2210 - A0390 Synaptic plasticity models predict that binocular treatments for amblyopia can outperform monocular treatments

Brian Blais[1], Eric Gaier[2,3]

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[2]Picower Institute for Learning and Memory, Massachusetts Institute of Technology
[3]Department of Ophthalmology, Boston Children's Hospital, Harvard Medical School

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Purpose

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- Compare the dynamics of amblyopia recovery at the neuronal level
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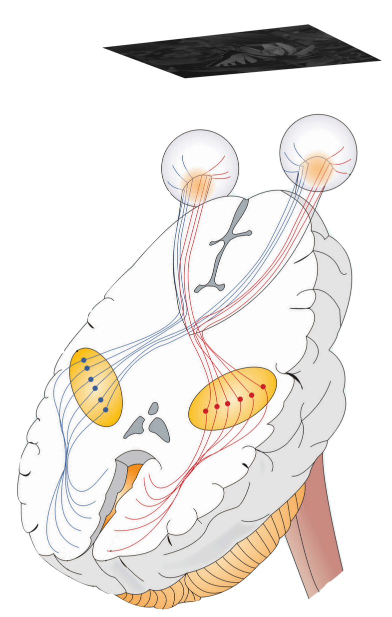
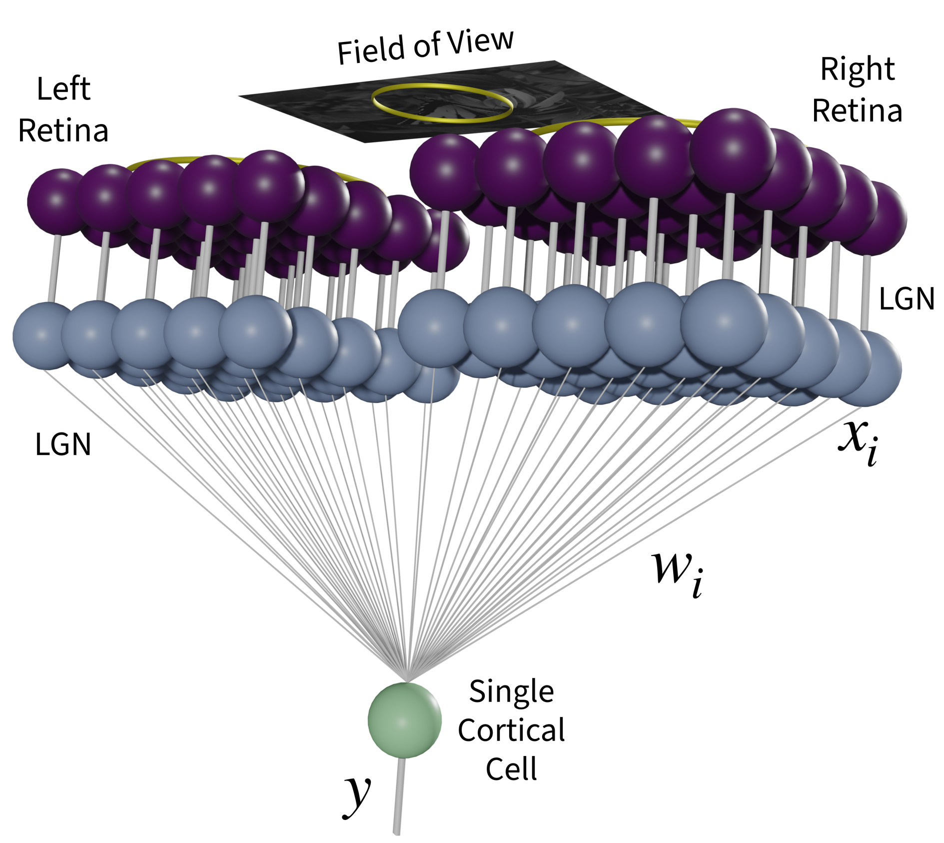
- Multiple sources for amblyogenesis
  - refractive error
  - strabismus





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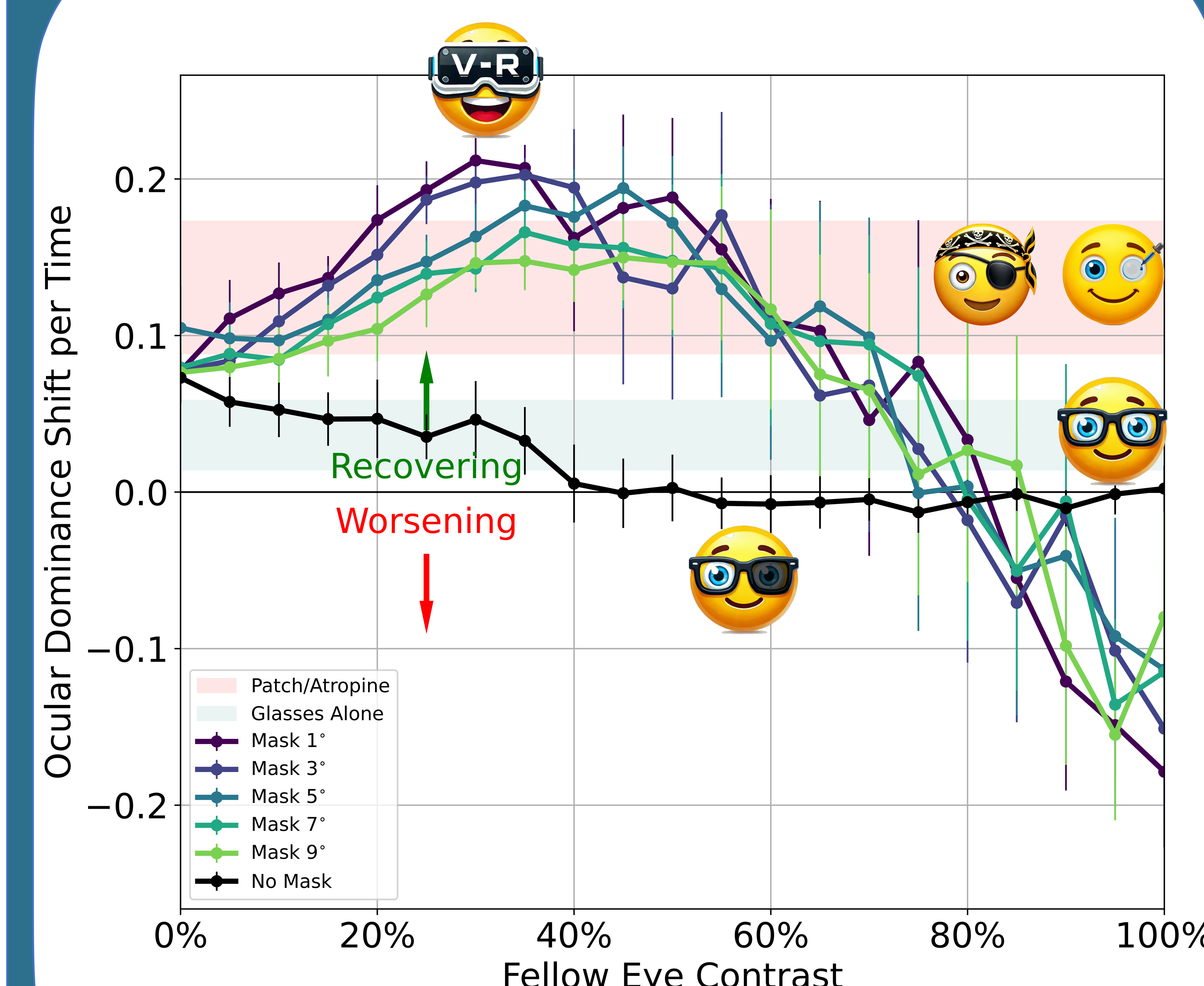

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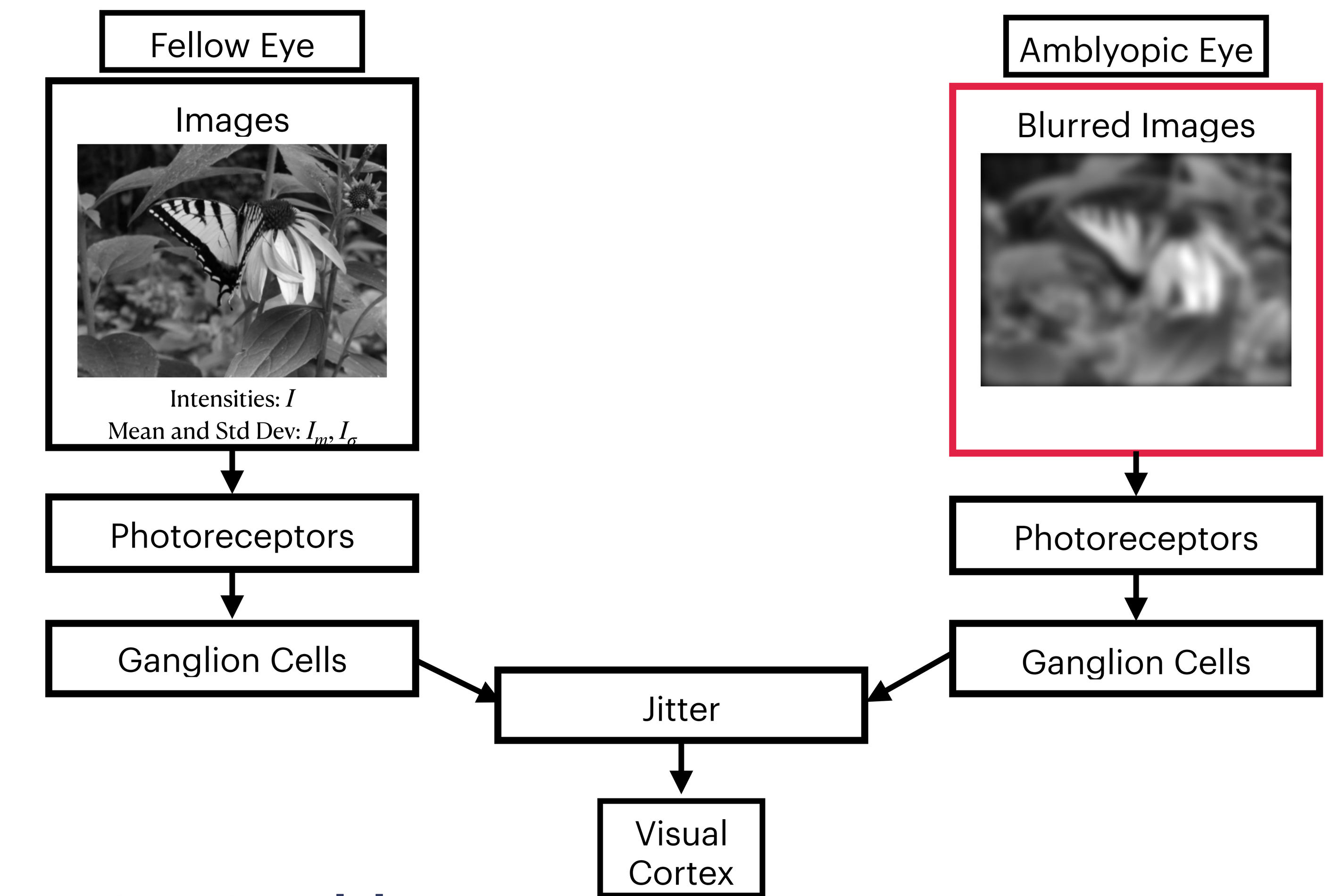

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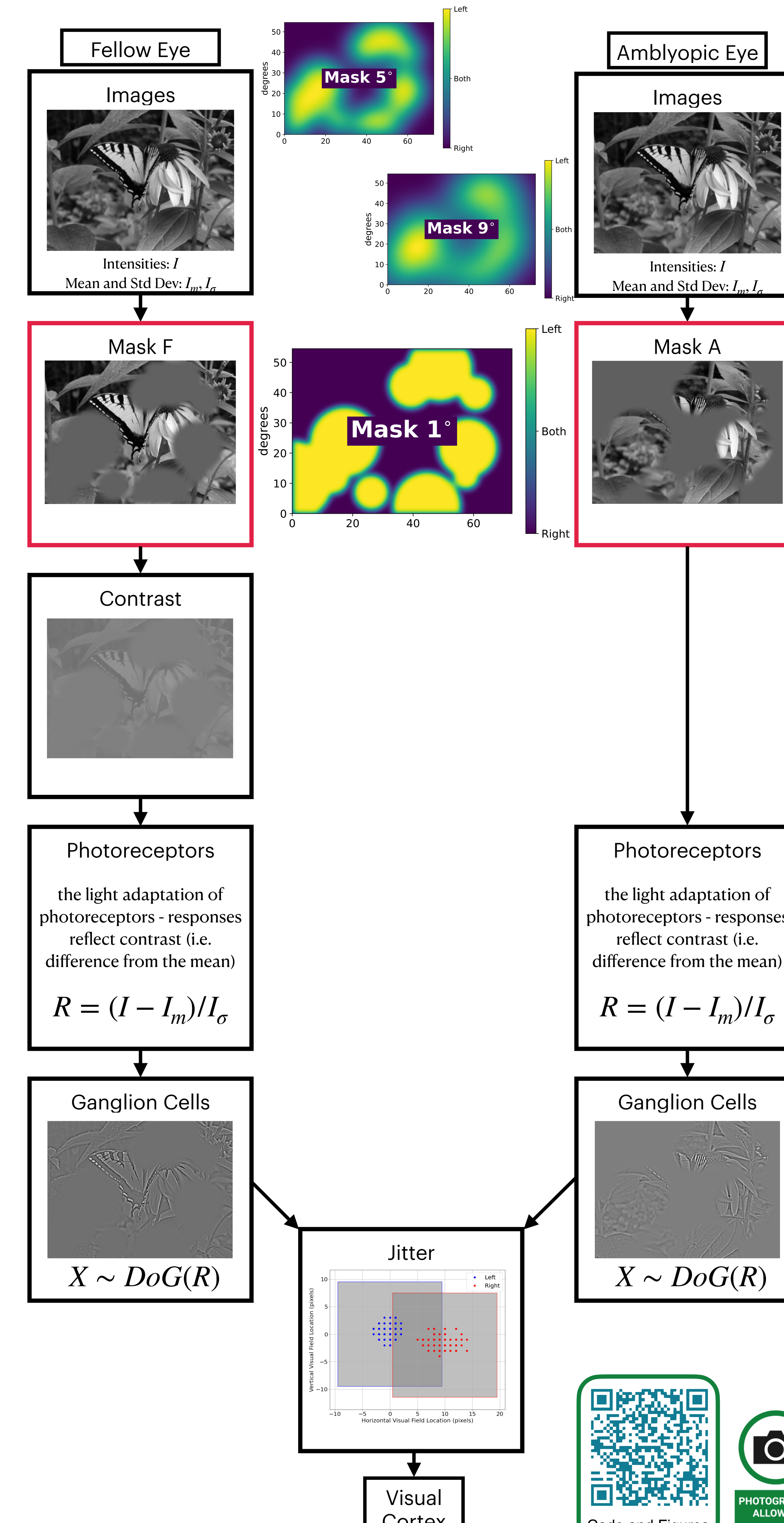

Code and Figures

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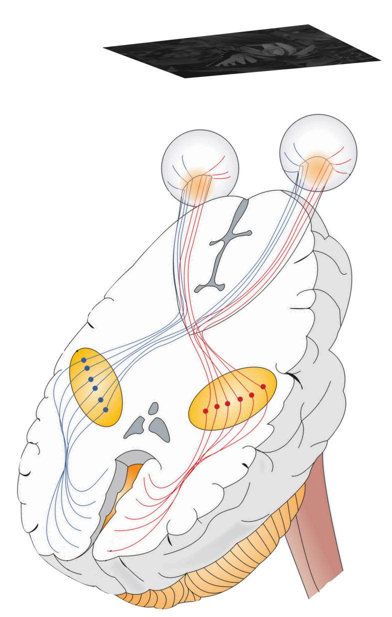

