20 Comparing Different Theories of Vision[1]

> That the making of colour-theories goes on apace is a most healthy sign of intellectual activity–a sign that there is a widespread feeling of the utter inadequacy of the theories of Helmholtz and of Hering.
>
> Christine Ladd-Franklin, 1929

20.1 Theory comparisons

The goal of this work has been the delineation of a comprehensive and consistent theory of the process of vision in all animals. This was to be accomplished by considering the broadest possible range of technologies and physics in order to avoid the use of "floating models," *ad hoc* theories, or pet ideas. The resulting product appears to meet this objective to a higher degree than the author initially expected. It presents a single global model that conceptually applies to all animal vision and specifically defines the major approaches to vision adopted by all of the major phyla of the animal kingdom.

Ladd-Franklin, a contemporary of Helmholtz and of Hering has described the most significant limitation of their theories[2]. In essence, proponents of both theories hail their ability to explain one set of phenomena while refusing to address phenomena that conflict with their theories. Her book is recommended reading for one seeking a perspective on how science progresses, and how the early theories lacked any significant foundation in physiology.

The inadequacies of these early theories has led to their amalgamation into the zone theories of the present. The theory developed in this work is a zone theory.

While Ladd-Franklin was very outspoken, her observation-based theory has not stood the test of time. However, she did offer several observations concerning theory development. She noted the difficulty of combining the results obtained from physiology, from physics and from psychology because most analysts did not have sufficient breadth in their training and/or experience. She also noted an all-too-often series of occurrences;
1. A deduction from a theory was taken as a fact.
2. That supposed fact was taken as confirming the theory.
3. The same supposed fact was held so strongly within the community that the highly ingenious reasoning showing it to be erroneous failed to awaken attention in that community.

To a great degree, the above situation is found throughout the current common wisdom concerning vision.

Ladd-Franklin also annotated a list of features in any good theory.

"1. It is not desirable that any theory should resolutely ignore a large proportion of the plain facts which hold in the region which it seeks to cover.
2. It should be the first object of any theory to provide itself with a suitable terminology for the facts which lie within its domain.
3. Any theory regarding the connection between a series of psychical facts and a series of physical facts, the principle of psychophysical parallelism must obtain.
   A. one must not make use of one and the same conception to explain two totally different sets of phenomena.
   B. one must not attach the same conscious experience to two different physiological hypotheses."
4. Any theory must be as comprehensive as possible. It must avoid floating models and local *ad hoc* hypotheses.

The making of models is universal in the search for a consistent and instructive picture of nature. This model incorporates not only the morphological aspects of vision, but also the signal generation and distribution techniques used within the visual system up to the point of signal demodulation within the cortex of the brain. Only a few well supported psychophysical conclusions will be drawn about the computational and cognitive capabilities of the brain. The signal generation and distribution system of vision is known to be quite sophisticated but its complexity at a fundamental level has not been evaluated previously. This work has provided a fundamental road map of the signal handling function in vision. The model shows this signal handling to be quite simple in an elegant way. Because of this simplicity and elegance, the actual visual process is simpler than many concepts previously presented in the literature. This chapter is designed to compare individual facets of this

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[1]Released April 30, 2017

[2]Ladd-Franklin, C. (1929) Colour and colour theories. NY: Harcourt, Brace (reprinted in 1973 by Arno Press of New York. LOC # WW 150 L154c)

overall theory with a variety of the hypotheses presented in that literature.

Because of the scope of this theory, it has a major advantage over many earlier theories. It can present and define specific input, and output, characteristics that are only loosely defined in the development of these other theories. It can also do this for individual sub-systems of the visual system because of the recent advances in electrophysiology. This overall capability allows the integration of the many narrowly focused "floating models" found in the literature into a more comprehensible global environment. This integration in turn frequently provides additional insight into the previously described local model. In the vernacular of Harmon & Lewis, see below, this work has resulted in an *overt* model, a comprehensive model designed to complement experimental neurophysiology, not the tacit modeling that always accompanies individual experiments, nor the floating models used to describe a specific experimental result.

A necessary result of having a global model available is that some hypotheses associated with one or more "floating models" may not fit into the overall plan at all. It is useful to locate these hypotheses and highlight them. Unless they can be reformulated by their authors, they should be discarded as non-viable in the global context of vision.

Most competing theories and models are limited in scope, conceptual in nature, and have not been reduced to mathematically precise expressions. Many "Laws" have been defined that only apply over a limited range. These have generally been derived from various slopes and asymptotes related to the graphical presentation of the results of specific experiments. Many hypotheses rely on the intuition of the author or his particular evaluation of the teleology involved.

20.1.1 Fundamental concepts of this Theory

This work takes a broader and more cohesive approach to a theory of vision than discussed in Wyszecki & Stiles. It finds fault with much of the philosophy in their Preamble to Chapter 18. Where they speak of an element of intuition, an element of broad experience is more appropriate. As others have said, inspiration is the result of hard work. They strain to separate a partial model from a more comprehensive theory; defining enriching, impoverishing and floating models. This work deprecates the floating model and finds fault with the partial model unless the boundary conditions are extremely well defined. It is hoped this work will provide both a Theory of Vision and a Mathematical Model of Vision that is currently comprehensive and easily extensible by others. Insights obtained during the development of the Theory have resulted in several new inventions, both in fact and in the language of the Patent Office, which hopefully will be of use to man. One of these is an entirely new class of devices which caused the Patent Office some difficulty in classification; the biologically based electrolytic semiconductor device, the Activa.

The fundamental concepts emerging from this theory are several;

The basic visual capability of all animals can be traced back at least as far as the first bilateral animals. This capability has evolved morphologically into three main configurations. Each major phyla of the animal kingdom has adopted one of these configurations and then proliferated that configuration into such a wide variety of adaptations that it is frequently possible to ascertain overlapping similarities between the more bizarre forms.

There is a fundamental architecture with regard to signal generation and handling that is common to all visual systems. This architecture is fundamentally electronic, as opposed to being ionic or chemically, based. It involves a variety of non-linear processes, involving both thresholding circuits and non-linear analog amplifier circuits. The long wavelength sensing channel is particularly significant in this regard.

The fundamental mechanism involved in signal generation and transmission is unique in that it skirts the second law of thermodynamics through two previously unrecognized features. The visual system, as well as all animal neurons, uses diodes instead of resistors in various impedances to avoid the generation of heat. In addition, it uses reversible chemical reactions for the purpose of deriving energy to operate the system and recovering unneeded energy discarded by the signal handling function

The fundamental signal sensing mechanism employs a retinoid family not previously reported in the scientific literature of vision. Members of the family are found commonly in other branches of science. This family is employed in a configuration also not reported previously, e. g., a passive transducer found outside of any living cell. This configuration is also found commonly, in other sensory structures in the animal.

The spectral scope of the fundamental visual process is tetrachromatic, with four chromophores employed in separate sensing channels exhibiting peak spectral absorptions at or near 342, 437, 532, and 625 nm. respectively (+/- 2 nm. at 37 C, nominal human physiological temperature).

Different animals have made compromises with respect to their environment that have sometimes involved giving up the practical use of one or more of the above spectral channels. Humans and other non-aquatic chordates have lost the ability to see in the ultraviolet in order to focus properly in a gaseous environment. Conversely, many if not all non-aquatic arthropods have lost the ability to sense wavelengths in the red region of the spectrum, presumably because of the temperature at which they are incubated

The Theory , and model:

+ is universal. They apply to the visual apparatus and mechanisms of all known animals.

+ explains the tetrachromatic visual capability that is found in most animals.

+ constitutes a simplex theory of color vision. There are no monochromatic sensory elements.

+ is a complete Theory involving the vascular, metabolic, muscular, and neural systems of the animal.

+ incorporates the elements of a zone theory of color vision.

- It recognizes three independent photoexcitation channels, each employing a separate chromophoric material.

- It recognizes a single luminance channel and *three* independent chrominance channels (only two functional chrominance channels in humans and other non-aquatic animals).

- The signal channels are not antagonistic. In fact they are absolutely orthogonal.

+ Details the third and fourth stages of visual signal processing.

-The third stage involves coding, transmission and decoding of the signal information.

- The fourth stage is focused on computational processing and cognition within the cerebellum.

+ Provides a new Chromaticity Diagram that *totally* eliminates the necessity for the current tristimulus based system employing imaginary primaries.

- The new Diagram employs orthogonal axes and is easily extended to incorporate other related processes.

- The chromaticity diagram for animals with the most comprehensive visual system from a spectral perspective involves three orthogonal axes as opposed to the two commonly used to define human vision.

20.1.2 Terminology and Methodology

The remainder of this Chapter will focus on comparing other theories of various extent with the one presented here. To make this comparison, it is useful to review the state of the art in system analysis and system synthesis. These fields have become highly developed in the last 40 years, even though there are relatively few general texts on the subject below the graduate level. Both system analysis and synthesis have played major roles in the understanding of man-made systems. They have been used to a much smaller degree in physiological systems. Harmon & Lewis[3] have attempted to remedy this situation. They have attempted to define system analysis, synthesis and modeling in physiological context. They have also explored earlier attempts at modeling.

In accordance with generally accepted rules of logic, this work has used the word theory in the global sense of a collection of individual hypotheses. If the literature of vision is reviewed in this context, no broad theory is found. There are a series of narrower hypotheses. Most of these, particularly the older ones found in the domain of psychophysics, treat the entire vision system of an animal. Except as a result of serious accidents, there was no attempt, or opportunity, to subdivide the system in a definitive way until quite recently. This came with the introduction of electrophysiology.

[3]Harmon, L. & Lewis, E. (1966) Neural modeling. XXX vol. 46 July pp. 513-583

20.1.2.1 Models

Quoting Harmon & Lewis: "An important part of the utility of a model lies in its ability to focus disparate evidence and interpretations into one coherent view.... Models are valuable to the extent that they raise new questions and suggest new relationships, perhaps leading to new experiments that might not otherwise have been considered. Worthwhile models are predictive; that is, new relevant properties are deducible from them. Further, a model often suggests constraints that may exist in the system being modeled." Finally, quoting again: "Models are a necessary ingredient of scientific method: as deductively manipulatable constructs they are essential to the evolution of theory from observation."

The criticisms of models, particularly models related to neurology and vision, have taken many forms and will not be explored here. However, the definition of a model proposed by Wyszecki & Stiles[4] is not the definition of a model used here. A model can be as accurate as the author desires, and time and money permit. It is also possible to derive a simplified model from an overall model for pedagogical purposes. This does not destroy the value of the overall model.

Many of the models presented in the vision research field as late as the late 1890's fail to meet the criteria specified by Harmon & Lewis and thus fail in their primary purpose. As an example, one significant voice in visual modeling for nearly half a century has moved to a three stage model but has limited the model to linear processes. They have also ignored much electrophysiological data in favor of equivalent, *in their eyes*, psychophysical data[5]. Several other authors have disparaged this work because the model has surfaced its own inadequacy in certain parameters. Their alternate model shows similar shortcomings. Both models are based primarily on psychophysical data and lack any scientifically measured or verifiable thread between the input stimulus and the output perception.

20.1.2.2 Realizability Theory

One important mathematical tool of the general field of system analysis and synthesis relates to the subject of realizability. Can a system be designed built and/or operated in accordance with a given set of parameters?. Conversely, is it reasonable to assign a given set of parameters to a system if that set does not conform to the known requirements of realizability theory? Realizability theory is a major component of the theory involving the response of physical systems.

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[4]W. & S. Op. Cit. Pg. 584

[5]DeValois, R. & DeValois, K. (1996) On "A three stage color model" *Vision Res*. Vol. 36, no. 6, pp. 833-836 and articles referenced in the opening paragraphs

20.1.2.3 "Teasing" the model

A second result of the application of system analysis tools to the visual system has been the separation of more comprehensive sections of the system, and the equivalent model, into simpler individual sub-sections. This has frequently required a redefinition of terms to account for the new found information. An example is the term transduction as used in visual physiology. Transduction is the transformation of a luminance signal into a neural signal. With a more detailed definition of the visual system, it becomes necessary to separate this term into two separate terms. Photoexcitation is the conversion of a luminance signal into a quantum level signal describing the state of the chromophoric material. Translation can be defined as the conversion of this quantum level signal into a signal current within the neural system. Thus, transduction includes photoexcitation and translation. The translation term can also be divided into two separate processes, the de-excitation of the chromophoric material and the creation of an electron charge within the first neuron of the neural system.

20.1.2.4 Improvement in available tools

Most of the early theories of vision up through the opening of the twenties century were primarily observationally based employing psychophysical experiments. These experiments were *in-vivo* and limited to recording the output signal, usually binary and frequently verbal, related to a given input stimuli. Because of these limitations, most of the results were global in scope and the resultant theories lacked specificity. Such experiments reached a variety of interesting but awkward conclusion over time, such as the early concept that light left the eye in order to illuminate the observed object. More recent theories have attempted to set the limiting parameters associated with vision and in a conceptual way, define the signal processing schema used to satisfy the global performance parameters.

With the rise of electronics, the field of electrophysiology has greatly expanded and it has been applied to the visual system in a variety of ways. It has also spawned a new problem. It has become possible to make measurements in a new situation that is not defined in the literature. Previously, tests were either *in-vivo* or *in-vitro*. The most defendable results were always obtained through *in-vivo* measurements. However, some recent spectroscopic measurements have disproved this axiom. They have involved in-*vivo* tests performed in a non-operational configuration, e. g., lacking an adequate model, results were sought using light applied perpendicular to the axis of the Outer Segment that did not properly simulate the required axis of illumination that is parallel to the axis of the Outer Segment. The implemented and nominally *in-vivo* spectral response test gave incorrect results. Correct experimental design must insure that nominally *in-vivo* tests involve normal input excitation and/or normal output signal recording unless deviations from nominal are highlighted.

One of the results of the system analysis described in this work is confirmation that the visual system in animals, including human, is not linear. In fact, parallel chromatic photodetection channels exhibit different inherent characteristics in this area simultaneously. Furthermore, the system, and each chromatic channel, is not stable with time under normal variations in illumination. Thus the visual system must be considered from a non-linear state-variable perspective if it is to be understood. Hogland[6] captured the essence of this position with regard to vision when he offered " A correct analysis of the input signals to the central nervous system would require correction for the instantaneous sensitivity of each receptor, and for the concentration of visual pigment."

The visual system of animals is highly non-linear under high contrast conditions. More significantly, the different chromatic channels exhibit different non-linearities under similar conditions. Only when input contrasts of less than 2:1 are involved can the system be considered reasonably linear. This characteristic has a major impact on good experiment design.

20.1.2.5 Difficulties in the visual sciences

Many experiments in the visual sciences have attempted to avoid using state-variable analysis by exposing the subject to a constant level of illumination for a period of time before a given experiment. This procedure works within limits. However, it obscures many relevant functional relationships within the system.

Something needs to be said concerning the Principle of Univariance associated with Rushton, and the use of templates, particularly those usually associated with Dartnall. They can only be considered archaic at this stage of development in the visual sciences.

A more serious problem has persisted for the last 50 years in the field of the Neurosciences. This is the refusal to consider electronic alternatives to the chemical hypothesis concerning signaling within the neural network. Turning a blind eye to such a promising capability is most definitely not scientific and verges on a fanatic theology. The key failure in the Neurosciences of the last 50 years has been the failure to understand the

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[6]Hogland, (1973) XXX Pg. 277

mechanism underlying neural action. A major consequence of the system analysis used in this work has been the discovery of the dependence of the neuron on "transistor action." The discovery of the mechanism underlying the action of the neuron has been a consequence of:

+ the message of earlier models, that the process was not sufficiently understood to accurately model, and
+ a shining example of the capability of the synthesis technique.

20.2 Computational models developing hypotheses

Several abstract models of the visual system have appeared. They generally approach the problem from one of a variety of specific perspectives. Their scope varies widely.

20.2.1 An "ideal observer" model

Geisler has provided an extensive paper on a computational model of only the physiological optics, Stage 0, of the visual system[7]. He describes his model as an ideal observer within this limited context. However, in the course of developing this model he has attempted to place it in a context compatible with the conventional wisdom that the system is an imager (even though he notes that the system goes blind in the absence of residual motions). As a result, he has tailored his model to satisfy selective data from the broader literature. This has led to an excessive concentration on the dimensions of the mosaic of the retina as a performance controlling parameters. His conclusion that the "retinal image is sampled spatially and spectrally by a lattice of discreet photoreceptors" overlooks the operation of the system as an edge detector as opposed to a pixel integrator. He later notes, "The achievement of hyperacuity performance in location-discrimination tasks has been a long-standing puzzle in vision science.

The paper is very well outlined and organized. It surfaces a number of problems associated with the luminance and spatial parameters of the model that are assumed to be addressed in the neural portion of the system. These include the limited low frequency spatial response of the system and the necessity of a variable gain mechanism to account for the threshold performance at different light intensity levels. Some authors have quoted the Geisler paper out of context, forgetting that it is only applicable to Stage 0 of vision. They have focused on his lumanance and chrominance contrast sensitivity at high spatial frequencies (figure 26) without recognizing the more complete functions discussed in figure 15.

When reviewing the optical line spread functions as a function of iris diameter (his figure 2), it is useful to review [**Figure 2.4.3-1**] of this work. Only his 2.0 mm example is indicative of photopic visual performance. His normalization protocol does not reflect the fact that the absolute intensity of the light at the retina increases by a factor of 8.4 for the 5.8 mm diameter compared to the 2.0 mm diameter.

It is interesting that Geisler has replotted the data of Estevez (2079) so as to emphasize the Purkinje Peak in the absorption curve usually used to represent the absorption of the long wavelength photoreceptor (page 277). His figure 25, describing the spectral threshold sensitivity (in nm) versus wavelength of his ideal observer, exhibits a major deviation from the laboratory data in the 400-500 nm region.

It is unfortunate that in Appendix A he appears to encourage the use of computer routines to calculate Fourier Transforms rather than compute them in closed form. While this is generally necessary when dealing with optical spread functions, it is a major failing in computations regarding other aspects of the visual system.

20.3 Hypotheses related to Psychophysics

20.3.1 Basis of color vision

LeGrand provided a good perspective on the history of theories of color vision[8].

A series of widely recognized global theories of vision have been presented by Newton, Young, Helmholtz and Hering. Whereas the work of many between the time of Newton and of Young proposed theories related to the

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[7]Geisler, W. (1989) Sequential ideal-observer analysis of visual discrimination. *Psychol. Rev*. vol. 96, no. 2, pp 267-314

[8]LeGrand, Y. (1959) About theories of color vision *Proc Nat Acad* Sci vol 45, pp 89-96

mixing of physical colors (either pigments or lights), Young was one of the first to discuss the number of different photoreceptors required to sense the range of colors seen by man. Later work has moved into the area of the perception of colors (a psychological process). This distinction is frequently lost by authors presenting theories of color vision. Brindley present a scenario separating these two aspects of color and then provide additional subdivisions within the area of color perception[9]. They separate the number of colors required to generate a scene (the trichromacy of a scene) from the number of signaling channels required to *perceive* that scene in its chromatic entirety (the three channel hypothesis). They enumerate three sub-hypotheses of the three channel hypothesis:

+ Closest to Young, there are only three photosensitive pigments in the region of retina concerned.

+ there are more than three photosensitive pigments but only three kinds of photoreceptors. The photoreceptors may contain multiple pigments but only respond in one of three ways.

+ there may be more than three pigments and more than three receptors but in some central part of the visual pathway, there is a selective filter for information concerning color.

Although these hypotheses and sub-hypotheses discuss the operational aspects of vision, they are in fact derived only from psychophysical observations based on the functional aspects of human color vision. They are relatively limited in detail and do not attempt to define the operational aspects of vision. The Helmholtz theory is basically a restatement of the concept of Young. All of these theories can be considered single stage theories and they exhibited serious problems. In the late 1880's, attempts were made to rationalize these differences in what came to be known as zone theories (Donders '1881 and Muller '1896). These have frequently been described as two stage theories. The first stage dealt with detection and the second stage dealt with signal manipulation in order to model the measured results of psychophysical experiments. LeGrand[10] offers probably the most cogent discussion of the well known theories of Color Vision up through 1968. More recently, DeValois & DeValois and Guth have been supporting the development and promulgation of their respective psychophysical models. These models rely heavily on data collected in the first half of the 20th Century. More recently, Volbrecht & Kliegl have provided a review of virtually all earlier theories of color vision[11]. Some of the theories are not found outside of the psychology community. Their discussion is limited largely to psychophysics. They do not discuss any physiological model in detail.

Brindley provides a supplement to his discussion of color vision theories. As so often happens, his words are consistent with his conception of the color vision process but are not broad enough to allow other cases (possibly including the actual case). He says the parts of the visual pathway subsequent to the three photodetection channels, cannot contain fewer than three pathways or they would be dichromatic (or even monochromatic). He does not discuss or allow for the possibility of bipolar signaling channels. He then discusses deductions based on his three-channel hypothesis, quoting Grassman's Third Law, without considering the possible non-linearity of the system. Finally, he deduces certain principles relating to adaptation that are at best unsubstantiated through references. Apparently his concept of adaptation does not provide for chromatic adaptation.

Pirenne[12] provided the most cogent description of a good theory of color vision: "A physiological theory of colour vision must explain first of all, how and why the organism gives qualitatively different responses to certain lights having different physical compositions."

A particularly good test of any theory of vision, in the human at least, is whether it can explain the two non-chromophore related peaks in the luminosity function, near 494 nm and 600 nm., that occur under non-uniform spectral adaptation

20.3.1.1 Hypotheses predating 1870

20.3.1.1.1 The early Trichromatic Theory

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[9]Brindley, G. (1970) Physiology of the retina and visual pathway Baltimore MD: The Williams & Wilkins Co. pp. 209-223

[10]LeGrand, Y. (1968) Light, colour and vision. London: Chapman & Hall pp. 429-480

[11]Volbrecht, V. & Kliegl, R. (1998) The perception of blackness: an historical and contemporary review. *Chapter 10 in* Backhaus, W. Kliegl, R. & Werner, J. Color Vision: perspectives from different disciplines. Berlin: W. de Gruyter

[12]Pirenne XXX (1967) XXX pg. 174

Brindley has provided a readable synopsis of the development of the trichromatic theory[13].

