

Excerpts from

The NEURONS and NEURAL SYSTEM: a 21st CENTURY PARADIGM

This material is excerpted from the full β -version of the text. The final printed version will be more concise due to further editing and economical constraints.

A Table of Contents and an index are located at the end of this paper.

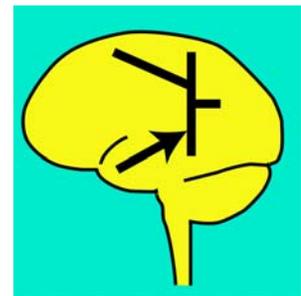
A few citations have yet to be defined and are indicated by "xxx."

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Neural Concepts

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2 Neurons & the Nervous System

4 The Architectures of Neural Systems¹

[xxx review cogn computation paper and incorporate into this chapter]
[xxx expand section 4.4.4 as a key area of importance]
[xxx Text and semantics needs a lot of work]

Don't believe everything you think. *Anonymous bumper sticker*

You must not fool yourself, and you are the easiest person to fool
Richard Feynman

I am never content until I have constructed a model of what I am studying. If I succeed in making one, I understand; otherwise, I do not.

William Thomson (Lord Kelvin)

It is the models that tell us whether we understand a process and where the uncertainties remain.

Bridgeman, 2000

4.1 Background

[xxx chapter is a hodge-podge at this time 29 Aug 11]

The animal kingdom shares a common neurological architecture that is ramified in a specific species in accordance with its station in the phylogenetic tree and the ecological domain. This ramification includes not only replication of existing features but further augmentation of the system using new and/or modified features.

Very significant differences are seen between the neural systems of the major animal kingdoms, *Arthropoda*, *Mollusca* and *Chordata*. One of the most important is the introduction of the elements of what will be described as stage 3, signal projection (**Chapter 9**). This new feature results in the formation of the spinal chord and the adoption of the name ***Chordata*** for the phylum exhibiting this feature. It also introduces the phenomenon of the "action potential," a signaling waveform of very specific properties. It is proposed, and the literature asserts, that the action potential phenomenon and signal projection technique are only found in *Chordata*. (a.k.a. vertebrata).

While this work will exhibit a homocentric tendency, it is important to note *Homo sapiens* is not superior to other species in a variety of respects. The muscles used to move the ears (and the associated neural elements) have largely atrophied in humans. The visual spectrum of *Homo sapiens*, like that of other large mammals, is constrained by the transmission of the lens of the eye and is deficient in the ultraviolet compared to the smaller mammals (**Section 8.2.xxx**). The hearing modality of *Homo sapiens* is inferior to that of other species in several significant aspects (**Section 8.3.xxx**).

This work will also develop the fact that the CNS of chimpanzee is not as sophisticated as that of *Homo sapiens*, and arguably that of the orangutan (genus *Pongo*) or the bottlenose dolphin (genus *Trisops truncatus*). The ability of the dolphins to image sound reflections provides them a capability beyond that of the humans (except potentially on a limited scale in a few individuals blind since very early childhood).

In developing the architecture of the neural system, it is useful to compare the circuitry to that of man-made microcircuit technology. Man started in the 1960's using what was called resistor-transistor logic (RTL). This technology was soon replaced by the more power efficient diode-transistor logic (DTL). Within a few years this technology was in turn replaced by a still more efficient transistor-transistor logic (TTL). The reader should immediately realize that the biological neural system is analogous to this highest level of man's technology. Adopting a similar framework, the neurons, synapses and

¹Released: July 19, 2015

Nodes of Ranvier of the biological neural system are used to implement Activa-Activa logic (AAL). To be complete, it is noteworthy the biological system does not use the man-made technology known as MOS or CMOS. Neither does it employ digital circuit technology. The biological system is an analog circuit based system and employs only a few binary (two-stable state) circuits.

The second introductory quotation describes the position of Lord Kelvin at the time the Scientific Method was being defined. While the quotation is pedagogically important, Lord Kelvin developed multiple conceptual models that failed miserably (in some cases catastrophically from a financial perspective), most significantly by ignoring the discoveries of Maxwell relative to acoustic, thermal and electro-magnetic propagation. In presenting the third quotation, Bridgeman characterized the current state of research into the neural system. He said, "The neuroanatomical analyses can tell us **where** to look for a particular mechanism, and neurophysiology can tell us **when** the critical information is being processed, but current techniques leave the '**how**' of the process tantalizingly elusive ²." The first quotation highlights the difficulties of relying upon intuition, or what is sometimes described as introspection. The goal of this Chapter is specific. It is to provide a series of both globally and internally consistent models that can support a wide range of experimental results and lead the way to a broader understanding of the neural systems in animals. Thus the goal of this work is to support the theoretical half of the Scientific Method.

[xxx modeling]

There are a number of problems associated with modeling the signal processing functions in vision. One of the biggest is the plethora of simplistic block diagrams and circuit diagrams found in the literature. The second is the extremely high impedance level found in the initial stages of signal processing. These impedance levels are to be expected; they relate to the extremely small size of the elements and they contribute to lower overall power consumption. A third is the reluctance of the biology community (at least until recently) to embrace the fact that there are synaptic junctions that involve only the movement of electrons across the boundary. No movement of chemical ions (much less complex organic molecules with the complexity of a protein) is involved.

Finally, the fact that 95% of the neurons in any organism (99.9% of the neurons in the retina) operate in the analog (not in the binary pulse) mode puts them in a class separate from much of the neural literature³. More specifically, the vast majority of neurons do not generate or process "action potentials."

It is noteworthy that the field of morphology is involved primarily with static conditions or very slowly changing conditions relative to growth. The field has largely overlooked the subject of neural signaling. One neurobiology text, that is heavily weighted toward morphology lists 14 types of cell-to-cell communications in hierarchal order but does not mention neural signaling based on electrolytics⁴.

It is also noteworthy that the literature contains no detailed description of the signals at different positions along the signal path from the input voltage at a neurite to the output voltage at the axon of a neuron.

Some of the material in this Chapter is designed for the actual laboratory researcher or serious analyst. It goes into more depth than required by the typical reader. The chapter is focused on the modeling of the larger parts of the neural system. The modeling of an individual Activa, an individual synapses and various individual circuits within a single neuron have been addressed in **Chapter 2**.

Section 4.1 can be read selectively as needed by the reader. **Sections 7.2** through **7.3** encompass the various phases of the detailed modeling of the neural system xxx.

Section 4.1.1 is critically important if one is to avoid the many conceptual traps found in the

²Bridgeman, B. (2000) Neuroanatomy and function in two visual systems. *Behav. Brain Sci.* vol. 23, no. 4, pp 535-536

³Xxx 95% analog

⁴Shepherd, G. (1994) Neurobiology, 5th ed. NY: Oxford Press. pg. 72 in the 1988 edition

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current literature. **Section 4.1.2** provides many detailed definitions that are required to insure consistency and correlation of the material in adjacent chapters.

Section 4.1.3 concentrates on the high level architecture of the overall neural system, using the non-visual system as a template for understanding the visual system xxx.

Section 4.1.4 provides an internally consistent set of morphological nomenclature for the neural system and **Section 4.1.5** does the same thing for the electrical waveforms normally associated with the neural system.

Section 4.1.6 provides a review of graphical techniques of specific value in modeling the visual system xxx.

Section 4.1.7 discusses the subtle differences between data and information rates.

Section 4.1.8 reviews some of the models used in other presentations on the system aspects of the visual process.

Section 4.2 develops the increasing complexity of the neural system as evolution has moved forward.

Section 4.3 xxx

Section 4.4 xxx and rest of sections.

4.1.1 A review of the Scientific Method and its application

This discussion will be brief. A more complete discussion appears in the Introduction to **Chapter 7**.

In the context of defining the neural system, the Scientific Method has not been used to its full advantage. There appear to be a variety of reasons for this. Until recently, there was little cross-discipline training of biological researchers. Second, the laboratory techniques required were often arduous and not easily reproduced by independent investigators. Third, the academic culture in biology has many of the hallmarks of a guild. New graduate students typically work along side more senior investigators, rather than in competitions directed at independently verifying the work of such senior investigators. This approach has suppressed the instinct of the young to question the foundation of previous investigations and strive to develop their own conceptions and investigatory approaches. This cultural problem, shared with very few other scientific disciplines, has also fostered the practice of using the same protocol as the previous investigator when attempting to validate the hypotheses of the earlier work. This practice is very dangerous and was the source of the famous Hubble Telescope fiasco. While, conventional practice in the optics field was to test large mirrors using two independent test protocols, the NASA Program Office decided to forego this luxury and repeat only one protocol twice. In a number of cases where validation has been performed using the same protocol, problems with the original hypothesis have remained hidden for years; the revered Hodgkin & Huxley experiments are the ultimate demonstration of this problem.

A strong involvement of the Scientific Method requires two parts, a carefully developed theory of the mechanism or process under study, and a well planned laboratory investigation guided by that theory. The laboratory investigation should announce in advance its null hypothesis, based on the theory, and the precision of the results required to validate that null hypothesis. If the experimental data fails to meet the criteria or confirm the null hypothesis, the null hypothesis must be considered falsified at least temporarily.

A major failure encountered all too frequently in biological research is the Bayesian Trap. The Bayesian approach requires the investigator to estimate the probability of each potential outcome of the planned experiments based on the available theory. However, failure to recognize results outside of the expected outcomes, because of an incomplete set of potential results, due primarily to a lurking variable or mechanism, leads to the Bayesian trap. The chemical theory of the neuron is the most obvious Bayesian trap of the last 100 years.

4.1.1.1 Failure of the chemical theory of the neuron and this work

This work is due in large part to the frustration resulting from attempts to rationalize the large number of floating models and dubious hypotheses in the biological literature relating to the neural system and specifically the sensory modalities. The application of the Scientific

Method surfaced new avenues of investigation that frequently had been dismissed previously based on the common wisdom resulting from these models and hypotheses.

A major problem with the current wisdom has been the reliance within the pedagogical community on the alkali-ion hypothesis of Hodgkin, Huxley & Katz dating from the 1940's resulting from their flawed null hypothesis that the "giant axon" of the squid *Loligo* was capable of generating action potentials. This reliance has been maintained in spite of the extensive documentation falsifying both hypotheses. However, it is beginning to change. Gartner, et. al. have noted the impermeability of the plasmalemma of the neurons to small ions in their study materials in Histology and for the current USMLE Step 1 Board Reviews⁵. Both activities are left to support the unverified pore or channel theory for transporting ions across the membrane. By adopting the Electrolytic Theory of the Neuron, a much more tractable and fruitful framework of neural formation and operation becomes available.

4.1.1.2 The need for more appropriate models and null hypotheses

Rigorous application of the Scientific Method demands the use of a detailed model to describe the current state of the art. While such models need not be graphical, the best ones are.

The critical feature of the method is that all of the parameters related to the process being modeled be stated explicitly using absolute scales to the greatest extent possible. The use of the Scientific Method deprecates the reliance on "common sense," intuition and introspection in the sciences. While reliance on these sources in the early stages of exploratory research may be acceptable, and even *disruptive* in a positive sense, they cannot play a role in applied research where reliance on defensible and quantifiable parameters is a necessity.

A second major feature of a good model is traceability back to a well founded, large scale model. **Lacking this traceability, the local model can only be considered a "floating model" that cannot be rigorously defended.**

In the absence of a detailed model with explicitly specified parameters, an investigation must be described as exploratory. This has been the character of much of the biological research of the last two centuries. When, a detailed model with explicit parameters has been obtained, investigations can move into the more advanced stage of applied research.

Frequently, a defining distinction between exploratory research and applied research is the tolerance on the defined parameters. Most biological research prior to the 1970's quoted accuracies of an order of magnitude. A standard deviation smaller than the mean of the measurements was presented in only a few exceptional cases. A standard deviation of less than one-third the mean is necessary to support any null hypothesis.

4.1.1.3 Types of Models and Diagrams used to aid understanding

To help interpret this work and the literature, it is useful to explicitly define a series of different types of models. The most basic classes of models are the abstract and the functional.

+ **Abstract models** typically present a conceptual block diagram or contain a mathematical equation. The conceptual block diagram is frequently found in pedagogical situations. The mathematical equation is usually intended to bound the performance of some process or mechanism in neuroscience without relating directly to they underlying mechanisms or processes. Both tend to be misleading with respect to the underlying electrophysiology of the system.

+ **Functional models** typically attempt to describe the actual mechanisms and processes of neuroscience and must conform to the electrophysiology of the system to be considered correct.

Historically, many texts have used functional in their titles, and in their texts, to describe what other disciplines would describe as the interconnections between neurons and

⁵Gartner, L. Hiatt, J. & Strum, J. (2003) Cell Biology and Histology, 4th Ed. NY: Lippincott, Williams & Wilkins. Page 1, section II, statement A.

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engines based on traffic analysis (the mapping of signal and information flow). These earlier works were seldom concerned with how the individual circuit actually functioned.

In this work, the subject of the interconnection between neurons and engines relates to traffic analysis. Traffic analysis has recently developed into its own field as a result of MRI and other imaging techniques. Hagmann et al describe it as the field of *connectomics*.

In this work, the function of a neuron or engine is used to describe its specific circuit topology and/or its specific input-output relationships. What is it for and what does it do?

A difference is noted here between emulation and simulation. Emulation is an attempt to precisely reproduce the operation of a mechanism with negligible error. Simulation is an attempt to reproduce the operation of a mechanism within an acceptable, and understood, margin of error. Computer emulations normally conform to the definition of the abstract model because the algorithms used seldom relate to the underlying electrophysical mechanisms and processes. Digital computers are incapable of emulating the analog circuits of the neural system.

Equivalent circuits and computer simulations (especially if sophisticated) on the other hand attempt to represent the electrophysiological situation using an equivalent topology in a different technology.

Specialists in system synthesis and analysis have long used a series of block, schematic and circuit diagrams to document the configuration and operation of a wide variety of systems. These tools attempt to represent the actual circuit topology of the neural system. The diagrams are used to aid in seeing both the forests and the trees simultaneously. Simultaneously, they provide a medium for documenting systemic relationships. Such systems may be of many types. They include electrical, hydraulic, mechanical, aerodynamic and *biological* types. Although not used widely or consistently in the neural field, an attempt will be made to use them consistently here according to the following hierarchy;

- + Global block diagram
- + Species specific block diagrams
- + Schematic diagrams
- + Multiple circuit diagrams
- + An individual circuit diagram

A block diagram is usually used to indicate fundamental but general relationships between major elements of the system. They are useful for orienting the reader and defining terms. They usually lack detail and are not indicative of the topology of the system. The schematic diagram is intended to illustrate relationships between the elements of a block diagram. The titles of the elements are frequently chosen to indicate the top level topology of the system and to indicate both feed forward and feedback paths. At the next level of detail are the circuit diagrams. These frequently occur in two classes, higher level circuit diagrams illustrating the interplay of several circuits and the individual circuit diagrams. The higher level circuit diagrams frequently employ high level symbolic representations of individual circuits to simplify the presentation and emphasize the topology of the system at this level.

The individual circuits on the other hand use the lowest possible level of symbology to provide a detailed understanding of the actual circuit. The symbols are usually of the most basic type and indicative of the most fundamental circuit elements. Because the symbology is so important to understanding within a profession, the actual symbols are usually standardized by professional organizations within each discipline.

A complete set of diagrams prevents floating models and inappropriate assignment of individual parameters.

4.1.1.4 Computational neuroscience

Section 7.1.4 discusses recent efforts to introduce computational modeling into the neurosciences. The resultant texts can only be described as introductory in nature and at the undergraduate level. The efforts has not been productive at the application level because of their focus on archaic and unrealistic representations of the neuron as a two port device embedded in a linear network unable to perform transcendental calculations beyond the summing and differencing of natural logarithms and exponentials to the base e . No significant attempt has been made in these works to recognize the complicated multiple engine operation of the stages of the neural system dedicated to stage 4 signal manipulation (information extraction) and stage 5 cognition.

4.2 Architectures of animal neural systems

Recent editions of widely used college level texts have presented introductory level material on the architecture of both the overall neural system and the individual neurons. These works concentrate on the morphology of the neural system and treat the physiology of that system superficially. While adequate in many ways for the study of simple animals (*Arthropoda* and lower *Mollusca*), these materials do not illustrate the actual architecture of the overall system as found in the higher animals (higher *Mollusca* and *Chordata*).

The neural system is one of the major distinguishing characteristics between animals, plants and other biological kingdoms. All but the simplest animals (those with less than a few thousand cells) exhibit a distinct neural system. The simplest systems may consist of only a single sensory neuron connected directly to a muscle cell designed to move the animal away from some irritation. However, the facility provided by a sensory capability controlling a muscular (or chemical) driven response adapted to many other functions as the complexity of animals increased.. In the higher animals, an entire hierarchy is required just to describe the functional classes of neural systems, much less the individual subsystems of the organism and types and functions of individual neurons.

An important distinction between the nervous system of invertebrates and vertebrates will appear frequently in this work. As Saavedra noted⁶, "The nervous system of invertebrates is often used as a model for neurobiological investigations because of its comparative simplicity and because some of the invertebrate neurons are giant in size. A number of experimental manipulations are thus possible in these cells." What Saavedra failed to note was that most of these giant neurons were specialized "swimming neurons" designed specifically to generate rhythmic patterns of command signals that are of negligible importance in mammals and found sparingly in other vertebrates. Neither did he note that these swimming neurons operate entirely in the analog domain. They are not myelinated; however, they frequently are surrounded by many small neurons in an attempt to reduce the axonal capacitance with respect to the surrounding neural matrix. They do not generate action potentials *in-vivo* (although, as Hodgkin & Huxley found, when stripped of their surrounding neurons, they can create signals under parametric excitation *in-vitro*) that appear "action potential-like" to the uninitiated. Thus, the evolution of the invertebrates has produced analog-based swimming neurons while the further evolution of the vertebrates (*Chordata*) has introduced phasic signaling neurons and action potentials.

4.2.1 The simplest neural architectures

⁶Saavedra, J. (1978) Microassay of biogenic amines in neurons of *Aplysia*, the coexistence of more than one transmitter molecule in a neuron *In* Osborne, N. *ed.* *Biochemistry of Characterized Neurons*. NY: Pergamon Press pp 217-238

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A variety of neural architectures can be defined based on the perspective of the investigator. The goal of this section is to develop an architecture that can be described concisely and contributes to the understanding of the neural system in greater detail.

As soon as animals evolved beyond their simplest possible configurations, their neural systems began to elaborate as suggested by **Figure 4.2.1-1**. These forms allowed simple signals from one neuron to cause the response of multiple cells capable of a variety of responses. Conversely, they also allowed the response of a single cell to be rationalized depending on the signal relayed through a computational element that received signals from multiple neurons.

The primitive neurosensory cell was described by Torrey. It is the type of cell that is seen in the most elementary animals where excitation of the sensory cell will cause the animal to contract a nearby muscle and turn away from the stimulus. The detailed signaling physiology of these cells is not well understood.

The above types of cells can be interconnected in a wide variety of ways. These include the simple local reflex arc, the more complex arcs associated with the knee-jerk and other autonomous responses that do not involve the central nervous system. One can build a hierarchy of ever more complex reflex arcs. Each of these arcs represents a more complex expression of a response to one or more stimuli. These responses can all be described in theory using boolean algebra. They are in general reproducible and do not involve time delays that are variable (except with respect to the temperature of the animal). However, at a certain point, the complexity of these arcs begins to involve cognitive processes. At this level, the response of the animal is no longer rigidly reproducible and the time of response may involve significant variation. These are the rudimentary signs of intelligence.

By combining some of the individual forms in this figure, even more complex forms were created.

4.2.2 The introduction of the bilateral and multi-segment neural systems

Two concurrent developments soon led to the development of ever more complex neural systems. The first was the organization of the neural system into segments that conformed with the segmented body form of the animal. This segmentation led to the replication of many neural circuits at the segment level, and called for a crude control system to coordinate the operation of these segments (which could number several hundred).

A major advance in neural system architecture paralleled the introduction of the bilateral animal form (as exemplified by *Planaria*). The neural systems began to be organized around two symmetrical neural paths that began to serve the two sides of the animal separately. While there may be many reasons for such a change, including redundancy and some measure against fatal injury by a predator, the change provided considerable flexibility in controlling the motion of the animal.

The evolution of two distinct neural signaling and control systems obviously required communications between the two structures and this is clearly seen at the segment level in early animals. As in any hierarchal organization, a need soon arose to provide some sort of overall coordination. As a result, a brain (or brains) was defined at the head (and/or tail) of

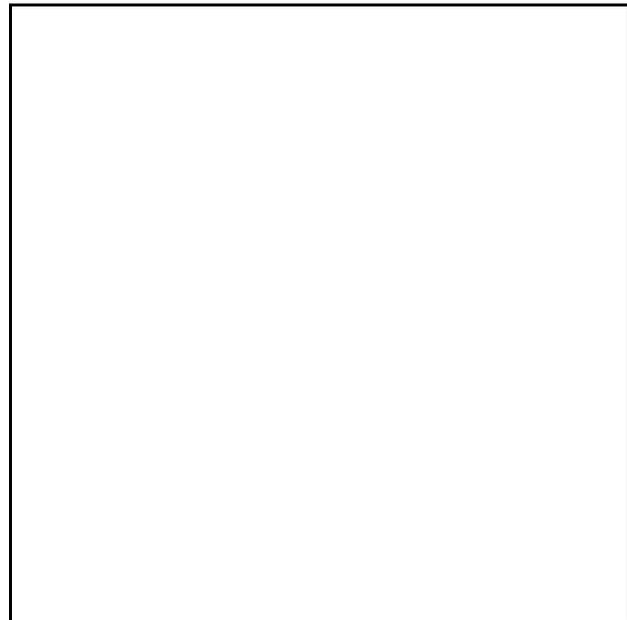


Figure 4.2.1-1 The simplest neural networks found in primitive animals.

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the animal that could influence these two neural subsystems. Many worms exhibit two brains that are difficult to distinguish from each other. However, as evolution continued, the head-end brain became dominant and was able to control more and more of the individual functions of the animal.

Early brains began to develop direct communications with a variety of sensory neurons and began to control the overall activity of the animal based on these sensory inputs. However, there was a missing function, the passing of signals from the individual segments back to the brain for purposes of supervision. Such supervisory signaling paths were soon introduced into many, if not all, of the phylum currently extant.

The full development of the bilateral form has followed a curious path. In the earliest animals larger than a few thousand cells, a notochord developed along the ventral surface of the animal and extending the length of the main body of the animal. This notochord divided into two separate chords that moved toward the lateral extremities of the midline of the animal. As evolution continued among many phyla, these two branch chords moved back toward each other but following different paths, **Figure 4.2.2-1**. In *Annelida* and *Arthropoda*, they reconverged in the ventral region of the sagittal plane. In Chordata, they reconverged in the dorsal region of the sagittal plane. The neural chords did not converge uniquely among *Mollusca*.

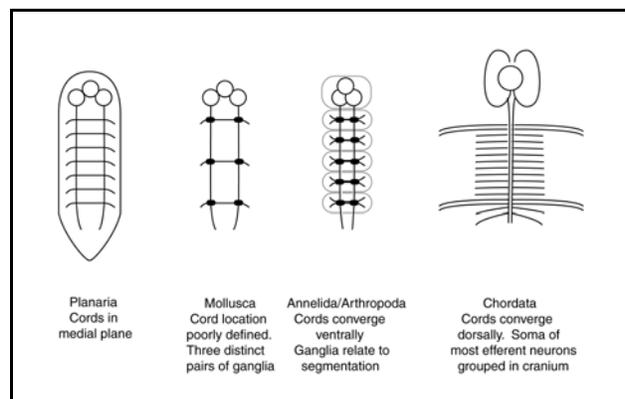


Figure 4.2.2-1 Comparison of neural system anatomies in various animals.

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It is important to focus attention on the chordates. In *Chordata*, the two chords remain distinct even though they are adjacent to each other and largely surrounded by non-neural (glial) tissue. In the members of *Chordata* known as *Vertebrata*, this non-neural material has become bone. However, it is important to note the neural architecture remains bilaterally symmetrical even in humans. This fact is illustrated in **Figure 4.2.2-2** that is similar to figures 17-8 and 17-14 in Torrey. The broad labels somatic and visceral are used. Somatic in this context refers to all functions related to the skin and its derivatives and the voluntary muscle system. Visceral relates to everything else. It is also noteworthy that the efferent and afferent neurons penetrate the vertebra at different locations.

The figure stresses the fact the spinal cord in vertebrates (and other members of *Chordata*) retains its bilateral symmetry up into the medulla.

[xxx add optic nerve layout to this fig and discussion]

[xxx review Barr, M. & Kiernan, J. (1983) the Human Nervous system: An anatomical viewpoint, 4th Ed.]

4.2.3 Architectures of advanced neural systems

A major feature of more advanced animals is the multiplicity of engines (frequently of a few million neurons each) working within a mesh configuration within each of the stage 4, 5 & 6 portions of the overall system. The multiplicity of stage 4 engines all contribute to the extraction of information from their signal inputs and placing that information in the appropriate portion of the saliency map assigned to that sensory modality. Similarly, the multiplicity of stage 6 engines draw instructions from the appropriate portion of the saliency map in order to create lower level commands for stage 7 affectation.

The saliency map is the major depository of current "declaratory memory" in the language of the psychologist and psychophysicist/psycho-physiologist. It is supported by additional long term memory facilities.

The precise location and other parameters of the saliency map are difficult to define. The map may be shared between elements of the posterior parietal lobe summarizing sensory information prepared for the benefit of the stage 5 engines, and elements of the anterior parietal lobe supporting the "premotor" engines of stage 6. **Section 4.6.2.3** will address this subject further.

Two interesting aspects of the saliency map is its plasticity, probably under limited control by the TRN, and the occasional failure of the assigned demarcations between the saliency map areas assigned to a specific modality to be respected by the stage 4, 5 & 6 engines. The result is a perceptual condition known as

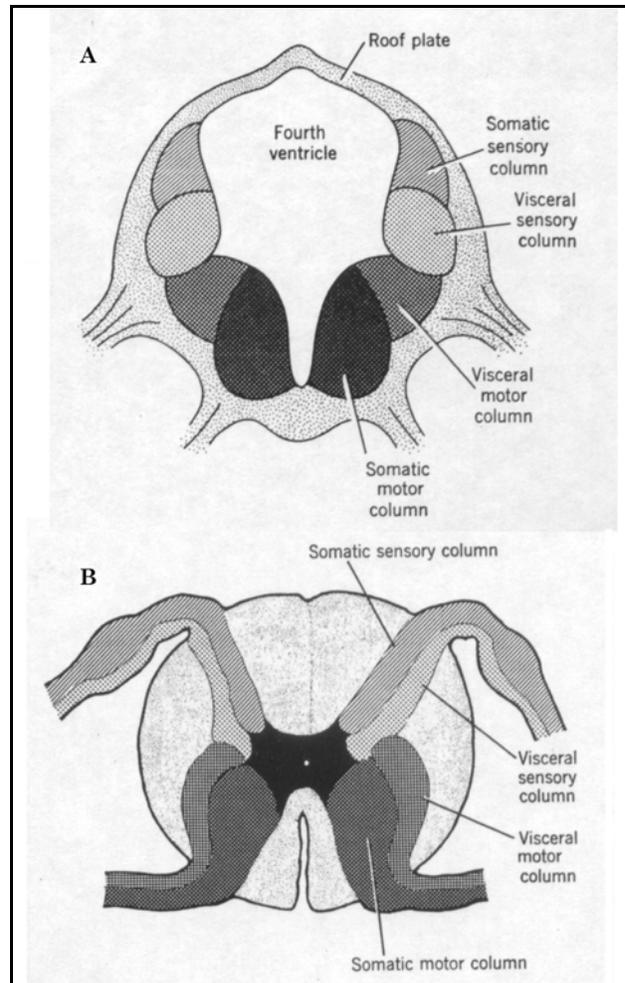


Figure 4.2.2-2 The bilateral symmetry of the vertebrate medulla (A) and spinal cord (B) REDRAW WITH BONE in LOWER FRAME. SEE Hickman, pg 639. Note the lateral symmetry. The areas in the center are devoted largely to metabolic support. The areas above and below the central areas are occupied by commissure providing lateral communication. Note the difference in ventral and dorsal organization of each lateral element.

synaesthesia (Section 4.xxx).

The tendency of research investigators to limit their activity to a single phylum, and frequently a single family or even species within that family has led to a great profusion in labels for similar functional neural units in the neurosciences. The recent convergence of the work of many investigators has begun to generate additional confusion in the labels used for many functional structures within the neural system. It is important to resolve some of these differences to avoid additional confusion. The fields of taxonomy have attempted to rationalize the nomenclature and labels used to describe the animal kingdom at the anatomical level, but much work remains to be done by some group at the morphological and cytological level applicable to neurons. One of the goals of this Chapter and Section is to provide a consistent set of labels for neurons based on their *function* within the overall organism. To avoid introducing entirely new labels, many morphological labels will be used, but frequently with more precise definitions that may appear arbitrary to some.

The complexity of the neural systems of higher animals makes it necessary to view the subsystems associated with the overall system from a variety of perspectives and levels. In the past, many investigators discussing these perspectives have attempted to avoid the interplay between them. This approach has tended to suppress the feedback mechanisms found in and between virtually all of these subsystems and to accentuate the visualization of these subsystems as a group of operational spheres or modes. **Figure 4.2.3-1** provides a simple description of the names of these spheres and their primary function. This figure does not represent the *operation* of the neural system realistically.

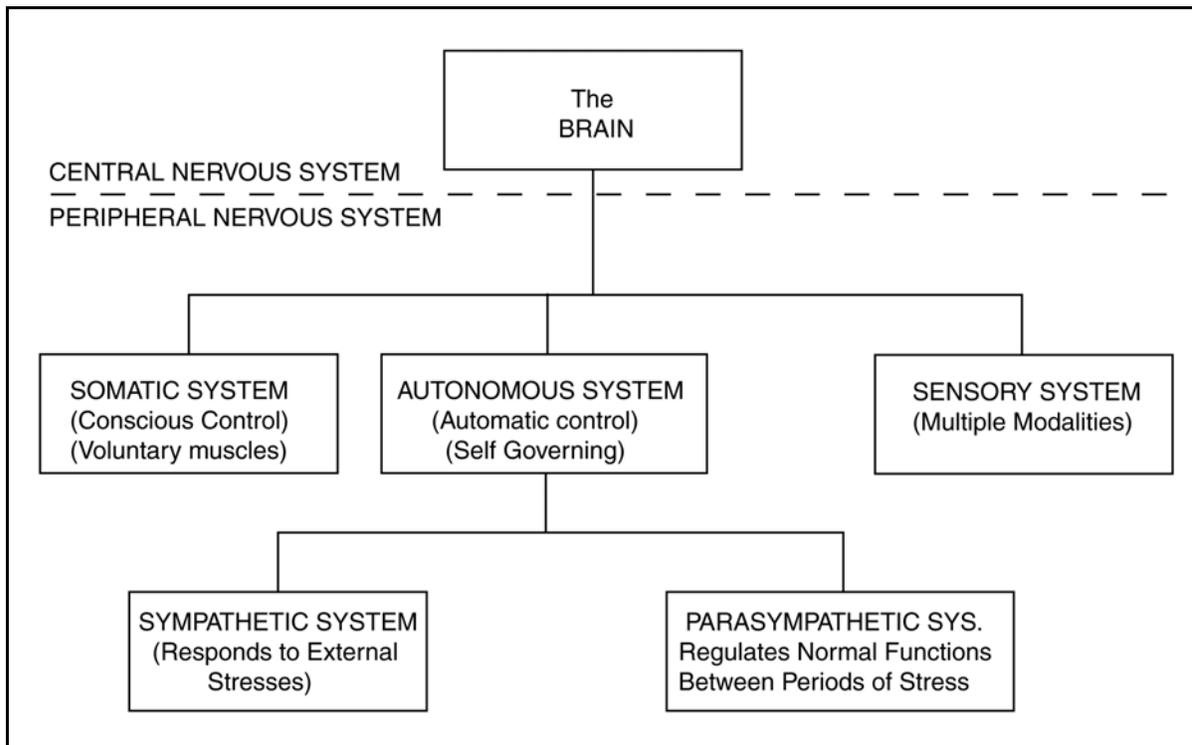


Figure 4.2.3-1 Conventional definitions of the spheres of the neural system in advanced animals
EDIT.

This figure appears in two forms. The first form is purely descriptive of subsets of the neural system and does not relate to any specific morphological entities. In this case, the top box is usually labeled "The Nervous System." The brain is not normally represented in this form and no demarcation between the central nervous system and the peripheral system is shown. The second form is shown here and is more topological. This form recognizes the position of the brain at the top of a hierarchy that will be expanded upon in the next figure. This hierarchy exhibits interaction between the sensory systems on the right and both the somatic and autonomous systems on the left. These interactions will be developed more explicitly in

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the next figure. Many of these interactions are carried out in the absence of any intervention by the brain (and particularly the neocortex).

An important consideration appears when considering this and the following figures. The efferent signaling paths associated with the somatic and autonomous systems labeled above rely heavily upon common neural paths within the peripheral neural system. Their postulated differences are more psycho-physiological than anatomical. This condition is easily recognized within the visual system. The process of blinking occurs routinely as a parasympathetic response of the autonomous system (not involving the neocortex). Blinking can occur as a sympathetic response of the autonomous system (generally not involving the neocortex based on the speed of response) and can obviously occur as a somatic response (at the volition of the neocortex). All of these responses rely upon the single neural path ending at the eyelids. A similar description can be given for the operation of the other oculomotor systems. The oculomotor muscles clearly operate under both the somatic and autonomous categories, virtually simultaneously. The larger saccades can be instigated by volition (conscious control) or due to an alarm (autonomous operation due to an external stress). Microsaccades and tremor are primarily autonomous but do not involve an external stress. Therefore, they would be described as parasympathetic in character. How these individual modes of operation are supported by the neural system will be discussed later (Section xxx).

[xxx need to redraw to include stage 3 projection neurons.]
Torrey has provided a collage of simple neuro/muscular systems that encompasses the

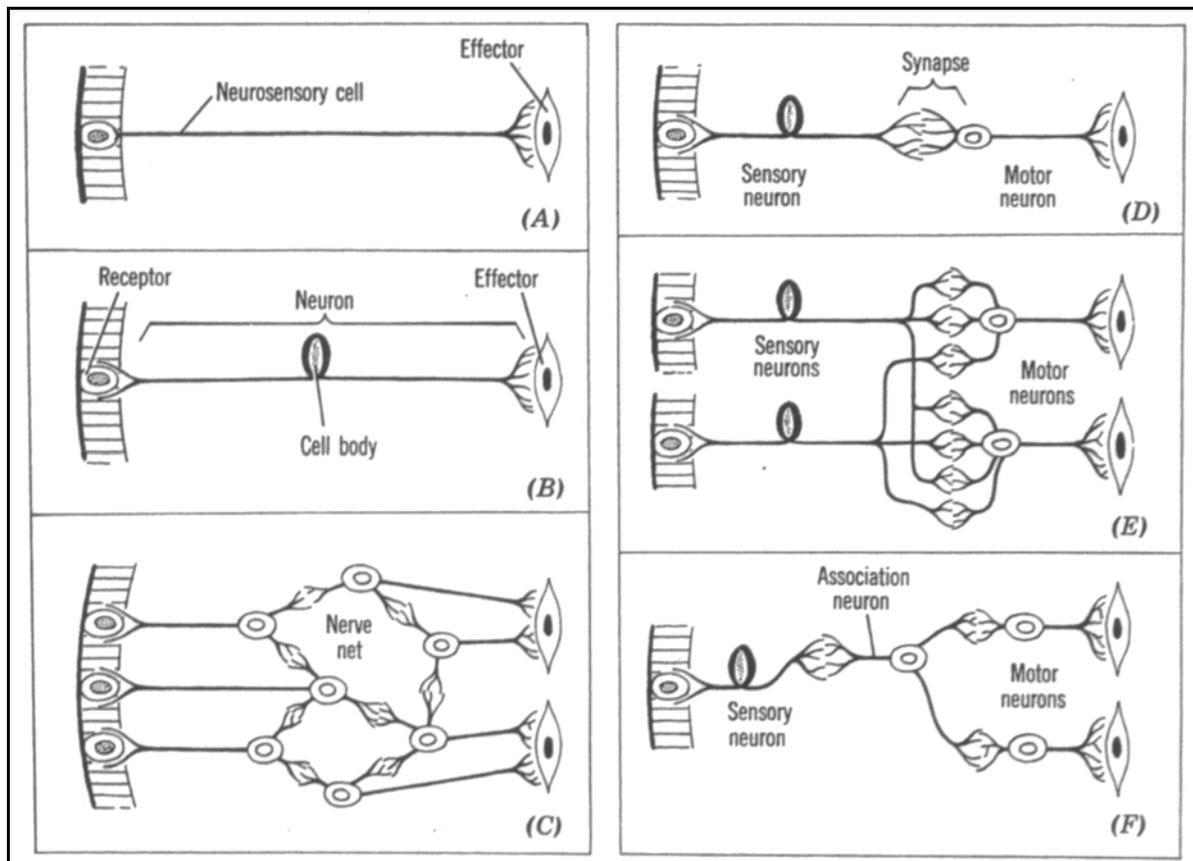


Figure 4.2.3-2 Neural circuits found at the most elementary level in non mammalian animals EDIT & REDRAW using same callouts.

simplest neurosensory cell path up through relatively complex reflex arcs⁷. **Figure 4.2.3-3** is an adaptation of fig 17-1 in that work. It de-emphasizes the nucleo-centric representation of the neuron in these simple networks (the soma is shown off to the side of the inter neurons) in favor of a Activa-centric approach (there is an Activa at the intersection of the dendrites and the axons in all of the neurons. These arcs involve sensory and motor cells interconnected by a signal processing matrix and what is labeled an association neuron.

However, there is no discussion of any cognitive element or central nervous system. Torrey also omits any discussion of analog versus pulse signaling over these circuits. Swanson uses the alternate term interneuron instead of just neuron or association neuron⁸. Shepherd has presented a similar collage at a single cell level where he speaks of intrinsic and projection neurons⁹. However, the projection neurons are characterized by having a high overall length to nucleus diameter ratio where the length is always less than two millimeters. Similarly, there is no discussion of analog versus pulse signaling over these neurons.

The neural circuits discussed by the above authors all relate to the lower animals, specifically non-mammals. When describing the mammals, a more complex circuit arrangement must be included that accommodates the much greater distances involved between the sensory and action locations and the central nervous system (CNS). The mammals have developed unique signal projection circuits (stage 3 in this work) that accommodate these greater distances in an energy efficient manner.

[xxx rework after reworking the above figure]

When approached from the signaling aspect of physiology, the architecture of the neural system appears quite different. Circuits (E) and (F) of the figure are only the low level circuits of a much more complex overall architecture and the so-called projection neurons of Shepherd are only the individual simple analog neurons of the detection and signal processing stages of the neural system. This work defines projection neurons quite differently from Shepherd. This definition is more aligned with the usage by those studying the central nervous system specifically.

Figure 4.2.3-3 illustrates a broader description of the types of neural paths. The simplest animals (even some acellular protozoa) employ a combination sensory/motor neuron to stimulate an effector muscle. Moving up the non-mammalian phyla, individual sensory and motor neurons operate in series to stimulate effectors. As the animals become larger, interneurons may appear between the sensory and motor neurons. However, all of these configurations rely upon analog voltage signaling. Such signaling becomes less efficient with distances exceeding a few millimeters. The primary problem is capacitance between the axoplasm and the surrounding interneural matrix. This capacitance causes analog signals to propagate very slowly within the axolemma. Some of the larger non-mammals have grouped neurons into bundles that effectively isolate the inner neurons from the interneural matrix and lower their effective capacitance. The giant axon of the squid is of this type (**Section xxx**).

A major innovation occurs with the evolution of the mammals. To accommodate their highly centralized neural system and large brains, it becomes necessary to relay many signals over distances much larger than a few millimeters at high speed and with high fidelity. Two elements were introduced to meet these requirements, the introduction of phasic signaling and closely spaced repeating devices (Nodes of Ranvier).

⁷Feduccia, A. & McCrady, E. (1991) Torrey's Morphogenesis of the Vertebrates, 5th ed. NY: John Wiley & Sons, pg. 406

⁸Swanson, L. (2003) Brain Architecture. NY: Oxford Univ Press page 24

⁹Shepherd, G. (1994) Neurobiology, 3rd ed. NY: Oxford Press, pg. 64

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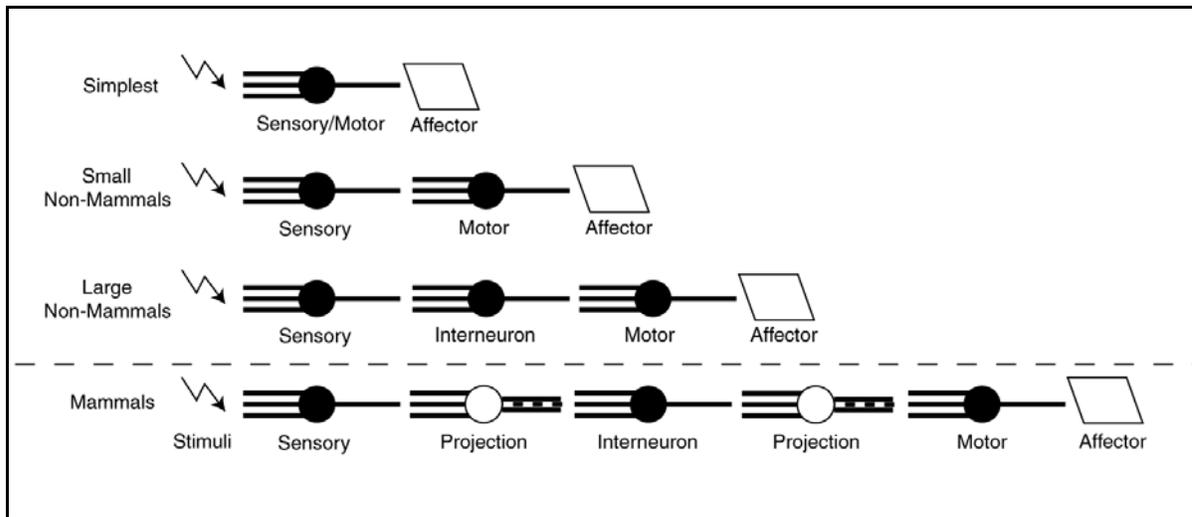


Figure 4.2.3-3 Fundamental neural paths among phyla. The simplest animals use a single combination sensor/motor neuron to activate a flagellum. Many small animals use a sensory and motor neurons in series to control an effector. The larger non-mammals employ an interneuron between the sensory and motor neurons. All of these configurations employ only analog signaling. To accommodate the centralized nervous system, the mammals employ stage 3 phasic signaling and projection neurons to propagate signals over long distances efficiently. Stage 3 signaling is only known to exist in mammals.

The innovation that allows the projection neurons to propagate their action potentials more efficiently is the introduction of myelination to the axons. Myelination reduces the capacitance between the axoplasm and the interneural matrix significantly and establishes a balance between the capacitance per unit distance and the inductance per unit distance that is highly optimized. The myelination also reduces any leakage of fluids or electrical charge through the axon lemma to zero (**Section xxx**).

It is remarkable that even recent texts and papers in neuroscience (including Swanson) have not recognized the significance of the 5% of the neurons generating action potentials are distinct from the analog signaling neurons which make up 95% of the neural system.

The dashed line in the above figure is extremely important. It separates the animals employing stage 3 signal projection, and employing action potentials, (exclusively *Chordata*) from the animals that do not (above the line). This separation has profound consequences. We now know that *Mollusca*, and specifically the squid, *Loligo*, *does not* employ stage 3 circuits, *does not* and *did not* generate action potentials as hypothesized by Hodgkin & Huxley at the time. Hodgkin & Huxley generated a long analog waveform (much longer than 1-2 msec.) in response to parametric stimulation of only the axon portion of a highly modified locomotion (swim) neuron *in-vitro*.

4.2.3.1 A hierarchy of the neural system architecture

This section will discuss reflex arcs in the broadest sense rather than the typical clinical sense. Clinically, the only reflexes typically examined are those responding to acute excitation via a small hammer.

It is important to note that the use of the hammer on the knee or elbow does not involve the stimulation of the sensory neuron at the beginning of a signal path. The impact stimulates a neural complex at these locations. Thus the hammer involves an indirect (or parametric) excitation of the neural path. An example of a direct excitation of a reflex arc is the transit of a pointed object (frequently a fingernail) across the surface of the bottom of the foot.

As discussed above, the neural system of all animals is designed as a hierarchy. The complexity of this hierarchy is determined by the evolutionary development of the animal and its needs. **Figure 4.2.3-4(A)** illustrates this architecture with respect to ever more complex

reflex arcs. Note that it is only at the lowest level that a signal is generated by a sensor and travels in only one direction, and generally to a node before arriving at an actuator mechanism (whether muscular or secretory). All higher level paths are shown as bidirectional. They actually involve two distinct paths, an initial afferent path (up-going arrows labeled s) and a subsequent efferent path (down-going arrows labeled m). Note also that all nodes receive signals from and transmit signals to at least four locations. It is the paths leading to the higher nodes that provide the capability of coordinated movement and eventually cognition. In this context, frame (D) of **Figure 4.2.3.2** can be considered as illustrating the lowest level reflex arc. There is an afferent neuron and a efferent neuron between the sensory cell and the responding cell. Frame (E) introduces cross-coupling between individual paths and corresponds to the next higher level reflex arc shown in **Figure 4.2.3-4(B)**. The final frame, (F), introduces the concept of an association neuron between two nodes. The mode of transmission used in these neural networks was not addressed in Torrey. As indicated above, this type of neuron is limited in length to only a fraction of a millimeter unless it uses phasic transmission techniques (see Section xxx).

[xxx rewrite this after symbology is changed.] Note the symbology used in the figure. The nuclei indicated by the black dots within the soma play no functional role in the neural system. They are involved in the support of the signaling function and the health of the cell. The Activa, indicated by the solid arrow within the soma, is the active and primary element within each neuron. ***Without at least one Activa, the cell is not, and cannot function as, a neuron.***

Up to this level of complexity, all signaling employs analog waveforms. This type of signaling becomes energy intensive for lengths greater than a fraction of a millimeters and an alternate, albeit more complex, system is needed. To meet this need, pulse signaling is introduced (recognized by the characteristic action potential). Introduction of this signaling mode requires replacing the single association neuron by a projection neuron *stage* consisting of a signal encoder neuron (typically, the ganglion cell of the nervous system), a signal decoder neuron (typically, the stellate cell of the CNS) and frequently signal regeneration mechanisms between the previous two neuron types (the Nodes of Ranvier). As a result of the introduction of this signal transmission technique and stage, it is useful to extend the concepts in Torrey to include those of **Figure 4.2.3-4(C)**. The shaded area encloses the signal projection stage and involves pulse signaling. Pulses are actually found from the output of the Activas within ganglion cells to the input of the Activas within the stellate cells (the region of darker shading). To the left of the projection stage is the signal processing stage associated with the sensory neurons. To the right is the signal processing stage associated with the effector neurons.

The pulse signaling code adopted throughout stage 3 of the neural system is uniquely appropriate for supporting reflex operations. The code is designed to provide a first pulse indicative of a change in the environment. This first pulse appears sooner after the environmental change the larger the intensity of the change. Bigger threat, earlier warning. The second pulse also occurs sooner after the first as the intensity of the change either is increased or continued at the former level. Beginning after the first few pulses, the sensory neurons begin their adaptation process that reduces the significance of the change within the neural reporting system.

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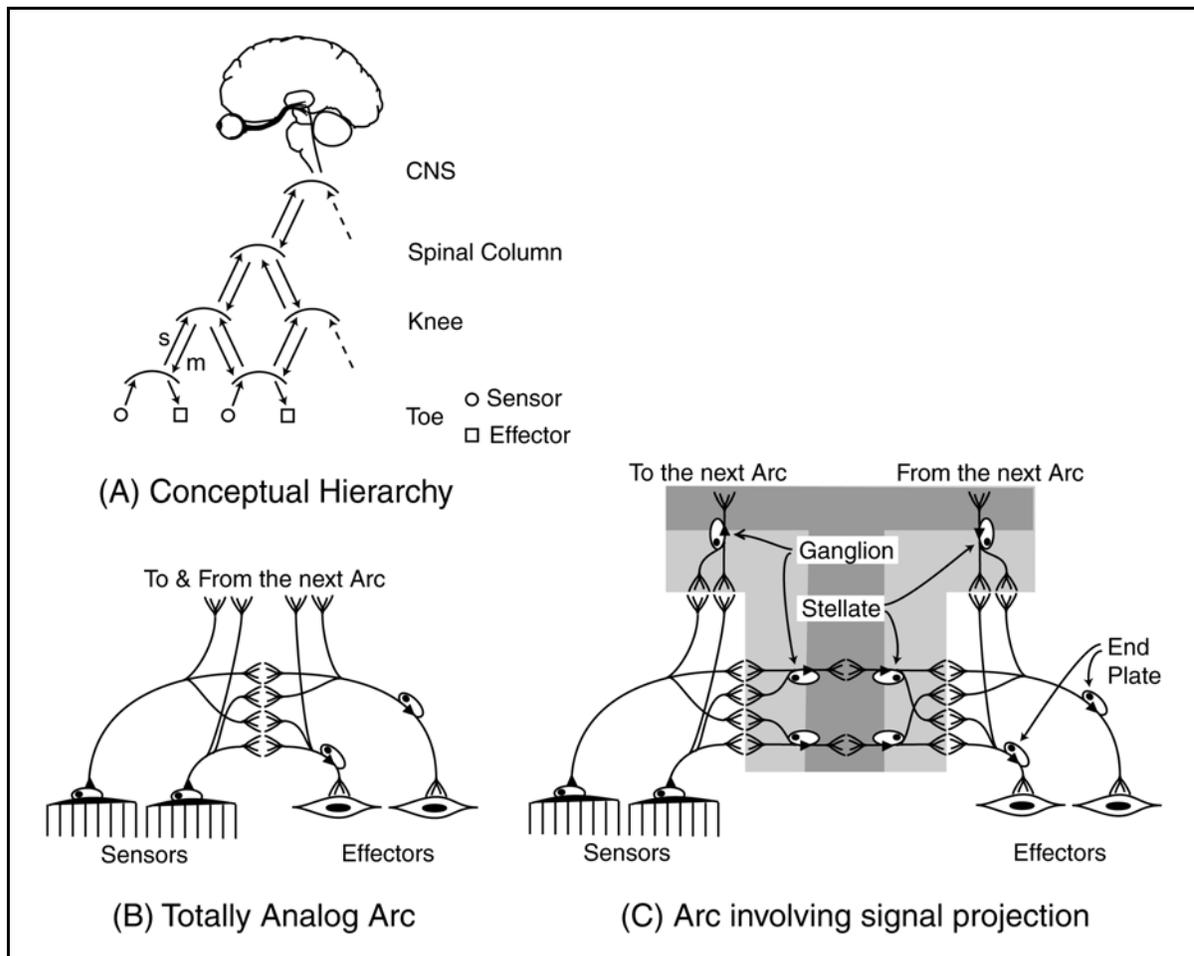


Figure 4.2.3-4 The hierarchy and signaling plan of neural pathways. (A); a partial representation of the typical hierarchy found in the nervous system. Each level can be considered a reflex arc. The lowest level is local (all elements within a fraction of a millimeter diameter) and involves only analog signaling. The higher levels are typically more remote and involve pulse transmission (action potentials) between levels. Within a level, analog signal processing may be employed. All neural signals, except possibly those of taste and smell, are routed through the midbrain initially. The labels on the right are only illustrative. The hierarchy can be applied to any of the numbered nerves of the system. (B); an example of the simplest reflex arc including paths to the next higher reflex arc but involving only analog signal processing. (C); a more extensive reflex arc involving signal projection (pulse signaling using action potential). The encoding ganglion cells and the decoding stellate cells are shown explicitly. This frame can be transformed into a higher level reflex arc by changing the lower labels to "from sensors" and "to effectors" and by removing the label "End Plate." Note the Activas, indicated by the solid arrowheads within each soma. The nuclei shown within each soma are not relevant to the neural signaling process.

Simple signal projection neurons are also limited in length to about 2mm for reasons to be discussed in xxx **Chapter 5**. Beyond this length, pulse signal regeneration is required to maintain pulse signal fidelity. Nodes of Ranvier are introduced near this spacing all along the axons of signal projection neurons. These Nodes are not shown at the scale of this drawing.

Dowling has presented a conceptual drawing similar to the networks in these figures¹⁰.

¹⁰Dowling, J. (1992) *Neurons and Networks*. Cambridge, MA: Harvard University Press pg 309

However, the details differ from those shown here.

A major problem with graphical component of these hierarchal diagrams is their suggestion that the major sensory systems, vision, hearing, taste and smell, are part of the central nervous system. While they are located within the cranium, they clearly are not part of the CNS from the operational perspective. Their location within the cranium is primarily a question of packaging to achieve maximum rate of response to a stimulus, and (in the case of vision) minimal transmission length for a very large number of individual neurons in the optic nerve. This fact is particularly evident when the complex servomechanisms supporting vision are examined in detail.

4.2.3.1.1 A top level schematic of a complete neural system

The complexity achieved in the mammalian neural system is amazing. The earliest efforts to describe it necessarily relied upon anatomy and morphology. It became clear early on that the system employed two major subdivisions, a somatic subdivision associated with the external sensory organs and the skeleto-muscular functions and an autonomous subdivision associated with the housekeeping aspects of a healthy body.

An early subsequent finding was the apparently duplicate innervation of many organs by what came to be known as the sympathetic and parasympathetic portions of the autonomous system. **Figure 4.2.3-5** reproduces a particularly clear schematic of the autonomic system.

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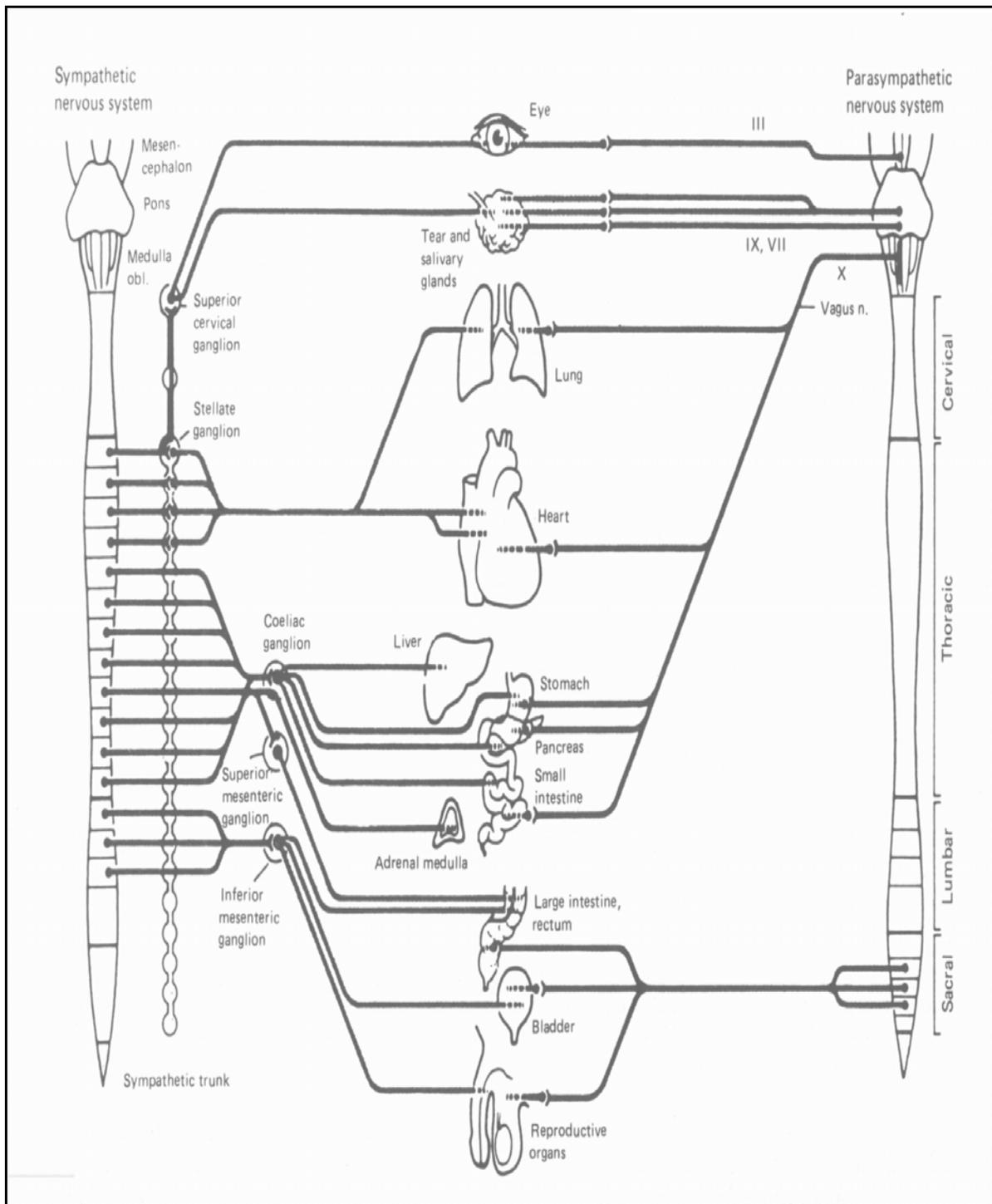


Figure 4.2.3-5 Top level schematic of the autonomic human nervous system. The sympathetic subsystem is on the left. The parasympathetic subsystem is on the right. The tenth (vagus) nerve travels outside of the spinal chord and, like the descending nerves of the spinal chord, serves a wide variety of visceral elements of the total system. From Schmidt & Thews, 1983.

Such complexity makes understanding the operation of the system difficult without an orderly subdivision of the system into multiple subsystems.

Figure 4.2.3-6 portrays many of the same elements in a more anatomical representation.

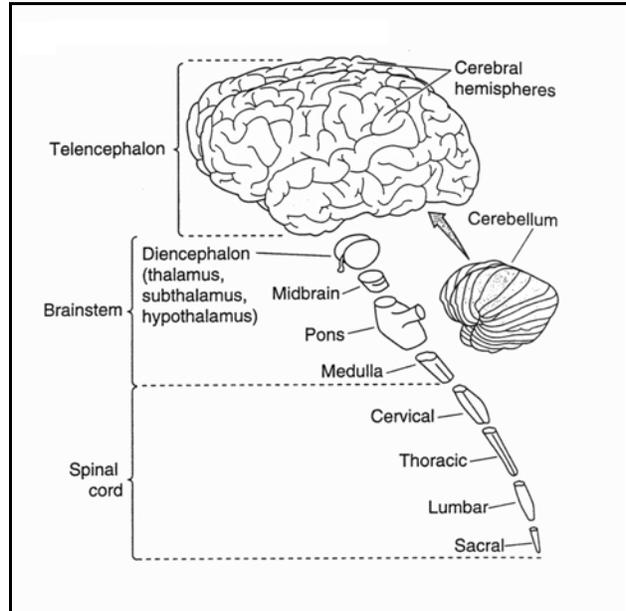


Figure 4.2.3-6 Gross anatomy of the human Central Nervous System. From Boron & Boulpaep, 2005.

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When discussing the neural system of the humans, and other primates in particular, the coordinate system becomes important. **Figure 4.2.3-7** illustrates the confluence of two different coordinate systems used in two different schools of anatomy. The additional framework when dissecting or recording parts of the CNS, based on Tailrach is addressed in **Section xxx**.