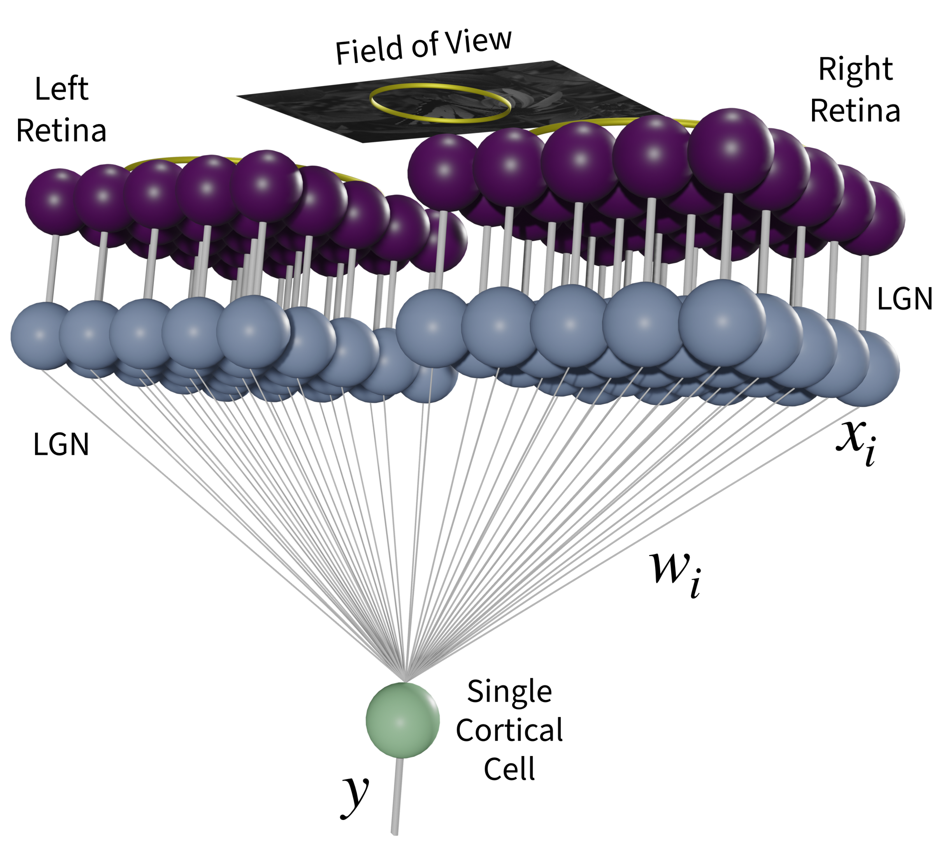

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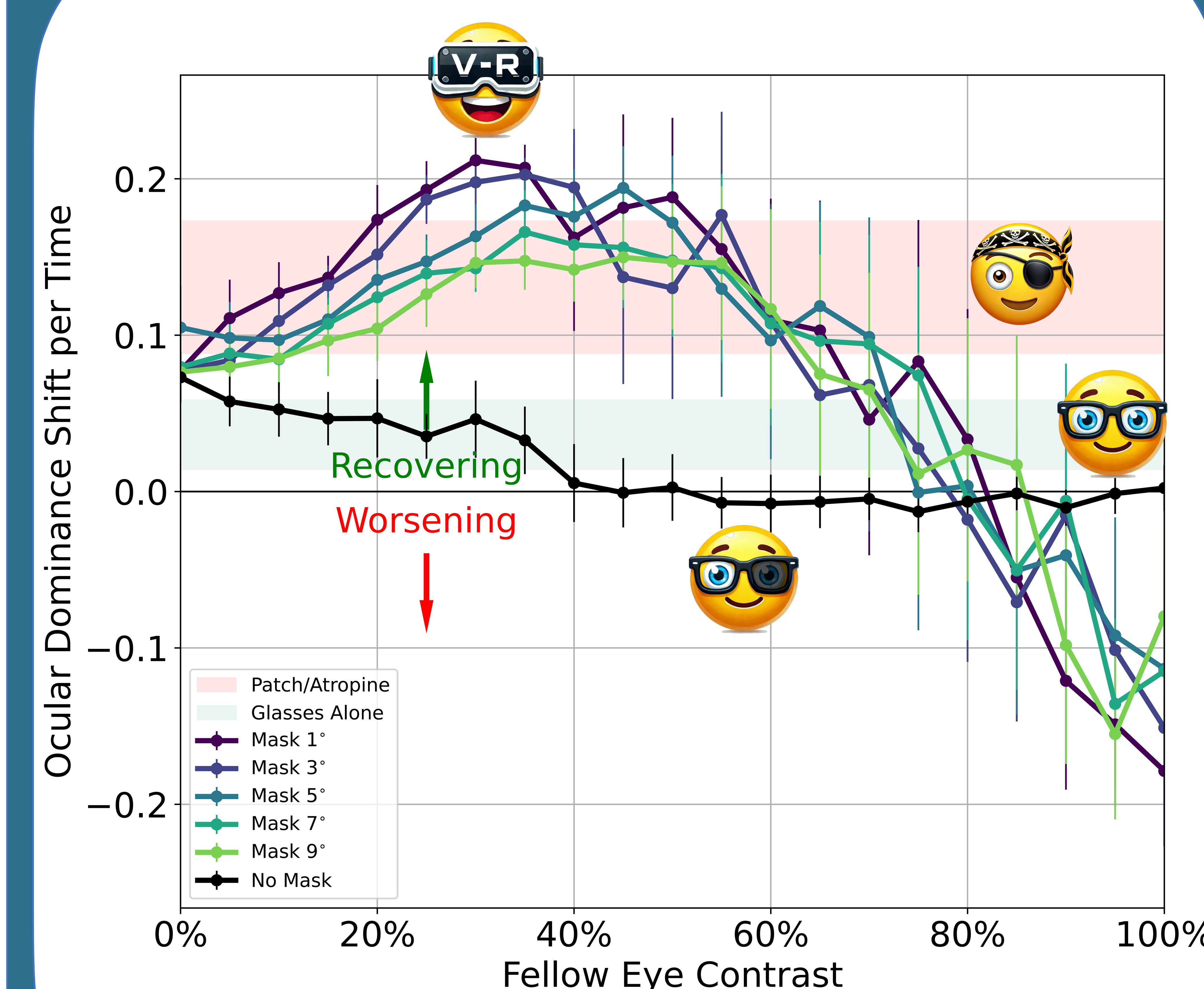

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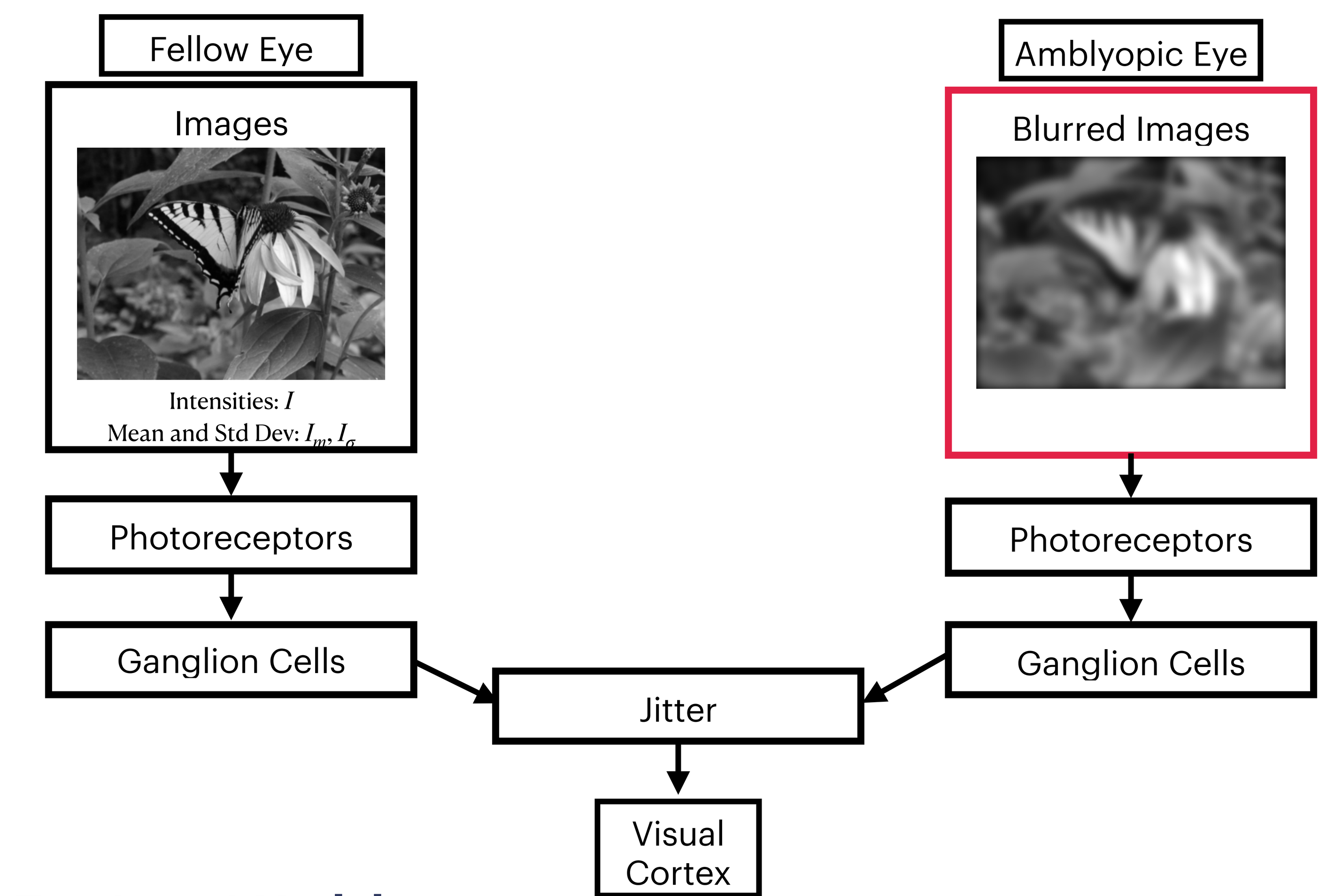

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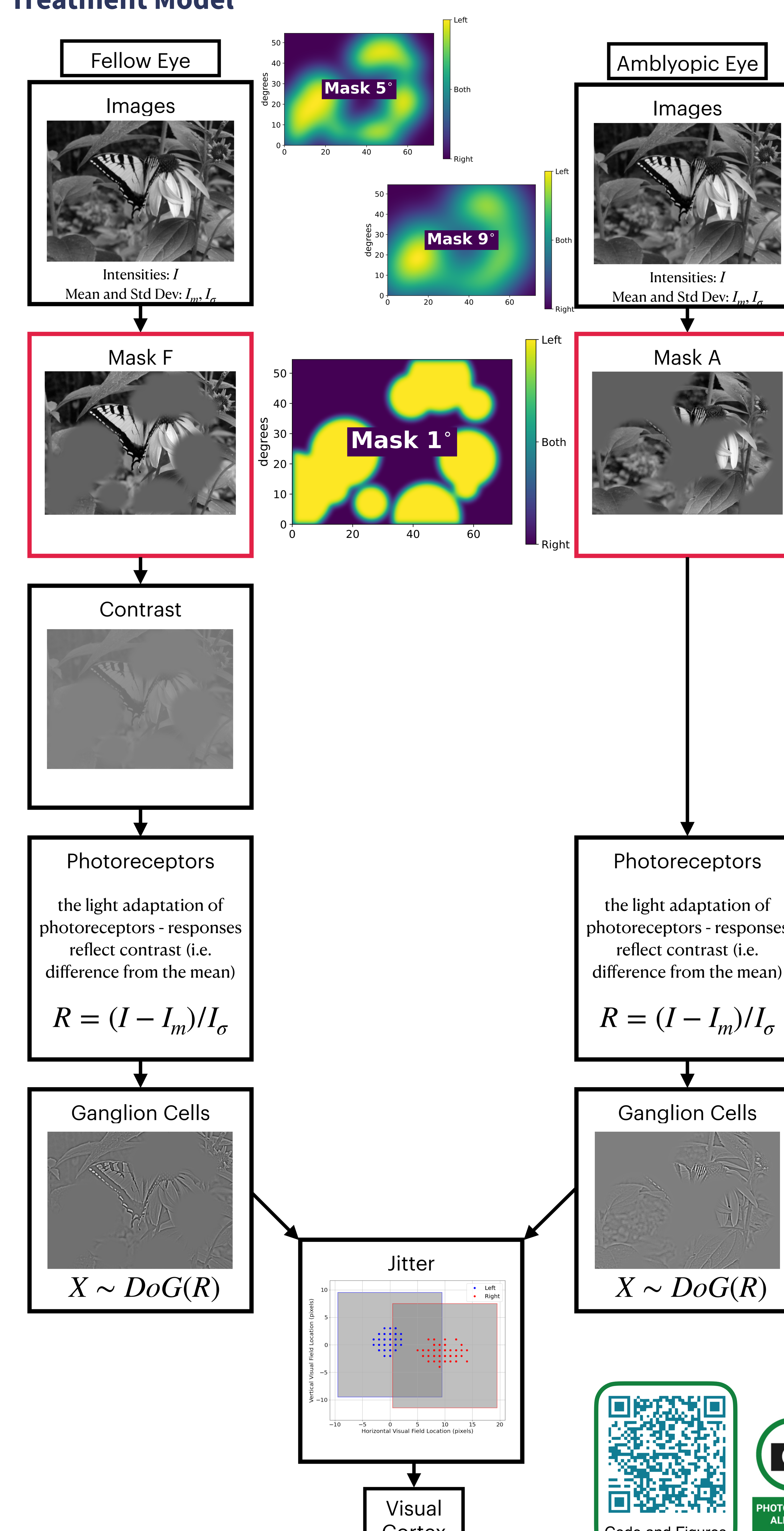

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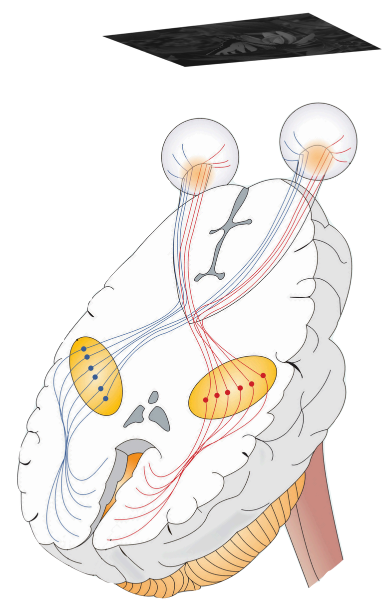

