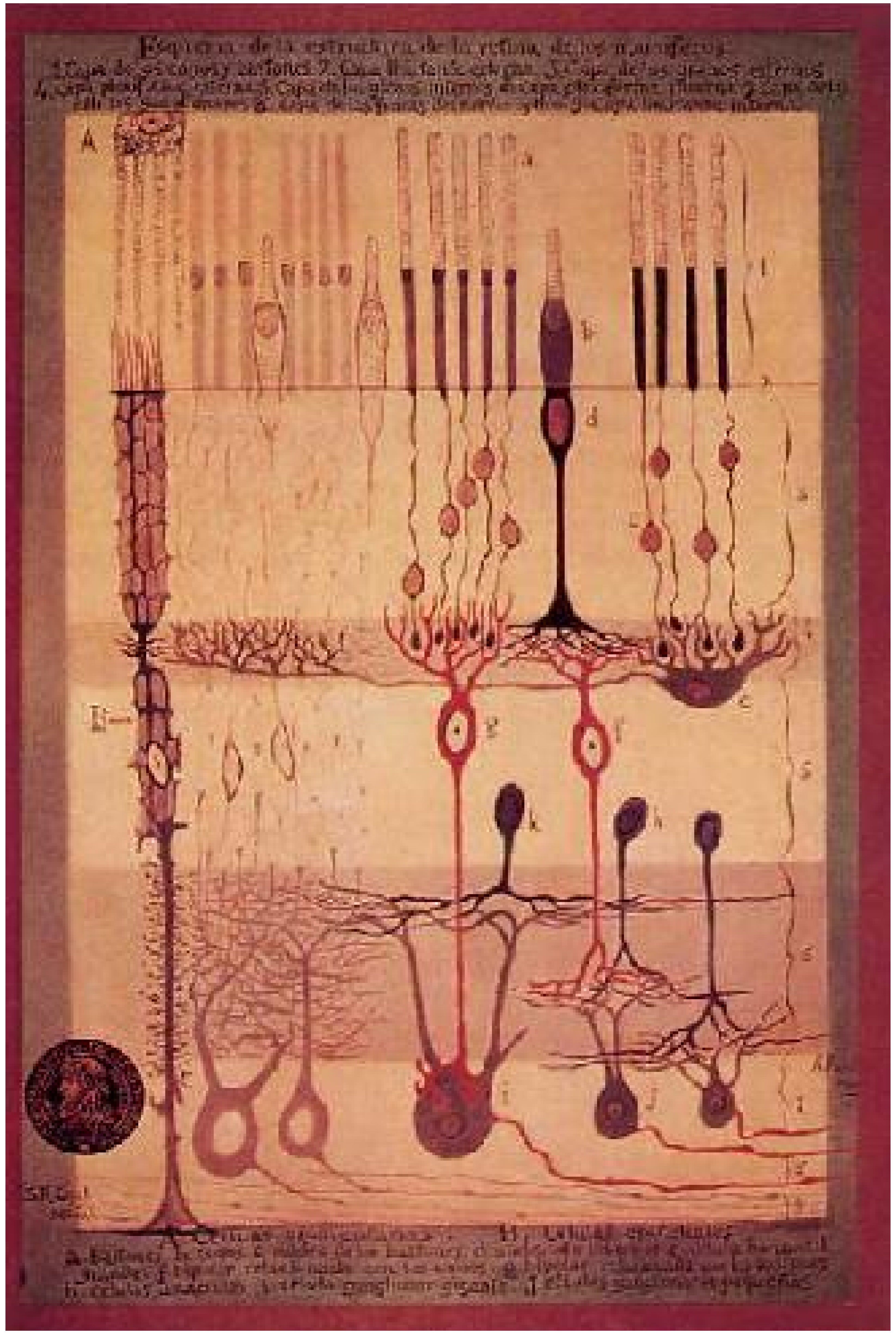


Ramon y Cajal

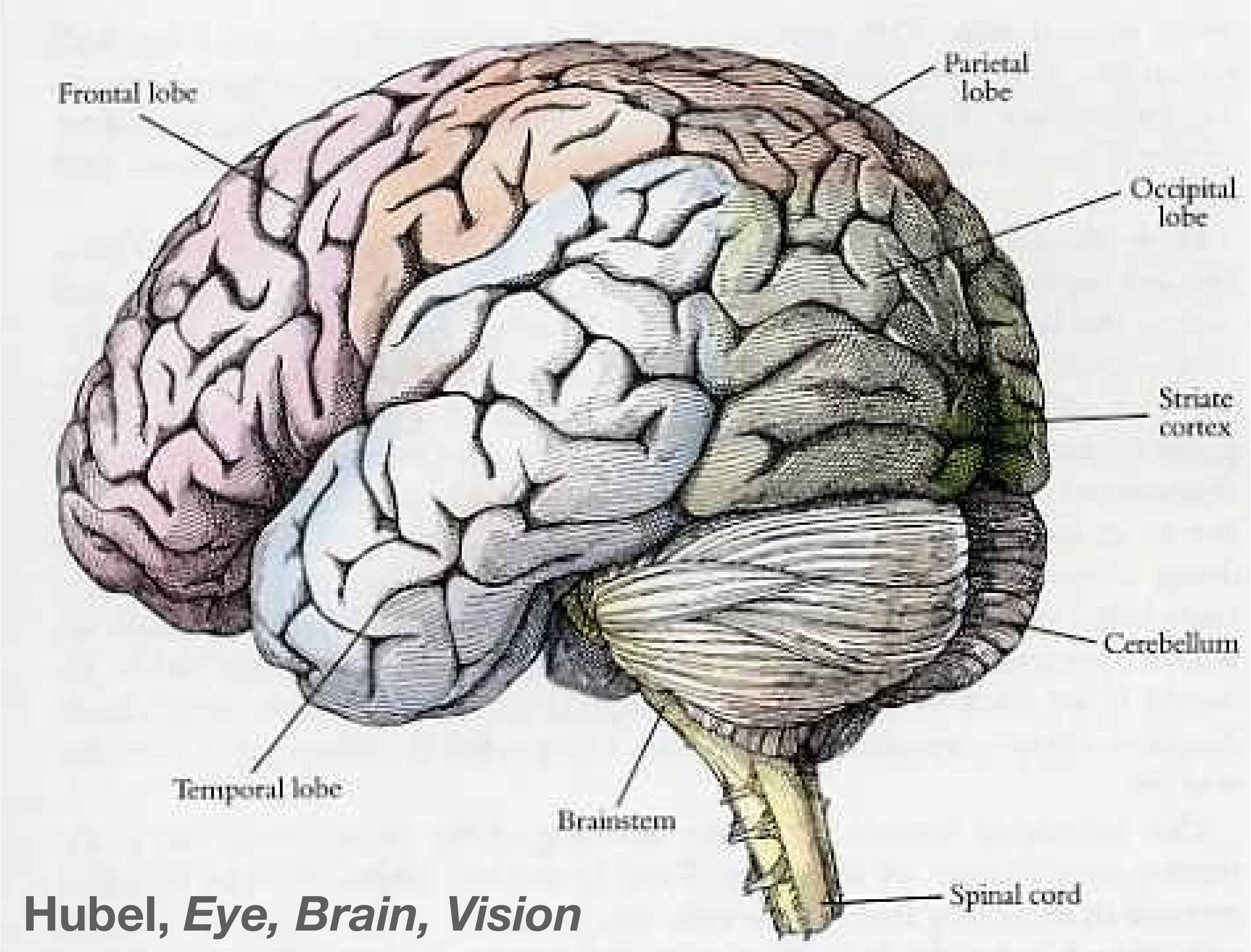
A coarse-graining approach to mapping cortical parameter space

Symposium on Machine Learning and Dynamical Systems
Fields Institute, Toronto
Sept. 28, 2022

