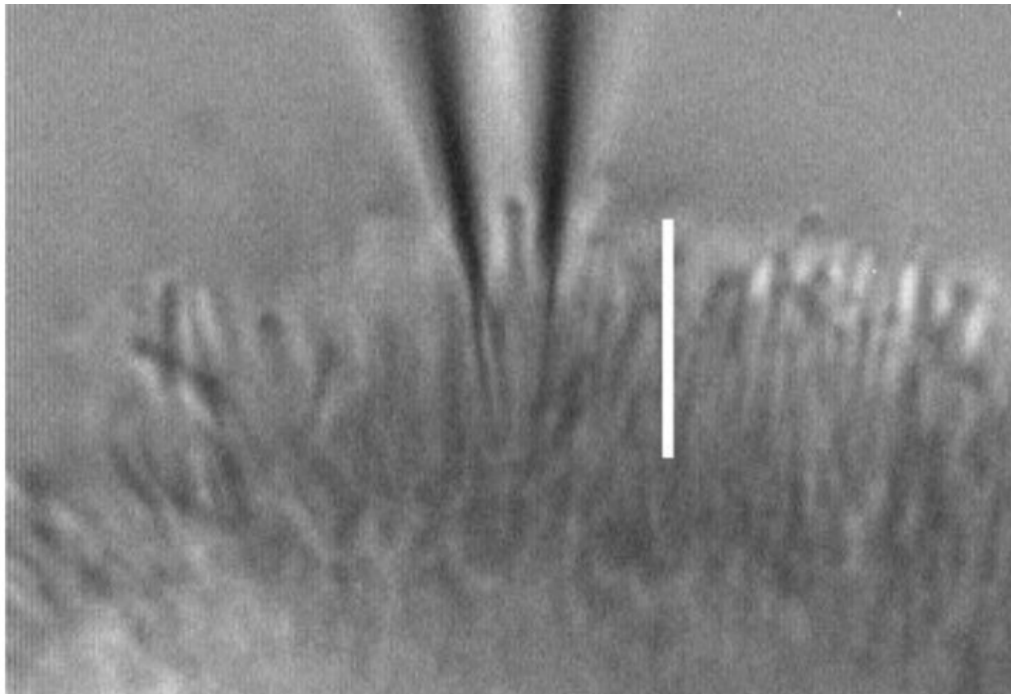


Research suggests revision to common view on how retinal cells in mammals process light

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Photomicrograph of a mouse rod drawn into an electrode during an experiment and imaged under infrared light. Credit: Daniel Silverman

Johns Hopkins Medicine scientists say that new experiments with mouse eye tissues strongly suggest that a longstanding "textbook concept" about the way a mammal's retina processes light needs a rewrite.

The enduring concept took root more than 30 years ago when

researchers doing experiments in frog retinas found that when a single particle of light, known as a photon, is absorbed by light-sensing cells called rods, it starts a cascade of biochemical reactions that involve around 500 [molecules](#) called G proteins.

Now, Johns Hopkins vision scientists say that their experiments, described March 12 in *Proceedings of the National Academy of Sciences*, show that the number of G protein molecules activated in the cascade of reactions is far fewer—involving only 10-20 of them in the rods of mice.

The new finding matters, say the scientists, because G proteins belong to a very large family of biochemical signaling pathways called G protein-coupled-receptors, which are among the most abundant signaling pathways in biology, says King-Wai Yau, Ph.D., professor of neuroscience and ophthalmology at the Johns Hopkins University School of Medicine.

"These pathways are a major target among pharmaceutical companies, because they control many diverse physiological processes, ranging from those that allow us to see images to those tied to heart disease," says Yau.

"We're beginning to understand our visual system better, and the more we understand a system, the better we are to develop treatments for its malfunction," says Daniel Silverman, Ph.D., postdoctoral fellow in Yau's laboratory.

When a photon of light hits a rod in the retina, it is absorbed by a light-sensing protein, called [rhodopsin](#), which is embedded in membranes within the cell. Rhodopsin then activates G proteins, which, in turn, activate other enzymes. It is the number of G protein molecules activated by one rhodopsin molecule that the new experiments challenge, Yau says. He notes that other scientists had speculated that the number of activated G protein molecules may be much less than the many hundred

originally proposed, but the number was difficult to directly measure in intact rods.

To do that, Yau and his colleagues devised two ways to measure the response to a single activated G protein in intact rods.

First, the scientists used mice engineered to express a mutant form of rhodopsin that interacts very poorly with the G protein so that most of the time no G protein is activated. But when rhodopsin was successful in interacting with G protein molecules, only one G protein was activated.

Second, the scientists looked at a derivative of normal rhodopsin called opsin, which is generated after rhodopsin is exposed to light. Opsin itself does not absorb light, but it can signal G proteins occasionally and very weakly. Opsin's signal is so weak that it can activate, at most, one G protein molecule, says Yau.

To make quantitative measurements, Silverman and former graduate student Wendy W.S. Yue used a tight-fitting glass pipette thinner than a human hair filled with saline solution and placed the glass pipette around a single rod, which sprouts from the retina of mice like a blade of grass. Then, Silverman and Yue recorded an [electrical current](#) from the rod that essentially reflects the signal coming from the rhodopsin/opsin-G protein cascade.

By using mathematical tools to analyze the electrical signal, Yue and Silverman found that the [electrical signal](#) triggered by a single G protein molecule was only one-twelfth to one-fourteenth the size of estimates of signals coming from a single rhodopsin molecule. Thus, they estimated that one rhodopsin activates approximately 10-20 G protein molecules.

Yau had previously found that, in a similar signaling cascade that facilitates the sense of smell in mice, one activated receptor molecule

has a very low probability of activating one G [protein](#) molecule. By comparison, the finding that such signaling systems in vision trigger 10-20 molecules may reflect the [visual system](#)'s unique need to detect light in very dim light conditions, without having to group together information from multiple rods, which would sacrifice spatial resolution.

More information: Wendy W. S. Yue et al, Elementary response triggered by transducin in retinal rods, *Proceedings of the National Academy of Sciences* (2019). [DOI: 10.1073/pnas.1817781116](https://doi.org/10.1073/pnas.1817781116)

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