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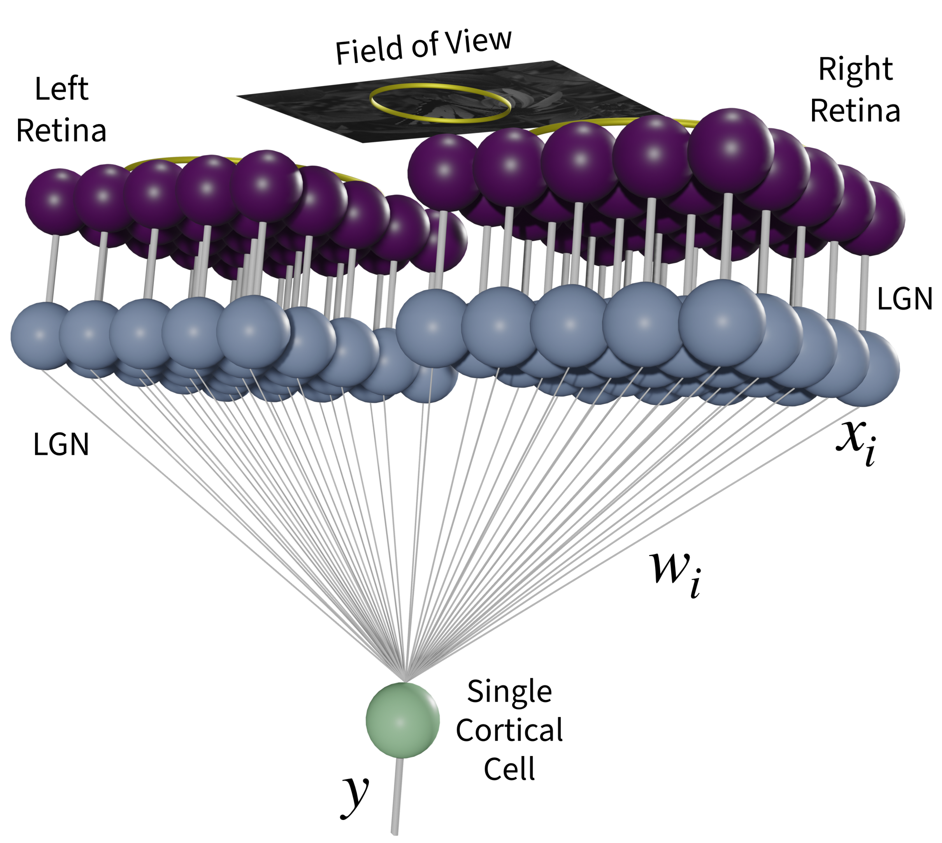

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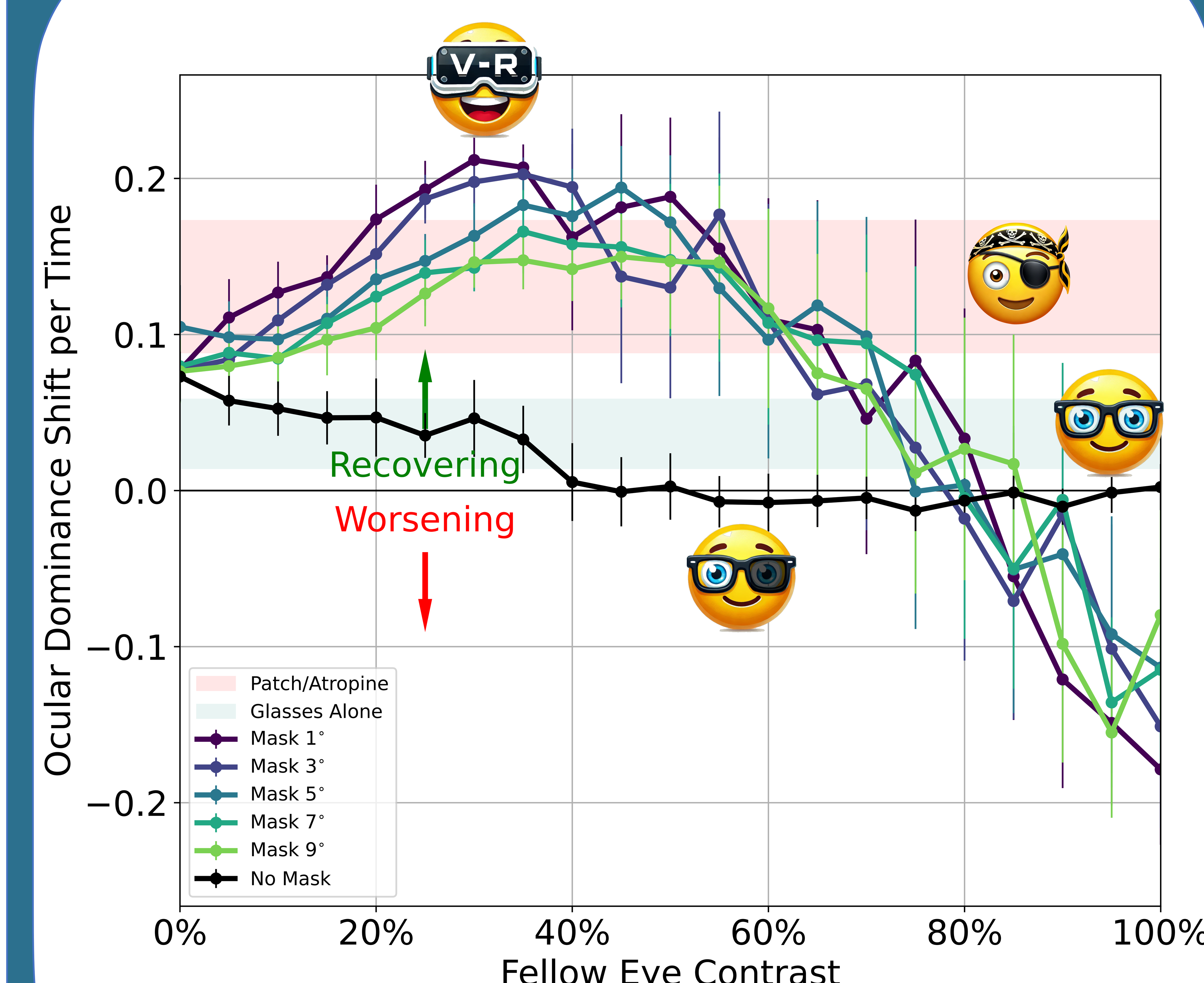

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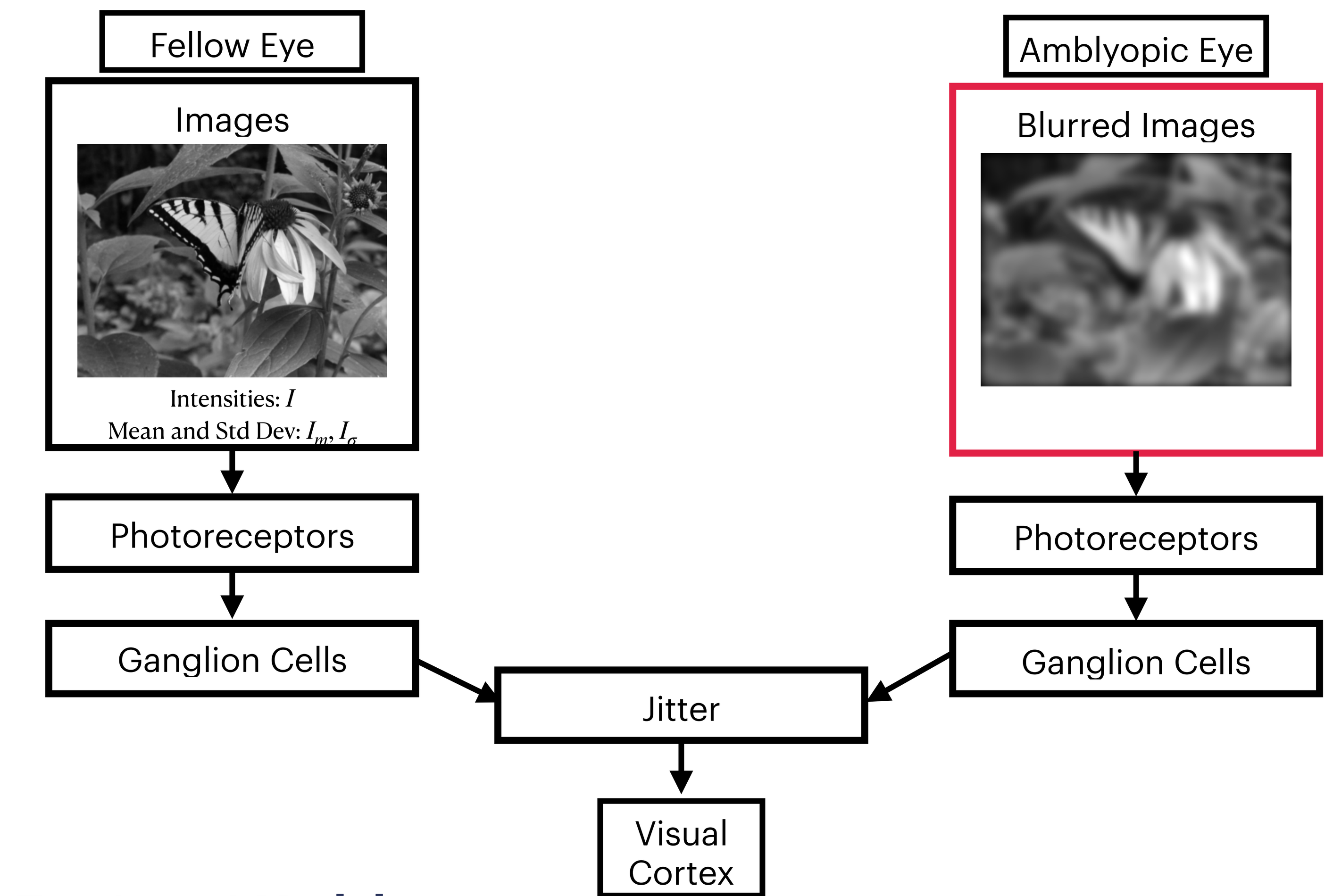

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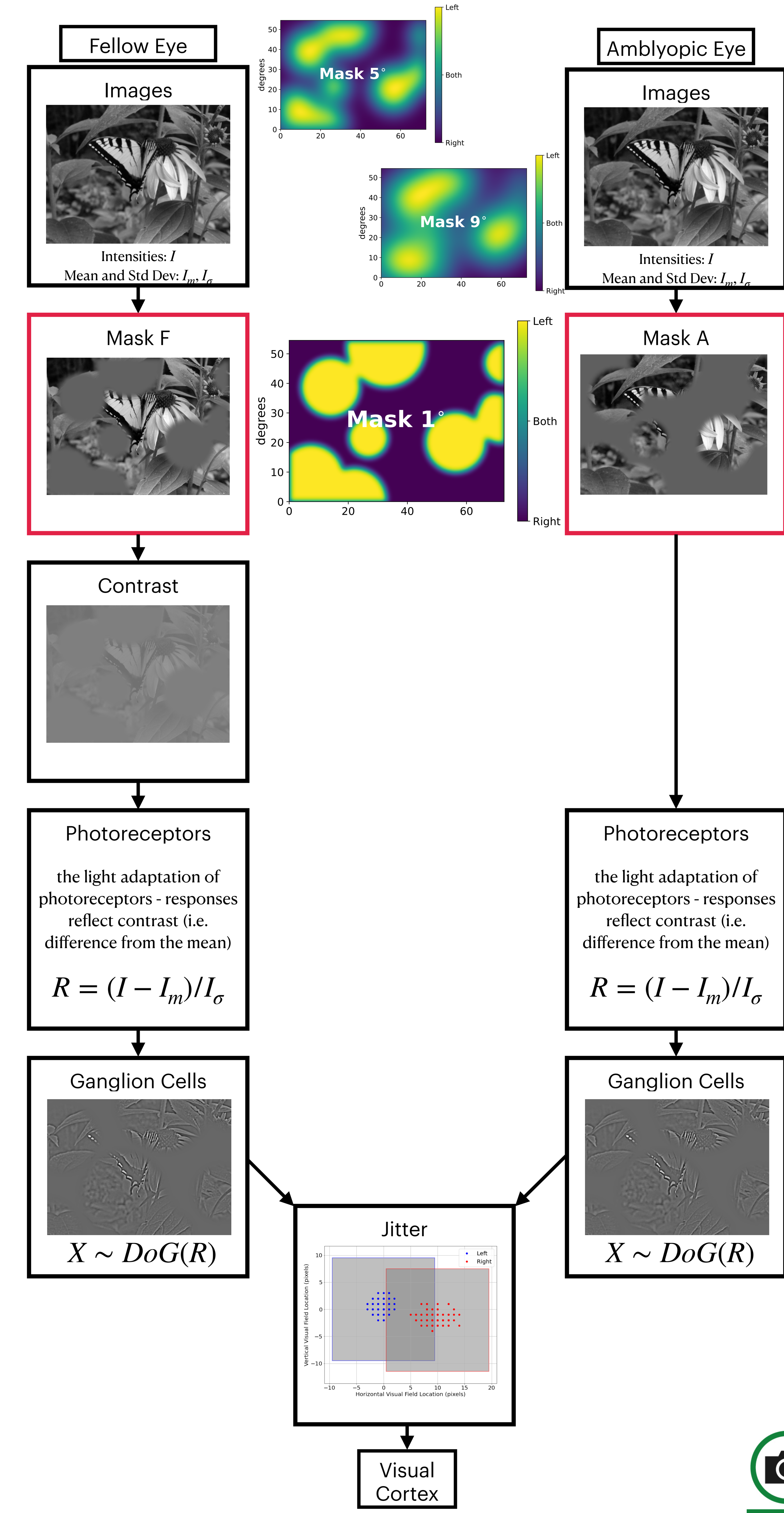

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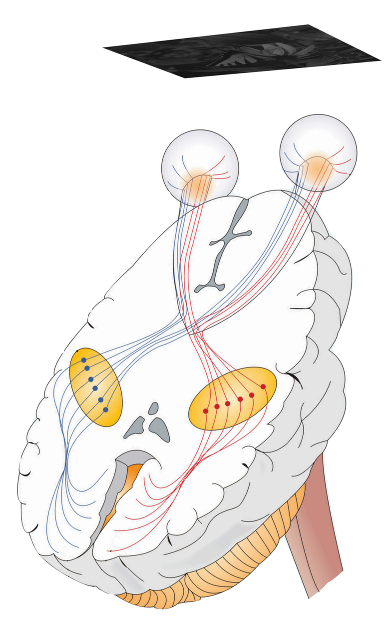