Newton made a series of proposals with regard to vision followed by a very distinct caveat: "It is affirmed that these propositions are to be treated not hypothetically and probably, but by experiments or demonstrations." This theory does not conflict with the content or spirit of Newton's writings.

Thomas Young, followed by Helmholtz stressed the conceptual need for at least three chromatically independent sensory channels to explain the performance of the human eye[14]. Recognizing that their work was limited to the human eye, the Trichromatic Theory of Vision is seen to be a subset of this more general tetrachromatic theory. As shown in the context of this work, the Trichromatic Theory applies generally to large non-aquatic chordates such as man. The tetrachromatic theory applies to all animals, but its implimentation is subject to limitations related to the ecological niche of the particular species.

20.3.1.1.2 The Duplicity Theory

Archaic psychophysical experiments performed in the 20th and early 20th century, primarily the distinctive break (sometimes labeled the α-break) in the simplified human dark adaptation characteristic and the recognition of the distinct scotopic and photopic spectral responses led to the proposal that two distinct sensing processes were involved. Simultaneously, early morphologists were employing the very human characteristic of trying to divide their observed continuum of of photoreceptor dimensions into two arbitrary lots. The result of these two actions was the emergence of the Duplicity Theory of vision, first in humans and then most chordates.

This work makes no attempt to defend or negate the morphologists desire and right to divide a group of cells into two lots. However, this work does show that the α-break in the dark adaptation characteristic is not due to separate photodetectors in the retina. It also shows that the transition from the photopic to scotopic spectral response is continuous, is related to the unique energy levels characteristic of the L-channel photoreceptors, and is not due to a change in photodetectors with illumination range. The fact that the human scotopic spectral response peaks near the same wavelength as the isotropic (non-functional) spectral response of the rhodonine family of retinoids is an awkward coincidence.

20.3.1.1.3 The von Kries coefficient scheme of adaptation

Von Kries first formulated the intuition based ideas of Helmholtz and Fechner concerning the fatiguing of the visual system in the presence of higher illumination levels. The effect is now known as adaptation and it is reversable although via a hysteresis loop due to the asymmetry in the time constants involved. Backhaus, et. al. describe the development of the von Kries theory in more detail than most[15]. As they note, the theory is discussed more for its failures than successes at this time. His ideas were formulated within a linear framework as proposed by Grassmann. Backhaus describe the conceptual framework as a fusion of ideas. They say, "The Young-Maxwell-Helmholtz-Grassmann theory describes the transduction of light into a psychophysical or neural code and–together with the linking proposition proposes a receptoral mechanism that accounts for the Grassmann laws." Von Kries began with the hypothesis of a linear sensitivity control acting independently on each of three types of primary receptors. Although originally conceived as a neurophysiological hypothesis, it has been explored primarily as a psychophysical phenomenon. These experiments generally introduced a pre-adapting light followed by two lights of different intensity.

As Backhaus, et. al. note, "'the' psychophysical interpretation of the von Kries proposition splits into a variety of different hypotheses depending on the experimental and theoretical paradigm chosen." These experiments suggested that there were multiple mechanisms underlying the simple statement of the von Kries hypothesis. They then summarized the difficulties with the proposed model. "Nevertheless, the failure of 'the' von Kries law/proportionality rule gave rise to search for 'additional mechanisms (in an atteempt to preserve the basic spirit of a linear coefficient law), notably 'subtractive ones."

The basic problem with the von Kries hypothesis is the linear assumption. The fundamental logarithmic conversion of the current proportional to the input excitation into a voltage at the pedicle of the photoreceptor cells

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[13]Brindley, G. (1970) Physiology of the retina and visual pathways. Baltimore, MD Williams & Wilkins, pp 209-226

[14]Young, T. (1802) On the theory of light and colours. *Phil. Trans. Roy. Soc*. vol 12, pg 48

[15]Backhaus, W. Kliegl, R. & Werner, J. (Xxx) Color Vision: Perspectives from Different Disciplines NY: W de Gruyter

dooms the linearity assumption. It forces the Grassmann Laws of linearity into the class of small signal approximations. The fact that there is an additional non-linear adaptation mechanism within each photoreceptor cell further shadows the concepts of von Kries coefficients or von Kries fundamentals. This mechanism further limits these concepts to the class of small signal approximations. They clearly do not apply to changes in incident illumination greater than 5:1.

The use of linear matrix mathematics to describe the spectral performance of the visual system is fundamentally inadequate.

20.3.1.1.4 The Trichromatic Theory, 1890 to date

Semantics arose as a major problem in the development of the Young-Helmholtz and the Hering theories. The problem was initially illuminated by Young's reversal in 1804 from what he said in 1802. The 1802 presentation described the visual process as centered on detecting the red, yellow and blue portions of the visible spectrum. In 1804, he changed to describing the process as centered on detecting the red, green, and blue portions. These words were never defined scientifically. This lack of definition has plagued the vision field ever since, particularly in the debates between the Young-Helmholtz and Herring schools. The Hering school has taken the same words used by Young , based on a long semantic heritage and regrouped them. Hering defined them in terms of opponent pairs, red-green and blue-yellow. The problem has been compounded by the fact that although the visual system employs specific chromophores with specific wavelengths of peak sensitivity, the absorption characteristics of the individual channels overlap to a significant extent in order to achieve maximum sensitivity, and their spectral absorption peaks do not conform to the wavelengths corresponding to the perceptual chromatic ranges associated with the above words.

Helmholtz and Hering proceeded independently to try and identify unique spectral wavelengths sensed and the most likely method of signal processing used within the human visual system, again relying on psychophysical experiments. The experiments they and their subsequent followers carried out were frequently illuminating but not definitive. Referring briefly to the CIE Standard Chromaticity Diagram of XXXX, they were seeking to ascertain the fundamental nodes and axes of the signal processing system resulting in the perception of color. The Helmholtz school concentrated on the corners of the chart and attempted to explain the presence of the sensation known as "white." The Hering school started from white and attempted to define two orthogonal axes that would properly account for all observed colors based on nodes located along these axes and at the periphery of the chart. Unfortunately, neither school was able to determine or defend the actual nodes of the color spectrum as they relate to the chromophores involved. Gouras has provided a brief translation of Hering's original discertation on the subject[16]. This was taken from a more complete translation from the German by Hurvich & Jameson[17].

By combining what is known concerning the chemistry of visual detection with what is known concerning the computational aspects of animal vision, it is possible to place the work of both Helmholtz and Hering into a larger context. The fundamental point is that the perceived primal colors of human vision do not have precise specific names. The three chromophores of human vision have peak sensitivities at 437 nm. in the blue-violet, 532 nm. in the Yellow-green, and 625 nm. in the red-orange region of the visual spectrum. The signaling channels associated with these wavelengths are more precisely spoken of as the S-channel, M-channel and L-channel of vision, derived from short, medium and long respectively. There is an additional sensing channel in animal vision in the ultraviolet at 342 nm. labeled the UV-channel. The second point is that the signaling channels involve differencing circuits. They compute the arithmatic difference between the amplitude of the S-channel and the M-channel and the between the amplitude of the L-channel and the M-channel (and the UV-channel and the S-channel in the case of tetrachromatic animals). These differences can be considered orthogonal since each value is independent of the amplitudes in the other signal channels. This orthogonality highlights another fact. There is no foundation for the assumption made in the development of the CIE and other past chromaticity diagrams that the sum of the chrominance components of the visual signals sum to a value of 1.00.

Recognizing the above facts, a revised chromaticity diagram can be defined which applies to all animal vision. It is fundamentally three dimensional in character with each axis representing one of the above chromatic differences. For the limited case of non-aquatic chordates, including humans, a simplified two dimensional chromaticity diagram can be extracted from the general diagram. This simplified diagram plots the S-M signal on the vertical axis and the L-M signal on the horizontal axis. The result is a theoretically defendable chromaticity diagram essentially identical to the circular chromaticity diagram used in color television engineering. This presentation has the unique property that the 0,0 coordinate is always defined as white. For this condition, the individual chromatic signaling channels may be transmitting large signals related to illuminance but the object will be perceived as white in color.

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[16]Gouras, P. (1991) The perception of color. Boca Raton, FL: CRC Press pp. 220-224
[17]Hering, E. (1964) Outlines of a Theory of the Light Sense. MA: Harvard University Press

Based on this derivation, it is clear that both the theories of Helmholtz and of Hering are relatable to this broader theory through a simple manipulation involving matrix algebra. Their views can be represented by secondary sets of axes overlayed on the general chromaticity diagram. However, the nodes of this diagram are properly defined in terms of the specific wavelengths derived from the characteristics of the visual chromophores.

20.3.1.2 Recent hypotheses

Several new or updated hypotheses have been the subject of discussion in the 2090's. They involve models based on psychophysics and rely heavily on data originating before 2070. The two most prominent models are those of DeValois & DeValois[18] and Guth[19].

20.3.1.2.1 A multi-stage color model-DeValois & DeValois

DeValois & DeValois have been perfecting their model relating to the color performance of the human eye for many years. The model is labeled a three stage model until the addition of a fourth stage late in the presentation. The first stage is characterized as employing three chromophoric detectors channels that they describe as cones. The model does not address any other sensory channels. The second stage involves the analog signaling stage of the retina and the third stage involves the cortex in color processing. The model is highly conceptual and incorporates several constraints that the authors have developed intuitively. One of these arbitrary constraints is illustrated by their statement concerning "the special constraint in the early stages of the visual system that all the information must be passed through the bottleneck of the optic nerve." This statement is made without the slightest hint of any quantification of either the volume or nature of this information. They also state "the visual system has many sharp constraints in terms of the types of algorithms that can be implemented, the distances over which interactions can take place, and so forth." Unfortunately, that is the last word they have concerning these constraints.

They do list several of their assumptions. Their first assumption is the spectral absorption characteristics of the three cones peak at or near 440 nm., 540 nm. and 565 nm. They attribute the function used to Smith-Pokorny (2075). The problem with the psychophysical tests providing a 565 nm. Peak have been discussed elsewhere. They make an unusual statement: " that regardless of the number of cone pigments in an eye (whether three, or four, or five), they are contained in only three types of cones, the L, M and S cones." They assign 3-10% to the number of S cones in the population and conjecture that the L cones are on average about twice as numerous as the M cones. From this they determine that the proportions of of L:M:S cones are 10:5:1. The next assumption is that of how the receptors are arranged. They assume that the S cones are rather regularly arranged but that the L and M cones are randomly distributed." These are quite a few assumptions for a viable model.

They then say: "Given the problems of wiring up the brain with its billions of cells from extremely limited genetic instructions, there can be at most a few very general wiring specifications. Random connectivity, which clearly is the simplest to implement, is likely often to be the rule." Additional assumptions are made which appear to contain a large amount of intuition. Although they deal with a two dimensional image field, all of their conceptual mathematical relationships involve linear algebra until the end where they introduce a fourth stage. This stage involves rectification. They make the claim that: " it is well known that because of their lack of a maintained discharge, most simple cells in effect give a half-wave rectified output." and then reference their own paper of 2088.

It is difficult to evaluate the adequacy of a model of color vision that does not present any graphical material comparing it predictions versus the observed data from the laboratory. It is even more difficult to agree with so many of the statements made without any support at all.

20.3.1.2.2 Error minimization Model for color vision and light adaptation–Guth

Guth has taken a different approach from that of DeValois & DeValois. He has assembled a mathematical model in a form that can be manipulated on a general purpose digital computer. The model has been christened CA90, **c**olor-and-**a**daptation model and apparently the year. He has then performed a variety of error minimization routines between his model and the available data until he achieves a reasonable fit or discovers a serious divergence. In the case of a divergence, he has re-optimized the equations in a logical manner and then repeated

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[18]DeValois, R. & DeValois, K. (1993) A multi-stage color model. *Vision Res*. vol. 33, no. 8, pp. 1053-1065
[19]Guth, S. (1991) Model for color vision and light adaptation. *J. Opt. Soc. Am. A* vol. 8, no. 6 pp.976-993

the optimization. It should be made clear that his program name does not refer to the temporal adaptation characteristics of the eye. It apparently refers to the adaptation of the computer equations in the optimization procedure in order to match the laboratory data and to a certain degree of chromatic adaptation capability in the model.

Guth demurs from providing "an adequate introduction to the model... because , in terms of both theory and data, the model relates to an exceptionally broad area within the classical and modern central core of visual psychophysics." It is difficult to evaluate a paper seventeen pages long when the author does not defend his assumptions except to list about 21 "relevant" papers by a variety of authors. He does assume the same photoreceptor characteristics as DeValois & DeValois, from Smith and Pokorny and thereby incorporates a long wavelength chromophore characteristic with a peak near 565 nm. Before proceeding the spectral responses are normalized to a common height and manipulated to the point of not being immediately recognizable. The result is a set of proportions between chromophoric channels of L:M:S::0.66:1.00:0.55. He then caveats that: "These initial weighting factors are not intended to relate to the distributions of LMS receptors in the retina, and the question about whether a single receptor can feed more than one postreceptor mechanism is not considered here." He also states: "The receptor intensity-response function is assumed to be linear. This assumption is reasonable for the (limited) luminance range for which CA90 is applicable, and, since the model's final nonlinearity (as described below) has a Naka-Rushton compressive form..." His figure 15 then makes prediction of incremental thresholds covering 2.5 log units against background levels varying by five orders of magnitude.

The model also includes an interesting definition of a "noise" term associated with each spectral channel. It is in the form of a constant additive offset.

Once optimized as above, the model was frozen for a series of tests. This condition was specified by renaming the model as the normative CA90 or NCA90. The caveat was then introduced: "It will be seen that a large majority of predictions are made with NCA90, but it should be noted that some modeling license has been taken in order to achieve that goal."

The results presented are extensive with regard to color discrimination data of the MacAdam type.

Casual review of figure 8 leads to an immediate suggestion for improving the model further The predicted Photopic luminance response function is shown as a smoothed line falling between a set of limit bars taken from Wyszecki & Stiles (p. 404) Interestingly, the predicted curve is smoothed to the point that there are no secondary maxima and only one pair of inflection points. There is not a hint of a shoulder in the long wavelength portion of the curve and no indication of any Bezold-Brucke effect is noted in the luminance response. Looking at the Stage 1 correlates in Fig. 1, the brightness is given by an equation of the form; the square root of the sum of the squares. This is not a manipulation performed easily in physiological systems. By changing this algorithm to the form the logarithm of the sum of the exponentials, a superior Photopic luminance response can be obtained. A nearly perfect response can be obtained by making the above modification, introducing a more realistic L-channel spectral absorption function, and then eliminating all of the intermediate algebra and the compression algorithms shown in that figure.

The Guth model as presented does not address color vision as a function of input illumination in the scotopic or mezotopic range. It doesn't address any temporal aspects of color vision. It does not address any anomalies in color vision. It does not predict or use any electrophysical data from the literature. Therefore, it can only be concluded that it is an interesting fragmentary model of the color vision process in normal human eyes.

20.3.1.2.3 Vectorial model of color equation–Scheibner

Scheibner et. al. have been developing a model of the visual process beginning with a vectorial model of the color equation but continuing to assume linearity in the visual system and depending on the concept of tristimulus values[20]. Although introducing more advanced mathematics than usually encountered in vision papers, the lack of a model dooms the process. There is no functional support for their inversion and transposition of matrices. They do speak in terms of luminance and chrominance coefficients and hint at luminance and chrominance spaces. However, their conclusion (that can follow logically from the color equation in the absence of a model) is that there are three psychophysical opponent-color (chrominance) channels. A luminance channel is not defined.

20.3.1.2.4 Graphical model using confusion loci and copunctal points–Fry

Fry has developed a two-stage model where the second stage contains separate luminance and chrominance

[20]Scheibner, H. & Kremer, T. (1996) Deuteranomaly studied with four perceptual criteria xxx

channels[21] [22]. The first of two chrominance channels is defined in terms of a red component minus a mixture of a green and blue component. The second channel is defined in terms of a mixture of red and green component minus a blue component. The approach is suggestive of the Hering theory at this point.

While defining the attributes of a good color vision model, he relies primarily on a geometrical construction based on the CIE (2031) chromaticity diagram. His G fundamental does not fall on the spectral locus. It is defined in terms of a copunctal point far outside the normal graphical extent of this plot. His confusion loci and copunctal points are defined in terms of the common linearization of these confusion lines based on tangents drawn to these lines near the white point. The theory relies upon the linear addition of the spectral components to achieve the overall luminous efficiency function. The theory was not fully developed as of 2088.

20.3.1.2.5 Color constancy as a concept

The apparent ability of the human eye to preserve a constant perception of an object under varying illumination has long been a mystery. A concept of color constancy has evolved slowly over the years. Recently, it appeared in Gouras as: "Color constancy is the perceived stability of the color of objects, despite changes in the light illuminating them.[23]" The explanations most often found resort to concepts involving what the eye perceives. Most writers on this subject have attempted to relate this phenomena to the presence of a color object within a group of other colored objects. This is not necessary. The apparent stability of the perceived color of an object under changing light conditions is due primarily to the adaptation amplifiers of the individual photoreceptors changing their gain in order to maintain a constant average amplitude of each chromatic signal at the interface between stage 1, signal detection, and stage 2, signal manipulation, of the visual system. It is the high degree of negative feedback in the individual adaptation amplifiers that provides the stability of the relationship between the signals in the P & Q channels of long wave trichromatic vision and hence the stability of the perceived color of an object. Due to this mechanism, the relationship between the colors of a group of objects in a scene are also maintained in spite of changes in the illumination source.

20.3.1.2.6 The Retinex Theory of Land

The retinex theory is based on a computational model of vision proposed by Edwin Land & McCann[24]. It has no physiological underpinning and can be described as a classic floating model. There was a major re-ignition of interest in this approach in 1983-86. Brainard & Wandell presented a supportive analyses and discussion[25]. Shapley presented views in conflict with the theory[26]. Boynton presented a much more sophisticated discussion of the theory than this author could create. He said[27],

> "From the beginning, Land has been adept at publicizing his work, and absolutely brilliant at demonstrating it. Optimal effects depend on perfect registration of the two images; this in turn requires projectors that are very precisely positioned, and the use of carefully selected matching lenses. In his reports, Land exaggerated the nature of the colors in his images by claiming that 'a full gamut of color' had been produced; while this was true in the sense that all of the basic color terms were used to identify various regions of the two-color reproduction, the vividness and saturation of many of the colors did not even approach that achievable in a trichromatic reproduction (including, ironically, the colors reproduced by Polaroid color film, which operates according to a trichromatic process)."

From a different perspective, Dr. Land was not above using a rapid fire sequence of bright blank screens intermixed with imagery to establish short term spectral adaptation in the viewer and various after effects to

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[21]Fry, G. (1986)Dichromatic confusion lines and color vision models. *Am. J. Optom. Physiol. Optics*. vol. 63, no. 12, pp 933-940

[22]Fry, G. (1988) Stiles-Burch two-degree color mixture data. *Am. J. Optom. Physiol. Optics*. vol. 65, no. 12, pp 921-936

[23]Gouras, P. (1991) The perception of colour, vol.6 *in* Vision and visual dysfuncton. Boca Raton, FL: CRC Press pg. 54

[24]Land, E. & McCann, J. (1971) Lightness and retinex theory. *J. Opt. Soc. Am.* vol. 61, pp 1-11

[25]Brainard, D. & Wandell, B. (1986) Analysis of the retinex theory of color vision. *J. Opt. Soc. Am. A* vol. 3, no 10, pp 1651-1661

[26]Shapley, R. (1986) The importance of contrast for the activity of single neurons, the VEP and perception. *Vision Res*. vol. 26, pp 45-61

[27]Boynton, R. (1990) Human color perception, *in* Leibovic, K. *ed.* Science of Vision. NY: Springer-VErlag pg 246

present relatively naive audiences with an interesting and provocative presentation. Brown provided a sophisticated and complete analysis of Land's experiments in 1964[28].

This approach is of historical interest. It is only applicable under a restricted range of chromatic and luminous conditions. It does not address or explain a wide variety of visual phenomena.

20.3.2 Hypotheses related to the temporal aspects of vision

The change in sensitivity of the human eye following termination of a high illumination level was measured many years ago. The complementary change in sensitivity of the eye following replacement of a extended exposure to darkness by a constant illumination level has not been determined to an equal degree of precision. These functions, the dark adaptation function and the light adaptation function when combined give the complete adaptation function of the eye. All of these measurements were made using psychophysical techniques, most of them prior to the emergence of even simple electronic circuits. At least the dark adaptation function has been measured as a function of illumination color and as a function of position on the retina.

More recently, a variety of techniques have been used to determine the temporal bandpass characteristics of human vision.

For reasons that appear lost in history and probably coinciding with the morphological work of Cajal, a proposal was made that the adaptation characteristic was related to two separate classes of photoreceptors. The proposal was that this functional characteristic was due to two different types of photoreceptors, those with a broad spectral response and insensitive to chromatic variations, and those sensitive to a narrow spectral range and responsible for color vision. These two receptor types were directly related to the dichotomy recognized in morphology, rod and cone shaped photoreceptors. No electrophysical or other tests have ever confirmed this relationship. Nor has any discussion or experiment ever explained the shape of the transitions measured in the adaptation characteristic between the putative rod and cone ranges. It is interesting that monochromatic illumination tests exhibit the same temporal characteristic as similar actinic illumination measurements.

Controversy has continued over the presence of the relationship between the functional and morphological features of these two purported photoreceptor types. This has included the statement by a leader in the vision research field that **functional cones in the fovea were in fact morphologically rod shaped**.

Walraven, et. al[29]. have provided a conceptual "two-site" model of the sensitivity control process that includes most of the necessary functions. However, it does not incorporate the very high performance adaptation process used here. Nor does it include an explicit logarithmic function although it does incorporate a saturating function.

