

## Comprehensive analysis of the retinal cell contributions to the human ERG

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**Purpose.** Standard electroretinogram (ERG) protocols are largely designed to isolate the responses of the rod and cone retinal pathways, including the use of adapting backgrounds to suppress unwanted off-pathway responses. Here, we record spectral ERGs in the low-to-high mesopic sensitivity range in the absence of any adapting background in order to assess interactions between the pathways.

**Methods.** We have developed a comprehensive neuroanalytic model of the component structure of the ERG driven by knowledge of the underlying retinal physiology, to enhance its power as a critical diagnostic tool for a broad range of both retinal and systemic dysfunctions. The ERG is conceptualized as a highly diagnostic signal of the retinal subsystems, each consisting of: an a-wave (photoreceptor extracellular current flow), a b-wave (transient bipolar cells), an inner retinal photopic negative response (PhNR; ganglion cells), and a melanopsin response (intrinsic ganglion-cell light response). This model is applied to an array of full-field spectral ERGs over a range of colors and intensities.

**Results and Conclusion.** Most of these response components are driven by both the rod and cone photoreceptor types, thus constituting about a dozen distinct components of the ERG, differentiated according to post-stimulus time of expression and the light level. At every light level, rod-driven components are typically slower than cone-driven components, equated for quantum catch. This neuroanalytic approach has been applied to a variety of spectral ERG datasets to account for as much as 95% of the variance of the ERG.

### ERG Model Equations

The additive component model implemented for the rod pathway ( $R$ ), cone pathway ( $C$ ), photopic negative response ( $Ph$ ) and melanopsin pathway ( $M$ ) contributions to the full-field spectral ERG response is:

$$ERG = a_{1,\lambda} \Xi_R(t) + a_{2,\lambda} \Gamma_R(t) + a_{3,\lambda} \Xi_C(t) + a_{4,\lambda} \Gamma_C(t) + a_{5,\lambda} \Gamma_{Ph}(t) + a_{6,\lambda} \Gamma_M(t)$$

where  $I$  is stimulus intensity,

$\lambda$  is wavelength,

$S(t)$  is the stimulus time course,

$$\Gamma_j(t) = t^{k_j-1} \cdot e^{-\frac{t}{\tau_j}},$$

$$\Xi_R(t) = \int \Gamma_j(t') \cdot S(t) dt,$$

$$a_{i,\lambda} = \kappa_i + \beta_i \cdot \rho_{i,\lambda} \cdot \log(I),$$

and where  $\rho_{i,\lambda}$  is the respective photopic, scotopic and melanopic spectral sensitivity for the  $R$ ,  $C$ ,  $Ph$ , and  $M$  pathways.

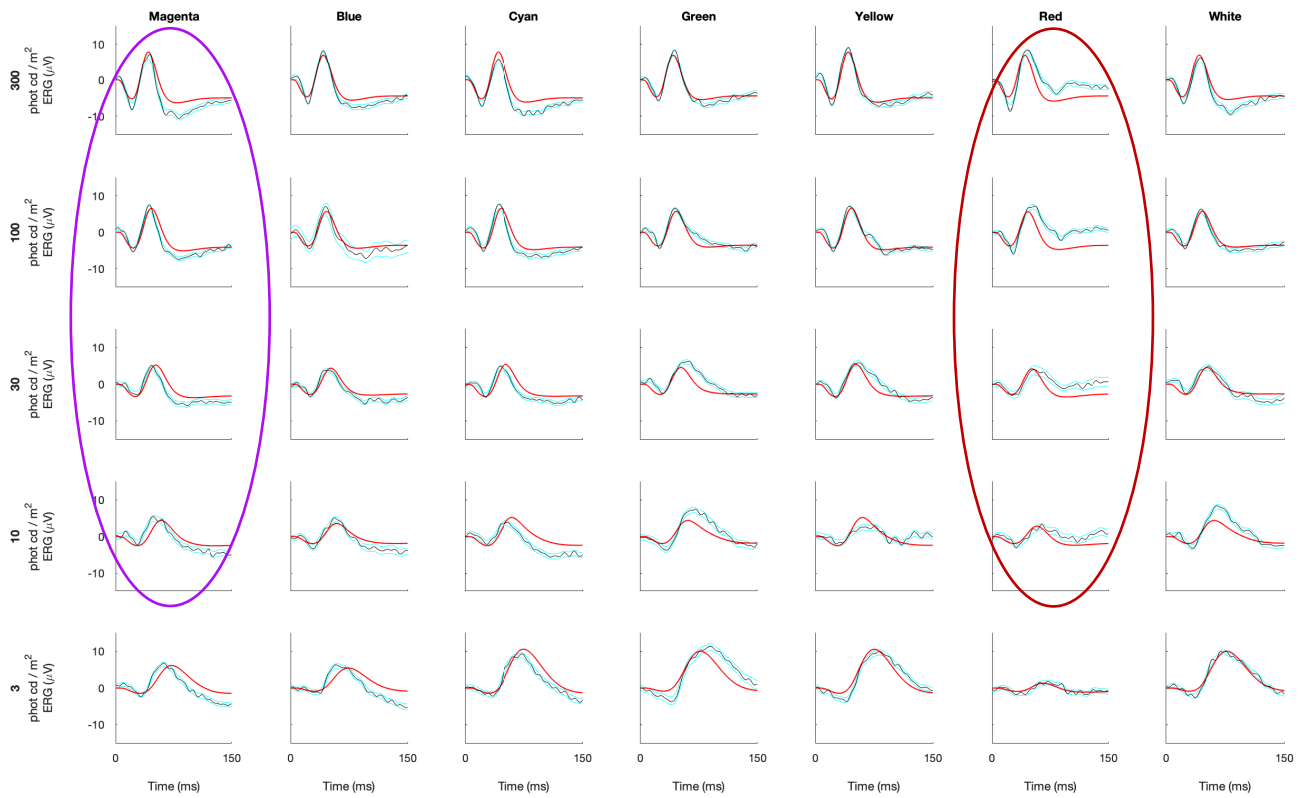


Fig. 1. Example of photopically-equated spectral ERGs for 6 color plus white (**black** curves  $\pm 1$  SEM error bounds, **cyan** curves), fitted with the structured intensity/spectral gamma-function model specified in the equation. Thus, the 24 parameter model structures the 210 free parameters of the model fits across the dataset. Note that there is nevertheless a consistent late negative deviation from the fit for the **red** column matched by a corresponding late positive deviation in the **magenta** column that deviates from any retinal receptor spectral sensitivity, and would require an extra **red-blue** opponent component to resolve.