Biophys. Struct. Mechanism 5, 113–116 (1979)

Biophysics of Structure and Mechanism

Introduction to the Symposium on Bistable and Sensitizing Pigments in Vision*

P. Hillman

Institute of Life Sciences, Hebrew University of Jerusalem,
Jerusalem, Israel

In recent years study of the mechanism of the transduction process in the vertebrate photoreceptor has particularly focused on "the calcium hypothesis" and on the possible role of the cyclic nucleotides. In the invertebrate, a good case has been made for Ca^{2+} as an essential intermediary of adaptation, but little progress has been made towards understanding the transduction process itself. However, a considerable amount of accessory information, which will closely constrain any future model of invertebrate transduction, has been accumulated. No extant model encompasses all this information. Much of it comprises a dissection of the overall process into stages and a characterization of these stages. This dissection has been made possible largely by the existence in many (if not all) invertebrates of a long-lived photoproduct of the visual pigment, metarhodopsin, and the consequent possibility of manipulating the pigment state at will. This manipulation has led to the discovery of prolonged after-processes in many preparations. These after-processes manifest themselves only following stimuli which result in a substantial net transfer of pigment between the stable state (rhodopsin) and the long-lived state (metarhodopsin). After-processes were the subject of many of the contributions to the Symposium and to the accompanying Poster session: The prolonged depolarizing after-potential (PDA) and the "anti-PDA".

Until now, the only published evidence of a clear role of metarhodopsin in invertebrate photoreceptor transduction has been in its contribution to the after-processes. Furthermore, the after-processes appear only in the upper range of light intensities. The statement appears in the literature that the after-processes are a phenomenon of "very high intensities" and, by implication, not relevant to the "normal" transduction process. Because of the long "integration time" of these after-processes, however, they may appear for intensities far down into the physiological range. Nevertheless, the relevance of a study of the after-processes to an understanding of the basic transduction process has been queried, and several papers at this meeting as well as some recent publications present evidence for and against this relevance.

---

* Based on material presented at the European Neurosciences Meeting, Florence, September 1978

0340-1057/79/0005/0113/$ 01.00

The evidence against relevance consists of action spectrum measurements, in several preparations (Barnes and Goldsmith, 1977; Strong and Lisman, 1978; Atzmon et al., 1978, 1979; Lisman and Strong, 1978), which appear to show that metarhodopsin does not influence the sensitivity or waveform of the stimulus-coincident response (late receptor potential) nor the state of light-dark adaptation. The evidence for relevance comprises (a) demonstration that the ionic bases of the two responses are similar (Brown and Cornwall, 1975); (b) demonstrations of similarity of the cell state during an after-potential and during a stimulus-coincident response (Hamdorf and Razmjoo, 1979); and (c) claims that under certain circumstances both the adaptation state and possibly the response waveform *are* influenced by metarhodopsin (Hanani and Hillman, 1979; Laiwand, private communication).

A reconciliation of these apparently conflicting points of view may lie in some combination of a stimulus intensity effect (metarhodopsin contributing only at higher intensities) and cell (metabolic?) state. The latter applies particularly to the light-adaptation effect: Cells with higher sensitivity (possibly a metabolic consequence) tend to exhibit less metarhodopsin effect (Hanani and Hillman, 1979) and the cells chosen for some of the studies which showed no metarhodopsin contribution to the adaptation (Strong and Lisman, 1978; Lisman and Strong, 1978) were just those of highest sensitivity.

The Symposium papers dealing with after-processes began with a review of the basic phenomenology, comparing in particular the properties of the PDA and LRP (Hochstein, 1979).

The Symposium then presented a paper examining further the properties of the PDA in insects and supporting the identity of the after-potential and stimulus-coincident response mechanisms on the ground of similar sensitivity effects (Hamdorf and Razmjoo, 1979). This paper also clarifies and provides supporting evidence for a "working model" for the receptor responses (Hamdorf and Razmjoo, 1977). The main difference between this model and previous suggestions (Hochstein et al., 1973) appears to be in its explanation of the "anti-PDA", the reduced PDA induction which follows a metarhodopsin-to-rhodopsin pigment transfer. Hochstein et al. (1973) called this an active inhibitory process, while Hamdorf and Razmjoo (1977, 1979) prefer to look at it as a passive process of (metabolically supported?) regeneration. It appears to be possible to reconcile most of the features of the two models, and remaining differences should be resolved experimentally in the near future. Both models hypothesize undiscovered states, processes or materials, whose existence will have to be demonstrated before either can be accepted as an approximation to the physiology; but both models have led to interesting new experiments – serving in this way as classical cases of the usefulness of speculative modeling.

Actually, even the *existence* of the anti-PDA in flies has been in some boubt, and Minke's paper (1979) is devoted partly to showing that it does indeed exist in (at least) several species of flies. Minke points out that the anti-PDA, together with other observations (especially in mutant *Drosophila*) of photoreceptor processes not manifesting themselves in potentials demonstrate that the transduction process has intermediate stages, as yet not directly detected. The usefulness of the mutant approach, in particular, is becoming more and more striking.

The final paper in the Symposium demonstrated that the photoreceptor after-processes in insects manifest themselves also in the pupillary response, suggesting that the pupillary response depends directly on the receptor potential (Stavenga, 1979).