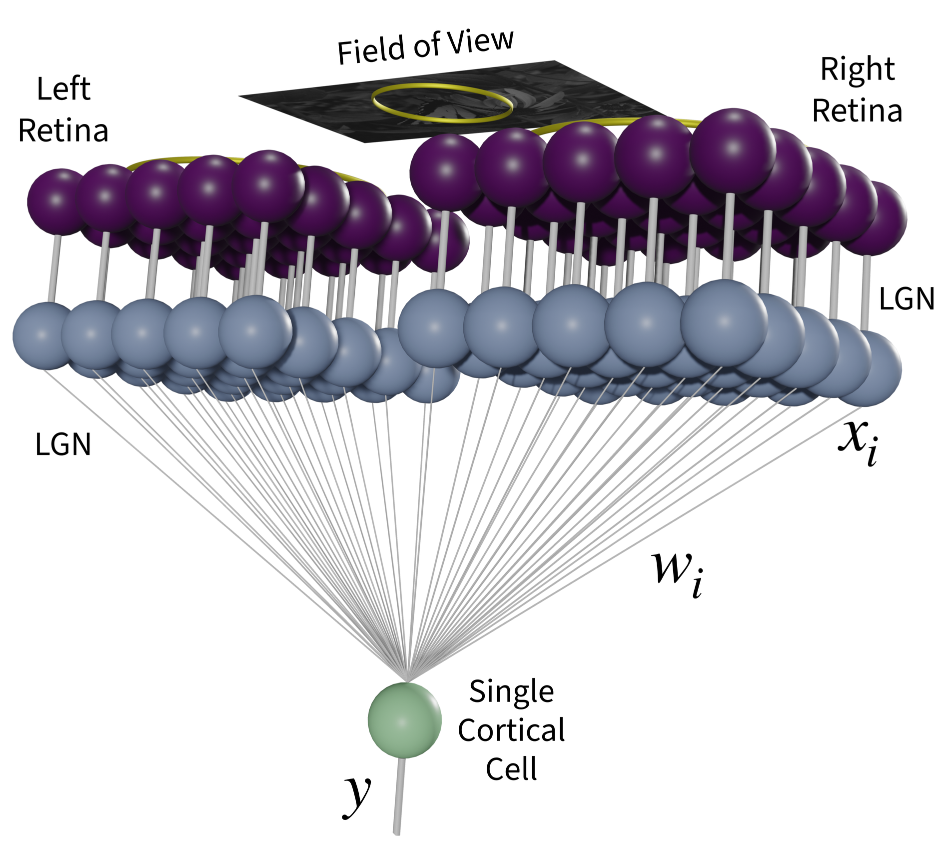

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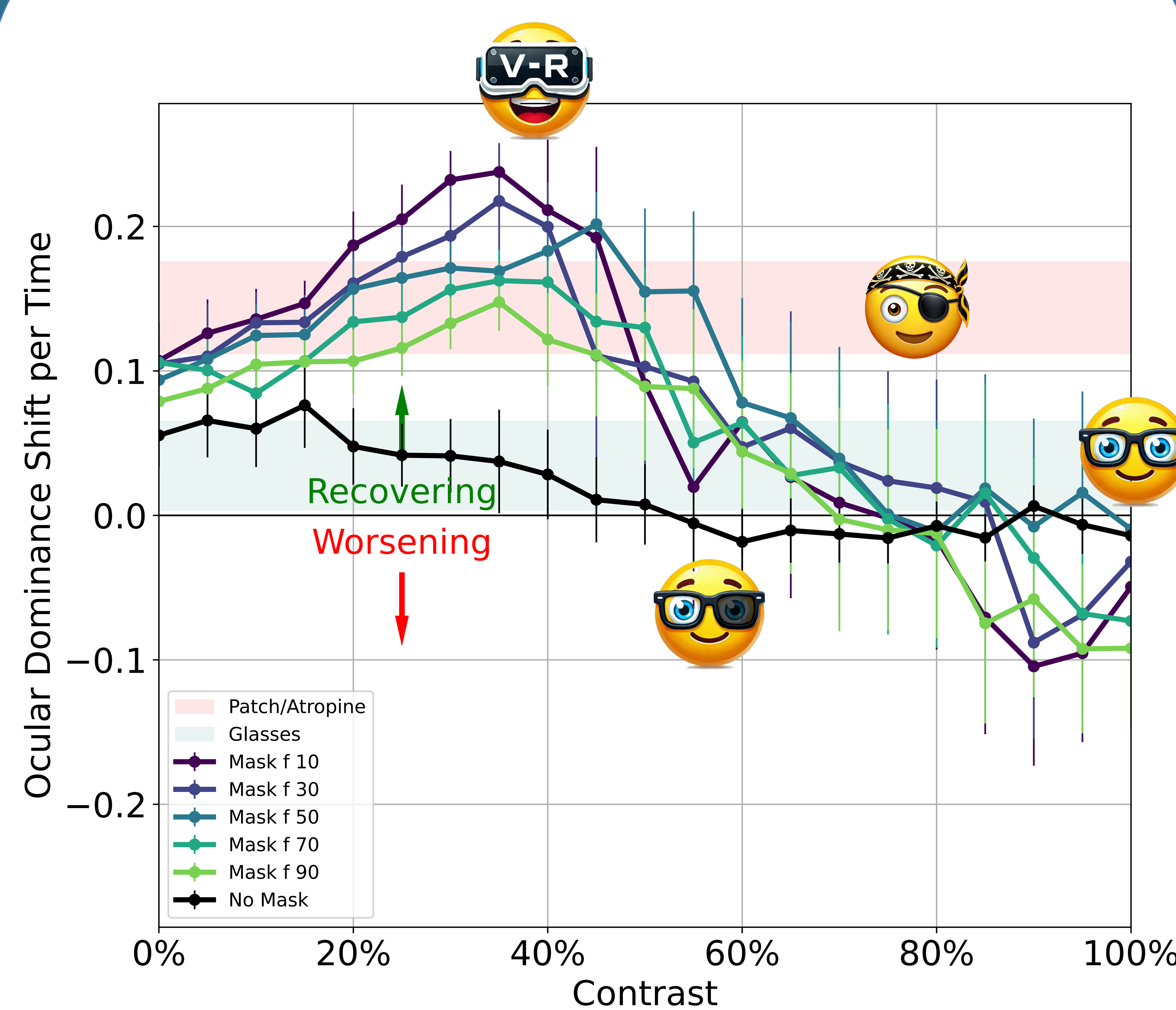

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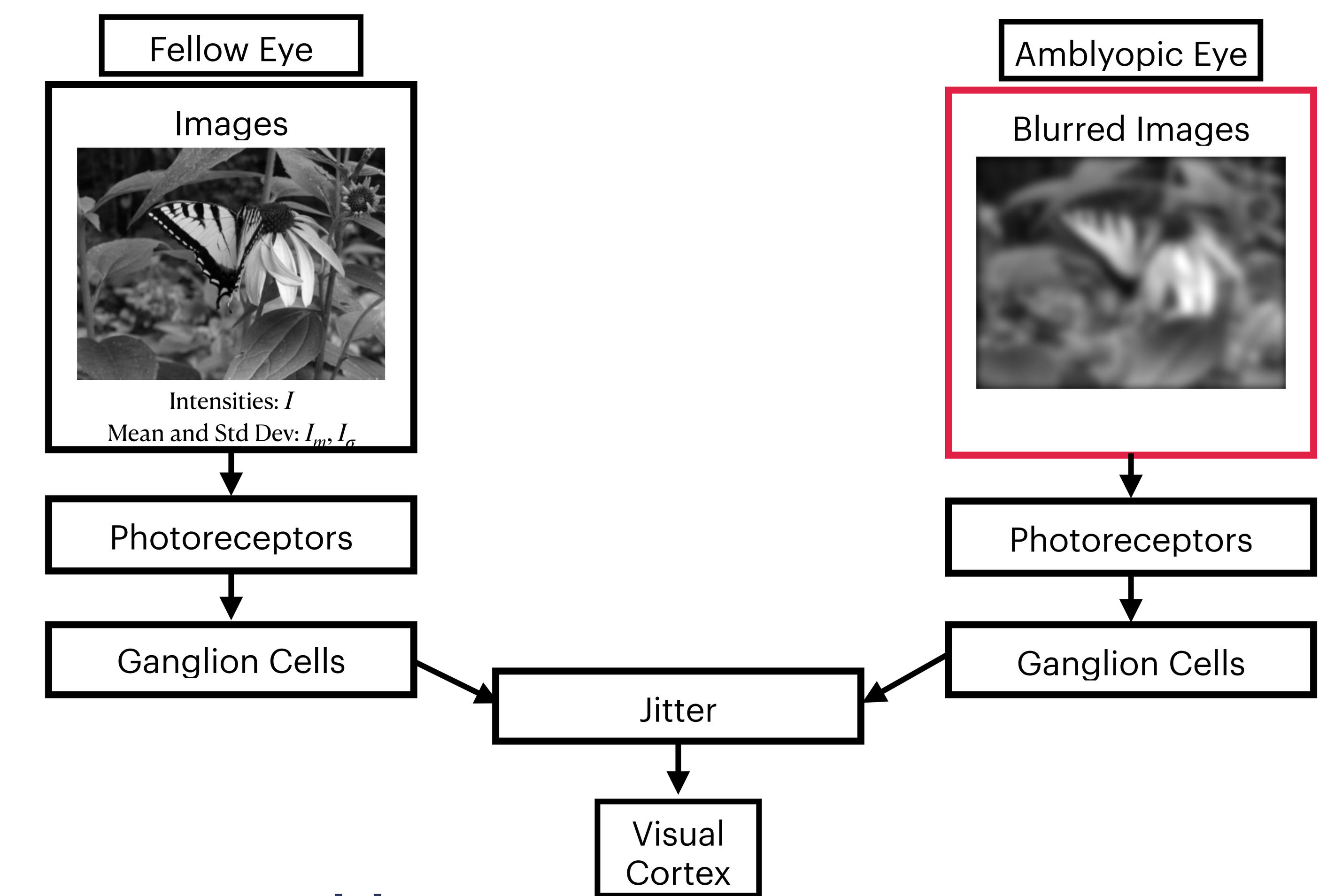

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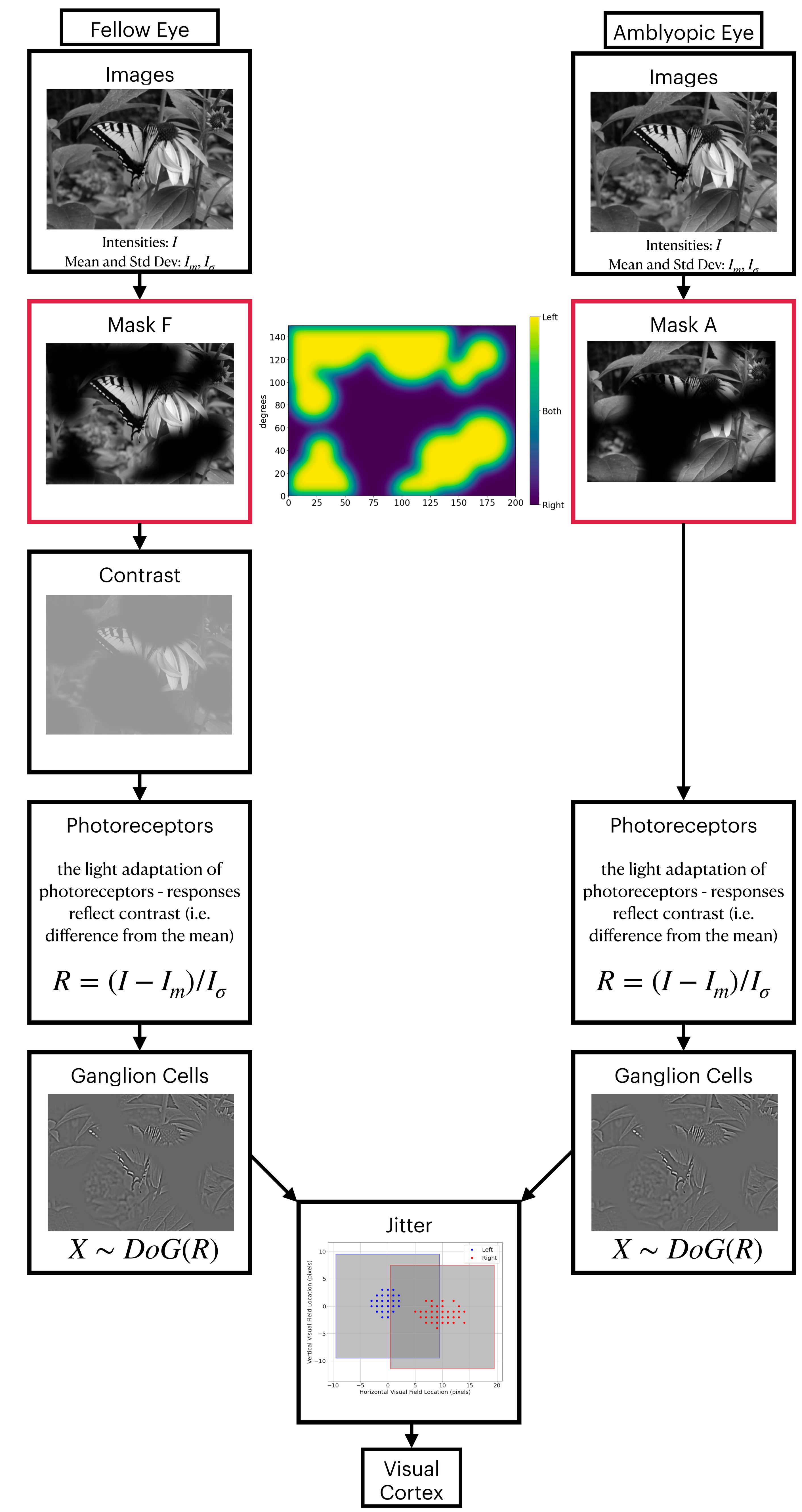

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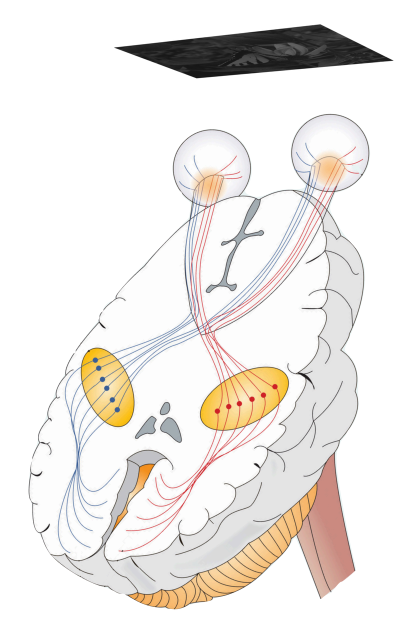