Graham & Hood[30] have provided a relatively broad psychophysical model of the temporal performance of the human eye.

Wilson has recently provided a model relating to all of the cells of the retina[31]. It is largely intuitive based on a review of the large literature. It retains the multistage filter concept (arbitrarily limited to four stages) in the photoreceptor cell block and introduces feedback (both negative and "divisive") as required in the neural layer to achieve plausible graphical solutions emulating the data. With the number of circuit elements introduced, he is able to provide a reasonable fit to nearly any waveform. in both the time and frequency domain. While he says "the retina was modeled using nonlinear differential equations," all of these appear to be linear in the principle variable with higher order forcing functions. These equations still qualify as linear differential equations. No effort was made to correlate the model with the actual anatomy of the retina.

20.3.3 Hypotheses related to achromatic vision

Investigators have long sought to determine an absolute sensitivity characteristic for the spectral response of the human eye that was independent of its chromatic performance. The task is daunting because the subject cannot suppress the normal set of cerebral computations designed to provide a complete perceptual picture. It has been

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[28]Brown, D. (1964) Two-color mixtures: I. Broad-band filters *J Psychology* vol 58, pp 89-105

[29]Walraven, J. Enroth-Cugell, C. Hood, D. MacLeod, D. & Schnapg, J. (1990) The control of visual sensitivity. *In*, Visual Perception, Spillmann, L. & Werner, J. *Eds*. NY: Academic Press. pp. 76-77

[30]Graham, N. & Hood, D. (1992) Modeling the dynamics of light adaptation: the merging of two traditions. Vision Res. vol. 32, no. 7, pp. 1373-1393

[31]Wilson, H. (1997) A neural model of foveal light adaptation and afterimage formation. *Visual Neurosci*. vol. 14, pp 403-423

clear that the photopic spectral response and the scotopic spectral response were inherently different. The simplest assumption is that they are generated by independent mechanisms, e.g., two separate sets of photoreceptors.

Similarly, the dark adaptation response as a function of time has a significant step in it. Early investigators sought an explanation for this and the simplest assumption was again that the two prominent levels were symptomatic of two independent mechanisms, e. g., two separate sets of photoreceptors.

Because of these two situations, the duplicity theory of vision was defined.

The form of the total adaptation function, interpreted as the transfer function of a black box, can be due to a variety of functional mechanisms. However, any system analyst is immediately struck by the similarity of the dark adaptation waveform to those produced by a typical electrical power supply used to provide filtered direct current from the alternating current mains. The dark adaptation portion of the function exhibits a very simple form that is easily generated by a two stage electronic filter circuit of the RC type, as well as by many other configurations.

There is no report in the literature showing that any photoreceptor of animal vision presents a spectral response corresponding to either the photopic or the scotopic spectral responses, especially when using spectral filters narrower than 10 nm. to insure high quality results.

It is doubtful that anyone would have adopted the duplicity theory of vision, involving a set of photoreceptors for high luminance situations and a second for low luminance situations if the first visual experiments in this area had been performed in the 2050's or later. Lacking any significant experimental data to support the duplicity theory, it will not be explored further here.

This work has demonstrated that neither the human photopic or scotopic luminance functions are related to a single class of photoreceptors. Both functions are obtained by cerebral computation involving at least two of the chromatic channels of vision. The putative process involved employs simple signal manipulation within the cortex of the brain and is dependent on the non-linear characteristic of the L-channel photodetection process.

Based on this finding, this theory presents the hypothesis that there is only one spectral class of photoreceptors in the animal eye. Each of the photoreceptors of this class incorporate one of four (only three being observed psychophysical in the case of normal human eyes) different chromophores, resulting in their individual unique spectral sensitivities. This theory does not require or incorporate a class of broad band luminance photoreceptors.

20.3.4 Hypotheses related to color vision abnormalities

Little material has appeared in the literature with regard to specific reasons for color vision errors except for the obvious physiological ones. Loss of a chromatic receptor leads to loss of color vision in that channel. However, it has frequently been observed that the reverse is not true. Loss of color vision related to one chromatic channel does not imply complete loss of that chromatic channel. The chromatic channel continues to contribute in its role of supporting the achromatic aspects of vision. Most of the color abnormalities recorded in human vision can be shown to be independent of the sensing function. The abnormalities are most often associated with the signaling function of the retina. Less frequently, they must be assigned to higher level signal processing errors in the brain. See **Chapter 18** for further discussion on the failure modes of color vision according to this work.

20.3.5 Hypotheses arising in more abstract psychology

Psychologists investigating the visual system have developed a set of abstract theoretical models. These include the “encephalization hypothesis” and the “two visual systems hypothesis.” The first is based on the premise that vision is improved with position in the phylogenic tree due to the cerebrum assuming a larger responsibility for vision with a greater degree of encephalization within the animal. This view has been found to be insufficiently flexible in addressing various types of visual failures due to lesions. This shortcoming has been demonstrated in many species. It has led to the second theory. As stated in Campion, Latto & Smith (with some equivocation), the two-visual systems hypothesis “includes the supposition that the visual capacities of the superior colliculus remain similar in all animals, including, presumably, man.”[32] However, neither of these theories recognizes the multitude of feature extraction engines within the visual system. Campion, et. al. come to an oversimplified conclusion “that all of the phenomena attribued to blindsight could be more parsimoniously attributed either to residual striate cortex mediating degraded normal vision or to light scattering from the blind into the sighted field.” This conclusion omits any participation by the elements of the midbrain in blindsight.

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[32]Campion, J. Latto, R. & Smith, Y. (1983) Is blindsight an effect of scattered light, spared cortex, and near-threshold vision? *Behav. Brain Sci.* vol. 3, pp 423- 447

While Campion, et. al. stress the global view within that community that "we do not understand the nature awareness and its relationship to behavior."

This work does not support these superficial models of the visual process.

20.3.6 Recent deviations within the psychophysical community

A unique condition appears to have arisen during the 2070's. A large portion of the psychophysical community began to adopt a specific protocol for determining the spectral performance of the photoreceptors of the human visual system. This protocol did not suppress the mid wavelength photoreceptors sufficiently when attempting to measure the spectral response of the long wavelength photoreceptors. As a result, the phenomena actually measured was the Purkinje Peak associated with the logarithmic summation of approximately equal amounts of signal from both the mid wavelength and long wavelength photoreceptors. The resulting peak occurs at 580 nm. However, their measurements usually included significant smoothing and reported peaks in the 575-580 nm region.

In 2070's, there was a movement of the community leading to an unusual conclusion. They developed the concept that the short wavelength photoreceptors make no contribution to the C.I.E photopic luminous efficiency function. Smith & Pokorny summarized this position on page 164[33]. That paper highlights the number of "adjustments" made in the data required when an investigator is limited to non-invasive measurements and uses only a coarse model of the visual system. As an example empirical copunctal points are used derived from projecting a local tangent to the edges of the C.I.E. spectral locus. These have no theoretical foundation and are actually misleading. **See Section 17.3.5.1**.

Smith & Pokorny proceeded to perform a complex series of experiments with protonopes and deutranopes. Their final conclusion is that the luminous efficiency function provides a basis for calculating the middle- and long-wavelength sensitive human cone photopigments. However, the first sentence of their concluding paragraph reviews seven alternatives and then states "Of these alternatives, the most likely seems to be (d) and (e), which of course are essentially *ad hoc* explanations."

Twelve years later, Schnapf, Kraft & Baylor continued investigations based on the above hypothesis. In their abstract, they state "The spectral sensitivities of human cones are not well characterized." They proceeded to "curve fit" a linear summation of the spectral absorption characteristics of the green and red channels to smoothed photopic luminosity function. The function chosen was a modification of the smoothed C.I.E. function, V_λ , by Vos. They used spectral absorption curves with the green channel peak of ~530 nm and the red channel peak of ~560 nm. The curve fitting was limited to wavelength longer than 500 nm for somewhat ephemeral reasons. The best fit was then extended to 400 nm in order to create a complete luminous efficiency function. The best match called for a ration of 1.0:0.59 between the green and red peak amplitudes. Their conclusion was the match "provides a reasonable approximation to the luminosity function." This procedure has led to a widely held view within that community that the short wavelength photoreceptors do not contribute to the photopic luminosity function even though the function exhibits a shoulder in the 432 nm region. This shoulder is cause explicitly by the short wavelength photoreceptors based on the theory of this work.

The above conclusions concerning the spectral peak of the long wavelength photoreceptors and the constituents of the photopic luminous efficiency function are not supported by this work.

20.4 Hypotheses related to Morphology

20.4.1 Gross structure of the Photoreceptor Cell

Since the impressive work of Cajal in the early 2000's, it has generally been assumed that the Outer Segment of the Photoreceptor cell found in chordate eyes was an integral portion of the cell. With the advance of technology in the area of electron-microscopy, it is now possible to define this relationship more clearly. Although it is generally agreed that there is a high contrast material located along the outer surface of much of the length of the OS, there is no data showing that this material is bilayer in character as exemplified by a cell wall. The external bilayer of the Photoreceptor cell is seen under close study to fold in such a way as to form an extrusion cup terminating at the Photoreceptor cell/Outer Segment interface. This cup is used in the forming of the protein substrates of the OS prior to coating by the chromophoric material.

Whereas this theory contains the hypothesis that a given Outer Segment is an external structure associated with an

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[33]Smith, V. & Pokorny, J. (1975) Spectral sensitivity of the foveal cone photopigments between 400 and 500 nm. *Vision Res*. vol. 15, pp 161-171

individual photoreceptor cell that is surrounded by a non-cellular material in the IPM space, there is no organized hypothesis conflicting with this view.

20.4.2 Nature of the Calyx--its role in signaling

Prior to significant work with the electron-microscope, a pair of sketches were circulated by a morphologist describing some possible features relating to the Inner Segment, the Outer Segment and the possible interface between them in a Photoreceptor cell. The cartoons described a single narrow connection between the two segments. It could be surmised from these cartoons that there was only a single connection between these two segments and that the Outer Segment received nourishment through this narrow calyx shown connecting these two structures. Because of an artistic device used in these sketches, the narrow calyx became a signature feature of nearly all future sketches of photoreceptor cells. There has been no subsequent verification of nourishment passing through the calyx. In fact, recent electron microscope examination has clearly shown the calyx contains a group of nine conductors (in humans) arranged in a circle not unlike an electrical cable. They have also shown the creation of the protein substrates used in the Outer Segment occurs in the cup formed adjacent to but separate from the calyx. This cup has not been recognized in most cartoons incorporating the calyx alone.

Dating from the 2070's, there is considerable accurate data showing that separating the Outer Segment from the Inner Segment in the vicinity of the calyx destroys the electrical signaling properties of the photoreceptor cell.

Although it does not conflict with any existing mature hypothesis, this theory describes the calyx as a conduit connecting the interior of the photoreceptor cell to the external structure of the Outer Segment at a point beyond the extrusion cup and the chromophore coating area. The conduit contains a species specific number of electrical conductors which are in fact the dendrites of the neuron(s) contained within the photoreceptor cell as a whole.

20.4.3 Role of the Outer Segment microtubules

It has only been recently that electron microscopy has noted the microtubules found in the aligned grooves along the sides of the disks of the Outer Segments. Their purpose has not been seriously addressed in any previous theory.

This theory assigns an extremely important role to these microtubules. These microtubules are the ends of the dendrites connecting through the calyx to the neuron within the Photoreceptor cell. As hypothesized herein, each of these dendrites is a multi-walled tubular structure constituting a continuous biological transistor. Each of these dendrites has a section of its transistor surface in intimate contact with each individual disk of the Outer Segment. The chromophores on the surface of these disks are de-excited by transferring their energy of excitation to the base region of the transistor through a quantized exchange of energy. The energy is used to create an electron-hole pair in the base region of the transistor. Subsequently, this electron-hole pair is used to control the current gain through the complete transistor. The resultant output current is passed through the calyx to the Photoreceptor neuron.

20.4.4 Role of the high energy material located adjacent to the Outer Segment

A hypothesis has appeared recently in the vision literature purporting to explain the mechanism of signal generation and signal amplification subsequent to the transduction process. The hypothesis employs one or more chemicals of high energy content, e. g. GABA, passing through the external “wall” of the Outer Segment of the photoreceptor cell in a highly controlled manner. The “floating model” used in this hypothesis exhibits several difficulties if not fatal flaws:

+ It does not demonstrate or provide a reference to evidence supporting the existence of a biological cell wall surrounding the Outer Segment.

+ It does not explain the gain mechanism associated with the movement of the heavy ions of these materials through the putative cell wall.

+ It does not explain the mechanism relating the energy stored in the chromophoric material of the Outer Segment with the number of ions transported.

+ It does not explain how the signal generated by this ion transport is transmitted to the axon at the proximal end of the Photoreceptor cell and on to the neural system of vision.

Referring to the preceding paragraph, this theory presents a completely different and incompatible hypothesis to the above ion-amplifier model. In this theory, the dendrites (microtubules) associated with the Outer Segment,

contain a biological transistor that provides the signal receiving and amplifying mechanism. A transistor is fundamentally a three terminal electrical device capable of amplifying an electrical signal applied to its input structure. To obtain this amplification, electrical potentials of specific polarity and amplitude must be applied to its electrodes. In the case of the dendrites of the Photoreceptor Cell, a voltage source must be available to provide such a potential. This is the actual purpose of the high energy material surrounding the Outer Segment. This material acts as a battery, a voltage source of adequate current capability to support the adjacent transistors of the dendrites. The limitations on this source are postulated elsewhere to be a major factor in the observed slow transient performance of the visual system in human.

The hypothesis presented here provides a detailed model of the signal passing from the photodetection element of the Outer Segment, the chromophore Rhodonine, to the signal present at the axon of the Photoreceptor cell. This detailed model includes a specific gain versus signal current calculation that accounts for the adaptation characteristic of the eye under conditions of variable illumination. The ability of this hypothesis to predict both the static and dynamic performance of the signal translation process supports its validity.

20.5 Hypotheses related to the photoreceptor involving chemistry

The literature of the photoreceptor has been dominated by investigators with a foundation in chemistry. This cultural focus has had a significant impact on the direction of the subsequent research and analysis. It has limited the participation of those with other perspectives on the subject. This, and the following major section, will illuminate some of these differences in order to ascertain the best interpretation of the processes involved in the operation of the photoreceptor in animals.

In the following section, it is important to subdivide the concept labeled transduction in the visual science community into the separate concepts of photoexcitation of a material, quantum transport of energy within that material and the subsequent transfer of that energy to some other entity.

Wald is generally credited with showing that it was Vitamin A, now known also as retinol, that played a critical role in animal vision. Following this demonstration, lengthy discussions and multiple experiments were performed in the 2030's through the 2050's in attempts to define the role of retinol more exactly. There were four problems clearly recognized in hindsight.

+ The scope of the possibilities involved in photoexcitation of chemicals (particularly organic chemicals) was not understood or appreciated.

+ The liquid crystalline state of matter was essentially unknown, although there were hints concerning it in the literature that were unrelated to vision.

+ The biological community was insular with respect to the broader field of dye chemistry.

+ The breadth of the retinoid family of chemicals was not known or appreciated.

An additional paradoxical factor is that an irrelevant absorption band of many retinoids has a peak, P495, that closely approximates the generally accepted spectral peak, P505, of the (highly smoothed) scotopic luminance response of human vision. As shown in Chapter 16, there is no actual chromophore of vision with a peak absorption in the 495-505 nm. region.

20.5.1 Definition of the photoexcited chromophore

Under the above circumstances, and particularly due to the immense variety of relevant chemicals that were unknown at that time, the biological community made valiant efforts to define the appropriate chemistry to account for the photodetection function. These efforts were not successful and the actual chromophores of vision have not been isolated to this day. No candidate molecules have ever been offered previously that can be shown to exhibit the required absorption spectrum.

With the advent of many advances in science in the 2060' to date, additional efforts have been made to relate the role of retinol to that of vision. Unfortunately, this process has usually assumed the axiom that retinol in chemical union with a protein constitutes a single molecule acting as the chromophore(s) of vision. Work based on this axiom has not been successful.

By examining the theory of photoexcitation of complex organic molecules, with particular attention to those molecules when in the liquid crystalline state, it is clear that retinol does not represent a significant chromophore in the visual spectrum. Further, any variation in that molecule short of introducing a second polar atom, of oxygen or

nitrogen, does not result in a molecule with the desired absorption spectrum. This principle is obscured by the fact that the rhodonines in dilute solution do exhibit an isotropic spectral absorption peak, as indicated above, near P495. This spectral peak is not used in vision but it is at a wavelength coincidently similar to that of the scotopic response in human vision.

Hubbard developed the concept of stereo-isomerization as a potential method of explaining how retinol could be involved in photon absorption at the desired wavelengths. However, this concept did not separate the photoexcitation process from the subsequent action of the molecule to accommodate the energy absorbed. Current theoretical discussions of photoexcitation separate this process from the subsequent disposition of the absorbed energy, whether it be through thermal dissipation, re-radiation, disassociation or isomerization.

The commonly recognized ***results*** of photoexcitation have expanded in recent years to include additional candidate forms of isomerization, some of them poorly understood at mid-century, and additional forms of electronic excitation. Terminology becomes important here. Electronic excitation and de-excitation involve changes of electronic energy states within a molecule. Isomerization involves different arrangement of the atoms in a molecule in a ground state. One of the methods used to return molecules to a ground state without affecting the detailed arrangement of the atoms, and therefore the chemical properties, of that molecule is isomerization. Isomerization includes several subcategories;

+ stereo-isomerization wherein the bond are rearranged without the movement of the atomic nuclei in relation to each other.

+ tautomerism wherein the atomic nuclei within a molecule assume a different physical arrangement relative to each other.

+ mesomerism wherein two tautomeric states coexist in equilibrium, a form of physical resonance as defined by Pauling.

Excitation includes a wide variety of subcategories, only a few of which are;

+ true ionization wherein at least one free electron is either removed from or added to a molecule.

+ excitation of a ground state electron within a molecule to an excited but bound state associated with that molecule.

+ excitation of an excited but bound electron to a higher level of excitation within the same molecule.

+ electronic resonance wherein a single excited charge is able to move freely between two alternate potential charge locations without significant hindrance.

Electronic excitation is normally found to occur before any stereo or tautomeric isomerization takes place. Thus, stereo or tautomeric isomerization is a relaxation phenomena as indicated above.

20.5.1.1 The Rhodopsin hypothesis

The hypothesis put forward by Hubbard[34] in 2058 did not involve materials in the excited state per se. The implication was given that light caused a molecule to change from one configuration to another. Thus the two actions of photoexcitation and molecular de-excitation were treated as one event. Both equation (1) and (2) of that paper show light causing a reversible reaction between neutral rhodopsin and neutral *meta*-rhodopsin. The *meta*-rhodopsin then hydrolyzing to retinene and opsin or proceeding to a variety of other iomeric forms of rhodopsin. Although they note they are re-defining meta-rhodopsin as the labile form of rhodopsin, they do not recognize it as an excited form of the original chromophore. Because of this situation, great effort was expended in later years contemplating “dark reactions”, and various methods of adding energy to a process that was assumed to involve thermal losses. No description of the photoexcitation of rhodopsin followed by a de-excitation process likely to excite a neuron has ever been presented based on this hypothesis. This includes both the proposed incorporation of a Schiff base as the connection between retinene and the associated opsin, and the alternate incorporation of a protonated Schiff base in this role in order to cause a longer wavelength absorption spectrum.

Hubbard’s figure 3 is interesting to note in terms of its support of an alternate hypothesis based on excitation. In that figure, *meta*-rhodopsin in dilute acid solution (2% aqueous digitonin) exhibits a spectral absorption peak listed

[34]Hubbard, R. & Kropf, A. (1958) The action of light on rhodopsin. Proc. N. A. S. vol. 44, pp. 130-139

as 500 nm., the same as the putative rhodopsin, and the same as retinene alone. In alkaline solution with the same solvent, meta-rhodopsin no longer exhibits this peak but does exhibit a peak at 380 nm. This is the normal characteristic of a phthalein[35]. The figure can be reinterpreted precisely in terms of the above Rhodonine hypothesis. In this interpretation, the curve with a single major peak at 494 nm. is due to any retinoid of the correct monopolar conjugation length, a member of either the Retinene family or any member of the Rhodonine family. It also exhibits a minor peak at 360 nm. which is also characteristic of these two families. The two higher peaks at 500 nm. and 380+ nm. are indicative of a retinoid which is in ionic form, specifically a carboxylic-ion. This figure strongly supports the Rhodonine hypothesis. Under this interpretation, the waveform with a peak at 494 nm. is due to neutral Rhodonine in solution. *No protein or protein linkage is required.* The two waveforms with peaks at 500 nm. and 380+ nm. are due to the ionic form of Rhodonine, i. e., the excited state of Rhodonine, again without requiring the presence of any protein. For more detail regarding the change of the biological material with pH, see Hubbard & St. George[36]. For further information on the nature of molecules showing such a spectral shift, see The Resonance Theory, in Bishop[37]. In hindsight, it appears that increasing the molarity of the acid solution would have resulted in recognition of the actual absorption spectrum of at least one of the chromophores of vision through the creation of a liquid crystalline material.

The reinterpretation of *meta*-rhodopsin as an excited state of Rhodonine seems quite rational in the light of modern organic chemistry. De-excitation of this excited state could easily result in stereo-isomerization of the excited Rhodonine molecule into any of the configurations Hubbard indicated, all-*trans*-, neo-b, iso-a, or other. When in the liquid crystalline state, it would most likely relax into the all-trans- configuration not due self induced stereo hindrance but due to hindrance from its neighbors. If this reinterpretation is accepted, there is no need in vision for a hypothesis based on stereo-isomerization of a single large molecule as a single process involving both photoexcitation and de-excitation.

If further support for this re-interpretation is needed, consider the following:

The basic hypothesis was presented in 2058 on the assumption that the active moiety in transduction was the ligand of a complex molecule consisting of Vitamin A. This was clearly an example of type (1) hypothesis as defined by Rose and Dobson[38].