Kevin K Lin
University of Arizona

Zhuo-Cheng Xiao & Lai-Sang Young
Courant Institute, NYU

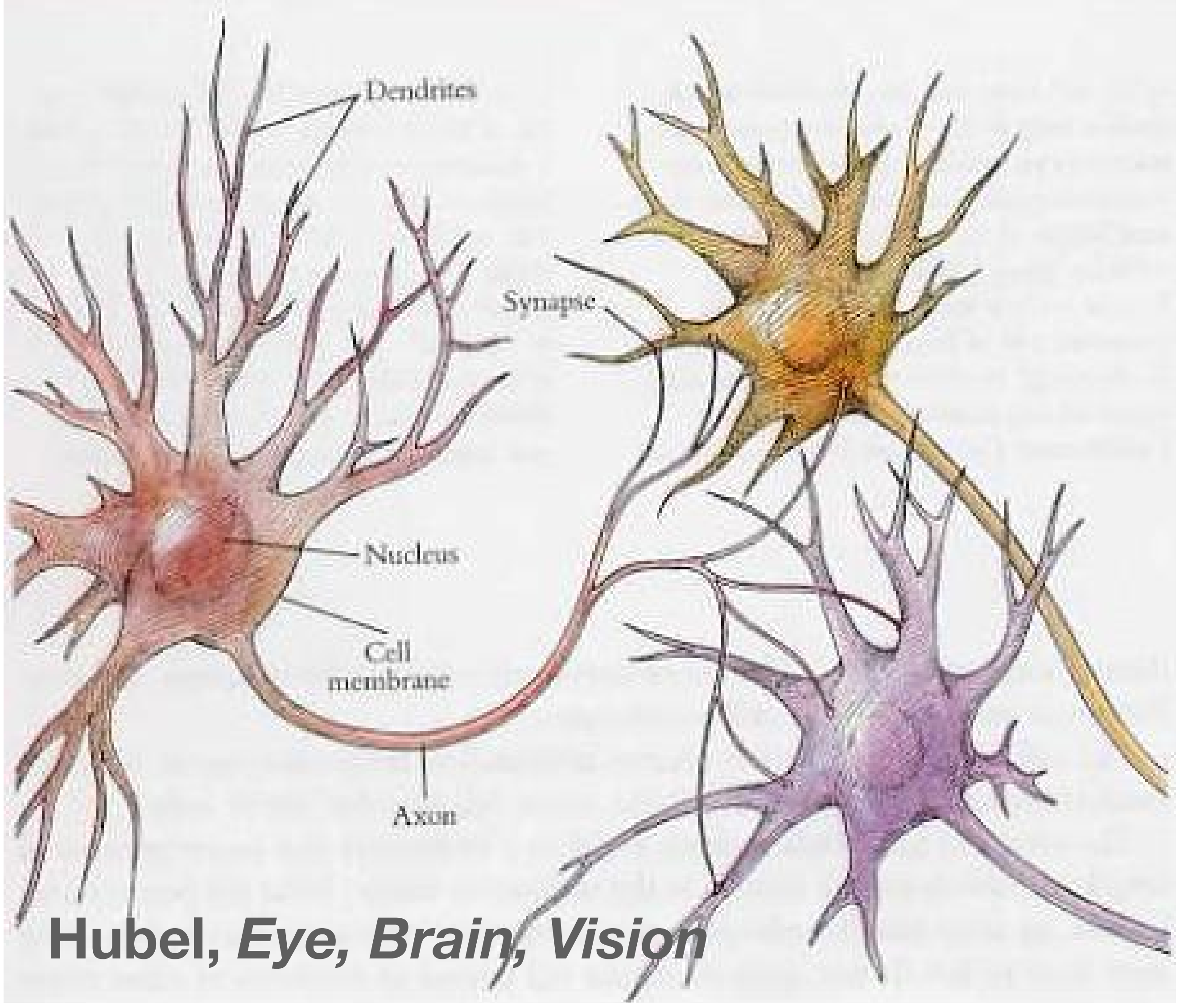
Cerebral cortex



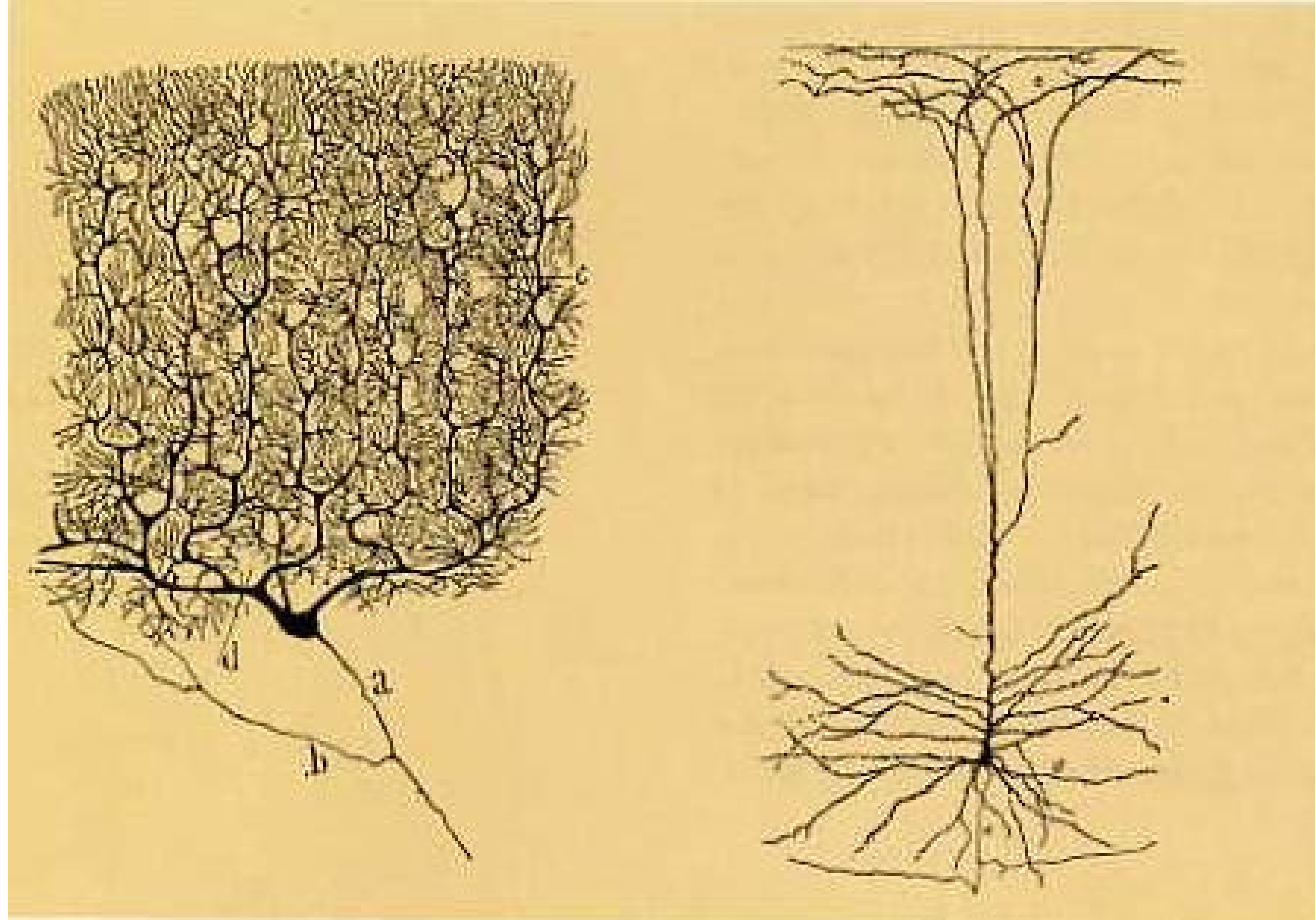
Hubel, *Eye, Brain, Vision*

- $\sim$ 1-2 $\text{ft}^2 \times 2\text{mm}$
- $6+$ layers
- (hyper)columns $\sim 0.5 \times 0.5\text{mm}^2$

