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September 12, 2012
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The Last Frontier of Sensitivity

The research group working at the Laboratory for Computational Photochemistry and Photobiology (LCPP) at the Center for Photochemical Sciences, Bowling Green State University (Ohio) has been investigating the so-called Purkinje effect: the blue-shift in the perceived color under the decreasing levels of illumination that are experienced at dusk. Their results have appeared in the September 7 issue of *Science Magazine*. By constructing sophisticated computer models of rod rhodopsin, the dim-light visual "sensor" of vertebrates, the group has provided a first-principle explanation for this effect in atomic detail. The effect can now be understood as a result of quantum mechanical effects that may some day be used to design the ultimate sub-nanoscale light detector.

The retina of vertebrate eyes, including humans, is the most powerful light detector that we know. In the human eye, light coming through the lens is projected onto the retina where it forms an image on a mosaic of photoreceptor cells that transmits information on the surrounding environment to the brain visual cortex, both during daytime and nighttime. Night (dim-light) vision represents the last frontier of light detection. In extremely poor illumination conditions, such as those of a star-studded night or of ocean depths, the retina is able to perceive intensities corresponding to only a few photons, the indivisible units of light. Such high sensitivity is due to specialized sensors called rod rhodopsins that appeared more than 250 million years ago on the retinas of vertebrate animals.

Similar to the much less sensitive cone rhodopsins employed in daylight (color) vision, rod rhodopsins provide the interface between the physical world responsible for light detection and the physiological world of brain signaling. All rhodopsins are proteins containing a derivative of vitamin A, which serves as an "antenna" for photon detection. When a photon is detected, rhodopsins are set in an activated state (via a chemical transformation), which ultimately results in a signal being sent to the brain. At the level of a single sensor, visual sensitivity is the result of a trade-off between two factors: light activation and dark noise. It is currently thought that light activation efficiency (i.e., the number of activation events relative to the total number of detected photons) is around 2/3 across all vertebrate studied. Thus, the higher sensitivity of the rod with respect to cone rhodopsins must depend on the extremely low level of thermal noise, namely on the number of activation events triggered by ambient body heat in absence of photon detection. Indeed, in primates, a single rod rhodopsin undergoes a thermal activation event once every 420 years. However, since there over 2 billions rodopsin molecules in a single rod, and, approximately 125 millions rod cells in the retina, such rare events become very important in setting the limit of light sensitivity.

An understanding of the mechanism determining this amazingly low thermal noise of rod rhodopsins opens up new pathways in the study of the evolution of vertebrate vision or to shed light on the molecular basis of currently incurable diseases such as the "night blindness". Moreover it provides a model for developing sub-nanoscale sensors approaching the sensitivity of a single-photon. For this reason, together with Dr. Nicolas Ferré, a French coworker at the Université d'Aix-Marseille, the LCPP group has completed a series of state-of-the-art computer simulations of the thermal activation of a set of rod rhodopsins. The results of such an effort, carried out entirely by BGSU graduate student Samer Gozem and research assistant Dr. Igor Schapiro, have appeared in the September 7 issue of *Science Magazine*. The rhodopsin models were built on Glenn, the IBM Cluster 1350 of the Ohio Supercomputer Center (OSC), which has provided two independent research grants to the group. The construction, validation and study of the model have taken more than two years to complete and were jointly funded by the BGSU Center of Photochemical Sciences and the College of Arts & Sciences, which helped to create the LCPP.

The rhodopsin models have provided, for the first time, an understanding of the thermal activation process. Through this model, the researchers have been able to formulate a theory of the thermal noise that explains a correlation between noise and perceived color first proposed by the British neuroscientist Horace Barlow in 1957. Barlow suggested that the ubiquitous bluish color perceived during night vision (the Purkinje effect) is determined by the need to minimize thermal noise in dim-light. In other words, the models successfully explain the existence of a link between the color of light perceived by the sensor and its thermal noise and establishes that the minimum possible thermal noise is achieved when the absorbing light has a wavelength around 470 nm which corresponds to blue light. Indeed, the theory predicts that thermal activation events will decrease in frequency when the perceived color changes from red to blue. Most remarkably, the same theory explains that a shift from blue to even shorter wavelengths (i.e. indigo and violet) will lead to an inversion of the trend and to an increase of the thermal noise towards the higher levels seen for a red color.

LCPP is part of the Center for Photochemical Sciences of BGSU. One of the Center's main missions is to develop novel light-responsive materials starting from concepts borrowed from Nature.

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