Visual Neuroscience (1988), **1**, 251–253. Printed in the USA.

Editorial: A symposium on retina

This issue of VISUAL NEUROSCIENCE is devoted to a symposium on retina, entitled "Membranes, Ions, Receptors; Cells, Circuits, and Synapses," which was held at the 1987 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in Sarasota, Florida, and was sponsored by the ARVO Electrophysiology Section. A symposium devoted to a similar topic, "Neural Interactions in the Vertebrate Retina," was held in 1982, and the recent symposium takes a detailed look at just a few of the major technical and conceptual advances in the area of basic electrophysiological investigations of retina that have occurred in the intervening 5 years.

The 1987 symposium represents a kind of "Rip Van Winkle" approach to an area of research that has moved quite rapidly during this period. In 1982, "patch clamp" recordings of retinal neurons, either in culture or in retinal slices, were unknown, and the minute photocurrents of the tiny, primate-photoreceptor outer segments had yet to be recorded. In retrospect, both suppressive-rod-cone interaction (SRCI) and scotopic-threshold responses (STR) had already been observed, sometimes on several occasions, but were not yet understood, nor was their proper significance recognized.

This issue of VISUAL NEUROSCIENCE includes manuscripts drawn from participants in the 1987 ARVO Electrophysiology Symposium; in addition, other papers have been solicited to highlight a few noteworthy presentations from the regular paper sessions of the meeting. What follows are short summaries of the symposium contents.

Primate visual pigments

In the first paper, Schnapf et al. report the spectral sensitivities of single (both human and monkey) rods and cones. These spectra were obtained from direct measurements of the minute photocurrents generated by individual photoreceptor outer segments. The method is more sensitive than spectrophotometric measures, as well as being less susceptible to contamination by photoproducts. It is also less troubled by spectral interactions than psychophysical methods. The outer-segment recording site is unique in the nervous system for obtaining such exquisite data about the first molecules of vision. Where else could the 600-nm sensitivity of short-wavelength sensitive ("blue") cones be determined or could the fact that these cells express short-wavelength opsin with a preference of at least 100,000:1, as compared with other opsin molecules? Are such molecular selectivities characteristic of other functional subtypes of neuron, both for molecules known and unknown? Remarkably, the results of psychophysical color-matching experiments, some of Stiles' π mechanisms, and the photopic-luminosity function can be calculated from weighted combinations of the cone spectral-sensitivity curves. These findings presage further understanding of visual pigment molecules, as well as an improved ability to sort out the neural-network aspects of color vision from those that are due to the nature of the transduction process itself.

Rod-cone interaction

The paper by Frumkes and Eysteinsson relates suppressive rod-cone interaction (SRCI) (a phenomenon seen in human psychophysics) to synaptic interactions between rods, horizontal cells, and cones. Small flickering spots, which selectively activate long-wavelength cones, produce flickering cone signals in a variety of retinal neurons. These responses can be increased by more than a factor of 2 by simultaneous presentation of rod-specific, adapting backgrounds. Agents that specifically block horizontal-cell responses prevent the effect, which also has a spatial extent equivalent to the horizontal-cell receptive field. Thus, remarkably, the perceived increase in cone-flicker sensation (brought about by rod-suppressing backgrounds in human psychophysical experiments) may have its origin at one of the first retinal synapses—the one mediating the lateral feedback interaction between horizontal cells and cones. Thus, the action of this synapse ultimately reaches the level of conscious sensation, convenient to both basic and clinical investigation.

GABA membrane

Neural membrane is "patchy," and physiologically important molecules such as those for receptors and ion channels are concentrated in specific regions of func-

tional importance. Tachibana and Kaneko extend this idea to benzodiazepine-coupled $GABA_A$ receptors on retinal bipolar cells. Not only can bipolar cells be readily distinguished from other neural types in dissociated goldfish retina, but one subtype of bipolar cell, the depolarizing rod bipolar, can be identified morphologically. Such solitary rod-bipolar cells responded at their bulbous axon terminals with about ten times more sensitivity and amplitude of GABA-induced chloride currents than occurred elsewhere on the cell. Since the axon terminal is the region where GABA-containing amacrine cells normally synapse onto such bipolar cells, the concentration of receptor molecules at that location supports the interpretation that a genuine subsynaptic membrane system has been studied. Like photoreceptor disk membranes, which contain only one species of opsin, such specialized regions of neural membrane may also represent naturally purified systems, where the pharmacological properties of a single functional receptor subtype can be accurately discerned.