Neurons & synapses



Hubel, *Eye, Brain, Vision*


Ramon y Cajal

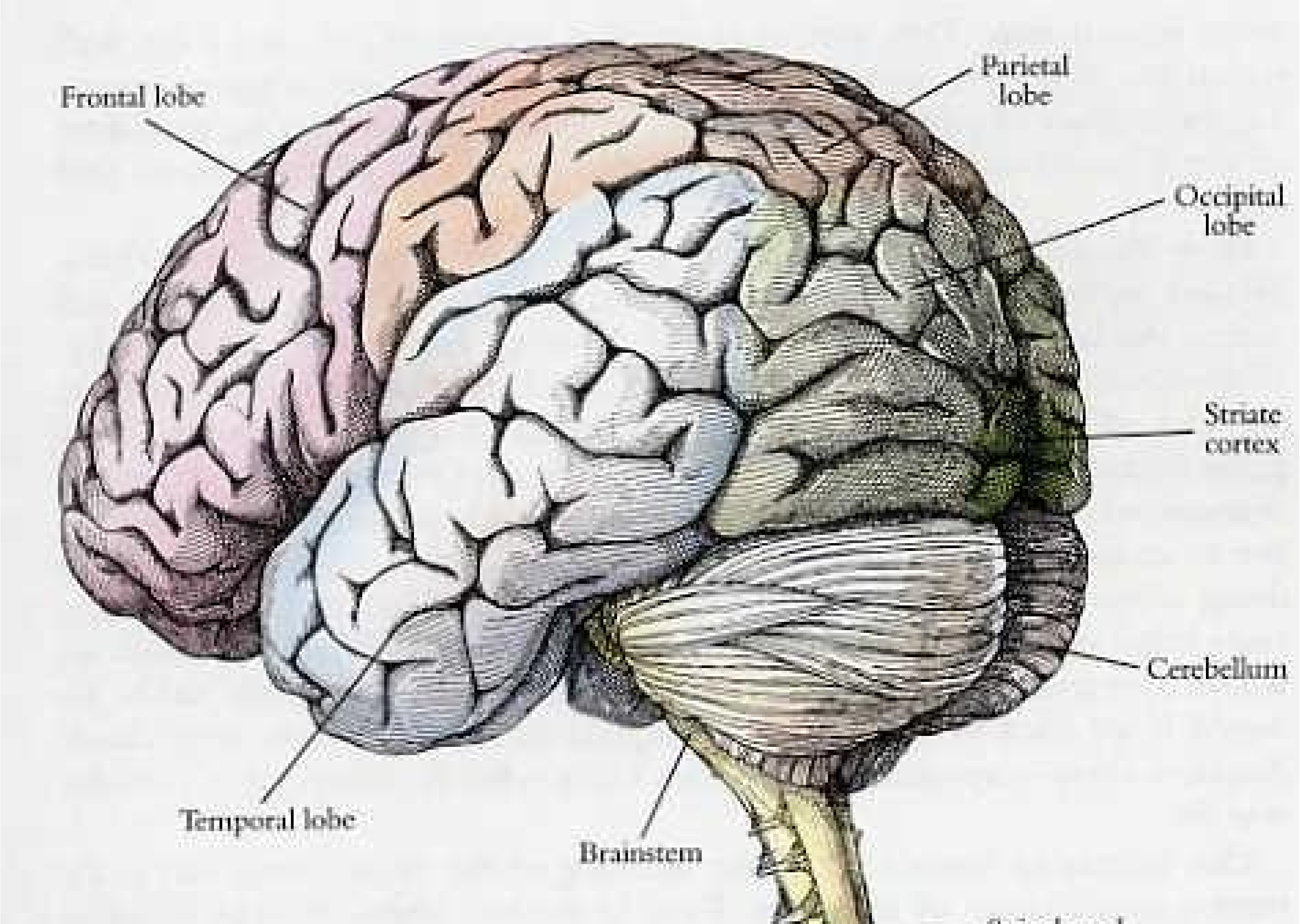
$\sim 10^{10}$ neurons

$\sim 10^{14}$ synapses

timescales: sub-ms up

Diverse
- morphology
- response properties

Cerebral cortex



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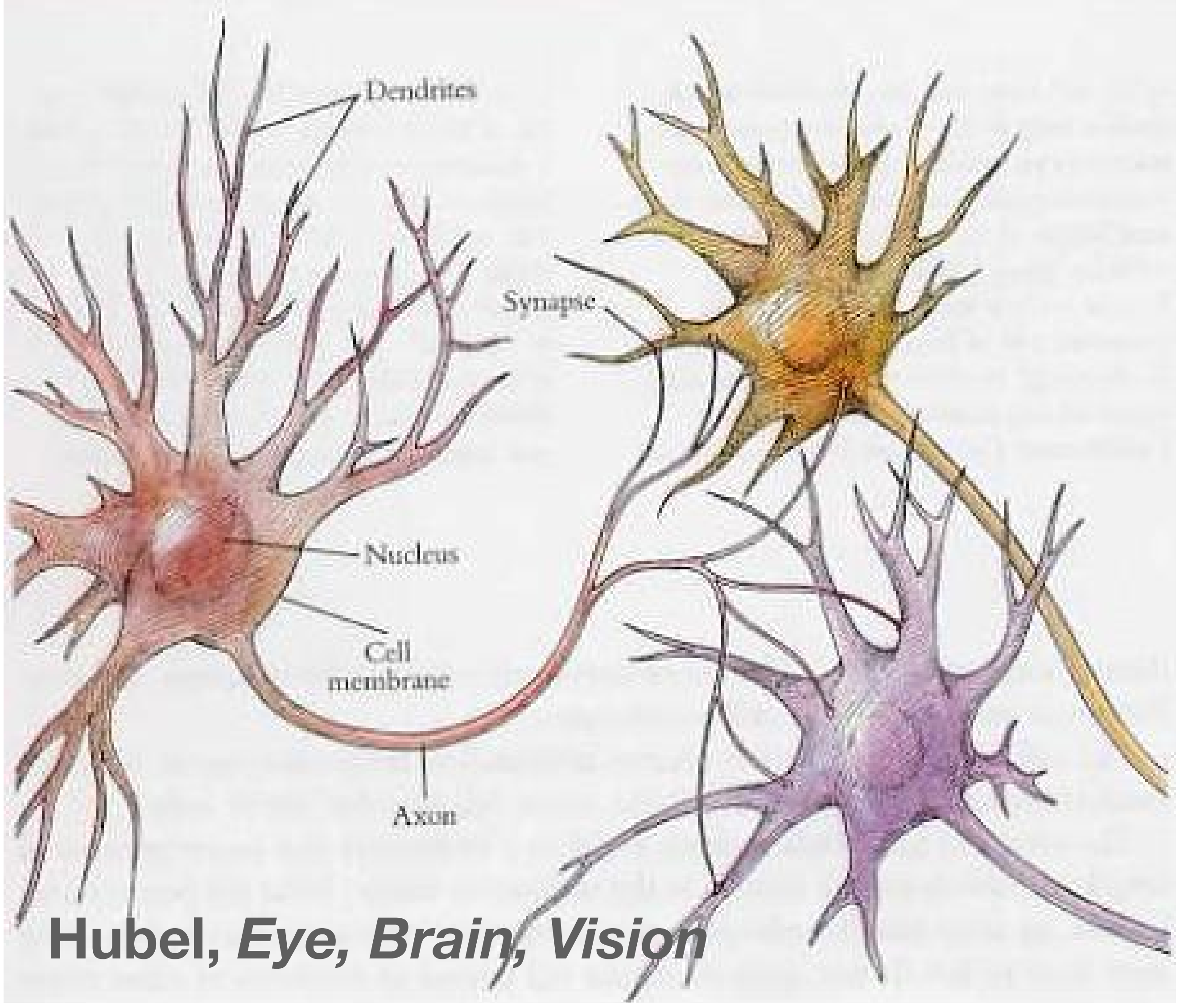

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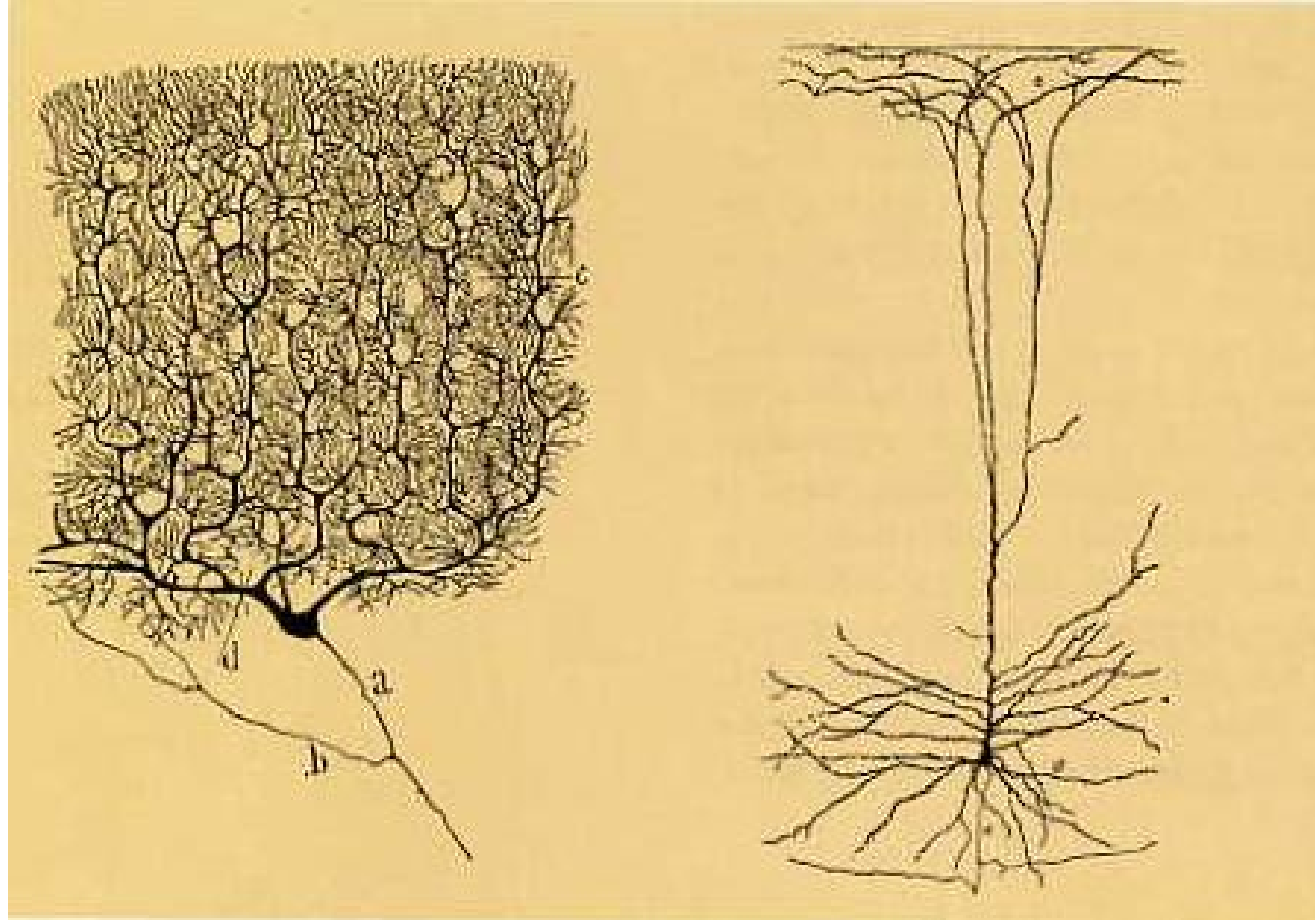


Ramon y Cajal

Diverse
- morphology
- response properties

Models
- summarize data
- dynamical mechanisms

Challenges
- Data: limited modalities
- **#model parameters**
- multiscale dynamics • *more*

This talk: *effort to address*

1) Constraining parameters from data (anatomy + physiology)?

2) Making sense of parameter space structure

This talk: *effort to address*

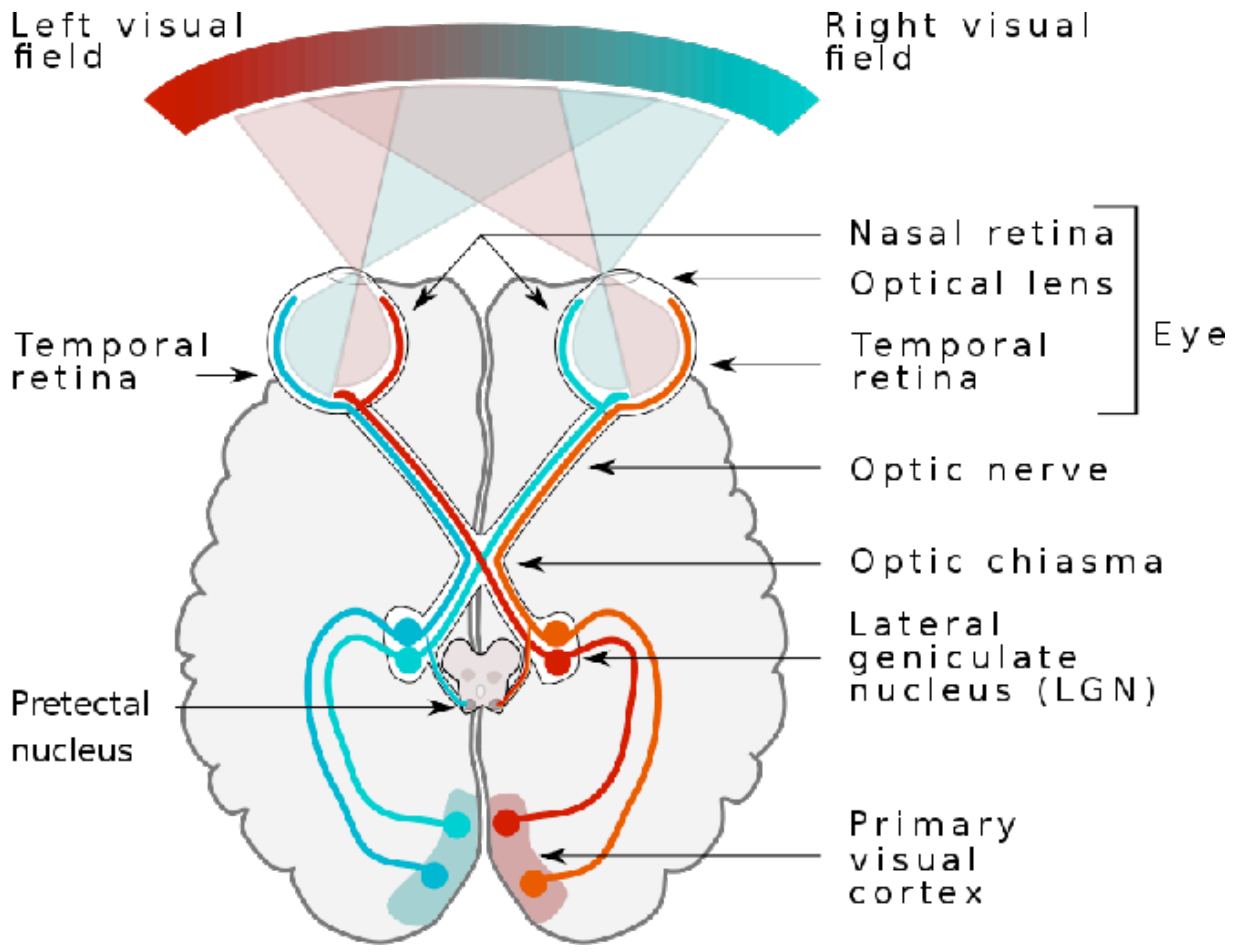
1) Constraining parameters from data (anatomy + physiology)?

