Supplementary Material for
DOI: 10.1098/rsob.180076

Implications of dimeric activation of PDE6 for rod phototransduction

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Equations for the downstream phototransduction cascade

We employed a well-established model of phototransduction, with Ca²⁺-mediated feedback onto cyclic GMP concentration via GCAPs and guanylyl cyclase, fundamentally the same as used in numerous previous investigations, and as set out explicitly in [9]. We included longitudinal diffusion of cGMP and Ca²⁺ within the outer segment [23], so that the expressions for cGMP and Ca²⁺ each required a partial differential equation (p.d.e.). Those two differential equations and the remaining equations for the downstream reactions are as follows. Most variables include the spatial coordinate (x) as well as time (t). The parameters in these equations are defined in Table 2, where their values are also listed.

cGMP p.d.e.: \[
\frac{\partial cG(x,t)}{\partial t} = \varphi_{cG}(x,t) + D_{cG} \frac{\partial^2 cG(x,t)}{\partial x^2}
\] (A.1)

Calcium p.d.e.: \[
\frac{\partial Ca(x,t)}{\partial t} = \varphi_{Ca}(x,t) + D_{Ca} \frac{\partial^2 Ca(x,t)}{\partial x^2}
\] (A.2)

cGMP net formation: \[
\varphi_{cG}(x,t) = \alpha(x,t) - \beta cG(x,t)
\] (A.3)

Calcium net influx: \[
\varphi_{Ca}(x,t) = \frac{1}{2} f_{Ca} L j_{cG}(x,t) - L j_{ex}(x,t)
\] (A.4)

Cyclase: \[
\alpha(x,t) = \frac{\alpha_{\text{max}}}{1 + [Ca(x,t)/K_{GCAP}]^m_{GCAP}}
\] (A.5)

Channels: \[
L j_{cG}(x,t) = J_{cG,\text{max}} \frac{cG(x,t)^3}{cG(x,t)^3 + K_{cG}^3}
\] (A.6)
Exchanger: \[ L \ j_{ex}(x,t) = J_{ex,\ max} \ \frac{Ca(x,t)}{Ca(x,t) + K_{ex}} \] (A.7)

OS current: \[ J(t) = \int_{L} \{ j_{cG}(x,t) + j_{ex}(x,t) \} \ dx . \] (A.8)

The membrane currents above are expressed as current density per unit length of outer segment, \( j_{cG}(x,t) \) and \( j_{ex}(x,t) \), but for convenience have been written in the form \( L \ j(x,t) \), with units of current over the entire outer segment length, \( L \).

**Hydrolytic activity at location of photoisomerization**

The PDE hydrolytic activity \( \beta \) in Eqn (A.3) above was set to

PDE activity (resting): \[ \beta = \beta_{\text{Dark}} \] (A.9)

at all longitudinal locations except where a photoisomerisation occurred.

For numerical simulation, we used spatial elements of finite width, \( \delta x \). In an element that received a photoisomerisation (typically at \( x = 0 \)), we set

PDE activity (isomerisation): \[ \beta = \beta_{\text{Dark}} + \beta_{E^{**}} \frac{L}{\delta x} PDE^{**}(t) \] (A.10)

meaning that the photon-induced PDE activity was distributed over the width \( \delta x \) of the element. The number of activated molecules, \( PDE^{**}(t) \), was obtained from the stochastic simulations described in the paper.

**Boundary conditions at ends**

The boundary conditions at each end of the outer segment are of the reflective (zero flux) kind. They apply for both cGMP and Ca\(^{2+} \), and can be written as:

At each end of OS: \[ \frac{\partial cG(x,t)}{\partial x} = 0 = \frac{\partial Ca(x,t)}{\partial x} . \] (A.11)

**Bright flash responses**

For bright flashes, we used a single compartment (i.e. a longitudinal element \( \delta x = L \)) and we dispensed with Eqns (A.1), (A.2), (A.9) and (A.11).

**Computer code**

The Matlab computer code used for solving these equations is part of the ‘WalkMat’ package, and has been deposited in Dryad with the link given under Data Accessibility.