

Master Thesis proposal

Minimal models of phototransduction response in vertebrates

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This proposal is for a Master thesis in the field of **Systems Biology**.

In the retina of vertebrates, phototransduction (i.e., the process of absorbing light and transforming it in an electrical signal) is performed by two types of photoreceptor cells, rods and cones, see [5] for an introductory overview. In patch-clamp experiments, the response of these neurons to various stimuli of light can be recorded as an electrical signal. Signals that are steps and pulses are normally used for this task.

The response registered is the result of several regulatory feedback loops occurring in the cell. Complex models describing each single molecular step exist see [2, 6] and references therein. In [1] we showed that for rods the basic regulatory action can be however captured well by simple qualitative reasoning, and has a clear interpretation in terms of different time scales between the faster direct (input to output) signal transduction and the slower feedback regulation. To understand these differences, steps responses and pairs of pulses at different lag times are used, see Fig. 1. The objective of this thesis is to perform a similar analysis on cone cells. These neurons (responsible for “color vision”) are much slower than rods, and their response also has slightly different features, see [4, 3]. Namely, the deactivation steps shown undershooting, a feature never observed in rod at the baseline, but only for step experiments in dim light (i.e. step on step). Compare Fig. 1 (B and D) and Fig. 2 (A, B, C). These features must be described by nonlinear models. The objective of the thesis is to investigate one such model and to fit it to the data (nonlinear identification).

References

- [1] G. De Palo, G. Facchetti, M. Mazzolini, A. Menini, V. Torre, and C. Altafini. Common dynamical features of sensory adaptation in photoreceptors and olfactory sensory neurons. *Nat. Sci. Rep.*, 3:1251, 2013.
- [2] R. Hamer, S. Nicholas, D. Tranchina, T. Lamb, and J. Jarvinen. Toward a unified model of vertebrate rod phototransduction. *Vis Neurosci*, 22(4):417–36, 2005.
- [3] J. I. Korenbrot. Speed, adaptation, and stability of the response to light in cone photoreceptors: the functional role of ca-dependent modulation of ligand sensitivity in cgmp-gated ion channels. *The Journal of general physiology*, 139(1):31–56, Jan 2012.
- [4] J. I. Korenbrot. Speed, sensitivity, and stability of the light response in rod and cone photoreceptors: Facts and models. *Prog Retin Eye Res*, 31(5):442–466, Sep 2012.