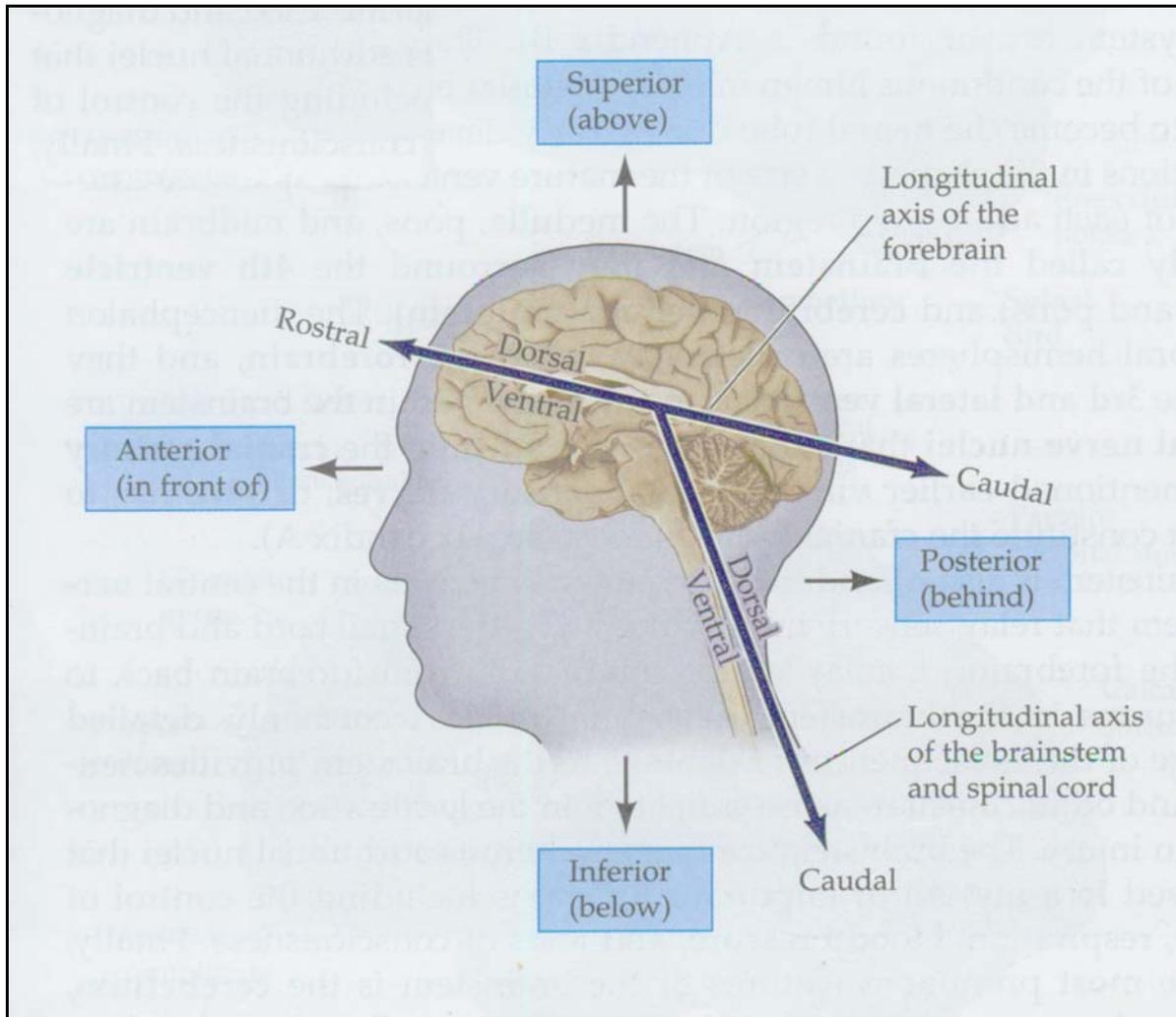


Figure 4.2.3-7 Two coordinates systems used in the anatomy of the neural system. The transition from the axes of the CNS to that of the spinal cord and rest of the body in the literature is not always clear. From Purvis et al., 2004.

4.2.3.1.2 A top level block diagram of a complete neural subsystem

To prepare to analyze the operation of any neural subsystem, it is appropriate to subdivide the neural system into a set of clear and distinct functional stages that can apply to any of the subsystems. The complexity of the visual system suggests it is a good candidate to use as a baseline for this modeling activity.

When employed in vision, many of the lower level arcs on the left of the above figure, up to the level of the interface of the optic nerve with the midbrain, are unidirectional. No evidence has been provided to support the interactive operation of (two way

communications between) the brain and the retina of the eye. However, the brain does play a major role within the overall servomechanisms used within the visual system. The hierarchy of lower level analog arcs associated with vision are combined and represented by the neural layers of the retina. They represent the signal detection and the initial signal manipulation stages of vision.

Figure 4.2.3-8 presents the neural system expressed in a more general top level block diagram form compatible with the rest of the neural system. The stages of the neural system are shown as defined below. The figure also shows the path of the two servomechanism subsystems associated with the neural system. The first involves a loop that turns at the midbrain and is labeled a reflex arc (RA_M). The second is a loop that turns at the cortex and is also labeled a reflex arc using a different subscript (RA_C). Whereas the first loop is essentially one complex loop serving the muscles associated with the multiple axes of the eye, the second is a broader designation for all high level reflex arcs involving the cortex. These latter high level arcs generally involve the cerebellum. Many of the functions associated with the cerebellum appear to be genetically "prewired." However, some of the reflex arcs involving the cerebellum can either be modified or over-ridden through training. It is the cerebrum (the cerebral cortex) that provides the great flexibility in neural system operation similar to that of a general purpose digital computer. Within a rather wide range of activities, the cerebrum can be considered totally flexible and re-programmable, limited in many respects only by its associated input and output signaling structures.

The figure represents the basal ganglia as a distinct part of the neural system (**Section xxx**). However, its function appears to be largely in support of the other stage 5 elements. The basal ganglia communicate closely with the thalamic reticular nucleus (TRN). This figure

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parallels but offers more formality than a similar figure by Swanson¹¹. Being at the top of the

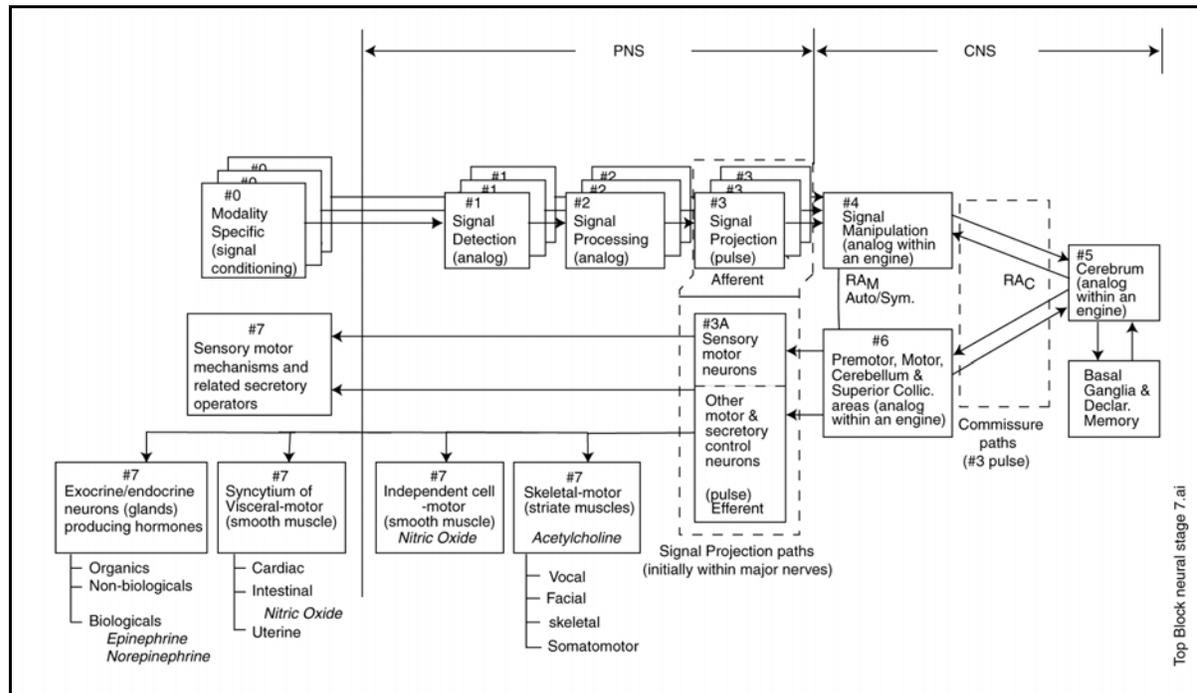


Figure 4.2.3-8 Top level block diagram of the neural system EDIT. The stages defined in the text are shown. The top level reflex arcs are designated RA_M for those turned in the midbrain and RA_C for those turned in the cortex. The role of the midbrain as a “gatekeeper” is emphasized. The parallel roles of the cerebellum and cerebrum are shown. Some reflexes involving the cerebellum are highly autonomous and can not be controlled by the midbrain as suggested by the dotted line. The signals controlling the oculomotor subsystem are a complex mixture of autonomous and sympathetic signals. Because of this situation, individual ganglion occur along the length of the neural paths designated 3A.

reflex pyramid, all of the high level reflex arcs involving the cortex are able to control large numbers of muscles simultaneously. This allows the animal to close its eyes, turn its head, and crouch simultaneously.

The nature of the signals are described cryptically at the bottom of each stage. In all cases, signal generation, signal processing and signal manipulation are performed in analog mode. Some short distance signal projection is performed in analog mode but statistically speaking, pulse signaling is the predominant form of signal projection. The arrows at the lower left represent the various nerves proceeding to the muscles and glands of the body.

In this figure, signals can originate in the cortex based on cognition. These signals can not be easily associated with a reflex although they may be reflexive, even after a long period of time. They are basically sympathetic, or at will, signals.

The efferent oculomotor signals are a complex mixture of autonomous and sympathetic signals where the autonomous signals are also a temporally complex mixture of reflexive and genetically programmed signals.

Although technically not part of the neural system, a **stage 0** can be defined to encompass the physiological elements prior to the sensory neuron receptors. This will allow the stages defined here to remain generally compatible with the two and three stage models currently found in the earlier literature.

¹¹Swanson, L. (2000) What is the Brain *Trends Neurosci* vol 23, pp 519-527

Each sensory modality employs a different stage 0 structure to support its interface with the ecological system. However, there are several functional features that are shared among the modalities. As an example, both terrestrial mammals and aquatic mammals share a horn type of antenna leading to and/or incorporating an external ear. The terrestrial mammals employ an air-filled horn while the members of *Cetacea* employ a fat filled horn. The terrestrial horn (the meatus) is generally rigid with dimensions that are tailored to the environment of the species. The terrestrial horn is typically terminated by a dynamic external ear that is steerable (except for most humans). Its frequently complex shape participates in frequency selection.

The cetacean horn on the other hand (at least in the dolphins), is generally flexible, and changes orientation during operation. The cetacean horn is typically terminated by a smooth skin supporting the hydrodynamics of the animal when swimming at speed. The termination is not known to be frequency selective.

From a different perspective, the cetacean horn is filled with a variable index of refraction material at audio wavelengths, while the generic eye of most mammals employs a "lens" that is formed from a variable index of refraction material at optical wavelengths. In the recent literature, the lens is described as a gradient index (GRIN) lens.

The stage 0 structures employed in taste and smell depend on the presence of a water-based film in which the sensory neurons are immersed and the stimulants can be dissolved. In both cases, the stimulants form coordinate bond (not a valence or covalent bond) with the outer chemistry of the sensory neurons. The use of a coordinate bond explains why no residue of a valence or covalent bond reaction has ever been isolated as a result of gustation or olfaction.

The specific features of each stage 0 structure will be addressed further in Chapter 8 when discussing a specific sensory modality. These structures are also discussed in detail in the works of this author dedicated to the "Processes in Biological Vision"¹², "Processes in Biological Hearing"¹³, and the Dolphin's Echolocation System¹⁴.

Stage 1, encompasses the neural circuits involved in **signal generation** subsequent to stimulation by some environmental mechanism. This stage will end with the presentation of the signals at the pedicels of the sensory neurons.

Stage 2, consists of the neurons associated with **signal processing** and manipulation carried out between the pedicels of sensory neurons and the input terminals of the *Activas* within the ganglion cells of stage 3 circuits. Being a functional element in the signal processing stage, the synapses associated with the pedicels of the sensory neurons will be considered part of Stage 2. Similarly, the neurites of the ganglion cells are also key players in the signal processing of Stage 2.

Stage 3, includes those neurons involved in the **signal projection** circuits of the neural system. The signal projection function is highly developed and easily characterized in *Chordata*. The techniques of stage 3 signal projection are believed to be used only in *Chordata*. It is used wherever it is necessary to transmit neural signals over significant distances (typically a millimeter or more). This includes both the efferent and afferent signal paths of the peripheral nervous system (PNS) and the paths within the brain, or central nervous system, (CNS).

Within the neural system, the projection function is used routinely. It is used to transmit signals over the optic nerve to both the LGN and the pretectum. It also used to transmit signals from the LGN to area 17 of the cortex and to transmit signals from the pretectum to area 5 of the cortex. Within the cortex, projection neurons are used to interconnect the different feature extraction engines and logic units of the brain with the initial motor system command generation centers.

¹²Fulton, J. (2004) Processes in Biological Vision, <http://neuronresearch.net/vision/>

¹³Fulton, J. (2008) Processes in Biological Hearing, <http://neuronresearch.net/hearing/>

¹⁴Fulton, J. (updated to 2015) Dolphin Biosonar Echolocation: A case study. <http://neuronresearch.net/hearing/pdf/appendL.pdf>

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In the nominal case, the projection function extends from the input terminal of the Activa within each ganglion cell to the output pedicel of each stellate cell within the brain that receives enervation from a neuron of the optic nerve. Note: the dendritic structure of the ganglion cell is looked upon as part of the signal manipulation function of **stage 2**, and not as part of the signal projection function of **stage 3**. Such a division highlights the role of ganglion and stellate cells as transition devices between analog and binary (pulse) signaling.

The further subdivision of **stage 3** to accommodate this situation will be addressed in **xxx Chapter 14**.

Stage 4 consists of all of the higher level **signal manipulation** and processing that occurs subsequent to the arrival of signals at the brain from **Stage 3**. It is often useful to subdivide this stage to clarify the fundamental difference in the signal manipulation occurring within the thalamus from that occurring in the cerebellum and the cerebral cortex.

Stage 5 consists of **information manipulation** and **volition instruction generation** within the prefrontal cortex and monitored by the thalamic reticular nucleus of the midbrain acting as gatekeeper.

Stage 6 consists of the **premotor and motor areas** of the cerebral cortex along with the motor portions of the **cerebellum and the superior colliculus**. This stage accepts volition instructions from the prefrontal cortex and generates adhesive instructions and command signals responding to the volition instructions emanating from the prefrontal cortex.

Stage 7 consists of the **command implementation neurons**. These include the muscle actuator neurons (end plates) and the enzyme secretion neurons.

It may be shown that most of the terminal neurons associated with stage 7 are secretory themselves.

In subsequent discussions, either the numbers or the descriptors highlighted above will be used to provide flexibility when speaking of these portions of neural subsystems.

A grand architecture of the complete neural system can be subdivided into a number of levels based on their functional characteristics. These levels can be defined by functional names:

4.2.3.1.3 A top level diagram showing parallelism of sensory modes

The top level block diagram shown above can be replicated for each of the sensory modalities as shown in **Figure 4.2.3-9**. It can be compared to an earlier and simpler version by Swanson in 2003¹⁵. (2003, pg 192). [duplic in 7.1.4-3]

¹⁵Swanson, L. (2003) Brain Architecture: Understanding the Basic Plan. NY: Oxford Univ Press. pg 192

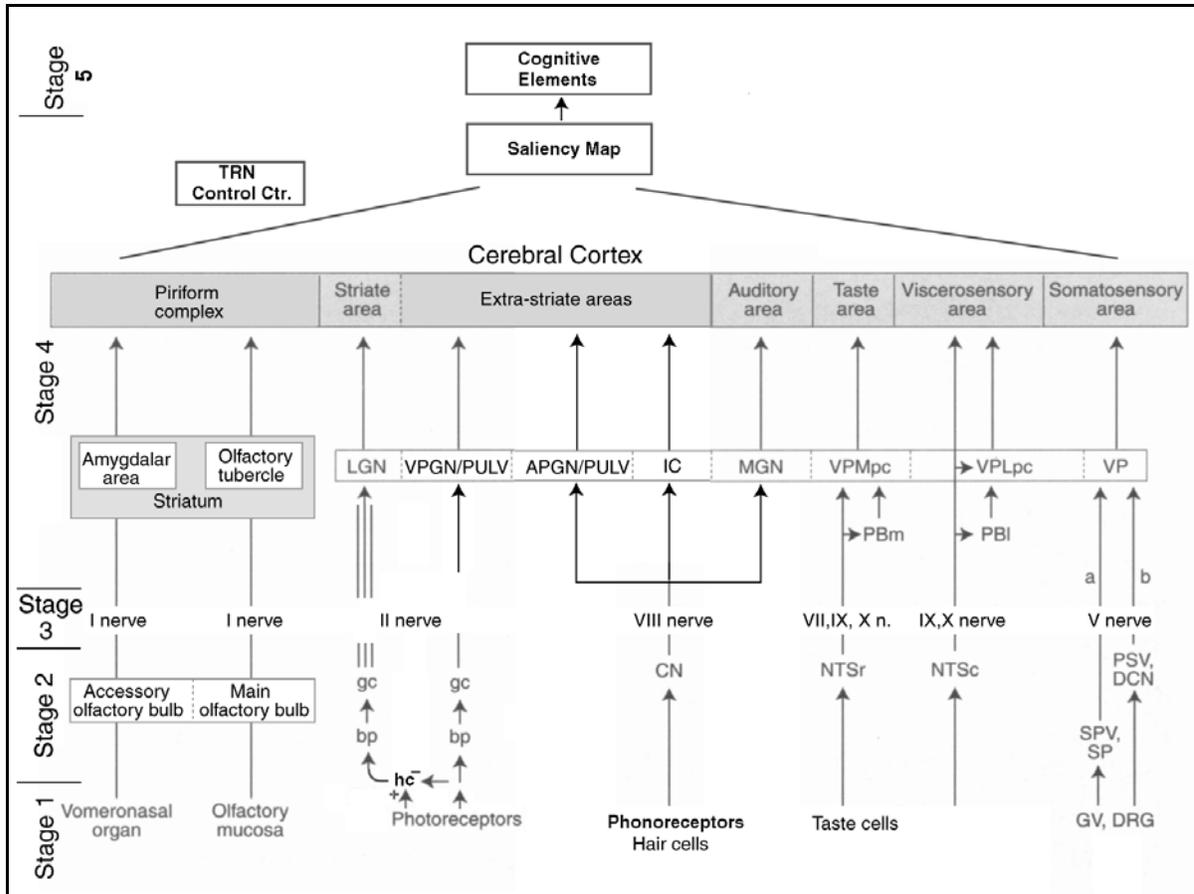


Figure 4.2.3-9 A top level schematic of the sensory modalities of the neural system. See text. Comparable to figure in Swanson, 2003.

This expanded version provides a larger context within which to highlight many features of the neural system. Much of the nomenclature will be left to later sections or to the comments of Swanson.

1. The figure extends the schematic to include the saliency map and thalamic reticular nucleus (TRN). The TRN acts as the control center for collecting information from the cerebral cortex (primarily the occipital and temporal lobes) and delivering the extracted information to the saliency map where it can be accessed by the cognitive elements of stage 5.
2. The main and accessory olfactory bulbs are shown as part of stage 2 (peripheral) signal processing rather than as integral elements of the CNS to make their organization consistent with all other sensory modalities (regardless of their morphological designation).
3. All sensory modality signals are projected to the CNS in phasic form by the stage 3 encoding/decoding system. The individual neural signals are accumulated and projected over a series of nerves to the CNS that generally retain a traceable geometric configuration..
4. The basal ganglia are separated into two sub-categories, those associated with stage 4, the elements of the striatum (Section xxx), and the elements associated with stage 6, the motor system (primarily the pallidum), .
5. All sensory information is received at the CNS in the diencephalon where the most time critical information is extracted. The diencephalon is indicated by the elongated white box on the right of stage 4. The expressions VPGN/PULV and APGN/PULV are used to indicate the very tight coupling between the visual and auditory portions of the PGN with their respective portions of the pulvinar.

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6. The piriform complex is generally associated with the cerebral cortex on morphological grounds. However, it is on the portion of the telencephalon directly associated with the diencephalon, which contains the other thalamic elements associated with the control of neural signals and the extraction of the most time critical information from the sensory channels. The striatum and piriform complex can be equally well associated with the diencephalon on functional grounds.

7. The major elements of the diencephalon frequently play two major roles; performing integration functions generally associated with the lateral geniculate nuclei (LGN) and medial geniculate nuclei (MGN), and extracting time critical information in the perigeniculate nuclei (PGN) for immediate use in alarm responses and both ocular and penic (external ear) steering in the general case.

8. In the case of the visual and auditory signals, both are delivered to both appropriate geniculate nuclei as indicated.

9. The complexity of the visual sensory signaling channels is highlighted by showing the dual paths to the diencephalon in more detail. While all bipolar neurons are simple non-inverting amplifiers (their outputs are always the same polarity as their input), the horizontal cells used in the chrominance channels perform a differencing function. This differencing (carried out in multiple parallel channels as indicated) can result in a signal inversion at their outputs for certain spectral inputs (primarily reds and blues).

10. The cochlear nucleus (CN) of the auditory modality is a stage 2 element in this description. Whereas the visual system employs computational techniques to derive stereoscopic information in both the LGN and PGN, the auditory system goes further and performs some stereophonic information extraction in the inferior colliculus (IC) as well as in the MGN and PGN.

11. The phonoreceptors are commonly described as hair cells from the early Latin designation of their outer segments as cilia. The internal construction of these outer segments is entirely different from hair cells of the somatosensory modality. The outer segments are piezoelectric sensory structures in their own right.

12. The taste, viscerosensory and somatosensory areas are shown as in Swanson and will not be developed here at this time.

This work will address stages 1 & 2 of the sensory modalities sequentially in **Chapter 8**. Additional details will be provided in the citations of that chapter.

4.2.3.1.4 An additional degree of parallelism within sensory modes

There is an additional degree of parallelism within the sensory paths of the higher mammals that is critically important, but seldom discussed in detail. Within vision, hearing and more widely, within olfaction and the touch aspect of somato-sensing, there are parallel channels that can be considered "high acuity" and focused on specific stimulant aspects. In vision, as an example, signals from the foveola, are distributed over dedicated signal paths to the perigeniculate nucleus and pulvinar for high acuity processing independent of the conventional "primary visual cortex" or V1. In olfaction, a distinctly separate path is provided between the sensory receptors associated with the auxiliary olfactory bulb, the auxiliary olfactory bulb and the CNS to support intra-species communications and mating. These parallel paths frequently provide alternate explanations for "paradoxes" encountered in neural research.

The parallel paths of vision, between the PGN/pulvinar and the LGN/occipital lobe, are so important, they will be developed in some detail below.

4.2.3.2 Redefining the peripheral and central nervous systems

The method of the presentation in [Figure 4.2.3-3] suggests that the visual system, if not other sensory systems found within the cranium, are part of the central nervous system. This conventional view within morphology circles deserves closer examination. At the start, it is important to provide a definition of the central and peripheral nervous systems.

Nolte provides several figures defining the topographic characteristics of the human brain at the introductory level¹⁶. At a more detailed level, Nolte & Angevine should be consulted¹⁷. The use of the term functional in those works does not refer to signaling, but only the topological arrangement of the morphological elements of the neural system based on neural traffic flow. The morphological description of the brain will be addressed in **Section XXX** along with Brodmann's original numerical identifications.

4.2.3.2.1 Initial embryology of the brain

A top level morphological view of the embryonic brain is presented in **Figure 4.2.3-10** to establish a baseline. It assimilates some of the terminology in the 5th edition of Torrey¹⁸, Pansky, et. al¹⁹, and the new edition of Afifi & Bergman²⁰. Many of the figures in these works are taken from the older text by Noback²¹. The material to the left of the vertical centerline is generally from Torrey. Hamilton has also provided a figure similar to the left half of the above figure²². The material to the right of the centerline is an expansion based on this work using the nomenclature of Afifi & Bergman. The opening paragraph of Afifi is particularly relevant to the following discussion. The figure attempts to show the morphogenesis of the brain of a higher chordate as a function of gestation time using three common anatomical forms. The most comprehensive discussion of morphogenesis appears in Noback.

¹⁶Nolte, J. (1999) *The Human Brain: An Introduction to its Functional Anatomy*, 4th ed. St. Louis, MO: Mosby

¹⁷Nolte, J. & Angevine, J (1995 & 2000) *The Human Brain in Photographs and Diagrams*. St. Louis, MO: Mosby

¹⁸Feduccia, A. & McCrady, E. (1991) *Torrey's Morphogenesis of the vertebrates*. NY: John Wiley & Sons.

¹⁹Pansky, B. Allen, D. & Budd, G. (1988) *Review of Neuroscience*. 2nd ed. NY: Macmillan Publishing Co.

²⁰Afifi, A. & Bergman, R. (1998) *Functional neuroanatomy*. NY: McGraw-Hill

²¹Noback, C. (1967) *The Human Nervous System*. NY: Blakiston Div. of McGraw-Hill

²²Hamilton, L. (1976) *Basic limbic system anatomy of the rat*. NY: Plenum Press. pg. 30

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The literature has generally presented two different topographies for the brain of the chordates depending on their level of morphological development. When examined more closely from a functional perspective, this dichotomy is not supported here. Torrey has exemplified this dichotomy by drawing the three heavy arrows indicating the general areas associated with the senses and then saying that the retinas connect to the diencephalon in

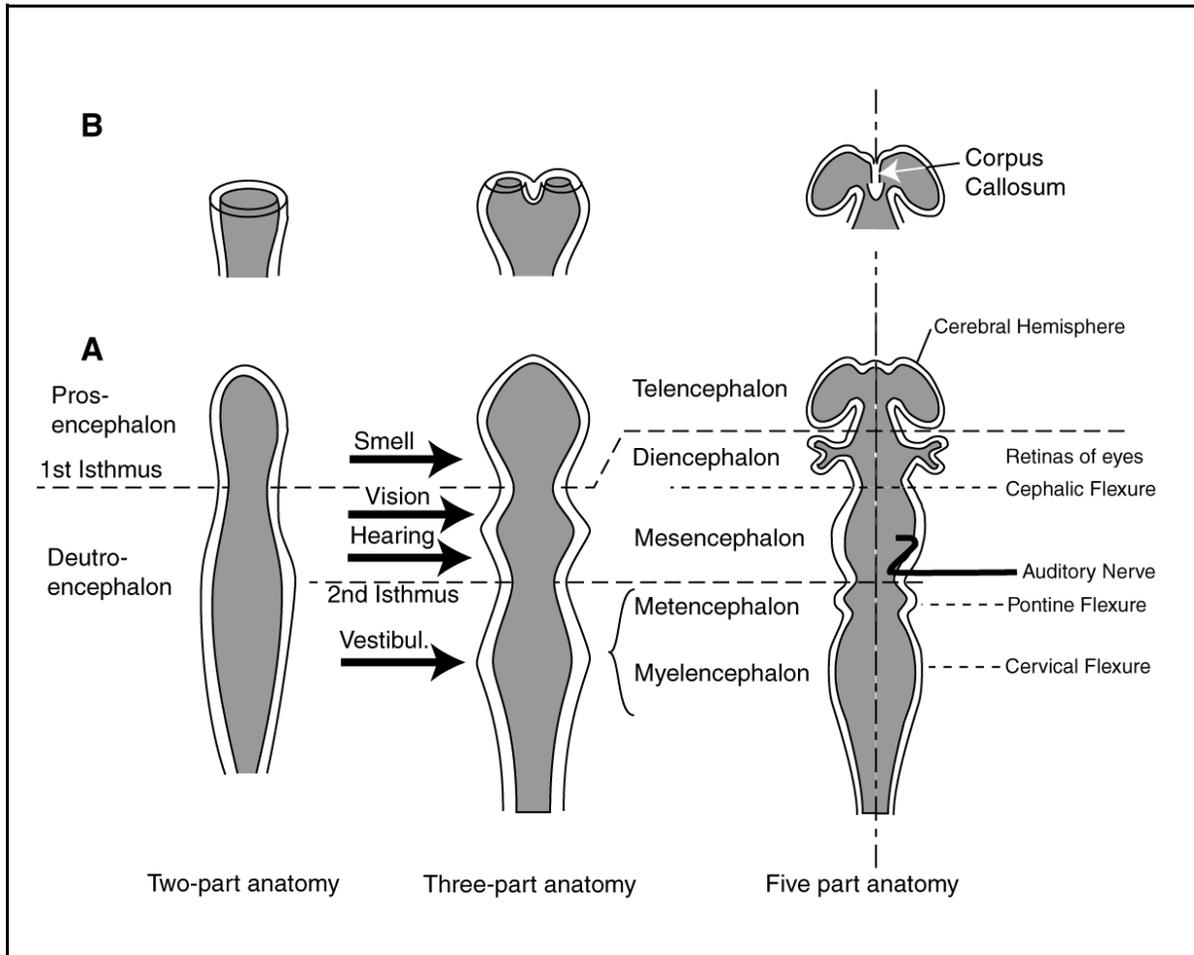


Figure 4.2.3-10 The morphogenesis and gross anatomy of the brain related to vision EDIT. The progression from two-part to five-part anatomy traces the morphogenesis of all brains. The figures to the left of the vertical centerline are similar to the fifth edition of Torrey. The four arrows differ from the three pen and ink entries made in Torrey by the new editors of that volume. In this case, the arrows refer to the location of the initial interface between the sensory neurons and the brain. Torrey has the lower arrow pointing to the lowest ventricle in the three-part anatomy, the Rhombencephalon. This area relates more directly to the vestibular than the auditory function. The figure to the right of the centerline represents the proposed interface between the retinas and the brain in greater detail. Paths **A** and **B** are afferent paths while path **C** is efferent. While the shaded area is frequently discussed in terms of ventricles or "spaces", they are generally filled with the association fibers and commissures connecting the various engines (Torrey describes as centers) of the brain.

the higher chordates and to the mesencephalon in the lower chordates. Hence the left side of the five-part anatomy of the higher chordates show the retinas interfacing with the diencephalon. This was as far as Torrey went. The arrows in the above figure are drawn at slightly different locations than the arrows (obviously added during editorial review) of Torrey. Since the brain has not completed its genesis at the three-part anatomy stage, the arrows point only to general areas. To go further based on only a two-dimensional drawing is

difficult. As an example, the optic chiasm cannot be shown easily within the context of the above drawing.

In addition, there is another level of detail that is critical to the understanding of vision in the higher chordates. These species exhibit a morphological fovea. Of greater importance, they exhibit a physiological foveola within the fovea. The presence or absence of a foveola is a significant physiological dichotomy among the chordates. This dichotomy influences the final morphological implementation of the visual system.

Whereas the neural interface between the optic nerves associated with the tectum is called the pretectum in the lower chordates, some authors call it the corpora quadrigemina in the higher chordates. The difference in this case is almost entirely morphological and not functional. Afifi discuss this matter in terms of the pretectum being reabsorbed as the corpora quadrigemina is formed. There is an additional problem in accounting for the portion of the tectum associated with the audio interface. This paired structure (not shown) is located within the area of the corpora quadrigemina. The area is analogous to an area of hills and mountains. The question becomes where do you draw the line between a hill and a mountain. The area could be called the corpora sexigemina equally well. The structures of both the thalamus and tectum that relate to vision are generally paired and arranged laterally from the sagittal plane (Pansky, et. al, pg. 325).

Torrey ends its discussion by suggesting that the anterior pair of the corpora quadrigemina are related to vision and the posterior pair are related to hearing. Noback presents the exact opposite impression when discussing the audio system²³. He does not differentiate between the nerves coming from the ears and those coming from the nearby vestibular system. This work takes a different view. It suggests corpora sexigemina is a better functional description of the roof of the tectum in all animals. It proposes that the two anterior bodies, the inferior colliculi are directly related to vision, the middle pair (which might be a part of the inferior colliculi based on Noback) are related to audition and the posterior pair, the superior colliculi are related to the oculomotor functions of vision as well as the motor functions of the body. This structure has a close tie to the vestibular system. This position is consistent with a merging of the figures on page XXX & 325 of Pansky, et. al.

The graphical description of the above relationships is further clouded by the three flexure points found particularly in the higher chordates. The brain cannot be properly presented on a 2-dimensional surface because of these flexures. These flexures are used to allow the brain to be packaged within a skull compatible with a face parallel to the ventral surface of the bipeds and quasi-bipeds. These flexures evolve in humans up to the time of birth. As shown, only the cephalic flexure is collocated with an isthmus. The cervical and pontine flexures actually reverse during the final genesis of the human.

[xxx clear pretectum and IC]

On initial examination, *most* of the neurons of the optic nerve are found to interface with the thalamus. However, this conclusion is not relevant to the functional performance of the visual system. When explored in detail, the retinas are seen to interface simultaneously with both the bottom of the diencephalon (the lateral geniculate nuclei of the thalamus, labeled **A** in the figure) and with the top of the mesencephalon (the roof of the tectum). The interface with the roof of the tectum actually consists of two distinct interfaces in the case of at least the higher chordates. There is an interface with the inferior colliculus (usually labeled the pretectum in the lower chordates and labeled **B** in the figure) and with the superior colliculus (labeled **C** in the figure). These interfaces are shown explicitly in Pansky, et. al²⁴. (Pansky, et. al. pairs the terminology pretectum and superior colliculus in their 1988 book and this terminology is frequently used in this work.) Their inferior colliculus interface is associated with the neurons emanating from the foveola and being processed by the Precision Optical System. The inferior colliculus will subsequently be defined as the perigeniculate nucleus in this work. The superior colliculus interface is associated with the few motor neurons of the ocular globes which also travel within the optic nerve and support the iris, lens, etc. The neurons interfacing with the inferior colliculus provide the fine spatial resolution associated with the foveola and so important to the visual system of humans and other advanced chordates (including birds). Hence, while *most* of the neurons of the optic nerves interface with the thalamus, the *most important* neurons of the optic nerves interface with the tectum (or visual PGN).

²³Noback, C. (1967) Op. Cit. pg. 6

²⁴Pansky, B. Allen, D. & Budd, G. (1988) Op. Cit. pg. 137

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MacLean provided **Figure 4.2.3-11** in 1967 to describe how the morphogenesis of different major phyla stopped at different point in the evolutionary process²⁵. The spinal cord of the reptile terminates in little more than a small bulge within the cranium. The limbic system took on a more important role in the expanded paleomammalian brain. Each of these major categories includes all of the major segments found in the neomammalian brain but their capabilities expand with the effective area of each segment (an indication of the number of neurons found in each segment).

In 1909, Brodmann described the relative size of the prefrontal cortex (PFC) of a group of animals to illustrate this growth in area. Humans allotted 29% of the cerebral cortex to the PFC, 17% in chimpanzee, 11.5% in the gibbon and the macaque, 8.5% in the lemur, 7% in the dog and 3.5% in the cat²⁶. While useful, these numbers may not be statistically adequate; their standard deviation may be quite significant relative to the mean.

McGovern has written on the MacLean concept of a "triune brain"²⁷. She provided a drawing more compatible with her investigations related to emotions in a variety of animals. She describes the elements of the human brain that would be associated with the reptilian and mammalian equivalents. As in MacLean, the mammalian (or paleomammalian brain of MacLean) consists of the limbic system overlaying the reptilian brain. The primate (neomammalian) brain brings additional expansion of the brain of the paleomammal. **Figure 4.2.3-12** shows her interpretation of the triune brain and its evolution.

Swanson has provided a figure (page 180) showing the expansion of the rat brain from the reptilian form to the paleomammalian form. He stressed the fact the entire cerebral cortex was a single sheet that in theory could be flattened and that it is fastened along its lower or ventral border to the cerebral nuclei.

Baars & Gage, 2nd Ed. (pp 520-521) addresses the subject of hydranencephaly, where the human baby is born without a neocortex. They note the infant illustrated appears to have a normal brainstem and cerebellum, citing Merker²⁸. Such a condition is consistent with the idea that the cerebral cortex has failed to elaborate from a simple reptilian "dorsal cap" to the thalamus. Further analysis of the images might suggest how much of the limbic system is present if any. The Merker paper is definitive on the subject of anencephaly and its ramifications. His note 1 defines the brainstem as including the diencephalon and describes

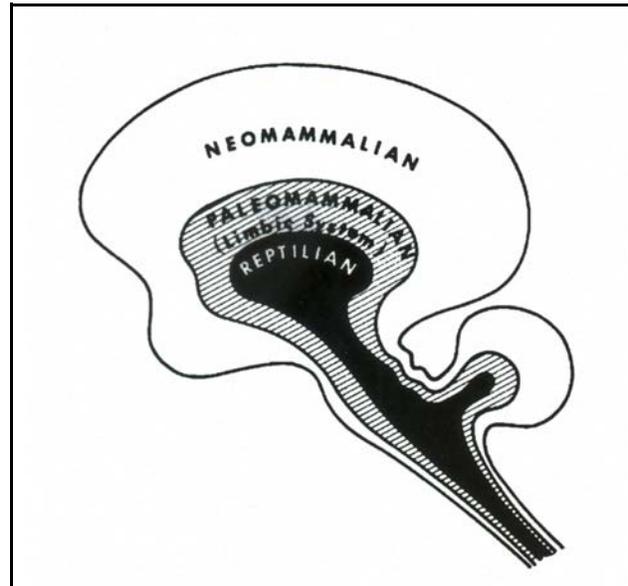


Figure 4.2.3-11 Evolutionary stages of the cerebral cortex. The forebrain evolves and expands along the lines of the three neural assemblies. All of the functions of the mammalian cortex and cerebellum are potentially available in the lower forms but only in more delimited surface areas and therefore presumed functional capability. From MacLean, 1967

²⁵MacLean, P. (1967) The brain in relation to empathy and medical education *J Nerv Ment Dis* vol 144(5), pp 374-382

²⁶Baars, B. & Gage, N. eds. (2010) *Cognition, Brain & Consciousness*, 2nd Ed. NY: Elsevier page 401

²⁷McGovern, K. (2008) Emotion *In* Baars, B. & Gage, N. eds. *Cognition, Brain, and Consciousness: Introduction to Cognitive Neuroscience*. NY: Academic Press Chapter 13

²⁸Merker, B. (2007) Consciousness without a cerebral cortex: a challenge for neuroscience and medicine *Behav Brain Sci* vol 30(1), pp 63-81

the origin of the critically important TRN. It is formed as an extension of the ventral thalamus and zona incerta (even though it encloses a large percentage of the dorsal thalamus). The paper supports the view that consciousness is not seated in the prefrontal cortex but in the diencephalon. The paper is followed by several commentaries of equal importance. A response by Anton M. L. Coenen on page 87 is particularly pertinent to this work. He appears to support the concept of this work that the diencephalon is the executive that controls signals to the prefrontal cortex; together they define a first and second level of consciousness. The response by Daniel Collerton and Elaine Perry appear equally relevant. The genetic problem resulting in this condition appears to center on the homeobox genes, called Hox, which are normally highly conserved among vertebrates²⁹.

While figure 3-23 of Nolte provides a tabular definition of his perception of the elements of the central nervous system, it does not show the interrelationship of these elements with the peripheral system. It also follows the historical approach of considering the spinal chord as a part of the central nervous system. It omits any discussion of a most important part of the diencephalon, the thalamic reticular nucleus (possibly in conjunction with the fornix and amygdala).

Figure 4.2.3-13 rearranges and extends the diagram of Nolte. In both figures, the Cerebrum is defined as including both the Diencephalon and the Cerebral hemispheres. These designations arise from different systems of notation. Few authors refer to the cerebral hemispheres as the telencephalon. Even at this time, terminology is evolving. Nolte (1999) defines the thalamus as part of the cerebrum but Nolte & Angevine (2000) define the thalamus as distinct from the cerebrum (page 1). In many documents related to the lower animals, the thalamus is usually considered the terminal portion of the brainstem instead of part of the cerebrum. As the earlier figure shows, still others consider the diencephalon as the third distinct major portion of the brain with the notation "diencephalon (literally the in-between brain)." This work will focus on a specific part of the diencephalon that is morphologically and topologically distinct from the remainder of the thalamus. This thalamic reticular nucleus appears to play a key role in the control of the both the supervision and the operation of the nervous system.

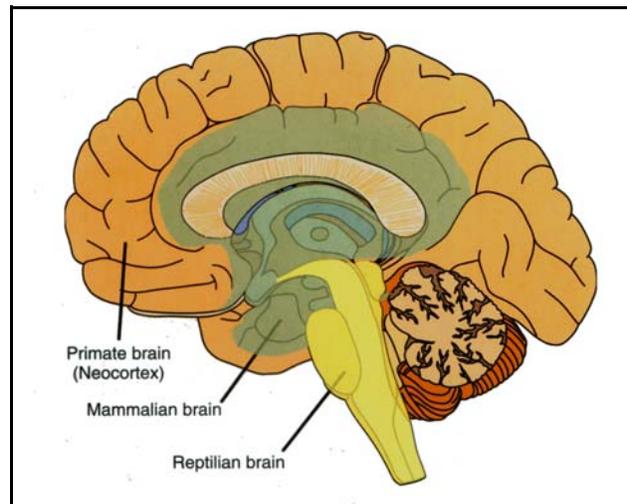


Figure 4.2.3-12 The triune brain of MacLean. Orange; neocortex. Green; mammalian addition to the reptilian brain. Yellow; reptilian brain. From McGovern, 2007.

²⁹Chambers, D. & McConnell, I. (2002) Neural crest” Facing the facts of head development *Trends Genetics* vol 18(8), pp 381+384

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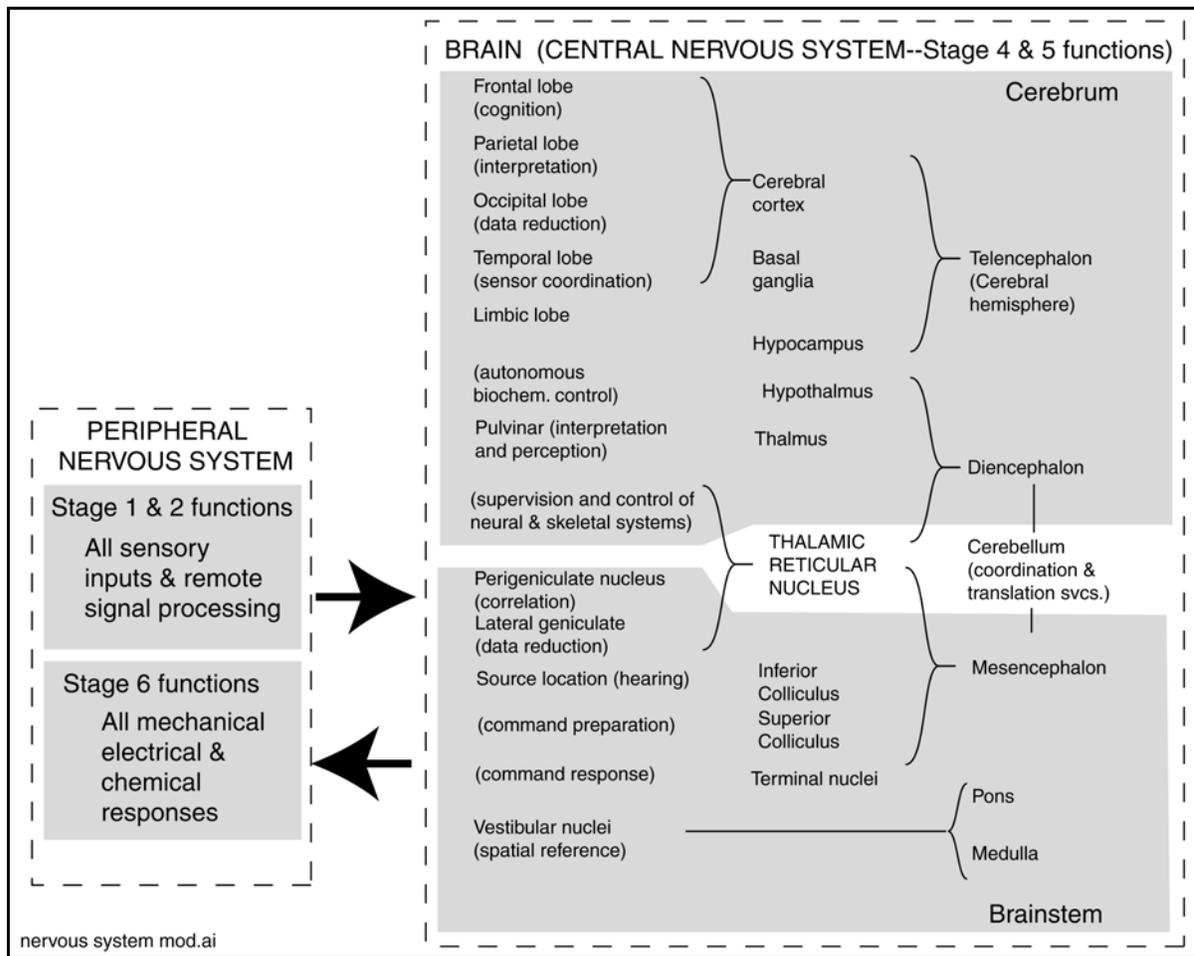


Figure 4.2.3-13 Tabular summary of the morphological subdivisions of the nervous system. Compare to Nolte, 1999. The figure has been expanded to illustrate both the efferent and afferent portions of the peripheral neural system. The large arrows represent the stage 3 signal transmission paths. Only a portion of these paths are found within the spinal chord. While the spinal chord contains a variety of interneurons supporting lower level reflex arcs, it is not a functional entity. The legends in parenthesis relate to the primary function of the element. The numbers in parenthesis of Nolte have been dropped to avoid implying a sequential relationship. As noted by Nolte, some of the functional elements shown overlap the borders implied by the connecting lines. He shows the vestibular nuclei at the junction between the pons and Medulla. The thalamic reticular nucleus takes on a greater role than envisioned by Nolte. See text.

In this context, the term cortex is synonymous with the brain and the spinal chord is exterior to the cortex. While the spinal chord is generally considered a morphological element, as noted above *there are actually a pair of spinal chords* encased in an armored articulated cable tray made up of vertebrae. The two chords support the bilateral organization of the human along with the appropriate reflex arcs between the two sides.

An alternate labeling makes the telencephalon the neo-cortex and the diencephalon and mesencephalon the paleo-cortex. This leaves the cerebellum a separate entity.

The spinal chord should not be considered part of the central nervous system for an additional reason. It is now known that the majority of the afferent stage 3 projection neurons extend from their source at the extremes of the body all of the way to the brain stem without interruption. In the case of a sensory neuron at a human toe, at least fifty percent of its total length is external to the spinal chord. This neuron does not change character where it enters the spinal chord. The question arises; is that part of the neuron within the spinal chord to be considered part of the CNS while the remainder is to be considered part of the

PNS? The obvious answer is the spinal chord is not a functional element with respect to signaling or with respect to individual neurons. Neurons found beyond the outer envelope formed by the stage 3 encoding or decoding functions of the cortex are peripheral neurons. The spinal chord is merely a portion of the neural path of some neurons that is offered special protection by the skeleton.

As portrayed in the figure, the cerebellum plays a major coordination and translation function. When it receives a high level command, it insures that all of the appropriate low level commands are generated to activate all of the necessary response functions. Moving smoothly without the cerebellum is known to be impossible. In the context of this figure, a great amount of information is transferred from the diencephalon to the telencephalon. However, a considerable amount of information is handled within the diencephalon, under the supervision of the thalamic reticular nucleus, and passed directly to the mesencephalon for action. It will be shown that the thalamic reticular nucleus is the most important supervisory and control element in the neural system. Without it, the organism cannot survive.

Figure 4.2.3-14 shows a useful graphic for understanding the development of the human brain presented by Baars (pg 128).

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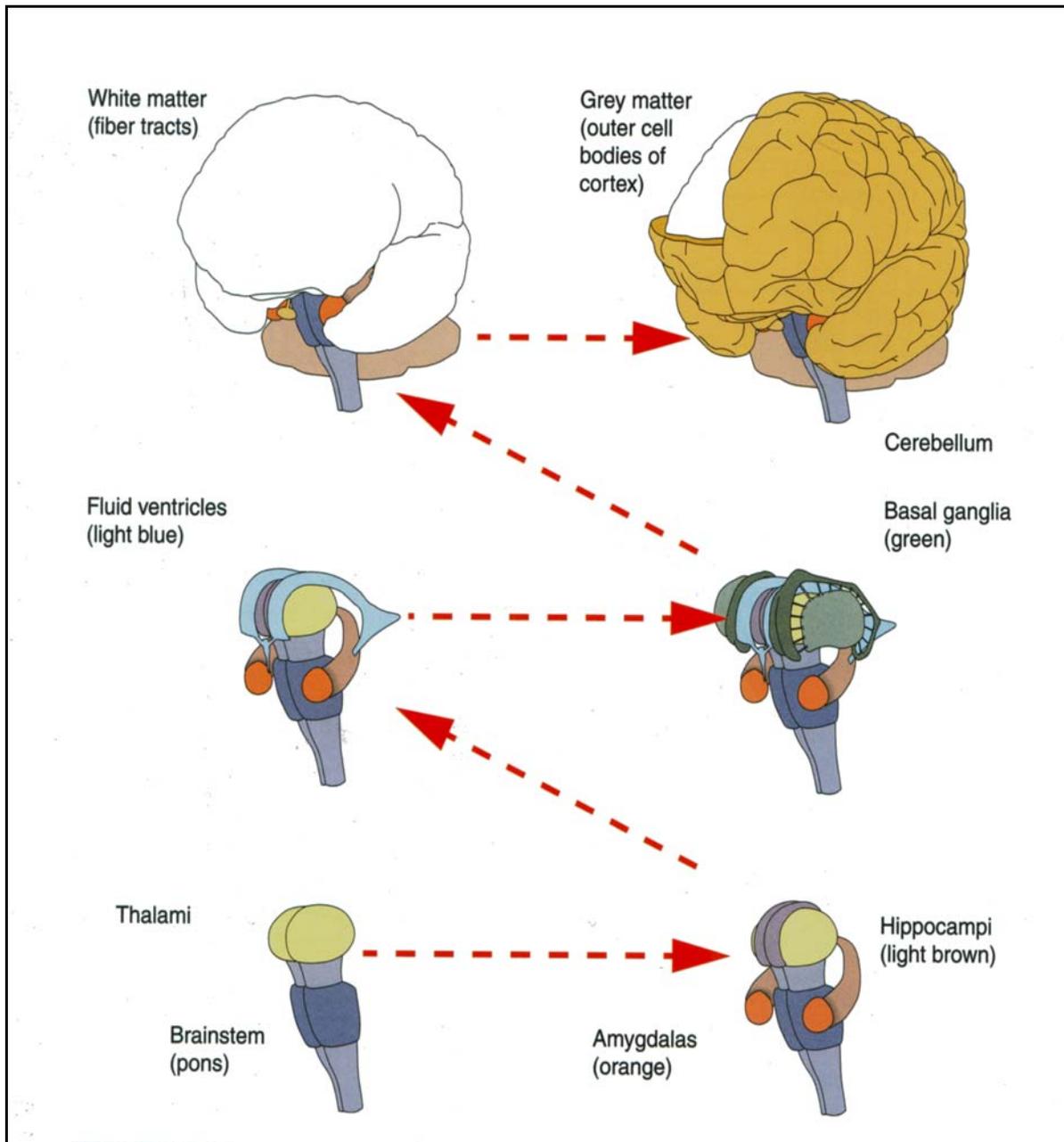


Figure 4.2.3-14 Growing the brain from the bottom up. If you memorize these basic shapes, you will have a solid framework for understanding the brain. The basal ganglia can be thought of as the output hub of the system. Figure and caption from Baars, 2008.

Many authors have proposed that the retina of the visual system is an intimate part of the central nervous system and is formed of neural material. This assertion is usually supported by the claim that the retina and the brain show a similar multilayer structure. **Section xxx** will show that the retina formed originally from ectodermal material. It will also show that while both the retina and some parts of the brain are multilayer, the functions of the layers are distinctly different. In fact the retinal pigment epithelial layer of the retina is more in common with a digestive organ (as opposed to merely supporting phagocytosis). No similar layer has been found in the cortex. **Chapter xxx** will also develop the lack of uniformity in the histology of the cortex. **Section xxx** will show the morphogenesis of most sensory neurons from

ectodermal material. In fact, a case can be made that all sensory neurons are derivatives of a common neurosecretory neuron that most frequently produces a single hair follicle.

The afferent neurons associated with stage 1 in each of the sensory systems can be matched with a matching stage 6 response mechanism. Although not obvious, the auditory input system is matched to an equivalent auditory pointing system. While only a few humans can wiggle their ears, other animals are much more proficient at this function. On the other hand, humans are adept at pointing their eyes while most other animals cannot perform this feat over any significant angle.

Under the above interpretation, the optic nerve of vertebrates can be considered a portion of the peripheral nervous system, PNS, just like any other large bundle of nerves except it contains a vascular component and is not enclosed by vertebra. In the context of this figure, the optic nerve is a peripheral nerve of considerable importance. However, it is functionally identical to, and competitive in size with, any commissure found within the central nervous system.

The morphogenesis of the human brain is well illustrated in figure 3-17 of Carpenter & Sutin³⁰.

4.2.3.3 The hierarchy within the CNS

Without discussing the details, the brain can be considered responsible for five primary functions:

1. To provide reflex responses of the most complex form at the highest level in the reflex pyramid,
2. To provide the animal with general situational awareness relative to the outside world,
3. To provide highly specific situational awareness relative to specific conditions (such as the color, smell, contour and texture of possible food items),
4. To provide a degree of memory for certain classes of events and situations,
5. To control communications with other animals based on the mechanisms available to the animal.

The human is noted particularly for its high level of evolution with respect to functions three (contour) and five (communications). This evolution has been highly dependent on the synthesis of a semantic system, language, followed by the development of a large memory mechanism external to the cerebral cortex, and then writing (and its subsequent ramifications).

The following discussion may conflict with many discussions based only on morphology or only on psychophysics. However, when the work in these fields is melded with the available work in physiology of the neural system, most investigators will agree with the following material.

At the top of the reflex arc pyramid is the brain. In the lower animals, it is typified by what is called the old or mid-brain in humans. It is essentially the top level reflex arc although it may involve considerable cross-coupling between individual signaling arcs. As these cross-couplings have become more complex, the brain has evolved a separate structure, the cerebellum to handle them. This structure continues to be primarily a correlation center for ever more complex reflex actions. It is generally considered the seat of autonomous responses. It does not involve memory or cognition and can be described in terms of, albeit complex, boolean algebra (no variable time delay elements).

Within the chordates and the higher molluscs, a need arose for a higher level of signal processing that included memory as a significant factor. For this purpose, the cerebrum evolved as another extension of the mid-brain. The functional complexity of this structure is so enormous that man has only begun to investigate and understand it. It differs from the cerebellum and the lower structures primarily in its employment of memory. The addition of this capability adds a new dimension to calculations based primarily on boolean algebra.

The addition of memory also adds a new dimension to the cross-coupling between the signals associated with a top level reflex arc. The response need no longer relate only to the

³⁰Carpenter, M. & Sutin, J. (1983) *Human Neuroanatomy*, 8th Ed. London: Williams & Wilkins pg 80

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present. It can relate to prior responses under similar (or all-together different) circumstances. In the extreme, the response can be the result of cross-correlation only involving prior events. This cross-coupling of signals stored previously in memory can be considered the kernel of cognition.

It is worth noting the recent recognition, primarily through MRI and fMRI techniques, that memory is not focussed in a specific portion of the brain. It is intrinsic to the individual processing centers of the cerebrum and the cerebellum. Because of the overall complexity of these individual centers, they are defined as engines in this work. This name correlates very well with the engines defined in current computer processing. An engine is a major hardware portion of a computer that incorporates memory as well as algebraic manipulation and frequently employs its own specialized software routines.

The cognitive process involves bringing a series of information vectors into the saliency plane of individual engines of the cerebrum and manipulating them.

As a result of this organization of the brain, the mid-brain has evolved to be a gate keeper. It is able to delay or influence a variety of autonomous responses from the cerebellum based on the information received from the cerebrum. It also controls virtually all sympathetic responses of the animal.

As the complexity of the brain has evolved into a mid-brain, a cerebellum and a cerebrum- plus a variety of auxiliary structures- it has become desirable to introduce an additional feature. This feature involves the bifurcation of individual (groups of) afferent signals to allow timely processing of the information by different portions of the brain. This bifurcation is extremely important to the operation of the visual system, apparently the audio system and probably the olfactory system. *This bifurcation has been largely overlooked in morphological studies but it is key to the understanding of these systems.*

In the case of the visual system, the signals from the optic nerve bifurcate upon arrival at the mid-brain. A portion of the signals associated with general situational awareness are initially processed by the lateral geniculate nuclei (LGN), a region of the diencephalon. The most time critical (change related) signals from the retina are stripped off the data stream by the LGN and returned to the Precision Optical System (POS) of the mid-brain immediately. The information required for stereo-optic vision is also stripped off at this point and returned to the POS. The remaining material is then passed to the posterior region (area 17) of the posterior lobe of the cerebrum by the LGN via the geniculocalcarine pathway for further processing. The material presented to the posterior lobe of the cerebrum is further processed by a variety of engines until it is entirely in vector form. This information is then passed to the cognitive and memory engines in the parietal and temporal lobes of the cerebrum.

The other information from the optic nerve, which is of higher spatial resolution, is more time critical from the perspective of information theory and originates in the foveola, are initially processed by the pretectum or forward portion of the mesencephalon. These signals are combined with other signals, primarily from the vestibular system and completely vectorized prior to being sent directly to one of the cognitive portions (area 7) of the parietal lobe of the cerebrum via the Pulvinar pathway. Although they are visual signals, these high precision, time sensitive signals do not pass through the so-called "primary visual cortex" at the posterior of the posterior lobe of the cerebrum.

It appears that the auditory signals from the ears are also bifurcated and processed simultaneously by two distinct areas of the mid-brain. This subject is addressed in detail in PBH xxx

Recognizing the above role of the midbrain as gatekeeper, the description of the suggested dual signal paths within the brain is slightly different than that in Figure 17-16 of Torrey. In this work, the mid-brain acts as a junction point involved in the receipt and issuance of virtually all signals associated with the CNS and capable of controlling the relay of some of these signals, particularly the efferent command signals to the peripheral system. This activity involves processing two separate classes of signals within two distinct areas of the midbrain. The first class relates to the general situational awareness of the animal. The second involves the specific situational awareness. These signal paths will be developed in more detail in **Chapter 15**. Recognizing this role, it is not clear that any signals from the cerebellum are ever passed through the midbrain to the cerebrum. However, ever and never are hard words to

defend in this field.

4.2.3.4 Consequences of introducing memory in the CNS

There are interesting side effects to the introduction of dynamic, as opposed to genetically encoded, memory into the CNS. These can generally be divided into those associated with short term memory and long term memory. It is evident that short term memory is shared with even the bees who are able to remember the path to a food supply long enough to return to the hive and perform their instructional dance for the benefit of other bees and the community as a whole. It is difficult to quantify the presence of long term memory versus genetically programmed procedures in the bees because of their short life span. Are they able to return to the same site some days later based on experience. Nearly all higher animals with a life span of over a few months are known to exhibit long term memory. Recent films have shown the ability of the octopus to return to one of a series of homes over a period of weeks with unexpectedly good precision. It generally does not rely upon intermediate landmarks nor does it take a previously defined path. Long term memory is generally associated with experience whereas genetic memory is provided across evolutionary time intervals.

4.2.3.4.1 Anachronistic consequences of memory in the CNS

With the availability of memory within the signal processing engines of the CNS, these engines are able to call upon experience, as stored in their individual memories, perform computations, and restore the results in other areas of memory and/or generate command signals. This capability can lead to relatively bizarre results. Fortunately, the mid-brain acting as gatekeeper can restrict some of these results. Also fortunately, these results can provide information about the importance of memory in the visual and other modalities (particularly hearing).