2) Making sense of parameter space structure

Setting

- Primary visual cortex (V1)
- Build on recent **experimental + modeling advances in V1 neurobiology,** *esp*. realistic but expensive model [Chariker-Hawken-Shapley-Young]
- Coarse grain while preserving biological interpretability

Visual pathway

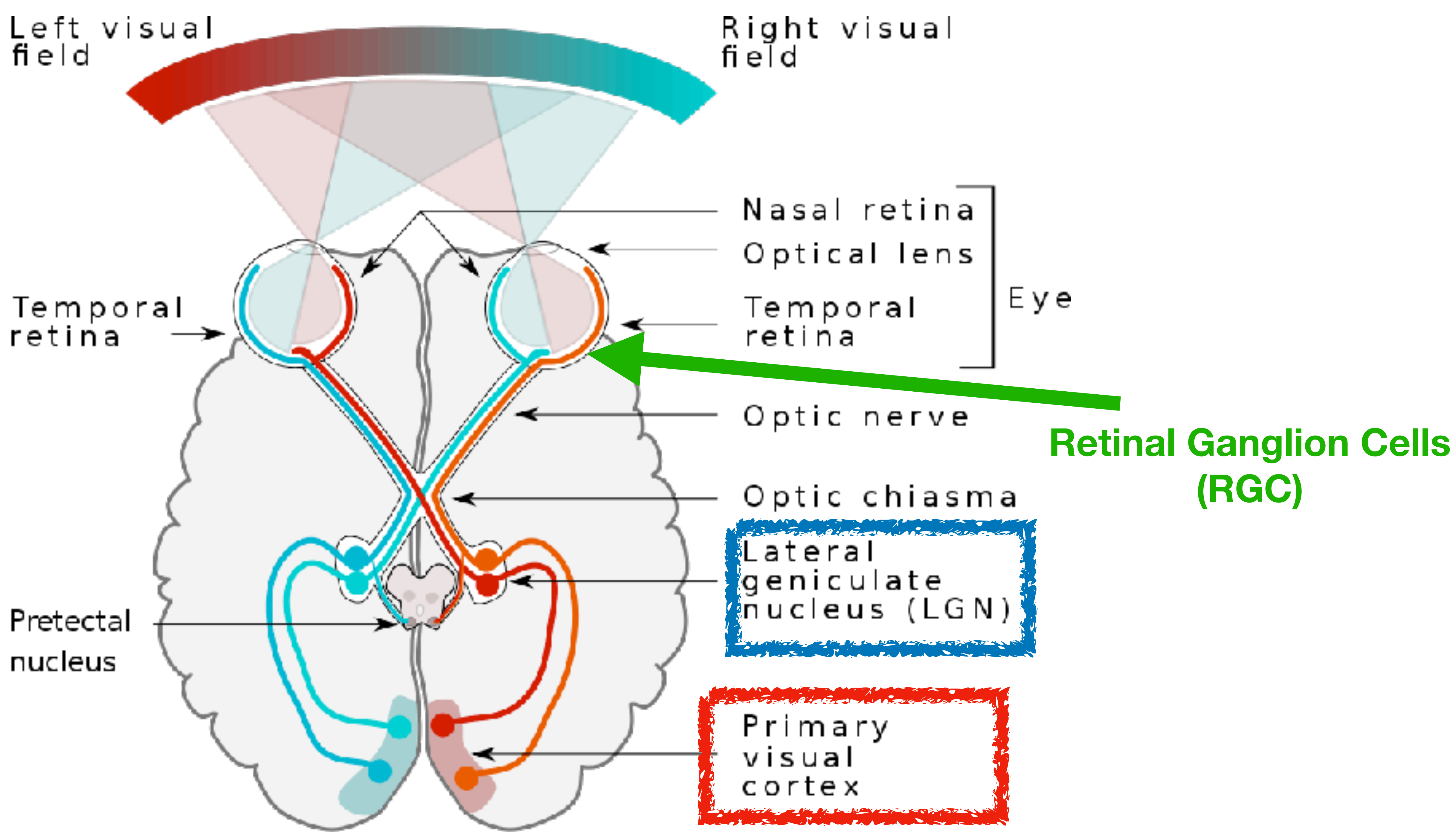


Wikimedia Commons (Miquel Perello Nieto)

ON center

OFF center

Visual pathway



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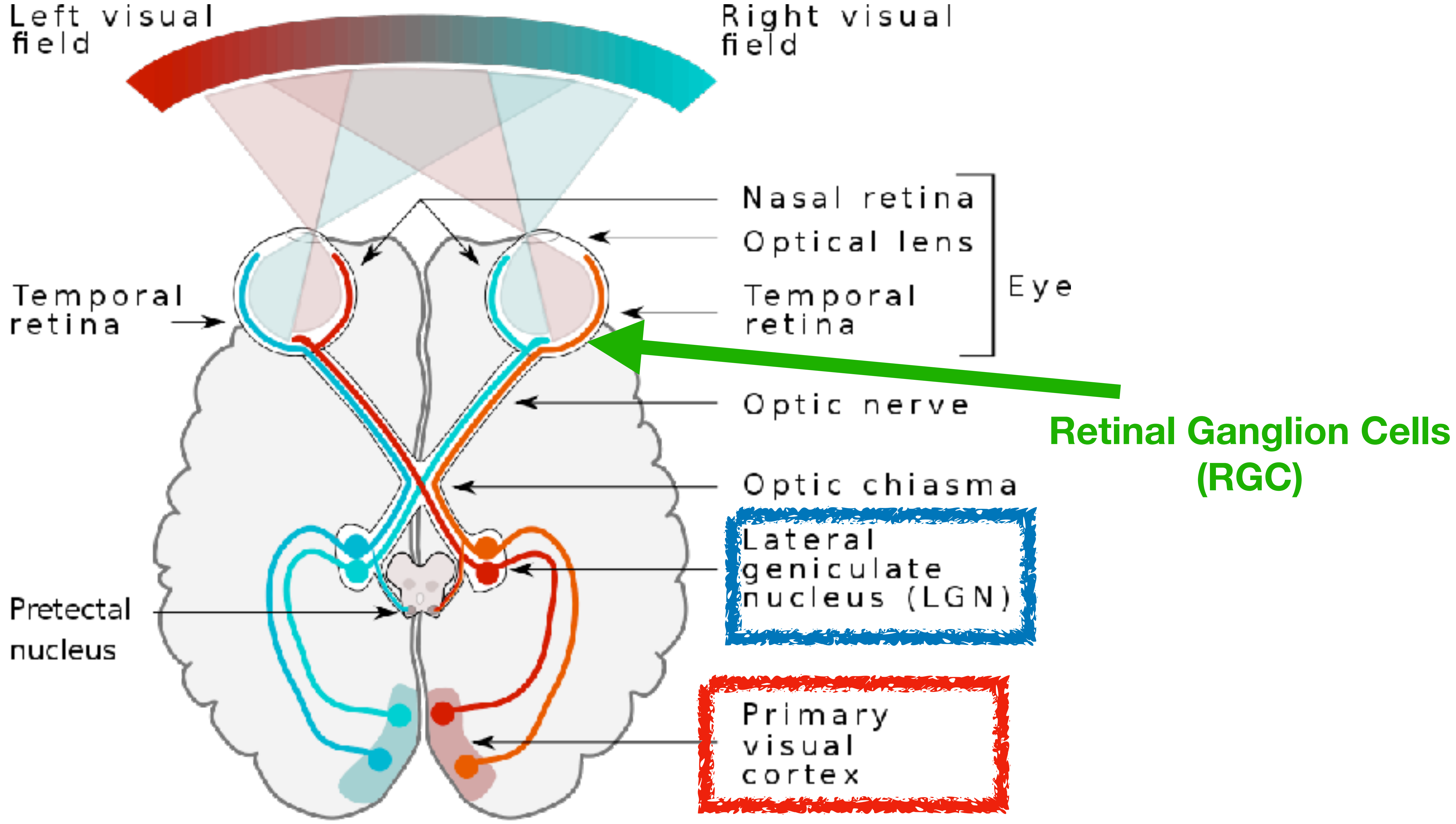