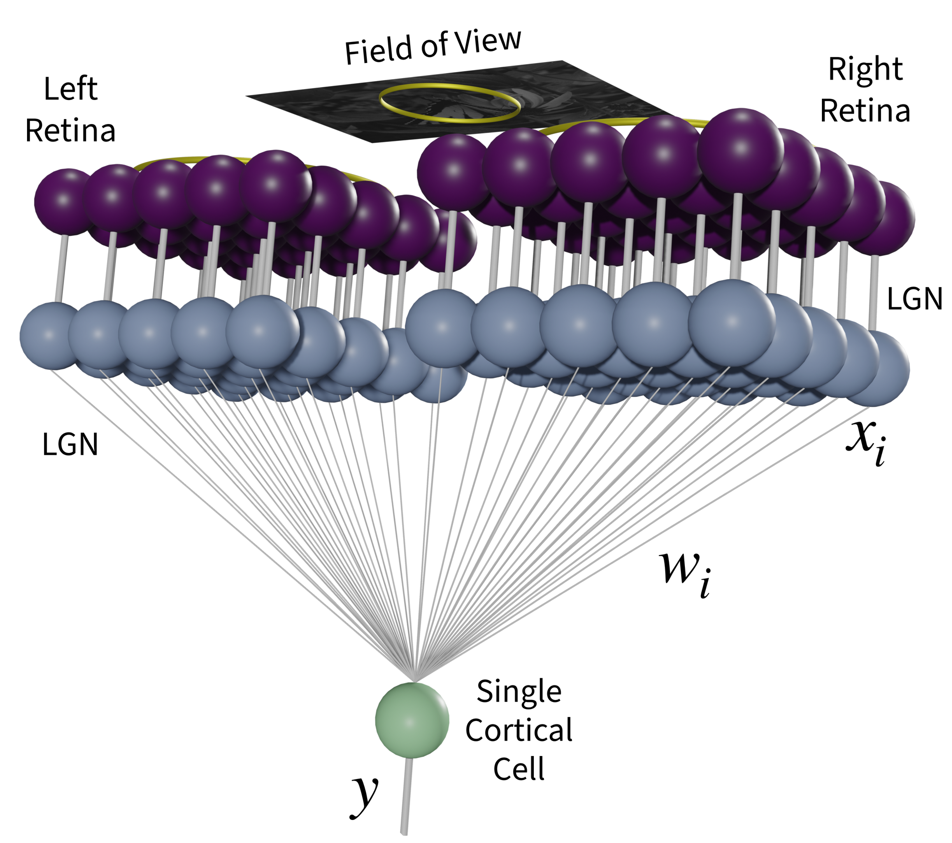

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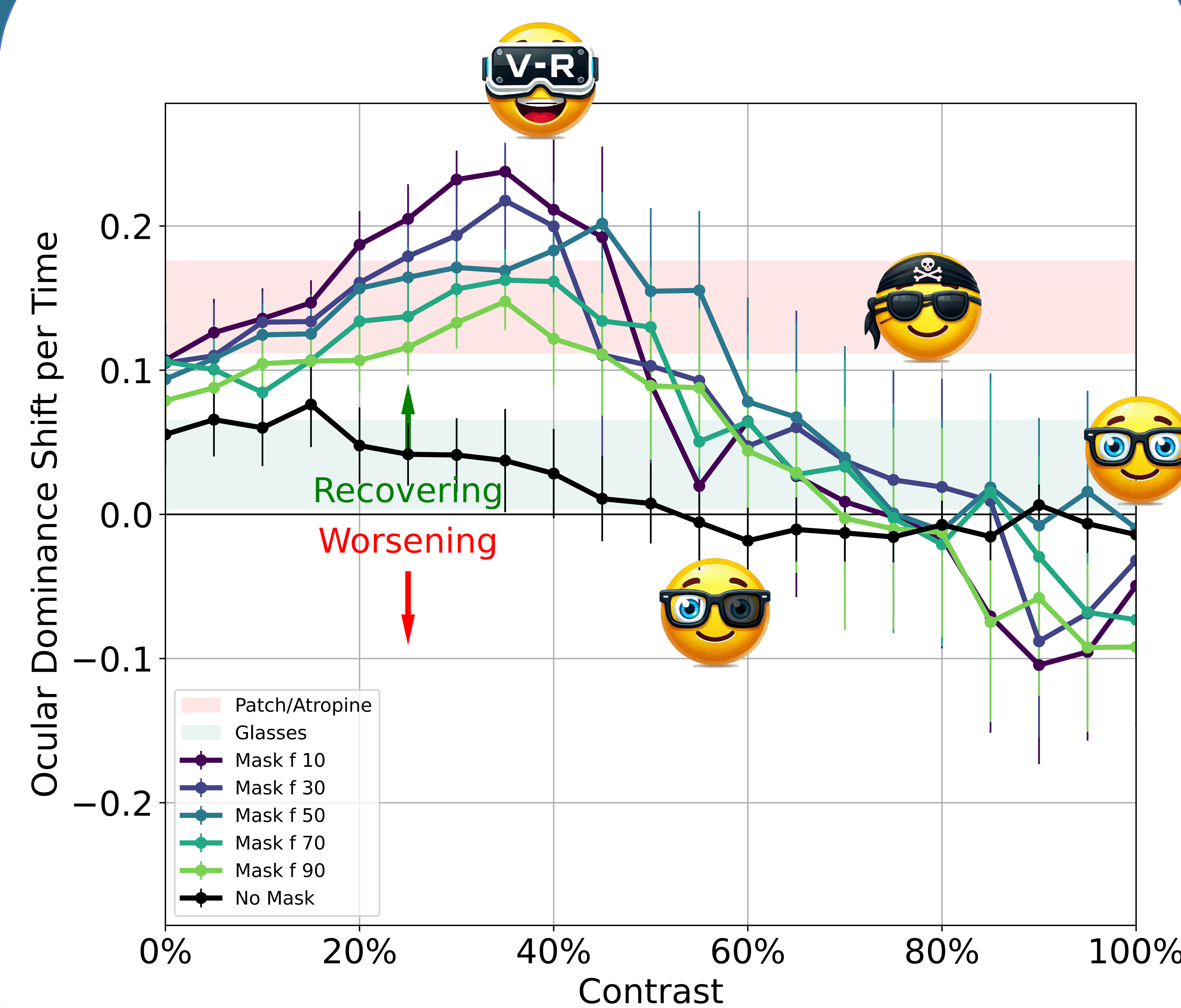

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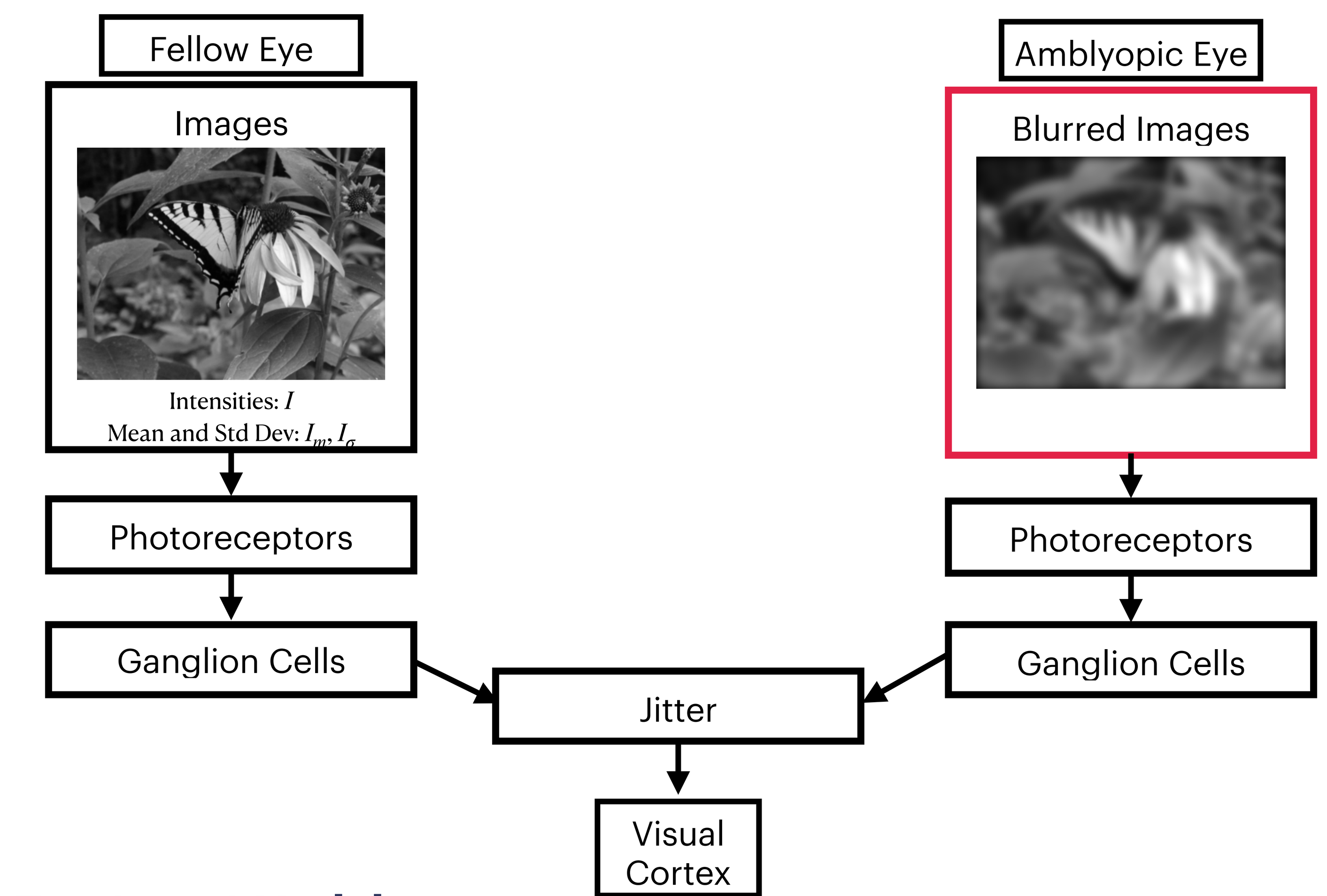

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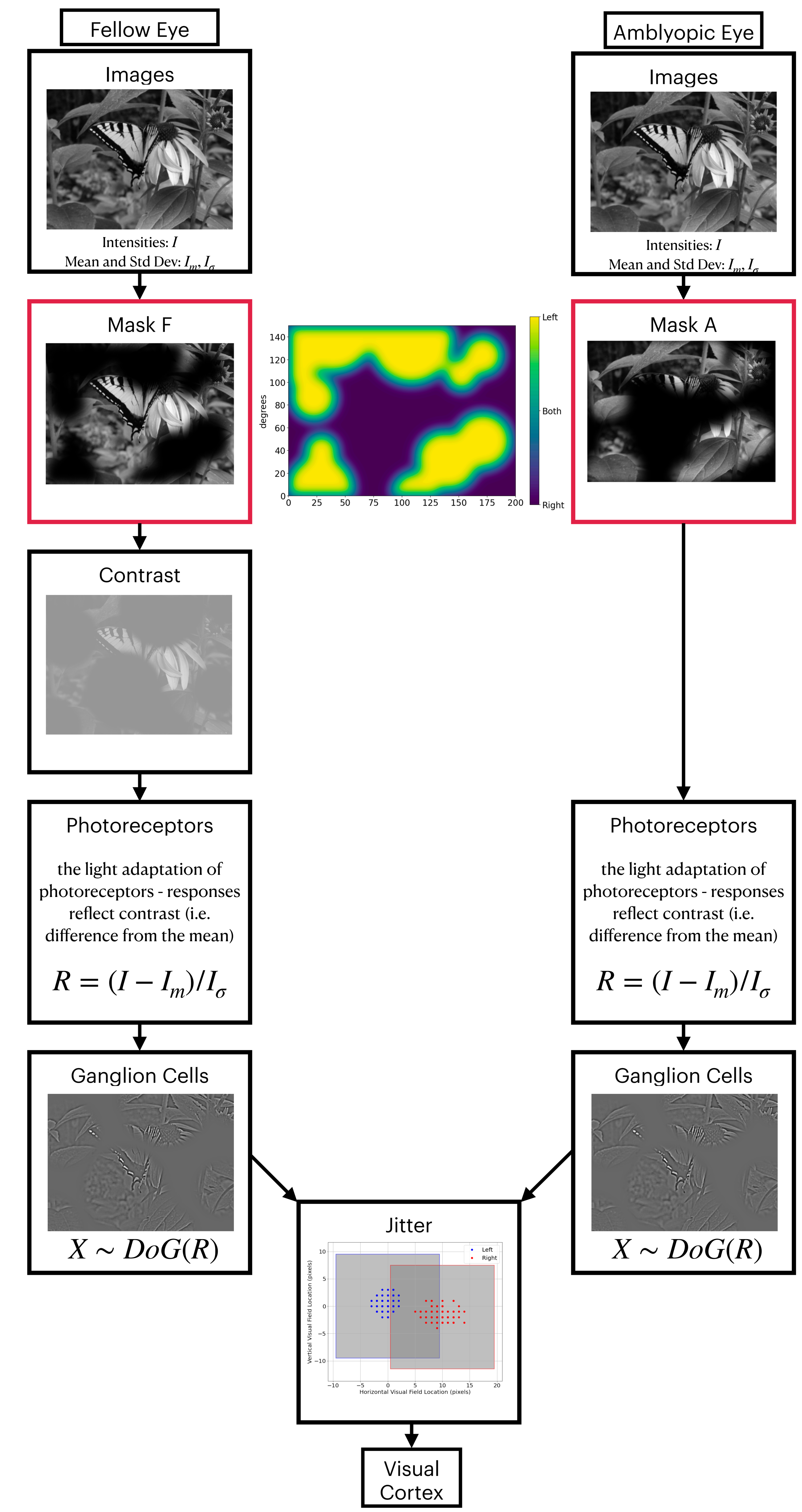

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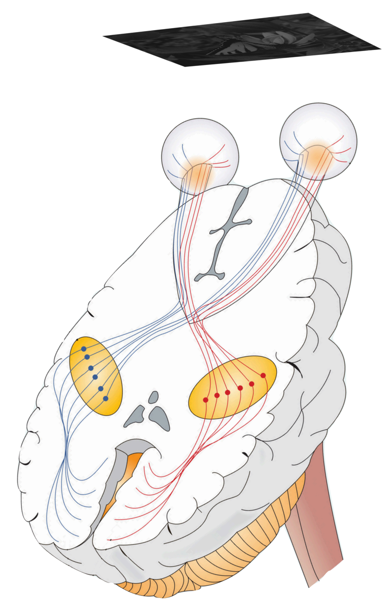

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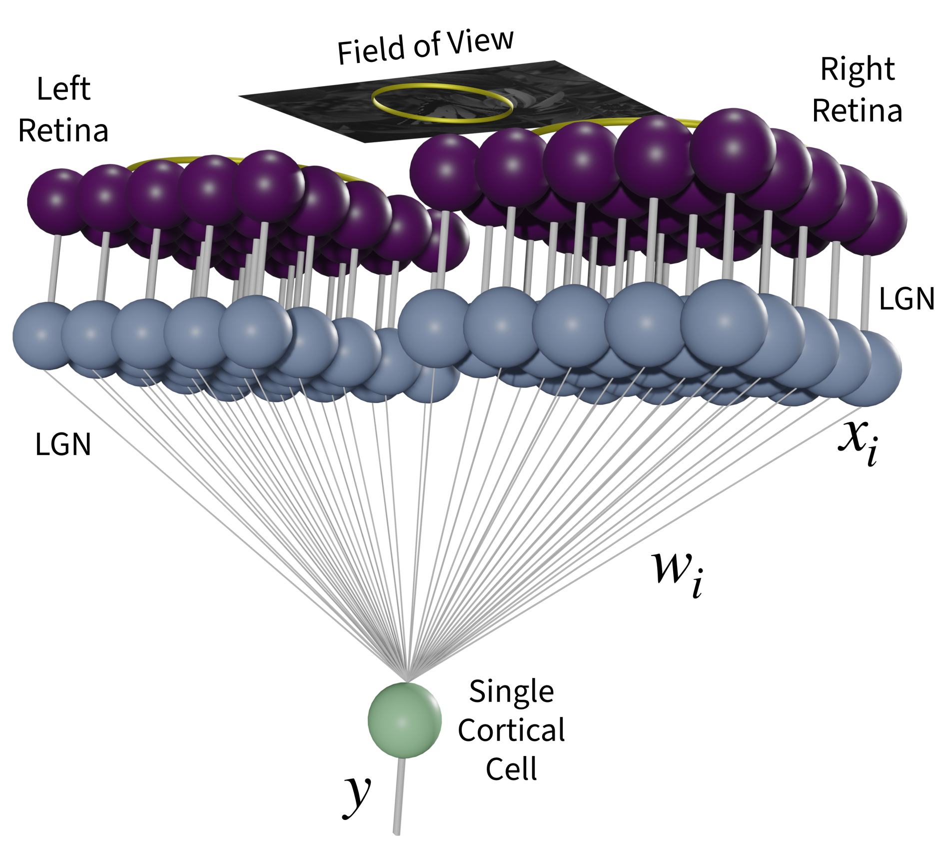

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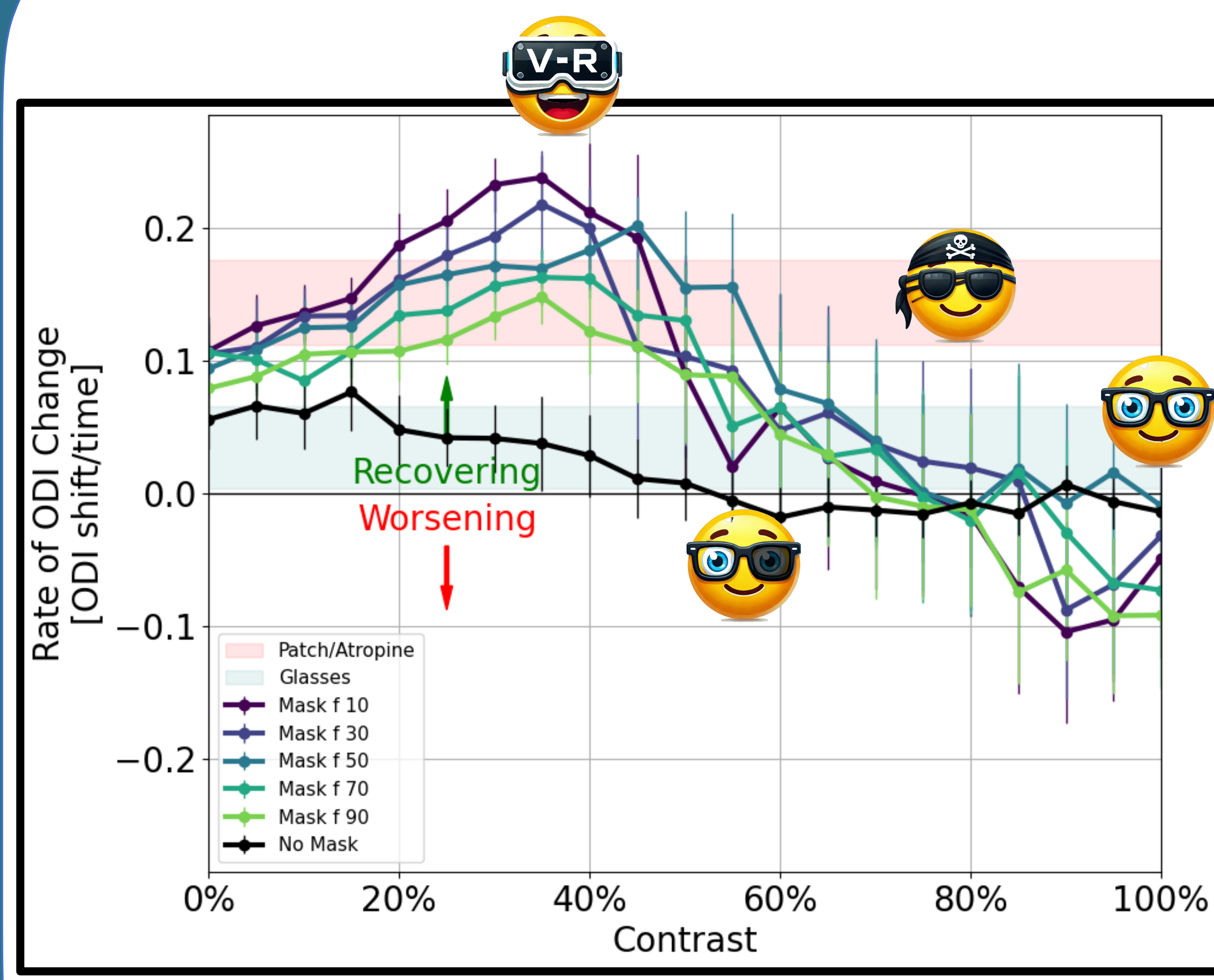