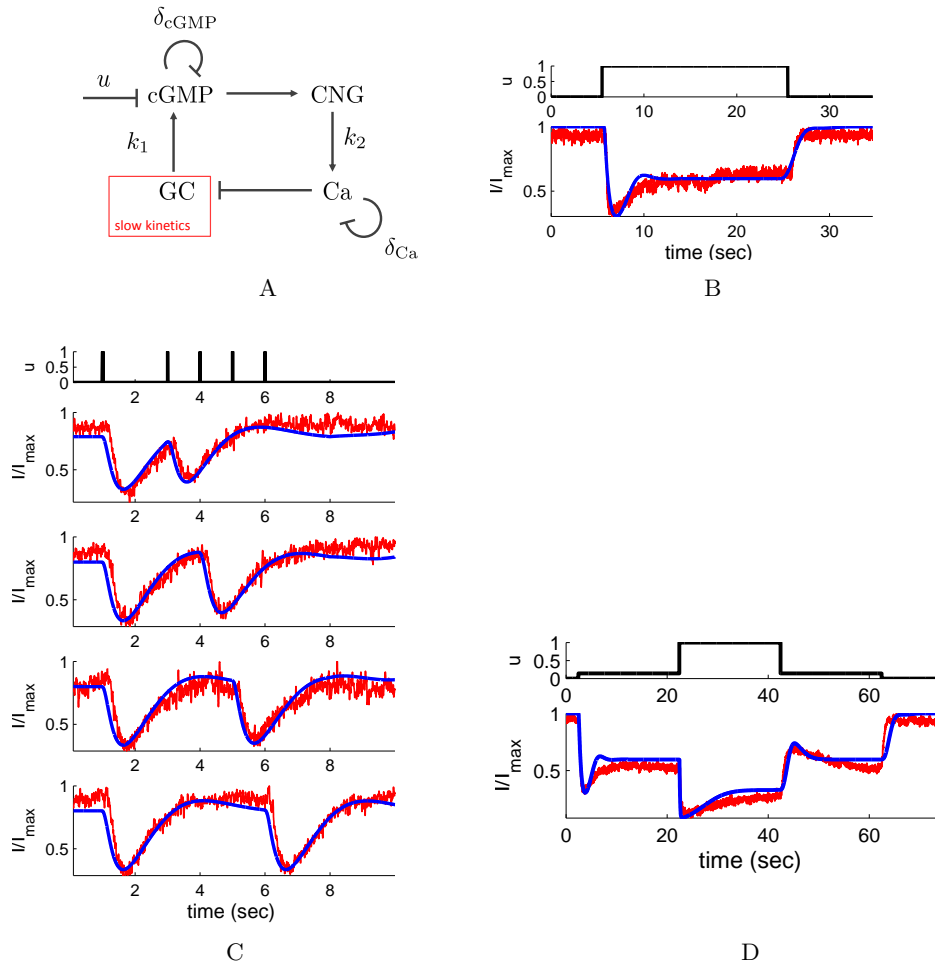


Figure 1: **Phototransduction.** A: basic pathway for phototransduction with its calcium-mediated GC feedback loop, see [1]. B: the red traces show an example of normalized response to a step. The step deactivation does not undershoot the baseline. The blue traces show the response of the dynamical model proposed in [1]. C: Example of normalized response from two identical non saturating light pulses applied at different time intervals (red traces; in blue the fit of the dynamical model). D: A step applied out of the natural baseline (step on step) shows undershooting in the deactivation phase.

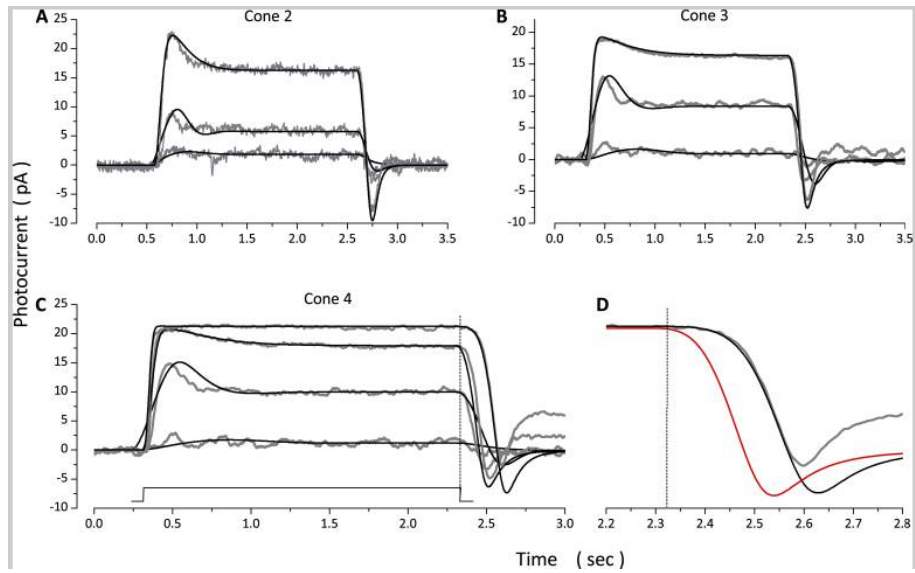


Figure 2: **Phototransduction in cones.** A, B, C: Step responses of cone cells showing undershoot in the deactivation phase. Figure from [3] (copyrighted).

- [5] E. Pugh Jr., S. Nikonov, and T. Lamb. Molecular mechanisms of vertebrate photoreceptor light adaptation. *Current Opinion in Neurobiology*, 9(4):410 – 418, 1999.
- [6] L. Shen, G. Caruso, P. Bisegna, D. Andreucci, V. Gurevich, H. Hamm, and E. DiBenedetto. Dynamics of mouse rod phototransduction and its sensitivity to variation of key parameters. *IET Systems Biology*, 4(1):12–32, 2010.