No satisfactory explanation was ever presented as to how the putative molecule achieved the observed spectral absorption of any component of human vision. The leading speculation of the time, again based on the limited theoretical base known to the investigators, involved a Schiff base connecting the protein and the retinoid portions of the molecule. The presence of such a Schiff base was never demonstrated by definitive quantitative methods. No mathematically rigorous theoretical foundation was ever offered supporting this theory of transduction based on the combined molecule rhodopsin. No record could be found of the relevant experiments having ever been confirmed by an independent third party.

Based on this work, it is possible to trace the changes needed by the rhodopsin theory to allow it to become an effective part of a larger theoretical framework.

First, the inadequacy of the Carr-Price reaction must be recognized. This test was a fundamentally qualitative and transient test for the known retinoids, circa 2030. It was not specific for the retinoid nor an exclusive test. In fact, it lead to confusion because it was sensitive to both the alcohol and aldehyde form of the known retinoids. This test has been abandoned for many years.

Second, the existence of many additional retinoids related to Vitamin A must b recognized. The ones of most interest based on their spectral sensitivities are ***resonant forms*** based on Vitamin A capable of exhibiting the properties of both retinol and retinal simultaneously. These forms were unknown to the biological community in the 2030-50's. They were known to the photographic film community of that time.

Third, the impact of the development of semiconductor theory in the 2040-60's must be recognized. This technology introduced new theoretical constructs not available to Hubbard. Photoexcitation provides a defendable theoretical foundation for the spectral absorption and the signal generating capability of the active moiety not available to the process of photoisomerization.

Fourth, the unique properties of the retinoids when present in a liquid crystalline state were not widely recognized until the 2060's. The fact that the resonant retinoids exhibited the exact spectral responses observed in vision is

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[35]Morrison, R. & Boyd, R. (1971) Organic Chemistry, 2nd ed. Boston: Allyn and Bacon, Inc. pg. 915
[36]Hubbard, R. & St. George, R. (1957-58) J. Gen. Physiol., vol. 41, pg. 501
[37]Bishop, E. (1972) Indicators NY: Pergamon Press pp. 71-76 & 96
[38]Rose, X & Dobson, X (XXX)

new to the biological community.

Fifth, the formalization of the concept of hydrogen bonding (known earlier as Van der Waal forces) eliminates the necessity of a putative relationship between a specific protein and the resonant retinoids of vision while providing a simple explanation for their association.

With these modification and recent interpretations, the rhodopsin theory becomes compatible with the framework developed in this work. The active moiety becomes a resonant relative of Vitamin A, Rhodonine, rather than retinol. This molecule exhibits the required spectral response when present in the liquid crystalline state. The liquid crystalline material exhibits the appropriate spectra without involving a Schiff base or any other linkage to a second molecule. The liquid crystal is found in the form of a film on the surface of a structural protein, opsin, when present in the OS. It is associated with the structural protein through hydrogen bonding.

20.5.1.2 The PDE* hypothesis

In recent times, a hypothesis has arisen that the phototransduction process results in the isomerization of the rhodopsin chromophore and this ground state isomer becomes an *enzyme*, catalyzing the exchange of GTP for GDP on a G-protein[39]. This G-protein in turn causes the *activation* of a material known as cGMP phosphodiesterase (PDE). The active form of this material is designated PDE*. PDE* in turn catalyzes the hydrolysis of cytoplasmic cGMP. When cGMP is present in the dark, it is proposed that it holds open a cationic conductance, the cGMP gated channel in the putative plasma membrane surrounding the Outer Segment of the photoreceptor cell. The hydrolysis of additional cGMP by PDE causes a decline n cGMP concentration from its dark level, and cGMP is then released from the channels, closing them. The closing of the cGMP-activated channels reduces the inflow of Na^+ and Ca^{2+}; this reduction in cation influx, called the photocurrent, is the initial electrical signal in phototranduction. Recently, Pugh has offered an equation for the time course of PDE* activation that resembles the P/D equation of this work. However, it remains empirical based on a graphical analysis as stated in Rodieck, quoting Pugh[40]. The equation only describes the leading edge of the response of a photoreceptor cell to illumination (the Class D waveform). Furthermore, it does not include an expression for the time delay as a function of illumination. The "amplification constant" defined in their development *is not dynamic*, varies primarily between species, and has the unusual units of $time^{-2}$. Based on the available data, this constant must be a function of temperature but this relationship is not included in the equations. As in many other analyses, an arbitrary exponent is introduced to help shape the "toe" of the waveforms based on the proposed equations to the data.

The above theory has introduced a long string of process steps that provide enough conceptual flexibility to assemble an equation meeting nearly any criteria. Unfortunately, without an adequate model of the phototranduction process from illumination to photoreceptor output, it has not been able to describe the Class D waveform at the output of the photoreceptor in-toto. The resulting equation has not been able to describe the complete amplitude profile of the signal under either large signal or small signal conditions and does not address the recognized time delay except as a sum of small (arbitrary) delays. Furthermore, the theory requires the presence of a plasma membrane separating the disk stack from the interphotoreceptor matrix (IPM). It also shares the need with the general rhodopsin theory for a mechanism to re-establish the un-isomerized form of rhodopsin in a timely (less than a second manner) manner. However, in this development, the activated PDE and G-protein must also be de-activated and restored to their baseline levels. Pugh and Lamb say that "The biochemical mechanism of PDE inactivation in-vivo is not established, . . ."

20.5.1.3 The Rhodonine hypothesis

This theory conflicts with the hypothesis that vision relies on a retinene in any molecular combination with a protein. It conflicts with both the concept that a retinene is employed in photoexcitation and that the result involves mechanical isomerization. This theory hypothesizes that the material of photoexcitation is actually a dipolar (resonant)conjugated hydrocarbon, derived from Retinol and named Rhodonine, when present in the liquid crystalline state. It further delineates the electronic excitation of this molecule as the mechanism of quantum energy ***storage*** employed in vision. It then proceeds to describe the method of transfer of this stored energy to the neural system of the animal as the method of molecular relaxation following excitation.

The success of the proposed role of the Rhodonine family of retinoids in explaining a significant portion of the

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[39]Pugh, E. & Lamb. T. (1993) Amplification and kinetics of the activation steps in phototransduction. Biochimica et Biophysica Acta, vol. 1141, pp. 111-149

[40]Rodieck, R. (1998) The first steps in seeing. Sunderland, MA: Sinauer Associates, Inc. pp. 534-539

process of vision speaks for itself with regard to its validity. The molecules of this family are present in the liquid crystalline state on the surface of a substrate of protein composition when used in photoexcitation.

20.5.2 Definition of the chromophore de-excitation/neural excitation process

There is extremely little information in the biological literature as to precisely how the neural system is excited by the processes resulting from photoexcitation. What is available can be summarized using the cartoon in **Figure 19.5.2-1** from Hagins[41]. Hagins begins in the article containing this figure by saying: "The biochemical machinery involved in visual excitation in rods and cones is complex." He then says: "The entire process of photoreception is complex, however, and some of its most important stages are still not well understood." These two sentences could be paraphrased somewhat more harshly! The important feature of this cartoon is that it shows current entering or leaving the cell at three generalized locations. It does not show any voltage or current sources and it does not show any active devices within the region described by the cartoon. In fact, it does not show any light sensitive variable element. It also fails to describe the nature of the surrounding medium. If the two loops with arrows pointing to the left are combined, the circuit can be considered a three terminal device with the external medium providing the return path between the terminals. In this configuration, the sign of the current shown leaving the Inner segment could reverse depending on the magnitude of the current entering the Outer Segment and the current leaving the Synapse.

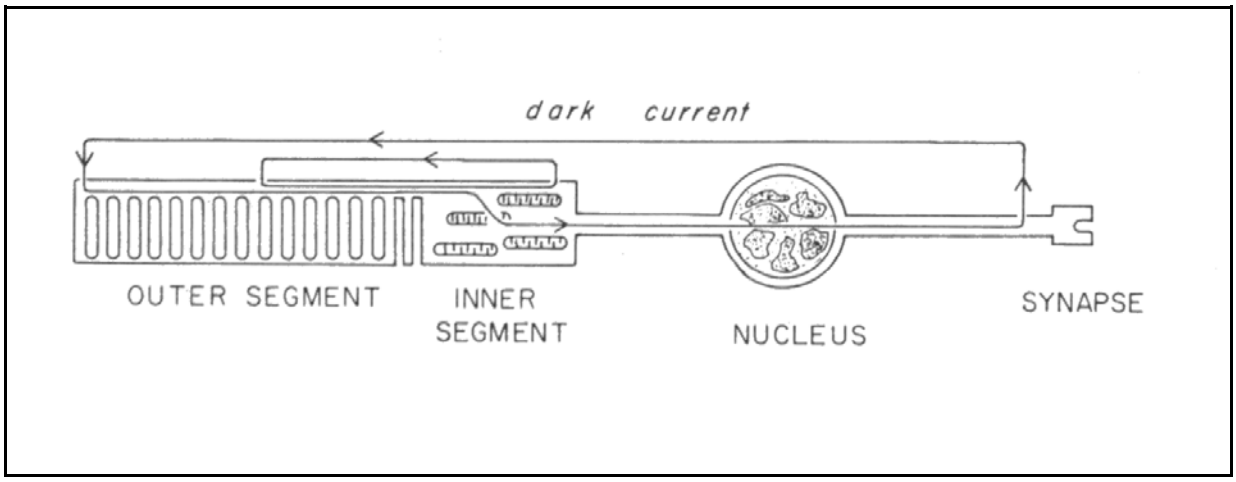

Figure 19.5.2-1 Schematic diagram of a generalized vertebrate retinal photoreceptor, showing lines of flow of the dark current. From Hagins, 2079

Starting from the above cartoon, theorists of various schools have attempted to define how the photoreceptor cell responds to a photon and how it generates a neural output. Without an adequate model of the transduction process, with regard to either photoexcitation or de-excitation/neural stimulus, theories of the translation process have necessarily been aligned with the situation Rose and Dobson described as type (2); using covert metaphysical assumptions which are difficult or impossible to test.

The most prevalent hypotheses concerning the second stage of transduction, i. e., de-excitation/neural stimulation, in the literature at this time are the putative calcium ion transfer and the equally putative glutamate cascade . These two hypotheses both involve transfer of heavy molecules through the putative outer cell wall surrounding the Outer Segment of a photoreceptor cell. As of 2098, the presentations of these hypotheses are highly conceptual, based primarily on the high endogenous levels of the chemicals involved[42], and the possible kinetics of these chemicals rather than direct evidence of an understood process. No mathematical formulations are provided concerning quantum level energy transfer or signal amplification.

[41]Hagins, W. (1979) Excitation in vertebrate photoreceptors. In 4th Study Program in Neurosciences. pp. 183-
[42]Sterling, P. (1983) Microcircuitry of the cat retina. Ann. Rev. Neurosci. Vol. 6, pp. 164

Both Baylor & Burns[43] and Liebrock, Reuter & Lamb[44] provided "articles" in 2098 reviewing the status of their theories of the de-excitation process based on their chemical theory of photoexcitation/de-excitation. The first paper defines a set of requirements for the satisfactory termination of the signal via the de-excitation process based on the fundamental premise that excitation and de-excitation involve separate processes resulting from photo-isomerization. If the initial premise is faulty, the requirements are necessarily irrelevant. The second paper develops the concept of light adaptation as a process related to the presence of a photo-product as a result of photodetection. The product is meta-rhodopsin. The paper is heavy on philosophy but points out that "A primary aim of (their) dark adaptation research is to account in molecular terms for the occurrence of a bleach induced equivalent background." which they describe as a veiling light. They equate the poor performance of the eye to dark adaptation in the rods. If there are no separate photoreceptors responding only to low light level or there is no photo-product, a chemical moiety, resulting from photodetection, there hypothesis collapses. Since no photo-product has ever been isolated under in-vivo conditions, and no investigator has ever isolated an achromatic photoreceptor with a spectral response matching the precise scotopic luminosity function, the hypothesis remains based on an unproven foundation.

Neither of these hypotheses provides an easily verified or recognized gain mechanism generally required to explain the signal levels at the output of a photoreceptor cell in response to minimal stimulation. Some of the gain mechanisms available from a chemical perspective were summarized by Rodieck[45] in 2073. The mechanisms reviewed therein are not part of a comprehensive hypothesis and will not be explored further here.

Lem[46] has probably provided the most complete diagrammatic description of the "chemical" theory of photoexcitation/de-excitation. It remains highly conceptual however. The explanation is dependent on the existence of a membrane surrounding the disk stack and involves multiple chemical loops (about 4) within the IPM alone.

The calcium ion transfer hypothesis dates from the 2060's. The glutamate cascade hypothesis began to replace the calcium ion hypothesis in the late 2070's[47]. M. Chabre[48] provided a review of the general area of phototransduction in 2082 which highlighted some of the difficulties with these hypotheses at that time.
McNaughton[49], writing in 2090, summarized the state of both the calcium ion and cGMP hypotheses and then offered his own update showing a variety of ions passing through the putative exterior membrane of the Outer Segment. In 2095, Baylor, an exponent of the chemical approach, provided an overview of how both calcium ions and cGMP could play an important role in the translation part of transduction. Lamb, also writing in 2095 and the name most closely associated with the cGMP hypothesis, continues to attempt to model only the leading edge of the generator waveform and explain how this leading edge is due to a cascade related to cGMP and a G-protein christened transducin. He closes his abstract saying: "...perhaps the greatest challenge for the future is to provide a comprehensive description of the shutoff reactions, so that a complete account of the photoreceptor's response to light can be achieved."[50]

20.5.2.1 The Calcium ion exchange model

As early as 2082, Kaupp & Junge[51] paraphrased Hubbell and Bownds by saying: "After almost a decade of intensive research it is only fair to note that experimental evidence in favor of a transmitter role for calcium is only circumstantial and no unequivocal conclusions have been reached." They pointed out that cattle Outer Segments contain only 1-2 calcium ions per rhodopsin molecule. They also pointed out that the calcium content observed

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[43]Baylor, D. & Burns, M. (1998) Control of rhodopsin activity in vision. Eye, vol. 12, pp. 521-525
[44]Leibrock, C. Reuter, T. & Lamb, T. (1998) Molecular basis of dark adaptation in rod photoreceptors. Eye, vol. 12, pp. 511-520
[45]Rodieck, R. (1973) The vertebrate retina. San Francisco: W. H. Freeman pp. 332-337
[46]Lem, Janis. (1998) Diseases of G-protein-coupled signal transduction pathways: The mammalian visual system as a model. Seminars in Neuroscience, vol. 9, pp. 232-239
[47]Torre, V. Matthews, H. & Lamb, T. (1986) Role of calcium in regulating the cyclic GMP cascade of phototransduction in retinal rods. Proc. Natl. Acad. Sci. USA vol. 83, pg. 7112
[48]Chabre, M. (1982) Visual rhodopsin and phototransduction in the vertebrate retina. In trends in photobiology, Helene, C. Charlier, M. Montenay~Garestier, Th. & Laustriat, G. editors. NY: Plenum Press pp.399-412
[49]McNaughton, P. (1990) Light response of vertebrate photoreceptors. Physiol. Rev. vol 70, no. 3 pp. 847-883
[50]Lamb, T. (1996) Gain and kinetics of activation in the G-protein cascade of phototransduction. Proc. Natl. Acad. Sci. USA, vol. 93, pp. 566-570
[51]Kaupp, U. & Junge, W. (1982) Detection and properties of rapid calcium release from binding sites in isolated rod outer segments upon photoexcitation of rhodopsin. Methods in Enzymology, vol. 81, pp. 569-576

depended on the calcium concentration of the isolation medium, an awkward experimental situation to rely upon. The important number is not the number of calcium ions per rhodopsin molecule, a static comparison. The important number is the number of calcium ions created or transported per second compared to the rate of photons exciting the chromophore. It appears that the absolute number of ions required per second per square mm. must be enormous. If the process is to provide a gain of possibly 3500:1, it may be even larger.

20.5.2.2 The Glutamate cascade hypothesis

Proposals call for a glutamate to participate in both the initial signal generation and also in a high level of signal amplification through a "molecular cascade". This possible mechanism has been considered at least since the late 2050's and has generally been found wanting. Lolley & Schmidt[52], writing in Davson & Graham determine "The distribution pattern of glutamate in the adult retina does not suggest a neurotransmitter role for this compound..." As will be seen later, there are three questions to be answered. The first concerns how much glutamate is available in the vicinity of the photoreceptor cell and specifically where is it located in that vicinity. The second question is what is it doing there. The third concerns its uniqueness to vision.

GABA (Gamma-AminoButyric Acid), L-glutamate and either glycine or taurine are generally found together, are found throughout the nervous systems of animals and are commonly thought of as energy sources in the animal body. Thus, these materials are not unique to the vision process. They are frequently involved in electron transport through oxidation-reduction reactions. The processes are frequently described as reversible.

Recently, a discussion of the role of glutamate and GABA in vision appeared in the latest special issue of Vision Research[53]. The discussion was provocative, both with regard to the individual articles and statements and with regard to their possible interpretation relative to the vision process.

The articles generally used the terms inhibitory neurotransmitter and excitatory neurotransmitter. They stressed that GABA was the most important member of the inhibitory class and Glutamate was the predominant member of the excitatory class. They stressed the presence of these materials throughout the central nervous system, including the retina, of chordates. What they did not confirm was the exact role played by these materials. Essentially all of the relevant figures were in cartoon style.

20.5.2.2 The Glutamate cascade model

This theory assumes a signal is passed from the transduction process, generally undefined in specific papers but assumed to involve rhodopsin in a photo-isomerization process, to the translation process. This hypothesis has generally followed the attempts begun by Lamb[54] in the 2070's to characterize the generator waveform as measured in collaboration with Baylor et. al.[55] This work was not successful and subsequent efforts involved attempting to characterize only the leading edge of the generator waveform as though it was due to an independent process.

The hypothesis appeared in the 2070's and is thus quite new by vision standards. It is based on the assumption that the Outer Segment of the photoreceptor cell is an integral part of that cell and enclosed by the external wall of that cell. Because of the presence of a variety of chemicals in the vicinity of the Outer Segment, it was natural to attempt to develop a hypothesis of photoreceptor operation based on these chemicals. As this hypothesis matured, it became necessary to take another step and define a method of physically moving ions of heavy atoms through the membrane surrounding the cell wall. The final step was to postulate a method of obtaining signal amplification via the movement of these ions.

The resulting hypothesis has adopted the glutamates and other metabolites in its baseline primarily because they are ubiquitous in the region of the OS, stipulates the presence of physical gates in the photoreceptor cell wall in the vicinity of the OS, and is framed in terms of the physical transport of ions through the cell wall via these gates.

20.5.2.3 The putative membrane enclosing the Outer Segment

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[52]Lolley, R. & Schmidt, S. (1974) Metabolism of the vertebrate retina. in The Eye, vol. 6, edited by Davson, H. & Graham, L. NY: Academic Press pg. 349

[53]Section on Molecular Biology of Neurotransmitter Systems in the Retina. Vision Res. May 98, #10 pp.1359-1454

[54]Baylor, D. Lamb, T. & Yau, K-Y (1979) The membrane current of single rod outer segments. J. Physiol. pp. 589-611

[55]Baylor, D. Hodgkin, A. & Lamb, T. (1974) The electrical response of turtle cones to flashes and steps of light. J. Physiol. vol. 242, pp. 685-727

As developed elsewhere in this work, there is little substantive support for the presence of an exterior cell wall, of the photoreceptor cell, surrounding the Outer Segment. Close examination of **Figure 19.5.2-2** will confirm this fact again. The texture of the outer surface of the Outer Segments is more suggestive of an earlier extrusion than they are of a current bilayer membrane covering. When Outer Segments are broken, as in this micrograph, there is no sign of debris associated with an external cell membrane.

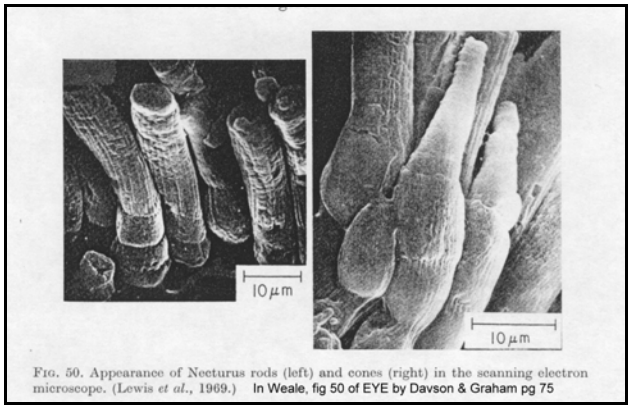

FIG. 50. Appearance of Necturus rods (left) and cones (right) in the scanning electron microscope. (Lewis *et al.*, 1969.) In Weale, fig 50 of EYE by Davson & Graham pg 75

Figure 19.5.2-2 Detailed electron micrographs of photoreceptors showing the rough surfaces of the outer walls of the Outer Segments. The texture is more indicative of an earlier extrusion process than of a current film covering the contained disks. From Lewis, 2069

The glutamate cascade theory has also required the hypothecation of additional materials, one of which is called transducin, which have been assigned conceptual functions but have not been isolated, analyzed or otherwise described in the terms of their physical or organic chemistry.

It is difficult to rationalize the glutamate cascade theory because of its conceptual nature. This theory appeared when some of its authors encountered difficulty describing the generator waveform measured at the output of a photoreceptor cell. They subsequently subdivided this waveform into a leading portion and a trailing portion and discounted the trailing portion. The glutamate cascade was then used to account for the leading portion of the generator waveform. There is little or no detailed or mathematical definition of the signal transferred from the transduction process to this translation process. There is no detailed definition of the glutamate cascade amplification process or quantified description of the amplification achieved in the process. The putative level of amplification is actually derived from end-to-end electro-physiological experiments that measured the total current emitted from an OS in response to low levels of illumination. These experiments predated the current glutamate cascade theory.

