Excerpts from

PROCESSES IN ANIMAL VISION:

including,

ELECTROCHEMISTRY OF THE NEURON

This material is excerpted from the full β-version of the text. The final printed version will be more concise due to further editing and economical constraints. A Table of Contents and an index are located at the end of this paper.

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PART B Bioelectrochemistry of the Photoreceptor & Dynamics of the Visual Process

To understand the operation of the visual system, one must understand the detailed cytology and molecular biology of the cells involved and their fundamental characteristics. These fundamental characteristics are electronic in origin. Gutmann & Keyzer have coined a new term that includes the necessary sciences in one expression, Bioelectrochemistry. This designation appears to include the study of the visual process and to incorporate the necessary subjects into a single global amalgam.

PART B introduces a new theory of the photosensitivity of the visual system based on modern physics that replaces the stereo-isomeric theory in use for the last 50 years. The previous mechanistic theory depended upon a putative structural change in the molecule named Rhodopsin. No investigation has ever been able to demonstrate the applicability of this molecule to the spectral performance of the chromophores of vision. The new theory is based on quantum-mechanical phenomena and leads to an explicit description of the photoexcitation process as well to the precise calculation of the absorption spectra of the individual chromophores as well as the detailed broadband spectra of the complete visual system.

PART B is divided into three chapters and will deal with the detailed mechanism and underlying quantum and molecular chemistry of the photodetection process in vision.

Chapter 5 explores the rules of photon-material interaction and defines the rules under which an efficient chromophore operates. **Section 5.5** concentrates on the description of the Rhodonines as the chromophores of vision. Chapter 5 concludes with suggested modifications to the previously used protocols designed to isolate the chromophores of vision. These protocols have not been successful in the past because they have employed excessively strong reagents and have not recognized the unique liquid crystalline nature of the material sought.

Chapter 6 collects the scientific knowledge currently available concerning the chromophores of vision and their chromogens (primarily retinol). Although most of this data only applies to the simple chromgen retinol in dilute solution, many features of the retinol data are shared with the Rhodonines. Pending the collection of new data, these shared features aid in the understanding of the structure of the chromophores. The unique application of Electron Paramagnetic Resonance (EPR) techniques to the role of oxygen in, and the evaluation of, the chromophores of vision is presented.

Chapter 7 focuses on a group of dynamic, but disparate, processes found in vision. **Section 7.1** is concerned with the dynamics of the chemistry related to photodetection in vision, including both the transport phenomena associated with moving the chromogens through the bloodstream and the transport phenomena associated with moving the chromophores from their point of creation to their place of operation and finally their point of phagocytosis. The unique transport mechanism used to simultaneously transport and begin the formation of the chromophores is defined. **Section 7.2** is concerned with the dynamics of radiation chemistry and the components of the Photoexcitation/De-excitation Equation of vision. This Section includes techniques for evaluating the various parameters related to the P/D process. **Section 7.3** develops the spatial performance characteristics of the Precision Optical System, POS, of the neural complex (including the oculomotor muscles). This section includes the first development of a comprehensive Theory of Image Fusion.

> **The proposed Theory of Image Fusion states:** Fusion is achieved among the higher chordates by dynamic merging of the information received from the two eyes through two-dimensional correlation. The process is inherently dependent on the tremor associated with vision in these species. The correlator is physically located within the perigeniculate nucleus of the thalamus, a major element of the POS. The optimum operation of the correlator also creates the final pointing, convergence and accommodation signals that are used by the physical layer, including the plant, to implement optimum acuity in three dimensions under the prevailing conditions of

illumination, scene contrast and target complexity. The perception of depth for individual targets within the field of the foveola is directly associated with the secondary statistics (residual disparity) relating those targets to the reference target.

Section 7.4 develops the temporal aspects of the POS. **Section 7.5 presents, for the first time in the literature**, a discussion of precisely how the visual system perceives and interprets the abstract symbols associated with reading. **Section 7.6** develops the unique mechanical dynamics of the photoreceptor cell/ retinal pigmented epithelium cell interface so critical to the visual process in long living animals. **Section 7.7** addresses the unique electrostenolytic processes of vision wherein the glutamate cycle is used to provide electrical power to the individual neurons of the visual and other neural systems.

At the conclusion of these three chapters, the reader should have a firm understanding of the biochemistry of the photoexcitation and de-excitation phases of the photodetection process within the overall visual process. When combined with the quantum mechanical processes involved in translation of the signal generated within the Outer Segments of the photoreceptor cell, the overall operation of the input structure of the photoreceptor cell becomes clear. This latter discussion appears in **Chapter 12** of PART D following development of the crucial features associated with the fundamental mechanisms of the neural system in PART C. The reader should also have a clear understanding of many of the dynamic mechanisms associated with vision.

As addressed in the Preface**, the concept of rhodopsin as the material facilitating photodetection in vision dates from the early 1800's.** The concept has gone through many re-formulations. With the turn of the 20th Century, biochemistry was able to show that a protein formed a significant fraction of the material in the Outer Segments. During the 1930's, the role of the newly defined Vitamin A in the visual process was demonstrated. This discovery started a flurry of activity to define the detailed molecular structure of rhodopsin based on the available knowledge of biochemistry. This knowledge base was quite limited compared to its state 30 years later.

