Comparison of nocturnal vs. diurnal phototransduction amplification: Theoretical analysis of frog electroretinograms

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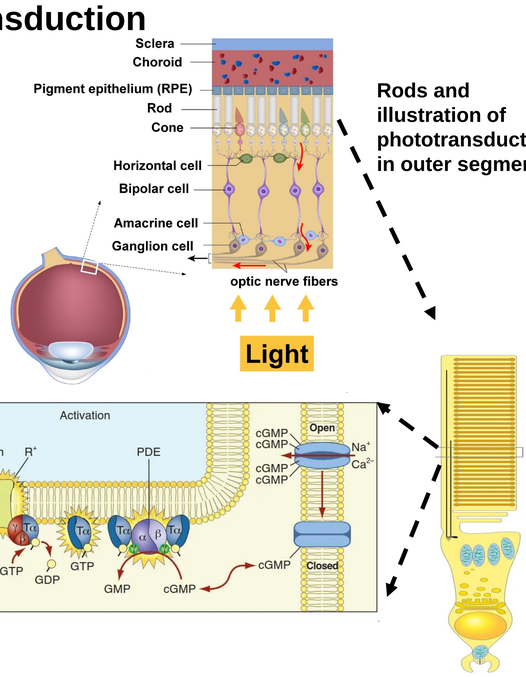
Introduction

Abstract: This study used an analytic approach to understand if amplification and temporal properties of phototransduction vary between retinas in nocturnal versus diurnal vertebrates. In vertebrate photoreceptors, phototransduction involves a cascade of biochemical steps leading to a reduction in membrane conductance, causing a decrease in membrane potential. In electroretinogram (ERG) recordings this change in potential is measured as the onset of the a-wave and can be modeled as a delayed Gaussian function. Previous theoretical analysis has shown that the function is scaled by an amplification constant (*A*) which reflects the product of the rate of phosphodiesterase activation to a single photoisomerization, the rate constant of cGMP hydrolysis by PDE, and the Hill coefficient of the cyclic GMP gated membrane channels. The rate by which the function changes is tau effective (τ_{eff}), a cumulative delay for the transduction processes. To determine *A* and τ_{eff} we used custom written software in the python virtual environment to fit the Gaussian function to the a-wave onset of ERGs in four species of frogs (2 diurnal, 2 nocturnal). A least-squares fit procedure determined the optimized values of *A* and τ_{eff}. Based on the analyses, we will test the hypothesis that the a-wave of nocturnal frogs exhibit greater amplification constants, reflecting the need for greater amplification of the reduced number of isomerizations in light-deprived environments.

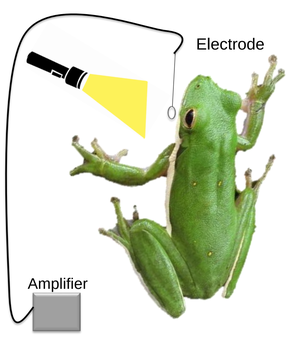
Phototransduction



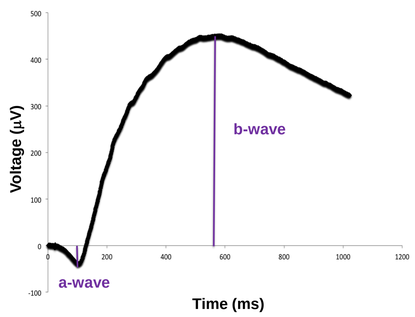
Rods and illustration of phototransduction in outer segments

The ERG a-wave: the response of photoreceptors

The change in circulating current in the photoreceptor outer segments is reflected in the change in voltage of the a-wave



Standard set-up for ERG. 1 ms white light flashes were delivered under scotopic conditions. Retinal responses were recorded using a AgCl electrode on the cornea.



ERG response. The a-wave represents the electrophysiological change of photoreceptors in the outer nuclear layer of the retina. The b-wave is the response of the bipolar cells in the inner nuclear layer.

Summer Project: Fit the Model

Summer Project: Write custom software to fit model to data

Analytic modeling of the a-wave allows for estimation of the circulating current in photoreceptors

For a brief flash of light, the normalized circulating rod current follows ***f(t)***

$$f(t) = \exp[-\frac{1}{2} * \Phi * A * (t - t_{eff})^2]$$

Φ is the number of photoisomerizations per rod produced by a light flash at time 0.

τ_{eff} is a delay that accounts for several steps in the activation reactions

A is cascade amplification parameter that is characteristic of a given species. It is the product of several cascade components

$$A = \upsilon_{RG} * C_{GP} * \beta_{sub} * \eta$$

υ_{RG} is the rate at which a single, fully active Rhodopsin* activates G-proteins

C_{GP} is coupling efficiency between activated G-proteins (G*) and Phosphodiesterase (PDE)

β_{sub} is the rate constant of a single, fully active catalytic subunit of the PDE

η is the Hill coefficient of the cGMP-activated current

Example of least squares fit of the model

Response of *Rana pipiens* female

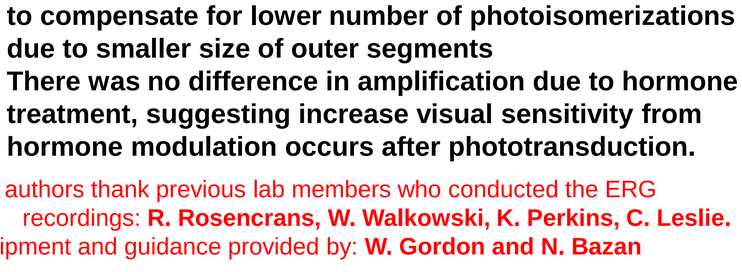
Φ = 209
τ_{eff} = 11.1 ms
A = 0.35633

Summer Project: After writing custom software to fit a-waves in many ERGs, we will compare *A* values across nocturnal and diurnal species

Results

Comparison of Amplification constant (*A*) in different populations of frogs

Nocturnal vs. Diurnal



Within Species: Male vs. Female

Reproductive vs. Non-Reproductive Endocrine state

Example Fits in Four Species

Conclusion

1. **First analysis of phototransduction parameters across species with different visual ecologies.**
2. **Diurnal eyes appear to have higher amplification, possibly to compensate for lower number of photoisomerizations due to smaller size of outer segments**
3. **There was no difference in amplification due to hormone treatment, suggesting increase visual sensitivity from hormone modulation occurs after phototransduction.**

The authors thank previous lab members who conducted the ERG recordings: **R. Rosencrans, W. Walkowski, K. Perkins, C. Leslie.**
Equipment and guidance provided by: **W. Gordon and N. Bazan**

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This research project was supported by Award Number: DBI-2051440 through the National Science Foundation (NSF), Research Experiences for Undergraduates (REU) Program