

## RESEARCH NEWS

# Synaptic vesicles burst into sight

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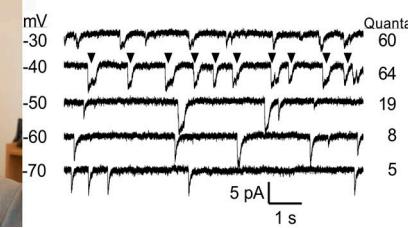
**JGP study shows that small voltage changes disrupt semi-regular bursts of vesicle release from rod photoreceptors, potentially facilitating low-light vision.**

The ability of vertebrates to see in low-light conditions depends on the extreme sensitivity of rod photoreceptors in the retina, which can detect single photons of light. However, the membrane potential of rod cells only changes by a few millivolts in response to a single photon (1), and it is unclear how such small signals are reliably transmitted to the rest of the visual system. In this issue of *JGP*, Hays et al. suggest that reliable transmission may involve distinct patterns of vesicle release by resting and stimulated rod cells (2).

In the dark, rod cells at a resting potential of approximately  $-40$  mV release a train of synaptic vesicles containing the neurotransmitter glutamate, which acts on downstream bipolar and horizontal cells. Upon stimulation, a slight hyperpolarization interrupts this release by reducing the activity of presynaptic L-type  $\text{Ca}^{2+}$  channels. “But how does a downstream cell know if a change in glutamate release is due to the absorption of a photon or just a random fluctuation?” asks Wallace Thoreson from the University of Nebraska Medical Center.

Based on modeling studies (3), one suggestion is that resting rod cells secrete vesicles at an extremely high rate—around 100 vesicles/s/synapse—thereby making it easier for downstream cells to detect a light-induced decrease in glutamate release. But this would be energetically expensive, and, when Thoreson and colleagues, including graduate student Cassandra Hays, measured vesicle release from voltage-clamped mouse rods, they found that individual cells secreted  $\sim 12$  vesicles/s under resting conditions.

An alternative suggestion is that downstream cells would be able to distinguish genuine from random signals if resting rod



Cassandra Hays (left), Asia Sladek (not pictured), and Wallace Thoreson (center) reveal that resting and stimulated mouse rod photoreceptors show distinct patterns of glutamate vesicle release. At a resting membrane potential of  $-40$  mV, release occurs in semi-regular bursts of 10–20 vesicles (arrowheads). Small voltage changes eliminate these bursts and, instead, single vesicles are released at random intervals. The researchers suggest these distinct patterns may help the visual system respond to single photons, thereby facilitating low-light vision.

cells secrete glutamate at regular, predictable intervals (4). Hays et al. found that mouse rods held at  $-40$  mV release glutamate in coordinated bursts of 10–20 vesicles (2).

“These bursts occurred at fairly regular intervals and were quite sensitive to small changes in voltage,” says Thoreson, explaining that, upon hyperpolarization, rod cells switched to secreting single vesicles at random intervals. In contrast, cone cells never showed bursts of vesicle release, suggesting that the ability of rod cells to change their release patterns in response to small voltage changes could be crucial for low-light vision.

Hays et al. found that the bursts of release by resting rod cells involve the readily releasable pool of vesicles (2). These vesicles are thought to be positioned near release sites by the synaptic ribbon, a large plate-like structure found at rod cell synapses. Indeed, the researchers determined that the bursts are triggered by the opening of ribbon-associated  $\text{Ca}^{2+}$  channels.

Hays et al. also found that the bursts are dependent on synaptotagmin 1 (Syt1), a  $\text{Ca}^{2+}$

sensor that binds to the SNARE proteins involved in vesicle fusion and promotes exocytosis in response to  $\text{Ca}^{2+}$  influx. But it remains to be seen how rod cells coordinate the bursts such that, after an extended pause, multiple vesicles are released in quick succession. Thoreson and colleagues are now examining the mechanisms underlying this behavior, as well as investigating its consequences for downstream cells.

“It seems like the regularity and voltage-sensitivity of the bursting might help downstream neurons detect single photons,” Thoreson says. “We’re now doing some modeling and additional experiments to determine whether this is actually true.”

## References

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