A particular example of anachronistic behavior is sleep walking in humans. This phenomenon stresses the capacity of the long term memory within the engines of the CNS associated with sensory system as a whole and the computational scope available to these engines. The engines can generate all of the necessary command instruction to effect the movement of the individual, without benefit of visual cues, over a considerable distance and along intricate paths. Fortunately, the mid-brain in its role as gatekeeper is usually able to prevent this activity from being implemented by the muscles. Sleep walking is frequently interrupted when the person encounters an unexpected obstacle that is not where memory indicated it should be.

A second example is the ability of a human to see ghostly images or hear sounds that clearly are not present. These perceptions are based on the engines of the CNS recalling stored vectors representing these (previously experienced-learned) events into saliency space. The problem arises when the individual believes these computed events (hallucinations) are real.

A more serious situation arises when a human recalls these above computed events from memory, performs computation upon them in saliency space, and then stores the new result in memory. As a result of this process, the individual can progressively lose the ability to separate real events stored in memory from computed but hallucinatory events. This can lead to a spiral into insanity.

4.2.3.5 Recent fMRI data confirming the distribution of the feature extraction engines of the brain

Within the last dozen years, our understanding of the operation of the neural portion of the brain has increased immensely with the introduction of functional magnetic resonance imaging (fMRI). The name is meant to describe the ability of the imaging device to record activity in the brain in response to images projected onto the retina. A particularly vivid example of this imaging technique was recently published by Logothetis, et al³¹. When combined with the VEP technique, it can be used to determine the time sequence of events relative to the different engines of the brain.

³¹Logothetis, N. (2002) Functional MRI probes monkey brain. *Biophotonic International*, April 2002, pp55-56

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Such techniques have already demonstrated the arrival of signals in the mid region of the cerebrum **before** the arrival of similar signals in the occipital cortex (the so-called primary visual cortex).

4.2.3.6 The connectome of the human CNS

Hagmann et al. have recently introduced a new MRI-based computer generated image of the brain that offers to document the individual commissure if not the individual neural path within the CNS³². The movement of water molecules along the neural paths is tracked. Currently, the complexity of the images puts them in the category of computer generated art. However, the ability to differentiate between different paths and to print out data in various identified groups offers considerable potential. **Figure 4.2.3-15** shows one of their early works of art.

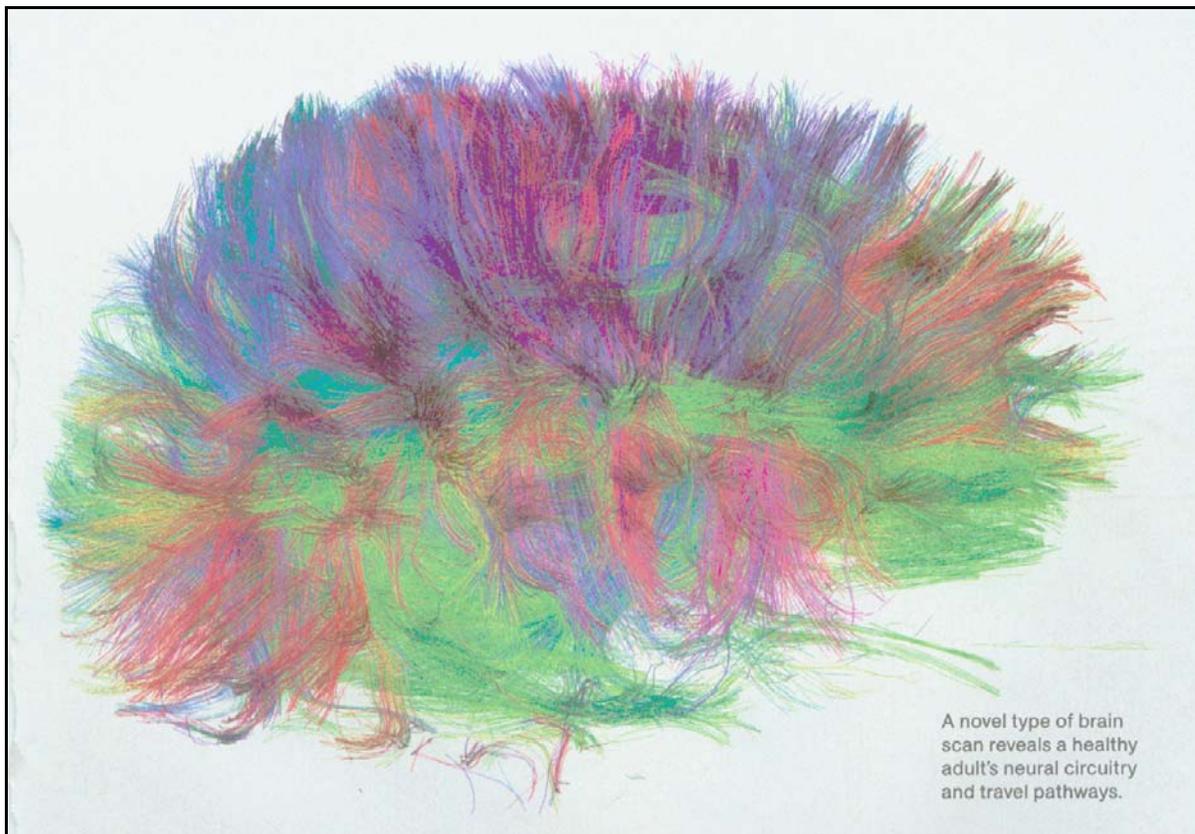


Figure 4.2.3-15 A composite mapping of the neural paths within the human CNS. From Hagmann et al., 2011.

4.2.4 Block diagrams reflect details of the architecture of neural systems

Once block diagrams have been used to define the stages of a neural system, they become even more valuable in defining the high level functional processes occurring within those

³²Hagmann, P. Cammoun, L. Gigandet, X. Gerhard, S. Grant, E. Wedeen, V. et al. (2011) MR connectomics: Principles and challenges *J Neurosci Meth* vol 194(1), pp 34-45

stages. The more complex of these high level blocks will be defined as engines in this work (typically containing one million to ten million active circuits—about the complexity of a modern desk top computer central processing unit, CPU. Block diagrams become equally useful in defining the next level of functions within these engines (typically 100,000 conexus) and eventually become useful in defining the individual servomechanisms and input/output circuitry associated with the neural system of interest. Using this nomenclature, the brain of the human contains on the order of a million individual high level blocks. In the context of the cerebral hemispheres, each block occupies about xxx square centimeters of topography (when flattened). [xxx review these numbers based on what is in old chapter 15 of Processes in Biol.]

[xxx check wording here]

Considerable work has been accomplished using this approach with the human visual system.

The visual system of humans and selected other carnivores (both mammalian and avian) exhibit extremely complex system level block diagrams. Many of these block diagrams have been prepared for a companion book, "Processes in Biological Vision" (PBV), and are currently available for downloading on the web at www.neuronresearch.net/vision . A few are presented here to illustrate the power of system modeling techniques discussed in the previous paragraph. **Figure 4.2.4-1** illustrates a very high level block diagram applying to only a small portion of the visual cortex and a variety of lower level engines supporting them (some only indicated by pathways to them).

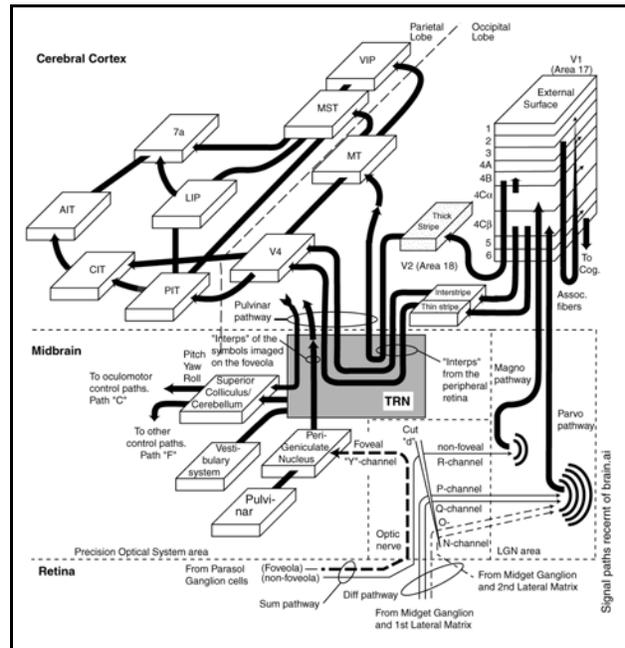


Figure 4.2.4-1 A preview of a high level block diagram of the engines supporting the human visual system. Discussed in detail in Chapter xxx.

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Figure 4.2.4-2 shows a slightly lower level block diagram representing only the signal manipulation associated with the afferent signals of stage 1, 2 and the initial parts of stage 3. It depicts the first thirteen steps in the visual process (using quite detailed labels) with the later steps shown at a higher level (and described by less precise labels).

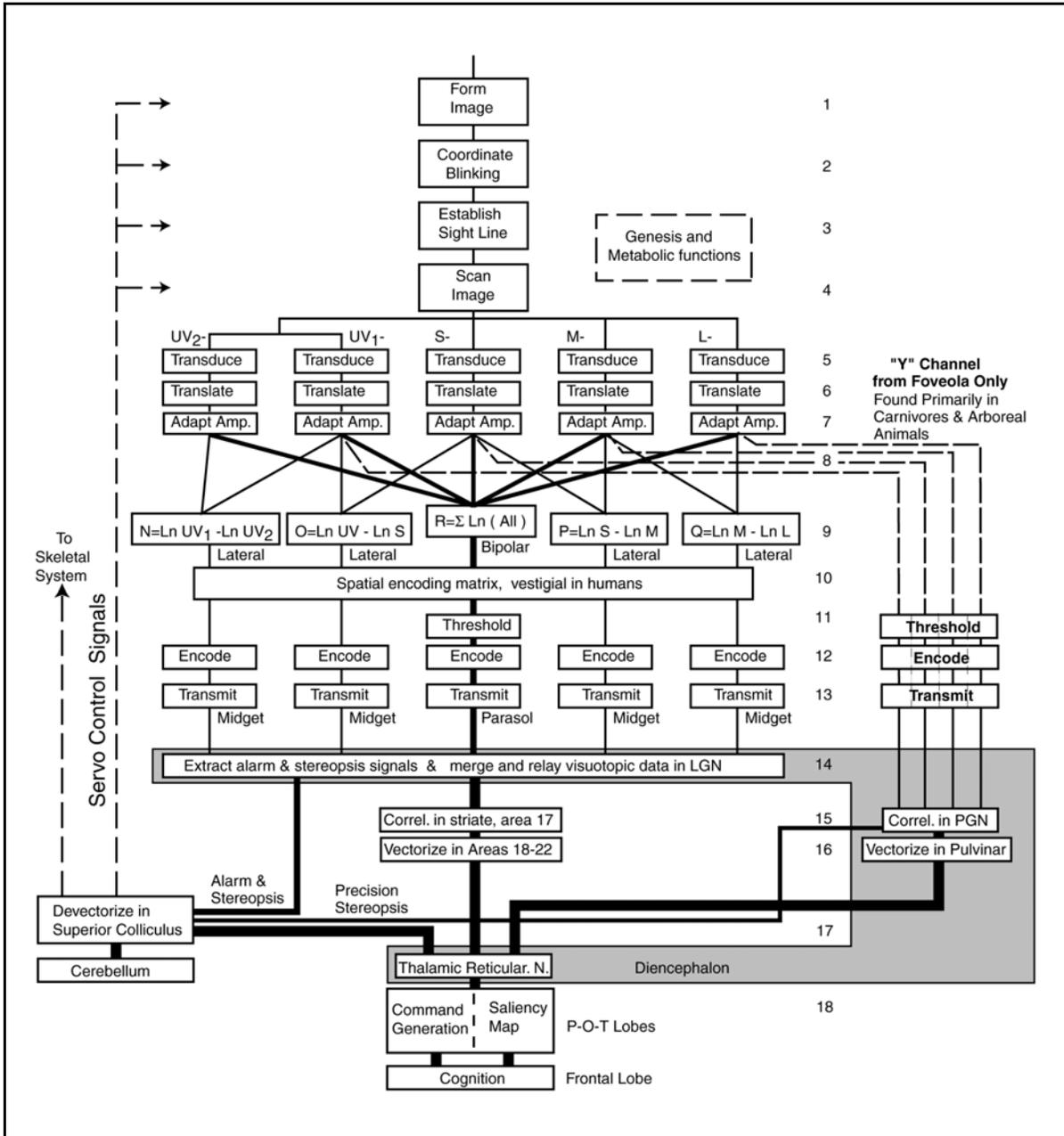


Figure 4.2.4-2A top level block diagram of the afferent signal manipulation paths of humans and other selected carnivores. See text.

[add text xxx][add text xxx]

A more comprehensive, but necessarily less detailed block diagram is shown in Figure 4.2.4-3.

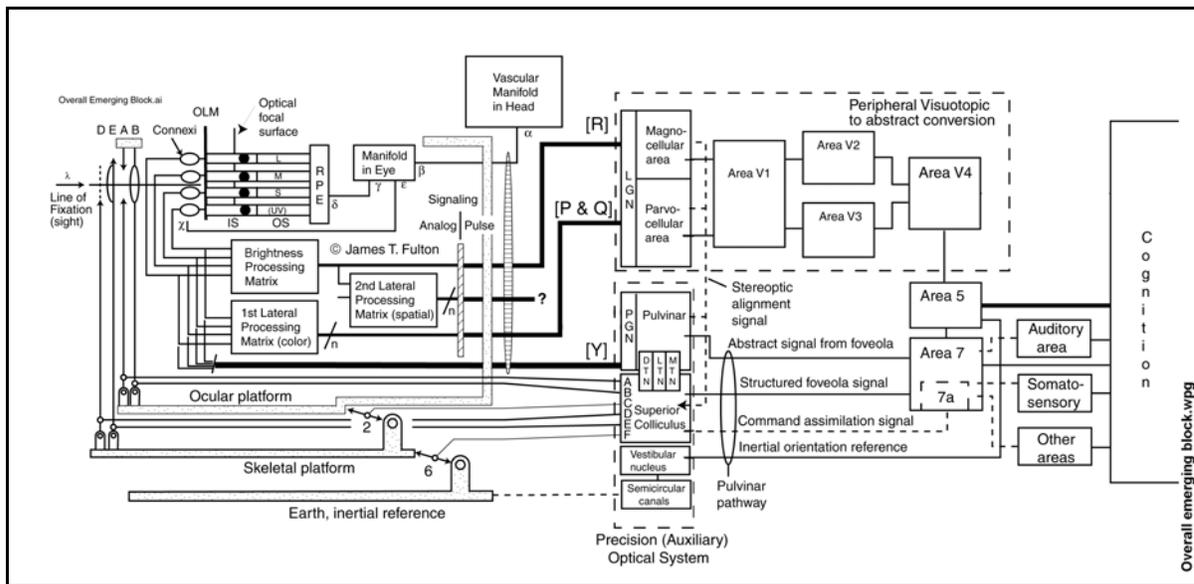


Figure 4.2.4-3 A block diagram of the overall visual system of humans highlighting the principal afferent, CNS (internal or circulating) and efferent signal paths, including the oculomotor servomechanisms.

Figure 4.2.4-4 shows a block diagram of the overall oculomotor servomechanism under a variety of operating circumstances. To show the performance of this complex set of servomechanism, it is useful to incorporate blocks representing different levels in the hierarchy of diagrams. At lower left, the symbology represents an individual pair of muscles whereas on the right blocks are shown that represent multiple engines within areas 7, 17, 18 & 19 of the cerebral cortex. The figure facilitates the definition of the six major (and largely autonomous) operating modes of the human neural system; awareness, alarm, analytic, information, volition and command. It is also able to highlight many very important relationships between this diverse set of circuits, engines and anatomical regions.

Many of the sensory modalities of the neural system exhibit similar architectures that can be discussed in term of a variety of operating modes. These operating modes can be considered overlays on the basic architecture, generally under the control of the TRN

[text from cognitive computation paper]

The **AWARENESS** mode is shared among all but the very lowest phylogeny of animals. This mode provides the interpretive and cognitive centers of the animal with a multi-sensor description of the surrounding environment. It employs an earth-oriented (generally gravity-oriented) inertial framework that is not related or restricted to the field of view of the eyes of the animal. The interpretations placed in the saliency map based on this framework, are not “-topic” to the sensory mode. They are -topic to the external environment of the animal.

The **ALARM** mode may be the primary mode of the neurological system. It is shared by all known animals (including those excluded from the awareness mode). The first order task of the alarm mode is to decide if the trajectory of an object in the environment will cause imminent danger to the animal. If true, the general response is some degree of flight to escape potential threats. If not, the threat is considerably reduced. Failure to escape by flight can lead to a defensive posture. However, this posture does not appear to represent a separate functional mode.

In many animals, the alarm mode appears to operate as several different levels in response to at least two distinct threat conditions. The simplest case involves the single threat level. The response at this level relates to the naivete of the subject. In small children, the appearance of a threat for the first time may not generate any response. However, this experience can be considered training. On the second appearance of this same threat, the response may be significantly different. Through further training, the response can become

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quite sophisticated.

The dual (multiple) threat level within the **ALARM** mode becomes quite important within the sports and military regimes. The response to near simultaneous threats at this level is also a strong function of training. Training frequently separates the successful player from the mundane players. The ability to respond to dual threats in the absence of cognition is intimately related to the attention-blink phenomenon discussed by Taylor³³.

[xxx edit below here]

The **ANALYSIS** mode is most common among the higher chordates and most optimized, both physiologically and programmatically, among humans. Within the visual modality, the mode depends on the fovea for its operation. For humans, it is optimized in the even more restricted area (1.2° diam.) of the foveola. The operation of this mode appears to differ significantly with respect to scene content.

For the natural scene, or non-symbolic image, the analysis mode appears to operate at one of two sub-levels. In the most general sub-level, the visual system performs a routine search of the field of view to analyze the characteristics of the scene of interest to the animal. This mode appears to rely upon previous images of the scene stored in memory to a remarkable degree. Through this reliance, the animal can restrict the time required to complete an evaluation of the scene based on a search. This type of analysis is encountered when a person enters a room for the first time. On subsequent entries, much less time is used to discover the features of the room. The second sub-level involves specific analyses, performed in response to a signal from the alarm mode, of a given scene element to decide whether it is a threat. These analyses go beyond the calculation of the trajectory of any object moving within the field of view. It seeks to determine the nature of the threat within a more precise context; does the scene element have big teeth?

For the symbolic image, there is a specific analysis mode, with two sub-levels, limited primarily to humans. It involves the detailed analysis of fine detail related to small objects within the instantaneous image on the foveola. These objects can be small objects of art or technology but most often are symbols related to communications (letters and words). The first or routine sub-level relates to objects of previously unknown characteristics. This is the typical analysis performed when a person picks up an unusually shaped rock or a sea shell on the beach. It is also the analytical mode used when someone looks at a document written in a foreign language or unfamiliar script. The analysis involves apparently random motions of the eyes within a few degree field of view. The amplitudes of many individual motions are measured in microradians. These motions are frequently related to tremor and are not random. They are programmed by the POS in accordance with memories associated with any similar object. To construct a perception of the whole object, the eye performs a series of microsaccades (tremor), minisaccades, and if necessary small saccades, to analyze the entire object. This mode involves a large degree of memorization of characteristics and can be considered training.

There is a second sub-level associated with the analysis of symbols. It is strongly influenced by training and memory. It allows the human to quickly evaluate a familiar member of a class of objects previously studied. Although not limited to text symbols, it is most recognizable in that context, i. e. reading. It is based on training in the syntax and vocabulary of a given language. For a language like English, written from left to right and where the first syllable of a word is usually important, the fixation point of the eyes will jump to the right after reading a word. The point of fixation will land on or about the third letter from the start of the word. This nominal motion is known as the "dumb default" in reading. The POS of the visual system will proceed to analyze the group of letters imaged on the foveola and store its interpretation temporarily until the remainder of the word is interpreted. Following sufficient time to analyze the first group of about five letters, the point of fixation will move to the next syllable until it completes analysis of all of the syllables of the word. It will then perform another dumb default to the start of the next word. At the end of a line of text, the point of fixation will drop down to the left end of the next line. Again, it will land on about the third letter from the start of the first word. The process will continue indefinitely. It is not clear how the POS works at the detail level. It may only assemble the interpretations associated with one complete word and pass that information on to the higher cognitive centers via the Pulvinar Pathway.

³³Taylor, J. (2006) *The Mind: A User's Manual*. NY: Wiley page 15

Alternately, it may assemble the interpretations related to whole phrases before performing a global interpretation and sending that interpretation on to the higher cognitive centers.

The analysis operating mode of the auditory modality of humans also appears to be optimized beyond that of most lower animals. This is particularly apparent with regard to music, where humans appear to appreciate tonal rhythms and sequences that most other species simply ignore. There is however, a growing recognition of the language capability of animals related to the auditory modality. Such a capability relies upon the analytical mode defined here.

The **COMMAND** mode is involved primarily with the execution of changes in the external environment (from the subjects perspective) in response to sensory inputs. These responses are predominantly timely but may involve significant delay at the will of the conscious executive. The command mode signals are primarily low level and directed to particular neuro-affectors. They are an expansion of higher level signals that have passed through the cerebellum and/or superior colliculus.

Besides the high level commands circulating within the nonconscious system in response to sensory inputs, there are signals labeled instructions received from the conscious cognitive stage via the **VOLITION** mode. The interplay between this mode and the modes related to sensing is complex and highlights the important role of the TRN. It is the switching and control portion of the TRN that controls the passing of sensory information to the anterior lobe via the cognition path and the passing of the initial (highly condensed) instructions formed in that lobe back via the volition path to the old brain for command generation and execution. The TRN has the final say as to whether to respond to volition generated commands or reflexive commands generated via the alarm mode.

These definitions of physical stages based on electrophysiology and histology and modes of operation based on behavioral characteristics appear compatible with the ideas of Revonsuo³⁴, of Schacter³⁵, of Baars³⁶, of Damasio³⁷ and others as cited in Sun (page 162-172), but are more detailed (such as showing procedural elements in both the afferent sensory modalities and the efferent motor-glandular modalities). They also appear able to explain some of the inconsistencies within the psychological literature such as those related to Underwood's saliency map hypothesis discussed below.

³⁴Revonsuo, A. (1993) Cognitive models of consciousness *In* Kamppinen, M. *ed.* Consciousness, Cognitive Schemata and Relativism. Dordrecht, Netherlands, Kluwer pp 27-130

³⁵Schacter, D. (1990) Toward a cognitive neuropsychology of awareness: implicit knowledge and anosagnosia *J Clin Exper Neuropsychol* vol 12(1), pp 155-178

³⁶Baars, B. (1988) *A Cognitive Theory of Consciousness*. NY: Cambridge Univ. Press

³⁷Damasio, A. (1994) *Descartes' Error: Emotion, Reason and the Human Brain*. NY: Grosset/Putnam

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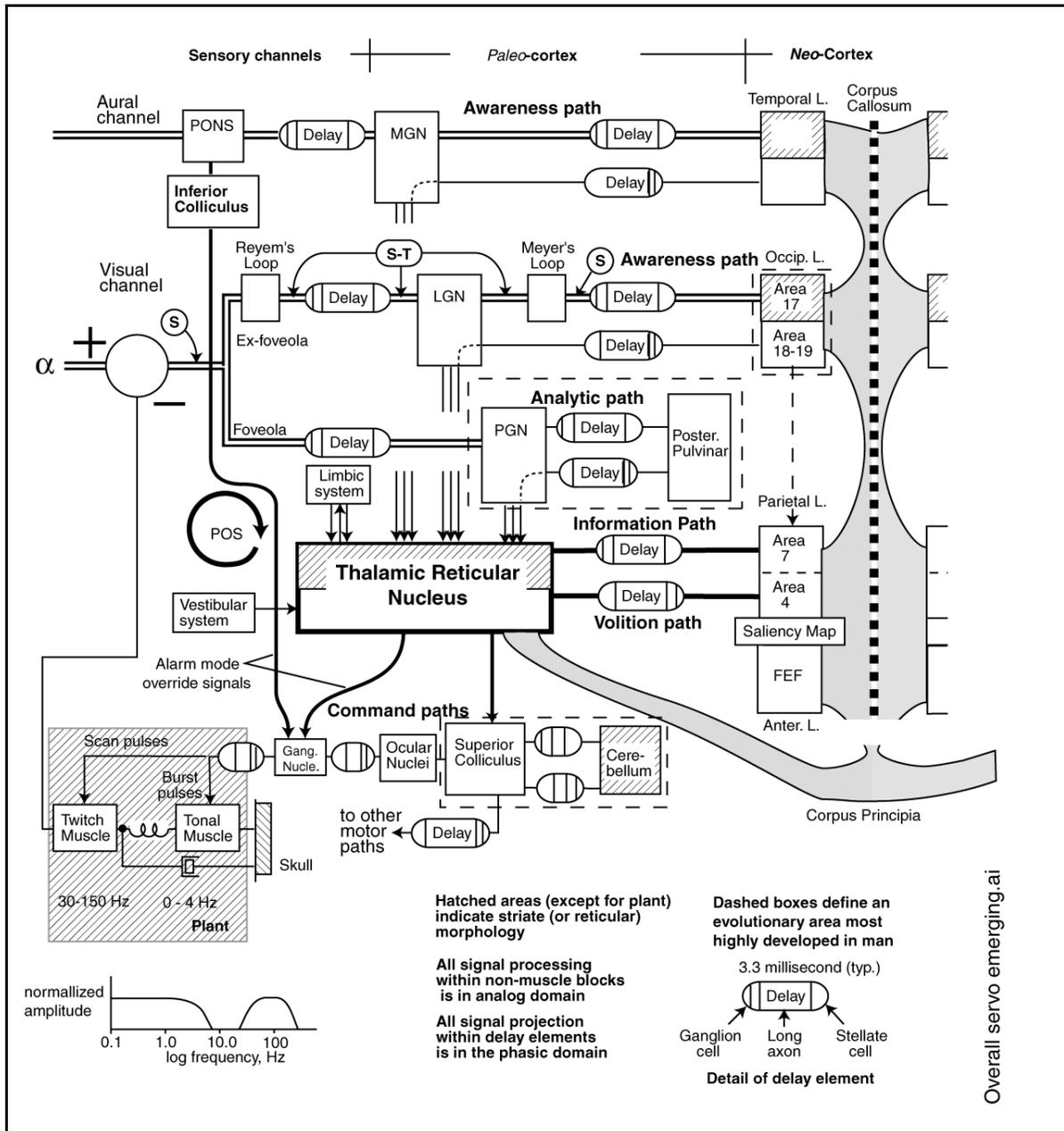


Figure 4.2.4-4 Overall block diagram describing the operation of the oculomotor servomechanism under a variety of circumstances. See text.

Most other sensory systems are simpler than the visual system. However, the auditory system employs a variety of uniquely configured multi-dimensional correlation techniques similar to those found within the thalamic reticular nucleus of the visual system.

4.2.4.1 Adding specificity: autonomous/somatic & sympathetic/parasympathetic operation

The above figure illustrates another advantage of a well documented lower level model. It allows the review and updating of earlier models. As an example, a more precise interpretations of the concepts of somatic versus autonomous operation and sympathetic versus parasympathetic operation is given in **Figure 4.2.4-5**. It is quickly recognized that the

concepts of autonomous versus somatic operation do not represent independent spheres of neural operation. These concepts are seen to be overlays upon the overall system. They relate to different levels of reflex arcs. Only what will be described as the somatic overlay involves volition commands originating in the cerebrum. These commands can arise spontaneously (an act of free will) but are generally in response to a sensory input, or the response to a stored perception related to an earlier sensory input. Sensory inputs arriving at the CNS are directed into distinct signal processing channels labeled modes following initial processing. The awareness mode is the major operating mode in the absence of danger to the organism. Much of the information in the awareness channel is not delivered to the neo-cortex. It is processed within the engines of the paleo-cortex or at lower levels in what will be described as the autonomous overlay. The autonomous overlay can be divided into two distinct sub-overlays. The high level sympathetic overlay involves the paleo-cortex and is focused on the merging of information from multiple sensory subsystems in order to create a coordinated response. These responses can be influenced by prior learning. Many of these reflex arcs are sufficiently complicated as to be described as servomechanisms later in this work. Examples are the operation of the oculomotor muscles in response to instructions from the paleocortex. Some of these responses are due to alarm mode inputs from the visual, aural or other sensory subsystems. These responses are clearly sympathetic in character. They frequently reflect unusual external conditions. Other responses of the oculomotor muscles are due to the more mundane commands generated within the paleocortex. These commands arise without volition mode signals from the cerebrum and are conventionally described as low-level sympathetic responses. In other neural pathways, these sympathetic responses may be generated within remote ganglia (the knee jerk response as an example). At the lowest level of neural system involvement are the parasympathetic overlays. These responses frequently involve local ganglia associated directly with the organ being supported by the neural system. Only minimal supervision of these reflex arcs is performed by the higher neural centers. Many of these reflex arcs are completely beyond the control of the somatic overlay.

While independent paths are shown between the various blocks in the figure, this is for clarity only. As suggested by an earlier figure, most of the supervisory signals are bridged across the lower level reflex arcs. Only single command paths (that may ramify in their terminal areas) extend to most muscles and glands.

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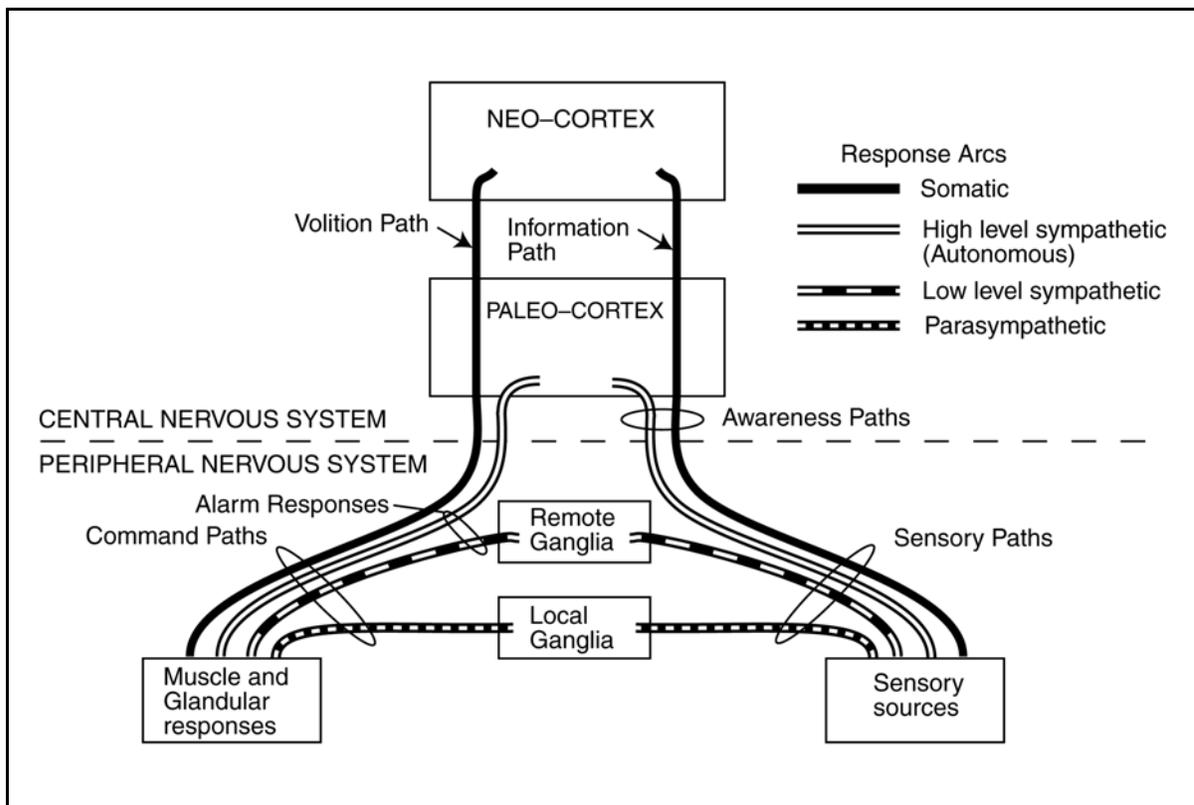


Figure 4.2.4-5 An improved description of the spheres of neural operation EDIT defined previously in [xxx Figure 4.3.2-1] . The high level sympathetic response arcs can merge data from multiple sensor subsystems.

Figure 4.2.4-6 from Schmidt & Thews provides greater detail related to the autonomic system³⁸. Note, only a small number of parasympathetic neurons travel down the spinal chord. The majority of the parasympathetic neurons travel down the vagus nerve (X^{th} nerve) from the medulla (medulla oblongata).

It is useful to note the column of sympathetic ganglia external to the spinal chord. No data could be found suggesting these ganglia contain analog (stage 6) neural circuits. These ganglia appear to receive stage 3 neurons from the spinal chord, and distribute an expanded group of stage 3 neurons to the target organs of the visceral system. There are even ganglia beyond the major column of sympathetic ganglia performing an additional nerve expansion function, primarily in support of the main intestinal tract.

³⁸Schmidt, R. Thews, G. (1983) Human physiology. Berlin: Springer-Verlag

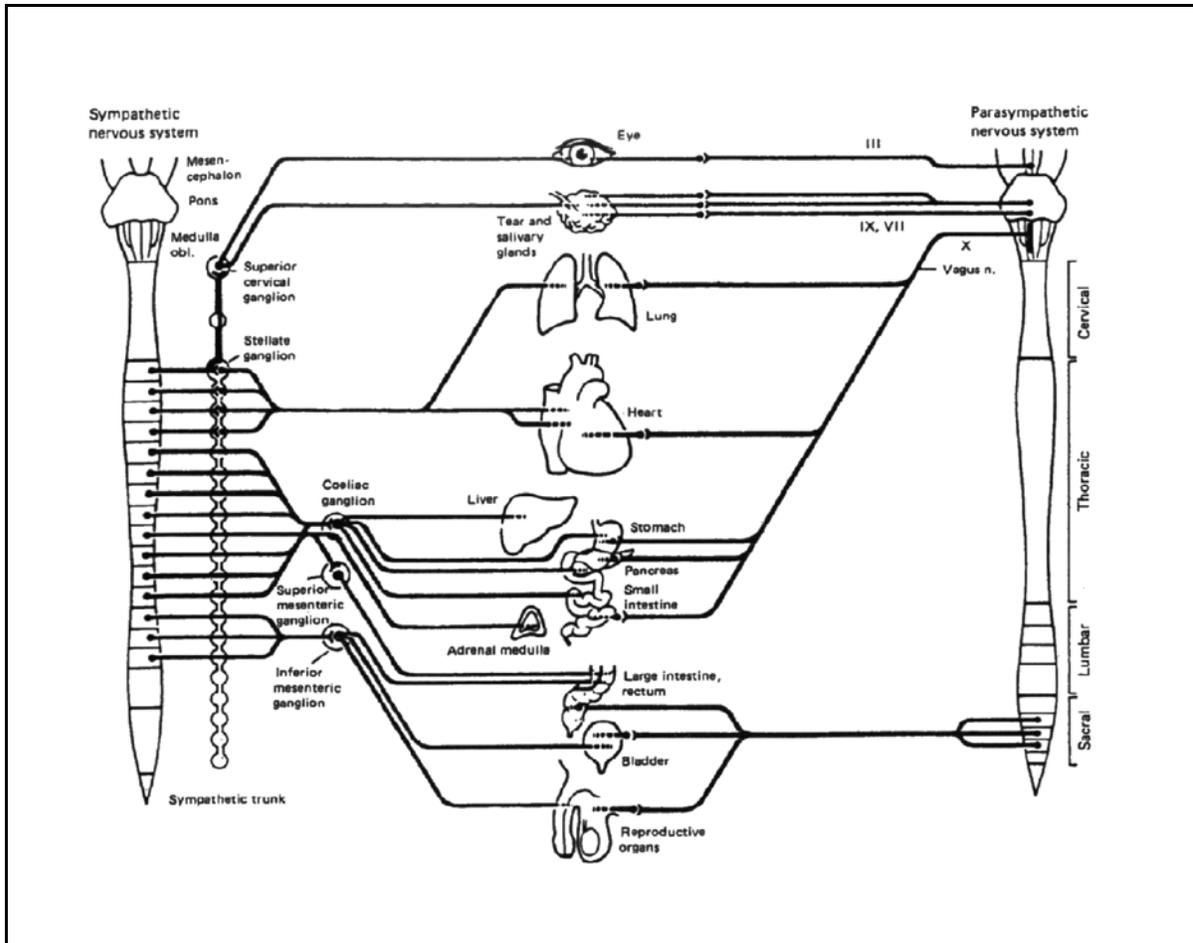


Figure 4.2.4-6 The complete autonomic system of human. The spinal chord is shown on both the left and right perimeters to support a clearer discussion. The sympathetic component is on the left and the parasympathetic component on the right. The sympathetic innervation of blood vessels, sweat glands and piloerector muscles is not shown. The sympathetic ganglia are shown on the left. See text. From Schmidt & Thews, 1983.

4.2.4.2 Clarifying the remarkable uniformity of the animal brain

The CNS consists of a single thin laminate of tissue typically two millimeters thick (the thickness of six business cards, or playing cards). It is represented by typically six active layers (~400 microns thick) and one nominal structural layer. The active layers are not physical layers. They are defined by the populations of neurons found in the tissue. If an investigator focuses on one population, he frequently assigns a different number of layers to the tissue because his criteria is different. The tissue layer is folded repeatedly to reduce its maximum linear dimension. It is folded further to reduce the distance between various regions of the tissue, thereby shortening the commissure required to propagate signals between these regions. In the case of the thalamus, its individual engines are frequently thought to be made of thicker material because of the great degree of folding actually present. Finally, it is folded further to maximize the amount of tissue within a given volume of the cranium. The degree of this final folding is usually taken as indicative of the phylogenetic sophistication of the animal.

The creases resulting from this folding, called sulci, are frequently used by the anatomist to identify regions of the CNS. However, it is important to realize the actual functional areas of the tissue sheet are not related to these sulci. The active neural tissue is not limited to the plateaus (gyri) between the sulci and the active neural tissue fills the sulci as well as the gyri. Hawkins (page 50) referenced Mountcastle (1978) concerning an additional point. "The regions of cortex that handle auditory input look like the regions that handle touch, which

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look like the regions that control muscles, which look like Broca's language area, which look like practically every other region of the cortex." While not technically correct, as noted below, "Mountcastle suggests that these regions are actually performing the same basic operations!" He goes on to suggest these regions use the same computational tools.

Mountcastle did not differentiate between the striated and smooth CNS tissue. While not functional in itself, striated tissue is indicative of the underlying function; the striations are due to long neurites arranged in one, two and multidimensional arrays and accessing large numbers of neuronal axon pedicles terminating at the nodes of such arrays. These striated areas employ tools from the same toolbox as other neural tissue but they achieve unique results such as Riemann surface transforms and large scale signal correlation without requiring transcendental mathematical calculations. The striated areas are also called reticulate areas. The thalamic reticular nucleus (TRN), a thin multidimensional array covering the majority of the thalamus, derives its ability to command and control the interplay between the afferent, cognitive and efferent subsystems of the neural system from the synapses occurring at the nodes of its reticulated structure.

Mountcastle's generalization plus the additional capability provided by the striated cortex and the TRN do suggest the degree of plasticity present, particularly during the formative period prenatally and during the first 18-24 months of life. Errors in connecting the specific neurons of the cerebral cortex by the appropriate circuit to the TRN can result in the condition of synesthesia. The subject may blur their perceptions, certain sounds evoke a perception of color, or certain textures evoke a perception of bitterness.

The human brain is bilaterally symmetrical to a remarkable degree, both morphologically and functionally. Only at the detail level do significant asymmetries appear; Broca's area is typically found on the left side of the brain and a stroke in this area can compromise the subject's ability to use the rules of grammar in speech.

4.2.4.3 Clarifying the role of time in the overall neural system

While the architecture of the neural system changes little during the lifetime of the organism, time plays a significant role in the operation of that neural system.

While the neural system does not employ a "clock" that is easily defined, it does exhibit an ability to relate to time, as if it employed a burning candle instead of a highly precise chronometer. As in the case of a candle, the neural system matures and ages much as a candle becomes shorter with time. And like the candle, the rate of shortening is subject to a wide range of variables that may themselves be functions of time. The biological clock does not employ an escapement or other highly stable mechanism to determine time intervals.

While the neural system does not employ a high degree of redundancy to provide enhanced reliability, it does employ multiple parallel and closely related channels in an architecture described below as a transversal filter. This means of operation combined with the employment of pattern recognition techniques in stages 4 & 5 does provide a high degree of individual neuron channel error rejection, and hence enhanced overall system reliability.

The perception of time while in one of the operating modes defined above may vary significantly. The observation by a subject that their perception of time stood still, or time appeared to speed up are common ones under various conditions of stress.

It may be asserted that the pulse rate is an example of the stability of operation of the heart with respect to time. However, additional thought will demonstrate this is a poor example. The pulse rate varies over a factor of three or more routinely. The relaxation oscillator circuits of the heart and other organs are fundamentally less stable than mechanical escapements or crystal-based clocks

4.2.4.3.1 The perception of external events vs time

The neural system employs a multitude of engines processing information generally in sequence. However, the system also employs a multitude of reflex loops that allows the response to a given environmental condition to occur rapidly.

The rapid response to environmental conditions via the alarm operating mode and various reflex paths results in the perception of an event to frequently occur after the response to the event has already begun, or even concluded. Batting a baseball is a classic example of this phenomenon but there are many others. "Training" is largely an exercise in learning to respond to an event before the event has been totally analyzed by, and perceived by, the cognitive elements of the neural system. Serious training in the military or sports is designed to prepare the subject to respond without involving cognition. The individual then responds via the alarm mode of neural activity. From this aspect, it is difficult to hold a soldier responsible for his actions on a moment-to-moment basis.

When a highly trained individual adopts a specific stance and a highly focused state of attention, it is safe to say he has transitioned to the alarm mode of neural operation.

4.2.4.3.2 Time dispersal within the neural system

The magnitude of the signal processing required within the neural system, the limited volume available for various processing engines, and the physical geometry of the sensory organs frequently causes the processing to occur in parallel paths and asynchronously. As a result, time delay plays an important role in the neural system. As in the above paragraph, it is not uncommon for visual signals to arrive at the visual cortex when those associated with the foveola have already been perceived by the pulvinar. This delay is enhanced by the physical distances involved and the significant amount of processing achieved within the LGN's prior to transmission of the partially processed information to the visual cortex. A similar situation appears to occur within the auditory system with respect to high levels of impulse-type sound. The circuits of the inferior colliculus may issue action commands before the auditory cortex, and even the audio PGN are aware of the threat.

A second aspect of time dispersal is used effectively in the neural system; particularly, but not exclusively, within the sensory stage of the auditory modality. The mechanism of frequency selection employed in hearing involves a slow acoustic wave traveling along Hensen's stripe within the cochlea. As a result, each frequency increment of the auditory spectrum is striped from the main signal path at a different time. These signal increments can then be processed individually without regard to their time coherence relative to other signal increments. The individual channels need not be processed in the same manner or to the same degree. It is only necessary to bring them back into time coherence when they are to be reassembled into a comprehensive signal representation. This means of signal processing is known as a transversal filter in engineering applications.

With the signals from a specific sensory modality dispersed in time and channels, it becomes quite easy to employ computational anatomy to achieve the equivalent of complex mathematical transform calculations between the channels without employing the Calculus of mathematics.

4.2.4.3.3 Stability of the neural system over time

An organism obviously completes implementation of its ultimate neural architecture during maturation, and degrades quite gracefully, on average, during aging. Between, and largely during, these two periods, the system operates largely without regard to time.

On a short term basis, the sensory modalities operate in real time, except for implementation of the time dispersals described above for operating convenience.

The sensory modalities generally operate in a change detection mode. This sensing mode leaves individual neural channels within the modality unresponsive to very slow changes in the environment related to times measured longer than minutes. However, in order to accommodate large changes in signal amplitude relative to the environment, the sensory channels employ a very high degree of adaptation, the ability to adjust their absolute sensitivity rapidly as a function of time to avoid any overload condition, typically described as signal channel saturation. Adaptation involves a very rapid change in sensory neuron sensitivity upon application of an excessive stimulation, but a relatively slow recovery of sensitivity following removal of the excessive stimulation. This recovery is frequently measured in minutes to tens of minutes. In vision, it is frequently labeled dark adaptation, but the equivalent recovery mechanism is also active in hearing and many other sensory modalities.

With multiple sensory channels operating at different levels of adaptation simultaneously

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within a sensory modality, planning experiments generally require including an adaptation period in the protocol of at least twenty minutes, and sometime, as in the case of snow blindness, as much as eight hours or more.

4.2.4.3.4 Stability of the CNS over time

The central nervous system is largely a system unto itself and under self direction. It is able to change operating modes largely at its own discretion. This ability can lead to very unfortunate results, such as those associated with Bipolar disorder and a variety of epileptic conditions. Although for different reasons, these mode changes frequently occur rapidly and are slow to return to a "normal" condition. Bipolar disorder is a good example of rapid mode switching in real time. A subject can change to an unstable state, frequently associated with the alarm mode and lacking cognitive rationality, very rapidly (within ten seconds) through a combination of neural and hormonal activity that they are generally unable to prevent or control. Because of the presence of significant hormonal activity, the subject generally takes minutes to hours to fully return to the expected rational and calm state where the awareness mode and conventional levels of attention are maintained.

4.2.5 The Top Level Feedback Loop of the Neural System

[xxx alternate figure saliency figure.wpg–stressing external feedback]
Static block diagrams describe the organization of the neural system but a top level feedback loop or state diagram is needed to describe the operation of the neural system. **Figure 4.2.5-1** presents a generic top level feedback loop attributable to virtually any operation within the neural system of any mammal. It is also applicable to other animals with a few changes in nomenclature. The figure can be compared to a 1991 figure by Fisher et al³⁹. It has been expanded and further annotated. A fundamental difference is the absence of any "efferent copy" of the motor commands. There is no documented record in the literature of an efferent copy within the neural system. The neurological system is designed on the assumption that the instructions given to stage 6 of the efferent neural (and motor) system are carried out faithfully and within the response time of the sensory system.

The lack of a precise efferent copy, and a true blanking circuit active during visual saccades, is readily demonstrated by looking at a strobe light on an airplane at night. If you move your eyes during the interval including a strobe pulse, your sensory system will report the location of the strobe with a gross error in position that is not consistent with an efferent copy signal.

Many authors (particularly psychologists and psycho-physicists) have introduced the concept of an efferent copy of an efferent neural signal using the example of a proprioceptor neuron reporting the position of a limb following muscular activity. However, it should be perfectly clear, the proprioceptor signal is generated following motion of the limb (such as being moved by someone trying to wake us up) irregardless of any muscular activity. In this case, an afferent signal is generated without any efferent activity. In any precise definition of external feedback, this afferent signal exhibits a best a quasi-relationship to a particular efferent signal and does not qualify as an external feedback loop in any engineering sense.

The figure has been expanded to include a number of functional elements between the sensory integration block and the motor planning block of Fischer et al.. To aid interpretation, the first informational block on the right provides labels to the individual neural paths between the blocks. These labels are augmented by a few labels on the left of the string of functional blocks. The second informational block on the right provides anatomical labels corresponding to the functional blocks.

The elements above the cognitive element form the afferent neural system and the elements below the cognitive element form the efferent neural system. It is noteworthy that the sensory cerebellum is functionally separate from the motor cerebellum although they are

³⁹Fisher, A. Murray, E. & Bundy, A. (1991) *Sensory Integration: Theory and Practice* Philadelphia, PA: F. A. Davis pg 86

both elements of the same morphological block, the cerebellum, and appear to be interconnected by commissure.

The top block in their figure is superfluous but has been retained for continuity. This block can not change the "intake" of sensory information without going through the blocks described

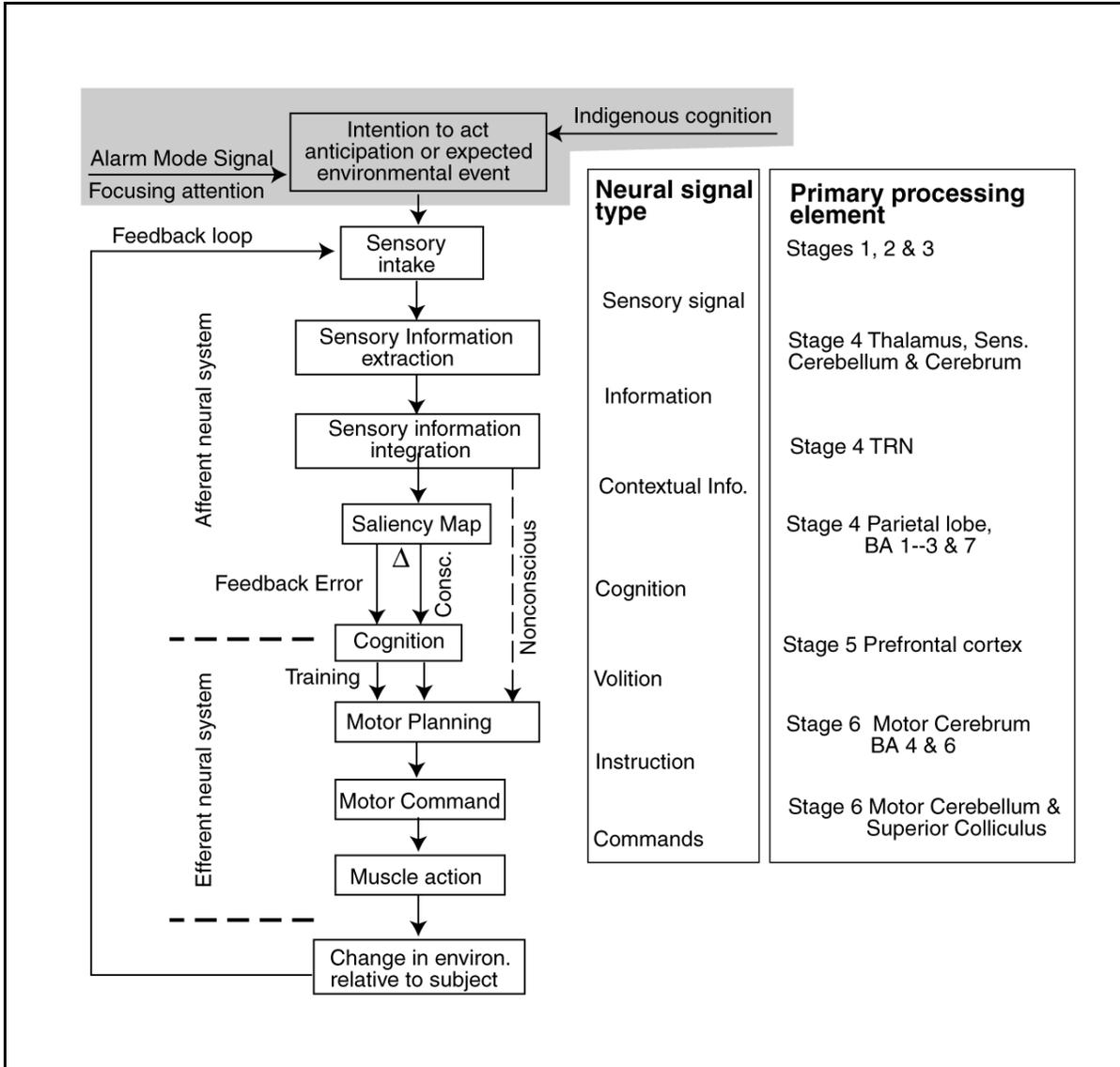


Figure 4.2.5-1 A generic top level feedback loop used in mammalian neural systems. The feedback loop is closed by a path *external* to the subject. The motor activity of stage 6 is primarily associated with the cerebellum, except for the visual modality where it is centered on the superior colliculus. See text.

within the efferent system. The block is a statement of the intention of the cognitive stage based on indigenous thought or stimulation by the awareness mode of sensory operation not otherwise discussed in this figure. It should be an integral part of the cognition element in the middle of the diagram. In that role, it sets the initial conditions (the state) of the state diagram or the feedback loop. These conditions are changed by the efferent neural system.

The saliency map incorporates what Fisher et al. describe as the "Reference of correctness." It might better be described as the "Perceived state of the environment and the subjects

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body" described largely within an inertial reference system.

The feedback loop path along the left side does not include an error component. The error component is developed at the saliency map by comparing the previous state of the saliency map with the latest state (note the delta symbol for change near the left channel). If greater than a selected magnitude, the cognitive system can decide to take action to reduce the magnitude of the error by issuing further volition channel signals.

Some variants of this figure show an efferent portion of the saliency map shown below the cognition block to indicate explicitly that a set of instructions is passed to the efferent saliency map before those instructions are passed to the cerebellum. For simplicity, the cognitive block is shown with two volition channels to the cerebellum. The goal of these channels varies with the state of learning of the subject. During ontogeny, the cognitive block sends training signals that aid the cerebellum in expanding or correcting its lookup tables. This activity helps the cerebellum improve the quality of its instructions to the superior colliculus.

The term lookup table is a form of non-declaratory memory in the language of the psycho-physicist/psycho-physiologist. The operational aspects of this term will be explored briefly below and more fully in **Chapter 17** xxx on memory.

The repeated operation of the generic top level feedback loop in the pedagogical (ontogenic) mode (sometimes described as self-actualization) appears frequently in the occupational therapy literature (pages 5, 19 & 36 of Fisher et al.) Rydeen described a similar, but less detailed, sensory-motor-sensory loop in the context of sensory integration and neurodevelopment⁴⁰. Fuster (page 218) describes the operation of this loop in a training mode as the "perception-action cycle." The difference between sensory integration during ontogeny and sensory integration during routine operation should be noted. The latter is not normally circular with respect to time unless the desired physical protocol calls for repetitious activity. After sufficient training, it is possible for the individual to short cut the complete top level feedback loop by employing a largely subconscious variant of the alarm mode of CNS operation. This mode of operation could be labeled preconscious because the subject is not aware of the action taken until after it has occurred. The subject perceives the implementation and results of the action through subsequent operation of the afferent portion of the feedback loop.

Failures in the functions, and/or signaling, between sensory integration by the thalamic reticular nucleus (TRN) and ultimate command generation by the cerebellum appear to be the primary source of problems related to dyspraxia in the diseases known collectively as autistic spectrum disorders. Although not generally recognized as such, many types of nystagmus in the visual sensory modality are also caused by problems in these same functional areas.

The superior colliculus uses its lookup tables to convert instructions from the superior colliculus into command signals encoded in the time-delay pulse format familiar to the electrophysiologist.. These signals are propagated to the muscular and glandular elements for ultimate implementation of the desired action.

4.2.5.1 Clarifying the role of feedback in the neural system

As noted earlier, neurobiological laboratory studies tend to be point studies. Such studies often overlook and frequently ignore the importance of feedback in the neural system.

The entire neural system relies upon feedback to accomplish its goals. This feedback can be described as both external feedback and internal feedback. The efferent motor system can change the orientation and posture of the subject relative to the external environment, but it is external feedback via the afferent sensory modalities that confirms the desired change has occurred. In the case of vision, this confirmation can occur at the individual photoreceptor channel level. In the case of hearing, it can occur with the precision of a fraction of a Hertz in frequency. Similarly, the muscles of the eyes can be activated by the efferent system to

⁴⁰Rydeen, K. (2001) Integration of sensorimotor and neurodevelopmental approaches *In* Huebner, R. *ed.* Autism: A Sensorimotor Approach to Management. Gaithersburg, MY: Aspen Chap 8

change the pointing of the eyes. However, it is the external feedback provided via the photoreceptor channels acting as a group that confirm the change in pointing was accomplished.

Within the CNS, internal feedback plays a largely unheralded roll. Textbooks frequently stress the visual signals proceeding from the thalamus to the visual cortex of the occipital lobe but they seldom describe the perceptual signals passed back to the thalamus. As Hawkins has noted⁴¹, "For example, in the circuit between the neocortex and a lower structure called the thalamus, connections going backward (toward the input) exceed the connections going forward by almost a factor of ten!" Not only are there more circuits in the feedback path, the signals carried by these circuits carry signals of higher information content.

4.2.6 Top level memory map supporting the feedback loop

The generic top level feedback loop can be more fully understood if the major regions of significant information storage (memory) are highlighted that support the elements in the previous figure. **Figure 4.2.6-1** provides this expansion.

The most important element of memory is the short term read-write memory shown as the saliency map. The location of the afferent saliency map and its presumed efferent equivalent, tentatively labeled the action map, remain obscure. It is associated with Brodmann's low numbered areas in this work (parts of areas 1 through 7), and therefore parts of the frontal and parietal lobes. However, it may not be a real physical area (it may be holonomic in character), and it may not be associated with the surface of the cerebral cortex.

Early work by Scoville & Milner showed major role in recording the contents of the saliency map in long term memory involved the hippocampus⁴². An ancient structure, the hippocampus is buried deep within the folds of the cerebral cortex and may be a morphological interface element between the paleocortex and the cerebral cortex. Their case history of HM has extended over a period of fifty years. The last line of the original paper noted they always removed the hippocampus, amygdala and uncus bilaterally as a group. There are indications that unilateral resection does not destroy the creation of new long term memories.

The case for the hippocampus participating in the recall of long term memory into the saliency map where it can be accessed by the cognitive function is less clear at this time although work is very active in this area. The subjects studied by Scoville & Milner were all able to recall memories created before their total resections of the hippocampus, amygdala and uncus.

⁴¹Hawkins, J. & Blakeslee, S.(2004) *On Intelligence*. NY: Times Books page 25

⁴²Scoville, W. & Milner, B. (2000) Loss of recent memory after bilateral hippocampal lesions *J Neuropsych. Clin Neurosci* vol 12(1), pp 103-113 A reprint of their 1957 paper.

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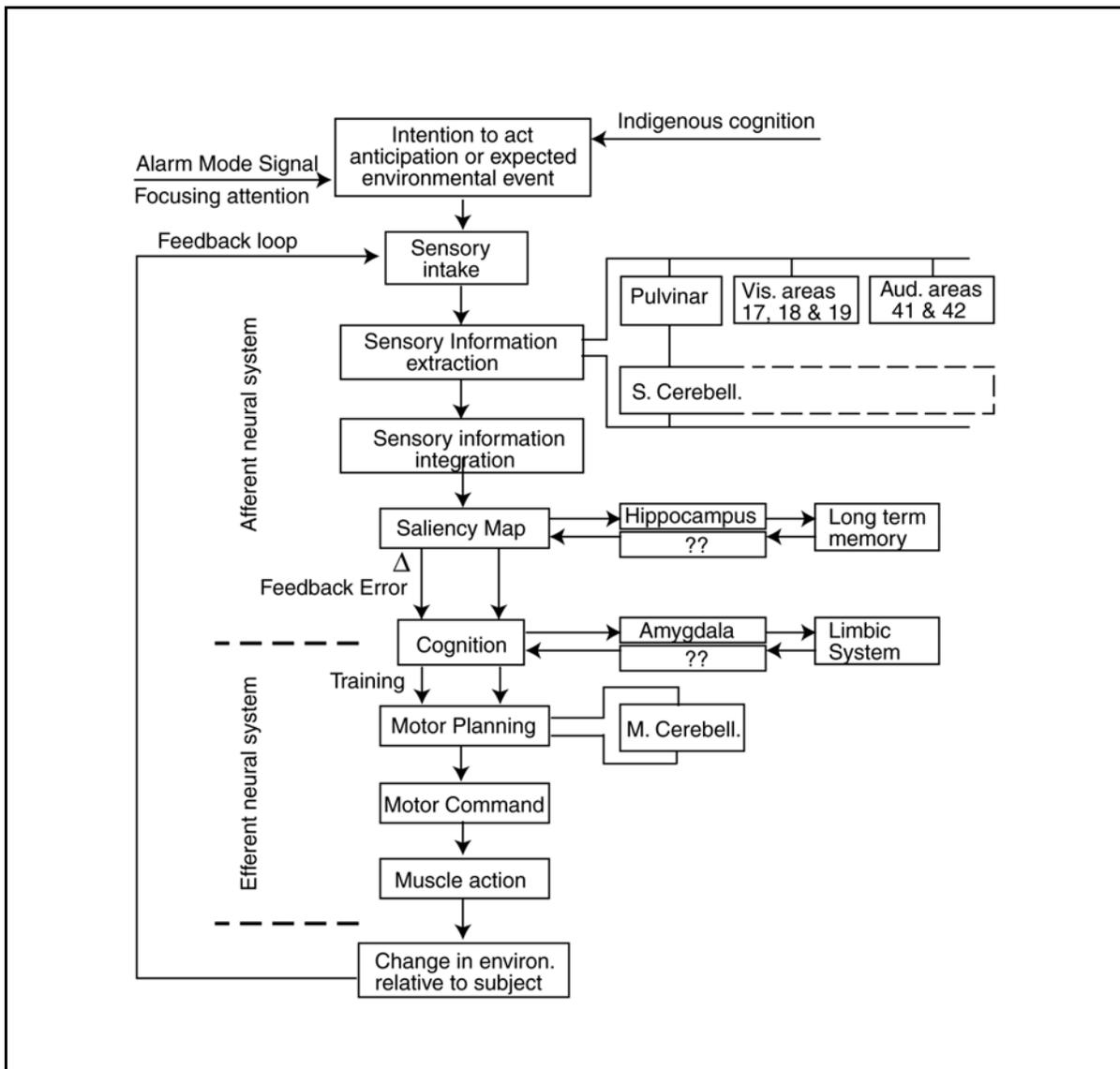


Figure 4.2.6-1 Major memory elements of the neural system. See text.