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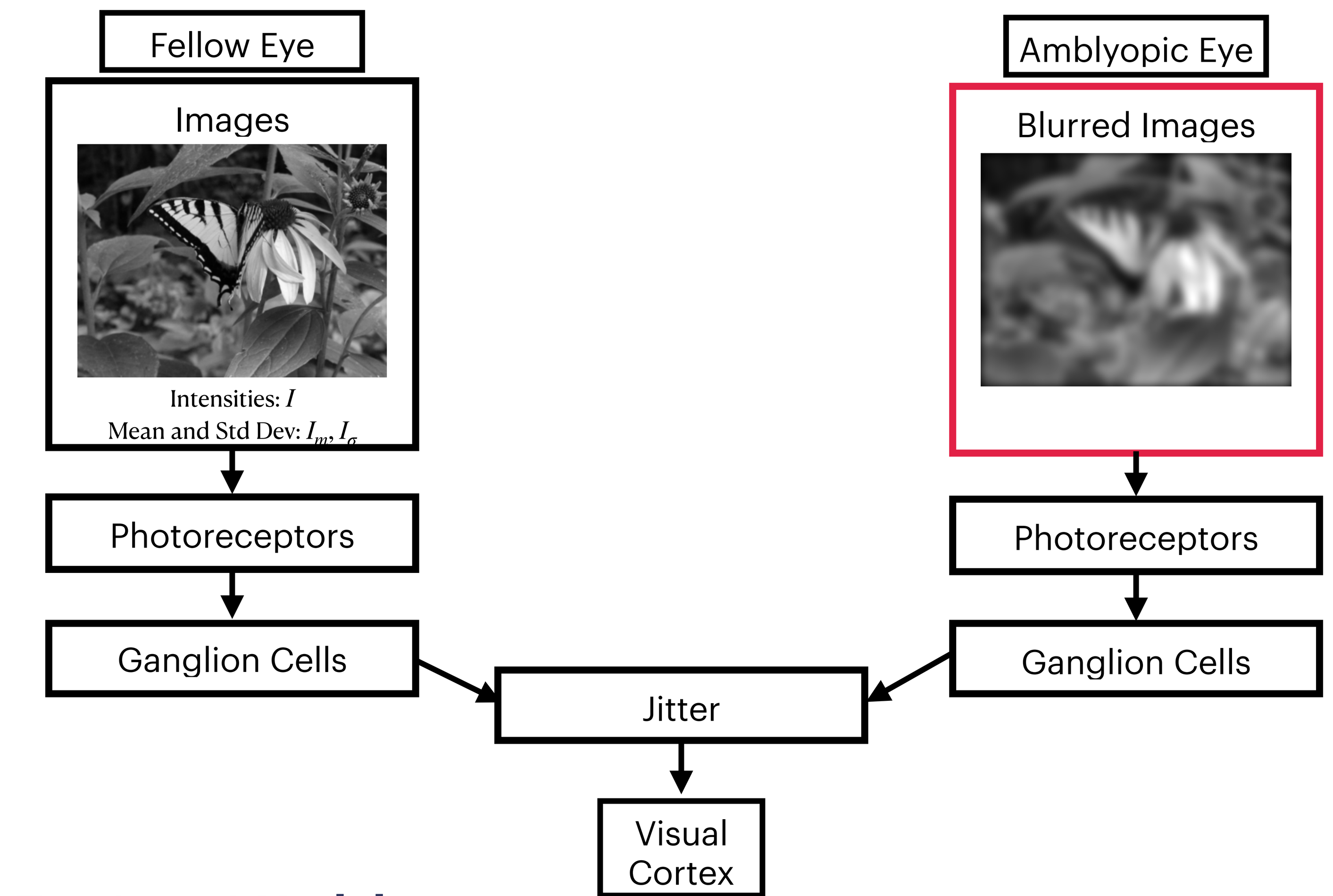

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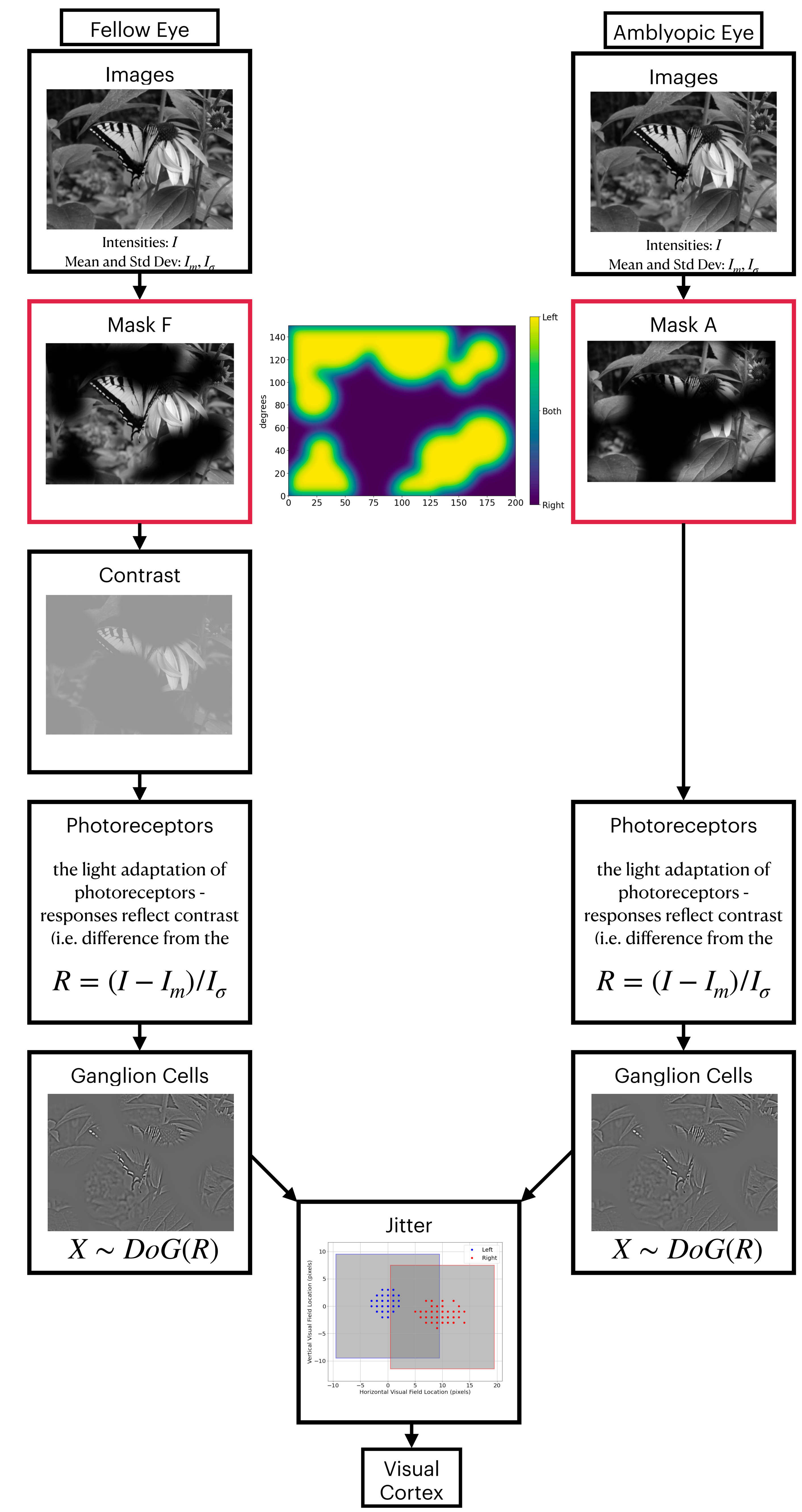

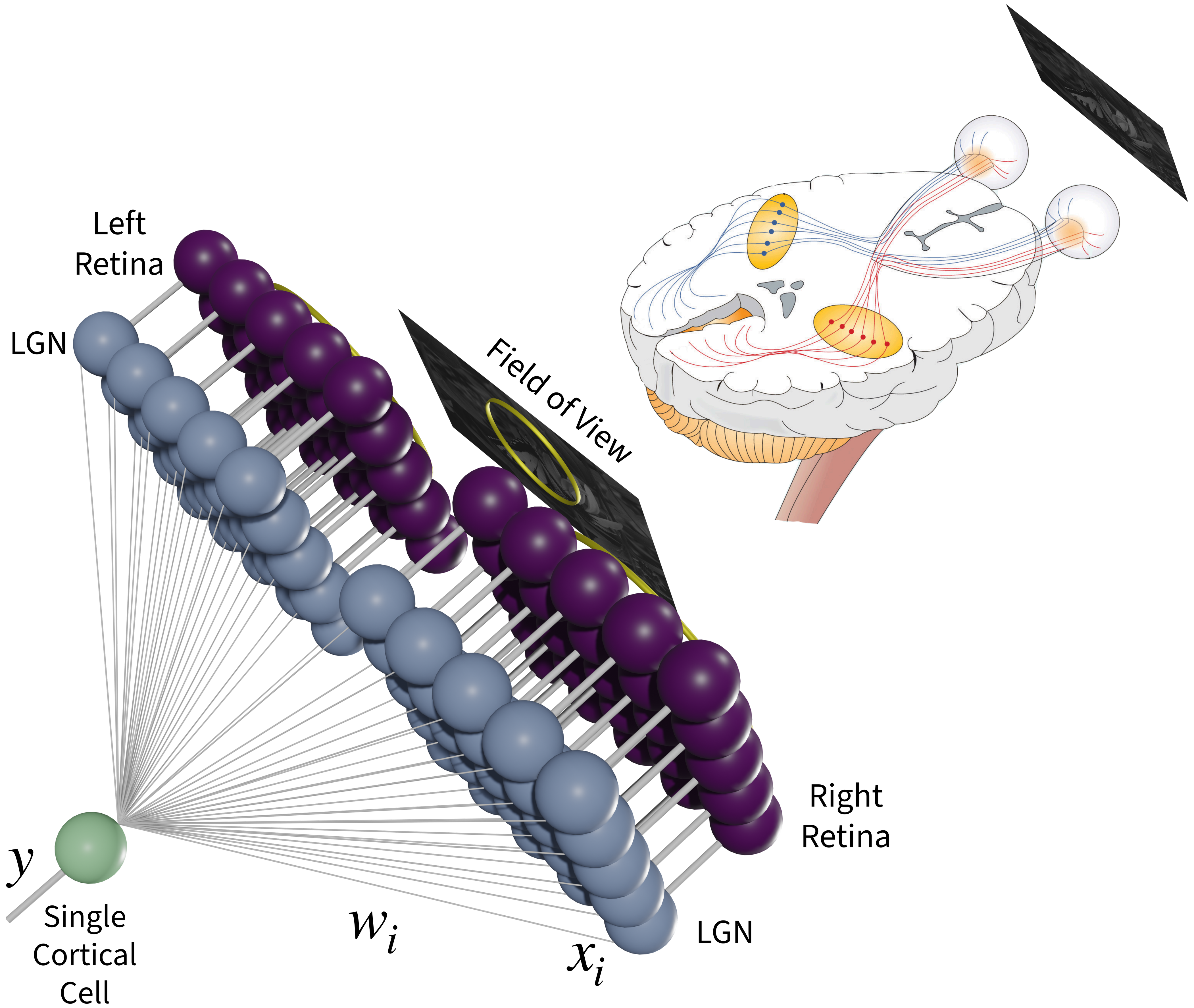
Left Retina
LGN
Field of View
Right Retina
LGN
y
Single Cortical Cell
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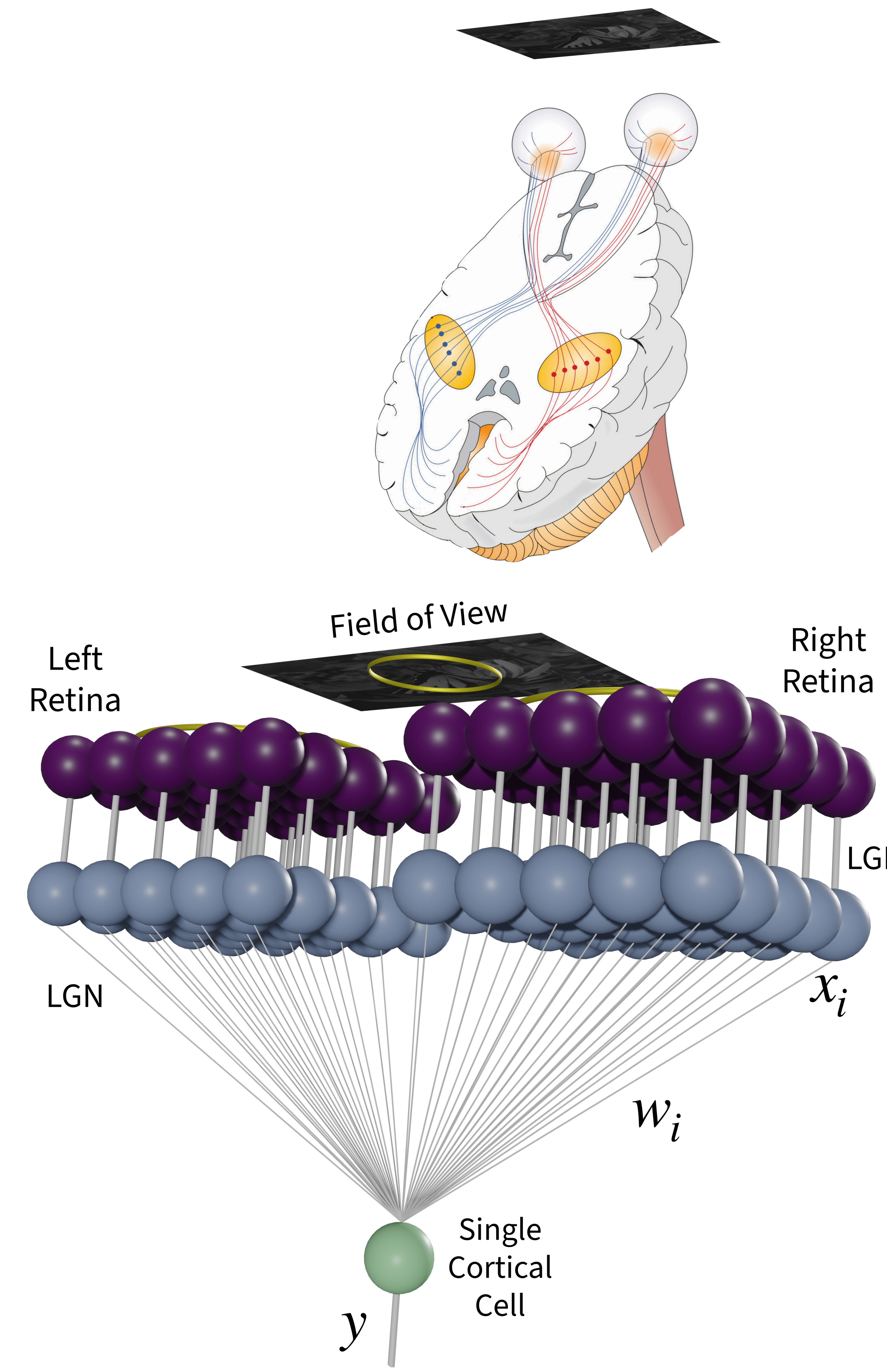
x_i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Modeling amblyopia treatment responses through principles of synaptic plasticity

Brian Blais[1], Eric Gaier[2,3], Scott Xiao[4]

[1]Department of Science, Bryant University
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[3]Department of Ophthalmology, Boston Children's Hospital, Harvard Medical School
[4]Luminopia

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Purpose

Amblyopia is a common cause of visual impairment that results from unequal visual inputs during development. The imbalance is known to manifest through synaptic alterations in visual cortex that shift ocular dominance. Understanding the effects of amblyogenic drivers and their reversal with synaptic plasticity could enable improvements in amblyopia treatment efficacy. This study uses a specific model of activity-dependent neural plasticity, the Bienenstock, Cooper, and Munro (BCM) model, to compare the dynamics of amblyopia recovery at the neuronal level under several treatment protocols, including optical correction, patching, atropine penalization, and binocular therapies.

