Modeling amblyopia treatment responses through principles of synaptic plasticity

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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

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

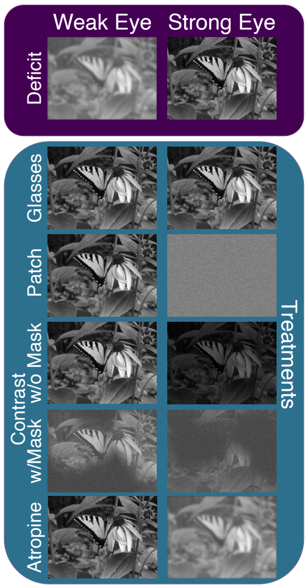
$$\frac{dw_i}{dt} = \eta y (y - \theta_M) x_i$$

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

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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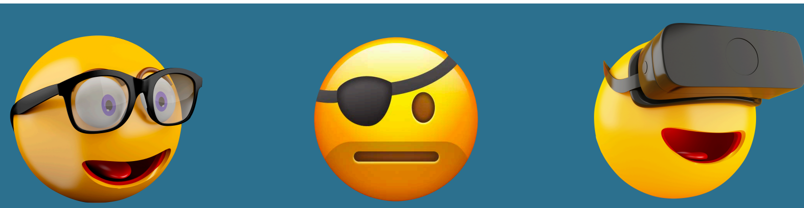
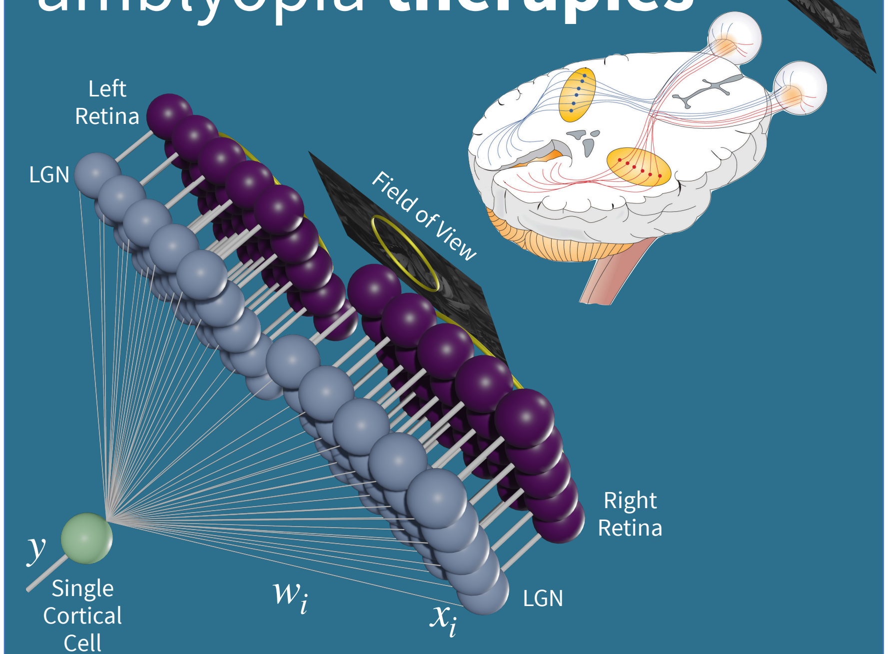


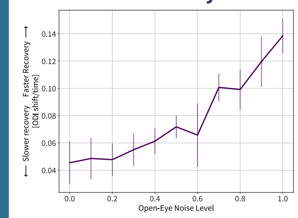
Synaptic plasticity **models** help us **understand** the **efficacy** of different amblyopia **therapies**



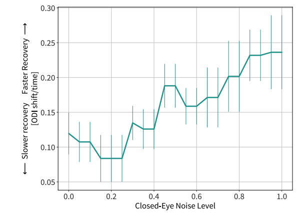
Discussion

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

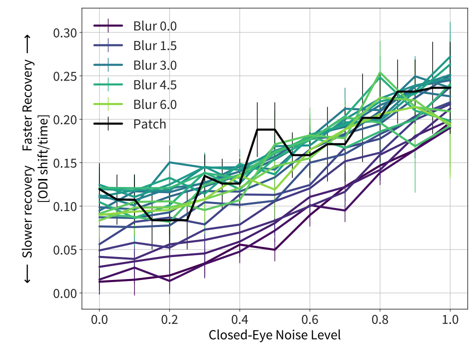
Glasses: open-eye noise enhances recovery



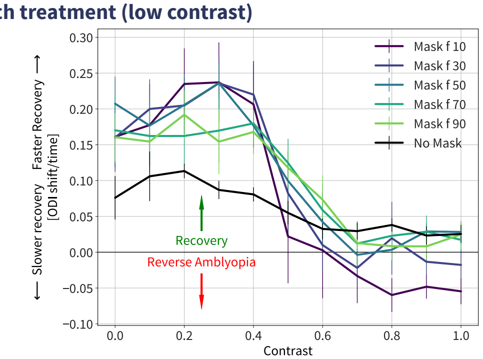
Patch Treatment: closed-eye noise enhances recovery



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