To the right of the cognition element are the elements of the limbic system, beginning with the limbic system. This portion of the neural system is totally within the CNS and appears to be the major gateway between the cognitive system and the glandular system. It is also involved directly with the emotional posture of the subject and may form the gateway for the olfactory modality into the CNS..

It is proposed in this work that sensory information extraction is largely under the control of the thalamic reticular nucleus (TRN). Major memory areas under control of the TRN are associated with the pulvinar of the thalamus and the multiple identified sensory portions of the cerebellum. It is proposed the visual, aural and probably olfactory areas of the cerebral cortex are also seats of unconscious memory associated with information extraction from the sensory signals. It is proposed this information extraction makes extensive use of pattern matching techniques.

The record appears clear that the visual and auditory sections of the pulvinar make extensive use of the sensory portions of the cerebellum to provide high level percepts related to the analytical signal paths of the respective modalities for inclusion in the saliency map. It is

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possible the visual and auditory areas of the cerebral cortex perform similar high level percept development for the peripheral "fields of view" of these modalities.

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4.2.6.1 Clarifying the role of time in the memory system

While one tends to think of individual memories as static, the majority of memories are stored as a sequence of memories as a function of time. This is a particularly important fact in the various portions of the cerebellum where it supports the creation of high level percepts (cognits) by assembling a temporal series of low level percepts. Similarly in the efferent motor planning function of the cerebellum, a single instruction from the volition channel can be expanded into a temporal series of motor commands destined for different muscles (or groups of muscles) at different times. Failure to expand such instructions into an appropriate temporal series of motor commands leads directly to the awkward body movements associated with dyspraxia.

4.2.6.2 An operating scenario

Richard Dobson has provided me with an operating scenario that needs to be incorporated into this work (19 Nov. 2012).

"I know that the workings of the somatosensory nervous system is in the future. But there is also the issue of sensorimotor coordination....the interface of the proprioceptive nerves and the motor nerves and the muscular effectors.

In my work, I have shown that a stick model of a human lifting a weight and analyzed and studied with Working Model, can be made to simulate the pattern demonstrated by normal people lifting up to 75 pounds. There are two phases of this pattern: elevation of the weight, with the spine leaning forward. This is accomplished with a constant and coordinated angular velocity at the ankles, knees and hips. The linear outline of the back raises in parallel to each previous position.

At about the time the hips and knees reach full extension, the trunk begins to rotate, with the tail pulled forward and the shoulders pulled upward and backward. The center of rotation of the spine is generally around the junction of the thoracic and lumbar spine. There is a clasp-like motion of the weight and trunk with the weight coming to rest against the thighs.

During this pattern of movement the center of momentum (a parameter that is strikingly absent in medical discussions)) moves smoothly upward and then backward, in a near parabolic curve. At the end of the lift the center of momentum, using this pattern, is moving horizontally. In that condition the normal stabilizing mechanisms in the torso and legs can work very effectively and efficiently to control the weight.

The main point I want to raise is about how the nervous system controls the angular velocity and/or the angular momentum at the joints. Once again I do not recall seeing much about "angular velocity" sensors, but at least in lifting a heavy load from the floor it is clear (at least to me) that the control and integration of angular velocity is a critical part of daily motor activities. These are also unconscious patterns of movement."

My response was as follows,

From a neural system perspective, I can provide a top level scenario that you might want to consider or comment on. To do this, I have attached an early draft of Chapter 4 of my book "The Neuron and Neural System." Particularly appropriate to the following comments are figures 4.2.3-7, 4.2.5-1, 4.2.6-1 and specifically 4.6.3-1 with the label at the lower right changed to the motor system in general.

When the cognitive circuits of stage 5 within the prefrontal lobe, it issues an instruction to the stage 6 command generation circuits. Stage 6 consists of three portions as shown in my figure 4.6.3-1. The instruction is first analyzed by the stage 6a circuits of the parietal lobe in order to determine what elements of the locomotion and other systems are affected. Stage 6a issues high level commands to these elements. With respect to muscle activity, the stage 6a commands are passed to the cerebellum of stage 6b. The cerebellum is the element

responsible for calling up prior learned motion protocols, and incorporating information about the current inertial position of the torso from the vestibular sensing system. These protocols involve the parameter of time and result in the issuance of a series of highly time-correlated commands to the stage 6c muscle activation circuits, of the superior colliculus and other circuits, and the actual muscles tasked with responding to the stage 5 instructions.

Note how the cerebellum is in a position to monitor the response of the system via inputs from the sensory system. If everything goes as planned, the instruction is completed without further participation by stage 5. If something goes off plan, stage 5 is made aware of that fact and additional cognition is required (including a response indicating surprise by the organism at the unusual (unexpected) response and corrective activity. See Figure 4.2.6-1.

The above material will be edited into appropriate areas of this manuscript xxx.

4.3 Expanding and definitizing the framework required in effective analysis

[xxx no Fourier Transforms, the alternate is computational anatomy]
[xxx transform processing only useful in off-line data reduction to discover underlying concepts]

[xxx shorten and refer to old 4.3 now awaiting integration into chapter 7]
[xxx move shortened version into top section of scientific method]

Before embarking on the detailed modeling of the neural system, there are a variety of major concepts that must be discussed. Following this discussion, it will be possible to further definitize the terminology and conventions used in neuroscience. The analysis of the neural system follows the same methodology as for any other "system," whether chemical, mechanical, electrical, hydraulic, etc. In fact, the neural system (like all biological systems) employs elements from each of the above disciplines. The rules of system analysis are well established and precisely documented. However, their development is beyond the scope of this work. For the non-mathematically inclined, Regan has provided a list of principles related to system analysis and a number of useful examples⁴³. While tending to bound the field and be very useful to the layman, his seventeen postulates should not be taken as mathematically rigorous. As he states, there are a variety of caveats applying to some of the postulates.

4.3.1 Applied research requires sophisticated statistical analyses

Statistics have traditionally been used in two ways in neuroscience research. The most important usage has been to properly describe the variation in a performance parameter measured among large populations. There are a variety of statistical environments that can be used to simplify the presentation of the statistical data. It is very important that the correct environment be selected before significant data analysis is undertaken.

The second usage has usually been as a crutch in order to present data based on a deterministic process that is not adequately understood or modeled. In a few cases, statistics have been used to skirt limitations in the test instrumentation that mask the actual desired measurements. While unfortunate, this latter situation should cause the researcher to redevelop his experimental protocols rather than report data that does not clearly describe his results.

It will be shown in this work that the individual neural system is highly deterministic under conditions of adequate sensory signal quality. Under more limited signal conditions, the selection of the appropriate statistical environment from the following paragraph is important.

4.3.1.1 Selection of the appropriate statistical environment

⁴³Regan, D. (1991) Spatial Vision. Vol. 10 of Vision and Visual Dysfunction, Cronly-Dillon, J. *general ed.* Boca Raton, FL: CRC Press pp 3-12

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As referred to above, selecting the correct statistical environment is important in the presentation of data. At the theoretical level, each statistical environment can be described by a distinct generating function. Most of the statistical approaches used in exploratory neuroscience research have been based on Gaussian Statistics, Normal statistics in the vernacular. The use of these statistics is founded on the Central Limit Theorem that states that all statistical distributions approach the Normal distribution if a sufficient number of underlying processes are statistically independent. The Theorem applies remarkably well even if only five or six independent processes are involved. However, there are a variety of instances in neuroscience where the number of independent processes are less than five or six. In this case, the correct statistical treatment must use Poisson statistics. The use of Poisson statistics will generally result in significantly different parameters describing a distribution than will the application of Gaussian statistics applied to the same data.

There are other cases where the individual processes are not statistically independent. Two important cases are metabolic growth and photo-electric molecular excitation.

Metabolic growth, along with many natural growth mechanism such as crystallography, do not follow Normal statistics because each growth interval is directly affected by the previous state of the specimen. In the simplest situation, the statistics of the process are described by Log-Normal statistics. The distribution of a Log-Normal process appears to be skewed when plotted on a linear axis because it is more properly plotted on a logarithmic axis. When plotted on a logarithmic axis, the distribution is symmetrical and satisfies all of the requirements of a Normal distribution. Hence the name Log-Normal distribution.

Photo-excitation of a chromophore, such as those used in the visual system, is a quantum-mechanical process that is not describable using Gaussian (Normal) statistics. The appropriate statistics for describing this process have been given several names over the years but are now known as Fermi-Dirac statistics. Following excitation of a molecule, the motion of the excited quanta within the quantum-mechanical energy bands of the molecule (or larger crystalline structure) are described using Bose-Einstein statistics. The parameters of these statistical classes are well known to the physicist. They differ significantly from the parameters associated with Gaussian statistics.

A clear clinical example of a condition that is not described properly by Normal (or Gaussian) statistics is emmetropia (inadequate accommodation of the lens system of the eye). The physical aspects of emmetropia involves only a few independent processes and these are related to growth. The physical errors related to emmetropia have been measured for millions of individuals over the years and reported in the literature. As a result, the distribution of emmetropia related to physical disease is well known to differ significantly from a Normal distribution. Unfortunately, the distribution is not purely Log-Normal either. The number of processes involved is sufficiently high that the Central Limit Theorem begins to apply. As a result, when plotted along a linear axis, the distribution reflects skewness and kurtosis on the lagging growth side. This is the primary reason why more people are nearsighted (hypometropes or myopes) than far sighted (hypermetropes).

As investigators move further into applied research, it is necessary that the appropriate statistical framework be used in presenting their findings.

4.3.1.2 Bayesian statistics require an accurate model

The statistical approach developed by Bayes in the 19th Century has become popular in the recent literature. It relates to conditional probabilities of events in a binary sequence of statistically stationary independent events. It is not always made clear by authors that the Bayesian approach requires a detailed understanding of the underlying processes in advance. It is basically a method of describing perturbations from an expected result. Bayes' approach requires an *a priori* estimate of the likely hood of a random event. If an inappropriate underlying model is assumed, the calculated parameters, based on the Bayesian approach can be wildly misleading⁴⁴.

The well known example of an inappropriate application of the Bayesian approach involves the "Lurking variable;" the presence of a significant variable not included in the *a priori* set

⁴⁴Cramer, H. (1955)The Elements of Probability Theory. NY: John Wiley & Sons pp 38-39

selected by the investigator. The Bayesian approach will proceed to allocate the likelihood of a given variable to be the source of the observed mechanism even though the mechanism is actually dominated by the lurking variable.

The Bayesian approach has little place in the field of exploratory research.

4.3.1.3 Obsolescence of the Michaelis Equation (aka Logistic Equation) in the neural context

[xxx rewrite in neural science context]

For more than the last half century, the experimentalists have not been able to provide an accurate mathematical equation for the generator potential and have developed a number of "rule of thumb" equations and simple models. Many of the investigators ignored the trailing edge of the generator potential and concentrated on the rising (or leading) edge of the waveform. They frequently applied a simple hyperbolic equation to their data using a variety of names depending on what their own discipline was⁴⁵. A common procedure was to associate any leading edge with a common statistical condition where the cumulative probability of any event rises from zero to nominally 100% in an orderly monotonic manner. This cumulative probability function has long been known as the Logistics Equation or the Michaelis Equation outside the field of statistical mathematics.

The cumulative probability function can be the result of a normal distribution function, a hyperbolic distribution function, or any other statistical distribution.

It will become clear that the neural system is deterministic in all its major features, except sensory neuron noise performance. Thus the Logistics or Michaelis Equation are of very limited use in describing the neural system.

It will be shown in this work that the leading edge of the action potential is not the result of a statistical process. It is the result of a deterministic process, resulting in a constant slope leading edge prior to saturation effects becoming significant.

Investigators have long attempted to explain the generator waveforms of the sensory neurons using the Logistics Equation. It will be shown that this waveform is also totally deterministic.

Some have gone further. They have adopted Lumped Constant Filter Theory to develop simple electrical models to account for the observed changes in the leading edge of the generator potential waveforms of the sensory neurons. Unfortunately, none of these equations and models are able to describe both the rising and trailing edge of the generator potential. The simple models based on Lumped Constant Filter theory required so many degrees of freedom that they could be used by the investigators to match any waveform if only the characteristics of the complete generator function were available.

The actual description of the sensory neuron generator potential is given by the totally deterministic Excitation/De-excitation Equation of this work (E/D equation, or the earlier P/D equation). The E/D Equation demonstrates successfully that:

- + it can describe the entire generator potential function for any sensory neuron under all conditions,
- + the actual process does not involve a hyperbolic rising edge, and
- + Transport Delay Theory, not Lumped Constant Filter Theory provides the correct solution to the problem.

4.3.1.4 Multi-dimensional analyses with axis rotation

Multi-dimensional analysis (MDA) is a very powerful statistical tool for determining the relationships between an apparently disparate set of elements.. It is frequently able to describe these elements in a multidimensional space using orthogonal axes. Unfortunately,

⁴⁵See Charlton & Naka ('70), Naka & Rushton ('66) ('67), Examples of Forti and of Lamb in Torre, et. al (1990)

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the technique requires the user to exhibit considerable sophistication and experience related to the technique. The user must make a judgement as to how many orthogonal axes are relevant to the data set after running the analysis; the user must frequently re-run the analysis using the selected number of axes. The axes selected by the mathematical manipulations performed, during the final run, may not correspond to the intrinsic orthogonal axes defined by the laws of physics and/or other appropriate laws. There are a set of axioms associated with the technique for rotating the axes, to conform with the potential intrinsic axes, but these have seldom been used in the past. An example of this rotation is found in **Section 8.xxx** related to the principle axes of the gustatory sensations.

4.3.2 Initial recognition of the electrical nature of the neural system

The initial chapters of this work introduced the reader to the rationality for an electrical approach to understanding the operation of the neuron. The intent was to show how it was possible to describe the detailed operation of the neuron as a signaling device without resorting to any hypotheses involving the transport or secretion of chemical materials in the signaling process.

Although early investigators proposed an electrolytic signaling mechanism, the chemical community has pushed a chemical mechanism to the forefront over the last 75 years or more. This competition has not incorporated the newly discovered biologically based electrolytic semiconductor device, the Activa. In the absence of this discovery, the chemical thesis for neural signaling has become ever more fanciful, daunting in the words of one author⁴⁶. However, it has not been able to demonstrate how an electrical signal within a neuron is converted to a chemical signal in the orthodromic interneural space and then back into an electrical signal within the next neuron. Based on the discovery of the Activa and the recognition that the synapse and the Node of Ranvier are simple electrolytic circuit elements based on the Activa, the fundamental electrical mechanism of the neural system becomes evident. In addition, a deterministic description of the neural system, external to the higher levels of the cortex, becomes possible.

Beginning with E. G. Gray in 1959, the electron microscopy community began delineating the structure of the synapse at the level of tens of nanometers. The result has been the description of the fundamental synaptic cleft as approximately 30 nm in width and less than 2 microns in diameter. This is the structure defined electrically as an Activa in this work. The discovery of the Activa was memorialized by a United States Patent in 1999. In many synapses, and related structures such as the Node of Ranvier, this fundamental structure is reproduced as an array of fundamental devices in order to achieve higher current carrying capacity. This mechanism provides a lower circuit impedance between orthodromic neural conduits.

In the following chapters, the utility of the Electrolytic Theory of the Neuron will be used to explore and explain many processes and effects never before addressed using only a chemical framework. The overall result will be the demonstration of the fact that the signaling function of the neural system is entirely electronic in character.

The above paragraphs are not meant to denigrate the role of chemistry in a supporting role to signaling. It has a profound role to play in providing the electromotive force energizing the neural system and it may play a significant role in causing the creation of short term and long term memory.

4.3.2.1 The grounding plan

When making measurements of the stages 1 & 2 of the neural system, it is critically important that an appropriate grounding plan be adopted that avoids to the degree possible, interference from other modalities, and particularly other stage 3 pulse circuits. This problem is particularly acute within the visual system where the electrical path between the analog signals of the retina and the surrounding tissue are quite convoluted. It is not uncommon to see reports of analog waveforms with a series of pulses riding along the top edge of the

⁴⁶Shepherd, G. (1988) *Neurobiology*, 2nd ed. NY: Oxford Press, pp. 75-76 reprinted with different page numbers as the 3rd ed. in 1994

waveforms that are completely spurious to the subject being discussed. This problem is addressed in greater detail in the author's PBV xxx.

4.3.2.2 Ohm's Law & homogeneous equations are inappropriate to neuroscience

As noted in **Chapter 2** and addressed again in **Chapters 8 & 9**, the neural system is fundamentally a logarithmic system based on the electrical diode and the capacitor. The fundamental laws of electrical circuit theory, Kirchoff's Laws are quite explicit; the realm of the simpler Ohm's Law is limited to linear circuits not involving time or the current flowing through them as a variable. This condition is not met within the neural system in general! **Ohm's Law does not apply to the vast majority of neural processes in animals** except under the most restrictive conditions. If an experimenter is making measurements over an exceedingly narrow range, of less than +/-10%, an effective resistance may be determined by measuring the *change* in voltage related to a change in current. The resulting value only applies for that operating range and an extremely narrow range near it. Kirchoff's Laws on the other hand allow for any kind of impedance, but the mathematics becomes more involved.

The basic fact is that the neurons of a living animal do not employ resistive elements as normally defined and manufactured by man. The basic impedance utilized in living tissue is represented by the diode. The voltage across a diode is not given by the product of a constant times the current passing through it, i.e., the common expression $E=I * R$; the voltage across an ideal diode is given by the natural logarithm of the current passing through the diode, $E \approx I * Z(I)$, conversely and more specifically, $I =I_0 * (e^{V/V_T} - 1)$ where V_T is related to the temperature and the material comprising the diode.

Because the impedance of neural tissue is not resistive, most of the algebra appearing in the literature is not appropriate to neural processes. Models employing common resistive elements are rarely appropriate.

Linear matrix algebra is not appropriate for the solution of neural problems if the excitation level changes by more than +/-10%. Linear matrix algebra is based on the use of linear homogeneous equations with constant coefficients. Mathematically, the terms are not homogeneous and the coefficients are clearly not constant over their typical operating range in neural tissue.

4.3.2.3 Inevitable results of the non-linearity of animal tissue

There are two inevitable results of the fact that animal neural tissue is not characterized by a resistor.

First, as will be shown in **Chapter 8**, the output of the Excitation/De-excitation process of the sensory channels is a quantity of electrons (which is normally changing with respect to time and constituting a current). When passed through a neural impedance, the resulting voltage is not linearly related to the charge (current). The voltage is related to the natural logarithm of the current. Thus, in probe experiments and ERG's, the measured quantity is generally not linearly related to the signal; the measured quantity is proportional to the natural logarithm of the signal parameter. Over the longer term, the quantity measured is also a function of the state of adaptation of the relevant sensory neurons.

Second, as is critically important in the visual modality (in order to maintain "color constancy"), the stage 2 signal channels associated with chrominance information rely on the linear summation of voltages; i.e., the linear summation of logarithmic functions of the underlying signals. In fact the signal channel associated with luminance information also relies upon the linear summation of voltages. *The summing of logarithmic quantities is equivalent to the multiplication of the underlying signal parameters.* Nearly all of the psychophysical and many of the electrophysical experiments in the literature measure parameters resulting from such logarithmic summations, but they do not recognize that fact and proceed to perform linear subtractions in order to separate spectral components of their data. There are two principal results of this failure to recognize the nature of the parameters measured.

The calculated visual spectrum, based on the arithmetic summation of the absorption coefficients for the individual chromophores, does not match the

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overall high irradiance (photopic) or low irradiance (scotopic) spectral performance of the eye. A logarithmic summation of the individual absorption coefficients *does give the measured overall spectra for all irradiance levels!*

The attempts to characterize the absorption coefficients of the individual chromophores by employing the linear subtraction of measured voltages invariably give incorrect spectral characteristics for at least one of the individual chromophores (typically the L-channel). Utilizing logarithmic subtraction, the *correct absorption coefficients can be obtained* for all three (four in appropriate animals) of the individual chromophores. Moreover, all of the absorption coefficients obtained are unipolar. No negative absorption in the blue region is required of the L-channel chromophore.

[xxx move to chapter on signal propagation or delete]

4.3.2.4 Electrotonic versus pulse signaling

The neural signaling system is divided into two classes of circuits. The vast majority of both the CNS and PNS circuits involve electrotonic signaling. Only the neurons of the signal projection stage, stage 3, employ pulse signaling. Although the method of signaling varies, the mechanisms used to generate and pass signals within neurons and between neurons do not. They are electrolytic mechanisms.

It is useful to re-examine the thesis of Bieda & Copenhagen in a recent paper⁴⁷. The paper is based on the conventional wisdom that signaling between neurons involves secretion of chemical neurotransmitters. It notes correctly that transfer of a signal from one neuron to another does not require sodium action potentials. However, it does not demonstrate or reference laboratory tests confirming that either GABA or glycine is required as a signaling mechanism between neurons. It merely assumes the conventional wisdom that since these substances are ubiquitous near neurons, the transfer involves these chemical substances. They are correct that these substances impact the transfer of signals because they impact the electrotonic power supply to the neurons.

4.3.2.4.1 Domains of signal manipulation

It is important to differentiate between the spatial, temporal and abstract (or saliency) domains of vision. The bulk of the operation of the neural system prior to perception in the midbrain occurs in the temporal signaling domain (See **Chapters 12 to 14**). Beyond the midbrain, the bulk of the interpretation and cognition occurs in a more abstract domain that will be called saliency space (see **Chapter 15**). Only a very limited amount of signal manipulation occurs in the spatial domain (See **Chapter 2** and xxx [tremor reference])

As a result of defining the functional model of the neural system in considerable detail, it becomes necessary to properly account for the different domains used for signal manipulation as well as the demarcations between them.

Chapter 15 of this work develops considerable information about the information extracted within the CNS of originally analog information obtained by the sensory neurons of the PNS. This processing involves a variety of relatively independent signaling paths. As signals proceed along these paths, their processing becomes more and more abstract and independent of both the spatial and temporal domains (although the vectors created to represent features may contain a time related tag). By properly interpreting the signal space associated with different locations along these paths, a new perspective becomes available concerning the signal manipulations employed in perception, interpretation and cognition.

Beyond the point of perception, the operation of the brain and the definition of the saliency space and saliency signals associated with memory remains quite enigmatic. This work will not proceed beyond discussing the framework for this processing and the rudimentary

⁴⁷Bieda, M. & Copenhagen, D. (1999) Sodium action potentials are not required for light-evoked release of GABA or glycine from retinal amacrine cells. *J. Neurophysiol.* vol. 83, pp 3092-3095

methodologies of perception and cognition, primarily related to reading and primitive shape recognition (See **Section 15.4 xxx**).

4.3.2.4.2 Inhibition versus differencing

The term inhibition occurs frequently in the neurological literature. The discussions are normally conceptual in nature. At the conceptual level, and particularly in behavioral testing, it is generally used to describe a putative throttling of the signal in one signal channel by a signal in a different channel. It is important to review the mathematical foundations appropriate to the interaction of two signals; in simple situations not involving a feedback loop containing a time delay, the options are a multiplication of two signals or a summing of two signals (which includes the concept of differencing). When electrophysiological tests are performed on *in-vivo* retinas, particularly involving spectrographic tests with more than one chromophoric channel excited, it is found that these so-called inhibitions of one signal by another actually involve the subtraction of one signal from another (a truly antagonistic situation), either to obtain hue information in the chromatic signaling channels or spatial size information in the geometric channels. The result is a situation where either input signal can be described as inhibiting the other (which implies a product relationship); however, the actual situation is that a change in either input signal will affect the output signal linearly (which implies a summing relationship). ***In general, the term inhibition should be viewed with suspicion when found in the neuroscience literature.***

4.3.2.5 Use of the term "Neural Networks"

While the use of an expression such as neural network is quite appropriate to the study of both the architecture of the neural system and the circuitry internal to a engine of the central nervous system, it has not been used extensively in these venues. Instead, the title neural network has been usurped by the high performance computational community. It was initially defined conceptually as involving a highly parallel set of nonlinear equations as thought to be found in a complex biological neural network. While this label was originally used to describe a class of networks ostensibly based on real neural networks of the biological sphere; in fact, it merely introducing a different class of nonlinear equations. The nonlinear character of these equations is not found in the biological sphere.

In the context of high performance computing, Jones & Creighton have recently defined a neural network⁴⁸. "A neural network is a set of nonlinear equations that predict output variables (Y's) from input variables (X's) in a flexible way using linear combinations of S-shaped functions." Such networks were contrasted with the more conventional linear set of quadratic polynomials which suffer from two problems. They lack the ability to treat high curvatures verging on discontinuities, they do not treat multiple maximums or minimums well, and they inevitably lead to expressions that go to infinity for large values of the X's.

In the biological sphere, neural networks associated with individual engines of the CNS appear to be highly complex Boolean circuits. A simple biological neural network may accept hundreds of input signals and generate an equally high number of output signals. Some of the input signals may be considered as acting simultaneously as input signals and as control signals within the overall Boolean circuit. The individual operators within such networks appear to consist of simple logical elements. These provide AND, OR, NOT AND (NAND), NOT OR (NOR), limiting and other simple conversion functions. These simple functions that can be assembled in a wide variety of ways to provide both signal processing and short term memory in a fundamentally analog signal environment. The environment of a specific engine operates in a self clocking mode due largely to the time constants of the underlying neurons and the circuit topology adopted to exploit those neurons.

4.3.3 Additional recognition of the electrical nature of the neural system

4.3.3.1 Emergence of the Biological Transistor

It is amazing to report in the year 2001, there is no mention in the scientific literature of the presence of a device or configuration in the neural system of any animal that has been

⁴⁸Jones, B. & Creighton, L. (2003) Using neural networks to model response surface designs Scientific Computing & Instrumentation, April pg 28-31

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described as a transistor--**a biological transistor**--when there is so much evidence, *overwhelming evidence*, for such a designation. It can only be explained by many investigators failing to see the forest for the trees. Giving credit where it is due Michael Bennett came very close to discovering such a device in the 1960's.

Interestingly, in mid 2001, a search of the Internet did not recover a single reference to the term "biological transistor," except at this authors site.

There is an immense amount of electrophysical evidence for the definition of a biological transistor as an analog to the semiconductor transistor. Some of this evidence will be presented here. More will be presented in Appendix B where the formal properties of the device will be developed and explanations of how the device is used within the neural system will be presented. The evidence is compelling and the acceptance of this reality greatly simplifies the investigator's task.

During the development of this Theory, the active electrolytic semiconductor device, the Activa, was discovered and awarded a United States Patent, #5,946,185.

Until the 1960's, it was categorically denied by the leaders of the vision community that the eye employed signaling by way of electrical currents (as opposed to chemical affecters) at synapses. This has changed considerably beginning in the 1980's. Similarly, there is now a large community of investigators whose work is based on the physical transport of large numbers of complete (and large) ions every second through a membrane surrounding the Outer Segment of each of the photoreceptors of the eye even though there are immense amounts of evidence from other investigations that ***there is no cellular membrane surrounding the Outer Segments***. The Outer Segments are actually extracellular.

4.3.3.2 The basic neural unit EDIT

The morphologist invariably insists that the neuron, as the minimal biological cell must be considered the fundamental neural unit. However, they have not been able to differentiate the minimal biological cell from the minimal biological neuron. On the other hand, Shepherd has held quite recently that the synapse is the fundamental building block of the neural system⁴⁹. These two views are quite far apart. Furthermore, it is quite clear that the synapse is a very complex functional structure.

The problem here is to differentiate the neuron from other cells and to describe the feature that makes the neuron different. There is one fundamental feature that differentiates all neurons from all other cells. There is also a secondary feature that is quite prominent. Both of these features are only discernible using the electron microscope at magnifications of over x100,000. Each neuron contains an active electrolytic semiconductor device that can provide electrical signal amplification. It is called an Activa. The secondary feature is the presence of multiple interior plasma spaces that are isolated from each other by membranes that are in close proximity in at least one area. The Activa is found in this area of very close, but very structured, proximity.

When examining the internal structure of a neural cell, compared to a non-neural cell, it becomes quite clear that the neural structure is an overlay. All of the normal elements of a cell are found in a neuron. However, there are additional elements not found in the non-neural cell. This makes it quite clear that the portion of the neuron in common with non-neural cells provides the housekeeping and growth capabilities of the cell. It is the Activa and the arrangement of the isolated plasmas that constitute the uniquely neural elements of the neuron. It will be shown that multiple copies of these features may be found in a single neuron. The photoreceptor cell is a particularly complicated example (**Chapter 12**). On the other hand, the projection neuron connecting a sensor or a muscle to the CNS is a particularly simple example showing considerable replication of the basic neural structure (**Chapter 14**).

Using the projection neuron as an example quickly shows that the synapse is not a basic unit of the neural system. It is only a particular configuration of the basic neural architecture that is shared with all of the Nodes of Ranvier and the internal amplifiers found within the soma.

⁴⁹Shepherd, G. Ed. (1998) *The Synaptic Organization of the Brain*. NY: Oxford University Press pg 3

Similarly, looking closely at the projection neuron shows that the neuron itself is not the basic unit. It contains a replicated structure centered on the Activa.

The basic unit of a neuron, that separates it from any non-neural cell, is the active electrolytic semiconductor device named an Activa that is formed in conjunction with a series of isolated plasmas within their individual conduits. The Activa need not occur within a neuron. It is also found connecting the plasma conduits of two adjacent neurons. In this situation, it is the major component of the synapse.

4.3.3.3 Ramifications of the Biological Transistor

As will also be developed in Appendix B, the mysterious purpose of the Nodes of Ranvier is easily and directly explained in the context of a biological transistor. And the critical test of this theory is provided by Tasaki, a leader in the field of nerve excitation. Quoting his 1975 paper⁵⁰, "We note that cleaned axons are incapable of developing action potentials when immersed in a medium completely free of divalent cations." Going further, it is proposed here that the actual situation was that axons are incapable of developing action potential when immersed in a non-conducting medium or a medium not capable of providing the proper ohmic contact to the middle layer or (poda) of the biological transistor located in the axon at the Node of Ranvier. The whole purpose of the break in the myelin (insulating) sheath of the axon is to allow such contact with the surrounding media.

It is a prediction of this work that investigators will find that complete photoreceptor cells will also malfunction if they are first washed and placed in a non-ionic or inappropriate ionic solution.

Going further, the key feature of a biological transistor circuit is the easy creation of a region of negative resistance in the voltage-current characteristic of the device. The simplest possible use of this feature is to recognize that such a characteristic cannot exist over an extended range; it requires a source of energy to create it over even a limited range. Therefore, in a typical situation, this region is bounded on both ends by a region of positive resistance. It is absolutely elementary to create a bistable circuit using a biological transistor that will exhibit two stable states. Hence, the *foundation* for the TWO-STATE THEORY of neural excitation is explained. The only trick is getting the device to switch states in the desired manner. To accomplish this, utilize a biological transistor and;

adjust the impedance of the electronic element in the poda lead properly and you will achieve an action potential regenerator.

adjust the electronic element in the dendritic and/or axonal leads of the biological transistor and you will produce an action potential with an interpulse time interval which is a direct function of the analog input signal (if it exceeds the threshold level).

adjust the impedances differently and you will obtain extremely high analog current amplification under very low noise conditions (and no spike will be generated).

use two biological transistors in what is commonly called a cascode arrangement and you can obtain extremely high analog current amplification under nearly thermal-noise free circumstances.

4.3.3.4 Rationalizing the confusion over polarity

There has been a long standing, and sometimes acrimonious, debate over whether the polarity of the generator potential observed in *Arthropoda*, *Mollusca* and *Chordata* are the same or different. Unfortunately, until the recent development of residual dye techniques, it was difficult for investigators to know precisely what cells they were actually obtaining electrophysical signals from--and whether these signals represented intracellular conditions or

⁵⁰Tasaki, I (1975) Evolution of theories of nerve excitation in vol. 1, The Nervous System, Tower, D. editor in chief NY: Raven Press pg. 177-195

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extracellular conditions. Furthermore, capacitive pickup from adjacent cells has frequently been a problem because of the high impedance levels involved.

There has also been the problem of relevance. Ottoson provided a side by side comparison of the output potentials from invertebrate and vertebrate photoreceptors⁵¹. However, his comparison suffered from several unstated factors. He used the response from an eccentric cell of *Limulus* as a typical invertebrate photoreceptor cell response, whereas most investigators consider this particular cell as a special case of a signal manipulation type cell. He also showed the response to a long pulse of light in the case of the invertebrate and the response to an impulse in the case of the vertebrate.

This problem will be examined carefully in **Chapters 12 & 13** in order to provide a defensible explanation of the actual situation--a necessity if many of the experimental programs under way in neural signaling are to be concluded successfully. In brief, the results of this examination are that all photoreceptor cells in animal vision operate similarly and generate the same polarity signals at the same location. The polarity of the signal sensed near the OS is opposite to that sensed by probing the axoplasm of the photoreceptor cell because of the differential amplifier circuit found in the IS of all photoreceptor cells.

4.3.4 Terminology and conventions used in this work

Some of the electrical terminology that has evolved in the biological field is not easily translated into conventional electronic engineering notation. Before proceeding, the relevant terms and conventions will be examined and some equalities defined.

⁵¹Ottoson, D. (1983) Physiology of the nervous system. NY: Oxford Press, pg. 365

4.3.4.1 Responses EDIT, too much on vision

With vision being a life science, investigatory work in this field necessarily involves biological-based experiments. These biophysical experiments fall into several categories, exhibiting various degrees of precision:

Psychophysical--based on the observed or reported response of an organism to application of a physical stimulus. Psychophysical experiments lead to psychophysical relationships rather than psychophysical measurements. They do not normally produce absolute values. They normally provide null values or suggest trends.

Electrophysical--based on the use of electrical probes to intercept signals generated by an organism in response to the application of a physical stimulus. Electrophysical experiments lead to exact measurements but, on the scale of the visual processes, may not involve exact knowledge of what is being measured.

Within the group of electrophysical measurements, there are a number of fundamental types:

mass responses--electrophysical measurements frequently taken at a remote point relative to the point of electrical signal generation, hence representing an average response of many circuits operating simultaneously (and frequently representing a voltage across a resistor in a "ground loop" in electrical engineering terms)

Electroretinographs (ERG)--mass responses taken by measuring the voltage on the surface of a complete eyeball with reference to the rest of the organism (and hence measuring the voltage on an equivalent impedance consisting of the impedance paths due to the entire optic nerve, the muscle tissue connecting to the eyeball and the liquid medium surrounding the eyeball plus any other impedance leading to the point where the return lead is connected)

Visual Evoked Potentials (VEP)--mass responses taken by measuring the voltage between a point on the scalp at the rear of the skull relative to a second point generally at a second point on the skull considered in some sense neutral or *indifferent* for purposes of the experiment

more specific responses

Local electroretinographs (LERG)--potentials measured with a probe, either extracellular or intracellular, and referenced to a more local reference point than the eye cup. A pair of concentric probes may be used resulting in a return signal lead connected to a point only 5-100 microns from the input signal probe.

Extracellular potential--potentials measured with respect to a return signal lead by using probes and frequently involving the capacitive coupling of signals from several adjacent cells. The return signal lead is frequently connected to some nearby structure, the eye cup, the retinal epithelium, etc.

A particularly important extracellular potential obtained with a probe is the potential in the vicinity of the Outer Segments due to the E/d process.

specific responses

Intracellular potential (current)--potentials (currents) measured utilizing microprobes to penetrate a given cell and measure its internal voltage with reference to the return lead. The return signal lead is frequently connected to some nearby structure, the eye cup, the retinal epithelium, etc.

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A particularly important intracellular potential obtained with a probe is the axoplasm potential of a photoreceptor cell and frequently labeled the generator potential.

The above descriptions surfaces a serious problem in vision research, **the frequently casual treatment of the return electrode**. Quoting the Brussels Symposium ad-hoc committee⁵² for VEP research in discussing the Electrode Montage, "The electrode montage and polarity convention (e.g., negative upward) should be clearly stated. The word 'indifferent' should not be used in describing the reference electrode, as it begs the question. The ear electrode, commonly designated a 'reference' is frequently anything but a passive reference in relation to the occipital response." The same can be said about other reference electrode positions. The conventional ERG is a classic case of this problem. The response measured is frequently described in terms of an a-wave, b-wave and c-wave, etc. based primarily on when they occur in time, not where they originate in the visual signal path. Little or no attempt is made to subtract the 'tail' of the a-wave from the start of the b-wave, etc.--although independent signals conforming to the a-wave are now generally available from intracellular recording.

Failure to adequately describe the electrode montage leads to data which is difficult to interpret because of frequent corruption by other unexpected signals. This is true when a probe is inserted into *the retina* a given physical distance and also when a probe is inserted into *a cell* a given physical distance. The signals resulting from such insertions are frequently indecipherable or misleading without a detailed model of the visual system being examined.

When attempting to record electrophysical waveforms, it is again necessary to be very specific with regard to the technique used. Ruben & Walls⁵³ make an important point in discussing probing the retina to various depths: "The signals within the retina to which the retinal nerves must attend are not necessarily the same as those recorded from the surface of the cornea, a mere 2 cm away. If the retina is penetrated slowly by a tiny electrode, beginning at the vitreous side and progressing toward the pigment epithelium, the polarity of the signal abruptly changes when the inner limiting membrane is crossed. The a-wave here is positive going, followed by a negative-going b-wave, a positive going c-wave, and a negative d-wave off-potential. *Except for the c-wave, all of these components are upside-down* in relationship to those recorded at the cornea." This reversal phenomenon is well illustrated in Figure 2 of Heynen & van Norren⁵⁴. Such reversals have caused long-standing arguments in the literature related to the signal paths in the retina.

Expanding on the above paragraph, Murikani & Pak⁵⁵ have provided material comparing the recording of intra-cellular and extra-cellular ERP's. Their actual comment is specific: "As was noted in the preceding section the intracellularly recorded waveform of the early receptor potential is substantially different from the extracellularly recorded waveform." They go on, with inserts by this author: "The intracellular recording represents a sum of the potential across the cell membrane and the potential drop along the resistance in the extracellular space {leading to the return electrode}, while the extracellular recording represents the latter alone {plus the signals from adjacent sources through capacitive coupling}."

Heynen & van Norren⁵⁶ provide an entirely different scenario of utilizing extracellular

⁵²Halliday, A. Arden, G. Bodis-Wollner, I. Jeffreys, A. Kulikowski, J. Spekrijse, H. & Regan, D. (1977) Methodology of patterned visual stimulation. in "Visual evoked potentials in man: new developments" ed. J. E. Desmedt Oxford: Clarendon Press pg 6

⁵³Rubin, M. & Walls, G. (1969) Fundamentals of Visual Science. Springfield, Il: Charles C. Thomas, pg 195

⁵⁴Heynen, H. & Norren, D. van (1985) Origin of the electroretinogram in the intact macaque eye--I. *Vision Res.* vol 25. pg. 700

⁵⁵Murikami, M. & Pak, W. (1970) Intraculluarly recorded early receptor potential of the vertebrate photoreceptors. *Vision Res.* vol. 10, pp. 965-975

⁵⁶Heynen, H. & Norren, D. van (1985) *Vision Res.* vol. 25, pp 697-707 & 709-715

recording with a concentric microprobe to obtain LERG waveforms. With a difference in tip position of 25-30 microns, they tend to be making differential voltage recordings between layers occupied by the OS, IS, ONL and INL. Furthermore, with an inner tip of 1-2 microns and an outer tip of 10 microns, the outer tip (and probably both since the probes were being retracted during data taking) is clearly integrating signals from a number of nearby cells. Both probes were at relatively high impedance introducing the likelihood of capacitive coupling. The probes penetrated the retina at an unspecified angle relative to the local surface of the retina and were not correlated with the local signal path geometry, although the sites were apparently extrafoveal.

Another area of difficulty is in the concept of linearity. There seems to be a great deal of confusion with regard to the concept of linearity as it is applied to an input stimulus or signal and as it is applied to a transfer function of a physical process, channel or system. Rodieck & Ford⁵⁷ have attempted to clarify this situation by separating the two situations. Whether an input stimulus, or any other signal, can be classified as linear depends on whether it can be represented by an equation of the first degree. Whether a transfer function associated with a process can be considered linear depends primarily on whether the process satisfies the Superposition Principle. This Principle states that the response to two stimuli presented simultaneously is equal to the algebraic sum of the responses to the two stimuli presented separately. They list four corollaries to this Principle:

1. The relative time course of the response is independent of the amplitude of the stimulus.
2. The amplitude of the response is proportional to the amplitude of the stimulus.
3. If the stimulus is inverted the resultant response is inverted.
4. Knowledge of the response to a simple stimulus, such as a 'pulse' or a 'step,' permits calculation of the response to any other stimulus.

They then draw a conclusion that is slightly too restrictive: "The response of a linear system to a pulse or step may thus be said to completely characterize the linear system." This statement is also true for the pulse response of a time-invariant nonlinear system.

The VEP technique will not be discussed in this work because of its limited specificity. Ffytche, Guy & Zeki have made some valid comments on this technique⁵⁸. Heckenlively & Arden present the general measurement regime⁵⁹. Recently, Ffytche, et. al. demonstrate that when combined with auxiliary magnetic intervention (mVEP), it is capable of a quite important degree of temporal precision. However, there is still considerable ambiguity in the precise spatial location of the events monitored and the spatial extent of those events. This leads to ambiguity in the specific type of circuit actually involved.

The Visually evoked potential (VEP) technique is described in Heckenlively & Arden. The evoked potential technique is a very coarse technique by any current standard. It typically uses half inch diameter electrodes placed on the scalp using a conducting jelly to make electrical contact. These electrodes are typically placed at a spacing on the order of two inches. Each of the resulting set of measurement points assimilate signals from at least 10 million neurons associated with unspecified engines of the brain. The stimulation generally involves a two color checkerboard arranged to reverse colors periodically at a rate on the order of once per second. Some recent VEP helmets have been prepared using closer spacing of the electrodes, but the measurements are still coarse and not well localized to the engines of the brain.

Any experimentalist in vision would be wise to read the introductory remarks of Rubin &

⁵⁷Rodieck, R. & Ford, R. (1969) The cat local electroretinogram to incremental stimuli. *Vision Res.* vol. 9, pp. 1-24

⁵⁸Ffytche, D. Guy, C. & Zeki, S. (1996) Motion specific responses from a blind hemifield. *Brain*, vol. 119, pp. 1971-1982

⁵⁹Heckenlively, J. & Arden, G. (1991) Principles and Practice of Clinical Electrophysiology of Vision. St Louis, MO: Mosby Year Book pp. 400-404

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Walls⁶⁰ before proceeding into the laboratory.

4.3.4.1.1 Mathematical manipulation of the responses

Historically, the mathematics associated with the field of vision research has been less sophisticated than the biological or psychophysical investigations with which it was associated. The equations of vision found in the literature have always tended toward linearity, even in the face of Weber's Law, Fechner's Law, etc. The CIE Chromaticity Diagram of 1931 was based heavily on the concept that color vision in humans involved linear responses to irradiance and that the various visual channels in the eye were linearly summed in order to create the sense of color. There is overwhelming evidence that this is not the case. In 1989, Flitcroft⁶¹ quotes Naka & Rushton from 1966: "For each pigment system, every quantum that is effectively absorbed makes an equal contribution to vision." One can argue with what Naka & Rushton meant by 'effectively absorbed', but the fact is that adaptation is a very nonlinear process and photons absorbed under different conditions of irradiance and time have vastly different impacts. Furthermore, the operation of the L-channel at mezotopic light levels does not satisfy Naka & Rushton's claim. Never-the-less, this Principle of Univariance has been widely pursued and has led to the use of the 'Silent Substitution' method in psychophysics. Flitcroft adopted this tenant and the foundation equations for the CIE Chromaticity Diagram to develop a theory based on matrix algebra of linear homogeneous equations. As will be shown in the next few chapters, the basic signal detection function is grossly nonlinear (it is optimized for change detection and not for good color rendition) and the basic signal processing function is based on logarithmic mathematical manipulations (which relates to multiplication in the underlying signals). **The result is that in the vision process, the appropriate equations, between input and output, are not linear, are not homogeneous, and are not of the first order!** This is true even for signal amplitude ranges of as little as 2:1.

When the appropriate arithmetic is used, a wide range of measurements and sensations can be explained without making arbitrary assumptions. These include adaptation, the transition from photopic to scotopic vision (in terms of both the change in spectral sensitivity and the loss of color sensation), the change in temporal frequency response with irradiance (and differential irradiance between signal channels) and the time delay as a function of irradiance found in vision.

4.3.4.1 Polarity

The adjective polar is overused when discussing vision. It is used to discuss the incoming optical radiation, the structure of the nerves involved, the voltage at certain nodes and to describe how the "action potential" is generated/transmitted along the nerve structures.

4.3.4.1.1 Polarization of radiation

In this work, the polarization of the incident optical radiation will be discussed in the conventional engineering sense, the polarization of light is described by the geometrical direction associated with the electrical field vector of the radiation.

4.3.4.1.2 Polarization in morphology

When discussing the structure of neurons, virtually every biology text illustrates the types of neurons using a nomenclature developed by the early histologists. An updated version of such an illustration is shown in **Figure 4.3.4-1**. The histologist defined essentially three types of neural structure based on how many structures emanated from the cell body (alias cyton/parikaryon). Thus, they named the neurons monopolar, bipolar and multipolar. Most authors caveat these figures by saying "these forms are not definitive, the geometry of nerves covers a wide continuum in between these three basic types." In fact, these designations have no functional significance and lead to endless confusion when discussing the related

⁶⁰Rubin, M. & Walls, G. (1969) *Fundamentals of Visual Science*. Springfield, IL: Charles C. Thomas, pg 50

⁶¹Flitcroft, D. (1989) The interactions between chromatic aberration, defocus and stimulus chromaticity:... *Vision Res.* vol. 29, no. 3, pp 349-360

electronic phenomena. There are three primary structures associated with the neuron. In the figure, the circle represents the nucleus or Soma, the black rectangles indicate the active electronic devices, the Activa, and the areas inside the dashed rectangles are the reticulum or electrical conduits of the neuron. Reticulums are usually separated into two classes, those associated with the input structure of the neuron, and enclosed within the neurites, and those associated with the output structure and enclosed within the axon. Note the term neurite is used to describe two types of input structure, the dendrites and the podites. All neurons contain at least one Activa. All Activa have a minimum of three electrical terminals. These terminals are best described in electronic terminology as the emitter or input, the base or common, and the collector or output terminals. More than three terminals can usually be associated with the Activa. Some of these additional terminals are associated with capacitances. The combination of each Activa with the other circuit elements supporting it, besides the neurites and axon, are defined as the **conexus** of the neuron. This conexus is entirely internal to the neuron and is only observable by high magnification electron microscopy (>50,000x) (A) shows a monopolar neuron with its three electronic terminals shown on the surface of the plasma membrane as dark bars. Note the identical functional organization in (B) for the bipolar neuron. Clearly, how close the nucleus is to the functional parts of the neuron is irrelevant. Whereas (A) and (B) show only the dendrite of significant physical size due to arborization, (C) shows the poditic or base terminal also being of significant size. The result is an easily identifiable three-terminal configuration related to the internal Activa. (D) shows the dendritic terminal further arborized. Neurites frequently arborize significantly, leading to thousands of input connections⁶².

Although there is only one nucleus in a given neuron, it is possible for there to be a great many Activa. (E) shows a typical projection neuron, such as a ganglion cell, containing three internal Activas. The sections between Activas are called internodes, or axon segments, or more appropriately conduit segments. The reason is that conduit segments exhibit terminals suggestive of both dendrites and axons.

⁶²Wassle & Boycott. *Physiology Reviews*, vol. 71, no. 2 April 1991 pp. 447-480.

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The biologist also speaks of the neural cell as “polarized,” meaning the signal is usually carried in the direction defined as beginning at the dendrite structure and ending at the pedicel (alias bouton/knob/end foot) of the axon structure. This is a relatively trivial use of the word and it should not cause any problem.

4.3.4.1.3 Potential and Polarization

The term polarization as used to describe an electronic condition in biology is usually used to describe the difference in voltage between the electrolyte on two sides of a membrane making up the wall of a cell. The inside of the cell is normally found to be at a negative potential with respect to an external electrode near the cell wall. The potential is typically 50 to 100 millivolts. This value is normally named the resting potential.

By associating the resting potential with the cell wall instead of the internal electrolyte, many biologists have considered this potential to be similar to the local polarization of a distributed capacitor. Based on the above notion of polarization, a cell wall becomes depolarized when the negative voltage of the internal plasma of the cell is reduced. Conversely, hyperpolarization is taken to be an increase in this negative voltage. This notion has delayed the advance of understanding in the area of neurology. In this work, depolarization and hyperpolarization relate to the relevant plasmas and not to the cell wall.

Figure 4.3.4-2 shows the typical voltage profiles of the three major functional classes of neurons in vision. The profiles focus on the axoplasm of a neuron. There is little data in the literature on the potential of the dendroplasm and podaplasm. However, the voltages of these plasmas are easily deduced from the theory in this work. Some care must be taken, in the case of photoreceptor cells, since some of their plasmas are in close electrical contact with the inter-photoreceptor cell-matrix, IPM, instead of the interneural matrix, INM). Both the photoreceptor and signal processing cells are electrotonic (they process analog voltage waveforms). The projection neurons are phasic and generate action potentials in response to an input signal greater than a specific DC potential.

The reference potential for these figures is the potential of the interneural matrix, INM. In most cases, this potential is significantly different from the circuit ground, V_{BB} of the individual neuron. The circuit ground is usually 10 mV more negative than the reference ground. The intrinsic membrane potential, V_{CC} , is the potential of the axoplasm in the absence of current flow through the membrane. This is not the potential usually reported in the literature. The commonly reported potential is the resting axoplasm potential, V_C . V_C and V_{CC} are approximately equal only in the case of the projection neurons during the interpulse interval. During this interval, the voltage drop related to the current passing through the cell wall is negligible. Under all other neurological conditions, V_C is less negative than V_{CC} . In frame **A** for the case of the photoreceptor cell, V_C is a state variable determined by the average illumination of the cell and the precise state of its adaptation. For this cell, V_C is typically -45 mV relative to the interneural matrix. The vertical bar shows the instantaneous dynamic voltage range of this cell to be approximately 35 mV. This range begins at the dark adapted

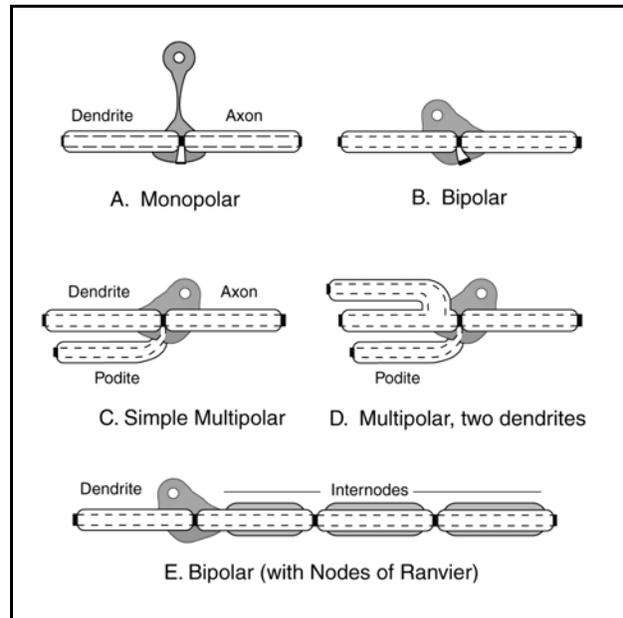


Figure 4.3.4-1 Correlation between the functional and morphological neuron. The nuclei of the cells are indicated by a circle. The Activa within each cell are indicated by black rectangles. The other circuit elements associated with the Activa and completing the conexus or Node of Ranvier are not shown. The reticulum are indicated by areas surrounded by a dashed line. (A), the simple monopolar neuron. (B), the simple bipolar neuron. (C), the simplest multipolar neuron. (D), a multipolar neuron with dual dendritic arborization. (E), A projection neuron containing multiple Activa located at Nodes of Ranvier.

set point of about -25 mV. In these cells, an increase in light causes the output voltage to approach the intrinsic electrotonic potential. This has traditionally been defined as hyperpolarization of the cell. The prefix hyper- is unwarranted in terms of the functioning of the circuit.

The signal processing neurons operate at a different set of nominal voltages than the photoreceptor cells as shown in frame **B**. In this case, the intrinsic electrotonic potential is typically -154 mV relative to the INM. However, the Axiolite is typically drawing current through the axolemma continuously. This results in a continuous voltage drop across the power source. The resulting axoplasm potential is typically near -70 mV and it can vary instantaneously over a span of about 130 mV. Its most negative potential is controlled by V_{CC} and its most positive potential is controlled by V_{CSAT} . V_{CSAT} is the lowest output voltage achievable by the Axiolite while the collector remains reverse biased. Note the overlap between the dynamic range of the photoreceptor cells and the signal processing cells.

The literature is unclear as to whether bipolar cells accept signals at their poditic terminals and are therefore biphasic in their output. For the following discussion, it will be assumed that only lateral cells can act as inverting amplifiers. This assumption has no impact on the overall theory.

For photoreceptor signals applied to the non-inverting input of a typical lateral cell, the gain of the signal processing cell is ~1.0 and the output at the axon of the signal processing cell is nearly identical in voltage to the input signal from the axon of the photoreceptor cell. However, in this case, the hyperpolarization in the photoreceptor has resulted in a depolarization (a reduction in the instantaneous voltage of the axoplasm relative to the INM) of the second cell relative to its resting potential.

For a signal from a photoreceptor cell that is applied to the inverting terminal of a lateral cell, the situation is different. The synapse between the cells must be of the appropriate size to shift the average DC potential of the signal while maintaining the voltage gain of the combination of the synapse and the inverting input circuit at or near 1.0. After this shifting and amplification, the instantaneous output signal of the signal processing neuron is nearly identical in shape to the input signal but it has been inverted and its DC level has been shifted by about 70 mV. The dark adapted set point of the photoreceptor cell is now represented by a voltage near -140 mV in the signal processing cell and a hyperpolarization in the photoreceptor cell due to an increase in illumination results in a depolarization in the signal processing cell, i.e., the signal is driven toward the resting axoplasm potential.

If two photoreceptor cells are excited equally and their signals are provided to opposite inputs of a lateral cell, the output level of the lateral cell remains essentially unchanged at its resting potential.

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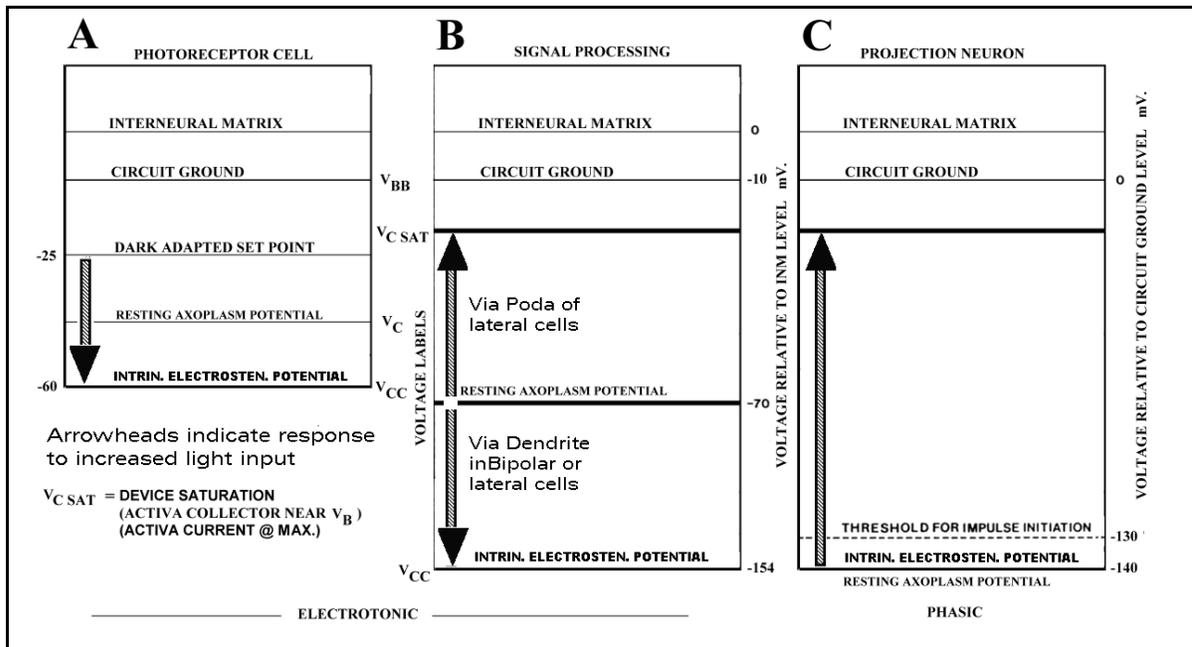


Figure 4.3.4-2 Fundamental voltage regimes in vision. A, for a photoreceptor cell. B, for a signal processing cell. C, for a signal projection cell.

Frame **C** illustrates the electrical profile of the third neuron type, the projection neuron. The potentials applied to the cell are essentially the same as those of a signal processing neuron. However, the cell is used in two diametrically opposite operating modes.

For those projection neurons designed to accept mono phase input signals (typically parasol ganglion cells accepting luminance signals), the internal Activa is normally biased at cutoff. In the absence of an input signal, no current flows through the internal Activa. The resting axoplasm potential is equal to that of the electrostenolytic process supporting that axon. For input signals below the threshold voltage for action potential generation, the projection neuron acts as a linear amplifier with a gain of about 1.0. The output terminal will display an output waveform that is a copy of the instantaneous input waveform. However, it will be at a DC value contained within the voltage range shown as -140 to -130 mV. However, for input signals exceeding a fixed DC potential, the circuit becomes unstable. It becomes a monopulse oscillator if the input signal exceeds the fixed threshold only briefly. Otherwise, it becomes a continuous pulse oscillator. When in the oscillatory mode, all of the generated pulses are of the same amplitude. This amplitude is given nominally by the voltage $V_{CC} - V_{CSAT}$. It is possible for a measured waveform to exceed this maximum amplitude depending on the size of the capacitances used in the oscillatory circuit. The voltage at -130 mV is labeled as the threshold for impulse initiation to conform to practice in the literature. There is no threshold in the axolemma potential. This level is the equivalent voltage to the actual response threshold voltage in the input circuit of the projection neuron.