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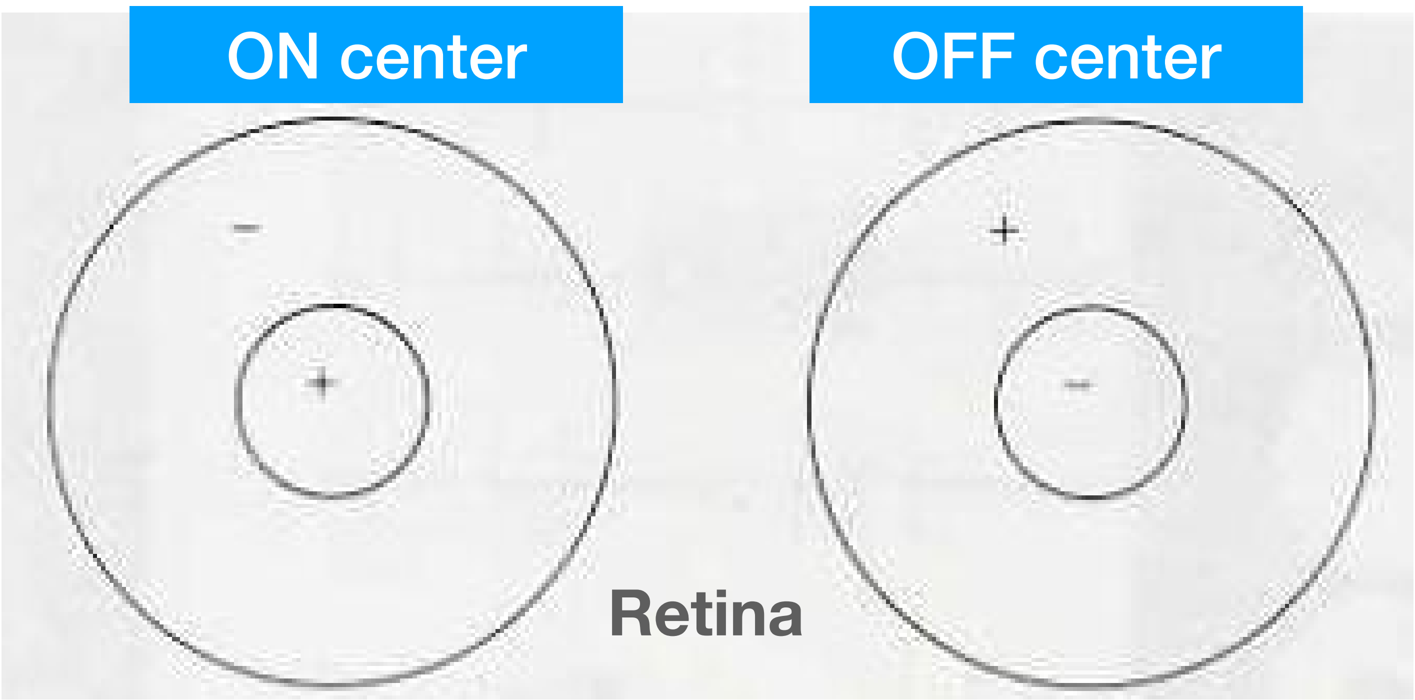
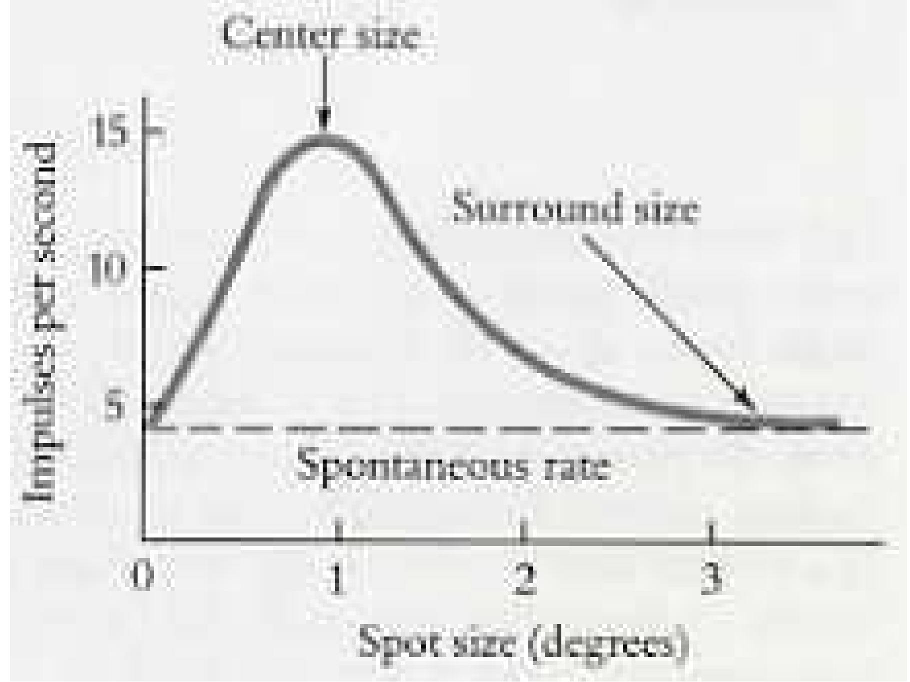
RGC *receptive field*





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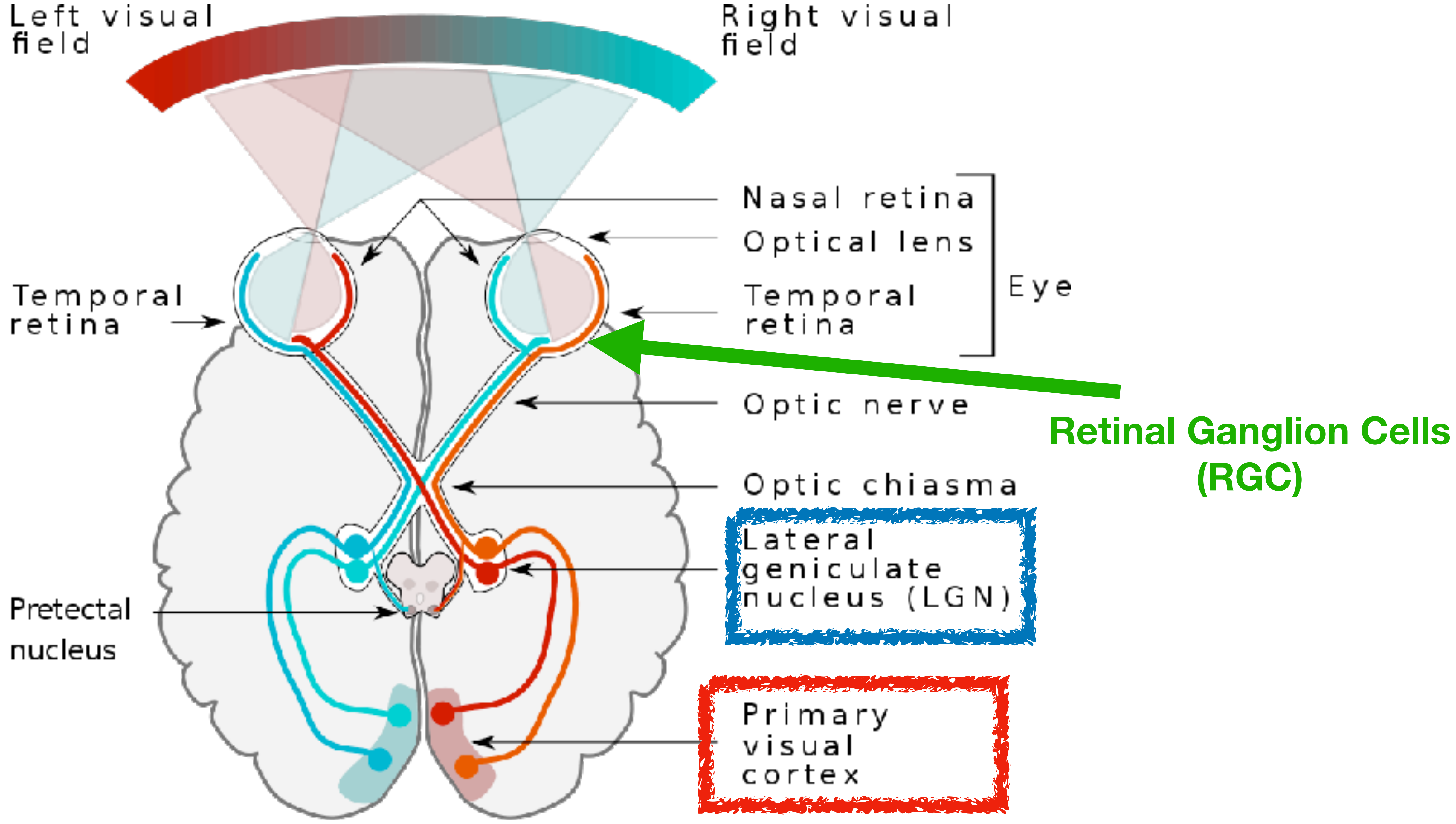