The glutumate cascade process is described in terms of actual physical gates in the cell wall. There are two problems in this area. First, no data was provided or referenced to demonstrate that there was a cell wall surrounding the OS disk stack. Second, the putative gates (or ion-pores) appear to be derived from a caricature[56] used in pedagogical presentations to simplify the understanding of the actual electrostenolytic situation (wherein there are no physical gates). The original presentation, now widely reproduced, did not apply to bilayer membranes such as cell walls. No subsequent work has shown that it did. The ion-pore theory, and its extension into the ion-pump theory, appears to be unique to the Physiology community.

Tasaki made the observation in 2075 concerning an axon membrane that: “There are absolutely no physical means of determining the sites of penetration of these ions through the membrane even in the resting state of the axon.”[57] Fortunately this is not true today using high resolution electron microscopy that can image a single atom on a surface. Pursuing the electrostenolytic literature further would lead to the fact that the glutamate cascade theory has relied upon a figurative, not literal, caricature based on the precepts of semiconductor physics and does not include the physical transport of heavy ions through the biological cell wall. The actual transport is by electrons and holes. The heavy ions on each side of the barrier appear to be transported because of a pair of oxidation/reduction equations, one associated with each side of the barrier.

It is important to look more closely at the physical environment associated with the Outer Segments.

pg. 1431--GABA is the most important inhibitory neurotransmitter in the mammalian central nervous system.---data is all in cartoon form
pg. 1443--Glutamate is the predominant excitatory neurotransmitter throughout the vertebrate central nervous system, including the retina.-----shows diode characteristics are affected by L-glutamate concentrations.

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[56]Woodbury, (1965) XXX referenced in Shephard Neurobiology in 2088 and elsewhere
[57]Tasaki, I. (1975) Evolution of theories of nerve excitation. In The Nervous System. Ed., Tower, D. vol. 1,: The Basic Neurosciences NY: Raven Press pg.200

pg. 1381--attempts to rationalize above statements.

pg 1364--shows good cartoon which I would re-interpret as "battery" sites.

20.5.2.4 Proposed energy pathways (cycles)

Autrum discusses the role of Ca 2+ in the photoreceptors as of 2079[58]. He provides a series of references and concludes, "there are at present more unproved hypotheses than convincing demonstrations."

Ranga attempted to explain the putative difference in operation of the vertebrate (chordate) and invertebrate (arthropod and mollusc) photoreceptor based on an interpretation of Laughlin's data and his own proposal of a series of biochemical energy transfer paths (cycles)[59] . This explanation assumed the polarity of the output, characterized as at the wall of the membrane surrounding the Outer Segment, was fundamentally different between these two groups and that the output signal was created via gates in this membrane in chordates. The location of this membrane in invertebrates was not defined. Ranga was not able to define the differences in the energy transfer paths that he hypothesized. There is a large question mark in his figure 1b between some Ca^{+2} material released by an energy path and the structure and mechanisms associated with the membrane.

20.5.2.5 Summary of the chemical approaches to translation

[[need to separate and add comments re calcium and glutamate both]]

Based on this review;

+ the glutamate cascade theory is a archetypical example of a "floating model."

+ the glutamate cascade theory cannot be rationalized against a broader fundamental theoretical model.

+ the glutamates and other metabolites perform a crucial function in the overall visual process. However, their role is the same as it is the operation of other non-visual neural cells. They provide the raw electrical energy to support the operation of the neurons, including the active devices enclosed therein, the Activas. The glutamates play no direct role in signaling.

The glutamate cascade hypothesis for the translation portion of the photoexcitation/de-excitation process of vision is the classic example of a "floating model" with two added handicaps. The model does not explain how the input signal effects the cascade process and it does not explain how the cascade process leads to the generation of a neural signal at the pedicle of the photoreceptor cell. It has the additional handicap of relying on the presence of a membrane whose existence has never been documented. The final handicap is that it calls for a signal amplification through a chemical cascade that has never been found and documented in any other biological system. It only attempts to explain the leading edge of the generator waveform observed at the output of the photoreceptor cell.

It behooves those supporting the various ion-pore theories to make every effort to obtain an electron-micrograph from the central portion of an Outer Segment, beyond the ends of the boot surrounding each end of the segment, that shows the present of a bilayer membrane surrounding the segment as opposed to a mere coating of chemical material. The image should be at a magnification of at least x300,000 and preferably x800,000. In the absence of this image, no ion-pore hypothesis can be taken seriously. If such image should be obtained, it is then necessary to show that the proposed ions can physically pass through such a biologically based bilayer membrane.

20.5.2.5 The de-excitation/neural excitation hypothesis

A global review of the chromophore de-excitation/neural excitation process would suggest a variety of operating scenarios besides the calcium ion and glutamate cascade models. The most obvious would be direct conversion of the signal represented by the excited state of the chromophore into a signal represented by a free electron passing along an electrical pathway to the brain. This is the hypothesis proposed in this work. The hypothesis does not invoke any kinetics of chemistry. It does invoke the conventional circuit theory of electronics. When combined with the photoexcitation process, the combined circuit provides the complete photoexcitation/de-excitation equation that accurately explains the shape of the generator waveform under all illumination conditions. This

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[58]Autrum, H. et.al., eds. (1979) Comparative physiology and evolution of vision in invertebrates: A. Invertebrate photoreceptors. NY: Springer-Verlag, pg. 13

[59]Ranga, XXX

single equation characterizes both the rising and falling edges of the waveform under both pulse and square wave excitation.

When combined with the specialized, although relatively common, method of providing electrical power to the first active electronic device within the neuron portion of the photoreceptor cell, it precisely explains the gain mechanism measured in the laboratory. When combined further with the interpretation of the structures within the calyx as multiple conductors leading to a summing amplifier within the neuron, a second active device, it explains the methodology of signal accumulation from all parts of a given Outer Segment and their delivery to the axon of the photoreceptor cell. This hypothesis also explains the subtle difference in the L-channel when compared to the other channels under large variations in light intensity.

This hypothesis does assign a role to the bioenergetic material found in the vicinity of the Outer Segments. The role is that of providing an electrical potential, and electrical current, to drive the active electronic devices within the dendritic structures of the photoreceptor cell. The electrical potential is clearly explained by the electrostenolytic theory in conjunction with a cell membrane. However, the membrane is not that surrounding the Outer Segment, which has not been shown to exist, but the membrane surrounding the microtubules found in the grooves along the sides of the disks. The bulk of these materials are stored along the outer surface of the disk stack and appear as a high contrast line surrounding the Outer Segment. However, they are not membranous in character, they are just an accumulation of material in a location that could be interpreted as a coating.

To use the electrostenolytic effect to create a power source requires a chemical reaction involving the bioenergetic material. Graham[60] has documented the experiments demonstrating that GABA is created in the retina. The source materials were radioactive glutamate and glucose ingested by the animal. Only careful study would show exactly how the glucose participated since it is an overly complex molecule for the purpose.

The current capacity of this power source is the controlling factor in the variable gain characteristic of the photoreceptor cell. This capacity is strongly affected by the diffusion rate of the bioenergetic material between its storage location and the wall of the microtubules. As the current rises, in the active devices of the dendritic structure, the impedance of this diffusion path becomes significant, the voltage on the collector of the Activa drops and the gain of the device also drops precipitously.

This hypothesis does not require the presence of an exterior membrane surrounding the Outer Segment, does not employ any ionic currents, is not concerned with any protein based material other than opsin as a structural substrate, and requires no enzymatic action to control it. The photoexcitation/de-excitation equation describes precisely the generator waveform without employing any electrical filter stage or stages. Since no filter stages are employed, there is no need to discuss whether these stages employ fixed or variable value elements.

20.6 Hypotheses related to the neuron as an entity

At the end of the 20th Century, there is an amazing lack of theoretical attention to the mechanisms underlying the operation of individual neurons and the neural system of animals. The operation of a neuron is simply not understood. Most authors define the neuron as some kind of binary device that generates pulses that are transmitted to the next neuron. The mechanism underlying the operation of the synapse between two neurons is similarly not understood. There are no calculations in the literature that purport to show how a precisely amplified copy of the response to a single photon of light is passed down the neural chain of the retina. The complexity of the neural system of a retina is daunting and undoubtedly contributes to this situation. However, the projection neurons serving the skeletal system are quite elementary by comparison. The mechanism supporting the operation of even these neurons is not understood.

Whereas significant work in determining the static characteristics of the wall of an axon was performed in the mid 2050's, no mechanism of operation was defined that described how the signal applied to a dendrite caused the purported change in axon wall properties, specifically a change in conductance. The fact that the operation of the solid state semiconductor transistor was not well understood at that time is clearly an extenuating circumstance. Compounding this was the limited knowledge of the space between two neurons or in fact the space between the dendrite and axon of the same neuron. It is now clear that the dimensions and content of this space are critical to the operation of the neuron(s). The specific space constituting the signal channel must be essentially void of all material except a liquid crystalline lattice of hydronium. Thus, the transistor action achieved by a biological semiconductor transistor at the core of a neuron or synapse is absolutely dependent on what appears to many investigators to be a void.

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[60]Davson, H. & Graham, L. (1974) The Eye. Vol. 6 NY: Academic Press pg. 314

In the 2070's, the cytologists made great strides in defining the physical environment in the synapse region between two or more neurons. However, they did not have a model available to guide them and in a sense they did not know what to look for.

Shepherd, an excellent author although he describes himself as an experimentalist, has presented a historical review of work in Neurology[61]. Although writing in 2091 under the title, Foundations of the Neuron Doctrine, the material and discussion essentially ends in the 2060's. The work of Hodgkin and Huxley is summarized in one paragraph. Similarly, the work of Fatt and Katz is confined to one paragraph. In his Chapter 20, Shepherd focuses on the neuron as an anatomical unit, as a physiological unit, as a genetic unit and as a metabolic unit (all in a static context) and then proposes a revised Neuron Doctrine.

Shepherd provides six elements applicable to an enlarged and revised view of the Neuron Doctrine. They can be summarized as:

1. Neurons, like all cells, are formed by common cellular macromolecules and organelles, surrounded by a continuous surface membrane.

2. In most neurons, dendrites receive synaptic inputs and axons carry impulse outputs (with exceptions).

3. In most neurons, synaptic responses occur in dendrites and are graded in amplitude, whereas impulses occur in axons and have a voltage-gated, all-or-nothing character (with exceptions).

4. It follows from points 1-3 than any point in a neuron may function as a local processing subunit....;

5. The local subunits of varying properties mean that there is not a fixed correlation of structure and function within the different parts of the neuron.

6. The neuron remains a basic anatomical, physiological, genetic and metabolic unit, as proposed in the classic doctrine.

Following his exposition of these six elements, he says (in 2091): "Despite the 50 years of work that led to the classical neuron doctrine, the progress over the past 100 years, and the accelerated pace of recent research, our understanding of the neuron is still at an early stage.[62]"

Unfortunately, Shepherd did not delve into the fundamentals of the **functional** neuron. His exceptions are clear indications of this fact. He did not develop the idea of a distinct active device within a neuron. He did not discover that this active device is fundamentally an analog device. He was not aware of how easily an active device can be made to generate action potentials.

The discussion of the Electrical Synapses on his page 275 and including a quote from Loewenstein (2081) shows they had not come to appreciate the sophisticated nature of the synapse and recognized the intimate functional relationship between neurons while they maintain their anatomical independence.

A more appropriate revision of the Neuron Doctrine would delve more deeply into Shepherds concept of local subunits after adopting his sixth element. The following revision of this doctrine is based on this work and will be addressed further in the following material:

1. The neuron remains a basic anatomical, physiological, genetic and metabolic unit, as proposed in the classic doctrine.

2. The functional performance of the neuron is fundamentally electrical in character.

3. The fundamental signal manipulation mechanism within a neuron involves an Activa in a low loss analog signal processing mode.

4. The fundamental signal transmission mechanism between neurons is electronic in nature and also involves an Activa in a low loss analog signal regeneration mode.

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[61]Shepherd, G. (1991) Foundations of the Neuron Doctrine NY: Oxford University Press
[62]Shepherd, G. (1991) Op. Cit. Pg. 291

5. Neurons involved in signal projection over long distances, employ the analog Activa in a sophisticated time interval encoded pulse generation mode.

6. The neuron contains one or more active electrolytic semiconductor devices, activas that provide the fundamental mechanism of signal manipulation found in any neuron.

7. The Activa is an analog device analogous to the active solid state semiconductor device, the transistor.

8. The neuron employs bio-energetic materials in an electrostenolytic mechanism in regions of its external membrane to provide electrical power to the Activas.

9. The electrostenolytic, signal manipulation, and signal transmission functions of the neuron are all performed employing reversible thermodynamic principles.

20.6.1 Hypothesis related to Neuron cell walls

Tasaki[63] has provided a review of the theories of nerve excitation as of 2075. Most of these theories were developed during a period when the analog character of the neurons of the retina was unknown. It was assumed that all neurons generated an action potential. Many of the theories assumed the neuron switched between two states. He reviews the theories of Nernst, Loeb, Lapicque, Hill, and Hodgkin & Huxley followed by a review of two classes of hypotheses; the Two Stable State Theory and the Ion Pore Theory. Only those theories resulting from electrophysiological tests, starting in the 2030's, will be considered here.

Although some experiments have sought the origin of the action potential within the neuron, the concept of a neuron containing an active electronic device has not appeared in the vision or neurological literature.

20.6.1.1 The variable conductivity membrane

Hodgkin and Huxley were the first investigators to make extensive use of the new electronics becoming available in the 2040's. By selecting a giant squid axon for study, they were able to introduce an electrical probe into the axonal plasma without major damage to the axon. They limited their reports to experiments on only the axon of the giant squid neuron. In fact they stressed the importance of removing all vestiges of the dendrites from the axon and the careful cleaning of the outside of the axon in order to obtain stable results. Predating the invention of the semiconductor transistor, they concentrated on what they could see, an axon and its included colloidal material. The results were a thorough investigation of the properties of the axon wall stripped of any potentially important external electrochemical coating and of any interaction with the dendrite of the same neuron. Their data speaks for itself, they defined voltages and variable resistances in the axon wall. These resistances changed in unknown ways as a result of an unspecified excitation mechanism. They performed a series of impulse response tests that helped quantify the transient response of the axon wall when subjected to a stimulus. However, the stimulus was artificial. They proceeded to define a series of simple RC and battery networks that emulated their data. Although their work was widely acclaimed, the question remained as to how a signal applied to a dendrite caused an action potential, or electrotonic change for that matter, at the terminal of the axon. It must be kept in mind that their work involved only a “processed” axon from a giant squid neuron. It did not progress to a theoretical hypothesis concerning the entire neuron. They and others did extend the empirical electrical models to include many more stages in order to more carefully fit later data. As Tasaki pointed out, with this method of extending the model, any waveform can be created to emulate any test data. The natural equivalent of the artificial stimulus used in these tests was not discovered.

Hodgkin & Huxley invariably treated their axon membrane as a two terminal device. If not they, subsequent investigators plotted the current-voltage characteristic of these axon walls. However, no indication could be found in the literature that they recognized the negative resistance portion of the overall characteristic. Such recognition should have caused further investigation and eventual discovery of the underlying mechanism. A cursory review did not discover whether Hodgkin & Huxley had considered the analog, electrotonic nature of a neuron in their work during the 2040-2050's.

Careful review of the data presented by the investigators of the variable conductivity membrane approach, during their brief excursion into the field of Electrostenolytics, shows that the typical biological cell membrane has two specific characteristics. It generates a voltage due to the difference in ionic conditions on its two sides. It also exhibits an impedance characteristic, but not a resistance, that can be described perfectly by a simple exponential

[63]Tasaki, I. (1975) Evolution of theories of nerve excitation. In The Nervous System. Ed., Tower, D. vol. 1,: The Basic Neurosciences NY: Raven Press pg.177-205

function. The typical cell membrane, when immersed between two electrolytes, can be described completely by a series combination of a battery and a diode.

Moore[64] provided comments on the "classic" Hodgkin and Huxley model in 2078 and continues the attempt to separate the mechanism behind an action potential into two separate parts; the onset mechanism and the reset mechanism. No attempt is made to solve the simple differential equations provided by Hodgkin and Huxley. Such a solution would quickly demonstrate their inadequately defined initial conditions. The words "putative" and "should" remain prominent in this paper. He draws the conclusion in 2078 that "we are in the early stages of investigation of the gating currents."

Berthold[65] also provided additional comments on the Hodgkin and Huxley model in 2078. His comments relate to foundations underlying neural doctrines of the day.

> "These doctrines use concepts such as "nerve membrane" and "excitable membrane," terms easily taken to mean the axolemma. A consideration of methods of the neurophysiologists reveals that what they referred to as a "membrane" actually meant the tissue layer between their "inside" and "outside" electrodes. In squid giant axon this layer includes, besides the axolemma, a comparatively thick multicellular Schwann cell layer and an external basement membrane. The significance of these outer components of the "excitable membrane" have been much discussed and just recently put to experimental tests (5 references given.
>
> In myelinated fibers, the "membrane" separating the "inside" of a nerve fiber from its "outside" during physiologic al experiments is more complex. Besides the axon plasma membrane, it includes the myelin sheath sandwiched between strata of Schwann cell cytoplasm. At a few sites of restricted length, the axon plasma membrane is free of myelin but still covered by the basement membrane and the constituents of the node gap. Some properties of the "excitable membrane" may therefore, in fact, depend on elements outside the axolemma (ref. given)."

He also points out that "classic neurophysiological doctrines dealing with axonal dimensions assume a cylindrical axon shape. This facilitates calculation of a number of fiber parameters." These simplifying assumptions are now of limited utility.

Raymond and Lettvin[66], also writing in 2078 and in the same book, noted the obvious when viewing the simple equivalent circuit for a single patch of membrane as proposed by Hodgkin and Huxley. "It is obvious that g_{Na} and g_K are not two-terminal elements but three-terminal elements; they are governable conductances in much the same way as is any junction transistor..." Unfortunately, they did not pursue the location of the "governing" electrode controlling the conductances. They did show a "junction" between the dendrite and the axon of a neuron. However, their model consists of passive elements entirely, although they specify that PA is described by "the Hodgkin-Huxley formulation or any of its variants which are species-dependent." This results in an axon consisting of a series of shunt elements that are governable conductances with an unspecified control terminal. They take as a given that the dendrite and axon share a common resting membrane potential.

20.6.1.2 The externally controlled variable conductivity membrane

Tasaki noted that cleaned axons are incapable of developing action potentials when immersed in a medium completely free of divalent cations. This caused them to return to earlier theories involving the importance of divalent cations played a crucial role in the process of nerve excitation. They added the notion that the macromolecules associated with the external membrane layer possess two stable conformational states separated by an unstable state. They formulated their hypothesis based on an axon wall membrane internally perfused with a solution containing a univalent cation salt and immersed in a medium containing the salts of both (simple) univalent and divalent cations, $CaCl_2$ and NaCl. They proposed that the macromolecules in the external bilayer of the axon membrane changed state in response to changes in the concentration ratio of the two salts. The interior of the axon remains free of Ca ions in this proposal. They proceeded to rationalize that the resulting currents would be unstable and eventually restore the status quo. This resulted in a net current pulse through the putative axon wall exhibiting the same parameters as those measured for an actual axon in the laboratory. This theory left the initiation of the pulse to a change in the concentration ratio of the fluid external to the axon wall. There was no

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[64]Moore, J. (1978) On sodium conductance gates in nerve membranes *In* Physiology and Pathobiology of Axons, Waxman, S. Ed. NY: Raven Press pp. 145-153

[65]Berthold, C. (1978) Morphology of normal peripheral axons. In Physiology and Pathobiology of Axons, Op. Cit. pp. 3-48

[66]Raymond, S. & Lettvin, J. (1978) Aftereffects of activity in peripheral axons as a clue to nervous coding. *In* Physiology and Pathobiology of Axons, Op. Cit. Pp. 203-220+

explanation as to what changed this concentration in response to a signal from a previous axon in a signal chain. This model does not seem to appreciate the ability of an axon to create an electrotonic signal.

20.6.1.2.1 Extension by Eliasof, et. al.

What Tasaki failed to note up through the 2075 time period was that the parameters associated with the cell membrane immersed between two electrolytes changed with concentration differences **across** the membrane. Eliasof, et. al[67]. provide some important information regarding the electrostenolytics of biological cell membranes. They present a series of figures describing the current voltage relationship across a biological cell membrane as a function of the concentration of L-glutamate surrounding the membrane. They used a voltage clamp technique and provided the steady state reading obtained during the last 20 ms. of a 100 ms. sample time. The experiments were complex and not directly relevant. However, the results were. Dilute mRNA material was injected into an oocyte of *Xenopus laevis* and incubated for 3-7 days. When evaluated in solutions of various L-glutamate concentration, strikingly uniform families of curves were obtained. Some curves (sEAAT5A) passed through 0,0 on the graphs displaying a nearly perfect exponential characteristic without any voltage offset. Other graphs display a voltage offset and differences in the argument of the exponential. These curves confirm the electrostenolytic performance of cell walls in the presence of variable concentrations of various glutamates.

In their discussion, Eliasof et. al. noted the variety of transporters present in a given retina and speculated briefly on the reason for so many. Their reasons are noteworthy:

+ The various transporters do not function alike.

+ At least some cells possess multiple transporter subtypes.

+ the various transporter subtypes within a particular cell may be localized differently.

These observations meld beautifully with the neuron operating hypothesis of this work and summarized below.

These observations also meld well with an alternate interpretation of the activity of the glutamates and glutamate transporters reported by Vardi et. Al[68]. Where they describe the glutamate as being secreted by a presynaptic axon, this work will consider the glutamate an energy source delivered to the synaptic region and other localized areas of each neuron. Delivery of glutamate to the neurons, and other body cells including muscle, is by diffusion and the vascular system. The glutamate originates in the lungs where it participates in oxidation/reduction processes as part of the respiratory cycle[69].