For those projection neurons designed to accept biphasic input signals (typically midget ganglion cells accepting chrominance, or other bipolar signals), the internal Activa is normally biased so as to oscillate continuously. The axoplasm potential is typically -140 mV during the interval between pulses and the amplitude of the individual pulses is as described above. The time interval between adjacent pulse peaks is a nearly linear function of the instantaneous biphasic voltage at the input terminal of the projection neuron.

As developed elsewhere in this work, all Nodes of Ranvier are also monopulse oscillators employing an Activa circuit identical to those discussed above that respond to monophasic input signals. They are normally biased to cutoff and only generate an action potential in response to an input signal exceeding the threshold voltage of its input circuit.

Historically, it has been very difficult to measure the voltage of the dendritic or poditic plasmas. It has been conventional to speak of the potential of the axoplasm as the potential

of all of the plasma inside the cell. As seen above, this convention is misleading and untenable.

The intercellular material in any organism is usually a very good insulator compared to metals, $\times 10^{xx}$ ohms per square (no units are needed here). And cell walls are usually very good insulators, except when disturbed. Although the dielectric constants involved are small, these walls are thin and relatively small numbers of electrons or ions can generate significant voltages.

Most of the biological literature, with its strong leaning toward chemistry, does not consider the transfer of charge along the surface of a membrane. It concentrates instead on the movement of ions perpendicular to the membrane surface. Furthermore, most biological literature does not consider the effect of individual electrons or ions on a membrane, preferring to work in units of moles or gram ions. This will not be adequate here where, in the limiting case, we are examining the signal generated by a relatively small number of photons (i. e. hundreds or less in the limiting cases). In addition, the distinct possibility of individual ions traveling along the surface of a membrane must not be ignored, especially in the case of the retina where distances can be extremely short (10's of microns). Thus a potential difference of one millivolt between the external surfaces at the opposite ends of a one micron long structure generates an electrical field of 10^3 volts per meter, a very significant field strength.

Juusola, et al. has recently provided a limited tabulation of some axoplasm and neurite potentials in general agreement with the above discussion⁶³.

4.3.4.2 Electrical fields

In the biological field, the vast majority of the older experimental work involved skeletal (alias principal/projection) neurons used to communicate over relatively long distances. More recently, much effort has been applied to describing the actions of signal processing (alias local circuit or /inter-) neurons.

The skeletal neurons exhibit electrical pulses traveling along the axon structures. These pulses are usually described in terms of "action potentials" in contrast to the resting potential. The "action potential" found in the giant Squid axon is found to have a peak amplitude of +95 millivolts. Several investigators have related this voltage to an assumed -60 millivolts resting potential for the axoplasm. Under this assumption, the axoplasm would become positive with respect to the surrounding matrix during the period of the action potential. As seen in **Figure 4.3.4-2(C)**, the axoplasm resting potential of projection neurons is normally -140 millivolts. Based on this value of the resting potential, the axoplasm is depolarized during the action pulse interval. However, there is no reversal of the potential across the axolemma.

Recent neurological literature has been concentrating on the dendritic portion of the skeletal and signal processing neurons. It recognizes that signaling may occur in an analog instead of a pulse mode. In this case, a sustained potential different from the resting potential is described as a "electrotonic potential." Smith indicates these electrotonic potentials (which are usually smaller in amplitude than the potentials associated with action potentials) are usually small depolarizations of a nerve cell membrane and are caused by essentially passive spread of electrical current through the conducting fluids inside and outside nerve cells and their extremities⁶⁴. As indicated above, many of the fluids involved in the signal processing environment may not be highly "conducting" and surface transport must also be considered viable. Frequently, the fluids are liquid crystalline in nature and ionic transport may not be possible. In this case, electron and hole transport may be the method of charge transport through the medium.

Smith also notes that, especially in the retina, "there are very few if any voltage dependent sodium gates present." Furthermore, the electrotonic signals recorded in the signal processing neurons of the retina are both positive going and negative going with respect to

⁶³Juusola, M. French, A. Uusitalo, R. & Weckstrom, M. (1996) Information processing by graded-potential transmission through tonically active synapses *TINS* vol. 19, pp 292-297, figure 4C

⁶⁴ Smith, C. (1989) *Elements of molecular neurobiology*. NY: John Wiley & Sons. page 257

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the axoplasm resting potential. This work proposes these electrotonic potentials are actually small polarizations and depolarizations of the axoplasm and not of the axolemma.

No report could be found in the literature where an investigator actually measured both the absolute resting potential of the axoplasm and the absolute amplitude of the action potential in the same projection neuron with respect to the surrounding fluid matrix.

4.3.4.3 Signal transfer between neurons

At the present state of the art in biophysics, the subject of how signals are passed from the axon of one neuron to the dendrite of a second neuron is expanding. Until recently, to imply the transfer of a signal by means other than the physical transport of ions was blasphemous. The existence of so-called gap junctions (alias electrical synapses) between neurons is now becoming accepted. However, their characteristics are not completely defined. Smith gives a brief description of a gap junction. However, the concept will be broadened here to accept the case of current sources as opposed to voltage controlled gates. Smith does define a crucial aspect of a gap junction, a hydrophilic pore created at the junction of two hydrophilic canals, one in each cell. He speaks of this pore being controlled by a voltage. Most morphologists speak of a reticulum inside the axon. It appears the canal is a conceptual version of the reticulum of morphology.

As developed in this work, Smith's concept of two canals connected by a pore can be replaced by two reticulum connected by a three terminal Activa. The Activa consists of the two neurolemma, the axolemma and the neurolemma separated by a liquid crystal of hydronium. The electrical transmission of the Activa is controlled by the potential between the axoplasm within the reticulum and the surrounding fluid. The potential of the orthodromic neuroplasm is inconsequential as long as it is more negative than the axoplasm and the surrounding fluid. Under these conditions, a current is transferred to the neuroplasm in response to the potential of the axon. The result is an all-electronic synapse. No other chemicals are required within the active region of the synapse. The all-electronic synapse is unidirectional because of the required bias potential between the neuroplasm and the surrounding fluid.

4.3.4.3.1 Cascaded Circuits

A problem of paramount importance in the neural system is that the circuits of the signal detection, signal manipulation and signal projection stages (stages 1, 2 & 3) are directly coupled. This method of coupling is not widely used in man-made electrical circuit designs for a variety of reasons. The primary reason is the difficulty of maintaining the signal in the center of the electrical voltage passband of subsequent circuits. For more than three circuit stages in man-made systems, the stability of the overall circuit usually requires provision of an external feedback loop. Otherwise, the signal is usually truncated at either high or low signal levels as it passes down the signal path. The neural system uses much less amplification and internal feedback within the individual stages to achieve the same goal.

4.3.4.4 Signal control

Smith describes the "membrane 'gates' or 'channels'" connecting two neurons as dividable "into two categories: those which are controlled by **chemical molecules (ligands)** and those which are controlled by transmembrane **voltage**." He continues: "In fact this division is not absolutely clear cut . . . Nevertheless, for the purposes of exposition, we shall consider each in turn." These words indicate clearly how tentative the science was in this area as of 1989. In fact, the words gates and channels are not synonyms in any context. A voltage may be used to control some other entity which carries a signal but a ligand as used here is clearly a signal carrying entity and not a controller. If the signal were to be carried by electrons instead of ligands (or ions), then it is quite reasonable to think in terms of a current source as generating these electrons as an alternative to a voltage controlling these electrons. The concept of an equivalent current source is always available when one speaks of a voltage controlled current, i. e. Thevenin's Theorem. In this case, with the high impedances involved and the presence of 'channels', a current source may be the more appropriate concept.

4.3.4.5 Signal measurement (Reserved)

This section is provided to collect and summarize the terminology and major concepts discussed in this and previous chapters.

4.3.4.5.1 Voltage polarization (Reserved)

It is important to point out that the topography of synapses associated with the pedicels of photoreceptor cells and the topography of Nodes of Ranvier are essentially convolutes. The signal path is along the axis of a Node of Ranvier and the electrostenolytic reservoirs surround it. In the case of the pedicel, the electrostenolytic reservoir is frequently in the center and the synapses are grouped around it.

4.3.4.5.2 Signal isolation

Figure 4.3.4-3 attempts to illustrate the importance of positioning the return electrode carefully while also illustrating the topographical location of the source of various waveforms. In the literature, the placement of this electrode is usually discussed in terms of finding an innocuous, or "indifferent" neutral location, such as the outside of the eye cup, the back surface of the RPE, etc. In fact, these are very poor locations for obtaining meaningful information. The return probe should be located in the INM or IPM as close to the probed location as possible in order to avoid extraneous signals due to "common impedances." When two circuits share a common impedance, the total signal measured by a probe located in one circuit will contain signals related to the other circuit. This is an especially important consideration in high impedance circuits where capacitive coupling as well as resistive coupling can occur. The problem is endemic to experiments in vision research where it is common to present waveforms clearly showing the summation of a low level analog (electronic) waveform measured at a high impedance point corrupted by a pulse (action potential) waveform capacitively coupled into the test circuitry from a higher voltage, and lower impedance, signal source. In this case, the extraneous pulse waveform frequently has a voltage higher than the desired electrotonic waveform. This result is easily calculated from the ratio of the impedances involved.

A related problem endemic to vision research is that of attempting to measure a waveform at a point of extremely high impedance. Frequently, the bandwidth of the original signal is wider than that of the test set used. The waveform obtained is therefore not that of the original signal but that of the test set. This problem is further complicated by the "loading" caused by the presence of the test set probe near or in contact with the signal node of interest. In this case, the resulting waveform may be a complex function of the combination of the test set and the signal under examination. This will be discussed in later sections when it will be pointed out that an open gate field effect transistor cannot normally be used in the testing of very high impedance circuits since the operation of the transistor is not symmetrical with regard to rapid voltage swings about a bias point (a resting potential). In these situations, it is not adequate to purchase and utilize a standard amplifier circuit without demonstrating that the performance of the amplifier alone is well understood and not distorting the signal waveforms.

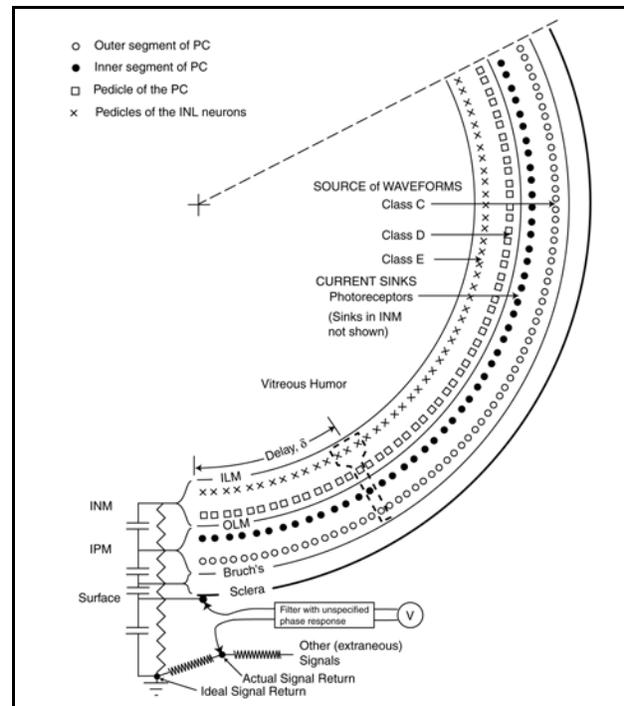


Figure 4.3.4-3 ERG lead placement relative to the topography of the retina. The source of the different classes of waveforms are shown on the right in this cross-sectional view of the retina. The ILM, OLM, Bruch's membrane and the sclera are shown as insulators shunted by conductive impedances on the left. The black dot indicates a signal probe in contact with the outer surface of the sclera. The return probe is shown connected to an "indifferent location." This probe location makes the test set susceptible to extraneous signal pickup.

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Baylor et. al.⁶⁵ have obtained some very high quality data while operating at the very low signal levels associated with the OS. By making current mode measurements, which are inherently low impedance, their data shows no discernable interference from higher level pulse waveforms generated in the nearby Inner Nuclear Layer.

4.3.4.5.3 Isolation from stimulus generator

Figure 3 of Baylor, et. al. (1984) shows a particularly insidious type of interference problem⁶⁶. When acquiring data at very low signal levels, it is generally not recognizable. However, when summing multiple data traces to improve the signal-to-noise ratio of the overall data collection, the synchronous noise associated with the stimulus generation circuitry is enhanced rather than suppressed. In this case, a nominally 15 Hz sinewave contaminates the data.

4.3.4.5.4 Decoupling

In electronic circuits, if the individual amplifier circuits are powered by a weak source, the source can be modeled as a voltage source and an associated resistance. The result under large signal conditions (see the following paragraphs for definitions) is that the measured signal will be corrupted by a signal related to the power source. The same situation occurs in the operation of the eye. The power source, the metabolic supply system, is tailored to be "just adequate" under normal conditions. Under large signal conditions, a drift or transient is observed in the measured signal which is directly relatable to the inadequacy of the metabolic system to provide an "absolutely stable" power supply to the photodetection process. In the case of the eye, this large signal problem has three ramifications:

1. The signal performance of an individual signal path will exhibit variable performance under different input illumination levels, including exhibiting a history of previous illumination, due to the marginal performance of the metabolic supply.
2. The signal performance of an individual signal path will exhibit variable performance based on the input illumination applied to nearby signal paths because of the common impedance in the metabolic supply. This is frequently labeled "cross-coupling" if the signals are of relatively high frequency.
3. The signal performance of an individual signal path will vary with its position in the retina due to the combination of both of the above effects.

Adjacent signal path coupling is a critical factor in the eye. The decoupling is usually inadequate under experimental conditions due to the application of large illumination signals. Because of geometric limitations of the metabolic supply available, the performance of the eye will vary in many ways with respect to geometric position in the retina.

4.3.4.5.5 Adaptation

Because of the relatively poor characteristics of the metabolic supply in the eye, the performance of the eye can exhibit significant temporal changes over short intervals based on the prior illumination history of the eye, i. e. the eye illustrates significant fatigue effects. When these fatigue effects are combined with the decay characteristics related to the photodetection process in the OS, these effects are generally described under the term adaptation. The eye exhibits significant sensitivity variations with time after either an increase or a decrease in average input illumination. These changes vary considerably with position in

⁶⁵Baylor, D. Lamb, T. & Yau, K. (1979) *ibid*

⁶⁶Baylor, D. Nunn, B. & Schnapf, J. (1984) The photocurrent, noise and spectral sensitivity of rods of the monkey *Macaca fascicularis*. *J. Physiol.* vol. 357, pp 575-607

the retina. The actual circuit used to provide the mechanism of adaptation is unique and based on the unique topography of the photoreceptor cell. This topography introduces a nonlinear mechanism into the collector structure of the first Activa found within the photoreceptor cell. This mechanism causes the circuit to exhibit a very large change in amplification factor as an inverse function of the input stimulus to the circuit. The result is an output that is essentially constant regardless of the input amplitude. The details of this process are presented in **Section 12.5.3**.

4.3.4.6 Signal classification

Because of the dynamic range of the vision system, it is necessary to carefully specify the signal level being applied to the eye, processed by the eye and/or measured in the eye. This is normal practice in the electronics field where the circuits normally perform in a linear mode when small signals are applied to them--and in a nonlinear mode when large signals are applied to them. A convenient criterion in electronic circuits is to classify the signals based on their amplitude as a percentage of the supply voltages. Large signals have amplitudes which are a significant percentage of the supply voltages; whereas, small signals always have an amplitude that is below 10% of the supply voltages.

In the case of vision, the signal circuits will be shown to exhibit an instantaneous maximum dynamic range of about 100:1, two orders of magnitude. The scene contrast applied to the eye is normally less than 6:1 for natural scenes and only approaches 20:1 as a maximum when viewing black ink on white paper. The average natural scene contrast is about 2:1 on an RMS (root mean square) basis.

The eye is normally exposed to low contrast, or small signals, except under abnormal conditions.

Much psychophysical testing is done under abnormal conditions. In fact, much of this testing involves the application of a large signal followed by a threshold test; this involves a combination of a large signal and small signal conditions and any analysis of the resulting data must account for the response of the system to both signals. Because of the transient response associated with all large signals, it is frequently found that the small signal threshold tests are a function of time from the application or cessation of the large signal.

In the case of large signals, the photodetection process in the eye exhibits a logarithmic response. This type of response exhibits interesting properties which will be developed below in later sections of this work.

4.3.4.6.1 "ON" and "OFF" in psychophysics

For those not initiated into the psychophysical community, a brief word is needed about "on" and "off" signals. These terms are not used in their literal sense. The psychophysicist uses these terms to describe the modulation of a baseline or carrier irradiance level. An "on" signal or excursion merely increases incrementally the total irradiance. An "off" signal does not turn off the irradiance. It merely reduces the irradiance level by turning off the incremental value associated with the "on" signal. They then report activity resulting from these changes. Thus, in a large signal situation, they will report activity resulting from an "off" signal which is actually related to the establishment--or reestablishment--of a new, non-zero, irradiance level.

4.3.4.7 Resonance

[xxx edit out ref. to eye and vision]

[xxx after extensive attempts by colleagues to locate resonant circuits in the neural system, it is safe to say they do not exist in the biological neural system. This is specifically true with regard to the auditory modality where the cochlea does not employ resonant circuits (resonators).]]

The term resonance must be carefully defined when discussing the eye. It is used differently in different disciplines and in fact appears in different forms in different functional areas.

The molecular structures found in the eye and utilized for photodetection are found to be quantum-mechanically resonant at wavelengths directly related to the wavelengths of visible light. Mathematically, their operation can be described in terms of second order

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differential equations.

The overall photodetection/electron excitation process performed by these structures does not involve a resonant process. This quantum statistical process can be described in terms of first order differential equations.

The basic analog signaling structures found in the eye do not exhibit either physical or electronic resonance; they only exhibit resistive and one type of reactive (in all known cases, capacitive) impedances. The responses of these structures are described mathematically by first order differential equations. However, it is possible through feedback of signals within the signaling structures to create electrically resonant circuits. The performance of these circuits must be defined utilizing second order differential equations.

4.3.4.8 Bandwidth and risetime

4.3.4.8.1 Spatial versus temporal frequency response

Before proceeding, it is important to provide a *cautionary note*. It is common in psychophysical, and some electrophysical, experiments to attempt to measure the spatial frequency response of the eye utilizing temporally varying signals as a substitute. Frequently, bar or checkerboard patterns of variable pitch are caused to reverse in contrast as a function of time. These experiments must be extremely carefully designed and compared to a relevant model if results are to be obtained that can stand close scrutiny. This is because of two things; the complex relationship between spatial features in the object plane and the temporal signals generated in the eye/brain *and* the determination of what is being measured in the experiment--the apparent spatial response measured at the output of a differencing amplifier, such as an amercine cell, can exhibit a different signal depending on the temporal phasing of the chromatic input signals. If the phasing is not carefully specified, confusion will result during the analysis and evaluation of the data.

4.3.4.8.2 Individual circuits EDIT

The description of the temporal performance of a signaling circuit can be relatively complex since it may be quite different under small signal and large signal conditions. Under large signal conditions, first order (i.e., non-resonant) circuits exhibit a temporal response consisting of one or more exponential response functions to a step input. The temporal response is usually described by way of the time constant of these exponential waveforms.

The output waveform presented by a first order circuit is quite distorted relative to the input signal. However, this is not of technical significance here. The eye does not make use of the *shape* of the input illumination waveform as a function of time. However, the effect is quite often presented in experimental waveforms and the source of this distortion should be understood.

4.3.4.8.3 Types of temporal frequency filters

The filtering topology and technology used in the neural system is far more sophisticated than recognized in the literature. The typical system employs at least four unique types of temporal frequency filters. To fully understand the effect of these filters, it is necessary to have some formal training in filter design. The concepts of poles and zeroes in filters is the key. The properties of the filters found in the system are unusual and not normally covered in introductory course material in "electronics for non-engineers:"

1. **A high frequency pole that is a function of the stimulation level** –The quantum-mechanical excitation/de-excitation process creates a high frequency pole that is sensitive to the stimulation level.
2. **A zero at zero frequency** –The adaptation mechanism found in virtually all sensory channels introduces a zero in the frequency response of the modality at zero frequency.
3. **A conventional high frequency pole**–Many circuits in the neural system exhibit an RC-type

high frequency pole due to the effect of circuit capacitance and the effective resistance of the circuit.

4. **A pre-emphasis circuit**—A circuit with a pole in both the numerator and the denominator of the transfer function that are at only slightly different frequencies can cause a narrow peak in the frequency response of the overall circuit.

5. **A sampling induced pole that is a function of the magnitude of a bipolar signal amplitude**—The encoding of bipolar information by the midget ganglion cells introduces a special form of filtering that results in a high frequency pole with a magnitude that is proportional to the signal amplitude.

When a signal is passed through a cascaded series of these different types of filters, the results cannot be accounted for using lumped constant filter theory. It is this fact that makes it so difficult to interpret the papers in the literature. Many authors have attempted to account for the performance of the neural system using multi-stage lumped constant filters. There are, in fact, no multistage lumped constant filters in the neural system and the use of a lumped constant filter as an analog of a dynamic filter is inappropriate.

It has also been common in the literature to consider the basic character of the neural passband a low pass filter. The presence of a zero in the system due to the adaptation mechanism makes this inappropriate. The simplest representation of the actual sensory modality from the sensory receptor of the sensory neuron on is a bandpass filter with a low pass pole near 0.3 Hz and a high pass pole below 300 Hz (depending on the stimulation level, see the following section).

The performance of these filters will be discussed individually in the following sections and chapters.

The unusual presence of the poles related to the E/D process suggests an unusual methodology when discussing the temporal frequency response of the neural system.

4.3.4.8.4 The variable pass band of the E/D Equation

As noted in Section 4.3.1.1, the quantum-mechanical statistics associated with sensory reception within the neural system are typically of the Fermi-Dirac type, and not the Gaussian type. The E/D equation has two poles in its denominator that exhibit arguably unique characteristics. At high stimulation levels, the lower frequency pole is fixed and the high frequency pole occurs at a variable frequency. This upper frequency pole typically describes the leading edge of the E/D temporal response and the lower frequency pole describes the invariant trailing edge temporal response. However, as the stimulation level decreases, a condition is reached where the two poles have the same value and form a double pole. Under, this condition, the E/D equation becomes equal to the Poisson Equation. The temporal response is then given by the normal distribution associated with the Poisson Equation and with Gaussian statistics. The stimulation level at which the response is given by the Poisson Equation is called the Hodgkin condition in this work, to recognize the failed attempts by Hodgkin to fit the Poisson Equation to the E/D equation without knowledge of the unique condition when he could accomplish such a fit.

If the stimulation level is reduced further, the previously upper frequency pole becomes the lower frequency pole and now describes the variable time constant of the trailing edge temporal response, and the previously fixed low frequency pole becomes the fixed upper frequency pole that now describes the leading edge of the temporal response..

4.3.4.8.5 Scene information modulation by saccadic motion-TREMOR

As discussed in the author's PBV xxx, the intrinsic animal visual system is blind to information in the far field that is not moving relative to the line of fixation. This is a major limitation in the visual system. Without an evolutionary fix for this problem, it is doubtful that the higher animals would have evolved at all. To overcome this limitation, the higher animals have introduced tremor as a mechanism of ocular muscle movement. Tremor, sometime referred to as micro-saccades, consists of a low amplitude signal that is continuously applied to those muscles except during other larger saccades. Tremor has a nominal temporal frequency of 50 Hz and a nominal amplitude of 30 arc seconds (or 1.5 photoreceptor cell diameters). By moving the line of fixation continuously, all of the information in the scene is modulated

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about this 50 Hz carrier. The effect is to move all of the information related to the scene into the passband of the visual system, 0.3 Hz to a nominal 100 Hz. To recover this information, the visual system must synchronously demodulate the neural signals related to luminance and other signals (such as chrominance) at a later point in the system.

An important consequence of introducing tremor to overcome the limitations introduced by adaptation is the fact that large areas of constant irradiance in the scene will still not be modulated by the tremor mechanism. Upon demodulation of the scene information, the brain will still not have information available concerning the luminance or chrominance of these areas. To compensate for this fact, the brain employs a "paint program" to compute the luminance and chrominance as part of the vectorization process. It uses the luminance and chrominance values it receives from points along the perimeter of a constant area, a contrast boundary, to compute these values. This technique is also used to eliminate the blind spot associated with the optic nerve usurping part of the retinal area at its point of exit.

Failure to recognize the importance of tremor in the signaling system of vision has led to great experimental difficulties in the laboratory.

The fine continuous tremor of the eye has a significant effect on the temporal frequency content of the signals in the neural system. If an edge is projected on the retina and the tremor causes a photoreceptor to continuously move back and forth across this edge, the effect is to modulate the irradiance signal applied to the photoreceptor at the frequency of the tremor. Under this condition, the signal may or may not be passed by the photoreceptor depending on the irradiance level. If it is passed,

1. it may or may not be pre-emphasized by a pre-emphasis circuit.
2. it may or may not be delivered into a high pass circuit channel for further processing.

This process is a major contributor to the color vision capability of the eye under dark adapted conditions. If the intensity is adequate, a point source of colored light will be recognized without difficulty on a black field.

4.3.4.9 Delay

The subject of delay, as used in neural research, is not usually defined clearly. Many authors have tried to interpret the delay times they measure in terms of the delay associated with lumped constant electrical circuits alone. They have largely or completely ignored the idea of transport delay due to the finite and relatively low velocity of transmission of electrical signals over biological pathways. These velocities are frequently in the 10 meter/second range as opposed to the velocity in metallic circuits, which is usually in the 10^8 meter/second range. This difference of 10^7 indicates the effects of low transport velocity must be considered in the calculation of the transport delays found in biological circuits..

It is very easy in biological circuits to have a transport delay that is larger than six or seven stages of conventional (copper wired) lumped constant delay. An investigator should always evaluate all contributing factors to the measured delays before beginning an analysis which assumes all delays are due to lumped constant effects.

The definition of delay used in small signal and large signal circuits is usually quite different. In small signal circuits involving sinusoidal signals, it is usually easy to define the delay in terms of the phase shift of a sinusoidal signal measured at one location compared to the same signal measured at another location. This phase shift will usually be a function of the frequency. If the delay times associated with these delays are plotted, the delay may be independent of frequency or it may contain an offset from zero that is independent of frequency. If it does, this constant value is defined as a group delay. A group delay is usually related to a transport phenomenon, not a lumped constant phenomenon. A frequency dependent portion of time delay is usually related to a circuit containing lumped constants. It is not possible to designate the nature of a particular small signal delay without taking measurements at several frequencies.

4.3.4.10 Feedback

Feedback involves the reinforcement of an input signal by a portion of the output from any amplifying device. The reinforcement can be positive or negative, or at any phase angle in between. It can also be internal or external (involving a signal path external to the basic circuit). In complex signaling systems, feedback can occur in a variety of scenarios--some not very obvious. In a circuit built from discrete components, it is usually easy to see the external (extrinsic) feedback loops around the major active elements. It is sometimes more difficult to recognize feedback due to common elements shared between two different current paths. This type of intrinsic feedback usually occurs where impedances are placed in the common base lead of man-made and biological transistor circuits. In fact, this type of intrinsic feedback is present in every transistor because of the inherent impedance associated with the base terminal of the device itself. Thus, virtually every active circuit involves internal feedback. The importance of this feedback is only a matter of degree. In most man-made transistor devices, the internal feedback due to the base impedance, r_b , is only important at high radio frequencies and above.

Typical circuits employing internal negative feedback are the lateral cells. Typical circuits employing internal positive feedback are the ganglion cells and the Nodes of Ranvier. There are no clear instances of external positive or external negative feedback in the biological circuits of the neural system that do not include the external environment in the loop.

4.3.4.11 Charge transport

Electrical charge transport is accomplished quite differently in different forms of matter. Table 4.1.11 gives a brief summary of the situation:

**Table 4.3.4-1
Charge carriers in matter**

Particle	-----Semiconductors*-----			
	Metal	Solid Crystal	Liquid Crystal	Liquid
electron	xx	xx	xx	
negative ion				xx
positive ion				xx
hole		xx	xx	

*The designation semiconductor implies a difference in net conductivity with direction through the material.

Very briefly, charge is transported exclusively by the movement of free electrons in metallic materials.

In the case of liquids, the situation was found to be different, and more complicated, long ago. In dilute solutions, not involving a semipermeable membrane or different types of electrodes, the charge is transported by the physical diffusion of both positive and negative ions through the solute under the influence of the externally applied electric field. Depending on the mobility of the various ions present, one ion may be the dominant current carrier. The current can then be described in terms of that ion type alone; i. e., the current can be described as n-type if it is carried primarily by the negative ions and p-type if carried primarily by the positive ions.

If the two electrodes are different, there will be an internally generated electric potential due to the difference in potential of the half-cells associated with each electrode and the electrolyte. The charge will still be carried by both positive and negative ions, and one type may dominate as above.

In discussing a semipermeable membrane, a distinction must be made between a membrane that is semipermeable to different size or chemical class of particles (hydrophilic, hydrophobic, etc.) and one that is semipermeable to electronic charges, i. e., a semiconductor.

If there is a membrane separating the solution into two chambers that is semipermeable based on particle size or chemical class and some of the particles are ions, there will be a partial separation of ions and a resulting non-uniform ion density; this will create an electrical potential generated by the membrane/solution system, which may support or oppose the

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potential due to the electrode half-cells. The resulting ion current may become considerably more complicated. The mobility of the various ions present can vary between the two bulk electrolytes and the interior of the membrane. It is even possible to describe the dominant charge carrier as a function of the region between the electrodes. The biochemistry of the neurons has traditionally assumed this type of charge transport through biological membranes.

A fundamental biologically based membrane is a bilayer of phospholipids that is not semipermeable to ions or large particles. It contains a hydrophobic core. If the membrane is electrically asymmetrical due to the two layers of the bilayer being different, it is normally semipermeable to electrical charges and is therefore an electrical semiconductor.

For the two semiconductor states associated with the metallic state and the liquid state, the situation is quite different. In these cases, as in the metallic case, the atoms of the material are not free to move under the effect of potential fields, but there are still two types of charge transport. One involves the motion of electrons through the conduction band of the crystalline material. The other involves the apparent motion of a positive charge through the valence band of the crystalline material following the loss of an electron from the valence band at the positive electrode. This motion of an apparent positive charge through a crystal lattice in the absence of any atomic motion is described as a "hole current."

Notice in the above case for a liquid crystal, ionic material must be present but it cannot move since it is locked into a lattice. The current is due to hole movement, not physical ion movement. This effect has been extensively explored and evaluated in the metal semiconductors. It is less well known in the liquid semiconductors. However, it can be easily demonstrated in liquid crystals. The mobility of the electrons and holes can be quite different, resulting in a dominant charge carrier in a given region; the material is describable as of the n-type due to predominantly electron movement or p-type due to predominantly hole movement. The mobility of these charge carriers is also typically much greater than that of the mobility of ions in equivalent but less concentrated solutions. ***This quantum-mechanical charge transfer mechanism is the mechanism that actually dominates in the biochemistry of neurons.***

4.3.5 Methods and capabilities of available tools DUPL of 7.1.3

4.3.5.1 Traffic analysis as a major adjunct to peripheral anatomy

When dealing with the peripheral neural system, anatomy can provide a nearly complete mapping of a neural system. However, it does not provide adequate information at the detail level or in areas of very complex circuit paths. Traffic analysis, using the term from military intelligence, is widely used at an elementary level by physiologists to learn more about the detailed circuit diagram of a given neural system. In its basic form, traffic analysis involves observing the volume of signals arriving at a given location by various means as a function of time and attempting to correlate that volume with the potential sources of such signals. Once the coarse relationships between the data arriving at a location and its sources are determined more sophisticated methods can be used to learn more about the traffic. These steps involve a more careful analysis of the origination time and arrival time of the signals to determine if any intermediate relays may have been involved. If a relay is inferred, the analysis is expanded to locate the path(s) involving the relay.

Once the signal traffic has been identified with respect to source, destination and timing, it is possible to attack individual messages in an attempt to determine their structure and information content. Determining their information content generally involves determining the language in which they are encoded. Here, the language may refer to the machine language of the transmission system, the human language of the sender, and any encryption method used to disguise the human language text. As an example there are multiple types of "Morse Code" used to transmit messages by teletype and multiple types of computer code used to transmit computer data. There are also multiple human languages and an infinite variety of encryption schemes.

At the current time, the traffic analyses used in studying the physiology of the central nervous system remains quite simple. Historically, the most common technique has been to insert a probe into neural tissue and then move a source of stimulation within the object field assumed to be associated with that tissue until an electrical response was observed. This

technique has produced a large volume of data with respect to the visual systems of many animals. However, this basic technique does not provide information about the path between the stimulus and the observed signal unless multiple probes are used. Multiple probes have only been introduced during the last ten years and the technique remains cumbersome and labor intensive. Most of the data collected has not included the transit time of the signals from the source to the probe location.

Recently, a series of non-intrusive techniques have appeared (MRI, fMRI, PET, magnetic VEP, etc. discussed in **Section 7.1.3**) that have offered a more comprehensive and less labor intensive traffic analysis capability. Except in the case of the magnetic visually evoked potential (magnetic VEP), these techniques have not provided information concerning the transit time of the signals.

Where the visual signal paths have been determined, attacks on the information content of the signals have been successful where ever the information exhibits a simple spatial relationship to the stimulus in object space. However, as the degree of spatial coherence of the signal with respect to the stimulus decreases, the ability to interpret the signals is reduced. This is the general case from the output of the cerebellum for afferent signals to the input of the cerebellum for efferent signals. At the current time, man has not determined the nature of the "machine language" used in the neural system to convey abstract (non-spatially coherent) information between these two locations. Determining the machine language used in this portion of the central nervous system is probably the next great frontier in neural research.

4.3.5.2 Spatial and temporal resolution of available tools ca. 1988

[xxx merge with 7.1.3 with this area surviving]]

Churchland & Sejnowski have provided a useful summary of the spatial and temporal resolution achieved prior to 1988 using a range of techniques⁶⁷. **Figure 4.3.5-1** extends their figure to differentiate between synapse investigation at the morphological/cytological level and such investigations at the molecular chemistry/crystallography level. The ranges are not meant to indicate theoretical limits. The inclusion of electron microscopy opens a vast area not considered by Churchland & Sejnowski. It allows the definitive description of the synapse and the electrostenolytic mechanism so crucial to understanding the neural system.

⁶⁷Churchland, P. & Sejnowski, T. (1988) Perspectives on cognitive neuroscience. *Science*, vol. 242, pp 741-745

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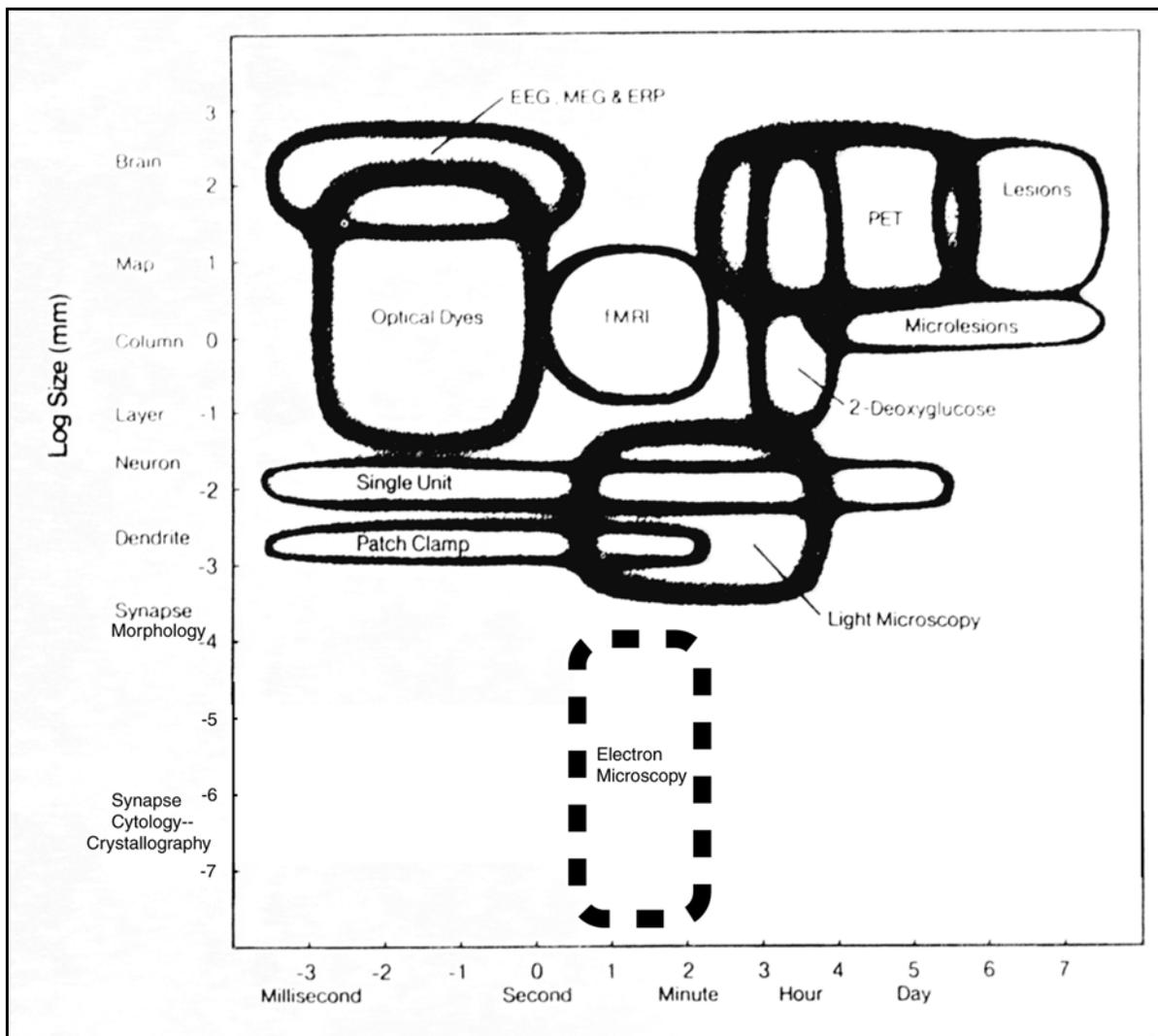


Figure 4.3.5-1 The spatial and temporal resolution range available with current techniques. Modified from Churchland & Sejnowski, 1988.

4.3.5.3 Spatial and temporal resolution of magnetic imaging tools

The recent application of magnetic imaging devices to medicine and the neurosciences has led to an explosion in new and more detailed knowledge. The technique of magnetic resonance imaging (MRI), combining the techniques of nuclear magnetic resonance (NMR) and computer aided tomography (CAT), is the basic technique. MRI has been expanded into a variety of special members of the family, including functional MRI or (fMRI). This technique promises to provide imagery at frame times approaching 1/30 sec as additional planned improvements are realized.

The current MRI and fMRI technologies employ 1.5 Tesla magnets large enough to allow passage of the human body. These machines are readily available in major hospitals and research centers. Higher performance machines with 3.5 T and 7-9.5 T magnets are available in smaller sizes. The first Atlas of the human brain obtained using a 7.0 T machine has now

appeared⁶⁸ and a similar volume focused on the white matter of the brain is in press⁶⁹.

fMRI is particularly useful in exploring the changes in blood oxygenation levels using the so-called BOLD technique (Blood Oxygenation Level Determination).

The spatial resolution of these machines is dependent on the magnet strength. Jackson et al. have provided a good tutorial on MRI as of 2005⁷⁰. While the operation of these machines is very complex, certain operating modes are becoming widely used. The expressions T1 and T2 weighting are playing an important role in the field presently. T1 refers to the time constant associated with the relaxation time of nuclei at the *atomic* level. T2 refers to the time constant associated with the relaxation time of nuclei at the *molecular* level. These two time constants are used to emphasize different constituents of the neural matrix, or other body tissues.

Currently, the resolution of these devices is measured in voxels, nominally 2 mm x 2mm x 2mm in volume, far too coarse for exploring individual neural paths or circuits. However, this size voxel is very useful in exploring the regional changes in blood flow and/or tissue density. The dimensions of the voxel are determined by the slice thickness set to collect data times the spatial resolution of the computed image. A tradeoff between the slice thickness and the spatial resolution associated with the area of the slice is available. This can lead to a false sense of spatial resolution if the investigator is not aware of the thickness of the slice being processed.

To place a 2 mm x 2mm x 2mm voxel in perspective, it can be compared to a very densely packed volume of neurons like the thalamus or to a very loosely packed area of cerebral cortex. a voxel of this size could contain up to 8 million neurons 10 microns in diameter. Clearly these neurons would not be resolvable, even in large groups. The folded thin sheet architecture of the cerebral cortex means a much lower number of neurons would contribute to the signal in each voxel. At the current time, the MRI technique is most useful in imaging the fluids associated with the neural matrix and not the neurons of the gray matter themselves. Similarly, it is very useful in imaging the lipids forming the myelination of large groups of commissure, the white matter (like the corpus callosum and the spinal cord)⁷¹. The mapping of the connectome mentioned in Section 4.2.3.6 is an example of this activity.

4.4 A coordinated (morphology-based) notation for the neurons

Based on the fundamental neuron defined in the previous Sections, it is now possible to define a series of more useful neurons that can be related to those real neurons defined by the anatomists and cytologists. This section will address these application-oriented neuron configurations with respect to their cytological and topological features.

The discussion will continue to be based on the fundamental premise of this work that all neural activity is electrolytically based and that the only chemical reactions associated with neural signaling relate to the electrostenolytic processes providing electrical power to the individual conduits forming neurons. No requirement or situation has arisen suggesting the need for chemical neurotransmitters between neurons even though many specific chemicals are found in the vicinity of elements of the neural system.

The discussion will also continue to be based on the premise that the fundamental functional unit of the neural system is NOT the neuron but the

⁶⁸Cho, Z-H. *ed.* (2010) 7.0 Tesla MRI brain atlas. NY: Springer

⁶⁹Cho, Z-H. Calamante, F. & Chi, J-G. (2013-14) 7.0 Tesla MRI Brain White Matter Atlas. Panmun.

⁷⁰Jackson, G. Kuzniecky, R. & Pell, G. (2005) Principles of magnetic resonance imaging *In* Kuzniescky, R. & Jackson, G. *eds.* Magnetic Resonance in Epilepsy. NY: Elsevier Chap 2

⁷¹Assaf, Y. & Pasternak, O. (2008) Diffusion tensor imaging (DTI)-based white matter mapping in brain research: a review *J Mol Neurosci.* vol 34(1), pp 51-61.

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neural conduit and the proper juxtaposition of two neural conduits to form an Activa. The neuron is the smallest living cell associated with the neural system. However, it is sometimes an incomplete functional unit since the myelin wrapping of the conduits is generally supplied by a distinctly separate cell. **Section 5.xxx** [xxx ne section 10.4.4 in vision] discusses this rationale in more detail.

Five functional types of neurons have been defined in this work that relate to the visual system.

- + Signal detection (neuro-secretory) neurons
- + Signal manipulation neurons
- + Hybrid neurons
- + Projection neurons
- + Neuro-muscular neurons

The only other significant class of neurons appears to be the neuro-secretory neurons related to genesis, growth (through the preparation of hormones) and metabolism. Except for those neurons involved in signal detection, the functional aspects of the neuro-secretory and neuro-muscular neurons will not be explored here.

The only type of signal detection neuron of interest here is the photoreceptor cell. These will be mentioned briefly for continuity. Their cytology is discussed in detail in **Chapter 4** and their operation is discussed in detail in **Chapter 12**. The signal manipulation neurons include the greatest functional variety of neurons and these will be discussed in detail. The hybrid neurons consist of two types, those that encode electrotonic (analog) signals into pulse signals and those that perform the inverse function. The first are defined as ganglion cells and the latter are defined as stellate cells. Projection neurons are those types that receive pulse signals at their input terminals and regenerate those signals at their output. The vast majority of the neurons in any neural system receive and deliver electrotonic (analog) signal waveforms. It is only the hybrid and projection neurons that treat pulse type signals (action potentials).

The definition of six stages within the operational neural system is compatible with a variety of signaling paths within the neural system. This includes the signal paths from sensory cells at the extremes of the peripheral nervous system to the brain as well as those within the brain, and those that return from the brain to the muscular-skeletal system.

A characteristic that is not explicit within the definition of these stages is the type of electrical signals found therein. All of the stages of neural signaling involve electrotonic (analog) waveforms except stage 3. Stage 3 alone uses phasic (pulse) signaling. The waveforms found within stage 3 circuits are described as action potentials. It should be noted again that **over 95% of the neurons within any animal are electrotonic and do not involve action potentials.**

The retina has frequently been considered a part of the central nervous system. It shows a similar (but not identical) layered structure like that of stages 4 and 5 cortical tissue. However, there is no contiguous membrane between the retina and the CNS sharing this layered structure. Hence the similarity in layered structure is based more on functional requirements than morphology. The retina is multilayered to accommodate stage 2 signal processing. The cortex is multilayered to accommodate the signal manipulation performed in stages 4 and 5.

The majority of the discussion concerning individual types of neurons will not address how they are connected to nearby neurons. It will be assumed that this is accomplished by electrolytic junctions. These junctions are frequently described as gap junctions, tight junctions or electronic junctions. A narrow definition of the (gap) junction associated with a synapse will be used here. The details of the junction between neurons, the synapse, will be addressed in **Sections 3.4 & 10.4 xxx**. This discussion will also focus on the quiescent or static parameters of the neurons. Their dynamic parameters will be examined in detail in the second half of **Chapter 10 xxx**.

Initially, this work attempted to model the neurons as general purpose circuits of unknown complexity, similar to man-made operational amplifiers. This was found to be unnecessary when the simplicity of the circuitry of each neuron was determined. The active element of

each circuit was then analyzed as to their electronic form, e. g., voltage controlled or current controlled devices. It was quickly determined that all of the active devices within the neural system could be characterized as of the current type and consisted of PNP class of active semiconductor electronic devices. ***Based on this work, there was no need to emulate the active devices of the neural system by complex networks of man-made active devices as found previously in the literature.*** The complete neural system can be represented by a highly replicated network of strings of remarkably simple individual circuits.

The various neuron configurations defined in this Chapter can generate signal waveforms in excellent agreement with the data base in the vision literature. These waveforms will be discussed and compared in the second part of **Chapter 10 xxx**.

4.4.1 Categorization of neurons by stage and function

[xxx pick up material from end of Chapter 2]

At a cursory level, the apprentice histologist finds "pyramid cells" in every layer of the CNS tissue. Only later does he find this classification unsatisfactory. The shape of the soma is not relevant to the operation of the neuron. The shape is only suggestive of the space available for packaging. Where space is not critical, the apex of the pyramid cell is the location of the arborization associated with its non-inverting (dendritic) electrolytic input terminals. Around the "base" of the pyramid cell are the arborizations associated with the inverting (poditic) electrolytic input terminals of the cell. Internally, the region near the base is the location of the Activa, the active electrolytic amplifier within the cell. The axon or output terminal of the neuron usually emanates from the center of the base of the pyramid. In cells functioning without using the poditic terminals as input circuits, the nominal pyramid cell is described morphologically as a bipolar (two ended) cell. In other cases, the nominal pyramid cell is described as an amercine (axon-less) cell.

Some "pyramid cells" interface with other neurons through as many as several thousand synapses divided between its various arborizations. In other cases, bipolar "pyramid" cells may employ less than five synapses on only a single dendrite (primarily to achieve a low electrical input impedance). Estimating the total number of neurons and synapses within a human CNS is not productive but 10 billion neurons is a commonly repeated number and Hawkins has given an estimate of 30 trillion synapses (page 48).

Some "pyramid cells," both within and outside of the CNS, generate action potentials as part of their stage 3 functional responsibilities. However, the vast majority (>98%) of "pyramid cells" only exhibit analog (or tonic) waveforms at the pedicles of their axons. These are the signal sensing, stage 1, and signal processing neurons of stages 2, 4 & 5.

In this section, the term function will be used in a much more precise mode than it is usually used in morphology and biology. Where the biologist frequently defines a type of neuron conceptually by the function it "mediates," the function of a neuron will be defined here in one of two more concrete ways. The first is how it modifies the (multiple) signal waveforms presented to it. The second is how it oscillates, either in free-running mode or in response to an instigating signal.

Books traditionally describe an abbreviated set of morphological types of neurons suitable to the purposes of the author. These sets are frequently incompatible. The most fundamental problem with such lists is their focus on the nucleus of the cell as a point of departure. This element has virtually no role in the function of the cell as shown in **Chapters 10 & 11**. As a shining example, the description of a neuron as monopolar, because it has only one appendage on the soma, is completely irrelevant to the function of the neuron. The so-called bipolar neuron actually has three appendages, although one may be difficult to see in the absence of electron microscopy. Similarly, an amercine cell has a fully functional axon, although it may be packaged with one of its neurites for anatomical efficiency. Steriade, et. al.⁷², and Pannese⁷³ provide a variety of morphological images of neurons that can be easily understood based on their electrical functions and electrolytic properties, as developed in **Chapter 8** and this chapter.

⁷²Steriade, M. Jones, E. & Llinas, R. (1990) Thalamic oscillations and signaling. NY: John Wiley, pp 132-133

⁷³Pannese, E. (1994) Neurocytology. NY: Thieme, pp 5 & 80-116

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A problem arises immediately with regard to the adaptation amplifier within the photoreceptor cell. A decision must be made as to whether a change in amplification associated with the adaptation amplifier should be considered signal processing and be discussed as a Stage 2 function or whether it should be considered an integral part of the Stage 1 function. Considering all of the functions occurring within the photoreceptor neuron as Stage 1 functions leads to a simpler model. With this question resolved, the earlier definitions regarding each stage can be definitized.

Although there are many idiosyncrasies associated with the physical structure of visual neurons, leading to difficulty in determining their proper morphological classification, **Figure 4.4.1-1** defines the more significant functional types to be addressed in the following chapters. A Type Designator is assigned to them for ease of cataloging. The common names are those usually found when discussing the visual system of chordates, probably the most sophisticated of the neural systems. Several names commonly used when discussing non-chordates can be added to the table. The reticular neurons can be listed as receptor neurons and probably contain the same internal circuitry as the photoreceptor cells. In the context of this work, the eccentric neuron of *Limulus* is a stage 3 projection neuron with its input structure performing stage 2 signal processing and its output structure encoding the resulting signals. This suggests it is functionally a ganglion neuron in the above table.

Shepherd has provided a good example of the fact that investigators examining the neural systems of different species have found it convenient to assign arbitrary names to the neurons of a sensory system⁷⁴. Only a cursory understanding of the signal flow within the systems is displayed in his figure that dates from 1978. Comparing the visual and olfactory sensory systems, horizontal cell is equated to periglomerular cell, amacrine cell is equated to granule cell, and ganglion cell is equated to mitral cell. No counterpart is shown for the bipolar cell of the visual system. The endless proliferation of morphological names found in the literature for the same functional element cannot be summarized here. It must be left to the reader to translate these designations as he encounters them.

⁷⁴Shepherd, G. (1988) Neurobiology, 2nd ed. NY: Oxford University Press pg 214

Class	Type	Common Name	Purpose/Features
In Chordata			
Stage 1 Signal Detection			
Receptor	AT	Photoreceptor (Vibrissal cell) (auditory cells) (vestibul. cells)	{ Adaptation Amplifier; strip line form, exponential internal feedback, collectors in parallel { Distribution amplifier; current to voltage converter
	AD		
Stage 2 Signal Processing (within PNS)			
	AB	In-line/Bipolar	Summing and isolation amplifiers; non-inverting
	AL	Lateral (Horizontal) (Amercine) (Pyramid)	Differencing amplifiers with two inputs; internal feedback
?	AX?	Interplexiform	Putative external feedback amplifier; from amercine to horizontal neurons
Stage 3 Signal Projection			
Signal Encoding	AG	Ganglion	Encoding: analog input to pulse output, internal feedback, oscillatory, action potential generator
Signal Decoding	AR	Stellate	Decoding: pulse input to analog output, capacitor integrator
Sig. Regenerator	AN	Node of Ranvier	Regeneration of action potentials
Stage 4 Signal Manipulation (within CNS)			
Signal correlation	AS	Sense amplifier	Sums signals in multi-dimensional correlators, found in LGN, PGN, pulvinar & cerebral cortex
Stage 5 Information Manipulation (within CNS)			
Stage 6 Action initiators (within PNS)			
Muscle Activation	AM	End plates	Decodes action potentials at high current level
Enzyme secretion	?	?	Secrete enzymes after decoding action potentials

Figure 4.4.1-1 A tabulation of neuron classes and their common names based primarily on the visual system. See text. The existence of an interplexiform neuron supporting external feedback in the retina is questionable. The orderly naming of neurosecretory neurons has not been pursued in this work.

The receptor neurons of Chordata appear to exhibit the full range of neuro-secretory functions available to the neuron. The ability of the photoreceptor neurons, the vibrissal neurons and the hair cells of both the vestibular system and the auditory system to secrete a protein is well established. These proteins form mechanical structures that support the sensory function. It is likely all these neurons exhibit the same internal topology as photoreceptor neurons, as this would explain their ability to vary their sensitivity significantly with stimulus intensity. It is likely that the receptors of taste and smell also secrete proteins.

The horizontal and the large group known as amercine neurons are all lateral cells in that they accept signals from neurons carrying signals from different spatial locations (which may also exhibit chromatic differences within the retina). They combine this information using a variety of algorithms that vary with their specific role (Chapter xxx). Pyramid neurons are lateral neurons that are found elsewhere in the PNS.

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The ganglion neurons of stage 3 exhibit a variety of individual features that will be described in greater detail in **Section xxx**.

The morphological descriptor's monopolar and bipolar do not relate well to the electrical performance of neurons and the morphological term monopolar will not be used in this Chapter. The bipolar name will be used to define a neuron primarily with respect to its in-line location in the retina between the photoreceptor cell and the ganglion cell in a signal path. This neuron is electrically monopolar (its signal waveforms proceed in only one direction from its resting potential when subject to an input stimulus) while it is morphologically bipolar.

Because of the fact that an active device may be formed upon the juxtaposition of any two membranes associated with neural conduits, amplification, in the broad sense, may occur at two different locations in the nervous system. It may occur inside a given neuron and also between two adjacent neurons. The Nodes of Ranvier are examples of multiple amplifiers within a single cell.

The circuit associated with the Active of Type AN (the N for Node of Ranvier), will be discussed briefly in **Section 3.3 xxx** because of its prototypical role in all signal projection and hybrid neurons within and outside of the eye.

- - - -

[xxx move most of this to section 4.4.1 of Chapter 4]

Five functional types of neurons have been defined in this work that relate to the visual system.

- + Signal detection (neuro-secretory) neurons
- + Signal manipulation neurons
- + Hybrid neurons
- + Projection neurons
- + Neuro-muscular neurons

The only other significant class of neurons appears to be the neuro-secretory neurons related to genesis, growth (through the preparation of hormones) and metabolism. Except for those neurons involved in signal detection, the functional aspects of the neuro-secretory and neuro-muscular neurons will not be explored here.

The only type of signal detection neuron of interest here is the photoreceptor cell xxx. These will be mentioned briefly for continuity. Their cytology is discussed in detail in **Chapter 4** and their operation is discussed in detail in **Chapter 12**. The signal manipulation neurons include the greatest functional variety of neurons and these will be discussed in detail. The hybrid neurons consist of two types, those that encode electrotonic (analog) signals into pulse signals and those that perform the inverse function. The first are defined as ganglion cells and the latter are defined as stellate cells. Projection neurons are those types that receive pulse signals at their input terminals and regenerate those signals at their output. The vast majority of the neurons in any neural system receive and deliver electrotonic (analog) signal waveforms. It is only the hybrid and projection neurons that treat pulse type signals (action potentials).

The above classification scheme supports a variety of signaling paths within the neural system. This includes the signal paths from sensory cells at the extremes of the peripheral nervous system to the brain as well as those within the brain, and those that return from the brain to the muscular-skeletal system. It also includes signaling paths within the central nervous system. The retina is appropriately considered a part of the central nervous system. In many morphological aspects, it is virtually identical to the rest of the cortex and the mid-brain. The hybrid and projection neurons are used to transmit signals among these cerebral units.

The majority of the discussion concerning individual types of neurons will not address how they are connected to nearby neurons. It will be assumed that this is accomplished by electrolytic junctions. These junctions are frequently described as gap junctions, tight junctions or electronic junctions. A narrow definition of the (gap) junction associated with a synapse will be used here. The details of the junction between neurons, the synapse, will be

addressed in **Sections 2.4 & 10.4**. This discussion will also focus on the quiescent or static parameters of the neurons. Their dynamic parameters will be examined in detail in the second half of **Chapter 10**.

Initially, this work attempted to model the neurons as general purpose circuits of unknown complexity, similar to man-made operational amplifiers. This was found to be unnecessary when the simplicity of the circuitry of each neuron was determined. The active element of each circuit was then analyzed as to their electronic form, e. g., voltage controlled or current controlled devices. It was quickly determined that all of the active devices within the neural system could be characterized as of the current type and consisted of PNP class of active semiconductor electronic devices. ***Based on this work, there was no need to emulate the active devices of the neural system by complex networks of man-made active devices as found previously in the literature.*** The complete neural system can be represented by a highly replicated network of strings of remarkably simple individual circuits.

The various neuron configurations defined in this Chapter can generate signal waveforms in excellent agreement with the data base in the vision literature. These waveforms will be discussed and compared in the second part of **Chapter 10**.

2.1.1 Categorization of neurons by function CONSOLIDATE into 4.1.1

In this section, the term function will be used in a much more precise mode than it is usually used in morphology and biology. Where the biologist frequently defines a type of neuron conceptually by the function it "mediates," the function of a neuron will be defined here in one of two more concrete ways. The first is how it modifies the (multiple) signal waveforms presented to it. The second is how it oscillates, either in free-running mode or in response to an instigating signal.

Books traditionally describe an abbreviated set of morphological types of neurons suitable to the purposes of the author. These sets are frequently incompatible. The most fundamental problem with such lists is their focus on the nucleus of the cell as a point of departure. This element has virtually no role in the function of the cell as shown in **Chapters 10 & 11**. As a shining example, the description of a neuron as monopolar, because it has only one appendage on the soma, is completely irrelevant to the function of the neuron. The so-called bipolar neuron actually has three appendages, although one may be difficult to see in the absence of electron microscopy. Similarly, an amercine cell has a fully functional axon, although it may be packaged with one of its neurites for anatomical efficiency. Steriade, et. al.⁷⁵, and Pannese⁷⁶ provide a variety of morphological images of neurons that can be easily understood based on their electrical functions and electrolytic properties, as developed in **Chapter 8** and this chapter.

There are many idiosyncrasies associated with the physical structure of visual neurons, leading to difficulty in determining their proper morphological classification. However, the neurons can be classified according to function much more easily. **Figure 4.4.1-2** provides an initial tabulation of the neuron types developed during this work. A Type designator will be assigned to them for ease of cataloging. Many additional "common names" can be added to the Common Morphological Name category. Appendix B provides independent data sheets (modeled after conventional transistor data sheets) on each of the neuron types using this table and the type designations.