Other papers presented at the meeting are led off by an elegant exploitation of the desensitizing effect of the PDA in cells R 1—6 and not in R 7/8 to link behaviour to specific receptors (Cosens, 1979). Further papers cover other properties of the after-processes: The dependence of the after-processes on pigment changes (Muijser and Stavenga, 1979), and on modulations of the ionic medium (Shaw et al., 1979). Laiwand et al. (1979) comment on the shape of the LRP under various circumstances, while Atzmon et al. (1979) suggest a general procedure for relating the response to the pigment scheme. Another paper looks carefully at the R-M photoconversion efficiency (Stark, 1979), and a final paper puts an upper limit on the pigment diffusion rate in intact, unfixed membranes (Almagor et al., 1979).

The Symposium opened with two papers by pioneers in demonstrating the role of a photo-stable pigment in sensitizing photoreceptors (Kirschfeld, 1979; Franceschini, 1979). The visible presence in many photoreceptors of a large quantity of photo-stable pigment has long been a puzzle (Rothschild, 1975). These Symposium contributors have now given such a pigment a role in phototransduction (Kirschfeld et al., 1977). Characterization and elaboration of this role is the subject of two Symposium talks. It appears that the photo-stable pigment has a multiple role of sensitizing and of modifying spectral and polarisation characteristics of different photoreceptors, through sensitization and screening.

It seems likely that clarification of the mechanisms by which the photo-stable pigment and the long-lived state of the visual pigment influence the transduction process will contribute greatly to our understanding of the process, and PDA studies may be particularly crucial to this end.

References

Almagor, E., Hillman, P., Minke, B.: Upper limit on translational diffusion of visual pigment in intact, unfixed barnacle photoreceptors. Biophys. Struct. Mech. **5**, 243—248 (1979)

Atzmon, Z., Hillman, P., Hochstein, S.: Visual response in barnacle photoreceptors is not initiated by transitions to and from metarhodopsin. Nature **274**, 74—76 (1978)

Atzmon, Z., Hochstein, S., Hillman, P.: Transduction in photoreceptors: Determination of pigment transition or state coupled to excitation. Biophys. Struct. Mech. **5**, 249—253 (1979)

Barnes, S. N., Goldsmith, T. H.: Dark adaptation sensitivity and rhodopsin level in the eye of the lobster, *Homarus*. J. Comp. Physiol. Psychol. **120**, 143—159 (1977)

Brown, H. M., Cornwall, M. C.: Ionic mechanism of a quasi-stable depolarization in barnacle photoreceptors following red light. J. Physiol. (Lond.) **248**, 579—593 (1975)

Cosens, D.: Blue adaptation: an experimental tool for studying behaviour of *Drosophila*. Biophys. Struct. Mech. **5**, 211—222 (1979)

Franceschini, N.: Bi-stable and photostable pigments in fly photoreceptor cells: Evidence from "ommatidial fundus fluoroscopy". Science (in press)

Hamdorf, K., Razmjoo, S.: Prolonged depolarizing after-potential and its contribution to understanding of photoreceptor function. Biophys. Struct. Mech. **3**, 163—170 (1977)

Hamdorf, K., Razmjoo, S.: Photoconvertible pigment states and excitation in *Calliphora*. The induction and properties of the prolonged depolarizing after-potential. Biophys. Struct. Mech. **5**, 137—161 (1979)

Hanani, M., Hillman, P.: Light absorption by metarhodopsin modifies the effect of a conditioning light on the barnacle photoreceptor. Biophys. Struct. Mech. **5**, 231—235 (1979)

Hochstein, S.: On the implications of bistability of visual pigment systems. Biophys. Struct. Mech. **5**, 129–136 (1979)

Hochstein, S., Minke, B., Hillman, P.: Antagonistic components of the late receptor potential arising from different stages of the pigment process. J. Gen. Physiol. **62**, 105–128 (1973)

Kirschfeld, K.: The function of photostable pigments in fly photoreceptors. Biophys. Struct. Mech. **5**, 117–128 (1979)

Kirschfeld, K., Franceschini, N., Minke, B.: Evidence for a sensitizing pigment in fly photoreceptors. Nature **269**, 386–390 (1977)

Laiwand, R., Atzmon, Z., Hochstein, S., Hillman, P.: Properties of the on-transient of the intracellular response in the barnacle photoreceptor. Biophys. Struct. Mech. **5**, 237–242 (1979)

Lisman, J. E., Strong, J.: The initiation of excitation and light-adaptation in *Limulus* ventral photoreceptors. J. Gen. Physiol. (In press, 1979)

Minke, B.: Transduction in photoreceptors with bistable pigments: Intermediate processes. Biophys. Struct. Mech. **5**, 163–174 (1979)

Muijser, H., Stavenga, D. G.: Receptor and after-potentials in blowfly visual sense cells: Dependence on rhodopsin-metarhodopsin ratio. Biophys. Struct. Mech. **5**, 187–196 (1979)

Rothschild, M.: Remarks on carotenoids in the evolution of signals. In: Coevolution of animals and plants. Gilbert, L. E., Raven, P. H. (eds.), pp. 20–51. Austin, London: University of Texas Press 1975

Shaw, C., Hananim, M., Hillman, P.: Effects of Mn^{2+} and Ca^{2+} on the prolonged depolarizing afterpotential. Biophys. Struct. Mech. **5**, 323–330 (1979)

Stark, W. S.: Photopigment conversion efficiency in fly compound eye and ocellar receptors. Biophys. Struct. Mech. **5**, 197–209 (1979)

Stavenga, D. G.: Prolonged effects of visual pigment conversions emerging in the pupillary response of the fly. Biophys. Struct. Mech. **5**, 175–185 (1979)

Strong, J., Lisman, J. E.: Initiation of light adaptation in barnacle photoreceptors. Science **200**, 1485–1487 (1978)

Received September 6, 1978/Accepted October 3, 1978