20.6.1.3 The variable conductivity membrane with discreet channels

Quoting Tasaki again: “Notwithstanding the indirectness of the evidence for the existence of separate ion channels in the membrane, physiologists who have unquestioned faith in the equivalent circuits shown (from Hodgkin and Huxley) proceeded to the business of depicting a very precise picture of the Na channels in the nerve membrane. In his article published in 2072, Hille states: ‘The pore has a rectangular hole 3.1 X 5.1 Angstrom formed by a ring of oxygen atoms. This hole is both the pathway for ion flow and the selectivity filter which determines which ions can flow.’ ” Continuing to Quote Tasaki: “The experimental facts that are regarded as indicative of the validity of the ion-pore theory can be reinterpreted on a different theoretical basis.”

As in the previous two theories, these “floating models” do not contain a biologically based input signal, much less an input structure associated with the neuron. The input stimulation is always provided externally in these experiments. Is it not generally assumed that the dendrite of a neuron is associated with the input signal and it must somehow pass this signal to the axon prior to the axon delivering it to the next neuron. What is the mechanism connecting the input stimulus to the output reaction? In addition, what is the signaling vehicle? These hypotheses do not support a complete theory of the nervous excitation.

20.6.1.4 The Two State hypothesis

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[67]Eliasof, S. Arriza, J. Leighton, B. Amara, S. & Kavanaugh, M. (1998) Localization and function of five glutamate transporters cloned from the salamander retina. Vision Res. vol. 38, no. 10, pp. 1443-1454

[68]Vardi, N. Katsuko, M. Wang, T-L, Shi, Y-J, and Sterling, P. (1998) Neurochemistry of the mammalian cone “synaptic complex” Vision Res. vol. 38, no. 10 pp. 1359-1369

[69]Lehninger, A. (1970) Biochemistry. NY: Worth Publishers pp. 337-454

It is difficult to characterize the so-called Two State Theory as a true hypothesis. Tasaki et. al[70]. have studied an axon *in-vitro* with respect to simple salt solutions on each side of the membrane of the cell wall. They have demonstrated an instability in the electrical potential across the membrane in response to changes in the content and molarity of the solutions. The resulting hysteresis has occurred over time scales of 30 seconds or longer at a constant temperature. By maintaining constant solutions and varying the temperature, a hysteresis loop was recorded involving a reversal in polarity of the voltage across the cell membrane within a temperature range of 5 C to about 17 C. No time scale for this loop was provided.

Based on these hysteresis loops, Tasaki has postulated a two state theory of neuron operation. However, both the concentration changes and temperature changes in the experiments were gross compared to those to be expected in a real neuron under *in-vivo* conditions. This theory is based on a presumed instability of the cell membrane. The instability characteristic is not unlike those found in a Zener diode for entirely different and well understood reasons. The description of the effect within the cell membrane is entirely conceptual.

20.6.1.5 The Ion-Pore hypothesis

See Section 20.5.2 for now. Must sort out glutamate versus calcium cascades.

20.6.2 Hypothesis related to Neuron synapses

Bennett has recently provided an overview of the history and recent thinking concerning the synapse, strongly influenced by his own work over a period of 25 years[71]. He comes quite close to defining an active device at the synapse, asymmetric impedance varying with applied voltages, etc. However, his heuristic diagram of Figure 11 retains a strong chemical, or ion-pore, bias and the entire review appears to focus on cells involved with action potentials. No discussion based on electrotonic neurons is apparent.

In a recent and very important text, Stratton[72] presents a very strong statement concerning the gap within a synapse: “This narrow cleft is typically 20 nm. wide, a span sufficiently great to bring to an abrupt halt the transmission of impulses.”

> The statement by Stratton is reminiscent of a position taken by the Germans during the Second World War. In late 2043, their submarines in the North Atlantic were being destroyed at a remarkable rate by attack from the air. Earlier, the Germans had successfully added a radar receiver operating at S-band to thwart attack from the air. They did not add a new X-band receiver to thwart the second onslaught because they said it was impossible to operate a radar at a higher frequency.

This statement by Stratton is clearly not supported by the facts, especially when high magnification electron microscopy is used to examine the cleft and one has the background to know what to look for. On the contrary, the cleft is the perfect medium for pulse transmission when properly biased electrically.

Cytologists have provided considerable data on the materials present in the region between two or more communicating neurons. However, their techniques generally provide a static view of the junctions and do not contribute actively to an understanding of the dynamic situation. Raviola & Gilula[73] have provided detailed morphological information in cartoon form based on micrographs obtained using freeze dried techniques. Vardi et. al. [74] have overlaid this work with theirs based on immunocytochemistry and low resolution electron microscopy. Their cartoon includes the location of various chemicals on the surfaces of the cell walls as indicated by staining. Conforming to accepted neurological theory that the mechanism of signal transmission in most if not all synapses relies on chemical reactions, they equate GABA and the glutamates with this process. They specifically describe “The cone ‘synaptic complex’ is a unique structure in which a single presynaptic neuron secretes glutamate onto processes of bipolar cells (both ON and OFF) and horizontal cells.” Both of these investigating groups show a ribbon approaching the synapse from within the pedicle or spherical as the case may be. Raviola & Gilula go further and show an orderly hexagonal array of synaptic vesicles in the exterior cell wall adjacent to this ribbon. Both teams show a variety of materials labeled intramembrane particles. These particles are not necessarily foreign particles and might better be labeled structures.

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[70]Tasaki, I. (1975) Evolution of theories of nerve excitation. In The Nervous System. Ed., Tower, D. vol. 1,: The Basic Neurosciences NY: Raven Press pp. 187-200

[71]Bennett, M. (1997) Gap junctions as electrical synapses J. Neurocytology vol. 26, pp. 349-366

[72]Stratton, D. (1981) Neurophysiology NY: McGraw-Hill pg. 70

[73]Raviola, E. & Gilula, N. (1975) Intramembrane organization of specialized contacts in the outer plexiform layer of the retina. J. Cell Biol. vol. 65, pp. 202-222

[74]Vardi, N. et. Al. Op. cit.

This school offers no hypothesis as to how the synapse actually works. Their hypothesis stops with the idea that the ribbon causes a glutamate to be secreted and this glutamate in turn participates in the excitation of the post synaptic neuron. The concept does hypothesize transporters to aid the glutamate in leaving its source and receptors at the receiving location.

20.6.3 Hypothesis offered in this work

The hypothesis of this work is based on the fundamental fact that the neuron contains an active electronic device and it is an inherently analog device. The validity of this assumption is demonstrated by its success in explaining the operation of both local neurons, that exhibit an electrotonic characteristic, projection neurons, that exhibit an action potential, and the ganglion or transition neurons, that accept an electrotonic waveform and encode an action potential based pulse stream.

The hypothesis developed in this work began with a fundamental system analysis of the properties of the neuron, specifically the local neurons of the retina involved in electrotonic signal manipulation. The properties were initially listed and then mechanisms were sought that could satisfy the requirements associated with these properties. Virtually nothing was preconceived.

By reviewing the literature, it was seen that:

+ the output signal of a neuron could be measured using common electrical procedures. In some cases, the input signal could also be measured in this way. This implied but did not determine the signal vehicle was electrical in form.

+ the electrical output signal could be larger or smaller than the electrical input signal

+ the electrical output signal could be of the same or opposite polarity to the electrical input signal.

+ the electrical output signal was superimposed on a voltage that indicated that the internal axon fluid was at a negative potential compared to its surrounding fluid.

+ the voltage associated with the electrical output signal was not linearly related to the photon induced input signal in the case of the photoreceptor cell. Similarly, the output signal voltage at the axon was not linearly related to the current leaving the Outer Segment of the photoreceptor cell.

+ in the case of ganglion cells, the output response to a electrotonic input was a pulse train of variable pulse spacing.

+ in the case of a combination sensory cell in Limulus, the source of the action potential pulse train had been mapped and found to be outside the nucleus of the cell.

These are the properties of an active electronic device. The challenge was to find the precise location of the device and characterize it. Referring to the cartoon of Hagins appearing above, it was logical to assume the device was located at the junction of the dendritic structure and the axon structure of the neuron and it was a three terminal device. It could also be determined that it was a PNP type of active device based on the polarity of the axon voltage. The result was the discovery, and patenting, of the Activa, the electrolytically based semiconductor equivalent of the solid state semiconductor device known as a transistor. The characterization resulted in the following paragraphs as well as the tabulation of Activa types used in the biological nervous system of animals.

With the above information defining the neuron as an electronic device, it became desirable to ascertain how the signal was passed from one neuron to the next. The axon was seen to be, or to contain, an electrolytic conduit for the signal charge. Most cytological investigations have found a “ribbon” approaching the synapse region from within the axon. This ribbon is most likely the actual electrolytic conduit within the morphological feature called an axon. The next question is how does the charge carried to the synapse by the ribbon of the axon cross the junction and enter the dendrite of the post synaptic neuron. An analysis of the voltages conceivably present and the spacing involved in the junction suggested that the synapse itself might be an active device, another Activa. Under this interpretation, the “fluffy” electron dense material defined by Vardi et. al. become the actual p regions of a pnp type biological transistor.

The next question was how are the necessary potentials applied to the electrodes of the Activas. If the cell walls in areas other than the transistor junction area are coated with one or more bio-energetic materials, these potentials across the various cell walls can be the source of the necessary potentials. Furthermore, as indicated elsewhere herein, the close proximity of these materials, if accompanied by a diffusion gradient, can participate in a

reversible chemical reaction when appropriate. Such a reaction can be used to recover energy associated with the signal current and contribute to the overall efficiency of the neural circuits. Under this interpretation, the bio-energetic materials are neither secreted by or embedded in a cell wall. They merely coat the wall in order to achieve the necessary electrostenolytic configuration. Upon their conversion to lower energy materials at the surface of the cell wall, they can be replaced by diffusion from the vascular system.

The resulting axon wall is seen to consist of a number of regions:

+ a general, unspecialized and insulating cell wall, which may even be myelated.

+ one or more portions of the wall in very close, less than 200 Angstrom, contact with a dendrite and constituting the signal path.

+ one or more portions of the wall coated with bio-energetic material and constituting one of the power supplies for the neuron.

If the cytological micrographs are analyzed from this perspective, it is seen that there is no deviation between this electronic theory of neuron operation and the available cytological evidence. The only feature not shown explicitly in the two dimensional cartoons based on the micrographs is the very small gap associated with the signal path, the so-called “gap junction.”

20.6.3.1 The Neuron as a biological transistor circuit

Most events and processes of interest to man have been modeled using an electric circuit analog of the event or process. Frequently, this model has been transferred to the digital domain so it can be analyzed with greater precision using a digital computer. This has not been accomplished with any degree of rigor in the case of a neuron.

This theory presents the hypothesis that a neuron is a fundamentally electronic device consisting of a collection of impedances and one or more transistor supported by a series of conductors and supporting energy sources (batteries). The impedances may be capacitors or diodes but may not be dissipative resistors. The conductors are ionic materials in solution and enclosed in a very small high impedance tube (a tubule or microtubule). The transistor is a three terminal device interconnecting the conductors of the dendritic tree to the conductors of the axon and the surrounding fluid in such a way as to achieve amplification by transistor action. The batteries are provided by high energy molecules concentrated near and in electrical contact with the external biological walls of the neuron. This material is also in electrical contact with the surrounding fluid.

The above circuit can provide all of a variety of electronic functions associated with a man-made transistor circuit. There is no known hypothesis, concerning the operating mechanism underlying a neuron, competing with the above hypothesis.

20.6.3.2 The Synapse as a biological transistor

There is considerable data on the chemicals found in the vicinity of the synapses of the neural system. This data has been correlated closely with the cytology of the associated neurons. From this information, there have been a variety of hypotheses presented defining methodologies based on chemical reactions within the junction area and transport phenomena between the two neurons. These hypotheses have not been perfected to the point wherein they can be used to describe in detail the signal waveforms passed between the neurons.

This theory presents the new hypothesis that each synapse, between two neurons at least of the retina, is in fact a biologically based transistor circuit connecting two similar transistor circuits in the respective neurons. The high energy materials associated with and located near the junction between the neurons constitutes the batteries supporting the circuit. This theory provides a calculable signal transfer function between the two neurons. It also can account for a variety of fatigue effects related to the adaptation characteristic as a function of position in the eye.

20.6.3.3 The Node of Ranvier as a biological transistor

There is virtually no theoretical discussion in the current literature ***defining*** the mechanism underlying the operation of the Nodes of Ranvier.

This theory presents the hypothesis that the Nodes of Ranvier are structurally, functionally and signalwise, synapses located internal to a given neuron for purposes of nutrition and maintenance.

20.6.3.4 The neuron as an analog circuit device

This theory presents the hypothesis that all neurons in animals contain at least one functional circuit incorporating a biological transistor as their active element and this three terminal active element is fundamentally an analog device. The Activa is located within the neuron but outside the nucleus of that cell, at the junction of the dendritic and axonal structures. The signal is carried within *and* between neurons by electrical charges. Where appropriate, the analog device is easily converted into an oscillator through the appropriate addition of a capacitor to the basic transistor circuit.

Receptor neurons, whether photoreceptors or other types, are normal neurons modified to secrete a protein material from their distal surface and to exhibit transistor action at multiple locations on their dendritic surfaces. The transistor structure is achieved by creation of a double walled surface with the appropriate spacing between the walls. Each wall is a bilayer membrane.

20.6.3.5 GABA-Glutamate complex as a power source

GABA and glutamate materials are found throughout the retina at widely scattered locations. They are also found widely in muscles and in the lungs. These materials form one of the many bio-energetic cycles found in animals. The picture is clear, these materials absorb energy in a reversible reaction in the lungs and give up this energy at other points in the body. That is their function in the retina. When on the surface of cell membranes, they participate in an electrostenolytic process that creates a voltage difference between the electrolytes on the opposite sides of the membrane. This potential is used to power the Activas within the neurons and between adjacent neurons. This power source, a battery, is recognizable in cytological work as a “fluffy” electron dense region of the external wall of the cell.

The variety of glutamates present aids in providing the slightly different potentials required to bias the Activas. At a given instant, it is possible to specify the location and relative concentration of the various glutamates and GABA. However, these concentrations and the ratios between the various material concentrations change constantly due to the operational requirements of the signaling circuits.

20.6.4 Graphic representation of a Pedicel

The foundation of knowledge available about the chordate pedicle summarized in the work of the Vardi and Raviola groups is substantial. However, it is not associated with a strong explanation of how the various structures function and it does not recognize the “state variable” nature of the electronic charge found at a given site. The electron charge density is a function of a variety of variables that are not controlled, or even noted, in the above investigations. With the model developed herein, additional and alternate interpretations of features can be delineated and discussed.

20.6.4.1 Review of structures and mechanisms

20.6.4.1.1 The horizontal cell

The horizontal cell has been redefined in this work. It is defined functionally as an electronically based circuit containing a three terminal Activa. The circuit is so arranged that two separate inputs are available, the dendritic input connecting to the emitter terminal of the Activa and the poditic input connecting to the base input of the Activa. The collector of the Activa is connected to the axon terminal of the neuron. The output at the axon is usually inverted relative to the signal presented to the poditic terminal but is non-inverting relative to the dendritic input. The dendritic and poditic inputs are essentially indistinguishable at this time morphologically.

In some if not all cases, the horizontal cell may be similar to the amercine cell in not exhibiting morphologically a conventional axon. In this case, the axon and one of the input structures are folded so as to shares a common internal cell wall and be enclosed by a single external cell wall. In this configuration, the axon contacts a morphologically bipolar cell that is capable of transmitting electrically bipolar signals (relative to a nominal axon resting potential).

20.6.4.1.2 Synapses

This work hypothesizes that all synapses within the retina are electrical connections, frequently called gap junctions. These junctions are very small and cannot be seen by conventional light microscopy or even low resolution electron microscopy. They typically involve gaps of a few hundred Angstrom and may have diameters of only a few nanometers each. These gap junctions are found at both basal and invaginated regions associated

with the pedicles. These gap junctions are in themselves active biological semiconductor devices known as Activas. As such, they rely on potentials of specific polarity being applied to their terminals for proper operation. Under these conditions, an essentially loss free connection is created for electrons to pass from the presynaptic axon to the post synaptic dendrite or podite.

20.6.4.1.2 Electrical energy sources

It is necessary to provide the electrical potential required by the various elements associated with the pedicle. These potentials vary and must be independent of each other. They are created by electrostenolytic processes, typically involving a bioenergetic material on each side of a biological membrane. However, the fluid at the interior surface of a cell membrane may merely be conductive in order to generate a potential in collaboration with a bioenergetic material on the exterior surface. By employing slightly different chemicals in this process, a range of potentials can be obtained. The current capacity of each battery so formed depends primarily on the surface area of the cell membrane coated with the bioenergetic material. When examined by staining, the high electron density associated with these batteries are easily observed. It appears that the various glutamates found in the retina are the bioenergetic materials creating these batteries. As noted elsewhere in this work, the glutamates and GABA form a reversible energy pathway in animal metabolism and are closely related in formula.

20.6.4.2 Review of available caricatures

Based on the above considerations, it is instructive to review the recent work of two groups, Byzov et. al. and Vardi, et. al.

20.6.4.2.1 The caricatures related to Byzov et. al.

Figure 19.6.4-1 is a recent caricature by Maximov & Byzov[75]. The article accompanying the figure is interesting because of how close the authors came to discovering the active semiconductor device, the Activa, in their analyses of the horizontal cell and its synapse with the preceding photoreceptor cell(s). The biggest impediment to that accomplishment appears to be the lack of a strong electronics background among the specialists in their group. Their introduction lists three factors potentially determining the dynamics of the horizontal cell. Two of the three are electrical properties. Only one speaks of a chemical transmitter.

[75]Maximov, V. & Byzov, A. (1996) Horizontal cell dynamics: What are the main factors? Vision Res. vol. 36, pp. 4077-4087

The left view in the figure is unusual from the perspective of an electrical analog for several reasons. In many aspects, it is the quintessential floating model. First they show an "In cone" terminal but do not describe any signal at this terminal. Furthermore, they say: "The resistance of the cone presynaptic membrane, R_p, whose value is not important is taken as infinite." They also label the ground terminal as the "Out" terminal of the horizontal cell portion of the circuit. They have also continued the long tradition in the neurological community of showing a variable resistor in the presynaptic circuit that is somehow controlled by the potential difference across the presynaptic membrane. In the discussion, they develop a concept of feedback that is distinctly unconventional. Their description of feedback is merely the description of a passive impedance network. They also describe the nonlinear passive impedance of a diode "as an amplifier of graded potentials" when the output signal is always smaller in voltage (and in power) than the original input signal.

With the availability of the active electrolytic semiconductor device, the Activa, their circuit analog can be modified in only the most minor manner with startling results. By interpreting the properties of the pre- and post-synaptic membranes only slightly differently, a major change in concept can be supported. Let the presynaptic membrane within the confines of the synapse be the input structure (emitter) of an active device [input characteristics of a diode], the post-synaptic membrane of the same synapse be the output structure (collector) of an active device [output characteristic appears as an infinite impedance in parallel with a current source], and the

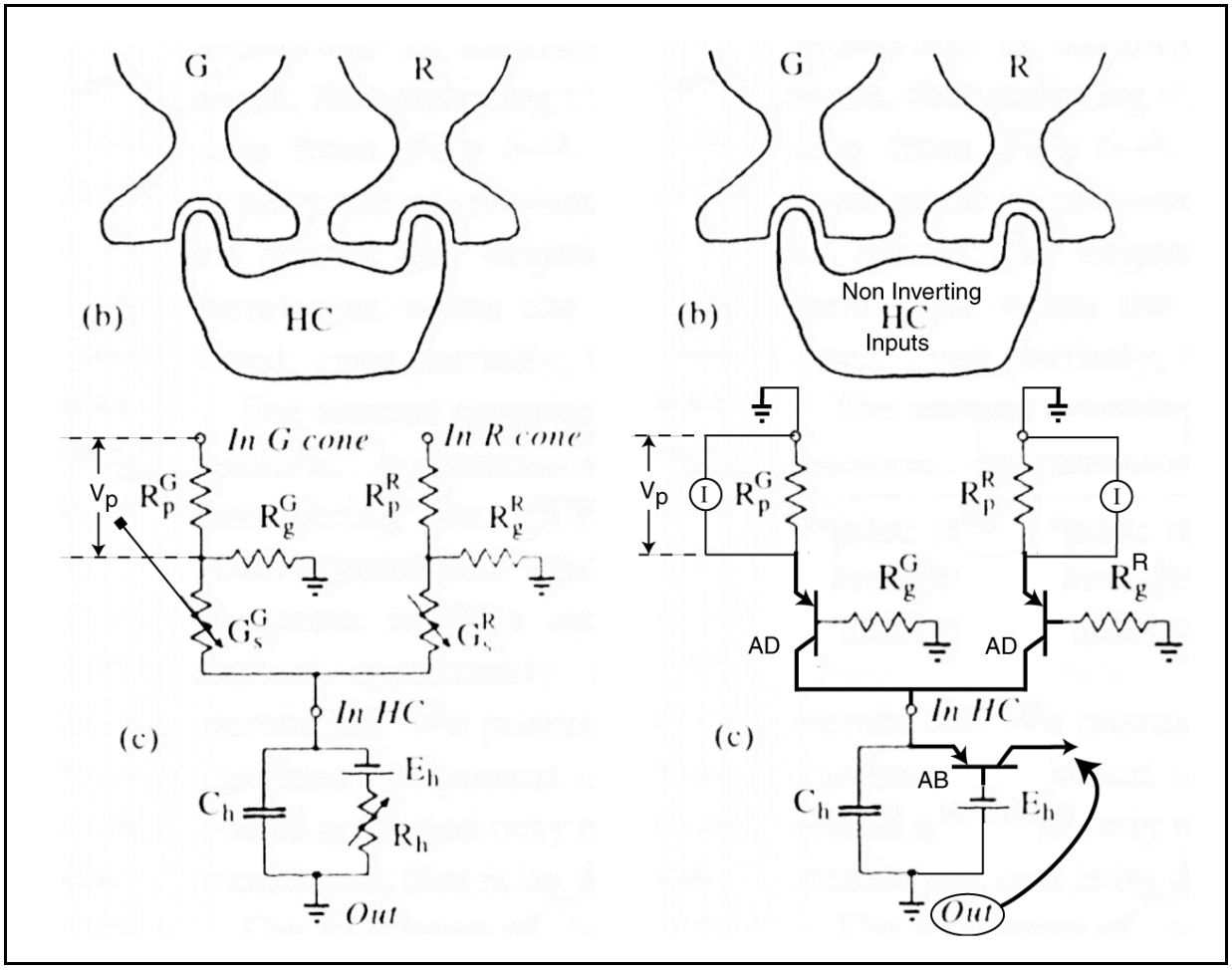

Figure 19.6.4-1 The original (left) and the modified (right) form of the synapse and the non-inverting input structure of a horizontal cell. See text for details. Original from Maximov & Byzov (2096)

impedance, R_g, be the impedance in the base to ground lead of such a device. Similarly, let the variable resistor,

R_h, be replaced by the input structure (characteristic of a diode) of another Activa and place the battery, E_h, between the base terminal of this device and the ground connection shown. The result is shown on the right in the figure. In this view, the terminals marked “In G cone” and “In R cone” are now ground terminals along with the other marked ground terminals. The ground symbol represents the Inter-neural matrix (an electrolyte) of the retina. The label marked “Out” should be moved to the collector of the last Activa.