⁷⁵Steriade, M. Jones, E. & Llinas, R. (1990) Thalamic oscillations and signaling. NY: John Wiley, pp 132-133

⁷⁶Pannese, E. (1994) Neurocytology. NY: Thieme, pp 5 & 80-116

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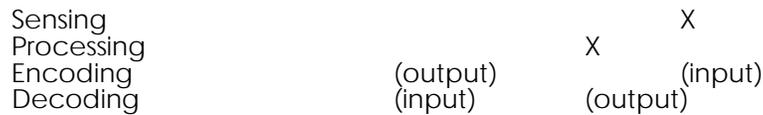
Stage	Functional Classification	Type	Common Morphological Nname	Purpose/Feature(s)
In Chordata				
1	SIGNAL DETECTION Receptor	AT	Photo/Phono/Chemo receptor, etc. Reticular cells in non-chordates	Asym. differential amplifier with high gain adaptation amplifier & unity gain distribution amp.
2,4,5,6	SIGNAL MANIPULATION Signal Process.	AB	Bipolar	Low output impedance distribution amp.
		AL	(Horizontal Amersine Pyramid)	Differential amplifiers with two inputs & internal feedback
	Signal Transfer	BS	Synapse	Active diode with unity gain (unidirectional <i>in-vivo</i>)
4	SIGNAL CORRELATION Sense Amplifier	AS	---	Long neurites, used in striated areas; PGN, LGN, pulvinar, occipital lobe etc.
3	SIGNAL PROJECTION Signal Encoding Signal Decoding Signal Regen.	AG AR AN	Ganglion Stellate xxx Node of Ranvier	Analog input, pulse output Pulse input, analog output Pulse input, pulse output
7	NEUROAFFECTORS Paracrine Endocrine Exocrine	AM	End plate exciters Glandular cells ---	Releases acetylcholine or Nitric Oxide Releases wide variety of hormones Releases a variety of enzymes, pheromones, etc.
Special Cases, Hybrids				
CARDIOCYTES				
	Timing gener.	CA	Nodal cells	Generate cardiac timing signals
		CB	Purkinje bundle cells	Distribute timing signals
		CC	Muscle cells	Excite sarcomere & relay timing sigs.
OTHER				
		DA	Eccentric Cell	Provides both stage 2 signal processing and stage 3 encoding in simple animals like <i>Limulus</i>

Figure 4.4.1-2 Tabulation of neurons by function. Some labels are incomplete

[[integrate into the above table]]

Class	Type	Suprathreshold (all or nothing)	Subthreshold (sustained or electrotonic)
Projection		X	
Myeloneurons		X	?

Interneurons



The horizontal, amercine, pyramid and interplexiform cells (if the latter exist) form part of a large group defined as signal manipulation neurons in this work. The signal manipulation capability of the eccentric cell of *Limulus*, and some other primitive animals, are special. They can be placed in this group with regard to their signal manipulation capabilities but they also exhibit a signal encoding function and are also classified as hybrid cells.

The morphological descriptor's monopolar and bipolar do not relate well to the electrical performance of neurons and will not be used in this Chapter. The Bipolar name will be used to define a neuron primarily with respect to its location in the retina between the photoreceptor cell and the ganglion cell in a signal path. This neuron usually exhibits an electrically monopolar waveform; i. e., proceeding in only one direction from its resting potential when subject to an input stimulus.

Because of the fact that an active device may be formed upon the juxtaposition of any two membranes associated with neural conduits, amplification, in the broad sense, may occur at two different locations in the nervous system. It may occur inside a given neuron and also between two adjacent neurons. The Nodes of Ranvier are examples of multiple amplifiers within a single cell.

The signal decoding neuron, labeled type AR, will be described by the functional classification, stellate neuron. The common morphological name stellate neuron has been used to identify almost any neuron that does not appear to be bipolar in geometry. Thus, the term stellate neuron is essentially useless in discussing the neural system among a group of investigators.

The circuit associated with the Activa of Type AN (the N for Node of Ranvier), will be discussed briefly in **Section 2.3** because of its prototypical role in all signal projection and hybrid neurons within and outside of the eye.

4.4.2 The electrotonic, or analog, neurons SHRINK OR MOVE FOLLOWING SECT.

The neurons exclusively involved in processing analog signals within the retina are, in order of complexity, the bipolar, lateral and photoreceptor cells of vision. They perform signal detection and a variety of signal manipulation functions. Similar analog neurons occur in the mid-brain, the cortex and elsewhere in the neural system. The primary signal manipulations involve the summing and differencing of voltage mode signals. All of the signal detection and manipulation neurons are derived from the basic topology of the bipolar neuron (which corresponds to the fundamental neuron of the previous Chapter when the poda impedance is minimal in value and insignificant in function).

In the following discussion, it will be seen that some of the signals are reversed in polarity as they pass along the signal path. This functional process removes any correlation between the nature of the signal and the concept of hyper- or de-polarization with respect to the signal at a given point. It will be shown that the direction of the potential change due to increased excitation of the eye by photons depends on the circuit under discussion. For the photoreceptor cells, increased excitation always results in a negative going potential change, a hyperpolarization. For the bipolar cells, the same excitation causes a negative going change, a depolarization. For the lateral cells and the ganglion cells, the situation is more complex and only anecdotal evidence (based primarily on after effects as detected by Bidwell's disk, etc.) is available. In general, it appears that the lateral cells produce a negative going change in output potential, a hyperpolarization, in the presence of increased excitation of the M- spectral channel. For illumination concentrated in the S- or the L- channel, the same increase in illumination results in a reduction in output potential, a depolarization.

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4.4.2.1 Bipolar Cells

The bipolar cell is the simplest extension of the second order cell defined in **Chapter 8** and therefore one of the simplest of neuron types. They are also the basic templates from which all of the other neurons can evolve. In the general case, the bipolar neuron acts as an isolation amplifier in the overall signal processing environment. In this mode, it is configured to accept multiple input signals and generate multiple output signals without causing impedance problems in the cells associated with it.

4.4.2.1.1 The Topology of the Bipolar Cell

The general morphology of the bipolar cell is straight forward although it is sometimes difficult for investigators to definitively describe the end structures associated with the dendrites and axons. The general cytology and topology of the bipolar cell is shown in detail in **Figure 4.4.2-1(a)**. This figure can help in understanding the morphology as well as the topology of the cell. The dendritic conduit of the cell is shown on the left. The wall of the conduit consists of several zones reflecting different types of BLM. Most of the wall acts as a simple insulator to the flow of all fundamental charges, ions and large molecules. It is probably made up of a symmetrical bilayer membrane at the molecular level. In areas juxtaposed to various other neurons, the cell wall consists of a zone(s) of asymmetrical bilayer membrane exhibiting an electrical characteristic typical of a diode. The area of this diode is a parameter controlling the reverse cutoff current of the diode and therefore its impedance. Two active connections to other neurons are shown as well as one potential or failed connection. Also shown is a zone of the BLM associated with the electrostenolytic process establishing the quiescent potential of the dendroplasm with respect to the surrounding matrix. Finally a zone is shown where the dendritic conduit is juxtaposed to the axon conduit. This juxtaposition comprises the Activa within the neuron. The axon conduit is shown to consist of a similar set of zones of BLM. The majority of the BLM is probably symmetrical at the molecular level and an insulator. One area is shown supporting an electrostenolytic function for biasing the axoplasm. Two areas are shown as connecting to following neurons.

The juxtaposition of the two conduits and the associated electrical path to the surrounding matrix through the podaplasm allows the Activa to function as an active electrical device when it is properly biased. It appears from the literature that, in the bipolar neuron, the base connection of the internal Activa is connected to the surrounding fluid environment via a low impedance path. This condition removes internal feedback as a factor in the operation of the bipolar neuron. However, the poditic battery or an additional electrostenolytic process associated with the poda may be important in establishing the overall bias structure of the cell. The dendrite is seen to exhibit one or more input sectors along its surface and it is conceivable that in certain physical locations the surface of the dendrite is a continuous Activa providing synapses anywhere along its length that is needed. Such a continuous or quasi-continuous surface is found in the photoreceptor neuron. In the figure, three conceptual inputs are shown:

- + an input from the output sector of a photoreceptor cell,
- + an input from the output sector of a second photoreceptor cell, or alternately from a horizontal cell, and
- + a failed input due to the failure of the two diodes to establish a common base region, e. g., achieve the ideal juxtaposition.

The last case is merely illustrative. If the two diodes do not establish a common base, no transistor action can occur and the diode associated with the dendrite will exhibit a high input impedance relative to the possible current from the potential input since it is reverse biased relative to the interneural plasma in that area. In the other two cases, the diodes of the dendrite are reverse biased but current is transferred into the dendroplasm by transistor action. In the absence of transistor action, a sector of the dendrite may act as a power source wherein the battery provides a potential to the dendroplasm relative to the surrounding interneural plasma. However, it cannot act as an input sector due its high impedance to input currents.

4.4.2.1.2 The Electrical Circuit

Figure 4.4.2-1(b) shows the electrical circuit of this cell. This circuit is a non-inverting current repeater for all input signals. The current delivered by the collector into the axoplasm is essentially identical to the current entering the emitter of the Activa. However, the delivered current may be at a higher impedance level, thereby providing power gain.

In the absence of input current, the circuit of the bipolar neuron is usually biased near cutoff by the various batteries and electrostenolytic processes involved. The axoplasm is therefore at its highest potential under quiescent conditions, i. e. fully polarized. Upon the application of a signal, the axoplasm becomes depolarized, the voltage relative to the interneural plasma drops.

The output current from the Activa is the sum of the input currents from all of the individual input sectors. Because of the presence of the load impedance associated with the axon power source, and possibly the output connections, the axoplasm exhibits a voltage relative to the surrounding medium. This voltage can be used to generate a current passing through any of the output sectors of the axon. If the contact with the proximal cell is intimate, transistor action will occur and signal amplification can occur at this junction, i. e., an impedance change although the current amplitude will remain the same. In general, the signal voltage at the emitter of the proximal cell will represent the logarithm of the current entering the cell.

In other simple cells of this type, a second type of output is conceivable, and has been widely proclaimed. The cell could emit a chemical substance into one or more synapse regions in response to the voltage of the axoplasm. This is not believed to occur in the retina.

The Bipolar Cell is representative of the simplest type of neuron. It accepts multiple input signals via transistor action which effectively isolates the sources of those signals from each other and the cell. Similarly, it generates a voltage in the axoplasm that can be used to drive multiple output sectors without causing the signals in proximally related cells to become cross coupled. It does not provide signal inversion and the output voltages appear to be depolarizing. No chemically based neurotransmitters are required to support the transfer of a signal to subsequent circuits. This situation will be addressed in more detail in **Section 3.4.**

4.4.2.1.3 Signal summation in the dendroplasm

The topology of the basic bipolar neuron suggests the answer to another question. In active semiconductor devices of the current (as opposed to the field) junction type, it is possible and common to have multiple emitters associated with a single base. The effect of this arrangement is to provide a degree of isolation between the signals applied to the individual emitters. This does not appear to be the case in the bipolar neuron. The total input current into the dendroplasm is the sum of the currents from the individual input zones. The current associated with each zone is a function of the impedance of each of the zones and the voltage of the previous conduit axoplasm. Because of the topology of the upper frame, the lower left frame shows multiple input signal paths converging on a single emitter of the Activa. Each signal path provides a current that is summed at the emitter of the Activa.

4.4.2.1.4 The Π Network Model of the Bipolar Cell

At a more basic level of schematic, an active semiconductor device, such as the Activa, is frequently represented by a fundamental circuit configuration of electrical engineering, a Π -network. Such a network is capable of accommodating and displaying all of the significant circuit elements within a given device regardless of frequency or application. The basic Π -network for this circuit configuration is shown in **Figure 4.4.2-1(c)**. Note that the impedance, Z_2 between terminals 1 and 3 (which would complete the π symbol) is so high it is normally not shown in low frequency networks such as neurons. This element is basically an open circuit at frequencies below a megahertz for signal manipulation neurons.

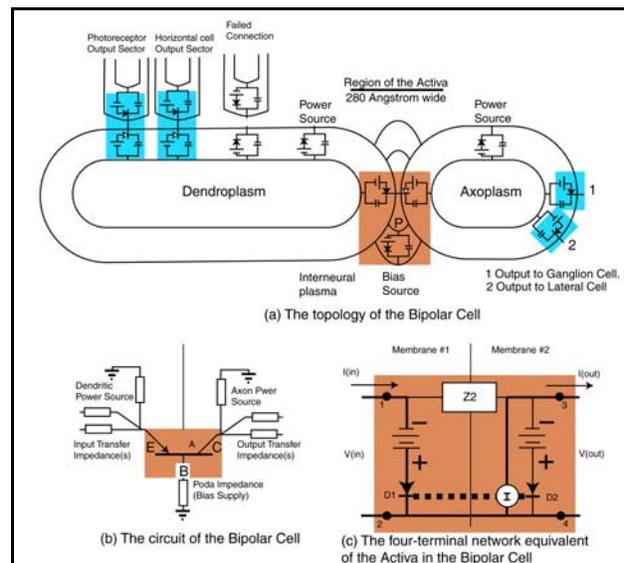


Figure 4.4.2-1 The topology of the bipolar cell. (A); the topology showing the interface with the surrounding circuits. (B); the schematic circuit of the bipolar cell. (C); the four-terminal network representation of the Activa within the bipolar cell.

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For purposes of emphasis, the two intrinsic voltage sources related to the membranes are shown explicitly. These voltage sources are internal to the Activa and distinguish it from a man-made transistor. They basically relate to the fundamental characteristics of an asymmetrical bilayer membrane immersed between two electrolytes, a critical element in the formation of an Activa. *It is important to note that these intrinsic BLM potentials are not necessarily the same or equal to the plasma potential they are commonly associated with.* In fact, each zone of a membrane may exhibit a different intrinsic membrane potential. In most cases, it is the potentials established by the electrostenolytic processes that control the operation of the circuit and not the intrinsic membrane potentials.

3.2.1.4.1 The unbiased Activa

In the absence of any external biases applied to the Activa, the input circuit consisting of the current path between terminals 1 and 2 can be represented by a small intrinsic potential and a diode. The output circuit can be represented by a similar battery and diode in series as shown between terminals 3 and 4. In this condition, the circuit between terminals 1 and 2 represents a high impedance in both directions. Similarly, the circuit between terminals 3 and 4 can be considered a high bidirectional impedance. There is no current through the current generator connected between terminals 3 and 4.

3.2.1.4.2 The biased Activa

If a significant positive voltage is applied to terminal 1 with respect to terminal 2, a current will flow through the input circuit. The value of this current will be controlled by the forward impedance of the input diode. In the absence of any external bias between terminals 3 and 4, no current will flow in the output circuit nor will there be any voltage between these two terminals except that due to the intrinsic potential associated with the output membrane.

If the bias between terminals 1 and 2 is removed and terminal 3 is made negative with respect to terminal 4, insuring that the diode is reverse biased, the impedance of the output diode will be high as represented by its reverse biased condition. No current will flow through the diode.

If a positive bias is applied to the input circuit and a negative bias is applied to the output circuit, a unique phenomenon occurs. A current appears in the output circuit essentially equal to the input current (typically greater than 99%) regardless of the potential between terminals 3 and 4 as long as it is maintained negative. This is the phenomenon of “transistor action” and it is suggested by the dashed line coupling the input diode to the output current generator. Note this generator is in parallel with the reverse biased output diode. The output circuit retains its high impedance characteristic regardless of the current through the generator.

It is important to note that the output current is of the same magnitude as the input current and flows in the same direction along the signal path as long as the input current forward biases the input diode. It is this fact that leads to the device exhibiting a transfer characteristic between its input and output that looks like a single diode. However, this transfer characteristic is only obtained when the device is biased as above. Otherwise, it exhibits a high impedance between terminal 1 and 3 under any condition.

4.4.2.1.5 The bias point of the bipolar neuron

The output potential of the bipolar neuron becomes more negative for increased levels of illumination applied to the eye. In the absence of illumination, the bipolar neuron is biased to a quiescent point compatible with the quiescent point of the photoreceptors connecting to it and the dynamic range required to support those photoreceptor cells.

3.2.2 The lateral and interplexiform Cells

In this work, a lateral cell is defined as a neuron with two distinct input structures that makes it capable of performing analog subtraction between two input signals. Such a neuron can assume a variety of morphological forms while still maintaining this fundamental capability. Lateral cells are frequently described by the morphological designations of horizontal, amercine and pyramid cells.

3.2.2.1 The definition and absence of interplexiform neurons

The interplexiform cell has been carried in this discussion to represent a cell that supports external feedback between cells of the retina. Discussions of such a cell have appeared occasionally in the literature. In the

course of this study, no definitive need for or example of a cell supporting external feedback has appeared. Therefore, this type designation will be dropped. On the other hand, the occurrence of internal feedback within a neuron is nearly universal and quite important.

3.2.2.2 The horizontal, pyramidal and amercine neurons

The horizontal cells and amercine cells belong to a distinctive class of cells, the lateral signal processing cells (or the lateral cells), used for signal processing in the retina and exhibiting a possibly unique characteristic in the neural system, at least outside of the brain. This class also includes the pyramid cell. These cells frequently vary in their degree of arborization. However, their basic functional characteristics are the same.

3.2.2.2.1 The topography (morphology) of the lateral cells

These cells exhibit two independent input structures that are not summed algebraically at the dendritic input to the Activa. They exhibit two input structures that appear similar to a histologist but seem to enter the cell at distinctly different locations. One is the conventional dendrite structure normally connected to the emitter of the Activa. The second neurite, the pseudo-dendrite or *podite*, is a similar structure but it connects to the base structure of the Activa. This characteristic provides a new dimension of circuit flexibility to the neuron. Shepherd⁷⁷ shows a good electron-micrograph of a cell of this class which he credits to his co-workers, Hersch and Peters. Unfortunately, it is imbedded in a surrounding structure that is not related to the functional aspects of the cell itself. The cell is labeled a pyramidal cell with an apical dendrite and a basal dendrite (podite) as well as the normal axon hillock and other conventional structures, **Figure 4.4.3-1**. The plane of the micrograph does not appear to contain the Activa. However, it is reasonable to say the dendrite and the axon are separated by structures related to the podite. To demonstrate the unique functional role of the two arborizations, it is necessary to examine their role in the cytology of the cell at x50,000 or better under an electron microscope.

The above figure can be compared with **Figure 4.4.3-2** showing the proposed idealized structure of the same type of cell at the cytological level (although at a slightly different orientation).

There is little discussion in the literature concerning a variety of lateral cell morphologies found near the pedicels of the photoreceptor cells at the distal edge of the inner nuclear layer. It is generally written that these cells are typified by the horizontal neuron with two fully arborized neurite structures. The same cannot be said of the lateral cells found proximally to the bipolar cells in the inner nuclear layer. At least six different types have been described in a single paper in the literature. These cells are frequently described as pyramid cells, amercine cells with no axon, and fully arborized lateral cells similar to the horizontal cells. It will be seen that these variations in morphology are due to the different functional role of these types of neurons

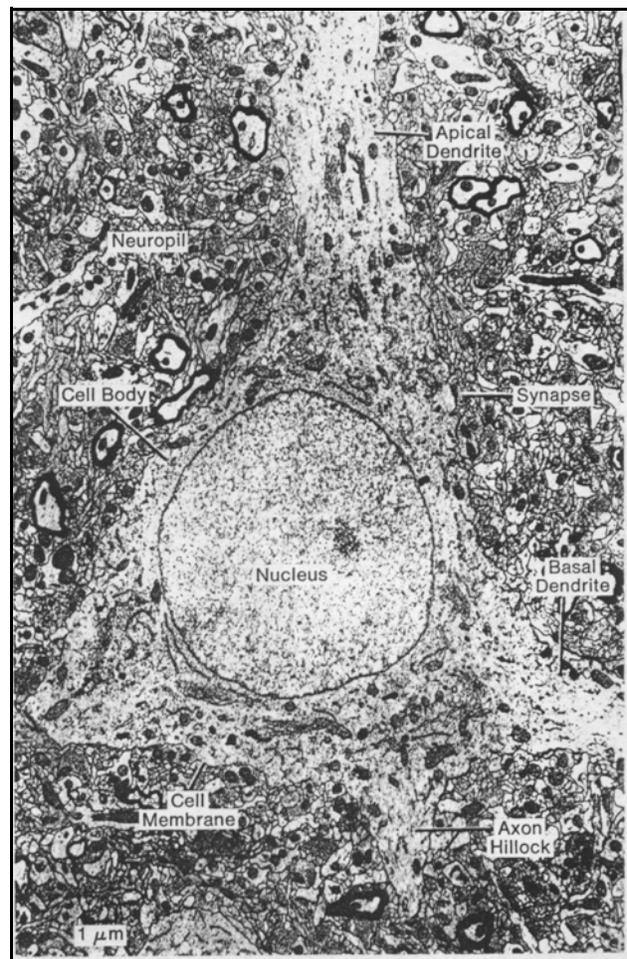


Figure 4.4.3-1 CR Electron micrograph of a pyramidal cell. Note the apical dendrite at the top, the basal dendrite (podite) at lower right and the axon exiting via the hillock at the bottom. In Shepherd, 1988, courtesy of Hersch & Peters.

⁷⁷Shepherd, G. (1988) Neurobiology. NY: Oxford University Press pg. 43

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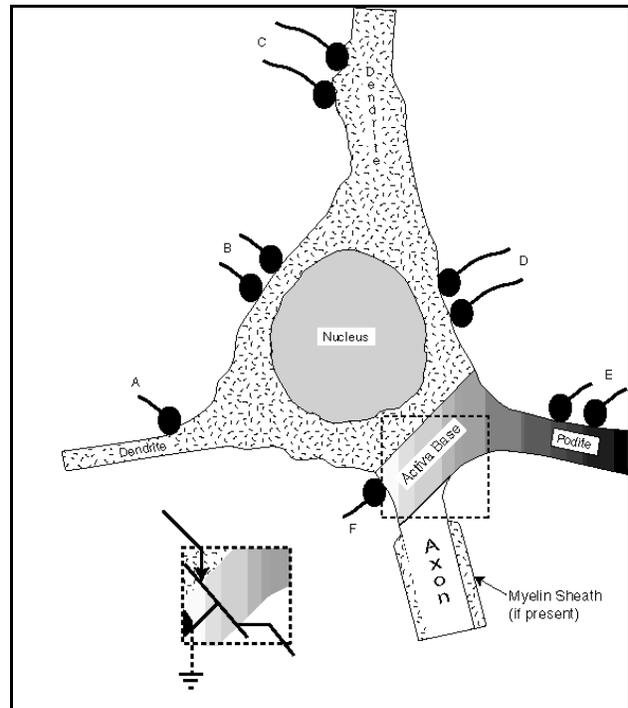


Figure 4.4.3-2 The cytoplological organization of a pyramidal cell. The structure labeled podite corresponds to the basal dendrite of the previous figure. The expanded inset shows the electrical topology of the active base region separating the dendritic structure from the axonal structure in the area of the hillock. A variety of synapses are shown interfacing with this cell. Note the synapses labeled E and F support inverting signal paths.

Dacey & Lee show several beautiful three-dimensional mappings of cells in this class, **Figure 4.4.3-3**. They carefully differentiate between the arborization of the dendritic conduit and the arborization of the poditic conduit which attaches to the soma at a distinctly different location.

3.2.2.2.2 Location of the lateral cells within the retina

From an overall signal circuit point of view, the difference between the horizontal cells and the amercine cells is their location in the retina. The conventional wisdom being that the horizontal cells are located in the distal area of the inner nuclear layer of the retina and are connected to the output of the photoreceptor cells and the input of the bipolar cells. The amercine cells are located at the proximal edge of the inner nuclear layer, connecting to the output of the bipolar cells and the input of the ganglion cells. Both cells may also interconnect with members of their own subclass in order to provide additional signal summation over large regions of the retina.

The morphologist occasionally sees and occasionally sketches another type of lateral cell but he has no clear way to describe their electrical topology. It may be the morphologist is seeing these cells because of a preconceived notion or input from others that an external signal feedback path is needed in the retina. These cells are described as having their inputs in the proximal edge of the inner nuclear layer and their outputs in the distal edge of the inner nuclear layer. These are the interplexiform neurons addressed in **Section 3.2.2.1**.

The tendency in the literature is to ascribe to these cells a roll in external feedback within the retina. Although this may be the case, no requirement has been found in the later parts of this work to justify an external feedback path within the retina. Much more work will be needed to confirm the existence and true topology of an interplexiform neuron.

Some lateral cells do not exhibit a highly arborized input structure. This is particularly true of the so-called amercine cells located at the proximal edge of the inner nuclear layer. It also appears to be particularly true of the higher chordates, such as the primates, who have poorly developed second lateral processing matrices. These neurons are frequently labeled amercine cells. The name amercine cell is misleading since it is derived from the Greek for “no axon.” Both the horizontal and amercine cells are atypical morphologically because their internal topology is different. In many cases, the dendritic regions and axonal regions lay side by side within a single structure relative to the cell nucleus; or the axonal length is merely short because it is connecting to a nearby dendrite. This is particularly common in cells located at the proximal edge of the inner nuclear layer. It appears that this may be a feature related to their signal processing role. Some of these cells appear to be involved in time difference signal processing. This processing involves collecting signals from remote neurons and subtracting it from other signals collected locally.

3.2.2.2.3 The functional characteristics of the lateral neurons

The lateral neurons exhibit intrinsic *internal feedback* due to the impedance of the poda circuit. ***This feedback is normally negative in these neurons*** (as opposed to the positive internal feedback found in the ganglion cells to be discussed below).

Briefly, the purpose of this class of cells is to perform algebraic summation in a circuit configuration capable of signal inversion (resulting in algebraic subtraction). Depending on the impedances involved, the cell can do this summation in the algebraic realm resulting in common addition and subtraction; or the cell can do this summation in the logarithmic domain resulting in *signal multiplication and division*.

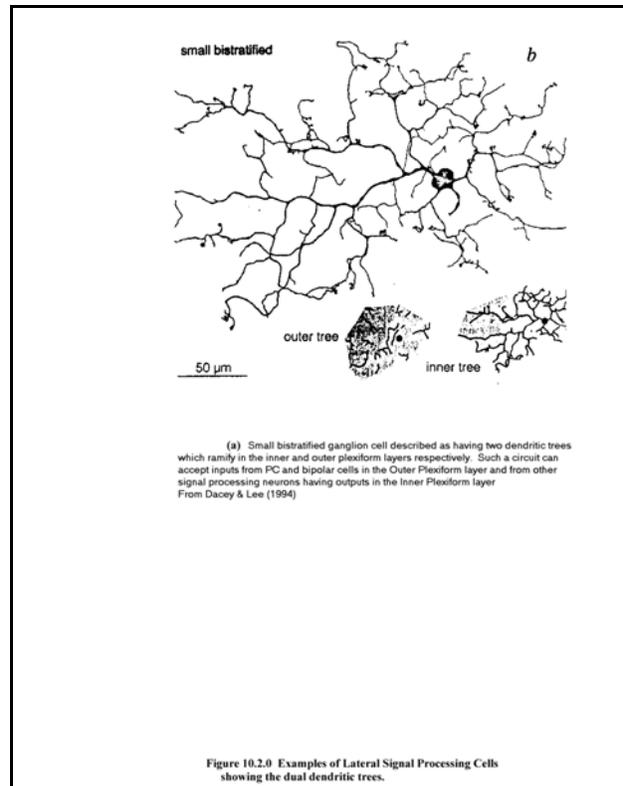


Figure 4.4.3-3 Examples of lateral signal processing cells showing the dual neurite (dendrite and podite) arborizations.

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By combining these operations, these cells are able to exhibit the wide range of output signals and resulting psychophysical conditions found in the literature.

A variety of morphological layouts for these types of cells can be found in the literature. **Figure 4.4.3-4(a)** illustrates the basic topological design. The cell is topologically similar to a bipolar cell except the poda region is expanded and includes signal input points. Thus, the podal region has taken on the same characteristics as the dendritic portion. The cell frequently appears in the literature to have two independent dendritic trees which will be differentiated here by describing them as the dendritic tree and the poditic tree.

There are also cartoons of many lateral cells in the literature which appear to have both input structures and output structures located along the same arm of the neuron, and often along both arms of the neuron.

Figure 4.4.3-4(b) presents the circuit diagram of a nominal Lateral Signal Processing Cell. It is only slightly modified slightly from the physical configuration of the Bipolar Cell. The main circuit difference consists of the poditic conduit providing a signal connection on the surface of the podalemma to the base terminal of the Activa. The functional difference is much greater than the physical difference for a number of reasons. Whereas the poda impedance in the bipolar neuron is of negligible value and significance, it plays a significant role in the lateral cell:

- + The presence of a significant poda impedance introduces negative feedback into the circuit with respect to any signal applied to the emitter terminal. This feedback normally introduces a loss in amplification with respect to the input signal over what would otherwise be obtained.

- + The presence of a significant poda impedance allows a signal to be introduced into the base terminal of the Activa. This alternate input signal can be derived from a voltage divider network between the poda impedance and the source impedance of this alternate signal. Although this signal does not suffer from any diminution due to negative feedback, it may suffer degeneration due to the ratio of the base input impedance and the emitter input source impedance.

- + The signal introduced through the base terminal is in phase opposition to any signal introduced via the emitter terminal, e. g., the net output is the difference between these two input signals.

- + The calculation of the net signal output is complicated by this differencing due to the phase of the two signals and the complex effective input signal amplitudes due to feedback on one hand and degeneration on the other.

The overall performance of this circuit is highly dependent upon the impedances found in the various circuit elements, the bias voltages applied and the recognition that the Activas involved are operating under large signal conditions. The detailed composition of the various membrane walls is an important characteristic of the overall cell. By varying the makeup of the phosphoglycerides in the membranes as a function of location, locations can be optimized as insulators, power sources, load impedances, signal input points and signal output points. The topology provides a great degree of flexibility with regard to the voltage sources. The principal criterion is that a given location of the neuron wall must be forward biased if it is to act as a signal output point and it must be reverse biased if it is to act as a signal input point. This bias is not determined by the membrane alone at that location; it is the net voltage applied to that membrane due to its internal as well as other voltage sources. This fact illuminates *the importance of not disturbing the cell or its surrounding interneural plasma* if results are desired that reflect normal cell operation.

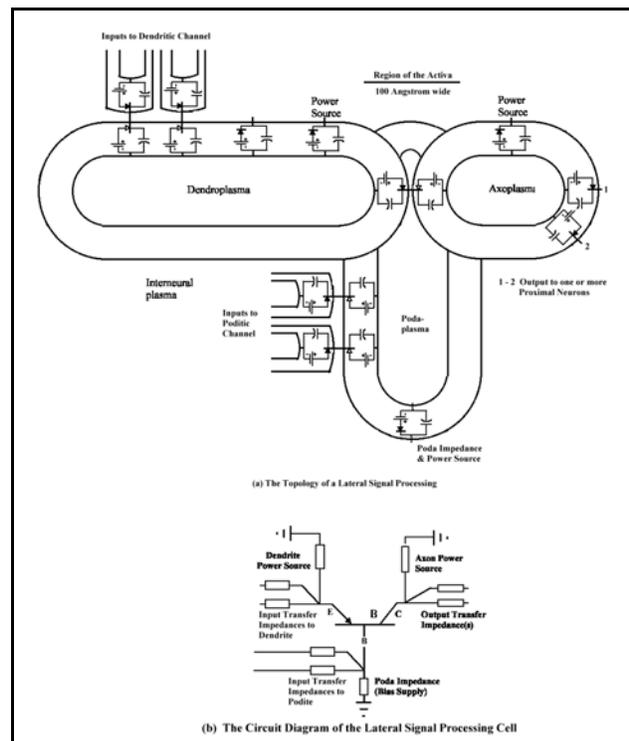


Figure 4.4.3-4 The topology and circuit diagram of the lateral cell. (A); the topology of the cell. (B); the circuit diagram of the lateral signal processing cell.

3.2.2.2.4 An alternate morphology of some lateral (amercine) cells

As will be discussed in detail in the following sections, some lateral cells associated with the 2nd lateral processing matrix may not require a significant level of arborization in either their dendritic or poditic input structures. Where they are employed in spatial filtering, they may only be differencing signals already aggregated by preceding bipolar cells. This limited role allows the employment of a simpler morphology for the cell.

Figure 4.4.3-5 shows an alternate topology illustrating how easy it is to obtain a structure that appears to have no axon; in which a portion of a dendrite (or in this case a podite) and a portion of an axon are wrapped within a single exterior cell wall for an extended distance. Clearly, the topology will accommodate almost any morphology. As an example, the axon region could be folded back along the dendrite also, resulting in a structure that had both inputs and outputs at each end--a configuration frequently shown in the literature. Each arm would then appear to a morphologist to have both input and output points along it. Only higher magnification examination would uncover the true nature of the structure, possibly using electron beam microscopy (as opposed to conventional electron microscopy) on living cells to expose the points, channels and directions of electron flow.

4.4.3 The phasic or pulse neurons EMPTY

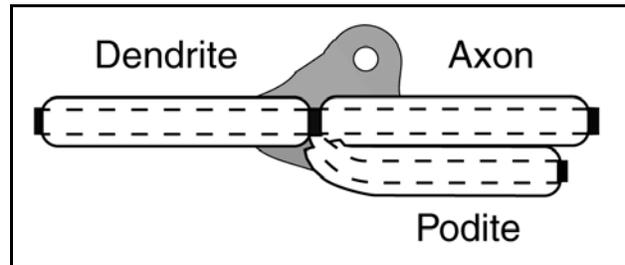


Figure 4.4.3-5 A common lateral neuron packaged to emulate a morphologically axonless (amercine) neuron.

4.4.3.xxx Notation for the ganglion neurons of vision

Investigators have chosen a wide variety of names to describe various ganglion neurons, usually without any concern for the functional parameters of the neurons. This practice is associated with exploratory rather than applied research. **Figure 4.4.4-1** provides a cross-index of the function and names associated with the ganglion cells in the publications of a few of these investigators.

Enroth-Cugell and Robinson described only two neuron types within the optic nerve of xxx in 1966⁷⁸. Boycott and Wasse used a different notation to describe only two neuron types in cat in 1974⁷⁹. Leventhal defined three distinct types of neurons in the optic nerve of monkey in 1981 but did not describe their functional significance⁸⁰. Wasse, et. al. identified the commonality between the X-Y and α - β classifications noted above⁸¹ in 1975.

After studying the various papers listed above, there is no obvious conflict among these designations. But the variety does lead to confusion, particularly when the abbreviations M and P are used to describe the neural paths within the optic nerve. Note the diametrically opposite designations when using M & P based on ganglion names versus the location these same neurons project to. The labels in the left-most column are consistent with those used in **[Figure 4.2.4-3 xxx]**. The designation R has been used to describe the neurons used to support the luminance signal path generated by stage 2 processing and that project to the magnocellular region of the LGN. The designation O, P & Q have been used to describe the neurons associated with the chrominance signal path generated in stage 2 and projecting to the parvocellular region. Y is used to describe those neurons associated with the signals from the foveola that are transmitted directly to the pulvinar (instead of the LGN) without

⁷⁸Enruth-Cugell xxx & Robinson, xxx (1966)

⁷⁹Boycott, xxx (1974)

⁸⁰Leventhal, xxx (1981)

⁸¹Wasse, H. Levick, W. :& Cleland, B. (1975) The distribution of the alpha-type of ganglion cells in the cat's retina. J. Comp. Neurology, vol. 159, pp. 175-193

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stage 2 encoding.

Pathway in Optic Nerve	Type of electrical Input to Ganglion	Ganglion name in this work	Ganglion projects to	Names in Selected Papers		
				Properties of Ganglia	Monkey (Leventhal,'81)	Cat (Boycott,'74)
R (brightness)	Monopolar	Parasol	Magnocel.	Y-like	A cells	α cells
Y (direct signals)	Monopolar	Parasol	Reticulocel.		A cells	
P & Q (chromin.)	Bipolar	Midget	Parvocel.	X-like	B cells	β cells

Figure 4.4.4-1 Correlation of ganglion cell names found in the vision literature.

4.4.4 The synapse and/or bouton arrays in information extraction

[xxx need some graphics in this section.]

As used here, a synapse is formed between two juxtaposed specialized areas of lemma, one on an axon and one on a dendrite. In some cases, the synaptic area is identified as being raised above the surface of the respective lemma whence it is identified as the pinnacle of a bouton. To date, no unique internal structure of a bouton has been identified. There are at least two, and probably three, fundamental architectures of synaptic couplings between neurons;

1. The simplest architecture is where a single axon is coupled to a single neurite in order to continue the propagation of an electrical signal along a single defined path. This architecture is frequently found as the inter-neural coupling between stage 3 signal projection neurons. It is very similar in architecture to the Node of Ranvier that is used intraneurally.
2. A commonly observed architecture involves one axon exhibiting a large number of synapses interconnecting with a large number of neurites. In general one specialized lemma of an axon interfaces with one similar specialized lemma area on either a dendrite or podite of a specific orthodromic neuron. Another specialized area of the axon connects with a second distinct specialized lemma on another neurite to form a distinctly different signaling path. This process may be repeated many times (possibly exceeding one thousand times) between a single axon and a great many neurons or conversely between many distinct axons and one or a few neurites.
3. At very high magnifications (using electron microscopy), the specialized areas of both the axon and the neurite have been shown to consist of arrays of synapses/boutons associated with only one axon and neurite. These arrays appear to be used to lower the overall impedance of the interconnection and mediate the transfer of greater amounts of charge between the axoplasm and the neuroplasm.

The second arrangement appears to be key to the parallel pattern matching mechanism used in the information extraction circuits of stage 4 and stage 5 engines. By employing essentially Boolean Algebra techniques, a large array of neurons can input signals from a large array of signals received from stage 2 neurons into a volume consisting of a cross-matrix of initial information extracting neurons. These initial information extraction neurons may be multiple in number. The result is that a single pattern associated with the incoming array is applied nearly simultaneously to a large number of pattern matching neurons in the cross-matrix. The interconnections between the axons and the neurites may be arranged so that a single neurite may report a specific pattern matching condition. By collecting these reports in a converging arrangement of initial information extraction neurons by a second set of neurons, a single signal can be created that provides very detailed information about the character of the originally introduced pattern.

To aid the above information extraction, the initial information extraction and the subsequent character extraction neurons may be bi-stratified; they may employ a distinct dendritic tree and a distinct poditic tree (with one of these trees (typically the poditic tree) introducing a subtractive function into the Boolean Algebra. This subtractive function is introduced after all of the signals from synapses on that tree have been summed. See **Section xxx** on stage 4 information extraction engines of this work.

The above method of comparing a large number of complex patterns essentially simultaneously appears to be the key to understanding the highly parallel (and time efficient) operation of the neural system. The method does not employ any transcendental calculations of the type usually assumed in man-made "Artificial Intelligence" networks. See Section xxx.

Similar techniques may be employed in stage 2 signal processing engines to optimize the transfer of information to multiple stage 4 engines simultaneously. They may also be employed in stage 5 cognition engines to efficiently combine information from multiple sensory modalities via the saliency map (as well as signals received from other stage 5 engines).

The morphological elements of the thalamus and the piriform areas of the CNS appear to employ the above form of parallel processing extensively but it is used throughout the CNS. The literature needs to be reviewed as to the extent that neurites with over an estimated 100 synapses per dendrite and/or neurite are found in a given area/volume.

4.4.5 The special purpose neurons *Loligo* EMPTY

A special purpose neuron has been developed to support the locomotion of multi-legged animals, snakes and other belly crawlers and swimmers. This is the type of neuron Hodgkin & Huxley studied in the squid, *Loligo*. It is designed to coordinate a large number of muscles so that they operate in a synchronous but time dispersed mode.

These neurons are believed to operate by chemical conduction along an axon exhibiting a large number of pedicles spaced at nominally equal intervals. As a result, the motor muscles connected to the sequential pedicles are caused to operate sequentially. It appears that the velocity of signal conduction along the axon can be controlled largely by electrical potentials. The waveforms expressed at the pedicles of the axon are analog waveforms of distinctive shape.

4.5 Additional tools needed to interpret the following material EDIT

It is helpful, when interpreting and evaluating the material in the following chapters, to have a good grounding in electronic practices. This section will address some of the more important concepts available from that field. The differences in performance between typical circuits under large signal and small signal conditions are particularly important in neuroscience. These differences will be addressed. It also becomes important to recognize that biological processes do not operate according to the reaction rate law defined by Arrhenius. They are restricted to the biological range of near the freezing point of water to less than fifty degrees centigrade.

4.6 The complexity & features of the neural architecture

The complexity of the architecture within the neural system varies considerably. Within the PNS, it begins with a very simple architecture among the stage 1 sensory neurons that closely follows the histological geometry of the specific modality. The sensory neurons of the auditory system follow a very simple mathematical equation dictated by the sound dispersion and transduction mechanisms employed within the cochlea. The visual sensory receptors generally follow a simple hexagonal packing arrangement with an element of a swirl to it. Virtually all of the sensory neurons exhibit the same internal topology and similar external topography except for their receptor area that interfaces with the modality specific transduction mechanism.

The stage 2 signal processing employed in the visual modality remains simple and follows directly from stage 1 (although varying somewhat with distance from the center of fixation).

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The architecture of Stage 2 of the olfactory modality is easy to recognize, however, stage 2 of the hearing modality rapidly becomes more complex and difficult to interpret without considerable electrophysiological test data. While many stage 2 neurons of vision and olfaction exhibit relatively simple bipolar or multipolar morphologies, those of hearing assume a wide variety of shapes. Many of these shapes have been given fanciful names that contribute little to understanding their functional role.

The definition and discussion of Stage 3 neurons, the action potentials and the specialized pulse neurons that process them will be delayed until Chapter 9. While action potential generating neurons are pervasive within the neural system, their numbers are small. The pulse processing (or phasic) neurons constitute less than 5% of the neuron population.

Omitting stage 3 for the moment, stage 4 within the CNS rapidly proliferates into a large number of individual engines for each modality that frequently involves a very complex set of interconnections between engines of the mesh configuration. **Chapter 15** will address some of the material in the following summary discussion in greater detail. The situation is similar for stage 5 and stage 6. An additional complication appears with regard to the cerebellum wherein engines associated with the afferent and efferent signal channels interact as part of a complex unconscious learning experience.

The complexity of the architectures of stages 4, 5 & 6 remain largely beyond human comprehension (other than for elementary traffic analysis). This traffic analysis has led to several first order concepts of CNS organization at various levels of detail.

Dehaene et al. have illustrated their conceptual view in cartoon form⁸². Their concepts are described as developing from the book by Baars⁸³. Dehaene et al. do not address any of the large number of engines associated with each of their labeled sectors. They do characterize the activity level within what they describe as "work space neurons" very usefully. The activity level was discerned after reviewing masses of data acquired during EEG, MEG and MRI experiments,

"In our simulation, workspace unit activation exhibits the following properties: (i) it is absent during routine tasks;
(ii) it appears suddenly when a novel, nonroutine task is introduced;
(iii) it varies semi-randomly during the initial learning of a novel task;
(iv) it is high and stable during execution of a known but not yet routinized effortful task;
(v) it decreases during routinization;
(vi) it resumes sharply following an error;
(vii) it is present during the delay period of a delayed-response task; and
(viii) it temporarily mobilizes, in a descending manner, other units involved in specific task components."

This listing is a very good summation of the activity by time interval that is developed below and in other chapters of this work. It corresponds to the steps in the context of learning, recalling from memory, evaluating and developing instructions for implementation by the conscious executive (generally associated with the prefrontal cortex). What it does not address is the role of the nonconscious executive engines, specifically the TRN of the thalamus, in detecting that some event has occurred that is not expected in the context of other events or has not been encountered before and been placed in memory after sufficient analysis. They discuss these activities in the context of the alarm (their vigilance), awareness (related to their conscious access) and analytical (related to their attention) modes associated with the sensory modalities of neural operation. Figure 2 of Dehaene et al. exhibits a strong analogy to **[Figure 15.1.1-1]** of this work, although it appears to combine the neurons of the saliency map and the analytical engines of the prefrontal cortex (PFC) of

⁸²Dehaene, S. Kerszberg, M & Changeux, J-P. (1998) A neuronal model of a global workspace in effortful cognitive tasks *PNAS-USA* vol 95, pp 14529-14534

⁸³Baars, B. (1988) A cognitive theory of consciousness Cambridge: Cambridge Univ Press Subsequently published in electronic form, including a Kindle edition <http://www.theassc.org/files/assc/BJBaars%20-%20Cognitive%20Theory%20of%20Consciousness%20%28Cambridge%201988%29.pdf>

this work in what they label “workspace neurons.”

Rolls & Deco have provided a series of figures focused on the flow of information related to the surface of the cerebrum of the macaque related primarily to vision (pages 17,19, 20, 58 & 82) without many citations⁸⁴. The figures ignore the role of the brainstem and particularly the thalamus and TRN in the overall neural system.

The fact that the typical engine of these stages employs two to four million analog neurons contributes to their opaqueness and explains the failure of “artificial intelligence” endeavors (based on binary phasic computer logic) to achieve their goals during the 1980's and 1990's. The morphology of individual neurons within these stages no longer show any significant relation to their function. Their form is dominated by packaging considerations; the volume available, and minimizing the circuit delay times between functionally related neurons. The locomotion sequence generating neurons of stage 6 are probably an exception. They tend to exhibit a shape determined by their internal signal diffusion requirements.

While the stage 3 signal projection neural paths were first identified orthodromically as connecting the stage 2 and stage 4 engines, these paths soon appeared as the normal connecting mechanism between all engines of any stage and between stages.

Rolls & Scott, writing in Doty, provide an early attempt to illustrate the parallelism between the different sensory modalities as they converge on the prefrontal lobe and associated elements of the limbic system⁸⁵. Section 4.6.3 of this chapter provides a more comprehensive view.

4.6.1 Afferent PNS neural pathways–Stages 1 & 2

Stage 3 signal paths leaving stage 2 engines are predominantly of the word serial/bit parallel type (individual words are sent serially over a nerve (a neuron bundle) and each word involves multiple neurons with parallel pulse trains carrying information.

4.6.1.1 Spatial summation and signal dispersal are key features of stage 2

In the chemical and mechanical sensory modalities in particular, spatial summation is used within stage 2 to increase the potential for stimulus detection and to contribute to the importance of the detected signals.

In the case of audition particularly, stage 2 incorporates significant dispersion of the signals to support multiple information extraction engines within both stage 2 and stage 4. Moller has illustrated how a single auditory fiber exhibits two stages of axon bifurcation to support three separate engines within the cochlear nucleus⁸⁶.

4.6.1.2 Time dispersal is a fundamental feature of the sensory modalities

It should be noted that the sensory modalities frequently introduce significant time dispersal between the individual signals transduced by the sensory neurons from the physical environment. In vision, this time dispersal is due to the significant differences in distance between the stage 3 encoding ganglia and their common exit path from the retina via the optic nerve. In the case of hearing, the situation is even more significant due to the coiled character of the cochlea and the extreme crowding of the sensory neurons. The transduced signals are believed to be encoded immediately by stage 3 neurons prior to delivery of the signals to the stage 2 circuits of the cochlear nucleus. As a result, many of the signals recorded in the past from the cochlear nucleus may exhibit a time dispersal not recognized by the original investigators.

Because of the time dispersals encountered within the vision and hearing modalities, most of

⁸⁴Rolls, E. & Deco, G. (2002) *Computational Neuroscience of Vision*. NY: Oxford Univ Press

⁸⁵Rolls, E. & Scott, T. (2003) Central taste anatomy and neurophysiology *In* Doty, R. *ed*. *Handbook of Olfaction and Gustation*, 2nd Ed, Revised & Expanded NY: Marcel Dekker page 681

⁸⁶Moller, A. (2003) *Sensory Systems: Anatomy and Physiology*. NY: Academic Press page 310

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the signals processed within the geniculate nuclei exhibit significant time dispersal. This time dispersal should be annotated when reviewing topographic maps of the lateral and medial geniculate nuclei in particular.

4.6.2 Afferent CNS neural pathways–Stage 4, the TRN & inferior colliculus

Most of the stage 2 signal processing was designed to minimize the complexity and power consumption involved in passing their signals to the CNS, and to provide support to the various reflex loops aiding in the defense of the organism. This activity was convergent in character.

The function of the stage 4 engines is to extract *information* from the largely unprocessed *signals* received from the PNS. To achieve this, stage 4 processing becomes highly multi-dimensional and highly divergent. The stage incorporates a mesh architecture with specific engines assigned to a variety of tasks determined by the sensory modality. The operation of these engines and their interconnection is largely controlled by the TRN (the unconscious switching and control center of the neural system). In most sensory modalities, one of the control tasks is to delineate processing of information related to three major operating modes, general situational awareness, detailed analytical analysis of the available information and inevitably the processing of alarm signals designed to protect the organism.

The processing of alarm mode information has the highest priority. Alarm mode processing to protect a specific limb is frequently achieved through low level reflex arcs as suggested in [Figure 4.xxx]. For more significant threats, the reflex arc frequently involves the cerebellum as discussed in greater detail in **Section 4.xxx**. Of primary interest in this section is the delineation of the awareness mode and analytical mode activities. Focusing on the visual and auditory modalities, the awareness mode efforts and a variety of housekeeping activities are concentrated in the geniculate nuclei of the diencephalon and dedicated areas of the cerebral cortex. The analytical mode efforts are concentrated in the PGN's and dedicated areas of the pulvinar, both within the diencephalon. In those animals where acoustic ranging plays a major role, the inferior colliculus, in conjunction with other dedicated areas of the pulvinar, also play a major role. The parallel nature of these activities have been recognized in the work of Karten & Shimizu discussed below.

To properly process complex threats, the necessary afferent stage 4 engines are concentrated within the diencephalon in order to save time. This alarm mechanism has recently, 2 Sept 2011, been a subject of discussion over the internet blog operated by the CVNet group (color vision group). The discussion centered on the ability of a baseball or cricket batter to hit the ball based on his reaction time. While the individual submissions frequently cited the role of the visual cortex, the visual cortex plays a negligible role in alarm mode activity such as involved in batting. The time delay associated with signals passing from the TRN to the cerebral cortex and back after information extraction is just too long. This alarm mode related activity is accomplished totally within the analytical mode engines of the diencephalon (thereby saving at least five milliseconds of transit time). The visual cortex plays no significant role in batting, whereas the PGN/pulvinar couple and the cerebellum play crucial roles. The submission by Dr. Christina J. Howard on 5 Sept. contains the most useful summation.

While stage 4 engines tend to receive their signals from stage 2 circuits in word serial/bit serial form, they tend to pass the extracted information up the neural pathways, and between associated stage 4 engines using word serial/bit parallel coding (individual words are sent serially but employ a group of parallel neurons to support information transfer in a bit parallel configuration). Thus, it is believed that the transfer of a single word of information occurs over the stage 3 nerves serving the output of stage 4 engines within a time window of a few milliseconds.

The inferior colliculus plays a major role in those animals depending on echolocation, it is the primary engine(s) that support this function. It is much larger and more highly developed in the bottle-nosed dolphin than in humans, and apparently any other species. Among those species using this capability, the processing of both direct reflections and Doppler modified reflections are critically important. In the dolphin, the data is primarily processed as analog information to provide a three-dimensional view of the environment from more than a meter to about 30 meters xxx from the snout of the animal. In this range, the whistle capability of the acoustic signal generation capability of the animal is primary. At closer ranges, the high

frequency pulse (click) capability of its acoustic signal generation capability is relied upon.

It should be noted, the dolphin has no capability to generate any sound through its mouth. Its major sound generation capability is within the nasal passages via the melon on its forehead. The sound heard at the zoo or in the pool with a dolphin is from its nasal passages via its blow-hole.

A major problem arises in discussing stage 4 signal processing and information extraction from the much earlier studies of the morphology of the human brain. The ease of seeing the pairs of superior colliculi and inferior colliculi gave rise to the term quadrigemina. This designation has no functional or architectural relevance as will be seen under the next heading.

A similar problem has arisen with regard to the term cyto-architecture, as will become evident in **Chapter 10**. This term does not relate to the architecture of the cell (cyto-). Instead it relates to the topography of the engines of the CNS, and more specifically the cerebrum since Brodmann did not provide numbers for the engines of the diencephalon and lower brain stem. The value of Brodmann's notation remains useful and will be used throughout this work where available. However, it refers to the topography of the major engines, and not the architecture, of the brain. In fact, the gyri and sulci described by the architecture of the human brain are largely incidental to its operation since at least 50% of the engines are buried in the sulci. To truly appreciate the topography of the brain and its functional organization, a so-called inflated model (created by computer) is required.

It is also important to note that the sulci of the human brain vary between individuals. While only a few graphics have been used to identify specific functions in relation to the sulci of that individual, any brain surgeon can tell you that these identifications are only correct within plus or minus six to a dozen millimeters.

[xxx rewrite and add figure make compatible with pages around 26 see next heading]
The study of the diencephalon has always been particularly difficult due to its highly protected location at the very center of the CNS (at the top of the brain stem and surrounded by the telencephalon or cerebrum or "new brain." Its critical importance has long been recognized by the reluctance of surgeons to even approach it with a scalpel. Injuries to the diencephalon frequently caused massive debilitation or death. On the other hand, the diencephalon, contains the thalamic reticular nucleus (TRN, not a nucleus at all but a thin covering of a majority of the pulvinar terminating in a set of structures commonly described as the quadrigemina in the anatomical literature. In this work, the quadrigemina will be expanded to a sexigemina, consisting of the lateral and medial geniculate bodies, the inferior colliculus, the superior colliculus and the two perigeniculate nuclei (related to vision and hearing). The relationship between the perigeniculate nuclei and the pulvinar within the TRN has not been reported previously in the neurological literature. The detailed discussion of the superior colliculus will be left to **Section 4.9** and the detailed discussion of the perigeniculate nuclei and the pulvinar will appear in **Section xxx**

The TRN and the pulvinar are the first elements of the neural system encountered in this work that are not bilateral in the conventional sense of two distinct elements separated significantly if not totally. The TRN, being a shell is difficult to characterized as symmetrical about the median and the pulvinar is horseshoe (or walnut shaped before the two halves are separated) with significant operational circuitry in the connecting portion. The so-called corona radiata actually emanates from all surfaces of the TRN after entering it from the corpus principia between the two halves of the pulvinar as well as the outer surfaces of the pulvinar.

4.6.2.1 The architecture and physiological of the mes- & di- encephalon

[xxx from hearing book pg 387]
The unique physiological character of the diencephalon and mesencephalon have been largely overlooked in the hearing literature. With its purpose unrecognized, the thalamic reticular nucleus (TRN), the outer shell of the thalamus, has also been largely overlooked. It is in fact the most important portion of each sensory modality (with the exception of smell/taste). The morphological designations mesencephalon and diencephalon have limited functional meaning. The elements described below on the posterior surface of the mesencephalon are actually formed from a fold of the tissue forming the thalamic reticular nucleus of the diencephalon.

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The coordination and control of auditory signal manipulation is controlled by the thalamic reticular nucleus (TRN), of the thalamus of the diencephalon. The TRN is described in the literature using a variety of names, most generally the reticular formation (or caudate nucleus in older texts). Although described as a nucleus, the TRN is a primarily a thin shell covering virtually all of the pulvinar within the thalamus. However, at the ventral posterior of the thalamus, the TRN expands into several multilayer folds that form the various geniculate nuclei and the four colliculi. The latter have been defined previously morphologically as the corpus quadrigemina. The geniculate nuclei and the colliculi as a group have been defined morphologically as the separate mesencephalon. This designation is too narrow as the folds include additional features of critical functional importance. Of particular importance are the perigeniculate nuclei found along the morphologically defined brachium of the superior and inferior colliculus (between each geniculate nucleus and its corresponding colliculus). These nuclei have not been studied in sufficient detail in the past although Aitkin et al. describe the inferior colliculus morphologically as consisting of three distinct nuclei⁸⁷. The crucial connections between the nuclei of the mesencephalon and the adjacent pulvinar have been generally ignored.

When mapped more globally in **Figure 4.6.2-1**, the functional projections of the major visual and auditory nerves are seen to be similar. In both cases, the appropriate sensory nerves project to the mesencephalon where they bifurcate repeatedly. The figure is designed to highlight the symmetry of the elements, and the fact that there are two colliculi of each type and two geniculate nuclei of each type. While there are two pulvinar lobes, their output is unitary. Beyond the pulvinar, the neurological system is no longer functionally bilateral. The cerebellum (not shown) and the parietal lobe function as unilateral engines. Only the left side of the figure has been detailed with respect to the neural paths. The right side shows only the two nerves emanating from the vicinity of the colliculi. The location is that described in a caricature (figure 7-3) by Noback⁸⁸.

The symmetry of the quadrigemina is not maintained at the functional level. The superior colliculi are primarily associated with stage 6, efferent command generation, while the inferior colliculi are primarily associated with stage 4, afferent signal manipulation. The signals within the optic nerve are bilateral to accommodate the command signals from the superior colliculus.

While it is common in the literature to suggest the hearing nerves arriving from the lemniscus first reach the inferior colliculus, this may not be the case at a more detailed level. One of the best caricatures available⁸⁹

⁸⁷Aitkin, L. Tran, L. & Syka, J. (1994) The responses of neurons in subdivisions of the inferior colliculus of cats to tonal, noise and vocal stimuli *J Exp Brain Res* vol 98(1), pp 53-64

⁸⁸Noback, C. (1967) *The Human Nervous System*. NY: McGraw-Hill

⁸⁹Mettler, F. (1948) *Neuroanatomy*, 2nd Ed. St Louis, Mo: Mosby

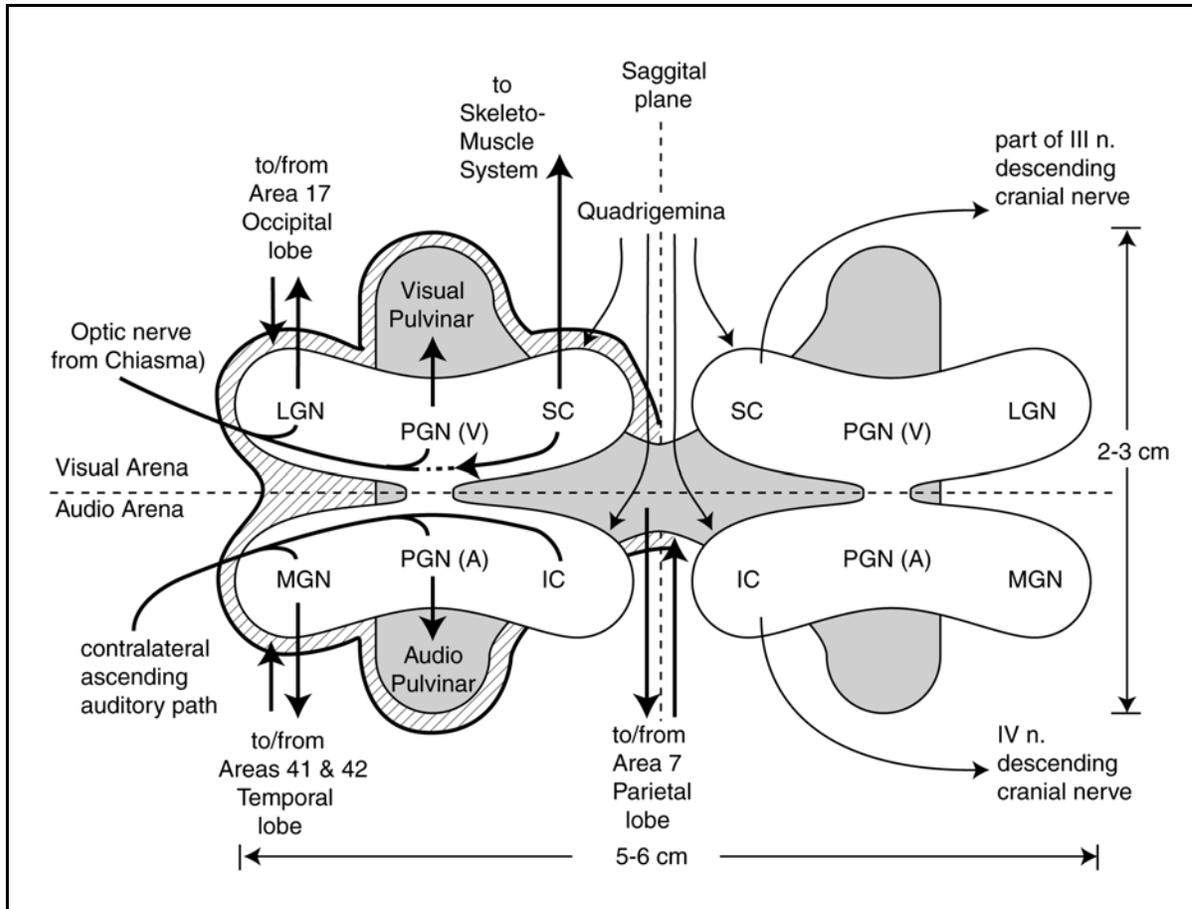


Figure 4.6.2-1 Functional arrangement of the posterior thalamus (or mesencephalon) facing the cisterna superior. Both the IInd and VIIIth nerves are intercepted by the TRN in either its control layer form (hatched) or by its functional elements, the geniculate nuclei and the colliculi. Except for the sensory nerves and the nerves of stage 6, all nerves shown contain two way elements. All signals being passed into or out of the diencephalon are subject to interception by the control portion of the TRN. The four colliculi are called the quadrigemina primarily because of their easy visibility from the cisterna superior while the other elements of the thalamus curve out of plane and are obscured by the bulk of the thalamus. See text.

suggests the vestibulocochlear nerve approaches the diencephalon so as to encounter the medial geniculate nucleus before the inferior colliculus. The detailed arrangement is species specific and in the human case, the inferior colliculus is often described as vestigial. In the case of the human, the portion of the nerve terminating in the perigeniculate nucleus (PGN) may include only a small number of neurons but it is of major importance.

