

The thermal limit to seeing

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IN BIOLOGY it is rare for a simple question to have a simple answer, so one might expect "Why can't we see dimmer lights?" to require a long and complicated answer. But the paper by Aho and colleagues¹ on page 348 of this issue goes a long way towards proving that a single physical factor, the thermal isomerization of the photosensitive rhodopsin molecules in the retinal rod photoreceptors, is the dominant factor setting the ultimate limit to visual sensitivity.

It was shown almost 50 years ago that the absorption of less than a dozen quanta is sufficient to cause a dim sensation of light in humans². Soon after this, it was argued³ that the reason why several quanta have to be absorbed before a light stimulus can be detected is the irregular thermal activation of the photosensitive molecules, which mimics their activation by single quanta. As there are 10^7 rhodopsin molecules in each receptor cell, thermal activation should happen frequently enough to cause noise at absolute threshold, even if the half-life of rhodopsin were about 100 years.

Hyperpolarizing 'bumps' exactly like those resulting from absorption of light quanta have indeed been shown to occur spontaneously in photoreceptors⁴; from other evidence, they seem to be caused by thermal isomerization of rhodopsin, and the rate at which they occur is close to that required to limit visual sensitivity in dim light.

The original speculation was based on human psychophysics and only established upper limits to the allowable noise. Aho *et al.*¹ now show that the toad *Bufo bufo* has a behavioural threshold about one eighth that of humans — as low as allowed by the known thermal isomerization rate in the toad's receptors. They also show that retinal ganglion cells, which process the signals from the photoreceptors, start to respond reliably at about the same level. This new work, together with that on the photoreceptors, now establishes a firm link between thermal events at a molecular level and their behavioural consequences.

The thermal isomerization rate has a predictable relationship with temperature, increasing about fourfold for a 10°C rise. Aho *et al.* test this by measuring the threshold for phototactic jumping in the frog *Rana temporaria* over a range of temperatures from 10 – 20°C and observe about a fourfold increase of threshold: the molecular rate of photoisomerizations at threshold is roughly equal to the molecular rate of thermal isomerizations. In

other experiments, the relationship also holds for *Bufo bufo* at 15°C and humans at 37°C .

This linear relationship gives pause for thought. Although it certainly indicates that the thermal rate is a limiting factor, there are complications. First, when the frog looks at a target, such as a worm, it is the number of thermal events in the target area over the duration of exposure to the target that sets the detection limit, rather than the molecular rate of isomerizations. Second, a square-root rather than a linear relation would be expected. Many other factors besides the molecular rate influence the actual numbers of events occurring during exposure to the target and it is strange that these factors conspire to produce a near-linear relation both in the across-species comparison and for the effects of temperature in a single species. Perhaps there is still more to understand about the problem, but the regular rise of threshold with temperature, together with the fact that the performance is close to the limit imposed by the known rates, would seem to establish the importance of thermal isomerization.

Why is it possible to point to a single dominant physical factor in this case, when the analogous question about other biological limits leads into a maze of interconnecting factors? In the case of the eye, the first point is that it was known where to look. Albert Rose⁵, while developing television cameras, first drew attention to the low quantum requirements of human vision; he was led to that directly from his experience with the comparatively high quantum requirements of the photocathodes of his day. He did not point to thermal noise as the limit of human vision but that was an obvious step because it is thermal emission that limits the ultimate sensitivity of photocathodes.

The second point is that good optics are required for intrinsic thermal noise to limit visual sensitivity. That means, among other things, well-packed and aligned photoreceptors and the appropriate connections with retinal ganglion cells that make suitable connections in the central nervous system. Thus there is also a maze of interconnecting factors in this case, and for thermal noise to stand out implies that evolution can successfully optimize the other factors but can go no further in improving the thermal stability of rhodopsin.

Nor should it be forgotten that basic physics dictates that the physical size of an eye is also important in limiting its ultimate sensitivity. Other things being equal,

both the number of quanta caught from a reflecting object of particular dimensions and the number of photosensitive molecules exposed to these quanta increase as the square of eye size; in contrast, thermal noise increases only linearly because it is proportional to the square root of the number of photosensitive molecules. Hence large eyes are more sensitive, which explains why nocturnal animals have large eyes and why small animals need eyes that are relatively large for their body size.

It is only the ultimate sensitivity, measured in the absence of all light except that from the target, that has been shown to be limited by thermal noise. But it is obviously a very great advantage to be able to catch and eat your prey in the dawn and dusk when your competitors, and the prey itself, are still blind; perhaps we can now discern the unalterable physical factors that limit the evolution of better visual performance under these conditions. □

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