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.*

Overall Impact/Merit *Write a paragraph summarizing the factors that informed your Overall Impact score.*
The goal of this revised proposal is to test whether color opponency and direction selectivity of RGC can be predicted from efficient coding theory, like their spatial and temporal structures can be. Overall this revision was strongly responsive to the reviewers' concerns, substantially clarifying the link between the two aims and the methodological approaches. The project is also substantially expanded to address not only L/M color opponency in midget cells, but also aims to predict other classes of color opponent and achromatic RGCs, as well as multiple classes of DSRGCs. However, the basis for the fundamental conceptual framework (the correlation across channels) is still not clearly described, leading to a number of concerns about the approach.

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.

1. Significance
Strengths • Efficient coding hypothesis has been a productive framework for understanding why systems adopt diverse of receptive field properties. • Color opponency and direction selectivity are two fundamental receptive field properties encoded in the retina. • Previous interrogation of these properties has been hindered by the correlation across channels. • Aims to explain why color opponency differs across retina and why there are four classes of dsRGCs **Weaknesses** • While it is stated that color and motion are both characterized by correlated input channels, it is not clearly delineated what this means- and where the correlation lies. It could also be more transparent how this correlation is managed by parameterizing the model. It is not clear how parameterization deals with correlation.

- More could be done in the significance to set up both the particular issues that the aims will address as well as the impact of this new framework on our understanding of either visual processing or efficient coding.

2. Innovation

Strengths

- Development of new theoretical approaches for addressing color and motion, dimensions that have increased numbers of parameters
- Novel hypothesis for the role of cone:RGC ratio in determining color opponency

Weaknesses

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3. Approach

Strengths

- Theoretical framework is based on long-standing literature and work in current lab
- Use of large database of natural images to train models
- Ability to resolve linear filters and defined parameters from trained model

Weaknesses

- Given that there are three color channels but potentially many more temporal latencies needed for direction discrimination, can the same parameterization framework solve both of these problems, or will direction selectivity be more difficult? In general, more information is needed about the number of channels (k) for each of these tasks, and the degree/source of correlation across channels.
- Will mutual information about pixel intensity be sufficient for generation of achromatic channels that exclude S cone signals? Or that don't make blue/red opponency, for example? Does the task need to be more selective? Or do the cone ratios need to be set?
- Similarly, will mutual information about pixel intensity be sufficient for driving selection of direction selectivity? Or does the model need a more direction specific task?
- In Aim 1, the d parameter is proposed to be the key parameter to describe the relative role of L, M, and S channels- yet it seems that both d and c are needed to describe opponency.
- In previous work, noise was an important factor in determining spatiotemporal RFs, yet there is no consideration of noise as an important parameter here.

Resubmission

Comments (if applicable):

- Revision is strongly responsive. There are major improvements in the motivation of the overall framework and the description of the modeling approach and un/expected outcomes. However, some of this was done in relatively broad strokes, and more explanation is needed.