Individual articles in the literature frequently describe the mesencephalon from different perspectives, resulting in different names for engines found to perform similar tasks. The engine labeled the perigeniculate nucleus is frequently described as part of the medial geniculate nucleus or as part of the inferior colliculus by different authors. While its morphology may be open to question, its performance is becoming clear. As described in Escabi & Read, it provides the octave wide correlator critical to extracting information concerning musical patterns and explaining spectral segregation phenomena⁹⁰.

Segregation refers to the ability of an auditory modality to identify a specific tone, or chord, as not belonging to a harmonically related ensemble (tone or chord) presented at the same time. This ability is key to one's level of music appreciation in humans. It

⁹⁰Escabi, M. & Read, H. (2005) Neural mechanisms for spectral analysis in the auditory midbrain, thalamus and cortex *In* Malmierca, M. & Irvine, D. eds. *Auditory Spectral Processing*. NY: Academic Press pp 207-251

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also appears to play a key role in the ability of a dolphin to differentiate between targets in its perception of the exterior environment provided by its active sonar system.

After signal manipulation within the posterior portion of the diencephalon, the major neural paths diverge. In the case of the auditory system, the medial geniculate projects primarily to the temporal lobe in support of the awareness mode. Simultaneously, the perigeniculate nuclei projects to the pulvinar/cerebellum couple in support of the analytical mode. This latter path is shorter and much more difficult to investigate *in-vivo*. The inferior colliculus projects back to both the control portion and the data formatting portion of the TRN. As noted in the figure, most of the paths projecting from the mesencephalon are bilateral. Their return portion generally terminates within the formatting portion of the TRN. When all of the necessary signals are available, the data formatting portion of the TRN delivers information, from the area described by Carpenter & Sutin as the ventral posterolateral and ventral posteromedial nuclei, to Area 7 of the parietal lobe for inclusion in the saliency map of the subject.

The signals delivered to the inferior colliculus appear to be a mixture of partially processed signals originating in the temporal or IHC sensory channels. However, some information originating in the frequency selective OHC and processed in the cochlear nuclei also appear to reach the IC. The signals delivered to the medial geniculate nuclei are known to originate from the frequency-selective OHC but may also be from the IHC. The signals delivered to the reticular portion of the perigeniculate nuclei can be shown to be from the OHC but may also be from the IHC.

While the signals projecting to the medial geniculate and the perigeniculate still show a strong tonotopic aspect, it is their receptive field (looking back toward the cochlear partition) that are of major importance. The signals projected over the great majority of these neurons are limited to pulse frequencies of about 600 pps. It is the physical location of their source along the cochlear partition that is known precisely due to their anatomical arrangement. For those signals that exhibit significant stage 2 signal processing, their receptive field may be associated with multiple locations along the cochlear partition, and therefore multiple frequencies in the acoustic field of stage 0.

Brodal⁹¹ and Carpenter & Sutin⁹² have provided valuable information on the thalamus and its elements. Brodal describes the right lobe of the thalamus morphologically. He shows the TRN (his reticular) cut away. Carpenter & Sutin (figure 15-14) describe the principle bidirectional nerve paths associated with each lobe of the thalamus followed by an extensive description of each element of the thalamus. They also note the laminated structure of the MGN closely resembles that of the LGN (page 646).

Kiang & Peake have provided a caricature attempting to describe the physiology of hearing as an overlay on an anatomical description⁹³. This work is in agreement with their description except in two areas. An area between the medial geniculate nucleus and the brachium of the inferior colliculus (or on the surface of the brachium) should be identified as the perigeniculate nucleus. Second, the role of the inferior colliculus should be de-emphasized in human hearing compared to its role in lower mammal hearing. Overall, their figure does not do justice to the complexity of the system.

Karten & Shimizu have provided two papers developing the similarity of the visual signal

⁹¹Brodal, A. (1981) *Neurological Anatomy in Relation to Clinical Medicine*. NY: Oxford University Press

⁹²Carpenter, M. Sutin, J. (1983) *Human neuroanatomy*, 8th Ed. Baltimore, MD: Williams & Wilkins

⁹³Kiang, N. & Peake, W. (1988) *Physics and physiology of hearing*. In: Atkinson, R. Herrnstein, G. Lindsey, & Luce, R. eds. *Stevens' Handbook of Experimental Psychology*. John Wiley & Sons. pp. 277-326.

paths of birds and mammals where they delineate the same two paths as in this work^{94,95}, although they do note their difference in performance, e.g., the broad field of view LGN/occipital couple and the high acuity PGN/pulvinar couple. They use the expression optic tectum to represent the visual perigeniculate nucleus, but the graphics make the commonality obvious. This work uses engine to describe both their area of the mammalian neural laminate and their non-mammalian clusters (or nuclei or aggregates). They discuss the laminated striate cortex and the non-laminated extra-striate. Their non-laminate is actually a rolled up laminate as seen in the structure of the LGN illustrated in **Chapter 10**. The lamination is more difficult to perceive with regard to the pulvinar until the cortex is inflated by recent computer programs and MRI techniques. The result is seen to be a single sheet of laminated cortex formed initially from a laminated tube. Their asserted advantage in packaging for laminates is equally true for the rolled LGN, PGN and pulvinar but based on a higher degree of performance.

Figure 4.6.2-2 shows the top level operational arrangement of the visual portion of the mesencephalon, and the two couples; the LGN/occipital couple and the PGN/pulvinar couple.

In this chapter, it is the striated portion of area 17 that is referred to as the occipital portion of the LGN/occipital couple. This is necessary to distinguish this couple from the similarly striated portion of the temporal lobe involved in the MGN/temporal couple described in a following section.

Where the analytical mode elements, the PGN's and the pulvinar are closely packaged to achieve the shortest possible input output delay time. In humans and most other mammals, the LGN/occipital couple involves considerably more delay due to their looser packaging.

⁹⁴Karten, H. & Shimizu, T. (1989) The origins of neocortex: connections and lamination as distinct events in evolution *J Cogn Ndeurosci* vol 1, pp 291-301

⁹⁵Shimizu, T. & Karten, H. (1990) Multiple origins of neocortex: contributions of the dorsal ventricular ridge *In* Finley, B. et al. *eds*. The Neocortex. NY: Plenum pp 75-86

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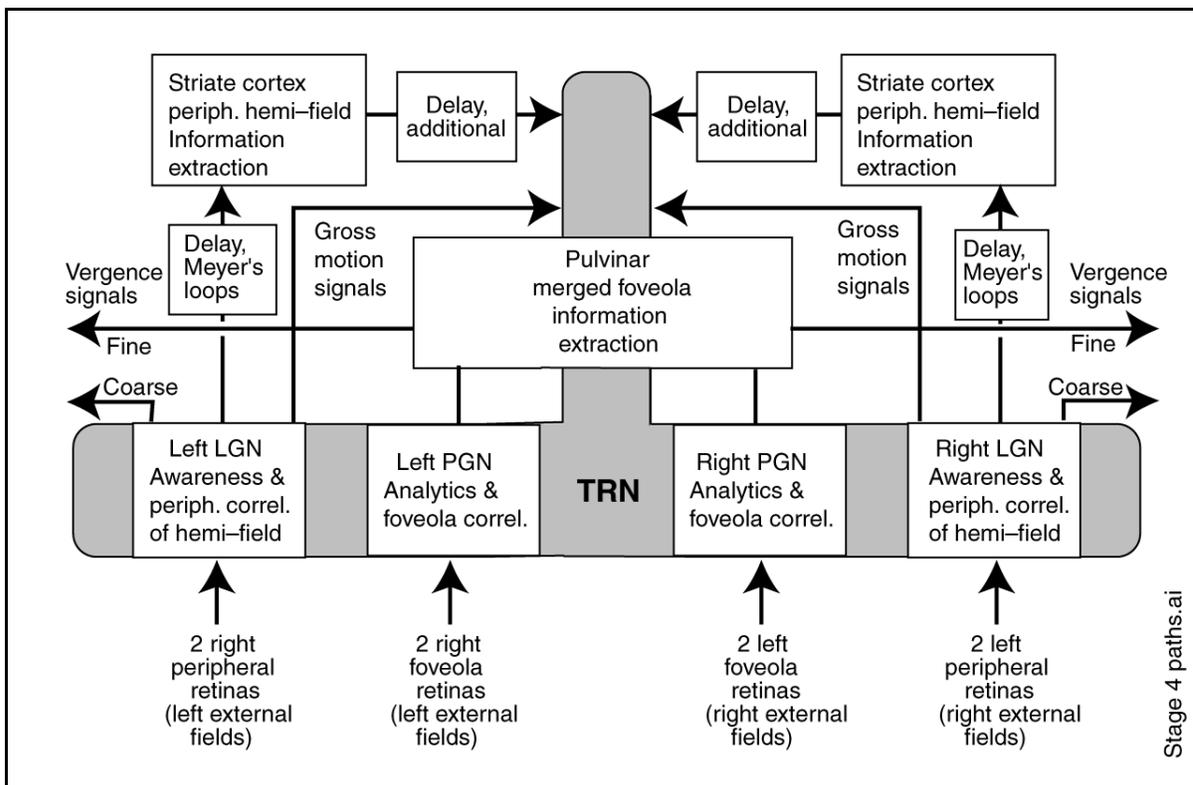


Figure 4.6.2-2 The top level architecture of the visual mesencephalon. The merging of the signals representing the external visual environment is performed in four initial steps followed by two final steps within the pulvinar and TRN before transferring the merged information to the saliency map. See text.

A theme of their papers is that significant damage to the striate cortex has remarkably little effect on the visual performance of birds, and that the same conclusion can be drawn for mammals. They also assert that V1 is not in a serial information extraction chain including V2, V3, V4 & MT.

4.6.2.1.1 The LGN and striated occipital cortex couple

The discussion of the LGN and striated occipital cortex requires introduction of another concept of great importance. The neural system accomplishes a variety of signal processing and information extraction without the ability to perform complex mathematical transformation, as performed in engineering and scientific calculations. Instead, it employs a much less demanding mechanism, computational anatomy. By rearranging the topography of neural paths, and then taking sums and differences, significant transforms can be accomplished virtually quickly, statically and virtually energy free. These transforms can be imaged at significant spatial resolution by staining living tissue while it is functioning. These transforms will be described extensively in Chapters 8, 11, 12?]. While researchers have generally described these topographies as retinotopic, exhibiting a relationship to the retinal map, this is inappropriate. There is a significant difference between the retinal image and the actual external field map.. In fact, these representations are generally scene-otopic, exhibiting a relationship to the actual external environment. [xxx add to spelling dictionary or pick a different expression first]

Some of these transforms by computational anatomy are needed to allow correlation between patterns that do not overlap each other well without it. The striate cortex employs a conformal transformation known mathematically as a bilateral transform. This transform converts a circle in the scene to a straight line on the striated cortex, and vice versa. (Section xxx).

After the necessary computational anatomy, the LGN merges the two fields supplied to it by using as many as four pairs of individual layers (not laminates) of neural tissue folded like a blanket. These pairs of layers merge the brightness channels (R-signals), and three chrominance channels, the O-channels, the P-channels, & the Q-channels from stage 2. To merge these signals accurately, the LGN must converge the individual layers. The layers are not one-to-one equivalents because of the presence of the nose in humans. In this process, information is obtained concerning the vergence signals required to steer the individual eyes into convergence and coarse information concerning the movement of large areas of the scene. The motion signals are multiple and reflect the greater likelihood of motion near the periphery of the field of view due to the subjects own motion. After merging these signals using summation neurites passing through these layers of the blanket in columns, the signals are passed on to the striate cortex.

While merging these signals within the LGN, the signals across an individual layer are not necessarily in temporal conformance due to the variable length of the neural paths from the retina to the LGN. This lack of temporal coherence, must be corrected before information can be extracted from the scene-topographic signals. This is the purpose of Meyer's loops shown in the figure. Meyer's loops are used to insure both appropriate topography and appropriate time coherence of the signals applied to the striate cortex.

There are two infrequently noted features of the signal topography at the striate cortex. First is that only one-half of the foveola is represented on each hemisphere of the occipital lobe. Each area is near the external ear and not near the center of the occipital lobes. Second is the very small area dedicated to the extremely important foveola. This situation supports the proposed greater importance of the PGN/pulvinar couple in the analytical mode of vision in humans.

4.6.2.1.2 The (visual) perigeniculate nuclei and pulvinar couple

There are two perigeniculate nuclei associated with vision as shown in the earlier figures of this section beginning with [Figure 4.6.2-1] which expands on the posterior fascia of the diencephalon provided by Broda in 1981. us. The visual PGN is found between the LGN and the SC, along what is described morphologically as the brachium of the SC. The auditory PGN is found between the MGN and the IC along the brachium leading to the IC. These structures are not large because they serve specialized functions in conjunction with much larger portions of the immediately adjacent pulvinar.

The PGN/pulvinar couple is responsible for many important functions. First, it is responsible for merging the signals received from the foveola of the two retinas into one spatially and temporally coherent representation. This action involves extraction of "fine" vergence signals that can be used to optimize the convergence of the two eyes and a similar "focus" signal used to adjust the stage 0 lenses of the eyes. Second, it is responsible for extracting the precision information about elements in the external scene imaged on the 1.2 degree diameter foveola of the converged eyes. Third, it is responsible for extracting the 3-dimensional spatial location of each element imaged onto the foveola. Fourth, it is responsible for identifying those elements and sending their identification and three-dimensional position to the saliency map.

The visual PGN/pulvinar couple is responsible for determining the optimum convergence angle between the two eyes and the associated optimum focus adjustment for the lenses of the two eyes. It accomplishes this by examining the signals from the foveola *en masse* while initially dithering the version angle between the two eyes, about the coarse version angle determined by the LGN, until signals of maximum amplitude are observed in the merged images from the two foveola. This "fine" version information is then sent to the oculomotor subsystem along with an optimal focus signal obtained from a lookup table given the optimum version angle. Once the fronto-parallel plane is established, it is possible for the pulvinar to determine the "version error" associated with each major element in the scene that is not in the fronto-parallel plane. This version error is a measure of the stereoscopic distance the element is in front of or behind the fronto-parallel plane.

Once optimum vergence and focus is achieved, the PGN/pulvinar examines each element

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within the volume created by the diameter of the foveola and the depth of focus of the visual system in an attempt to identify that element. It achieves this identification using a lookup table generally associated with the pulvinar. For elements of very sophisticated spatial structure, it is believed the couple calls on the larger capacity of the cerebellum to provide an extended lookup capability based on previous experience. If the element cannot be readily identified, a new record is prepared and incorporated into the pulvinar or cerebellum lookup tables to aid identification of similar elements in the future.

The combined identification and 3-D location information for each element within the above volume is transferred from the couple to the saliency map for subsequent stage 5 cognition.

The visual system is not limited to vision along a line perpendicular to the line drawn between the centers of the lenses of the two eyes. As a result, a volume in object space can be explored at high acuity by the visual system that is defined at any instant by the above volume (foveola area in object space times the depth of focus of the visual system) and the version angle of the oculomotor system. The composite volume of this space along the horizontal plane and the median plane is known as the horopter. The horopter describes the range of best viewing relative to a single putative "cyclopean eye" at the center of the forehead. Performance away from these two planes declines rapidly due to the mounting arrangement of the oculomotor muscles to the ocular globes. The horopter has been defined conceptually since ancient times. However, the detailed description of these two features is quite involved (**Sections 15.xxx and/or 19.xxx**).

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Several failures within the PGN/pulvinar couple account for behavioural shortcomings that have been well documented within the psychology community.

One of the responsibilities of the PGN/pulvinar explains a well known but poorly explained phenomenon, that of agnosia. Following a failure in the PGN/pulvinar couple, the subject loses the ability to appreciate images of a variety of common words (alexia), objects, places, concepts or faces (prosopagnosia), even though the subject is still able to perceive these objects because the LGN/occipital couple provides information to the saliency map, albeit at lower than optimal spatial resolution, .

Another phenomenon associated with the PGN/pulvinar couple is "macular sparing." This is the clinical situation where even people with total destruction of the visual cortex, V1, are still able to perceive objects near their point of fixation. This condition is due to the processing of the signals from the foveola by the PGN/pulvinar without the participation of the LGN/occipital couple.

Many laboratory investigators have used a small light in object space for the subject to use as a point of fixation during the evaluation of subjects with significant striate damage. Because of this protocol, they do not normally evaluate the performance of the PGN/pulvinar. However, they frequently report the subject is able to report movement of objects in the peripheral field of view even though the relevant part of the striate cortex, V1, has been totally destroyed.

While appearing paradoxical, and christened "blindsight" by Weiskrantz⁹⁶, this ability to report motion of an object within a field that the subject cannot perceive is clearly an example of the version and motion signals from the LGN still being processed and used to converge the eyes and report motions within the field of view to the saliency map. This occurs in spite of the inability to perceive the object moving in this part of object space corresponding to the destroyed part of V1 and outside of the foveola served by the PGN/pulvinar couple.

As noted in the citation in the next section, there is every reason to believe the bottle-nosed dolphin, *Tursiops truncatus* is able to perceive language via its PGN/pulvinar couple. Baby dolphins are known to identify themselves by acoustic signature (a "name" showing a resemblance but distinct difference from that of its mother) within minutes of its birth.

⁹⁶Weiskrantz, L. (1997) *Consciousness Lost and Found*. NY: Oxford Press

4.6.2.1.3 The MGN and striated temporal lobe couple

The function of the MGN/temporal lobe couple has not been investigated in as much detail as the LGN/occipital lobe couple. Its primary responsibility can be expected to be merging the signals from the two ears into a composite representation that can be passed to the striate auditory area of the temporal lobe. The reticulated area of the temporal lobe dedicated to hearing is largely buried within a major sulcus (a.k.a. the lateral fissure of Sylvius) along the dorsal surface of the temporal lobe (Brodmann's areas 41 & 42).

It is likely the MGN is mapped topographically into parallel stripes associated with octave long sections representing the auditory acoustic range. This would involve the use of computational anatomy to perform a Riemann transform. In mammals with mobile pinna, the act of aligning these representations would generate coarse source direction information that could be used to generate pinna-motor pointing commands much like those generated by the LGN/occipital couple. As in the case of the LGN, variations in the frequencies between the two sets of data could be interpreted as Doppler shifts due to the motion of the source in object space.

The topology of the candidate 1st stage auditory correlator follows the morphology of the cochlear partition, spiral ganglia and PGN closely.

Figure 4.6.2-3 shows how this mathematical manipulation can be achieved easily using computational anatomy. The left frame depicts the uncoiled rows of OHC along the Organ of Corti divided into major groups of L signaling channels each. This size group is probably correlated with the individual knots of the spiral ganglia. The axons associated with each of these major groups are arranged into a linear array forming a horizontal row in the middle frame. This transform of a long one dimensional array into a group of shorter stacked arrays can be described as a Riemann Transform. The resulting linear arrays are stacked vertically with the neurites of sensing neurons contacting each of the axons in a vertical row. Thus, each intersection of a horizontal line and a vertical line is a node occupied by a pedicle of an axon, from part of the auditory nerve, synapsing with a neurite of a sensing neuron. There is also the option of a unique storage neuron associated with each node.

Until further morphology can establish the location of this two-dimensional array in hearing, it will be associated with a specific portion of the TRN located adjacent to the medial geniculate nucleus, MGN. This area closely parallels a similar region in the visual system and will be defined as the auditory perigeniculate nucleus, PGN. This area of the TRN is reticulated, a common appearance of correlation circuitry.

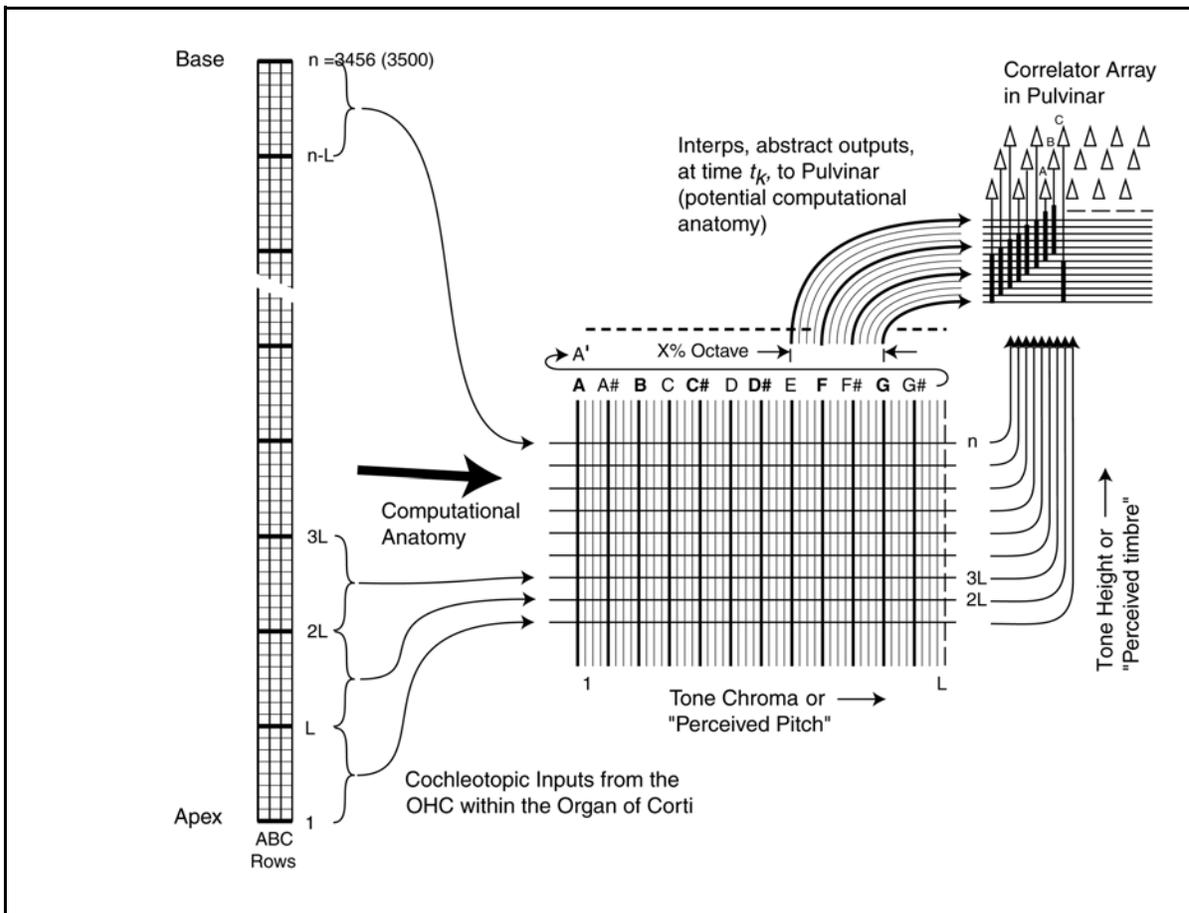


Figure 4.6.2-3 Computational anatomy and correlation in the primary correlator of the thalamus. Left; schematic of the OHC groups along the Organ of Corti. Center; schematic of the correlator in the auditory perigeniculate nucleus of the thalamus. Computational anatomy changes the one-dimensional cochleotopic array into a two-dimensional array. The fineness of the resulting array is controlled by Stage 2 signal processing between these two arrays. The dendrites of the pitch correlation neurons are aligned in vertical columns and contact each octave of the input structure. The dendrites of the timbre correlation neurons are aligned in horizontal rows. An axon associated with each of these dendrites extends to the pulvinar. The axons of the correlation neurons form the multichannel output signal from the two-dimensional array. Only the group going to one secondary pitch correlator is shown. This correlator accepts signals from approximately X% of an octave of the main correlator as shown. This output is abstract with respect to the Organ of Corti. It can be considered an initial interp. Right; the secondary pitch correlator in the pulvinar. Consists of individual correlators examining groups of inputs. The instantaneous output of these correlators can be considered a complete interp. The secondary timbre correlator is similar but not shown. See text.

While the use of the Riemann Transform is convenient for illustration, the folding of the top frequency of one octave back on to the lowest frequency of the next higher octave may seem unwieldy. Many other conformal transformation exist that can transform a straight line into a series of concentric circles⁹⁷. In that case, the sensing lines would become radials emanating from the center of the set of concentric circles, see the following discussion..

4.6.2.1.4 The (audio) perigeniculate nuclei and pulvinar couple

⁹⁷Kober, H. (1957) Dictionary of Conformal Representations. NY: Dover Publications. Publication S160

An alternate hypothesis to the Riemann transform suggested above in connection with the MGN, is the use of a similar Riemann transform in the PGN to generate precise information about the tones applied to the ear relative to the musical scale. There is an interesting difference between speakers of tonal and atonal languages. Tonal language speakers learn at an early age to distinguish not only the musical note associated with an acoustic frequency but also the octave range of that tone. Atonal language speakers, except those exposed to sophisticated musical training at a very early age are able to recognize the musical note associated with an acoustic frequency but are unable to reliably describe the octave of the frequency. A small percentage of the atonal language speakers (generally limited to some of those exposed to music very early) are able to identify both the musical note and octave of a frequency. These people are said to have "perfect pitch." On the other hand virtually all tonal language speakers exhibit perfect pitch, to the degree that the term is largely unknown in the orient, and is certainly not a distinguishing feature of an individual.

It is proposed the PGN incorporates a topographical representation of acoustic frequency space formed into a logarithmic helix similar to that of Hensen's stripe but precisely organized at one octave range per turn of the helix.

[xxx edit text if necessary to fit current volume]

Figure 4.6.2-4 represents the performance of the multidimensional correlator of the human PGN in *circular* coordinates. Each octave range is represented by a nominally equal distance along the cochlear partition. It has been associated with a loop of a spiral to provide a frequency continuum. The pitch of the spiral is unimportant. Nominal frequencies have been associated with each loop as indicated at the bottom of the spiral. The frequency advances exponentially based on two to the nth power. The lowest frequency shown is arbitrarily taken as 125 Hz. The scarcity of spectral channels below this value and the secondary order curvature of Hensen's stripe in the cochlear partition make analyses below this frequency more complicated. The highest relevant frequency is above 16 kHz but less than 22.6 kHz. The highest spectral channel of the human auditory system is not well documented. The notes of the musical scale are shown surrounding the spiral and show how the same note is associated with multiple frequencies (depending on their octave range).

The orientation of the figure relative to the named musical notes is arbitrary. The precise frequency associated with these names has changed irregularly throughout history and as recently as the 1930's.

Every radial in the figure represents a single perceived pitch. That pitch can be generated by a single tone at the intersection of the radial and a specific loop of the spiral. Alternately, it can be generated by a series of harmonics appearing at the intersections of the radial with one or more of the loops. The series need not be regular or complete. The series need not start with the lowest frequency intersection.

employment of this information extraction approach largely resolves the missing fundamental paradox of hearing and also explains the tritone paradox. (See Chapter 9 of PBH available in draft on the internet⁹⁸)

4.6.2.1.5 The inferior colliculus in direction finding & acoustic imaging

The inferior colliculus of humans is of lesser importance than in other advanced species. The human inferior colliculus, IC, is frequently described as rudimentary and hard to identify by morphological means. In the bottle-nosed dolphin, the IC is a dominant feature of the posterior diencephalon because it is used to perform sophisticated acoustic image analysis, probably in conjunction with the pulvinar, beyond human capabilities. Its size makes morphological identification of the adjacent PGN difficult.

The role of the advanced versions of the IC can be compared to the role of the PGN described above in many particulars. However, operation in cooperation with an active acoustic source offers additional capabilities.. These can be separated into two categories, those associated with a continuous source, usually associated with a variable frequency whistle, and those associated with a pulse source, usually associated with a train of clicks. Less well known is the ability of the bottle-nosed dolphin to utilize two distinct and spatially separated acoustic sources and its ability to steer its outer ears. Its outer ears are not associated with its rudimentary and atrophied pinna left over from its days as a land animal. It employs a pair of streamlined fat-filled horn receiving antenna, just below, behind and outboard to its lower jaw bone (www.neuronresearch.net/dolphin)

After transfer of the energy collected by its antenna to the cochlea via an alternate wall of the vestibule (bypassing the impedance transformer of the middle ear, which is not needed in the water environment), the auditory modality operates like that of any other mammal. An exception is in the more sophisticated curl of Hensen's stripe within the cochlea that is optimized for hearing at much higher frequencies than in most mammals (bats being another exception).

Overall, the acoustic imaging capability of the bottle-nosed dolphin is as sophisticated as any man-made radar or sonar system (and believed to be better than any man-made sonar on a pound-for-pound basis. It employs steerable transmitting and receiving antenna, the transmitting antenna are in a non-horizontal plane to provide limited vertical spatial resolution the continuous sources are dynamically variable in frequency and the pulse sources are controllable in both frequency and pulse duration characteristics. The receiving system is capable of Doppler signal processing and very sophisticated target identification (equivalent to the best of any current submarine system). The system appears capable of simultaneous wide-angle search and narrow-angle attack modes of operation.

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To achieve the above modes of operation, the IC is appropriately complex. It has not been studied histologically in the detail that other auditory tissue has been in other animals. However, the behavior and measured performance of the dolphin allows the operation of its IC (and possibly related engines) to be sketched.

The operation of the IC related to its associated continuous wave sources appears analogous to the adjacent PGN/pulvinar couple describe in the previous section. The size of its antenna, and the nominal target ranges relative to the wavelength of sound in water, makes fixed-focus operation of the acoustic imaging system adequate. In other aspects, the systems are quite similar. When desired, the two source beams can be used together to establish a horopter of considerable depth of field (nominally a few meters to a power-limited 600 meters using the frequency range of 30-80 kHz.

As in other mammalian auditory systems, only frequencies below about 600 Hz (3 dB point) are actually represented within the neural system. The sensory receptors are envelope detectors and the actual frequency of the signals received are identified to the IC by the specific location of the neuron delivering the signal within the cochlea (or

⁹⁸Fulton, J. (2008) Processes in Biological Hearing: A 21st Century Paradigm. www.neuronresearch.net/hearing/pdf/9Performance in draft form

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equivalent label within the nerve providing the neural signals).

In general, after locating a school of fish, the dolphin establishes a line of approach placing the school within about ± 5 degrees of, and 5 degrees above, the intersection of nominal horizontal and medial planes through its head (corresponding to the nominal beam pattern of its acoustic transmission system).

The quite stable whistle pattern used by an individual dolphin provides excellent range and range-rate information relating to the centroid of the target school. The difference in the frequency transmitted and the median frequency received is indicative of the range. The change in this difference over a short interval is indicative of the changing distance (or the relative velocity) between the school and dolphin. Similarly, the frequency width of the returning signal describes the Doppler frequency associated with the school and is generally associated with the swirling of the school (very valuable information suggesting whether another dolphin is cooperating in herding the school). If there is another dolphin in the area, he can easily be identified by the asynchronous character of his whistles relative to the first dolphin. The other dolphin can probably also be identified by his signature via the PGN/pulvinar couple of the first dolphin.

As the dolphin approaches the school, he is generally able to determine the thickness of the school by noting the difference in time of arrival of the first and last echoes. These echoes are generally due to the swim bladders in the fish or other marine animals, not due to reflections from the acoustically transparent skin of the fish.. The dolphin can estimate the breadth of the school by the Doppler frequency shift associated with the return. Thus, the IC provides a 3-D image of the target school to the TRN for deposition in the saliency map. This image improves in quality as the dolphin approaches the school.

The operation of the IC related to its associated pulse wave sources appears quite sophisticated. It operates in the 80–150 kHz range. While it appears largely ineffective at ranges less than a meter, the dolphin is moving toward the school with its mouth open at that range, and ready to capture anything that his mouth encounters. At ranges from one meter out to about ten meters, the dolphin appears to use single pulse stimulation to provide range and range-rate information that helps it identify individual fish within its instantaneous field of view. The agility of the pulse generator suggests the dolphin (and the bats as well) uses transmitter pulse to received pulse coincidence to determine range using a lookup table rather than perform any computations.

The curvature of Hensen's stripe has been observed in the bottle-nosed dolphin. It is recognized that the changes in curvature associated with the high and middle frequency ranges identified above have been reduced in order to provide more precise frequency resolution in these regions.

In summary, the IC of the dolphin *Tursiops truncatus* and almost certainly its relatives, exhibit an ability to acoustically image, and potentially identify coarsely, targets in front of it in a manner completely analogous to that performed by the visual PGN/pulvinar couple in terrestrial animals. The IC may call on the adjacent pulvinar, or even the cerebellum, for image interpretation support. Simultaneously, it can identify its hunting partners using its auditory PGN/pulvinar capabilities just as humans and other terrestrial mammals do.

4.6.2.2 Aconscious role of the TRN of the diencephalon

This section will introduce the first element of the "mind" encountered in the architecture of the neural system. The totally abstract mind can be subdivided into three major elements, the conventional conscious and sub-conscious mind and the aconscious mind. The first two of these will be addressed beginning initially in **Chapter 15** and more fully in **Chapter 18**. The aconscious mind refers to the thalamic reticular nucleus of the diencephalon. The TRN is the primary control and switching center of the brain. It controls what is passed through the stage 4 and stage 6 engines to and from the saliency map; it thereby plays a major role in

what the conscious and subconscious minds perceive and can access. Its capabilities are labeled unconscious because they are beyond the perceivable by either the conscious or subconscious mind yet they play a major role in the decision-making processes of the subject. The TRN is the gatekeeper to the conscious and subconscious mind.

The TRN constitutes our first encounter with reticulated (or striated) cortex, although is needed to recognize its appearance in the closely associated geniculate and colliculus structures as well. The term applies to the distinct appearance of this type of neural tissue. It appears to have a corrugated appearance in either one dimension or sometimes two orthogonal directions on the surface of the brain. This appearance is due primarily to a series of long, nominally straight neurites forming a grid associated with a "diode matrix" commonly known in engineering as a cross-bar switch and used extensively in telephone central offices. In some cases, the orthogonal reticulation is formed by long axons embedded within the surface as well. In other cases, the long axons are below the surface of the tissue and the reticulation due to them is less prominent.

The reticulated *structure* of the TRN provides the functional *architecture* for the TRN to manipulate signal paths through the diode matrix formed by the active diode synapses.. While much of the diode matrix appears to be "hard-wired" beyond after the age of puberty in humans, it does provide a degree of both long-term and short-term plasticity throughout life. The short term plasticity of the TRN allows it to support the operating modes introduced earlier in **Section 4.2.4**, awareness, alarm, analytic, informative volition and command.

The TRN controls and switches all of the afferent sensory signals of the neural system. It also controls most if not all of the efferent volition and command signals emanating from the CNS. It is frequently said by the morphologist that the TRN is bypassed by the olfactory signals because they proceed directly to the cerebrum. Upon closer examination, the majority of the olfactory signals enter the CNS in the area of the insula immediately adjacent to the thalamus. As seen on an inflated map of the CNS (**Sections 10.2.2-4 or 10.8.xxx fig 10.8.1-1 showing notch by Swanson03pg77 mod**) , the insula of the cerebral nuclei and the thalamus of the mesencephalon are adjacent to each other. It is proposed the TRN constitutes a surface structure through which the PNS signals pass to make connections with the stage 4 engines of both the diencephalon and the insula.

4.6.2.2.1 Proposed architecture of the TRN

Figure 4.6.2-5 illustrates the proposed complex relationships involving the TRN in the mature organism. This figure expands on a figure in Lozsadi⁹⁹ and is similar to figures in Mitrofanis & Guillery (93, fg 1 & 4). In the literature, vision is frequently associated with the dorsal and caudal portion of the TRN. However, the LGN and PGN are located more ventrally. The TRN itself can be divided into at least three distinct physiological regions;

1. Areas describable as supporting the switching (and/or combining) of abstract signals from multiple sensory inputs.
2. Areas performing a two-dimensional correlation function, specifically the perigeniculate nucleus, PGN, in the visual regime.
3. Areas involved in the supervision of the processes occurring in other nuclei of the old brain and lobes of the *neo*-cortex.

⁹⁹Lozsadi, D. Gonzalez-Soriano, J. & Guillery, R. (1996) The course and termination of corticothalamic fibres arising in the visual cortex of the rat E. Jour. Neurosci. vol. 8, pp 2416-2427, fig 11

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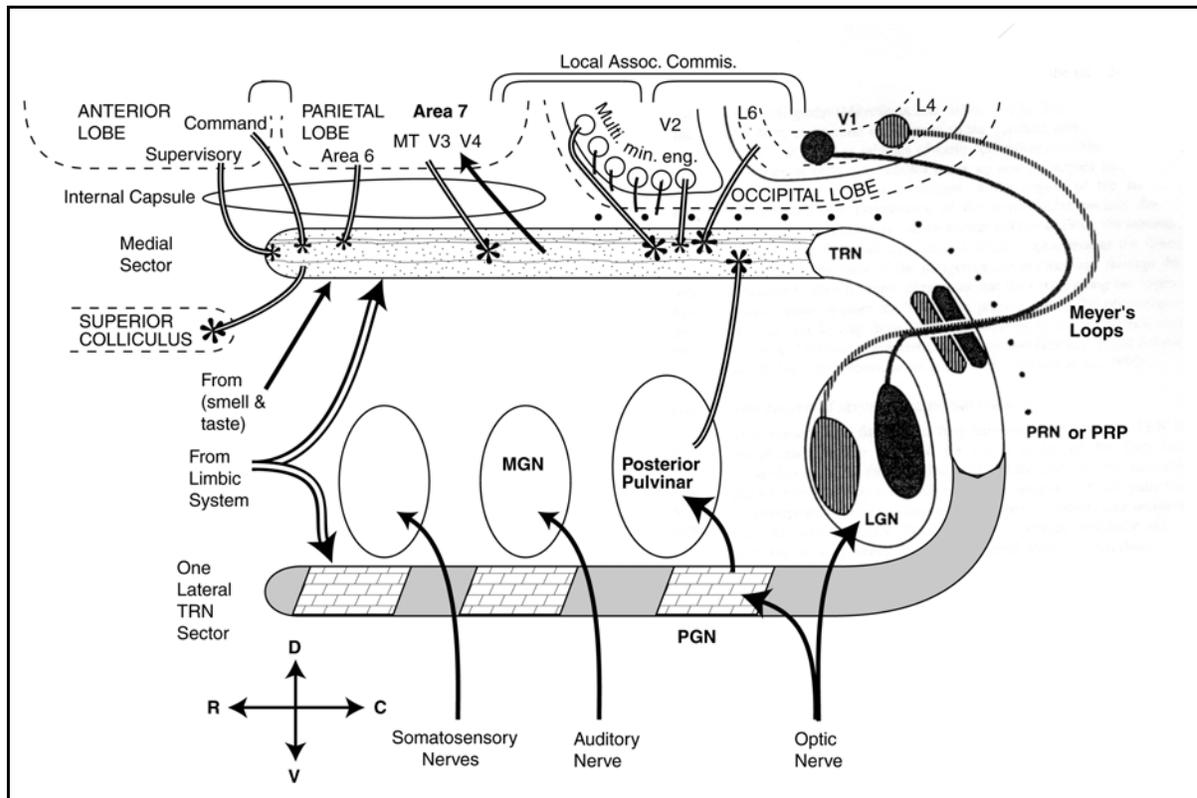


Figure 4.6.2-5 The functional role of the thalamic reticular nucleus. The U-shaped TRN is shown in three sections. The lower section is focused on processing sensory inputs. It includes the perigeniculate nucleus processing 2-dimensional data from the foveola. The right section is concerned with supervising centrifugal signals from the TRN. The top section is concerned with selecting and switching signals based on alarm mode inputs and previous experience. Solid paths are spatially oriented sensory inputs. Paths with white core are abstract signals.

These three areas are highlighted in the figure by different background patterns. The two lateral TRN sectors perform several poorly documented functions. The most important with respect to vision is the two-dimensional correlation of the imagery from the foveola in the perigeniculate nucleus, PGN. The supervisory function is highlighted on the right. This compartment is known to contain "slabs" showing a topological resemblance to similar areas in the thalamus and in the *neo*-cortex. However, it is also known to contain areas that appear to be comparing signals from adjacent slabs related to different sensory modalities.

The solid signal paths in the figure represent afferent signals. The signals between the LGN and the *neo*-cortex represent signals from two areas representing equal elevations above the horizontal meridian in object space. The signal paths with a white core represent efferent signals.

Mitrofanis & Guillery have noted several key facts. "All of the axons that pass either way between the cortex and the thalamus must go through the thalamic reticular nucleus, and many of them, possibly all, give off collateral, excitatory branches that innervate the reticular nucleus." Further, "These thalamic relays themselves receive their heaviest innervation not from the periphery, but instead from axons that return from the cortex to the thalamus." Lozsadi, et. al. went further and noted that the neural paths to and from the occipital lobe do not pass through the same area of the TRN¹⁰⁰. The striate portion receives signals from the

¹⁰⁰Lozsadi, D. Gonzalez-Soriano, J. & Guillery, R. (1996) Op. Cit. pg 2416

laterally symmetrical parts of the LGN via the lateral (outer) two-thirds of the visual sector of the TRN. The prestriate portion returns signals to the medial third of the TRN. These comments were consistent with earlier remarks by Lozsadi that the TRN was not heterogeneous in rats^{101,102}. The Lozsadi papers provide other references related to the interface of the TRN to the limbic, somatosensory and motor subsystems. These papers provide a wide range of specific features of different regions of the TRN. Most of them note the long linear neurites and axons of specific classes of neurons, and the general size and spacing of the various engines found within the TRN. They also note the more abstract (diffuse) nature of the signals returning to the TRN from the *neo*-cortex.

This work will generally follow the terminology used in the above papers, by Jones¹⁰³.

A major function of the TRN is highlighted by the medial TRN compartment. This compartment appears to collect abstract signals from a variety of sources, both internal to the thalamus and from other sources. It processes these signals in two distinctly different ways. It combines many abstract signals into more complex abstract signals associated with the saliency map. It appears to direct these abstract signals to other areas, primarily in the neo-cortex. Alternately, it accepts abstract command signals from the higher cortical centers (shown at upper left) and directs them to the appropriate part of the superior colliculus. There, they are processed further into specific oculomotor and skeletomotor commands. Jones, et. al. have described this switching and consolidation activity of the medial compartment as a 'global' function and described the connections between this compartment of the TRN "and the neo-cortex and thalamus as **not** being mapped in a clearly defined topographical manner." Lozsadi also discusses the multiple minute maps in the prestriate cortex. Based on the assumption these are visuotopically mapped instead of reflecting a visuotopic receptive field, he claims their neural paths back to the TRN terminate in topographically mapped order ('96, pg24-26). More recently, Tootell & Hadjikhani show the local sign within the area including dorsal V4 varies "seemingly randomly." Such action suggests this area is not visuotopically mapped but consists of many feature extraction engines exhibiting a variety of receptive fields related to object space.

The anterior lobe is shown directing supervisory commands to the medial portion of the TRN (extreme left). The associated action commands may be sent from the anterior lobe itself or they may be sent via the pre-motor complexes in area 6 of the parietal lobe. The name pre-motor is very appropriate because these abstract commands must be decoded into action commands within the superior colliculus.

Note that as the signals become more abstract, laterally symmetrical processing areas in the brain, to accommodate these signals, become redundant. Thus many identified processing areas of the parietal and anterior lobes are not paired and there is no reason for the TRN to maintain a visuotopic organization for abstract signals returning from feature extraction engines in the *neo*-cortex. Tootell & Hadjikhani have addressed this conceptual area when they ask "Where is 'Dorsal V4?'"¹⁰⁴. In the same paper, they note that the middle temporal area, MT, is not paired. They also noted that V4 was not topographically mapped in the monkey. Born & Tootell provide additional data concerning the columnar nature of the MT in owl monkeys¹⁰⁵.

Mitrofanis & Guillery provide a caricature showing the neurons of layer 6, apparently of area 17, returning to both the TRN and portion of the thalamus related to vision. The caricature is

¹⁰¹Lozsadi, D. (1994) Organization of cortical afferents to the rostral, limbic sector of the rat thalamic reticular nucleus *J. Comp. Neurol.* vol. 341, pp 520-533

¹⁰²Lozsadi, D. (1995) Organization of connections between the thalamic reticular and the anterior thalamic nuclei in the rat *J. Comp. Neurol.* vol. 358, pp 233-246

¹⁰³Jones, E. (1985) *Thalamus*. NY: Plenum

¹⁰⁴Tootell, R. & Hadjikhani, N. (2001) Where is 'Dorsal V4' in human visual cortex? Retinotopic, topographic and functional evidence *Cerebral Cortex* vol 11, pp 298-311

¹⁰⁵Born, R. & Tootell, R. (1992) Segregation of global and local motion processing in primate middle temporal visual area *Nature*, vol. 357, pp 497-499

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not detailed enough to discriminate between the switching and supervisory compartments of the TRN¹⁰⁶.

There is a significant interplay between the limbic system and the TRN as shown on the left. The limbic system, particularly the fornix, literally surrounds the diencephalon in many sectional views¹⁰⁷. This would suggest it interconnects with the TRN and thalamus in many roles. Lozsadi has provided information of the rostral TRN associated with the limbic system and noted the unusual characteristics of the neural terminations¹⁰⁸. His discussion seems to apply to both the switching and the correlation portions of the TRN. The discussion supports the heterogenic nature of the TRN with modality and location within the TRN. Multiple zones were found in some areas of the TRN that were essentially parallel to the surface of the TRN. However, the limbic terminations within individual zones formed "slabs" of neurons that were not parallel to the surface of the TRN. They note the more dorsal portions of the TRN exhibit slabs perpendicular to the surface of the TRN.

Besides addressing the gross signaling architecture of the vision related portions and the morphogenesis of the TRN, Mitrofanis has also addressed the architecture of the commissure adjacent to the TRN in ferrets¹⁰⁹. He develops his discussion in terms of the commissure associated with the internal capsule, which he defines as the perireticular nucleus. This structure already has several names due to its complex shape. Here the name perireticular nucleus will be reserved for the area of the nucleus lateral to either lobe of the TRN. The commissure change direction significantly in this area. This designation is in general agreement with the 2-dimensional line drawings in figure 2 of Mitrofanis. Mitrofanis & Guillery address the commissure architecture showing it lateral to the TRN in both line drawings and electron-micrographs.

While the morphological community has addressed the interweaving of commissure at the lateral extremes of the diencephalon in terms of peri-reticular nuclei, PRN, the physiologist describes this area in terms of a peri-reticular plexiform layer, PRP. Mitrofanis & Guillery suggest, "it may be more useful to think of the perireticular cells as more of a sorting mechanism, separating fibres that have different properties." The various neural paths interweave to establish the most expedient paths to their terminating points. In the thalamocortical neurons, this interweaving also involves both the removal of time diversity (using Meyer's loops) and the computational anatomy leading to the visuotopic presentation at the striate cortex.

Steriade, et. al. have noted the direct connections between the basal forebrain and the thalamic reticular nucleus¹¹⁰. In addition, they note the widespread proliferation of the axons from the forebrain throughout the TRN. These connections are considered crucial to the supervisory and switching role of the TRN. They probably determine the operating mode of the TRN, and hence the organism.

The last paragraph of Lozsadi, et. al. is critical to understanding the operation of the LGN and the PGN. He notes a difference in path between the foveal and peripheral neurons as they pass through the TRN. They note further, that "this may prove to be a true difference either between the pathways that represent central vision and those that represent peripheral vision, or between fibres that originate from area 17 and those from the prestriate cortex. Further experiments are needed to resolve this issue." This work sides with separate paths related to both of these options.

¹⁰⁶Mitrofanis, J. & Guillery, R. (1993) Op. Cit. fig. 1

¹⁰⁷Kretschmann, H. & Wienrich, W. (1998) Neurofunctional Systems. NY: Thieme pg. 90

¹⁰⁸Lozsadi, D. (1994) Op. cit. pg 241-244

¹⁰⁹Mitrofanis, J. (1994) Development of the thalamic reticular nucleus in ferrets. *E. Jour. Neurosci.* vol. 6, pp 253-256

¹¹⁰Steriade, M. Jones, E. & McCormick, D. (1997) Thalamus, vols 1 & 2. NY: Elsevier, Sect. 3.2.4.2

The geometric details of interweaving of the commissure are not critical to this discussion.

4.6.2.2 Supervisory & switching architecture & topology of the TRN

The detailed discussion of the TRN must recognize the differences between species in this area. The relative sizes and functions of the sections of the TRN change significantly among members of *Chordata*. The differentiation is particularly striking between the pro-simians and simians. Thus the papers of investigators must be carefully studied to determine the specific phylogenetic context in which they apply.

Davenport provides a reference point in the phylogenetic development process¹¹¹. He notes that after the first week in chick embryos, the chiasm degenerates to a simple crossing. All remaining connections between the eyes and the brain are contralateral. His caricature presents a visual system that is quite simple. Because of the minimal binocular vision in chicks, there are no obvious lateral geniculate nuclei. The perigeniculate nuclei also seem absent in the chicken.

Ohara & Lieberman performed early studies, using horseradish peroxidase, to determine the nature of the neurons passing through and terminating in the TRN of the rat¹¹². They did not study the neurons found entirely within the TRN. Later investigators have generally found that the neurons passing through the TRN do not have an in-line synapse within the TRN but many have collateral axons that terminate within the TRN. On the other hand, many other neurons, both from the neo-cortex and the thalamus, project axons terminating in the TRN.

The primary feature of the morphology of the TRN is due to the underlying nature of the neurons comprising the switching and correlation functions. These neurons have long neurites and/or axons, many of which are aligned with the surface of the TRN. These neural elements contribute to the woven appearance of the surface of the TRN from which it gets its name the reticular nucleus.

This section will review the architecture and topology of the supervisory and the switching compartments of the TRN. These characteristics are similar among all chordates. The architecture and topology of the correlation portions are uniquely well developed in human. The discussion of those characteristics will be found in **Section 15.6.3**.

4.6.2.3 The role of the inferior temporal lobe in vision

Data continues to accumulate showing the important role of the inferior temporal lobe in the extraction and identification of features serving the visual modality¹¹³. Rolls & Deco focus on the extraction of information concerning faces in and along the superior temporal sulcus (STS) of macaque. The list of citations is good, but the specificity of their conclusions is limited. "This evidence makes it clear that a single cortical visual neuron tuned to faces conveys information not just about one face, but about a whole set of faces, . . . (page 93)." Thus, they have still not identified an individual "grandma" neuron among the face neurons, if one exists. Most of their information is based on action potential firing rates.

As part of their analysis, Rolls & Deco address the question of how the neural signals are projected from engine to engine. They define three potential situations,

- Local representation– one in which all the information that a particular stimulus or event occurred is provided by the activity of one of the neurons.
- Fully distributed representation– one in which all the information that a particular stimulus or event occurred is provided by the activity of the full set of neurons.

¹¹¹Davenport, R. Thies, E. & Nelson, P.. (1996) Cellular localization of guidance components in the establishment of retinotectal topography, *J Neuroscience*, 16(6): 2074-2085.

¹¹²Ohara, P. & Lieberman, A. (1981) Thalamic reticular nucleus: anatomical evidence that cortico-reticular axons establish monosynaptic contact. *Brain Res.* vol.207, pp 153-156

¹¹³Rolls, E. & Deco, G. (2002) Computational Neuroscience of Vision. NY: Oxford Univ Press Chap. 5

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- Sparse distribution representation– is a distributed representation in which a small proportion of the neurons is active at any one time.

The first definition corresponds to the simple case of a single neuron projecting signals in a word serial format where the word consists of only a single amplitude value. This is the mode used extensively in the peripheral sensory modalities, including vision and hearing.

The last two definitions clearly suggest the encoding of information in the word serial/bit parallel format within these engines of the inferior temporal lobe (and in fact in any stage 4, 5 or 6 engine).. Their data also supports the continued graded output of individual neurons, even though this grading may be embedded in the coding of an action potential pulse stream. Their data also shows the variation in the output of a single stage 3 neurons (presumably part of a set of neurons within an identifiable nerve) upon stimulation by a variety of faces (page 90). Their figure 5.9 shows the activity of a series of closely related neurons to a set of face stimuli. The differences appear statistically relevant. The different action potential response rates provide a pattern that could readily be compared to other patterns previous stored in memory.

Rolls & Deco make some significant assertions in their section 5.5.4 concerning the exponentially high coding capacity of a group of neurons employing graded responses. They do not attempt to identify the number of neurons in a nerve required to identify a particular stimulus, however their discussion mentions a number varying from about 20 to “on the order of 100.” The capacity suggested by their binary representations on page 101 is greatly increased if the analog amplitude associated with each neuron can support 5 information bits rather than the single bit supported by a binary signal.

They also note how easy it is for neurons of an orthodromic engine to “read” the patterns delivered by a stage 3 nerve, and presumably to compare the pattern to a previously stored pattern using what they call dot product mathematics. However, keep in mind their information remains in analog form even though encoded into a pulse format for stage 3 projection. Thus their calculations based on binary bit patterns are conservative. Operating in the large signal mode, the dynamic range is quite large and each neural output can support 5-10 bits of information.

Rolls & Deco have addressed the actual encoding of action potentials only to the extent of defining potential options (their section 5.5.6). “It is possible that there is information contained in the relative time of firing of spikes within the spike train of a single neuron.” Their discussion does discriminate between what they describe as temporal pulse coding and rate pulse coding. The remainder of their discussion suggests more research in this area is needed. This work has identified the specific coding used in stage 3 signal projection in Chapter 9. It involves what is known in engineering circles as phase encoding. This type of encoding incorporates both temporal and rate encoding in one versatile code.

While not discussed explicitly, Rolls & Deco appear to accept the fact that the signals on parallel neural paths are asynchronous (even their pulse streams are asynchronous internally). At the same time they speak repeatedly of employing time windows fo 20, 50, up to 500 ms in their investigations. This procedure suggests they expect the neural system to employ a sampling interval (and sampling duration) commensurate with the fusion frequency of the visual system (on the order of 30-40 ms depending on light level). This appears to be the sampling interval and duration associated with the stage 5 cognition process, even though information is presented to stage 5 on a nominally continuous basis.

Rolls & Deco describe their symbology for a two port neuron on page 4. As noted, the neural system employs three port neurons built around a three port Activa (Chapter xxx). On pages 101, 146, 160, 180 & 181 they describe selected multi-input neural circuits based on their two-port concept. In their section 5.5.4.2, Rolls & Deco discuss the concept of “reading” an multiple signal stream from a nerve. Their text varies between discussing reading and pattern matching as the function of a set of neurons associated with a given stimulus pattern delivered via a specific nerve. In the context of this work, these two functions are distinct. Their dot product decoding is a step in the pattern matching function. However, their stick character figure based on a two port neuron can be made much more realistic by introducing a three port neuron. With the introduction of a sampling aperture from a separate source, and potentially a clearing signal as well, a very complete pattern recognition architecture can be suggested. This architecture is also compatible with the

physiology of the neural system. **Figure 4.6.2-6** shows an alternate to their figure on page 160 that can be simplified to more closely resemble their simpler figures.

The figure uses their notation as far as possible but employs three-port neurons. This requires reversing their symbol for a soma. This reversal turns it into a standard symbol for an operational amplifier within the context of the Electrolytic Theory of the Neuron. An operational amplifier is always a three-port network. It has two inputs and one output (plus several support terminals). One input is normally inverting relative to the output and the other is normally non-inverting.

There is not enough information in the Rolls & Deco material to ascertain whether the signal input is the inverting or non-inverting input. The input from the preceding axons is shown arbitrarily as applied to the inverting (poditic) input. The memory loop is shown incorporating the non-inverting (dendritic) input to each neuron. Recognizing that every synapse is an active-diode, it is possible to adjust the circuit parameters associated with the signal inputs and with the sampling inputs to arrange for the feedback loops to act as a short term or long term memory with respect to the sampling window. The other input to each neuron can be used to accept a clear or erase signal that can affect all of the neurons acting in parallel. Thus, this circuit can act as a multiple bit word sampling window or a bit by bit pattern matching circuit. Two of these circuits in series can perform both the sampling function and the pattern matching function.

The sample and hold feature of the dendritic loops can have an effective holding time of 30 ms, or of longer duration depending on the impedances employed. The sample and/or clear feature can be implemented in several ways depending on the polarity of the separately supplied sample and clear signals

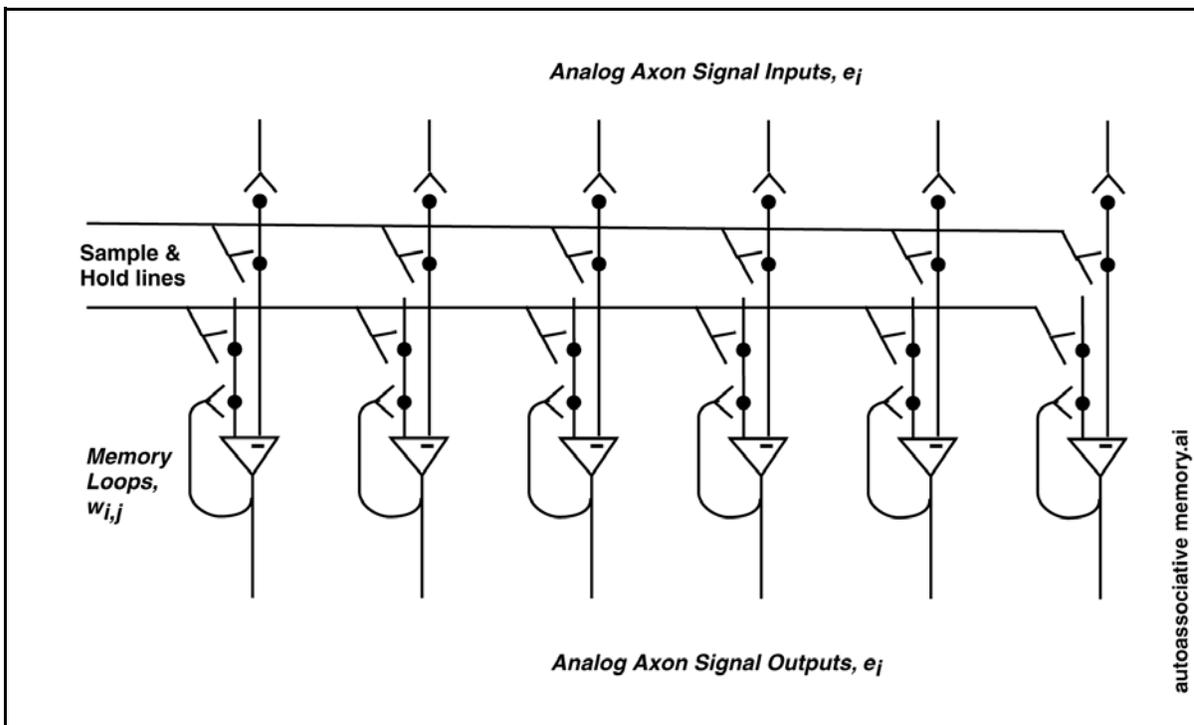


Figure 4.6.2-6 An autoassociative neural network for sampling or pattern matching circuit. The multiple synapse (with different time constants) can act as sample and hold circuits when in a feedback loop (as shown at lower left) or as either sampling or clearing inputs (as shown at upper left).. See text.

The circuit is shown as consisting of six neurons fed by six signal axons. However, this number can be extended to any arbitrary number.