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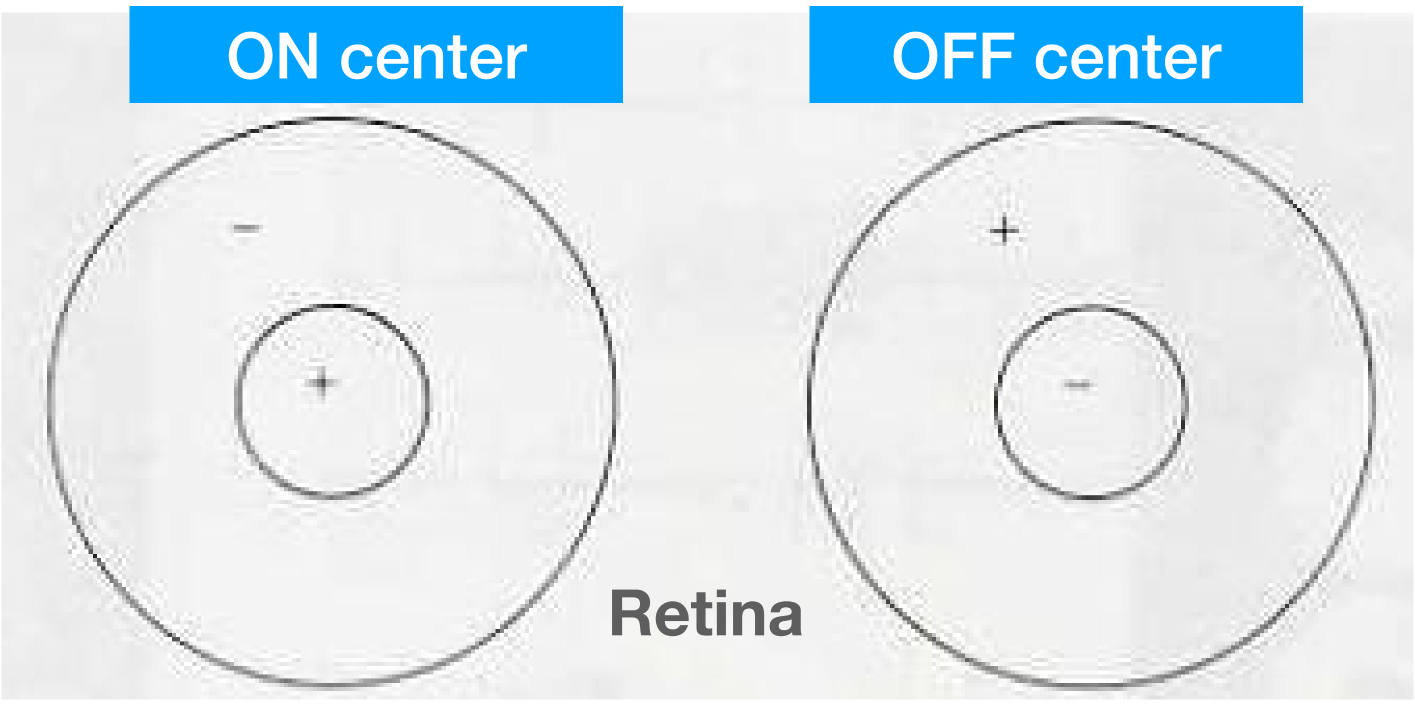
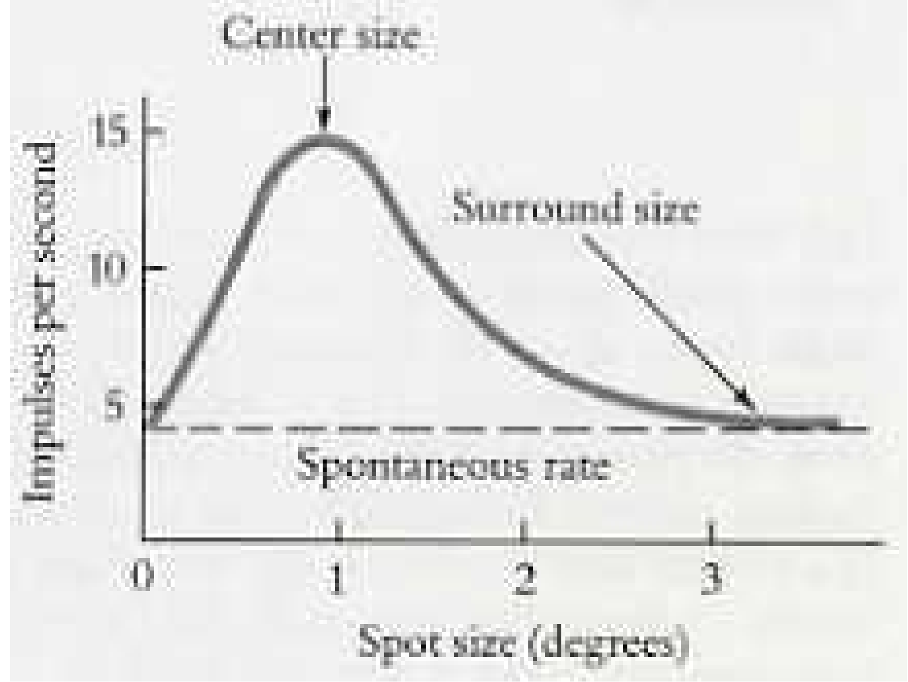
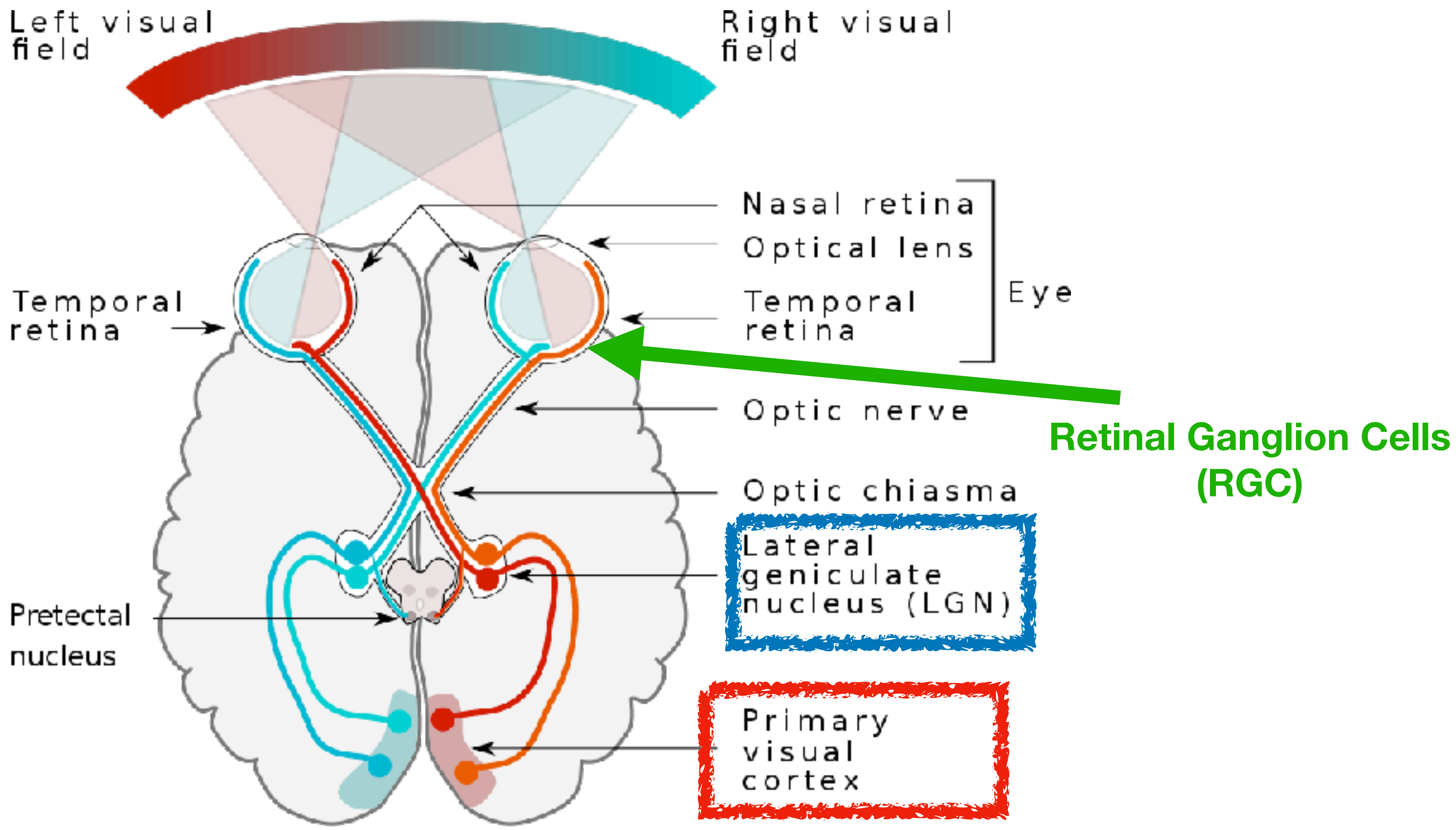




LGN: "similar"

Visual pathway



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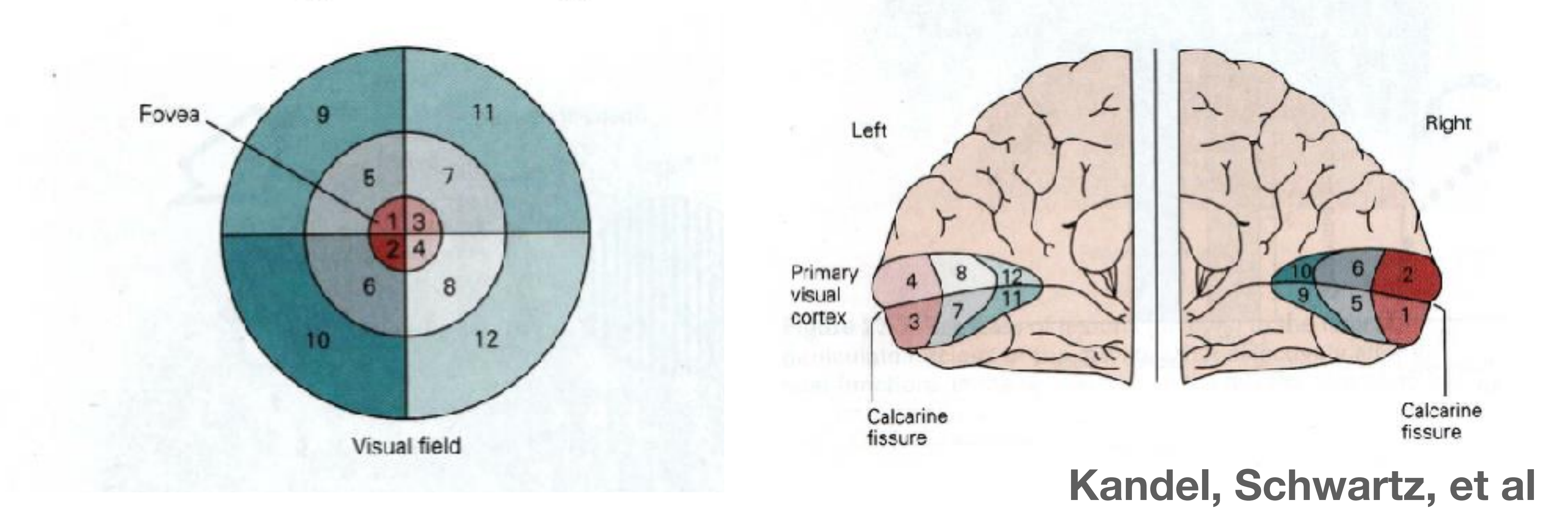
retinotopic map in V1



Kandel, Schwartz, et al

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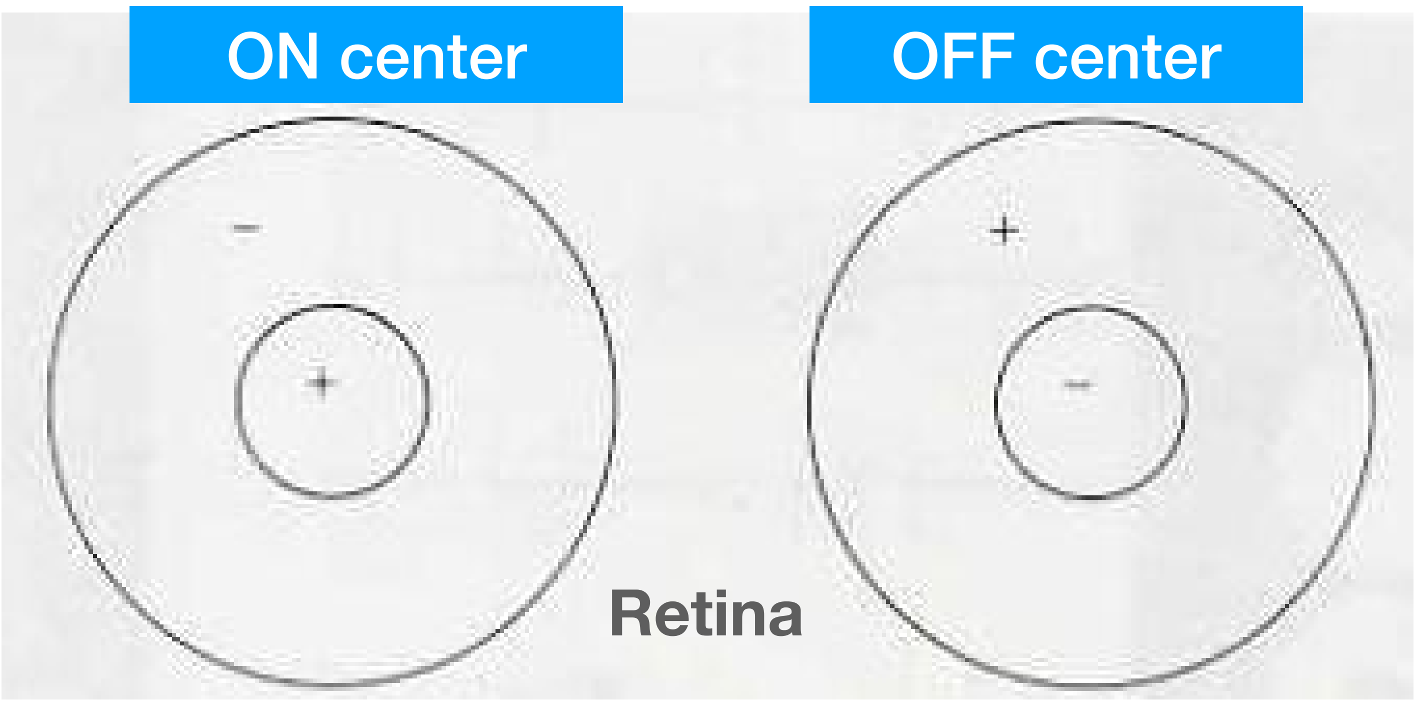

