F30/F31/F32/F33 Review

Applicant: David St-Amand

# Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood that the fellowship will enhance the candidate’s potential for, and commitment to, a productive independent scientific research career in a health-related field, in consideration of the following scored and additional review criteria. An application does not need to be strong in all categories to be judged likely to have a major impact. *See BIOTRAIN 720 review criteria rubric for guidance in evaluating proposals and writing critiques.*

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| Overall Impact/Merit *Write a paragraph summarizing the factors that informed your Overall Impact score.* |
| In this resubmission, the applicant has thoughtfully responded to comments from reviewers, presenting a compelling proposal for developing efficient coding models that predict the responses of retinal ganglion cells to color (Aim 1) and motion (Aim 2). Current efficient coding models cannot sufficiently explain retinal processing of chromatic or moving stimuli without including biologically implausible assumptions, limiting understanding of why the retina processes critical components of natural scenes the way that it does. Therefore, the applicant proposes to use “multiple correlated channels as inputs” instead of a single channel, which the applicant hypothesizes will better model the physiological properties of actual retinal ganglion cells. To achieve this, the applicant must increase the number of parameters, a computationally intensive task that has posed a barrier to progress. The applicant presents a well-reasoned strategy to “parameterize the linear filters . . . to be [the] difference-of-gaussians,” citing preliminary data from the applicant’s lab that demonstrates feasibility. Moreover, the applicant is in a lab with expertise in efficient coding, an ideal training environment. The efficient coding models developed in this proposal will represent a significant technical advance with the potential to better model biological phenomena within the vision field and beyond. The applicant’s plan to compare the novel modeling results with recorded electrophysiological data has the potential to significantly advance understanding of color and motion processing in the retina. This is an exciting proposal that rigorously addresses an important neurobiological question, demonstrates the applicant’s computational ability, and could have a significant influence on the field. |

# Review Criteria

Reviewers will consider each of the review criteria below in the determination of the candidate’s qualifications, scientific and technical merit of the proposed research, candidate’s training potential, and institutional environment and commitment to training.

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| 1. Significance |
| **Strengths**   * Explains that the field has achieved “descriptive” and “mechanistic” explanations for retinal processing but lacks “normative” explanations, a barrier to understanding early visual processing at the level of the retina. * Highlights how prior applications of the efficient coding hypothesis for retinal processing included biologically inaccurate or implausible assumptions (“an infinite number of neurons and linear output responses”), limiting the ability of these models to provide normative explanations. * Discusses how the field has progressed by “incorporat[ing] non-linear output responses and a limited number of neurons” into efficient coding models that can now predict retinal processing of achromatic stimuli (the current frontier of knowledge). * Articulates the specific gap in knowledge, that efficient coding models cannot yet predict “how the retina processes strongly correlated inputs across multiple channels,” and conveys that filling this gap is important because natural stimuli include both color and motion (which “involve multiple correlated channels as inputs”). * This proposal will “develop new machine learning techniques to train efficient coding models with multiple correlated channels,” which will require solving the “overparameterizing problem” that limits the number of parameters in current models. Future computational research will strongly benefit from this achievement, both within and outside the vision field. * This proposal will enable the applicant to “learn how efficient coding models handle correlated channels, and whether this solution is similar to the computations RGCs perform.” The understanding gained by comparing the new computational data with existing electrophysiological data is likely to have a powerful influence on the vision field.   **Weaknesses**   * Could expand upon what we will be able to do once the gap in knowledge – developing an efficient coding model for retinal processing of color and motion – is filled. How will successful completion of these aims change the way that we think about retinal function (beyond filling the specific gap in knowledge)? What next steps would we be able to take? * Could explain “space-time separability” and why this assumption is “difficult to relate to retinal physiology.” * Could discuss whether an alternative to efficient coding has been used in an attempt to normatively explain retinal processing of color and/or motion and what the outcome was (to further strengthen the argument for using efficient coding models to understand retinal processing). |

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| 2. [Innovation](http://grants.nih.gov/grants/peer/critiques/rpg_D.htm%23rpg_03) |
| **Strengths**   * This proposal is technically innovative because it will “solve [the] overparameterizing problem” to deliver efficient coding models with “multiple correlated channels as input.” The development of efficient coding models with “multiple folds” more parameters will be novel and is likely to significantly advance computational research in the vision field and beyond. * This proposal is conceptually innovative because it will develop efficient coding models that, unlike prior efficient coding models that take a single channel as input, take “multiple correlated channels as input” like the retina does. The approach will enable the applicant to test whether the novel models can predict experimental data from retinal processing of color and motion, an achievement that is likely to advance the vision field.   **Weaknesses**   * Previous points addressed in the resubmission. |

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| 3. Approach |
| **Strengths**   * Discusses preliminary data from the applicant’s lab for efficient coding models of retinal processing, establishing that the appliciant is in a training environment with the expertise and resources to accomplish the proposed aims. * Explains the conceptual basis of the efficient coding model so that a non-computational reviewer can understand, while also including details that convey the applicant’s computational ability and the rigor of the experimental approach. * Presents a well-reasoned plan to build an efficient coding model with a higher number of parameters (“parameterize the linear filters of each neuron to be difference-of-gaussians”), suggesting that the applicant is likely to be successful in tackling this challenge. * Discusses potential problems and alternative strategies for both Aims.   **Weaknesses**   * Mentions “a fixed average firing rate” for model retinal ganglion cells as a method “[t]o represent the metabolic cost of firing spikes,” but how the firing rate restriction represents metabolic cost is unclear. Also, to what extent does the constrained firing of model retinal ganglion cells reflect the firing of actual retinal ganglion cells? * In Aim 1, the applicant mentions changing “the RGC-cones ratio” but does not specify the different ratios that will be used or how they are chosen. * Could add a discussion of future directions. * Other points addressed in the resubmission. |

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| Resubmission |
| Comments (if applicable):   * I have revised my comments above to reflect the changes made in the resubmission. |