Methods: Model Construction

- Model of the single cortical cell
- Natural scene stimuli from two eyes
- Thalamocortical synaptic modification obeys the BCM learning rule
- Competition between *patterns* in the two eyes drives changes in ocular dominance

BCM equations for Synaptic Plasticity

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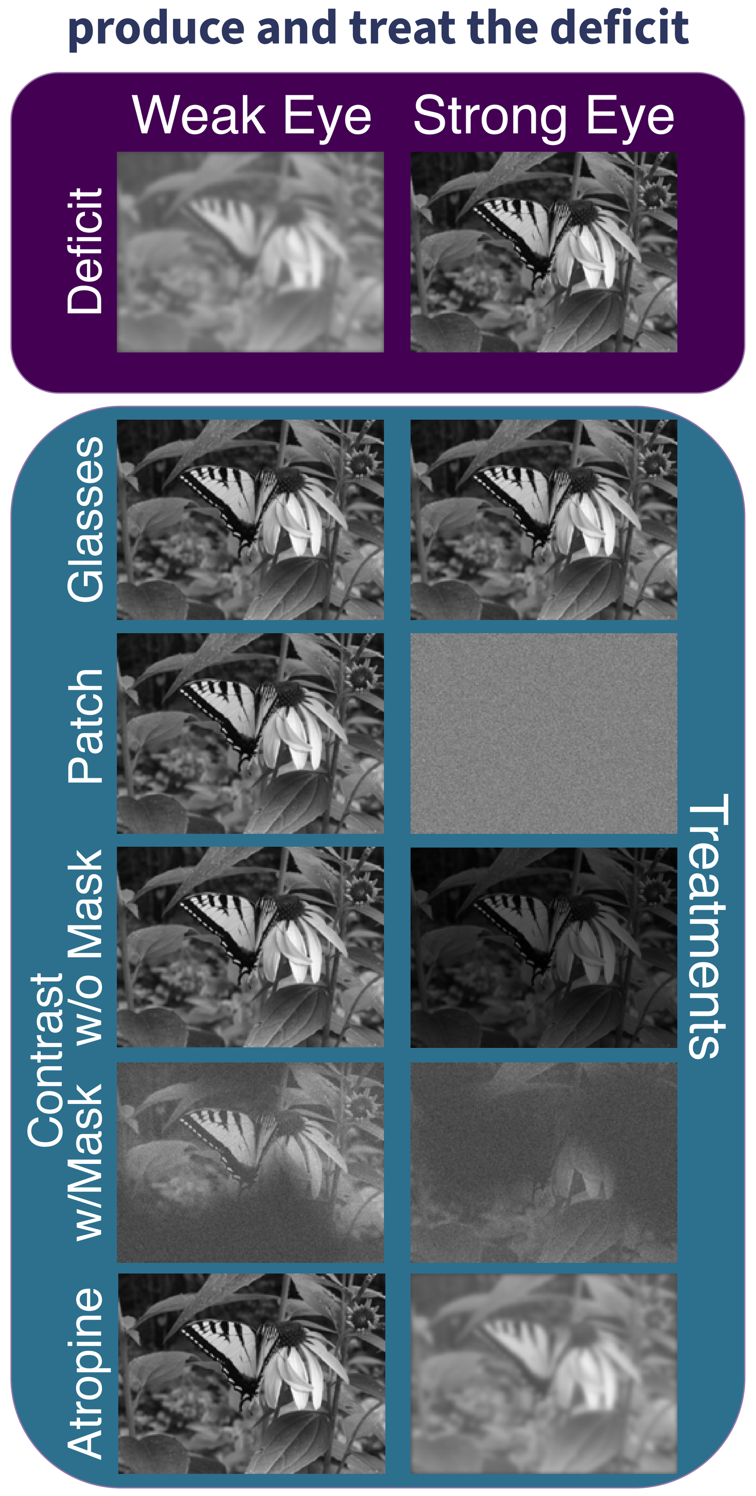
Methods: Interventions

- Anisometropic amblyopia is modeled by blurring input to the affected eye
- The fix (with glasses) rebalances the structure of inputs
- Patching is modeled with unstructured activity (noise) in the fellow eye
- Atropine penalization uses both noise and blurred input to the fellow eye
- Binocular therapies involving contrast modification and dichoptic masks are modeled with established input filters

Example input image to the weak- and strong-eyes to produce and treat the deficit



Results

- Imbalanced structure of inputs produce a long-lasting ocular dominance shift in favor of the one eye (usually the fellow eye)
- Rate of recovery increases with greater input *pattern* disparity.
- Rate of recovery is greater with patch and atropine treatment models as compared to contrast disparity alone
- Addition of dichoptic masks enhances the rate of recovery with the binocular treatment model
- Rate of recovery with binocular treatment comparable to or faster than patch treatment, parameter dependent

References

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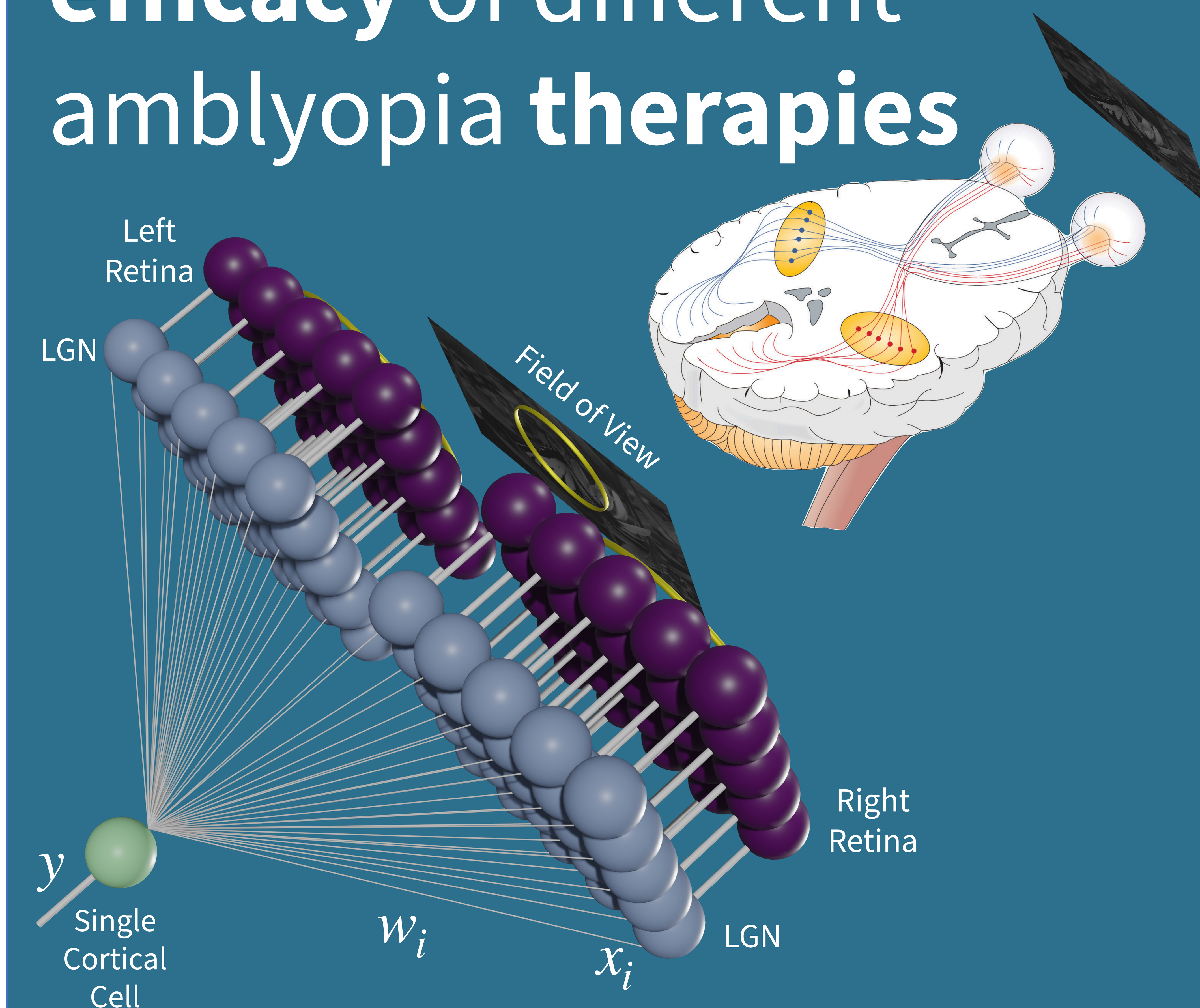
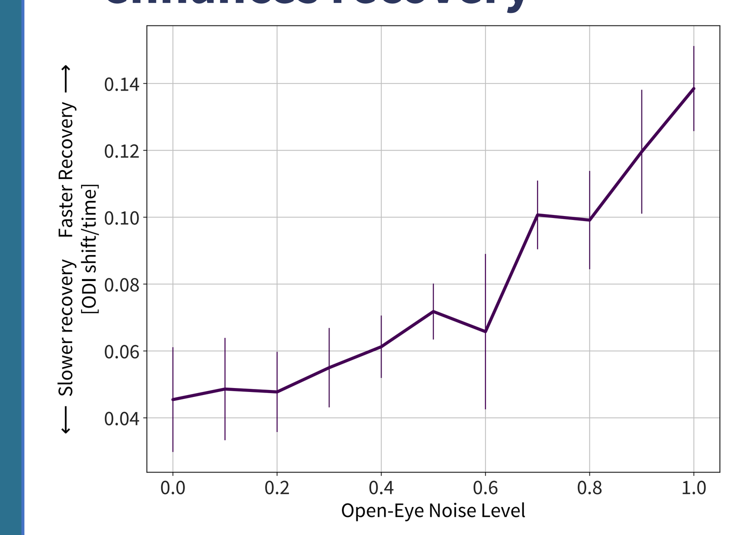
Synaptic plasticity **models** help us **understand** the **efficacy** of different amblyopia **therapies**



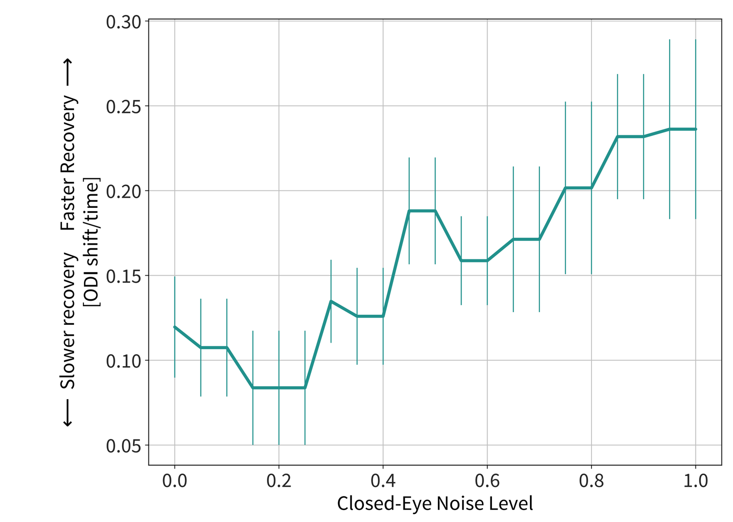
Discussion

Simulations demonstrate that masks enhance the contrast-based therapy	Simulations demonstrate the relative rates of recovery under different treatment protocols
Rate of recovery with binocular treatment comparable to or faster than patch treatment, parameter dependent	
Models allow us to explore the statistics of the input patterns and their affect on plasticity and cortical activity	Models allow us to spin out many scenarios that would be prohibitive to do experimentally

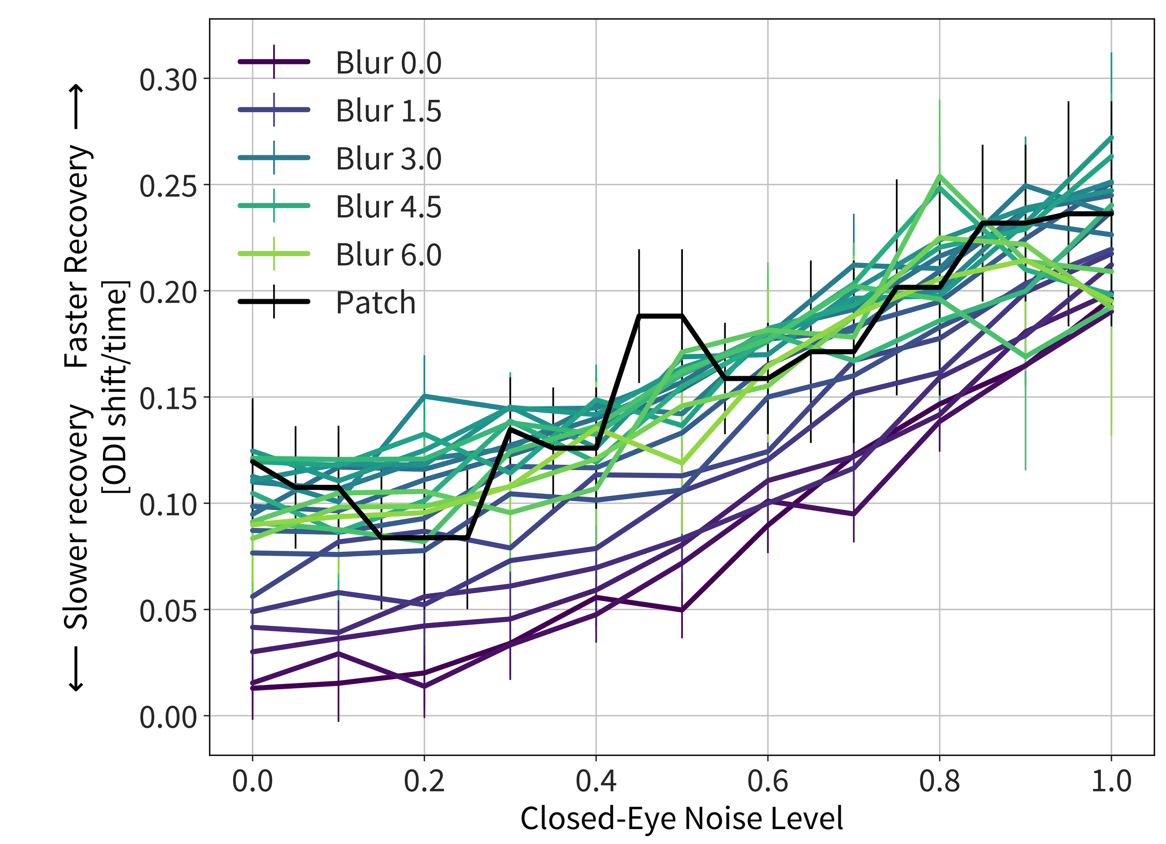
Glasses: open-eye noise enhances recovery