Transient bipolars and motion detection

How does a system of neurons in the inner retina detect movement? This question appears to be related to another: How are transient responses generated from sustained inputs? Werblin et al. have developed a retinal-slice preparation that allows pharmacological-sensitivity profiles of inner-plexiform layer neurons to be determined directly *in situ*. Transient, wide-field amacrines are sensitive to excitatory and inhibitory neurotransmitters *only* in the center of their dendritic fields. Solitary impulses propagate into the peripheral dendritic tree and trigger the release of glycine. For narrow-field, sustained-amacrine cells, the dendritic regions of input and output coincide. These GABAergic neurons, which are driven by sustained bipolars, activate $GABA_B$ receptors on another bipolar type. The $GABA_B$ receptors terminate the release of transmitter from this bipolar terminal by a presynaptic mechanism, making the release of excitatory transmitter a transient one. Wide-field amacrines are excited by these transient bipolars. Systems of wide-field amacrine cells, responding transiently at ON and at OFF, appear to be the fundamental subunits for detection of motion.

Inner-retina electroretinogram

In cat and man, the eye's electrical response to threshold stimulation is corneal negative in polarity. Retinal depth recordings described by Frishman et al. locate the source of this "scotopic threshold response" (STR) in the inner retina near amacrine and ganglion cells, far from the photoreceptors where conventional, corneal-negative, a-wave components originate. The STR is associated with a local increase in extracellular potassium. The b-wave, or PII, response is, of course, the most prominent of the eye's suprathreshold electrical responses. Its maximal amplitude lies deeper in the retina, near horizontal cells, and inverts in polarity from negative within the retina to positive at the retino-vitreal surface. The STR, however, enjoys a different retinal arithmetic: Its polarity is the same on either side of the retino-vitreal boundary. The eye's response to suprathreshold stimuli can be mimicked by a weighted subtraction of intraretinal PII from STR. Just as SRCI (above) provides a noninvasive window on the function of the distal retina, the STR provides just such a window for proximal retina.

Retinal serotonin circuits

Brunken and Daw probe the neural organization of the rabbit inner-plexiform layer with pharmacological tools. The action and locus of action of indoleamine-specific pathways are explored with ligands specific to the $5HT_1$ and $5HT_2$ serotonin receptors. The selective blockade of ON, but not OFF, responses by $5HT_2$ serotonin antagonists suggests the existence of endogenous, serotoninlike neurotransmitters. Serotonin receptors are self-opposing, like other biogenic amine receptor systems: $5HT_1$ serotonin receptors are inhibitory, while $5HT_2$ serotonin receptors are excitatory. As a consequence, $5HT_1$ serotonin-receptor *agonists* have the same effect as $5HT_2$ serotonin-receptor *antagonists*, i.e., the selective reduction of ON responses. Furthermore, both receptors may exist at a common site; however, blockade of this site does not affect the generation of complex trigger features, such as directional selectivity. Brunken and Daw argue for an important role for serotonin at the reciprocal synapses of the mammalian rod-bipolar axon terminal.

From chaos black boxes

What is the best stimulus for retinal physiology? Sakai et al. summarize the advantages of photic white-noise stimulation for retinal neurons. In the distal retina, background-induced changes in sensitivity and dynamics of horizontal cells are efficiently tracked by h_1, the first-order Wiener kernel, or impulse response. In the proximal retina, second-order (h_2) kernels (first found in amacrine cells) suggest models of retinal processing. The "four-eyed" kernel seen in C-type amacrine cells is consistent with a static nonlinearity (squaring) applied to a band-pass-filtered signal. A more complicated second-order kernel occurs in type N amacrine cells. This fits a "Korenberg model": a cascade of a bandpass filter, followed by squaring, followed by another bandpass filter. Furthermore, the authors' data suggest that signal transformations produced by amacrine and bipolar cells are passed relatively unaltered to ganglion cells.

The white-noise type of analysis is like other sorts of

https://doi.org/10.1017/S0952523800001905 Published online by Cambridge University Press

conceptual dissections of the visual system in that it suggests functional operations that can be performed by retinal neurons, but leaves open the challenge of how one may hope to identify the membrane receptor mechanisms, neural circuits, and other neurobiological processes subserving these functions. Ultimately, there is a continuing need to "reverse engineer" our logic and thought patterns to produce and refine a set of concepts that are natural and appropriate to the retinal-biological system, which will also provide a middle ground that well serves the needs of both analysis and experimentation.

I would very much like to thank the authors and reviewers for their efforts, the Electrophysiology Section Program Committee for devoting its slender meeting resources to the endeavor, and, in particular, Katherine Fite and the editorial board of VISUAL NEUROSCIENCE, for their consistent and persistent support of this project. It has been a privilege to participate so thoroughly in discussions and decisions concerning one of the first issues of this high-quality journal.

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