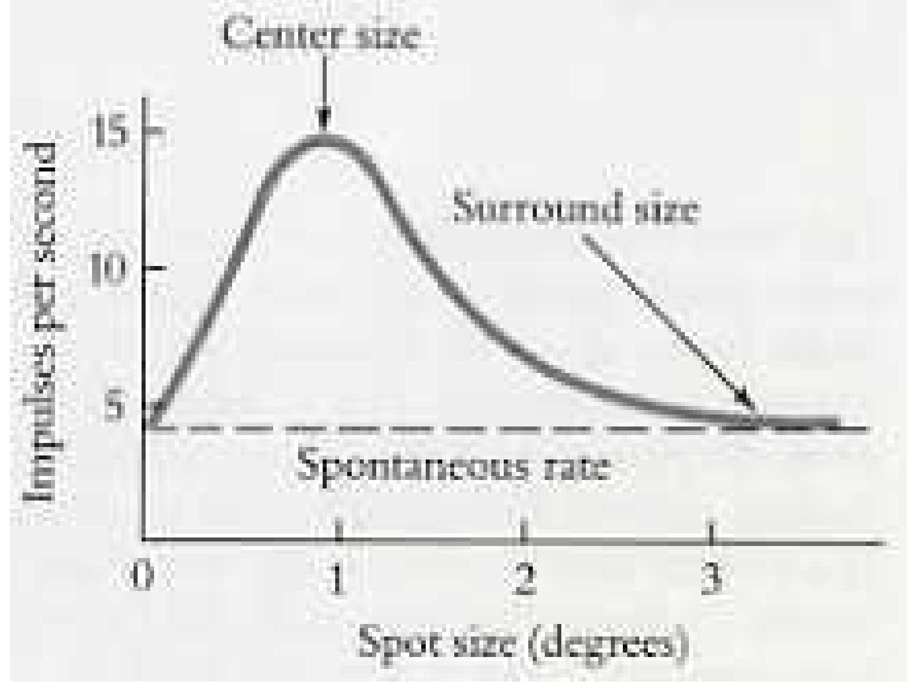

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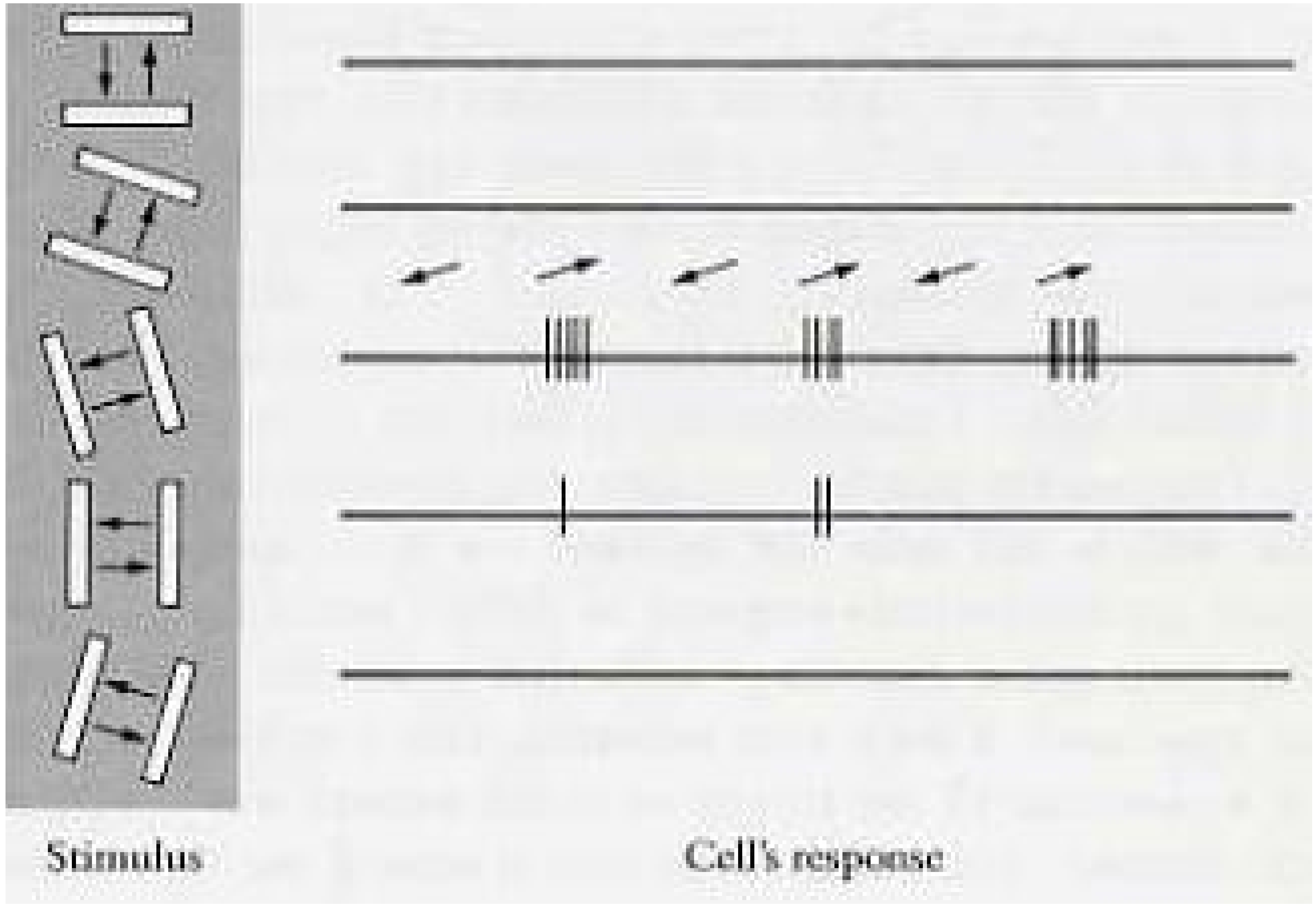

Hubel, *Eye, Brain, Vision*

CHSY cortical model

Kirchoff's current law

$$\tau_i \dot{v}_i(t) = -g^L(v(t) - V_{rest}) - \underbrace{g_i^E(t)(v_i(t) - v^E)}_{\text{E current}} - \underbrace{g_i^I(t)(v_i(t) - v^I)}_{\text{I current}}$$

$v_i(t)$ = membrane voltage of ith cell

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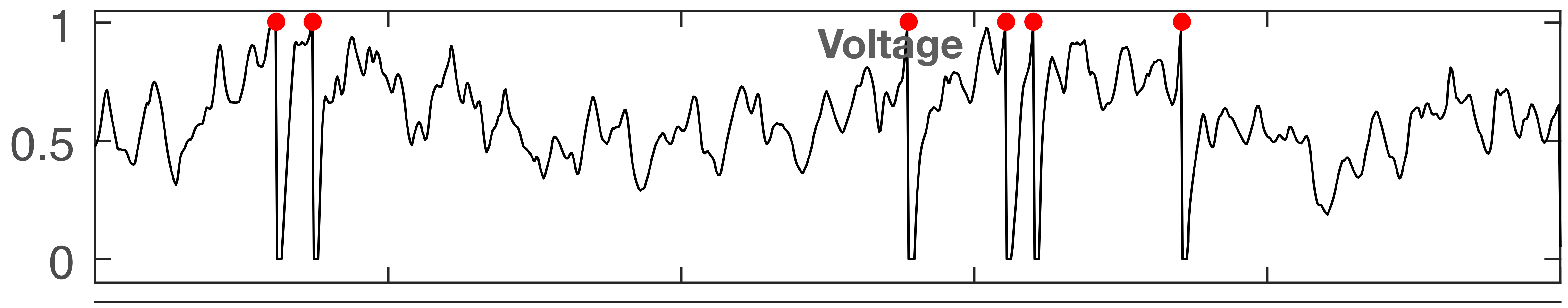
Leaky Integrate-and-Fire (LIF) neuron

$v(t) = \text{threshold} \implies$ spike + reset

Chariker, Young, *J Neurosci 2018*



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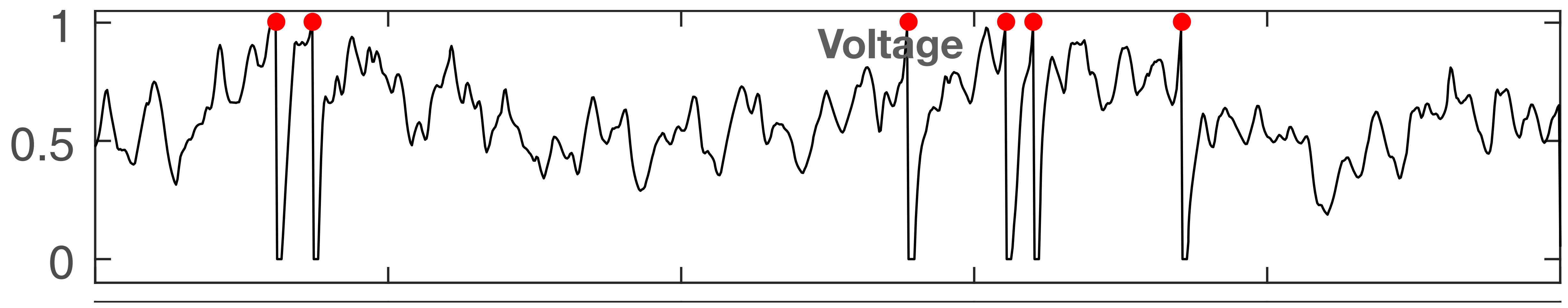