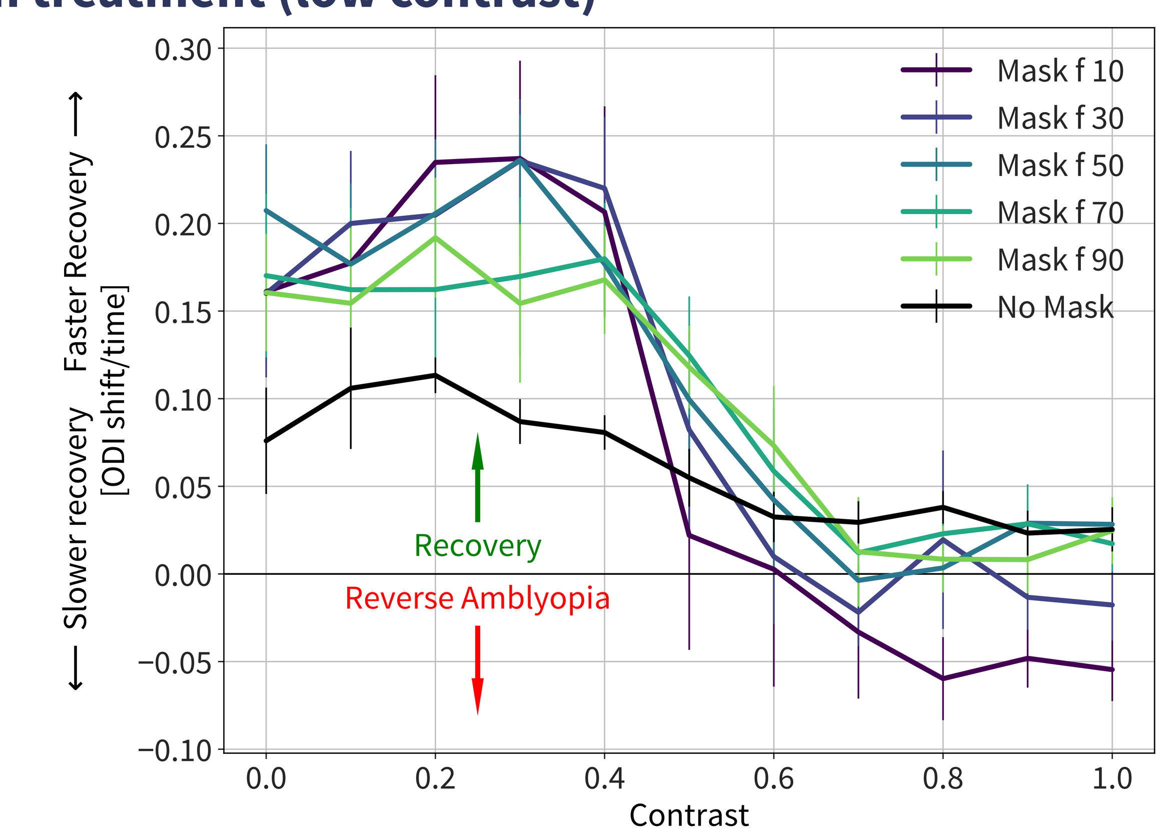
Patch Treatment: closed-eye noise enhances recovery



Patch treatment comparable or faster than atropine treatment



Contrast+Mask faster than contrast-only and comparable to patch treatment (low contrast)



Limitations

- Model uses ocular dominance instead of spatial frequency for convenience
- Model does not use network inhibition or downstream decision processes for simplicity

Clinically relevant future directions

- Plateauing in patch treatment → Reduction in learning rate over time
- Critical period → Explicit role of inhibition and its changes
- Treatment contrast level changes over recovery → Include time-dependent contrast levels
- Interocular suppression → Include additional activity-effect in learning rule

Discussion (cont.)

- Simulations also demonstrate the underlying neural parameters (e.g. activity variability)
- Model highlights the differences between traditional monocular therapies and binocular therapies

Synaptic plasticity models predict that binocular treatments for amblyopia can outperform monocular treatments

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Purpose

Amblyopia is a common cause of visual impairment that results from unequal visual inputs during development, known to manifest through synaptic alterations in the visual cortex. What is not known is the detailed mechanisms of these synaptic changes and how these mechanisms impact the dynamics of recovery. Here we use a computational model of neural plasticity to compare multiple treatment strategies.

Methods

This study used a specific model of activity-dependent neural plasticity, the Bienenstock, Cooper, and Munro (BCM) model, to compare the dynamics of amblyopia recovery at the neuronal level under several treatment protocols, including optical correction, patching, atropine penalization, and binocular therapies. This study extends prior work in this area by exploring multiple sources for amblyogenesis including refractive error and strabismus, and it compares multiple treatment protocols.

BCM equations for Synaptic Plasticity

$$y = \sigma\left(\sum_i x_i w_i\right)$$

$$\frac{dw_i}{dt} = \eta y (y - \theta_M) x_i$$

$$\frac{d\theta_M}{dt} = (y^2 - \theta_M)/\tau$$

Results

BCM modeling recapitulated anisometropic amblyopia, but ocular dominance remained stable even when simulating large angle strabismus. The recovery achieved with dichoptic masks combined with an interocular contrast disparity exceeded that of patch and atropine treatments. Patch and atropine treatment models produced faster recovery compared to a contrast disparity alone, highlighting the importance of the dichoptic masks. The rate of recovery depended on treatment features such as the size of the dichoptic masks and the magnitude of the contrast disparity, both experimentally accessible. The model suggests optimal values for these modifications.

Conclusions

The BCM theory of synaptic plasticity is sufficient to model anisometropic but not all of strabismic amblyopia, suggesting additional aspects of synaptic plasticity and/or circuit dynamics that produce an ocular dominance shift with strabismus (e.g. suppression). The near infinite potential modifications and combinations of eye-selective visual input in dichoptic therapy cannot be practically tested in dedicated clinical trials. Computational modeling can thus serve as a useful tool to compare therapeutic approaches and make specific clinical predictions to answer key lingering questions and inform improvements to binocular treatments using principles of neuroplasticity.

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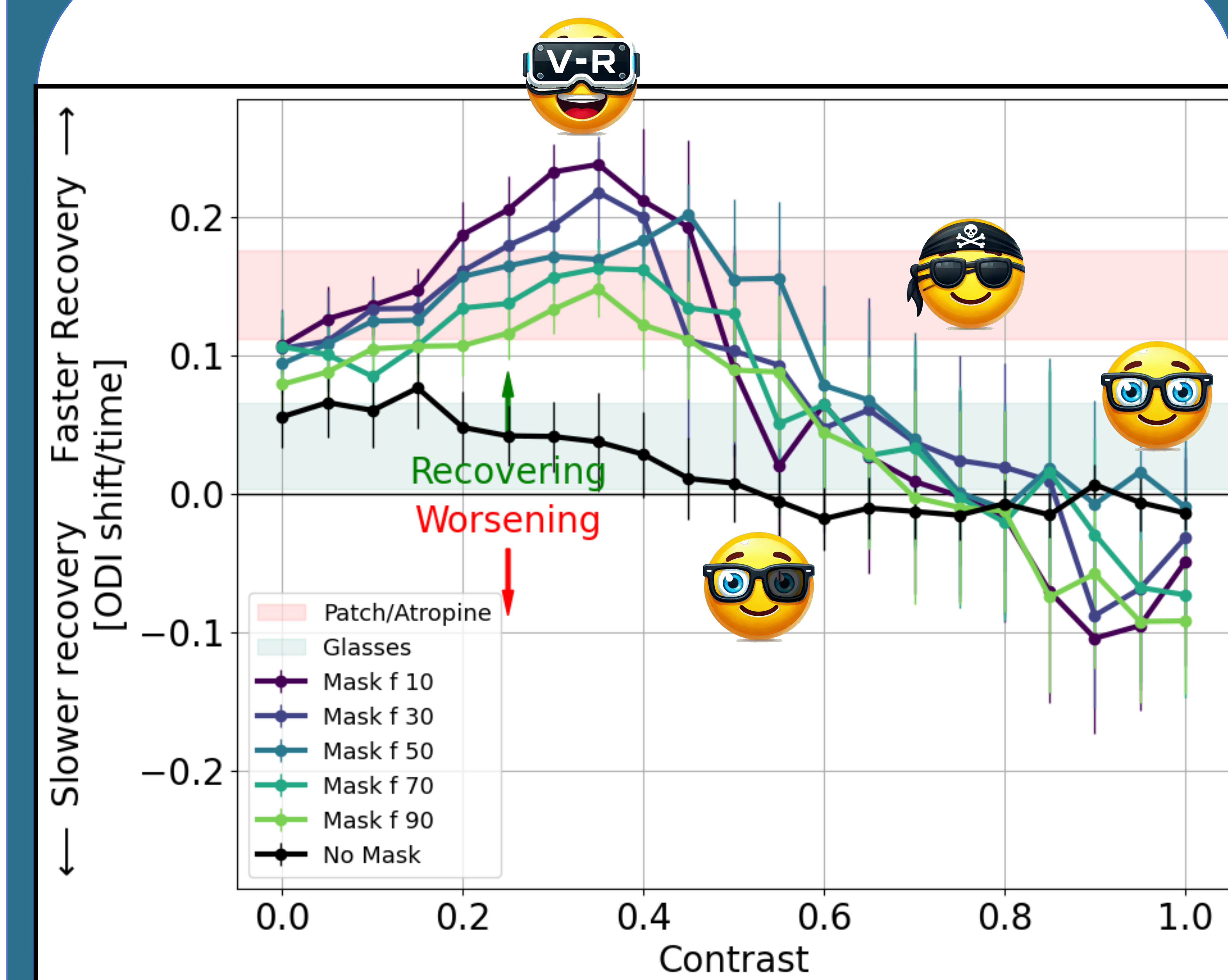
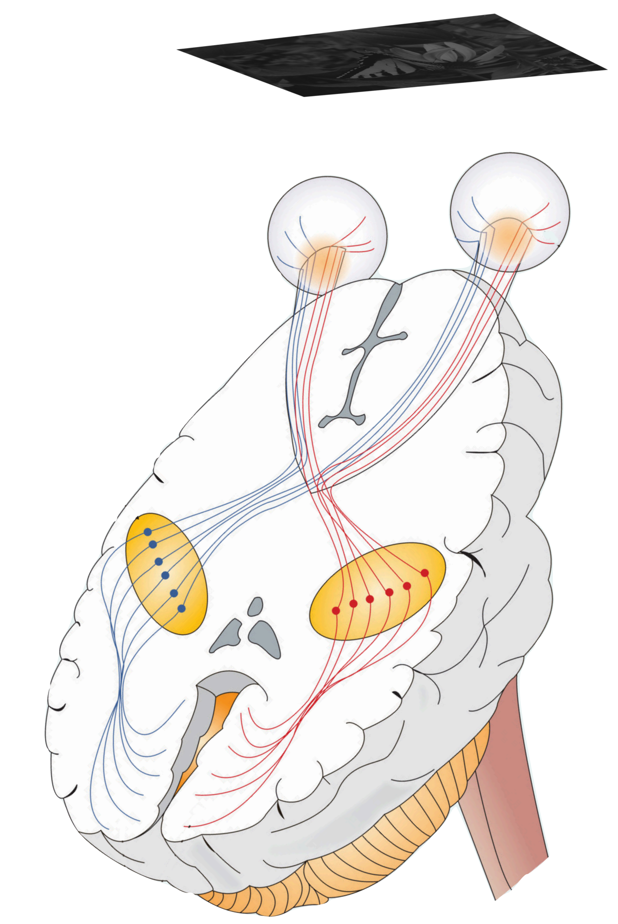
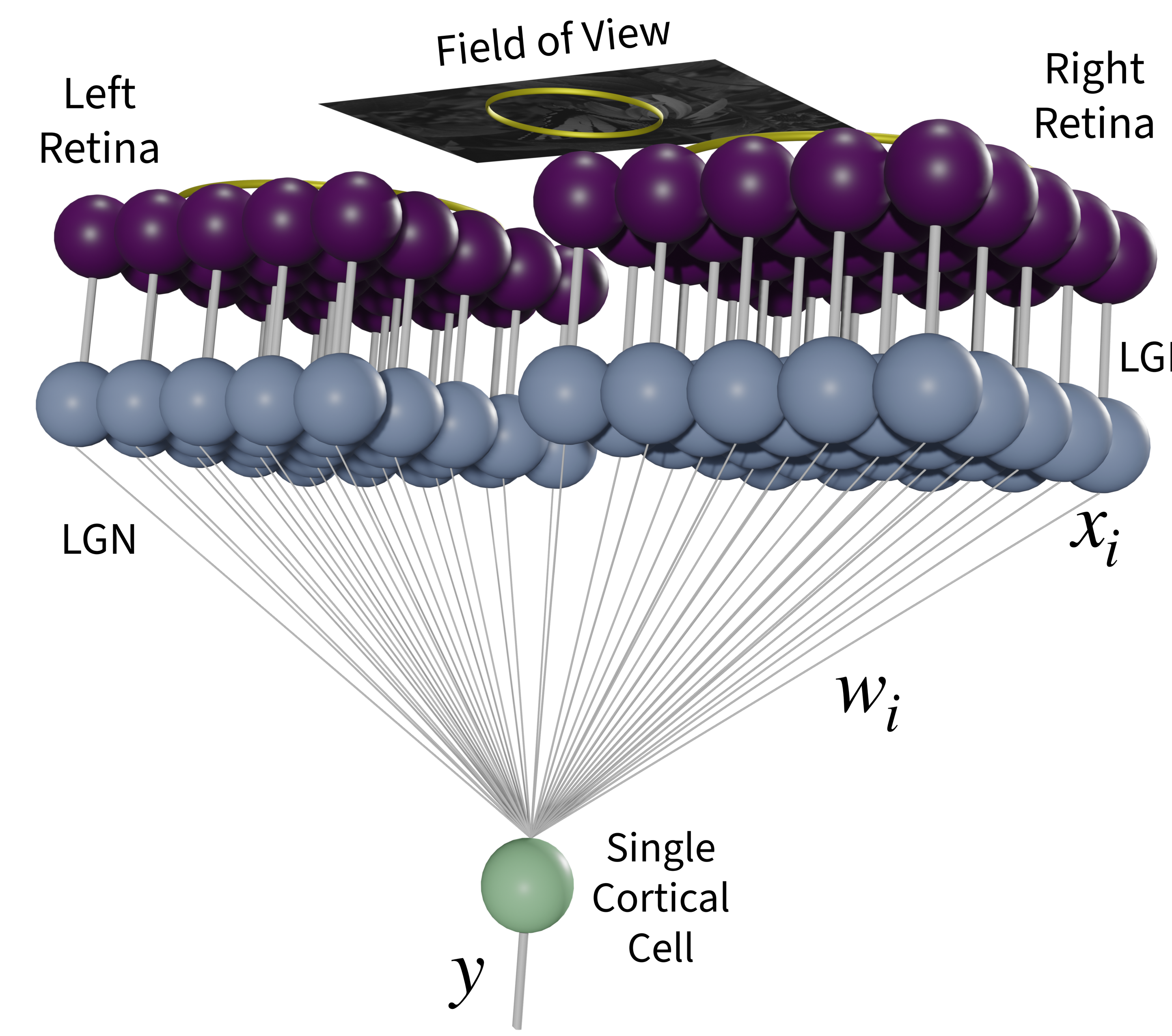
References

3/7/2025

Synaptic plasticity models predict that **binocular treatments** for amblyopia can <u>outperform</u> **monocular treatments**







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