

Constraints on synaptic transmission from sensory receptors to target neurons
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Extraordinarily sensitive sensory systems face two problems. First, the receptor cells must be able to transduce a very small stimulus, a single photon in the case of a rod photoreceptor, nanoscopic bending in the case of a hair cell, and microvolts in the case of an electroreceptor. Second, and the subject of this work, the receptor cell must be able to transmit its small electrical signal to its target neurons by a small change in a small number of quanta (Q) of neurotransmitter. The rod typically transmits its signal to a small number, just two, of its target rod bipolar cells, whereas the other receptor cells transmit their signals to many target neurons. The quantal and stochastic nature of neurotransmitter release, along with the small numbers involved, impose inescapable mathematical constraints on successful synaptic transmission from receptor cell to target neurons.

These receptor cells all have a specialization in their synaptic terminals, the synaptic ribbon, that is believed to enable them to release quanta of neurotransmitter continuously at a high rate. In the case of the rod photoreceptors, the quantal release rate in the dark ($Q_{\text{rate,dark}}$) is estimated to be ~ 100 Q/sec but may be lower. Because a rod bipolar dendrite accumulates quanta of neurotransmitter within an epoch of ~ 0.1 sec, considerably longer than the ~ 10 ms interval between quanta, the dendrite may be regarded as a quantal counter, and the mean quantal count in the dark ($Q_{\text{count,dark}}$) is small (~ 10 Q). Moreover, quantal release is a stochastic process, and the $Q_{\text{count,dark}}$ varies from epoch to epoch and is distributed. Upon absorption of one photon and isomerization of one rhodopsin molecule (from R to R^*), the mammalian rod hyperpolarizes by only one millivolt and reduces its Q_{rate} by only $\sim 20\%$ (Schein and Ahmad, 2005). The quantal count for one R^* ($Q_{\text{count,R}^*}$) is also distributed, its mean count is also small, perhaps ~ 8 Q, and the change in Q_{count} is very small, just ~ 2 Q.

To discriminate R^* events ($Q_{\text{count}} \leq Q_T$) from darkness ($Q_{\text{count}} > Q_T$), the quantal counter – the rod bipolar dendrite – must have a threshold quantal count (Q_T). Given the two Q_{count} distributions, Q_T determines the probability of a false positive, when $Q_{\text{count}} \leq Q_T$ in the dark, and efficiency, the probability that $Q_{\text{count}} \leq Q_T$ after production of one R^* . We have described several ways to reduce overlap and thereby improve efficiency (Schein and Ahmad, 2005). Foremost, we argue that release cannot be random (Poisson) but must instead be regular ("clockwork") to narrow the Q_{count} distributions. From study of four $Q_{\text{rates,dark}}$ (50, 100, 200, and 400 Q/sec with Q_T set to optimize efficiency in each case), we also showed, not surprisingly, that efficiency rises as Q_{rate} rises.

Here we show the effect of increasing Q_{rates} in finer increments and necessarily fixed Q_T . We show that efficiency is determined by a single parameter that combines degree of regularity and Q_{count} , so suitable adjustment of degree of regularity can achieve high efficiency (e.g., 50%), even for very low quantal release rates (e.g., 12 Q/sec). However, for a fixed Q_T , a small increase in the quantal release rate in the dark ($Q_{\text{rate,dark}}$) greatly reduces efficiency. To stabilize efficiency, the postsynaptic target, the rod bipolar cell, must be able to regulate the relationship between its (biochemical) Q_T and its (biochemical) $Q_{\text{count,R}^*}$, thus clarifying the role of negative feedback involving Ca^{2+} and suggesting a helpful role for spontaneous isomerizations of rhodopsin. Efficiency could be stabilized in the face of drift in degree of regularity as well if $Q_{\text{count,R}^*} = Q_T$ and efficiency = 50%, similar to what has been measured.