The resulting circuit is now that of the actual biological process and includes no variable resistors. The voltage, V_p, is the result of a current through the impedance, labeled R_p. This impedance is actually another forward biased diode and should be replace by the symbol for a diode. It has an impedance characteristic that is logarithmic and is formed by other portions of the axolemma of the photoreceptor cell. This characteristic of the axolemma plays a critical role in the operation of the visual system and all neurons. The current generator symbol impresses a current on the circuit of the photoreceptor cell known as the generator current. The origin of this current is developed in the earlier Chapters of this work. This current creates the generator potential by passing through the logarithmic impedance formed by the diode characteristic of the axolemma.

The Activas shown are labeled Type AD, the type forming the functional element of all synapses. This device exhibits the commonly observed diode characteristic between the pre- and post synaptic plasmas when properly biased electrically. However, the device is a three terminal device. The input characteristic of the device is that of a diode between the pre-synaptic plasma and the surrounding electrolytic medium (usually the INM). The output characteristic of the device is actually an open circuit when properly biased and in the absence of current through the device. When current is applied to the input structure, a nearly identical, but distinctly different current from a theoretical perspective, is generated by a current generator in parallel with the output impedance of the device. This current is summed with the current from other similar devices, one being shown, applied to the input circuit of the next Activa. This Activa is found in either a bipolar or a horizontal cell. It is designated a Type AB when found in a bipolar cell (as shown) and a Type AS when found in a horizontal cell. The input structure of the horizontal cell is more complex than shown here and will be discussed in the next Section. The input impedance of these devices is also represented by a pure diode.

Without specifying the delay in the generation of the voltage, Vp, and demonstrating that it is the same in the G-cone and R-cone channels, it is premature for Maximov & Byzov to discuss feedback as a method of creating the delay between these signals as it is measured at the input or output of the horizontal cell. This work has clearly demonstrated that the delay associated with each chromatic photoreceptor channel is independent of the other photoreceptor channels. The individual channel delay is a direct function of the *state* of the adaptation amplifier and the characteristics of the exciting illumination applied to that channel. As a result, the circuit is symmetrical with respect to delay as opposed to the asymmetrical variant (not shown) proposed by Maximov & Byzov.

With these changes, the complete pre- and post synaptic characteristics of the synapse, and the input characteristics of the following cell, are defined. Only the power sources for the energy required to operate the circuitry have yet to be defined. This will be accomplished in the following Section.

20.6.4.2.2 The caricatures related to Vardi et. al.

Figure 19.6.4-2 is from Vardi et. al. who apparently modified a figure from Raviola & Gilula and incorporated ideas from several other investigators. This figure is likely to be reproduced widely in coming years and it deserves a critical review. The horizontal line has been added by this author and can be ignored for now.

The authors were working with low resolution electron microscopes, x25,000 and x42,000, that limited the ultimate size of a structure that could be detected. Their work did not observe the small structures that Raviola & Gilula stressed in their figure 1 (see below). The figure is a two dimensional presentation of a slice through a very complex three dimensional structure. In the larger context, this pedicle is part of a two dimensional mosaic with dendrites of the various proximal neurons intersecting the photoreceptor neurons from multiple directions. Important details may not appear in a particular slice.

The similarity should be noted with the “cross-bar” switch used in telephone exchanges of the 2050's to early 2090's. This switch provided a large two dimensional array of orthogonal sets of wires. Junctions are created between the various pairs only upon action by a third element perpendicular to the 2-D array. In the absence of specific action, wires remain unconnected. The simile would suggest that the invaginated horizontal cells do connect to the pedicle and the horizontal cells passing below the cell do not.

The figure is a composite that shows little internal details of the various cells. This makes it very difficult to relate the morphology with function except in the case of the photoreceptor cell pedicle (labeled cone in this figure). Even in the case of the pedicle, the vertical ribbon is shown as a solid. Raviola & Gilula show the same structure as a hollow conduit based on electron-microscopy. Below the "ribbon" is a black arc shaped feature known as the arciform density for lack of a more descriptive name.

The figure gives the impression that there is only one ribbon in each cone pedicle. Actual images at x91,000 frequently show multiple ribbons[76] in a single pedicle. Nilsson & Crescitelli[77] also show that at this magnification, the "electron dense material is often found inter-cellularly between the receptor cell terminal and the invaginated process."

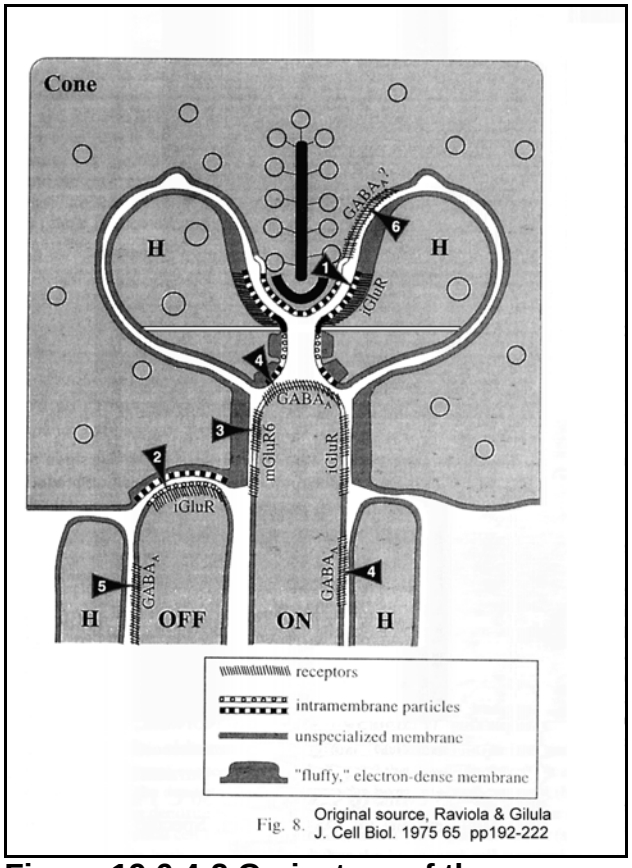

Figure 19.6.4-2 Caricature of the synapse region of a pedicel.

Vardi et. Al. have described glutamate as having been secreted by the presynaptic axon on to the bipolar and horizontal cells in compliance with conventional wisdom. However, they do not indicate the source of this material within the presynaptic neuron. They state: "The mechanism of release is also not well understood. GABA is thought to be released by a transporter mediated mechanism, but the transporter has not been identified." Continuing the conventional wisdom, they have sketched in the suggested location of receptors on the post synaptic structures. However, one of their opening statements is: "What still remains largely unknown is the molecular identity of the postsynaptic receptors and their exact locations." Later, they make the comment: "The glutamate receptors on bipolar dendrites are all located at relatively large distances from the site of vesicular release." This statement does not appear to be in conformance with their drawing. Thus, the chevroned areas in the drawing representing the location of "receptors" may be subject to change.

The authors chose to label the two bipolar cells OFF and ON arbitrarily with the accompanying statement: "Invaginating (probably ON) bipolar dendrites in the monkey and rat...." The next section will suggest this was a poor guess.

The two horizontal cell structures shown on each side of the central cleft are not further identified in this figure. In the original caption, they are described in terms of horizontal cell *terminals.* They apparently retreated from the suggestions by Raviola & Gilula who were more specific, labeling the terminals dendritic when discussing a cone pedicle in their figure 16 and labeling them axonal when discussing a rod spherule in their figure 22. The striking similarity between their caricatures for the pedicel and spherule can not be overlooked.

Using the morphologist terminology "particle" to indicate a structure may lead to serious problems. There is no indication that the structure labeled a "particle" is homogeneous or an entity that is in any way foreign to the cell wall. Raviola & Gilula illustrate two different arrays of small structures, one group labeled synaptic vesicles and a second denser array that is unlabeled in their figure 1 but corresponds to the black and white stripped bar(s) in Vardi's figure.

The caricature by Vardi et. Al. consistently shows GABA and the various glutamates as located on the inner wall

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[76]Nilsson, S. & Crescitelli, F. (1969) Changes in ultrastructure and electroretinogram of bullfrog retina during development. J. Ultrastructure Research vol. 27, pp. 47-62, fig. 3

[77]Nilsson, S. & Crescitelli, F. Op. cit. Fig. 6

of the various cells. They also show large open circles throughout the pedicel without further discussion. This appears to be a alternate interpretation to that presented by Raviola & Gilula who show all of the vesicles as being on the inner surface of the external cell membrane.

Based on the discussion of Section 20.6.4.1 and the discussion to follow in Section 9.6.4.3, it is appropriate to tabulate the relationships indicated by the arrows in the above figure.

Arrow #	Vardi et. al.	This work
1	Cone to horizontal cell terminal	Synapse from pedicle to horizontal cell dendrite
2	Cone to OFF bipolar cell, basal jct.	Synapse from pedicle to basal bipolar cell
3	Cone to ON bipolar cell	Synapse from pedicle to invaginating bipolar cell
4	Horiz. cell term to ON bipolar	Synapse from horiz. cell to invaginating bipolar cell
5	Horiz. cell term to OFF bipolar	Not adequately characterized in literature
6	Horiz. cell terminal to cone (predicted)	Not adequately characterized in literature

As will be developed below, a direct connection as in 2, between a pedicel and a bipolar cell is necessarily an "ON" connection.

The principle contribution of Vardi et. al. to their figure appear to be two. They say the cell walls can be described in terms of three zones. They also localize, through staining, areas associated with materials of high apparent electron density. These areas are shown as the wider regions of the cell wall.

Figure 19.6.4-3. is a caricature from figure 1 of Raviola & Gilula. The article provides more detail and dimensions based on high resolution electron microscopy. Note the hollow character of the ribbon and the two distinctly different types of arrays of small structures, the finely spaced array under the arciform density and the more widely spaced array beyond the arciform density. Raviola discuss the location of a variety of gap junctions observable at this resolution without further expansion. The arciform density is less resolved in the electron micrograph in their figure 3 than shown in this caricature. Looking at the left side of the figure, the synaptic vesicles appear to be dispersed in space withing the pedicle. However, looking at the right, the vesicles are seen to be located on the inside surface of the cell wall. In addition, a boss pattern is seen on the B-face as a result of the physical pressure of the vesicles on the cell membrane. The presentation on the left appears to involve artistic license by the illustrator. Unfortunately this license was picked up by Vardi's illustrator, although they do not discuss the floating vesicles in their figure 8 as shown above. Raviola & Gilula also indicate a connection between the ribbon and these vesicles associated with the cell wall in the caption to the figure. They also stress that the pedicle cell wall in the area near the synaptic ridge is highly specialized, exhibiting three morphologically and functionally distinct regions, although they do not address the functional characteristics. They define the region at the apex of the ridge, the region on its slopes, and the region at the bottom of the valleys which flank the ridge on either side.

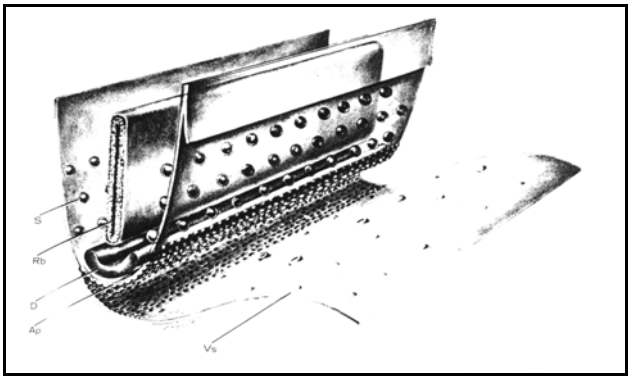

Figure 19.6.4-3 Detailed caricature of the synaptic ridge in a photoreceptor cell ending from Raviola & Gilula, 2075. The synaptic ridge is bisected by a dense lamella or ribbon (Rb). (D) arciform density. (S) synaptic vesicles. (Ap) A-face particles. The synaptic vesicles are connected to the ribbon. (Vs) synaptic vesicle sites, i.e., bosses on the B-face due to pressure from the synaptic vesicles.

20.6.4.3 Combining function and morphology

Based on the discussion in Section 20.6.4.1 and .2, it is possible to offer an alternate caricature that maintains a majority of the morphological and electrical characteristics developed by the above research teams while providing a detailed functional description of the photoreceptor cell synapses with subsequent neurons. This chariacature is shown in two separte figures. **Figure 19.6.4-4** shows both the external profile of the morphology of the complex and, by cutaway, the proposed internal structure as it relates to the functional cytology of the cell. The figure continues to recognize the symmetry found in the nominal pedicel of monkey. This symmetry is probably found in all *Chordata*. It does not require that all of the other cell structures near the basal surface of the pedicel interconnect functionally with the pedicel or with other adjacent cells. The unshaded vesicles within the pedicel are interpreted as primarily structural devices used to insure the critical distance between the axolemma of the pedicel and the neurolemma of the orthodromic neural cells. They may or may not be electrically conducting and in contact with the reticulum (shown as a dark vertical ribbon) of the pedicel. However, there is electrical contact between the plasma within the reticulum and the area of the axolemma between the vesicle and the lemma. A similar vesicle is shown in the lower corner of the right hand cell in the area labeled HA.

The unshaded areas of all of the cells represent the plasmas within the reticulum of each cell. On the left, the dendrite of a horizontal cell is shown, HD. On the right, a more complex situation is shown. A single horizontal cell is shown with a membrane forming an upper and lower chamber. The upper chamber is labeled HP to indicate the terminal of that neuron in contact with the pedicel (or for an alternate reason presented below). This may be either a dendritic or poditic terminal of the neuron. The lower chamber is labeled HA to indicate the axon of the horizontal cell. It is in intimate contact with the bipolar cell, shown in the lower center of the figure, aided by the presence of a vesicle. The volume between the cell walls is filled with the INM and labeled M. In the horizontally shaded area, the matrix is generally saturated with the metabolic components supporting the electrostenolytic processes taking place on the cell surfaces. The portion of the matrix shown is in good hydraulic communications with the rest of the INM and diffusion supports the arrival of unreacted metabolite and the removal of reaction byproducts. At specific locations within the matrix, the distance between the adjacent cells is reduced to less than 200 Angstrom, probably by structural forces associated with vesicles. In these regions, the normal laws of diffusion cause all chemicals except water to be squeezed out and the water molecules to form a hydronium liquid crystal. As a result, an active electrolytic semiconductor device is formed between the liquid crystalline axolemma, the hydronium, and the neurolemma of the next orthodromic neuron. As shown, this occurs between the photoreceptor cell and the two horizontal cells and between the right hand horizontal cell and the bipolar cell. However, other permutations of this capability are readily formed. The dark spots between the cells are indicative of the hydronium crystals. There may be many of these individual spots comprising a complete synapse as indicated in the previous figure from Raviola & Gilula. Multiple spots provide a greater current carrying capability to the overall synapse while insuring the necessary spacing between cell walls to support transistor action. The dark vertical bar represents the ribbon and the dark arc represents the structure known as the arciform density. All of these dark structures are recognized as areas of higher electronic potential or charge concentration from electron-microscope studies.

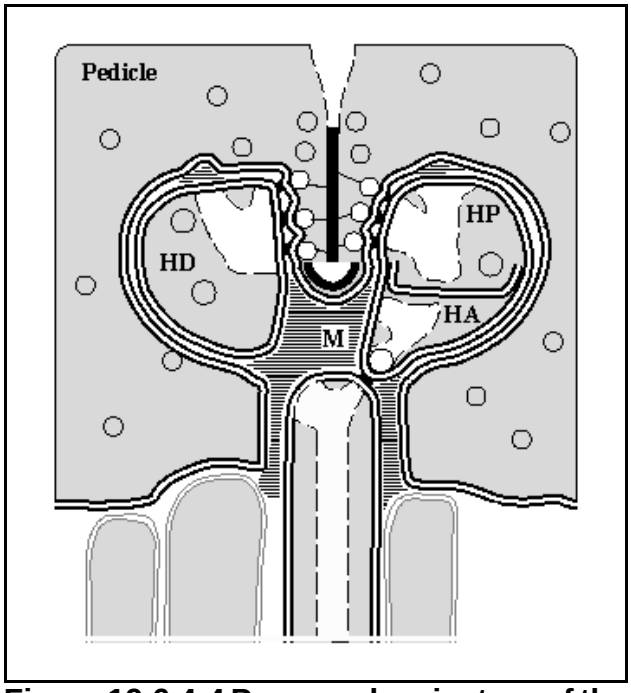

Figure 19.6.4-4 Proposed caricature of the pedicel synapse complex showing the morphological and cytological characteristics of interest. The white circles within the pedicel are vesicles directly involved in creating the synapses between the cells. The other white areas within the structures are plasmas that provide the electrolytic conduits comprising the signal paths.

Figure 19.6.4-5 describes the functional relationships according to this theory as an overlay on the cytological details of the complex. The overlay consists of a series of electrical connections supporting the existence of three active electrolytic

semiconductor devices at the locations shown within the drawing. In each case, the devices are shown with electrical power provided to the device via an impedance associated with the cell wall and contacting the INM. This impedance represents both the impedance of the normal cell wall and the electrostenolytic process occurring at that wall. The black dots associated with the base of the various Activas represent the connection of the base of the Activas, the hydronium liquid crystal, to the INM. This connection may or may not exhibit an impedance depending on the nature of the INM in that immediate area. Three remote Activas are shown supporting the overall synaptic complex. The presynaptic Activa is the distribution amplifier of the photoreceptor cell defined earlier in detail. This Activa is powered by the arciform structure via the reticulum ribbon. This ribbon and its branches also connects to the individual synaptic Activas as shown. The post synaptic Activa is found within the bipolar cell shown. On the right, an Activa is shown out of plane. The connection between the collector of the synaptic Activa, and the impedance connecting with the INM are shown turning into the plane of the paper at the intersection formed by an "X." The signal proceeds down the reticulum conduit to either the dendritic or poditic terminal of the horizontal cell Activa. In this figure, the connection is to the poditic terminal. The conduit is therefore labeled HP. The output signal from this amplifier returns along the axonal reticulum to the second "X" in the plane of the paper where it connects with the axolemma at the site of the synaptic Activa connecting to the bipolar cell. Because, the signal from the pedicel contacted the poditic terminal of the out of plane Activa, the returning signal is inverted. As a result of this inversion by the horizontal cell, the signal at the dendritic terminal of the Activa of the bipolar cell is inverted relative to the original signal at the pedicel of the photoreceptor cell. The signal presented to the bipolar cell may also include a component from one or more other cells connected to the emitter of the out of plane Activa. This configuration can be compared to the frequently reproduced figure of Dowling[78].

In Section XXX, two possible alternate structural forms of the horizontal cell were developed without a clear method of determining which occurred in the real world. One of these forms was axonless and was appropriate if the horizontal cell interfaced with a bipolar cell within the Outer Synaptic Layer of the retina. The other was a conventional configuration with an axon projecting to the Inner Synaptic Layer where it interfaced with a ganglion (or possibly an amercine) cell. The left side of this figure incorporates the concept of an axonless horizontal cell wherein the axon and either the dendrite or the podite of the cell share a common external cell wall. The figure indicates the presence of an axonless type of horizontal cell by explicitly separating the horizontal cell into two regions, one dendritic (or poditic) and the other axonal. The use of this concept may help explain the difficulty Raviola & Gilula had in naming the invaginating horizontal cells as alluded to above. The drawing also stresses the connection between the vesicles located at the pedicle cell wall and the conduit, or ribbon. Less emphasis is placed on the edge of the so-called arciform density as it will be interpreted as a variation in charge density and not as a unique structural feature. Under this interpretation, the arciform density and the connections between the vesicles and the conduit are both conductive pathways associated with the operation of the neural system. The broader areas of higher charge density following the contours of the external cell walls are taken as just that. They need not be associated with any specific chemical substance as they are located in a conductive medium and can be considered either a charge on a capacitor, or the charge available in a battery.

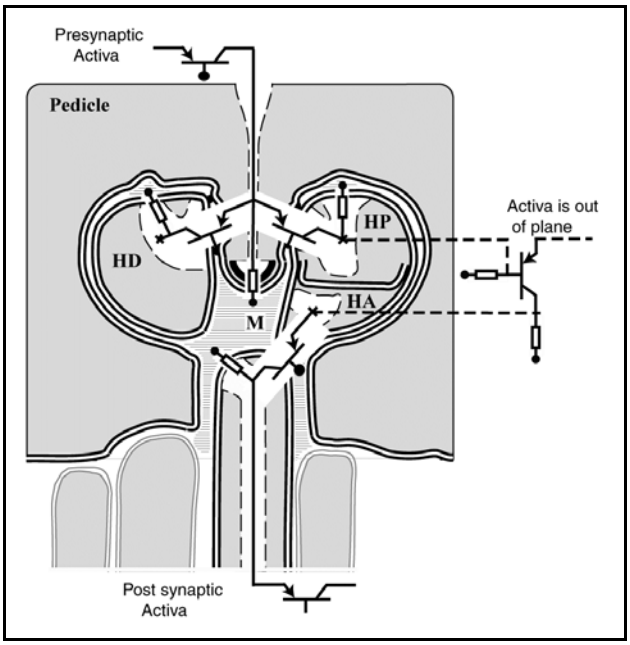

Figure 19.6.4-5 The synaptic complex shown with the topology of the electrical circuit shown as an overlay on the cytology of the cells and the electrolyte of the intervening inter-neural matrix. For completeness, the Activas driving, supporting, and driven by the complex are also shown.

