The Nobel Prize in Physiology or Medicine 1967

Presentation Speech

Presentation Speech by Professor C.G. Bernhard, Member of the Nobel Committee for Physiology or Medicine of the Royal Caroline Institute

Your Majesty, Royal Highnesses, Ladies and Gentlemen.

Light, shadows and colours do not exist in the world around us. What we perceive visually and call light is the result of the action of a certain portion of the electromagnetic radiation on the sensory cells in the retina of the eye. Our awareness of the play of light in nature, the multiplicity of the forms and the richness of the colours is ultimately dependent on the pattern of this radiation with respect to frequency and intensity. The light is composed of packets of energy, which combine the properties of waves and particles. When these particles - the quanta - strike the retina of the eye they are caught by the specialized sense cells - rods and cones. It is known that one quantum, which represents the least possible amount of light, is sufficient to initiate a reaction in a single rod. The excitation of the sensory cells results in messages directed towards the brain. As there are no direct connections from the eye to the brain the messages must be transmitted through several relays which combine signals from several sensory cells and translate the message into a language which can be understood by the brain. The primary relay is in the retina itself, represented by an intricate nerve net, the structural beauty of which was revealed by the neurohistologist Ramón y Cajal, Nobel laureate of 1906. In this complex structure messages from a great number of sensory cells converge on a far smaller number of optic nerve fibers and this results in a transformation of the pattern of signals.

Picasso has said: «To me painting is a sum of destructions. I paint a motif, then I destroy it». The painting goes through a series of metamorphoses but «in the solution of the problem nothing has been lost. The final impression is still there in spite of all revisions». However, it is obvious to everyone that in the finished work a re-evaluation has taken place of the original elements of the motif. In some way this is a description of what happens in the visual system. An image of the outer world is formed on the retina in the same way as it is formed in the film of the camera. The image that falls on the closely packed mosaic of light sensory cells is disintegrated, since different cell types respond to various parts and qualities of the image. The primary data are then brought together in the nerve net in which a considerable processing takes place involving not only addition but also subtraction. This characterization of the message induces an impression in which there is a re-evaluation of the image projected on the retina. Does it mean that we cannot rely on what the eye tells us? No, not in the sense that there is full agreement between the external stimulus pattern and the composition of the impression. But rather in the sense that certain characteristics of the picture with essential biological and psychological significance are emphasized. There is a sharpening of contrast so that forms stand out more clearly, colours are exaggerated and movements accentuated.

We now know the mechanism by which light triggers off the reaction in the sensory cells of the eye thanks to the discoveries by George Wald and his coworkers among whom Ruth Hubbard - now Mrs. Wald - should be mentioned in the first place. The light-sensitive substances in the sensory cells, the visual pigments, consist in principle of two pieces. One, containing vitamin A, the smaller piece or the chromophore, fits like a hooked puzzle piece in the surface profile of the larger protein piece, the opsin. When a light quantum is taken up by the visual pigment the chromophore changes its form: there is an isomerization from II-*cis* to all-*trans*. The puzzle piece straightens out and releases itself from its position so that a successive splitting of the visual pigment follows. This molecular transformation induced by light - the isomerization triggers the subsequent events in the visual system. All later changes - chemical, physiological and psychological - are as Wald says «dark» consequences of this single light reaction. Wald's conclusion that this reaction applies to the whole animal world also emphasizes the broad significance of his discovery.

Our ability to differentiate colours requires that different visual cells respond characteristically to different parts of the spectrum. Theories concerning the physiological basis of colour vision originated with Isaac Newton, Thomas Young and Hermann von Helmholtz. These theories were based on perception experiments. Today it is possible to attack this problem more directly with the aid of electronics which permits interpretation of the language of the nerve cells, thanks to the pioneer work in the 1920's by E.D. Adrian, Nobel laureate 1932. It is a great pleasure to see Lord Adrian here today and in this context I am reminded of his work with Yngve Zotterman which 40 years ago taught us the ABC's of the symbols in the sensory cells' language.

We honour Ragnar Granit for his discovery of elements in the retina possessing differential spectral sensitivities as determined by means of electrophysiological methods. The first work together with Svaetichin appeared in 1939. It was followed by an impressive series of investigations which led to the conclusion that there are different types of cones representing three characteristic spectral sensitivities. This important conclusion of Granit has recently been confirmed by Wald and collaborators as well as by research groups in U.S.A. and Great Britain using other methods. The discovery implies that the signal patterns which the optic nerve transmits to the brain and which result in perception of colours are dependent on the contributions from the three types of cone cells.

Keffer Hartline's elegant analysis of impulse generation in the sensory cells and the code they transmit in response to illumination of different intensity and duration has given us the basic understanding of how they evaluate the light stimulus. His later studies have led to the discovery of fundamental principles according to which the rough data from the sensory cells are re-evaluated. A precise quantitative analysis of the results was made possible by a refined technique and a careful choice of a suitable object - the eye of the horseshoe crab, a large marine spider. This approach to the problem led him to the discovery of the lateral inhibition, which in this eye was shown to be mediated by simple neuronal connections. Already in the 1930's Granit had shown the existence and importance of inhibition in the complex vertebrate retina. After having shown the interconnections of adjacent visual cells Hartline employed his discovery in a most imaginative way in order to obtain a quantitative description how a nerve-net processes the data from the sensory cells by means of inhibition. His discoveries have in a unique manner contributed to our understanding of the physiological mechanism whereby heightened contrast sharpens the visual impressions of form and movement.

Professor Granit, Professor Hartline, Professor Wald. Your discoveries have deepened our insight into the nature of the subtle processes in the eye which form the basis of our ability to perceive light and to distinguish brightness, colour, form and movement. They have also proved to be of paramount importance for the understanding of sensory processes in general.

Professor Granit. About 100 years ago the distinguished physiologist in Uppsala, Frithiof Holmgren, discovered the electrical response of the eye to light. The hopes that he expressed for the future regarding the possibilities of all electrophysiological analysis of the retinal processes and the mechanism of colour vision have been realized by your distinguished discoveries. These show the importance of inhibition in the integrative action of the retina and the principles for spectral discrimination by retinal elements. Your discoveries have pointed the way in modern physiology of vision and your stimulating research work has contributed to the fruitful development of this field.

Professor Hartline. Your laboratory has been described as a «slightly disorganized but extremely fertile chaos». Your work which - by the same right has been characterized by «elegance in design, expertise in manipulation and clarity in exposition» has resulted in an exemplary limited number of publications, each of which is a corner-stone in sensory physiology. They have given us the basic knowledge about the impulse coding in the visual receptors and presented discoveries of the most fundamental principles for data processing in neuronal networks which serve sensory functions. In the case of vision they are vital for the understanding of the mechanisms underlying perceptions of brightness, form and movement.

Professor Wald. With a deep biological insight and a great biochemical skill you have successfully identified visual pigments and their precursors. As a byproduct you were able to describe the absorption spectra of the different types of cones serving colour vision. Your most important discovery of the primary molecular reaction to light in the eye represents a dramatic advance in vision since it plays the role of a trigger in the photoreceptors of all living animals.

Gentlemen. It is with great satisfaction that Karolinska Institutet has decided to award you this year's Nobel Prize for physiology or medicine for your discoveries concerning the primary physiological and chemical visual processes. On behalf of the Institute I wish to extend to you our warm congratulations and I ask you to receive the prize from the hands of His Majesty the King.

From *Les Prix Nobel en 1967*, Editor Ragnar Granit, [Nobel Foundation], Stockholm, 1968