Their discussions within Section 7.3 apply to this configuration with only minor changes to accommodate the three-port configuration. However, it is critically important that this circuit

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is used in the analog mode of operation within stages 4, 5 and potentially 6. The inputs are not pulse sequences, and the outputs are not pulse sequences. The pulse sequences are associated with stage 3 neurons and nerves interconnecting engines of the higher numbered stages.

The remainder of chapter 5 of Rolls & Deco explore how invariant representations of a stimulus might be obtained. Their information is very useful, but must be interpreted with the knowledge that the eyes are change detectors and tremor plays a major role in converting them into "pseudo-imaging" detectors as part of the information extraction processes of stage 4.

Most of the detailed discussion in the later chapters of Rolls & Deco become largely academic based on their employment of the never demonstrated two port character of the nominal neuron and the assumption that most information extraction neurons (defined as stage 4 & 5 neurons in this work) employ pulse signaling.

4.6.2.4 Loading the saliency map

Figure 4.6.2-7 shows a simplified schematic of the saliency map embedded in a larger scale representation of the neural system. It omits most of the cognitive circuitry of stage 5 and the efferent neural activity associated with stage 6 which is explored separately below..

As noted in **Section 4.2.3**, the precise location of the saliency map remains morphologically undefined. It may remain a dispersed read-write lookup table of non-declaratory memory shared among a variety of stage 4 information extraction engines and stage 6 information to command translation engines; or it may be a relatively small centralized lookup table currently below the "resolution" of current electrophysiology protocols. In either case, the function of the saliency map is clear; to provide stage 5 engines access to an internal representation of the primarily external environment, and to provide stage 5 engines a means of transferring instructions to stage 6 engines in an orderly manner.

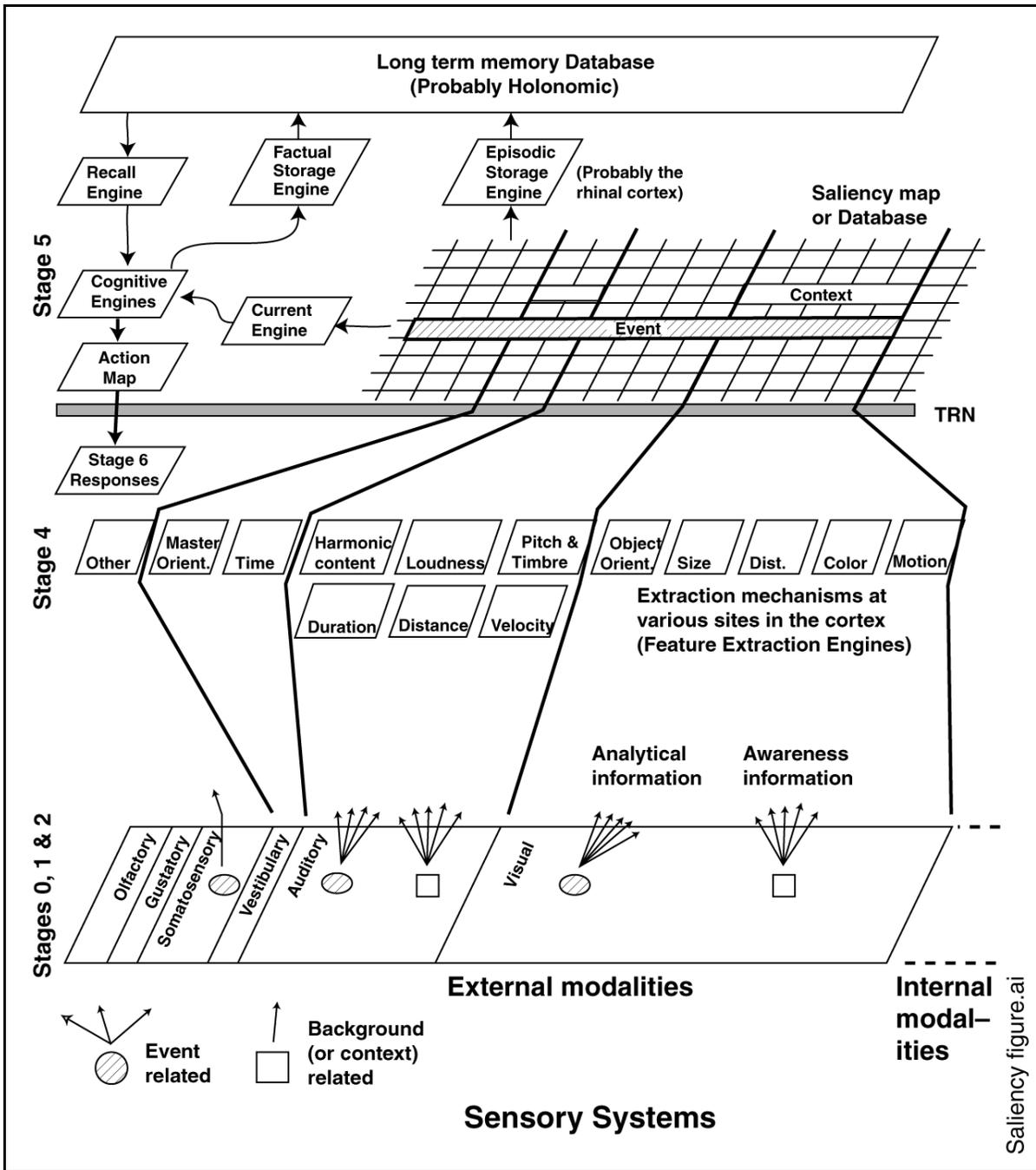


Figure 4.6.2-7 The top level signaling plan associated with the external sensory modalities of the mammal focused on the saliency map as the interface between the stage 4 (information extraction) and stage 5 (cognitive) engines. The bridge labeled TRN represents the thalamic reticular nucleus; the TRN is the main switchboard between the sensory modalities and the central nervous system. It also has a significant role to play in directing signals from stage 2 to various stage 4 engines (not shown).

The major feature illustrated by the figure is the ability of the TRN to assemble an interpretation of the environment and place it in the saliency map for accessing by the cognitive engines of stage 5. The merged signals from the five historical senses, when combined in the saliency map and presented to the cognitive stage, constitute the "common sense" described originally by Aristotle.

Like the long-term memory of stage 5, the location of the saliency map has not been

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determined. It may be largely holonomic and spread over large areas of the CNS. Alternately, it may be holonomic and spread over significant areas of the parietal lobe of the cerebrum. However, this poses problems for chordate animals lacking a significant cerebrum. The saliency map in these organism may be located on the surface of the upper extremity of the spinal cord.

The figure also illustrates the nominal demarcation lines between sections of the saliency map dedicated to the individual sensory modalities.

4.6.2.4.1 Plasticity & Synaesthesia at the saliency map boundaries

The subject of plasticity of the brain has become more important in recent years. The subject is particularly relevant in those subjects with a major failure in their sensory modalities at or shortly after birth. With the advent of MRI and fMRI imaging, it has become possible to document events in the brain of such subjects that is completely unexpected theoretically. However, it has long been assumed from behavioural studies. The ability of blind people to achieve remarkable facility in music and the ability of other blind people to demonstrate remarkable echolocation capability has long fascinated scientists.

A misalignment within the saliency map between the demarcations anticipated by the TRN in loading the sensory information into the map and the cognitive engines accessing that information leads to the condition of synaesthesia. People with this condition report an inappropriate perception of sensory inputs; they frequently report a specific smell being associated with a color, or a specific sound causing the perception of motion, etc. This is not a common condition, but it is frequent enough for it to support a small association of people with such perceptions and to attract its share of space in the popular scientific press. It can be expected that a similar demarcation error may occur between the instructions placed in the saliency map by the cognitive engines and that accessed by the stage 6 command generation engines. Such results have been hard to document but might account for a variety of ticks and other abnormal muscular events.

4.6.2.4.2 The “acuity” of saliency map loading

An important feature of saliency map loading relates to timeliness and “attention.” Noting the parallel, high and low acuity, signal paths associated with many sensory modalities introduced above, the saliency map is generally populated with information from the low acuity paths as quickly as possible after data acquisition. The quality of the stored information is then upgraded in a timely manner under control of the stage 5 circuits, primarily of the prefrontal lobe, as it directs its attention to specific areas of the incoming signals (**Chapter 18**). The process is verified in chapter 18 using the visual system as an exemplar.

4.6.3 Cognitive CNS neural pathways–Stage 5 & Saliency map

Stage 5 engines are believed to operate primarily using the word serial/bit parallel manner, which leads to much faster information transfer within stage 5 and bidirectionally with the saliency map. Thus individual word transfer is accomplished within millisecond windows within stage 5. The word serial/bit parallel format calls for groups of neurons to follow parallel paths between major engines. These paths are identified as commissure within the CNS. Note, the time delays longer than milliseconds can still occur due to the distances traveled at stage 3 propagation rates. However, time dispersal due to different commissure (or neural) paths is minimized.

There appears to be an exception to the use of word serial/bit parallel operation within the CNS related specifically to vision. It appears the “commissure” radiating from the diencephalon to the visual area of area 17, known as Meyer’s loops, may be operating in the word serial/bit serial manner to allow easy compensation for the significant time dispersion introduced by Meyer’s loops in the retina. This dispersion is primarily to the nominally spherical shape of the retina in *Chordata*.

It is believed the saliency map represents information in the form of words related to each sensory input or instructional output that involve no time dispersal, although the sensory information is clearly delayed with respect to the environment.

The use of word serial/bit parallel signaling obviously places a greater requirement on investigators to employ multiple channel recording techniques and to recognize potential time dispersion between their stimuli and their data recordings.

4.6.3.1 xxx

4.6.3.2 Major neural paths to & from the prefrontal lobe

[xxx how do the saliency map and premotor cortex differ. should the left box be marked with area for sensory inputs at perital lobe?]

Fuster has provided his view of the major connections to the prefrontal cortex¹¹⁴. He has provided one schematic associated with motor functions and one associated with emotional functions. The motor figure lacks clarity because it does not separate the sensory related elements from the true motor related elements of the brain. This is a common problem in the psychology literature. **Figure 4.6.3-1** shows an alternate figure to his figure 2.16 that addresses this issue. It separates the afferent sensory signal paths (shown on the left) from the efferent signal paths (shown on the right). It also focuses on the forward (or information carrying, fundamental) flow of information, and largely omits the potential backflow of status related command and control signals. Virtually all of the paths shown contain a reverse or backflow component. These presumably carry supervisory signals confirming signal or information receipt in good order. In some cases, the return signals (such as those from the occipital lobe) go to a different portion of the diencephalon (in this case the TRN) than where the forward signals originate (in the LGN).

The prefrontal cortex is described in terms defined in **Section 12.2**. However, some of the assignments within the prefrontal cortex remain tentative. The morphological terminology related to the prefrontal cortex remains confused in the literature (LeDoux, 2007). Price, writing in Zald & Rauch, assert the amygdala connects primarily to BA 24, 32, 25 & portions of 14 (at least in the monkey). Barbas & Zikopoulos, also writing in Zald & Rauch, provide a series of conceptual block diagrams of connections to the orbitofrontal cortex apparently based primarily on traffic analysis.

Stage 4 briefly illustrates the operation of the visual and auditory channels (LGN, PGN & MGN, etc.) in lieu of showing all the sensory input channels.

The TRN plays a significant supervisory and control function related to the motor system. It inhibits motor action during sleep and other special situations. In conformity with its switching and control function, the TRN influence on the motor system is inhibitory rather than graded. The figure replaces "midbrain pons" of Funster with the more definitive superior colliculus and hypophysis. It also shows the outputs of the superior colliculus projecting to the stage 7 neuro-affectors. the hypophysis (pituitary gland) is the major transition element between the neural system and the glandular system.

The dual roles of the cerebellum and the basal ganglia are emphasized in this figure. Both appear to have elements that are associated with the afferent sensory system (labeled stage 4b) and the efferent motor system (labeled stage 6b). The close cooperation of the two halves of each element becomes most clear during training of the subject. The cooperation is especially important during training for a new motor task that involves

¹¹⁴Fuster, J. (2008) *The Prefrontal Cortex*, 4th Ed. NY: Academic Press page 41

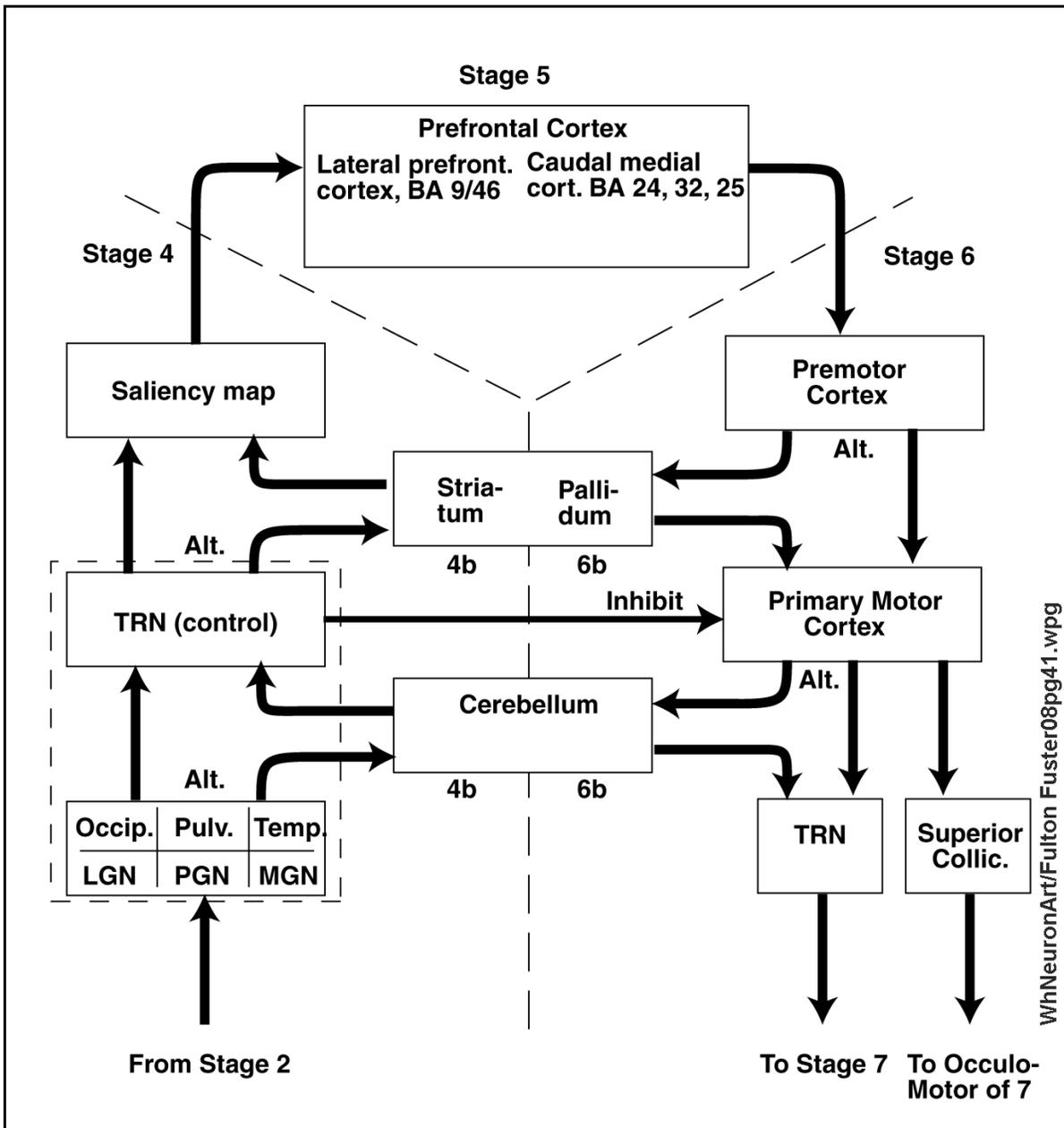


Figure 4.6.3-1 Traffic flow to and from the prefrontal cortex related to the motor function. The afferent stage 4 activity is shown for reference. The afferent role of the diencephalon is shown in greater detail within the dashed box (along with the occipital and temporal lobes of the posterior association cortex), but does not include chemical and somatosensory inputs. The sensory signal outputs of the diencephalon can come from any of its engines. The dual roles of the cerebellum and basal ganglia are shown explicitly. Alt; alternate paths available under the supervisory control of the TRN. See text. Compare to Fuster, 2008, pg 41.

visual or acoustic sensory information if optimum results are to be achieved.

The term alternate appears at several points in the figure. It indicates a choice can be made between a direct path and a circuitous path through a portion of the cerebellum or basal ganglia. For simple activities, or alarm mode operations, the direct forward signaling path can be taken. This path may result in a clumsy motor response but it may be necessary during alarm mode operations. In a young child, the direct path is a precursor to starting the

learning process. For learning, and especially learning of more complex operating activities, it may be necessary to use the circuitous path. Initially, the circuitous path is used to learn a new sensory response profile or to learn a new complex motor activity. It is clear the two halves of the cerebellum coordinate their signaling states during the process of a learning episode.

A distinctly separate path is shown at lower right in support of the oculomotor system. Time delay is of the essence in the higher primates, specifically related to reading. The superior colliculus appears dedicated to supporting this function. The SC may also support pinna pointing in some other species.

The figure includes an explicit saliency map describing the environment of the subject. This saliency map is believed to be stored in the yet undefined short term memory facility of the neural system. There are opposing proposals in the literature. Some suggest both short term memory and long term memory are initially stored in the hippocampus, with selected short term memories made permanent under instructions from the prefrontal cortex. Others suggest a separate short term memory wherein its contents are transferred to long term memory via the hippocampus and under the instruction of the prefrontal cortex.

The role of long term memory is not shown explicitly in this figure. Long term memory is becoming closely associated with the hippocampus with access from BA 10 of the prefrontal cortex. This work has not made a determination as to whether long term memory should be considered part of the sensory (afferent) neural system, part of the cognitive system (stage 5), or part of the efferent system (stage 6). Its role may justify a separate characterization with respect to its functional area.

Damasio et al¹¹⁵. have also provided a largely conceptual block diagram of the human brain focused on stages 5 and 6 and resulting primarily from one specific medical case, an individual known as EVR. They suggest the prefrontal lobe can be divided into two distinct neuroanatomic systems based on the results of their observations of the subjects response to a series of delayed response (DR) and xxx (DA) tasks.. They do not associate particular physical areas of the prefrontal lobe with specific subordinate areas or specific motor functions. However, their delineation appears to be compatible with that described here and in **Sections 12.1.2 & 12.2.**

The role of the cerebellum and the striatum and pallidum will be addressed in **Section 4.6.4.**

Wolters & Raffone have provided an extensive paper on the PFC using only conceptual schematics¹¹⁶.

4.6.3.2.1 Recent histological location of stage 6 neurons in fruit flies

Sanders has provided a recent popular article¹¹⁷ describing the work of Zlatic et al¹¹⁸ with specifically mutated *Drosophila melanogaster*. They employed a highly automated protocol to determine the role of multiple individual neurons within the simple neural system of this species. In particular, they identified individual premotor stage 6 neurons providing initial commands that are subsequently elaborated into multiple commands within stage 6 with the result that complex movements are performed by elements of stage 7.

After defining 29 behaviors, the researchers noted the lack of a one-to-one relationship between some neurons and specific responses. Such differences may be due to the still complex signal processing within the brain of this simple species or in the failure to probe the

¹¹⁵Damasio, A. Tranel, D. & Danasio, H. (1991) Somatic markers and the guidance of behaviour: theory and preliminary testing *In* Levin, H. Eisenberg, H. & Benton, A. eds. *Frontal Lobe Function and Dysfunction*. NY: Oxford Univ Press Chapter 11

¹¹⁶Wolters, G. & Raffone, A. (2008) Coherence and recurrency: maintenance, control and integration in working memory *Cogn Process* vol 9, pp 1–17 DOI 10.1007/s10339-007-0185-8

¹¹⁷Sanders, L. (2014) Neurons linked to specific behaviors *Sci News*, 3 May, pg 6

¹¹⁸Vogelstein, J. Park, Y. Ohyama, T. Kerr, R. Truman, J. Priebe, C. & Zlatic, M. (2014) Discovery of Brainwide Neural-Behavioral Maps via Multiscale Unsupervised Structure Learning *Science* 25 April, pp 386-392

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same neuron in repeated experiments or in associated but different fruit flies.

4.6.3.3 A “fundamental mode” of prefrontal cortex operation

Following the ideas of Edelman in 1980 and the earlier material in this book, it is possible to begin the definition of a functional block diagram of the executive (cognitive) portion of the brain. **Figure 4.6.3-2** shows an initial block diagram describing the proposed fundamental mode of operation irrespective of the sensory material presented to it. The goal of this figure is to describe to the greatest extent possible what inputs and outputs are expected of the executive based on the known external topology of the CNS. The figure is delineated into the stages defined previously in this work but recognizes a potential need for an expansion. The work has not previously addressed the emotion aspects of the neural system, typically associated with the limbic system, explicitly, or the location of long term memory (LTM). It may be advisable to define additional stages to group these neural activities in areas distinct from the cognitive aspects associated with stage 5. Alternately, it may be useful to define an input stage related to the limbic sensory channels and an output stage related to limbic related responses (although these may all fall within the signal definitions of stages 6-7)

The reports of Barbas & Zikopoulos relating to the emotional aspects of the PFC appear to offer information on extending this diagram (pages 80-81). Similarly, Gottfried et al. offer additional information related to the olfactory and gustatory inputs to the PFC (Section 11.7.9 and Zaid & Rauch). They suggest areas 11l and 13l are involved in olfactory cognition.

As in other areas of the cerebral cortex, the left and right portions of the prefrontal lobe are able to operate independently. They normally coordinate via commissure. When operating more independently than desired they can become the source of serious disease that in the past have led to prefrontal lobotomies designed to sever these commissure.

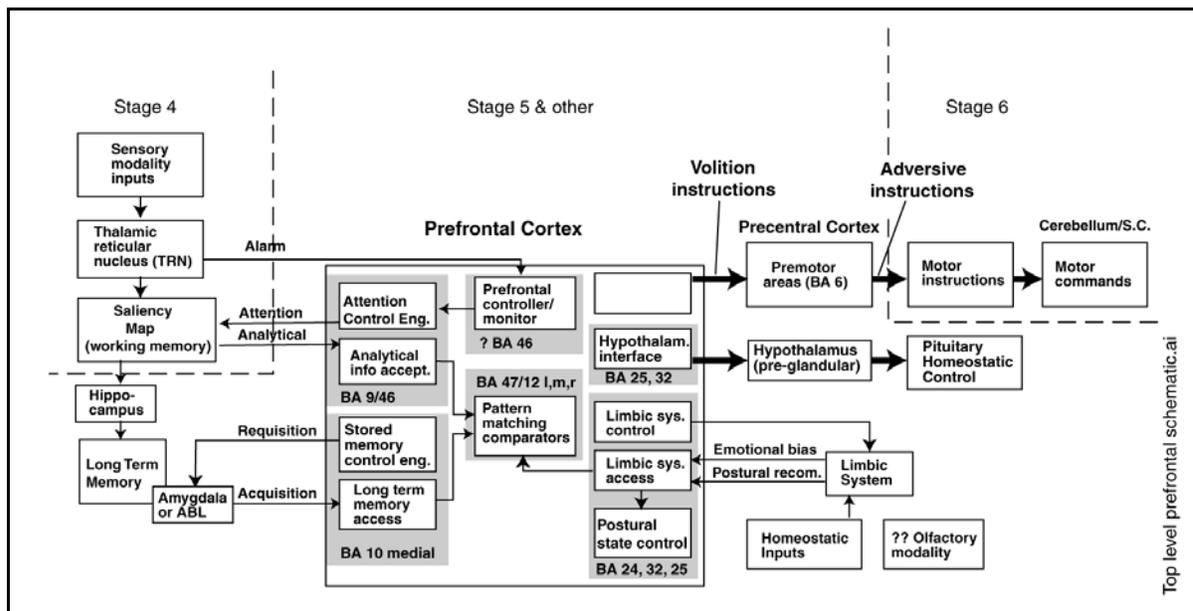


Figure 4.6.3-2 Candidate top level block diagram of prefrontal cortex with cytoarchitecture overlay ADD. While stages 4 & 6 are clearly delineated, stage 5 is subject to further subdivision. A clear role and location for the major prefrontal cortex element associated with the “mind” and issuing volition instructions to the premotor areas has yet to be isolated. See text.

It is very likely that the executive contains a master controller (labeled the prefrontal controller in this figure) that is capable of choosing the mode of operation of the executive. This function is the source of the mind’s ability to act spontaneously, its “volition.” This controller is proposed to be in contact with all of the individual engines within the prefrontal cortex directly associated with the executive; it would be in contact with engines not yet defined in this figure..

It is highly likely the operation of the prefrontal controller of the executive is highly responsive to any alarm mode signal received from the TRN. If true, this response to an alarm signal provides a logical starting point for the analysis of the operation of the executive. **Section 8.xxx** defines a series of operating modes within the sensory modalities of the neural system. It is likely a similar set of operating modes is found within the executive of the prefrontal cortex.

Initially, it is clear the executive lacks a sophisticated computational capability. This means no transcendental calculations in accordance with the rest of the system. It also means the executive relies primarily on pattern matching; it probably can perform pattern matching on multiple reference patterns in parallel. The reference patterns may represent memories that are parallel in relative time or the memories may consist of a series of patterns that are sequential in character. See **Section 12.2.xxx**.

4.6.4 Efferent CNS neural pathways–Stage 6, the cerebellum and SC

Stage 6 engines are believed to operate in the inverse manner of stage 4 engines. It is believed they receive information from the saliency map (and potentially other stage 6 engines) in word serial/bit parallel form over commissure (multiple neuron paths within the CNS) and deliver their commands to the stage 7 effectors of the PNS using word serial/bit serial formats over individual neuron paths (which may be grouped as nerve, multiple neuron, paths for morphological simplicity).

4.6.4.1 The Cerebellum and striatum/pallidum couple

The cerebellum and the striatum and pallidum of the previous section appear to operate in conjunction with a variety of stage 4 and stage 6 engines, but to be focused on more complex operations including actions exhibiting a specific time sequence. The cerebellum is believed to generate output commands that occur over a period of time and in a specific sequence. These commands may involve one hundred or more individual muscles. See **Chapter 17**.

The operations of the cerebellum and striatum/pallidum couple are more sophisticated than the simple reflex arcs of the PNS. The engines of these elements provide significant levels of information extraction, or information insertion into the signaling streams. Bizzi & Mussa-Ivaldi have discussed the role of these engines in greater detail¹¹⁹. [xxx may be wrong citation]

When speaking of training, as found in sports, the military, professional dancing, etc., one is generally speaking of complex procedures involving the cerebellum, and potentially the striatum/pallidum couple, acting as a read/write lookup table (non-declaratory memory). In each case, these engines are able to accept complex temporally distributed sequences from stage 4 as well as memorize the prescribed response sequences (stage 5 instructions). The training generally involves minor variations in these distributed sequences to insure the subject is ready to respond optimally to any situation (even physical missteps that require rapid recovery to the prescribed sequence of actions).

The TRN provides aconscious control and switching operations of both the cerebellum and the superior colliculus. In the absence of a more effective set of commands from the cerebellum, it will forward the coarse commands from the pre-motor areas of the parietal lobe to the superior colliculus. The results of this action are clearly evident during training and following failure of the involved part of the cerebellum. Football, rugby and similar sports provide a good example. A young child will attempt to throw the ball in a highly uncoordinated manner with poor results. However, with practice, he can become an expert, if not professional, thrower. However, if he should sustain a significant injury to or intrinsic failure of the appropriate cerebellum area, his skill will revert to a child like capability, a very awkward, uncoordinated throwing style.

4.6.4.1.1 The striatum/pallidum couple

The role of the striatum/pallidum couple remains poorly understood from a functional

¹¹⁹Bizzi, E. & Mussa-Ivaldi, F. (2009) Neurobiology of coordinate transformations *In Gazzaniga, M. ed. in chief, The Cognitive Neurosciences*. Cambridge, MA: MIT Press Chap 37

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perspective. Morphologically, they are considered a part of the basal ganglia and have been identified using a variety of names over the years. They are generally associated with fine motor movements. This couple has not been researched as part of this work. Differentiating their role from that of the cerebellum and superior colliculus may require a sophisticated protocol that accounts for the normal operation of the SC and cerebellum. The discussion in Noback remains one of the better and more interesting discussions of these engines, even though it remains largely conceptual and based on limited behavioral analysis¹²⁰. It stresses the high degree of mesh-based interconnections with other stage 4 and stage 6 engines.

Afifi & Bergman have provided a more recent description of the brain in this area¹²¹. They spend much of only a few pages discussing the variety of names associated with these engines by various investigators and provide a selection of block diagrams summarizing the traffic analyses performed with respect to these elements. While the title of their volume uses the term "functional," the material is based primarily on traffic analysis, not electrophysiology. Signaling is largely absent from their work. They do stress the striated or reticulated character of these elements, indicative of their correlation and/or switching capabilities. They note the striations are associated with myelinated fibers traversing the gray matter. They also note the close association between these elements and the diencephalon and mesencephalon. Their discussion of dopaminergic systems and various neurotransmitters, neuromodulators, etc. are deprecated in this work.

4.6.4.2 The superior colliculus BRIEF

The superior colliculus consists of a set of engines dedicated primarily to the operation of the visual system. It operates primarily in the aconscious domain, supporting the pointing of the eyes and head. It is located within the mesencephalon, adjacent to the PGN/pulvinar couple in order to provide the least possible delay within the visual operating loop that includes the external environment. In a sense, it is a dedicated mini-cerebellum for vision. It plays a major role in the ability of humans, and potentially a few other primates, to master the eye movements necessary to analyze fine detail and read. The superior colliculus tends to operate in near real time and command hundreds of muscles.

4.6.5 Efferent neural pathways–Stage 7 and the neuroeffectors

Stage 3 neurons have been defined as neurons carrying phasic signals over long distances between engines employing analog signal processing and manipulation. If a stage 3 neuron actually terminates at an interface with a non-neuron, it is defined here as a stage 7 neuron. Such terminations occur commonly at both striated and smooth muscle and at the interface with the hormonal system. The majority of the stage 7 neuron may operate as a stage 3 neuron, incorporating multiple sections replicating the conventional axon segment–Node of Ranvier pair but the last axon segment interfaces with non-neural tissue. This termination can take a variety of forms, and involve a variety of chemicals as discussed briefly in **Section 3.5** and in detail in **Section 16.3.4**. These chemicals are the neuroeffectors of this work. Section 3.5 defined several environments for the release of these chemicals, including a very localized (pericrine), a less localized (paracrine) environment generally restricted to the CNS within the blood–brain–barrier, a generalized (endocrine) environment within the organism, and an exocrine environment extending external to the organism.

The neuroeffectors can be subdivided into neurons supporting electrostenolytic sites that;

- Disassemble complex molecules and release simpler neuroeffector agents, e. g., nitric oxide.
- Assemble and release simple peptides, e. g., up to about ten residues, before more complex assembly techniques are required.
- Assemble and release more complex molecules, e. g., species specific variants of complex proteins.

¹²⁰Noback, C. (1867) *The Human Nervous System*. NY: McGraw-Hill pp 215-220

¹²¹Afifi, A. & Bergman, R.(1998) *Functional Neuroanatomy: Text and Atlas*. NY: McGraw-Hill pp 275-286

Those electrostenolytic sites supporting disassembly of initial components in order to release either acetylcholine or nitric oxide attract the initial component in the reaction by establishing a specific stereochemical environment accompanied by a specific electrical potential that is compatible with the dipole potential of the component. Once the initial component is in place, the disassembly is instigated by a change in the axoplasm potential of the neuroaffector neuron. This change causes the active component to be released into the extra-neural environment. Subsequently, the residue of the reaction is no longer well matched to the stereochemical site and electrical potential of the neuroaffector neuron site and its is also released.

Those electrostenolytic sites supporting assembly of hormones attract the initial component in the reaction by establishing a specific stereochemical environment accompanied by a specific electrical potential that is compatible with the dipole potential of the component. The combination of the electrostenolytic site and initial component establish an attractive stereochemical environment and electrical potential for any additional component required. Once the neuroaffector is formed, its release is caused and controlled by a change in the axoplasm potential of the neuroaffector neuron.

For more complex hormones, the above process is extended to support the incorporation of additional chemical elements into the final hormone structure. The chemical complexity of these hormones (21,000 to 40,000 Daltons), and their minor species specific variations suggest they require the full capability of mitochondria implementing a part of the genetic code to achieve satisfactory results.

[xxx edit the following to follow this position]

After reviewing the formation of the hormone suite of even a mid level animal, it appears only the first (disassembly) and last (full mitochondria involvement and secretion) potential methods of formation and release are viable.

4.6.5.1 Chemical complexity of agents released in stage 7

The range of chemical complexity and the means of release of these chemicals by stage 7 neurons appears to vary broadly in the neural system. The chemicals range from acetylcholine and the ultra simple nitrogen oxide, through a variety of simple peptides, to more complex peptides and finally to the very chemically complex pheromones.

Ganong has identified six hormones released by the neuro-secretory neurons of the anterior pituitary gland that were believed to be simple peptides in 1975. He defined neurosecretion by these neurons as the release of hormonal material into the circulating body fluids whether the neurons contained Gomori-positive staining granules or not (page 166).

The presence of these Gomori-positive staining granules may form a useful distinction between those neuro-secretory neurons and the cells releasing more complex hormones through internal (as opposed to electrostenolytic) operations.

Swanson has provided a more complete, but still less than adequately structured discussion of the initial neuro-endocrine interface.

4.6.4.1.1 The simplest neuroeffectors

The two chemicals of the broadest application are also two of the simplest, acetylcholine and nitrogen oxide. The data suggests neither of these chemicals is secreted by stage 7 neurons; but rather, they are released from receptor sites similar to those used in the electrostenolytic processes.

4.6.5.2 Origins of the hormonal system

4.6.5.3 Hypothalamus releases mostly peptides

The hypothalamus releases eight initial endocrine hormones, primarily peptides of between three and 44 amino acid residues, designated by the shorthand notation XRH or XIH for –releasing hormone or –inhibiting hormone respectively. One, known as the prolactin inhibiting hormone, PIH, is actually dopamine, a catecholamine. These initial hormones are used

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to control a wide variety of second generation endocrine hormones. They are released by the hypothalamus into the hypophysial portal vessels leading to the anterior lobe of the pituitary gland and the general circulatory system of the organism. Dopamine is also released as a paracrine hormone within the CNS itself.

Figure 4.6.5-1 shows it is appropriate to use a symbology similar to that for other electrostenolytic mechanisms for the assembly of the simpler hormones on the surface of the neuroeffector neuron. In this case, the reactants and residues are all listed next to the symbol as appropriate. The pair of vertical lines within the arc indicate the reaction is controlled. In this case by the axoplasm to external environment potential, V_A . pGLU is pyroglutamic acid, a cyclic form of glutamic acid created by the condensation of glutamic acid. HIS is histidine and PRO is proline. The product of this assembly of essential amino acids is the tripeptide, TRH (thyrotropin releasing hormone), also known earlier as TRF (thyrotropin releasing factor).

There are eight relatively well established hormones released by the neuro-endocrine interface neurons. They are all believed to be peptides of up to 44 amino acid residues, although one is frequently claimed to be dopamine. Three are peptides of ten amino acid residues or less. Achieving a 44 amino acid residue peptide by the method described in this paragraph may be difficult. In those cases, the more complex secretion procedure described below may be required.

Two additional "simple" peptides are also released by the hypothalamus. They are vasopressin, VAS, and oxytocin, OXY, nine amino acid residue peptides that also contain a disulfide bridge. This bridge may put their assembly into a different class than that suggested above.

The larger of the peptide hormones may require the presence of the Gomori-positive staining granules inside the axolemma to create the hormones prior to their secretion through the axolemma.

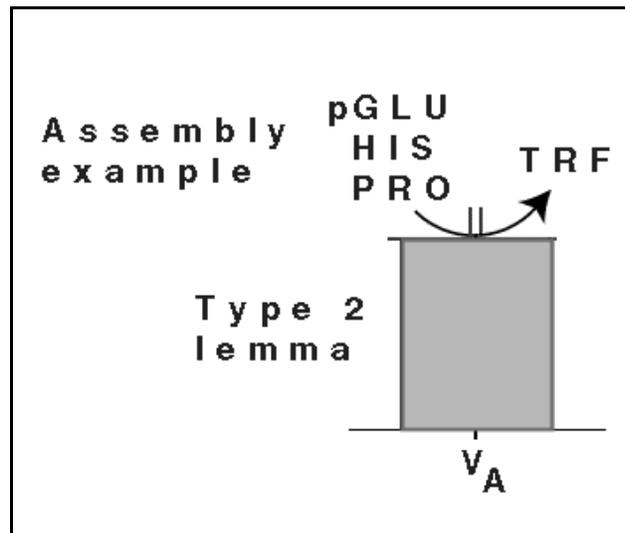


Figure 4.6.5-1 The extended electrostenolytic symbology used for the hormonal neuroeffectors. The axoplasm potential, V_A , and the stereochemical arrangement of the electrostenolytic site control the assembly of the tripeptide, TRF, from its constituents.

4.6.5.3 The majority of the hormones are high molecular weight molecules

Most of the hormones controlled by the hormones released by the hypothalamus are much more complex proteins and glycoproteins. These are generally released by cells that are not considered neuro-secretory but hormonal cells in their own right. A discussion of these types of hormones is outside the scope of this work.

4.6.5.4 Pheromones

A pheromone is a secreted or excreted chemical factor that triggers a social response in members of the same species. There are alarm pheromones, food trail pheromones, sex pheromones, and many others that affect behavior or physiology. Pheromones may be volatile or non-volatile. Pheromones vary greatly in their chemical complexity and the character of a specific pheromone may appear quite generic to most species but have a major specific effect in the target species. Pheromones are fundamental examples of exocrine hormones, sometimes labeled ecto-hormones.

The pheromones of lower animals have been studied much more aggressively than that of higher animals. However, many of these studies have been based more on observation of behavioral activity than on use of the scientific method to design experiments demonstrating activity as defined by a pheromone. Wikipedia provides a good but elementary discussion

of these study areas.

An extended discussion of the pheromones is outside the scope of this work.

4.6.5.4.1 The potential pheromones of cats

Many of the remarkable “attractants” to cats, believed to be pheromones, are multi-cyclic hydrocarbons containing oxygen or nitrogen substitutions. Other cat pheromones appear to be aliphatic thiols.

4.6.5.4.1.2 The potential pheromones of bees

According to Wikipedia, “Honeybees have one of the most complex pheromonal communication systems found in nature, possessing 15 known glands that produce an array of compounds. Pheromones are produced as a liquid and transmitted by direct contact as a liquid or as a vapor. One of the most studied pheromonal glands in the bee is believed to release more than 40 chemical compounds, including isopentyl acetate (IPA), butyl acetate, 1-hexanol, n-butanol, 1-octanol, hexyl acetate, octyl acetate, n-pentyl acetate and 2-nonanol.” It can be argued that this group of simple chemicals could represent the lexicon of a simple language, rather than a pheromonal system.

A majority of the reported pheromones of bees are more complex chemicals with very specific effects upon the target bees.

4.7 Material from vision and hearing modalities as exemplars

A variety of figures previously published by the author provide additional perspective relative to the architecture of the neural system.

4.7.1 Effectiveness of information extraction–by traffic count

Figure 4.7.1-1 provides an estimate of the traffic flow in the visual system based on nominal number of neural paths between major stages and/or engines. Note the nominal 15 million sensory neurons of each retina has been reduced to about one million neural paths at the optic nerve. Of this million, only about 23,000 serve the high acuity foveola path to the perigeniculate nuclei and the analytical capabilities of the pulvinar.

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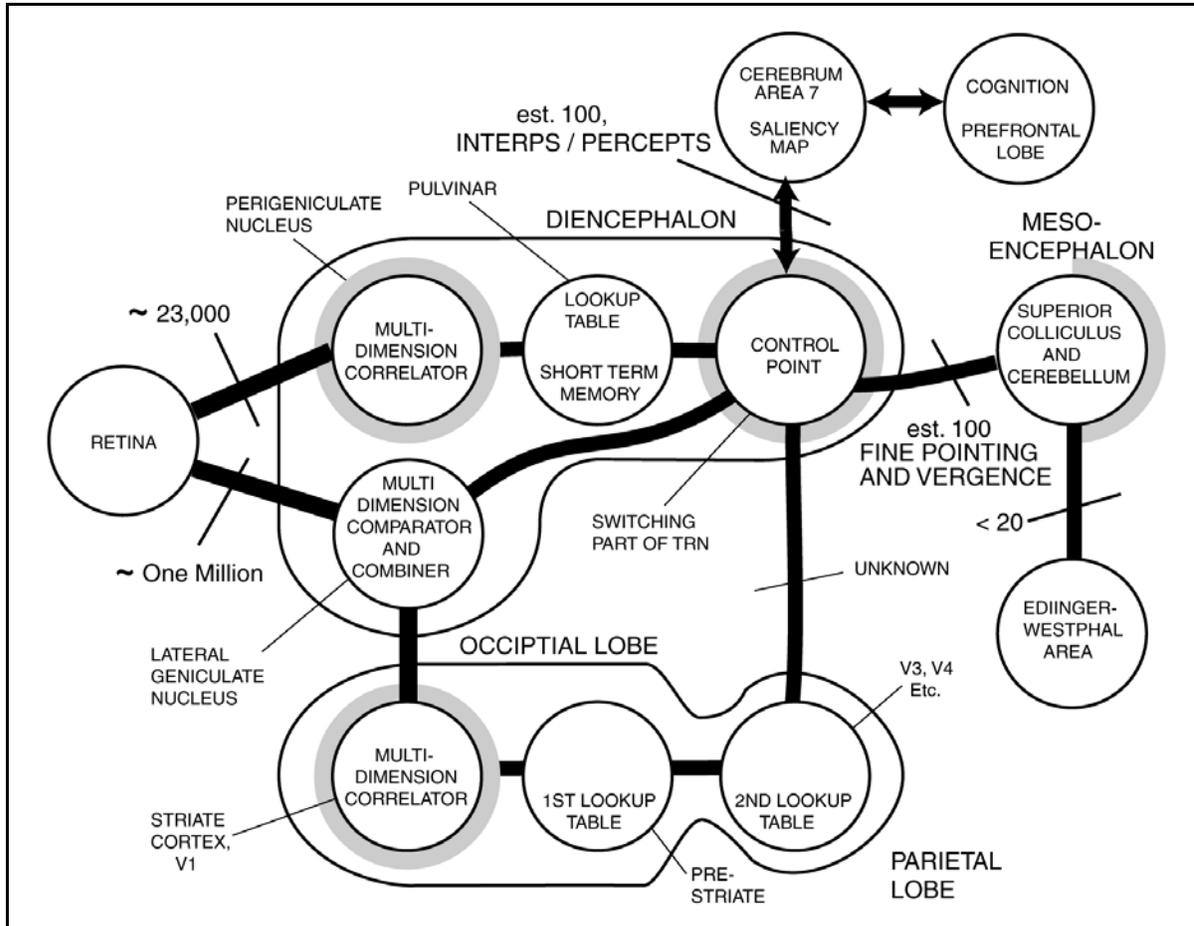


Figure 4.7.1-1 Traffic flow through the complete visual modality based on neural path count. The high path count via the lateral geniculate nucleus and V1 is important. However, the low path count by high visual acuity path via the perigeniculate nucleus is key to human analytical vision. The two-way commissure path to and from the saliency map and stage 5 cognition has not been quantified. See text. The major areas of reticulated tissue are shown with a gray halo. Many special purpose mesh network paths are not shown.

Most of the signal paths shown are unidirectional. The proposed commissure carrying word serial/bit parallel messages between the TRN, the saliency map and the stage 5 cognition engines are shown by the double arrowhead connections.

The multiple paths to the control point (TRN) help explain the phenomenon of blindsight discussed in **Chapter 15**. It is clear from the schematic that the occipital lobe is not required for the cognitive engines to receive color and motion information from the retina via the LGN. . ADD words. Nor is it required to receive high acuity information from the foveola and PGN.

Similar levels of signal path compression (convergence) are found in the hearing and olfactory modalities.

4.8 Architectures of the individual neuron types ADD

[xxx five basic neural types;
Sensory neurons,
signal processing neurons,
signal projection neurons,
locomotion neurons, and
affecter neurons.

The sensory neurons are the most topologically complex, with two distinct connexions found within the same envelope, a few distinct pedicles of their axon tree and a myriad of receptor sites associated with their (frequently complex) dendritic structures.

The signal processing neurons exhibit the simplest topology, containing only one connexion within the plasmalemma and exhibiting only two input and one output structures. However, their morphological structure may appear quite complex.

The signal projection neurons are by far the longest of the neurons with their distinct repeating topological structure of a Node of Ranvier and associated axon segment. In addition, they are the only neurons that employ myelination to achieve efficient phasic signaling.

The locomotion neuron exhibits a relatively simple topology but with operational features not found in the other neurons. That topology includes a series of axon segments or pedicles emanating from a primary axoplasm compartment.

The neuroeffector neurons exhibit a relatively simple neural topology but accommodate a wide variety of specialized chemical acquisition and release structures, frequently identified by a vesicular structure associated with the axon compartment. Their association in large knots to form primary "glands" are a distinguishing feature.

[xxx The specialized locomotion neuron may be found across the broadest sector of the animal phyla. It appears to be used within the non-arthropod invertebrate animals (a vast array of annelids (earthworms), nematodes (roundworms)), larvae of insects, *Arthropoda* (insects, arachnids, crustaceans),

Mollusca,
Reptilia, and potentially
Mammalia.

4.9 Architectures of the visceral systems ADEQUATE

Chapter 20 xxx will go into considerable detail relative to the visceral mini-neural systems. They are noted here primarily for completeness.

Key features of these mini-systems are their truly autonomous operation and their different pace of operations. In most cases, these systems continue to operate normally following their complete isolation from the parent neural system. Women believed to be brain-dead have given birth. A woman in Florida is believed to have remained alive for years in a hospice situation after being defined as medically brain-dead.

The difference in pace is frequently represented by different time constants for the circuit elements like those found in other modalities of the neural system.

4.9.1 Cardiac mini-system EMPTY

4.9.2 Enteric mini-system EMPTY

4.9.3 Uterine mini-system EMPTY

4.10 Summary-

4.10.1 Signature waveforms of the neural system

The above sections have introduced a variety of very unique signaling waveforms found within the typical neural system. Most of these waveforms exhibit specific, and frequently unique, temperature sensitivities. They vary with temperature based on a constrained

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biological temperature range and do not follow the absolute or Kelvin temperature of conventional Arrhenius Theory. They are most recognizable following stimulation by an *impulse* function (or another action potential of low amplitude in the case of the stage 3 action potential).

Five characteristic waveforms have been identified in this work. A wide variety of uncharacterized analog waveforms are found within stage 2 signal processing, resulting from a variety of signal processing activities..

- Generator Waveform– The nominal analog waveform of all stage 1 sensory neurons examined. It is a continuous waveform of quantum mechanical origin employing two time constants, one of which is stimulus intensity sensitive. It exhibits a unique stimulus condition, the Hodgkin Condition, when the two time constants are equal and the resulting waveform is a solution of the Poisson Equation.

- The generator waveforms have been described as the result of processes implementing the excitation/de-excitation (E/D) equation or photo-excitation/de-excitation (P/D) equation in this work.

- Action potential waveform– The nominal monopulse (phasic, but not binary) waveform of all stage 3 signal propagation neurons. It is a discontinuous waveform resulting from the action of a neuron operated in the switching mode of a relaxation oscillator. The leading edge of this waveform is virtually a straight line below the saturation regime of the Activa within the connexus. Closely associated with myelinated axon segments.

- Intermittent action potential streams–Streams of action potentials encoding monopolar information, derived principally from individual stage 1 stimulus channels or sums of individual stage 1 channels (ex. brightness information encoded by parasol ganglion neurons; conceived as Class 1 by Hodgkin, 1948).

- Continuous action potential streams– Streams of action potentials encoding bipolar information, derived principally from the differences between stage 1 stimulus channels (ex. chrominance information encoded by midget ganglion neurons; conceived as Class 2 by Hodgkin, 1948).

- Locomotion waveform– A waveform used widely within the animal kingdom to control the coordinated motion of a large number of muscles. Typically, a large number of pedicles are found along the length of a locomotion generating neuron, such as the giant axon of the squid *Loligo*. The neuron is not myelinated but is surrounded by a large number of neurons that aid in controlling its timing.

- Neuroeffector waveform– A waveform of stage 7 neurons that can be a feature of neuro-muscular or hormonal signaling. Generally represented by the decoding of stage 3 phasic signals representing commands issued by stage 6 neurons. Their precise form, analog electrical signal or hormonal concentration per unit time, can vary widely as the command signal directs.

- Cardiocyte timing waveform– A waveform very similar to the action potential waveform but of considerably longer duration. It is also a discontinuous waveform resulting from the action of a neuron operated in the switching mode of a relaxation oscillator. While the term syncytium has frequently been associated with the neurons generating these waveforms, reliability considerations would suggest they operate independently, possibly as a set with the determination of which neurons oscillate and when under separate neural control..

- Cardiocyte effector waveform– A waveform resulting from over-driving a cardiocyte using a cardiocyte timing waveform or orthodromic cardiocyte effector waveform. The resulting waveform exhibits a saturated maximum amplitude and a variable duration.

The waveforms of stages 2, 4, 5 & 6 are not represented in the above list as they are analog waveforms covering a very large range based on their diverse applications. They have usually been overlooked and only the stage 3 pulse streams encoding the output analog waveforms of very large signal processing engines have been reported. They are typically reported without any explanation as to their origin.

It is likely that many of the stage 4 & 5 waveforms are associated with word serial/bit parallel

signal projection. Such signaling requires multi-probe recording techniques which are only now becoming practical in neural research.

4.10.2 Electrolytic Serape used to analyze discontinuous neural waveforms

Section 4.4.4 has introduced and Section 9.2.4 has developed an important tool for interpreting the operation of the stage 3 ganglion neurons, synapses and Nodes of Ranvier and the action potential waveforms they produce (or reproduce).

4.10.3 Lack of a role for efferescent waves in the neural system

No dedicated efferescent waves have been defined within the neural system. While many sensory channels appear to be reporting on the results of motor neurons, they typically are reporting on changes in the configuration of the organism (orientation or physical relationship) relative to its exterior environment, and not just echoing a command signal back to as CNS source.

4.xxx.xxx Circuit diagrams of vision as exemplars

The visual system can be used as a model for each of the sensory modalities. It is the most intensely studied modality and there is a surfeit of exploratory information available. Unfortunately, a wide variety of schematics of the modality can be found in the literature. Most of these do not differentiate between the stages of the neural system in a consistent manner. Rose has provided a recent version exhibiting this problem¹²². His designation of the stage 3 parvocellular and magnocellular pathways differs from the typical presentation where those paths lead to the stage 4 lateral geniculate nucleus, not away from it. The circuits leading away from the LGN are designated anatomically as Meyer's loop and more functionally as the koniocellular pathway. Similarly, the posterior parietal area (BA 7) contains stage 4 neurons presenting high level information to stage 5 while the frontal eye fields of Brodmann area 8 are stage 6 premotor circuits receiving volition instructions from stage 5 and issuing adverse instructions to the motor system. These areas do not normally communicate with each other, except via the stage 5 cognitive circuits.

Figure 4.10.3-1 shows a proposed revision to his figure 2.10. The footprints of the two fields of view have been modified to include foveola in their centers. At the scale of the figure, both the stage 1 and stage 2 circuits of the retina are shown within the footprints of the fields of view. The neural signals from these foveola are shown traveling to the left and then up to the perigeniculate nucleus (next to the lateral geniculate nucleus on the surface of the thalamus). The PGN is shown analyzing the word PRESS imaged on the foveola. The interp derived from this process is passed to the pulvinar for further processing and assembly into a percept that can be passed to the saliency map of the posterior parietal lobe (area 7). The paths and elements at lower left constitute the analytical mode of the visual modality.

The frontal eye fields of stage 6 found in Brodmann area 8 are shown at upper left receiving volition instructions from the cognitive circuits of stage 5 and issuing adverse instructions to the oculomotor circuits. These efferent circuits associated with conscious motor activity are separate from the oculomotor servo loops that drive the oculars subconsciously (not shown).

All of the engines and architectonic regions shown below stage 5 and above the field of view footprints are afferent stage 4 signal manipulation circuits. The pathways shown connecting all of the sources and targets are stage 3 signal propagation circuits. The stage 3 pathways to and from the lateral geniculate nucleus have been re-labeled to follow more generally accepted practice.

¹²²Rose, S. (2005) *The 21st Century Brain*. London: Jonathan Cape pg 49

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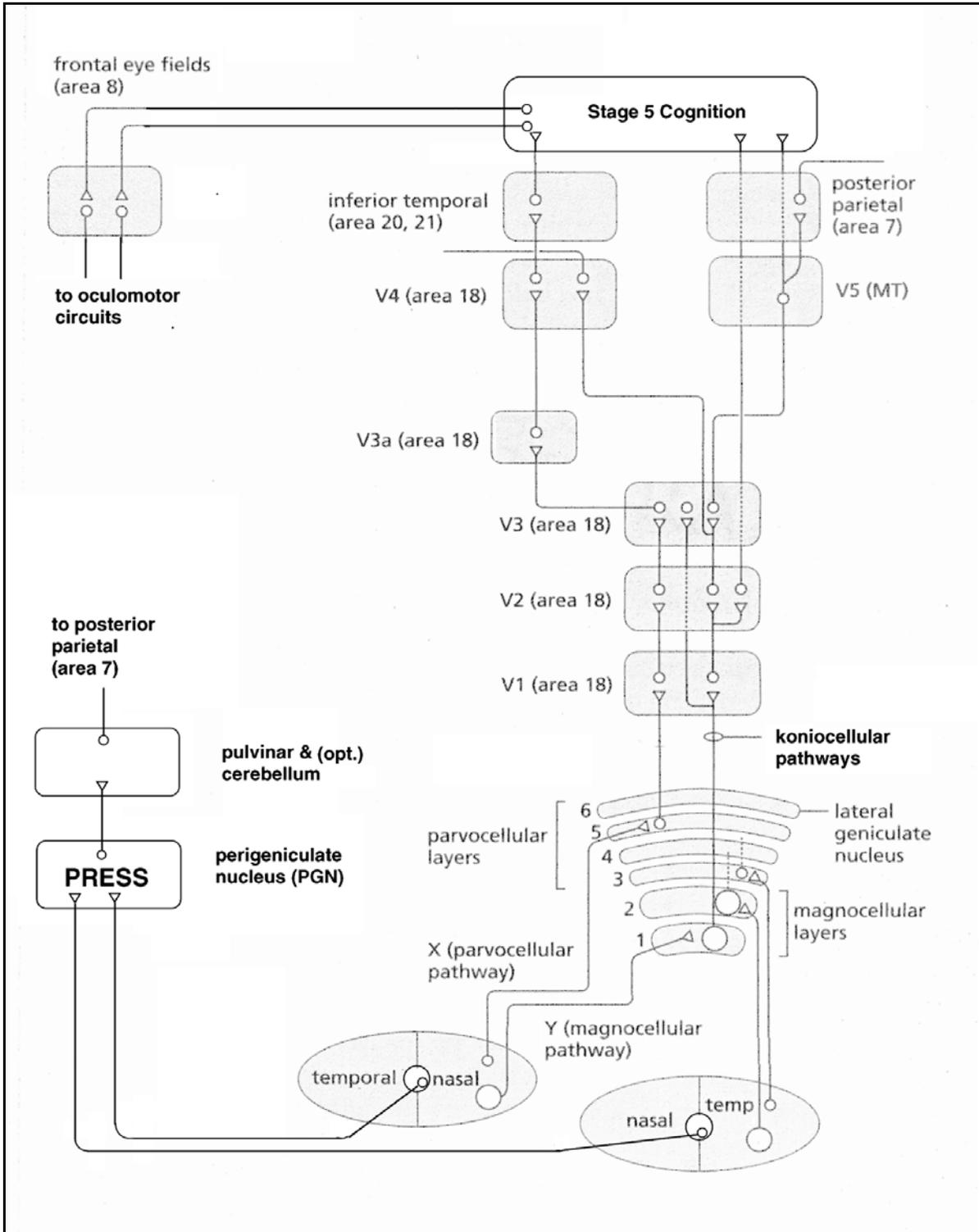


Figure 4.10.3-1 Fundamental neural pathways of the vision modality. The circular foveola of the retinas have been added to expand the schematic to include the analytical mode of vision at lower left and the awareness mode of vision on the lower right.. See text. Modified from Rose, 2005.

4.11 Circuit diagrams of vision as exemplars MOVE TO STAGE 1

It is common to find simple circuit diagrams in the vision literature. It is uncommon to find precise statements about the applicability of these diagrams. They are invariably "floating models" based on the assumption of circuit linearity. When electronic test circuitry is attached to the actual visual circuits, it is invariably done in a less than precise manner because of a lack of knowledge concerning the design of the biological circuitry under study. This Section will present some of the pertinent design information and the applicable circuit diagrams. The diagrams presented in this section begin with the detailed, large signal, diagrams and progress to a selection of simpler diagrams of less general applicability.

It is important to note that the large signal diagram is not an "equivalent circuit." It is the actual circuit employed in animal vision presented in human linguistic and graphical notation. This circuit can be used to accurately predict the performance of the visual system of a generic animal. It can be tailored to more accurately represent the visual system of a specific animal by making minor circuit modifications to account for specific features resulting from evolutionary adaptation. As discussed elsewhere in this work, an "equivalent circuit" can be constructed using man-made components that will faithfully reproduce the performance of the biological eye. However, the equivalent circuit must be constructed of carefully selected components and operated at the appropriate electrical voltages if it is to emulate the biological eye over even a fraction of its dynamic range. Each component must exhibit (frequently nonlinear) characteristics that are the same as those of its biological counterpart. This is particularly true with respect to the avalanche type transistor used to emulate the first Activa of each photoreceptor cell.

4.11.1 Background

To describe the actual circuit topology of the visual process, many of the procedures used in electronics are available. The first step in developing a circuit diagram is usually to determine what signaling environment is involved. What is the dynamic range of the amplitude of the signal and what is the frequency of the signal spectrum? In high performance circuits, it is also important to determine the "grounding plan."

4.11.2 Effects of temperature

Temperature plays a much larger role in biological electronic circuits than in typical man-made circuits for two primary reasons. First, man-made circuits tend to use circuit elements (other than semiconductor devices) that are not significantly affected by temperature variations between zero and 100 degrees Celsius. The conductors (wires) used for interconnection are virtually immune to temperature change. In the case of semiconductor devices, temperature plays a major role and special "balanced" circuitry is frequently used to reduce the effect of temperature on the performance of the overall circuit.

Biological circuits are even more limited than metallic semiconductor circuits. Essentially all of the circuit elements and interconnections of the neural system are either electrolytic or semiconductive in nature. The wires used in biological circuits are invariably insulating conduits filled with an electrolyte. Both the conduit and the electrolyte are of organic origin. They frequently operate over a restricted biological range and exhibit a change in electrical parameters with temperature that is much greater than found in inorganic circuitry. The predominant circuit element in the biological circuits of vision is the semiconductor diode and its progeny, the active electrolytic semiconductor device or Activa. Both of these devices are sensitive to temperature according to the basic diode equation. The result of these factors is that biological circuits will not operate as designed beyond the biological temperature range and they exhibit significant changes in performance over the biological temperature range, from near the freezing point of water to less than fifty degrees centigrade. Outside of this range, the materials change to different states of matter. These changes are irreversible and frequently described as denaturation.

The temperature must be accurately recorded and specified when making precise laboratory measurements related to neurons. In warm blooded animals, this requirement is frequently overlooked. However, it is important to specify the temperature of the specimen (not just a nearby substrate, whether *in-vivo* or *in-vitro*) to within 0.1 Celsius to insure repeatability of the results by independent investigators.

END of TEXT xxx

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