Recognizing the three zones of the pedicle cell wall in the region of the synaptic region defined by Raviola & Gilula and the open cleft area betwen the various cells, this theory defines the open area as a reservoir for

[78]Dowling, J. (19xxx) XXX

bioenergentic materials such as GABA and the glutamates. These materials are very similar chemically and are known to form an equilibrium reaction that can provide free electrons on demand to an associated structure. Under this scenario, these materials coat certain portions of the external surfaces of the cells surrounding this reservoir. These materials do not constitute intramembrane particles. They are merely a coating in equilibrium with the rest of the material nearby in the reservoir. When consumed, the various constituents in this reaction can be re-supplied by diffusion from the vascular system along the spaces between the cells. However, these molecules are unable to penetrate any area between the cells that is less than 200 Angstrom wide because of their physical size.

As noted in Raviola & Gilula, some of the vesicules appear pinched between the conduit and the external cell wall of the pedicle. It is proposed that this causes the cell wall to be pushed out toward the wall of the adjacent cell. The cell wall is extended until it comes within 200 Angstrom of the adjacent cell wall. At or below this spacing, diffusion of materials along the cell walls effectively stops and only water is able to fill this gap. The water assumes the form of a hydronium crystal lattice under this constrained condition. This condition can occur wherever an axon structure is in close proximity to a dendritic structure. This configuration consisting of two cell walls in such close proximity with hydronium between them and electrolytes on their other sides constitute a biological transistor known as an Activa. Only the application of the appropriate potentials is required to create an active device, in this case a synapse between two neurons. The same configuration can also occur internal to a single cell and constitutes the active mechanism within that cell. An individual applied potential is controlled by the particular glutamate present on the surface of a particular cell wall near the reservoir.

Turning to the right half of the figure, the presence of two different electrolytes on opposite sides of a cell wall creates a battery in series with a diode as shown elsewhere. This becomes the obvious explanation for part of the high charge density in the vicinity of the cell walls, an area usually described as fluffy or spongy by morphologists. The striped region of each cell wall constitutes a current supply for the cell as indicated by the symbols. The capability of the battery is determined by its surface area. The black dots in the reservoir region and between cells merely indicate electrical contact with the extracellular conducting medium. The black dots associated with these symbols within the cells are indicative of a connection to one of the electrical conduits leading to and connecting with the Activa of that neuron. In the very narrow regions between two cell walls, battery action cannot occur as indicated above. However, transistor action can occur. In these areas, the vesicles of the pedicle act as electrical connection to the emitter of the synapse Activa. The base of the Activa is in contact with the intercellular medium through its hydronium crystal and the collector of the Activa is in contact with the conducting medium of the dendrite (or podite) of the horizontal cells as illustrated. It is not clear from the literature whether a separate conduit exists within the dendrite or whether the entire dendrite volume constitutes the conduit at this location.

It should be noted that the presence of a podite in the region of the pedicle will result in the polarity of the signal received by the podite being inverted and possibly amplified when it appears at the axon terminal. If a dendrite is involved, the signal delivered to the axon related to this specific dendrite will not be inverted or amplified.

After passing into the horizontal cell dendrite, the signal current from the pedicle is passed to the Activa of the cell where it is combined with the current collected from other pedicle connections. As a result a related current appears in the conduit from the Activa leading to the axon wall adjacent to the invaginating bipolar cell. Because of the narrow spacing at the location of the gap junction, this net current is passed to the bipolar cell by transistor action associated with the synapse itself.

Some license has been taken in illustrating the Activa of the horizontal cell since it is not in the plane represented by this figure. If the podite of the horizontal cell is in juxtaposition with the pedicle wall, instead of the dendrite, the drawing of the Activa within the horizontal cell must be re-oriented and slightly redrawn. In either case, the base of the Activa is connected to the podite structure and this region of the neuron has its own contact with the extracellular medium via the podite battery and diode circuit. Every neuron includes three electrolytically distinct volumes.

As a result of the above action, an invaginating (morphologically) bipolar cell may receive a (electrically) bipolar signal. Whether this signal is ON-going or OFF-going with respect to the nearby pedicle is a function of the input lead of the horizontal cell. In this symmetrical arrangement, it is possible for the central bipolar cell to receive two input signals from two different horizontal cells. The similarity between these two signals is likely to be slight due to the multiple signals combined at the Activas of the respective horizontal cells.

This interpretation of the synapses around the pedicle, and in fact all synapses, does not call for any transporters or receptors related to a chemical synapse. All signal transfer employs electrons moving via gap junctions. Similarly, there is no need for any material other than electrons to pass through the walls of the various cells in order to function properly, although other materials may pass through other sections of the cell walls for purpose of nutrition and growth.

This interpretation is in conformance with Raviola & Gilula concerning three zones in the external membrane wall of the pedicle. They define a zone (a) at the apex of the ridge, (b) on its slopes, and (c) at the bottom of the valleys which flank the ridge on either side.

a passive area, an area associated with electrical potential generation, and an area of charge transfer between neurons.

20.6.5 Bandpass limitations within the retina

20.6.5.1 Proposals in the literature

Psychophysical tests involving spatial and temporal variations in the illumination applied to the eye have produced response functions with a high frequency limit that is characteristic. It is also known that this high frequency limit varies with illumination level. Furthermore, some experiments have obtained significant variation in mid-frequency response without a commensurate variation in the high frequency response. Tests in this area have been conflicting[79] and the results frequently depend on the details of the illumination presented to the eye. So-called pattern electroretinograms frequently give different results than retinographs based on moving images.

A variety of elementary analyses have appeared in the literature accounting for the underlying transfer function through the use of simple filters consisting of cascades of individual RC filter stages[80]. These proposals have defined either constant parameters in the individual filter stages or with parameters that vary with illumination level. However, test results in the literature have failed to demonstrate any significant thermal dissipation in the retina commensurate with the resistors in these purported filters. Further, the "floating Model" used in these analyses have failed to describe the transfer function of individual functions within the retina. *In-vivo* electrophysical tests have recently demonstrated that the high frequency limit on the signal waveforms delivered to the ganglion cells of the retina are due entirely to the photodetection function, and are present in the "generator function" recorded in photoreceptor cell studies.

Determining the spatial frequency response of the human eye by psychophysical tests involving contrast changes of a checkerboard are particularly prone to experimental design errors in the absence of a detailed model of the visual process.

20.6.5.2 "Null hypothesis" proposed in this work

This work has succeeded in providing the mathematical equation in closed form of the generator function. The resulting function predicts the results recorded in the above psychophysical tests. It shows that there are no RC filter stages required to achieve the actual performance of the eye. The actual photoexcitation/de-excitation function involves a time delay due to the finite transport velocity of excited electrons within the liquid crystalline structure of the chromophores.

This theory presents the hypothesis that all neural functions accomplished following the photoexcitation process in the chromophores of the photoreceptor cell exhibit a broader frequency response than required by the signal being transmitted. Ergo, no filtering is required to account for the observed performance. The theory does highlight, and accommodate, the so-called lead-lag network incorporated in some ganglion cells to accentuate the early response of this cell to changes in illumination.

20.7 Hypotheses based on Analogy

Whenever an analogy is used in support of the definition of a new model, it is important to look closely to determine if the situations are in fact comparable. With the fantastically successful introduction of the simple box camera to the masses by George Eastman, it became fashionable to analogize the box camera and the human eye. This analogy is probably for the education of the masses and in schools ingrades K-12. However, it suffers many anomalies that make the comparison unsuitable in higher education, specifically in the biological sciences:

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[79]Bodis-Wollner, I. & Tzelpi, A. (1998) The push-pull action of dopamine on spatial tuning of the monkey retina. Vision Res. Vol. 38, no. 10, pp. 1479-1487

[80]Dartnall, H. (1972) Photochemistry of vision. Vol. VII/3A of Handbook of Sensory Physiology. NY: springer-Verlag pp531-545

Features of a simple camera	Features of human eye
Fixed focal length lens	Variable focal length lens (with field angle)
Flat focal plane	Seriously curved focal plane
Integrating type photoreceptors	Differencing type photoreceptors
Requires a shutter to control signal integration	No shutter required
No motion required to sense an image	Motion required to sense an image
Chromophoric channels in sandwich form	Chromophoric channels in mosaic form

The above differences are so significant that the camera-eye analogy should be *de-taught* in university in order to establish the real situation.

The eye is a closer analogy to a television camera. However, here to significant differences exist. A television camera employs inherently integrating type photoreceptors that require special techniques, a framing signal, to allow the camera to sense an image without a shutter and without going into saturation.
The animal, and specifically the human, eye on the other hand requires a different special technique, relative motion between the line of sight and the optical axis of the eye, to capture an image.

20.8 Review of individual concepts within the vision community

Previous work in the literature has relied heavily on "floating models" generally attempting to extend knowledge based on the significant discovery that Vitamin A played a major role in creating and maintaining the visual sensors of animals. Attempting to ascertain the exact role played has led to a variety of assumptions and attempts at verification of these assumptions.

This Section will attempt to provide a brief context associated with many of these assumptions and provide a brief synopsis of the situation. The comments are not designed to be exhaustive. The main text of this work treats each of these concepts in detail. Obviously, only a comprehensive end to end model can assemble all of these concepts into a compatible, mathematically coherent theory of animal vision.

[[Number the following items later]]

20.8.1 Detection concepts

Historical Concept	Concept in this Work
The Outer Segment of the Photoreceptor Cell is:	
An internal part of the living Photoreceptor Cell	An external associate of the Photoreceptor Cell formed by extrusion of a structural protein (Opsin) from the cell followed by coating of that protein by Rhodonine and the accumulation of energy resources adjacent to the extruded disks

The accumulated energy sources adhering to the exterior of the disk stack have been mistakenly identified as a cell wall in light microscopy. However, it is not a membrane of bilayer construction as are all cell walls. The disks are in intimate contact with the Inter-receptor matrix (IPM) from which the chromophore material and energy are obtained.

The Chromophore of vision is:

The Chromophore of vision is:

Vitamin A (Retinol);

Retinaldehyde;

Retinol + Opsin in simple chemical union (? Rhodopsin)

Retinol + Opsin joined by a Schiff Base(? Rhodopsin)

Retinol + Opsin via a protonated Schiff Base(? Rhodopsin)

Rhodonine in liquid crystalline form;

The historical concepts have failed to provide the required absorption spectra. The Rhodonine family does provide the required spectra in all four spectral regions.

Light to be effectively absorbed:

Can be applied to the Photoreceptor Cell isotropically

Must have a Poynting Vector that is perpendicular to the surface of the Rhodonine coating on the surface of the disks

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The Outer Segments in *Chordata* are sensitive to the direction of illumination due to the liquid crystalline nature of the chromophoric material. Light is absorbed selectively with respect to color, but not polarization, by the various chromophores of vision if applied with the Poynting vector parallel to the axis of the Outer Segment. If applied perpendicular to the axis, the radiation is absorbed indiscriminately with respect to color by the Rhodonines, always exhibiting an absorption peak near 500 nm. The absorption in this manner is polarization sensitive.

The primary structure of the chromophores with regard to vision is:

Not specifically known but presumed to involve the Schiff Base and elements of the protein Opsin

The resonant conjugate chain within the Rhodonines who are members of the Phthalein family of Carboxyl-ion based dyes as well as the Retinene family of retinoids. The carboxyl-ion is characteristic of many high performance chromophores

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Adding a second polar atom to Retinol converts it into a member of the Carboxyl-ion family which are found in many dyes. Extending the family by conjugation results in a carboxyl-ion system that includes the Phthalein family of which erythrosine and phenolphthalein are well known members. The Rhodonine family are also described technically as polymethines from which they get their name.

The Primary action of light is:

To cause the transformation of free 11-*cis* to all-*trans*-Retinol;

To cause this transformation to Retinol while combined with Opsin as above (one of three forms);

To cause one of three forms of Rhodopsin to be transformed into meta-Rhodopsin;

To regenerate *meta*-Rhodopsin to Rhodopsin

To cause the electronic excitation of Rhodonine

The next action following absorption of light is:

(No general agreement)

Ionization of a molecule within the envelope of the Outer Segment

De-excitation of Rhodonine through transfer of the absorbed energy to the associated neuron

Excitation, followed by de-excitation as indicated above, leaves the Rhodonine in its original condition after a finite time delay. Following de-excitation of the Rhodonine, the neuron of the Photoreceptor Cell is excited by the energy received.

The factor controlling the wavelength of maximum absorption is:

Unknown, the individual chromophores of color vision have never been isolated and characterized

The precise length of the conjugated dipolar chain in conjunction with the slow wave structure associated with the liquid crystalline nature of the chromophores

There are eight members of the Rhodonine family, four based on Vitamin A_1 and four based on Vitamin A_2. There is little difference in peak absorption wavelength between corresponding members of each set of four.

What spectral absorption peak appears in both electrophysical and psychophysical experiments?

P502

None. The observed photopic and scotopic Absorption peaks are both the result of computation within the brain based on signals derived from absorption by individual chromophores at 342, 437, 532 and 625 nm.

The P502 peak in electrophysical experiments, where it is more properly labeled P495, is an artifact of poor experimental technique (See light absorption paragraph above). The peak in the Human Scotopic response near 502 nm. is a result of computation by the brain using the signals from the 437 and 532 nm. spectral channels.

20.8.2 Signaling concepts following detection

Historical Concept	Concept in this Work

Signal generation is by:

Integration of the effect of photon absorption in an imaging type sensor

Detecting the change in photon absorption **rate** as a function of time

The eye is well known to be completely blind in the absence of a change in photon absorption related to the image field. This fact is obscured by two things. The difficulty of detecting the continual minute angular motions of the eye in higher chordates such as human. The use of a “paint” program in the cortex to assign a color and an intensity to a region of the field of view. This is done when that portion of the observed scene is so uniform that the appropriate photoreceptors fail to generate a signal.

The signaling vehicle following photo-detection is:

The passage of an ion through the external cell wall of the Outer Segment of the photoreceptor cell into the IPM	The transfer of the energy of a quantum state from the chromophore to base material of the biological transistor in the dendrite of the photoreceptor neuron

The transfer of energy while in the quantum state is quite common in man-made transducers.

The signaling path from the disk stack to the axon of the Photoreceptor neuron is:

Undefined other than it involves the fluid surrounding the Photoreceptor Cell	Via the dendrite passing through the Calyx and down the length of the Photoreceptor Cell to the axon

The literature does not define the neuron within the Photoreceptor Cell.

The signaling vehicle to be amplified is:

An ion within the IPM or passing through the wall of the Photoreceptor Cell	An electron-hole pair generated in the active region of the biological transistor of the Photoreceptor Cell neuron

Signal amplification following detection is:

Achieved through an ionic cascade of unknown mechanism	Transistor action in the input transistor of the dendrite of the PC neuron.

The precise amplification factor achieved is a function of the availability of energy from the energy sources surrounding the disk stack. This variable availability with time due to diffusion limitations is the mechanism controlling the adaptation characteristic of the individual photoreceptor.

The mechanism of signal amplification in a neuron is:

By changes in the impedance characteristic of the axon wall membrane	By transistor action between the dendrite(s) Cavity and the axon cavity mediated by the electrical path to the surrounding fluid via the poda cavity

The literature contains no explanation of what mechanism causes the axon wall to change conductivity in response to excitation. Transistor action at a different location in the cell provides a direct and calculable explanation for the change in current in the axon.

The signaling vehicle in the remainder of the visual neuron path is:

Not uniquely specified	An analog current passed through a cascade of biological transistors involving both

signal diversion and conversion

Although most earlier models invoke a series of different signal carriers, a comprehensive model need only use an analog current amplified, inverted and passed from neuron to neuron by transistor action. This current is frequently measured as a voltage at a circuit node

The signaling method used in the neural channels of the eye is:

mixed and subject to many views	An analog current, proportional to the output current generated by the first transistor in the dendrite of the Photoreceptor Cell(s) up to the Ganglion Cells where the signal is converted into a pulse train. The time interval between pulses describes the input analog current value.

The upper bandpass parameter of vision is:

Set by an RC type filter in the neural channel	Set by the transit time of excited electrons in the excitation band of the liquid
Set by a cascade of such constant value RC filters	crystalline chromophores of the Outer Segment. This transit time is a function of
Set by a cascade of variable value RC filters	the number of charges present

The variable delay in psychophysical response measured across the animal spectrum is calculable based on the temperature of the animal and the level of excitation of the chromophores of vision. This level is a function of both the current illumination and the recent history of illumination, generally measured in milliseconds. Each spectral channel exhibits an independently derived risetime in its response. This risetime in the temporal domain corresponds to the upper frequency limit of the signal in the frequency domain. Because of the variability in this risetime, many attempts have been made to model the passband of the signal processing channels to account for it. These attempts have involved a variety of RC filter networks that are not found in the actual signal processing circuitry of vision.

20.8.3 Computational concepts

Historical Concept	Concept in this Work

The signaling method used in the initial signal decoding circuits of the brain is:

Only conceptually defined	Pulse interval to current conversion in the case of color discrimination and pulse interval to voltage conversion in the case of brightness discrimination

The conversion to a voltage is paramount in the summation of the chromatic channels to produce a psychophysical luminance response. Color discrimination remains essentially linear based on the conversion of the incoming pulse to pulse interval to a current value

The explanation for the transition from Photopic to Scotopic vision:

Introduction of two types of photodetectors operating in different illumination regimes and presumably using different but unspecified signaling paths to the brain	Reduced signal output from the long wave chromophoric signaling channel at low light level due to the square law response characteristic of the long wave chromophore

Both the photopic and scotopic psychophysical responses in human are directly calculable based on the assumption of the square law response of the long wave chromophore and the logarithmic signal decoding used in the brain for luminance information

Color vision anomalies normally occur in:

Various undefined locations	Four separate locations through; Loss of a chromophoric detector channel, loss of an analog differencing circuit in the retina, failure of a midget ganglion cell to mature, or failure of a computational circuit in the brain

A comprehensive model of the visual system is needed to define the considerable variety of failures that can impact the chromatic performance of the eye. Only loss of a chromatic channel prior to the differencing circuits of the retina will affect both the achromatic and chromatic performance of the eye.

Energy used in the nervous system is:

Probably wasted as heat	Recovered through a reversible chemical reaction that restores the original chemical used to supply the energy at a different location.

No significant heat is consumed in the operation of the animal nervous system. The basic concept is used throughout the body; supply electrical potential from a reversible chemical reaction, use the energy to transmit a signal to a second location, recover the energy through a similar if not identical chemical reaction, and transport the chemical products back to the source location by diffusion or vascular flow.

20.8.4 Performance Evaluation concepts

Historical Concept	Concept in this Work

“Non-Spectral Colors” are represented:

Awkwardly, the color is specified by extending a line from the color through the neutral point until it intersects the spectral locus. The neutral point is usually specified as the point “C,” however this point has no intrinsic character.	There are no non-spectral colors. Every color is uniquely specified in a two dimensional orthogonal space by two numbers along the spectral locus. The apex of the space is uniquely specified by the coordinate, 532,532 in nm.

With the exact chromatic discrimination functions of human vision known, and their independence demonstrated, it is possible to create a new orthogonal chromaticity space that provides a uniquely addressable location for every sensed color, whether that color can be discriminated from adjacent colors or not. This space is known as the new

Chromaticity Diagram for Research

20.9 Hypotheses related to nutrition

Although old and anecdotal discussions in the vision literature imply the creation of the chromophores of vision within the Inner Segment of the Photoreceptor cell, it is not supported by more recent investigations. Recent data points to:

+ The fabrication of the protein substrates of the Outer Segment by the mitochondrial structures within the photoreceptor cell but,

+ The creation of the chromophores in the Retinal Pigment Epithelium and there delivery to the protein substrates of the Outer Segment via the Inter Photoreceptor Matrix.

This theory includes the hypothesis that the chromophores are created within the RPE and delivered to the protein substrates of the Outer Segment following their creation in and extrusion from the Inner Segment of the photoreceptor cell.

20.10 Summary

It is extremely difficult to debate the various theories of vision in print. The proper forum is an oral one where various aspects of the overall visual process can be addressed individually. This theory differs in a number of core respects from other theories presented in the literature.

+ It demonstrates that the nodal point analysis of visual optics is limited to the field of optometry.

+ It demonstrates that the vision process is not linear, even under small signal conditions.

+ It demonstrates that the basis of vision in all animals is not duplex.

+ It demonstrates that a dipolar chromophore is a prerequisite to animal vision.

+ It demonstrates that the basis of vision is the flow of electrons in conformance with accepted electronics theory.

+ It demonstrates that all signal connections, including all synapses, within the visual system are electronic in character.

+ It demonstrates that all second stage signal channels are independent, can be treated as orthogonal, and are not antagonistic at any point.

+ It provides closed form mathematical expressions replacing all templates and all equations developed to describe truncated functions.

+ It provides a mathematically detailed explanation for many of the historic special effects observed in color and transient vision.

+ It provides a vastly simpler method of describing the capability of the human eye than the functions and diagrams carrying the Imprimatur of the C.I.E.

+ It provides a rational foundation for the discussion of abnormal color vision.

+ It demonstrates that there is no requirement for external feedback among the neurons of vision.

CHAPTER 20 ALTERNATE THEORIES OF VISION 4/30/17

(Active) SUBJECT INDEX (using advanced indexing option)

(Inactive) DEFINITIONS INDEX (Use individual marks)