Photon detection lecture outline
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The absolute sensitivity of our visual system is remarkably good. This sensitivity poses several constraints on the neural mechanisms responsible for detecting and processing single photon signals, and similar constraints arise in other sensory systems. My main aim today is to tell you where we are in understanding how this sensitivity is achieved. But I also have another aim — to start to convince you that there are interesting things happening in the retina.

1. **Introduction and motivation**

   - retina is nothing like a camera — different rgc classes and their specializations. Thus circuitry between photoreceptors and ganglion cells provides excellent opportunity to understand how functionally important computations are implemented by neural mechanisms.
   - even better if we can study computations in context of task with clear relation to behavior and clearly defined physical limits to performance — hence photon detection
   - dark-adapted visual system can detect absorption of a handful of photons, thus approaching fundamental limit to performance. This constrains fidelity of transduction process in rods and signal transfer throughout rest of visual system. Examples in other sensory systems: hearing, invertebrate vision, olfaction.
   - relate photon counting to underlying biophysical mechanisms. Excellent opportunity to understand behavioral significance of these mechanisms

2. **Behavior**

   Existing behavioral experiments leave some ambiguity about behavioral threshold and magnitude of internal noise. This primarily comes about because the quantum efficiency estimates from behavior are substantially lower than estimates from physical measures of losses in the eye. This could mean that some photon responses are discarded, or could mean the estimates of behavioral threshold and noise usually given are too low. Resolving this is a big deal because what is at stake is how we view the retinal processing of the rod signals!

   Despite these ambiguities, behavioral experiments suggest visual system can access signals from a few, perhaps a single, photon and provide an estimate of noise source that limits photon detection. These observations provide specific constraints on retina:

   - phototransduction: single photon responses reliably transduced
   - synaptic transmission: in contrast to central synapses, synapses must be reliable
   - neural coding: absorption of a few photons must produce noticeable change in optic nerve activity

3. **Phototransduction**

   Functional requirements of photon detection

   - Amplification. Quantitatively explained by known properties of phototransduction. Nice case where we can generate quantitative model based on underlying biochemical events.
   - Dark noise. Consists of two components: discrete events produced by spontaneous activation of rhodopsin (rate 0.005-0.01 sec^{-1}) and continuous rumbling.
   - Reproducibility. Signals from each absorbed photon vary less from one to another than expected for signals produced by single molecules. Functional significance unclear, but may be critical for preserving information about time of photon arrival.

4. **Rod noise and behavior**

   Existing comparison of rod noise with behavior has focussed on discrete noise and neglected continuous noise. Lowest estimates of rod noise from behavior (i.e. lowest quantum efficiencies) are close to rate of discrete noise events in rods. This identification is tenuous, however, because of experimental imprecision in behavior and rod noise measurements.

5. **Retinal readout of rod responses**

   Convergence and sparseness pose a particular problem for rod-bipolar signal transfer

   - At visual threshold photons sparse — only about 1 rod in 10,000 absorbs photon within integration time of rod signals, but all rods generate noise.
   - Sparse signals means that retaining signals from rods receiving photons and rejecting noise from other rods can substantially improve sensitivity.
   - General problem. Signals in many parts of nervous system (olfactory system, V1, ...) are sparsely represented, and computations based on these sparse signals could benefit from separation of signal from noise. This issue can be posed precisely in retina because relevant signal and noise can be measured and photon detection is of clear behavioral relevance (so you think system would take advantage of opportunity to be much more sensitive).
   - Rod-bipolar synapse is the last opportunity to do this because rod bipolars receive input from multiple rods; once rod signals are mixed cannot separate signal and noise.

   Rod-to-rod bipolar synapse indeed implements a threshold-like nonlinearity that separates rod signals from noise.

   - Rod-rod bipolar signal transfer is nonlinear, causing rod bipolar single photon responses to be more discrete and identifiable than those in the rods.
   - Nonlinearity eliminates majority of rod's single photon responses. This could explain discrepancy between behavioral and physical estimates of quantum efficiency.
   - Rod bipolar provides near-optimal readout of rod array at visual threshold. Rejection of small single photon responses more than compensated by rejection of noise.