The current concept of rhodopsin is not supported in this work. Although widely promulgated, this concept of rhodopsin developed by the Harvard school during the late 1930's through the 1960's has not been able to explain the operation of the photodetection process in vision. The most glaring problem with this concept has been its inability to demonstrate the spectral absorption characteristic(s) found in vision. The concept developed during that period was of rhodopsin as a discrete molecule formed in the photoreceptor cells as a chemical combination of retinol (Vitamin A) with a protein (Opsin). Various methods of combining these two materials were proposed but none has proven successful. Both retinol and opsin are inherently colorless in the visual region of the spectrum. The initial concept during this period was that the retinoid was the chromophore and employed the mechanism of stereo isomerism. However, this mechanism did not exhibit the required spectrum. Recent research has generally failed to confirm the presence of *cis*-retinol in the visual systems of the animal world. At that time, the revised proposal was offered that the materials were joined via a Schiff Base. In this configuration, the oxygen atom of the retinol was replaced by nitrogen which acted as a coupling agent. Neither theoretical calculations or laboratory tests supported an appropriate visual absorption characteristic for this material. It was then proposed that a delocalized proton associated with the nitrogen in the Schiff Base could provide the necessary electronic configuration. This proposal also lacked confirmation and was criticized theoretically based on energy considerations. Finally, it was proposed that the coupling was via a sulfuryl group instead of a Schiff base. This approach did not succeed in defining the spectrum of the chromophores. Subsequent investigations have attempted to show it is the protein that is the chromophore and not the retinoid. These proposals have generated many theoretical technical articles but no laboratory confirmation. In the absence of a conjugate carbon chain, it is difficult to show that a protein can exhibit the necessary electronic resonance typical of a good visible wavelength photon detector.

Each of the above proposals suffers serious inconsistencies with the rules of “dye chemistry,” the specialized field involved in determining the rules applicable to the molecular chemistry of good photo-absorbers. In addition, it is now known that the material secreted by the photoreceptor cells consists of only Opsin. No retinol or retinol derivative is associated with this secretion process. The chromophores of vision are actually formed within the RPE cells of the retina.

A key fact was recorded but not interpreted during the 1950's. The chromophores of vision were found to change

spectral absorption as a function of pH. This is a characteristic of an electronically resonant molecule now described as a member of the "indicator family." A key problem in the laboratory was that the chromophores contain both an alcohol group and an aldehyde group in each molecule. The relative concentration of these two ligands is determined by the pH of the experiment. This explains the confusion in the literature over the precise formulation of the chromophores.

Another difficulty was the uncontrolled bleaching of the chromophores *in-vitro*. The recovery time of the chromophores after bleaching was very long with a time constant of over 3 hours. This was not consistent with the time constant *in-vivo*.

A new concept of rhodopsin is presented in this PART. It is based on the above rules of "dye chemistry" and is far more successful in defining the detailed molecular chemistry of the four forms of the conceptual material. It is also compatible with the greatly expanded knowledge bases of quantum physics, semiconductor physics, and the liquid crystalline state of matter. Each of these disciplines plays a critical role in the actual process of photoexcitation and subsequent de-excitation of the material called rhodopsin.

In this concept, Opsin remains present as a significant percentage of the dry weight of the Outer Segment of the photoreceptor cell. However, its role is entirely passive and that of a simple substrate. The polar material retinol (which does exhibit a conjugated carbon chain as a backbone and is a polyene) is looked upon as the chromogen of vision but not a chromophore. The chromophores of vision (there are four) are the Rhodonines. This homologous series exhibits the exact spectral absorption properties associated with animal vision, including the ultraviolet spectrum found in insects and other selected animals. The Rhodonines are resonant forms (dienes) derived from the polar conjugated form of retinol by the addition of a second heavy atom to the molecule (proposed to also be oxygen). These materials exhibit a spectral absorption characteristic that is identical to that of the individual visual chromophores under only one condition. They must be present in a liquid crystalline state. In vision, this is accomplished by the chromophores being coated on the surface of the passive substrate Opsin. Thus, rhodopsin is redefined as a weak combination of Opsin and Rhodonine involving hydrogen bonding as the mechanism. The combination is not defined at the molecular level. A single molecule of Opsin combined with a single ligand of Rhodonine does not exhibit the spectral characteristics of a chromophore. However, at the aggregated state associated with the liquid crystalline state, the combination does. Furthermore, when in the liquid crystalline state, the Rhodonines exhibit the high absorption cross-section of an effective chromophore and a unique decay characteristic when in a photon-induced excited state.

In summary, **the chromophores of animal vision are the homologous family of four Rhodonines when present in the liquid crystalline state. The Rhodonines are resonant, polar, conjugated hydrocarbons and members of a variety of chemical families due to their unique structure. They are dienes, carbonyl ions, retinoids and members of the indicator family of electrically resonant molecules and the carboxyl ion system of photographic dye chemistry. They are easily derived from the chromogen, retinol. They also exhibit extremely long relaxation times in the absence of other biological mechanisms. This unique property is due to the dual oxygen atoms present as auxochromes.**