Membrane conductances $g_i^{E,I}(t)$

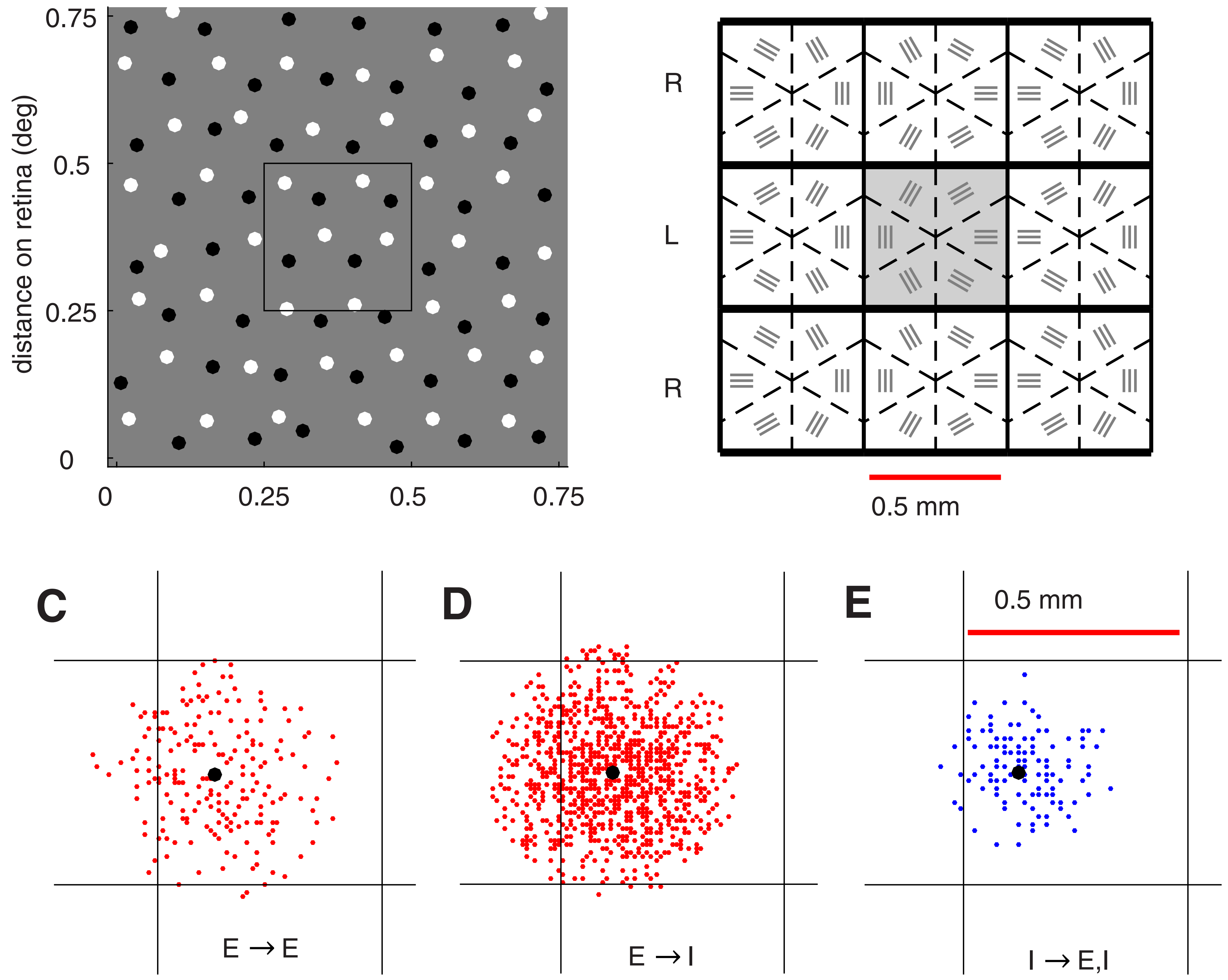
$$g_i^{\{E,I\}}(t) = \sum_j S_{ij} \sum_{t_i<t} \gamma^{\{E,I\}}(t - t_i)$$

$\gamma^E(t), \gamma^I(t)$: given

S_{ij} : network structure

- Connection prob: ↓ with dist
- $S_{ij} = S^{EE}$ if $i, j \in E$, etc.
- LGN: 5 ON, 5 OFF
- *More: L6, ambient*

Chariker et al, J Neurosci 2016



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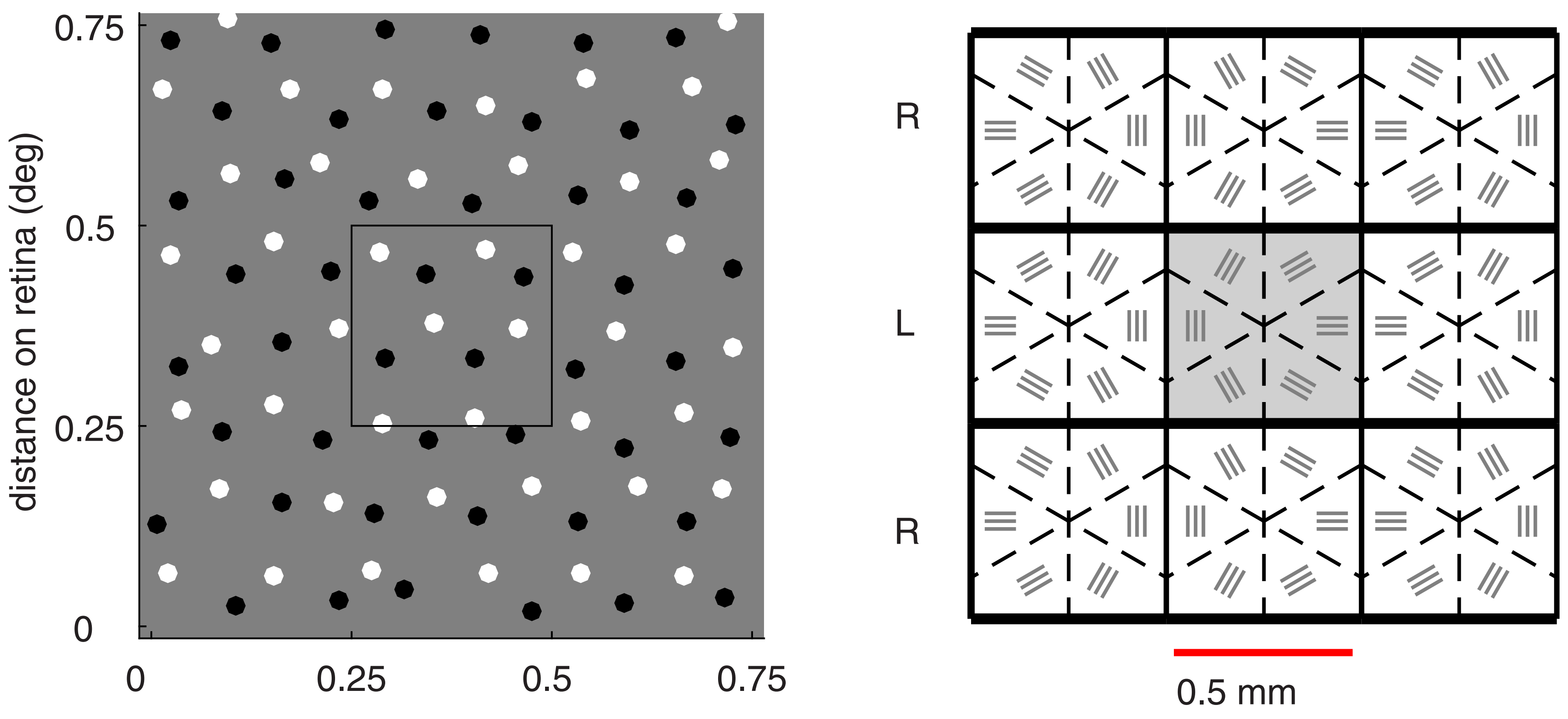

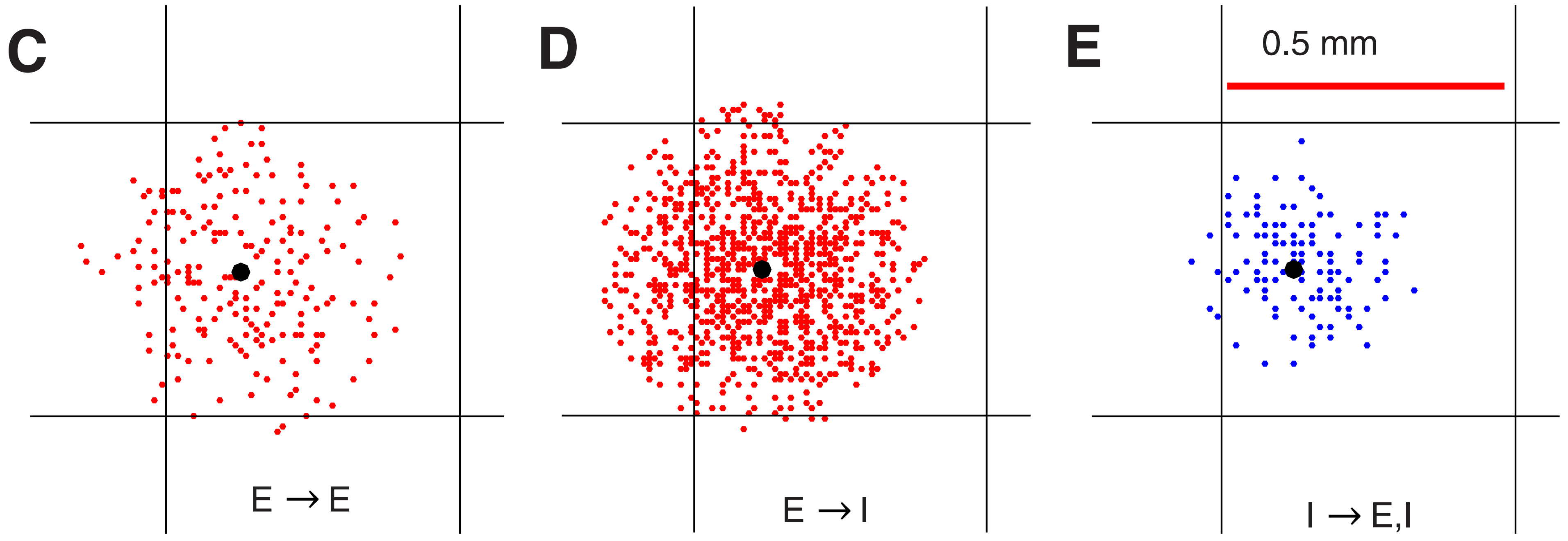

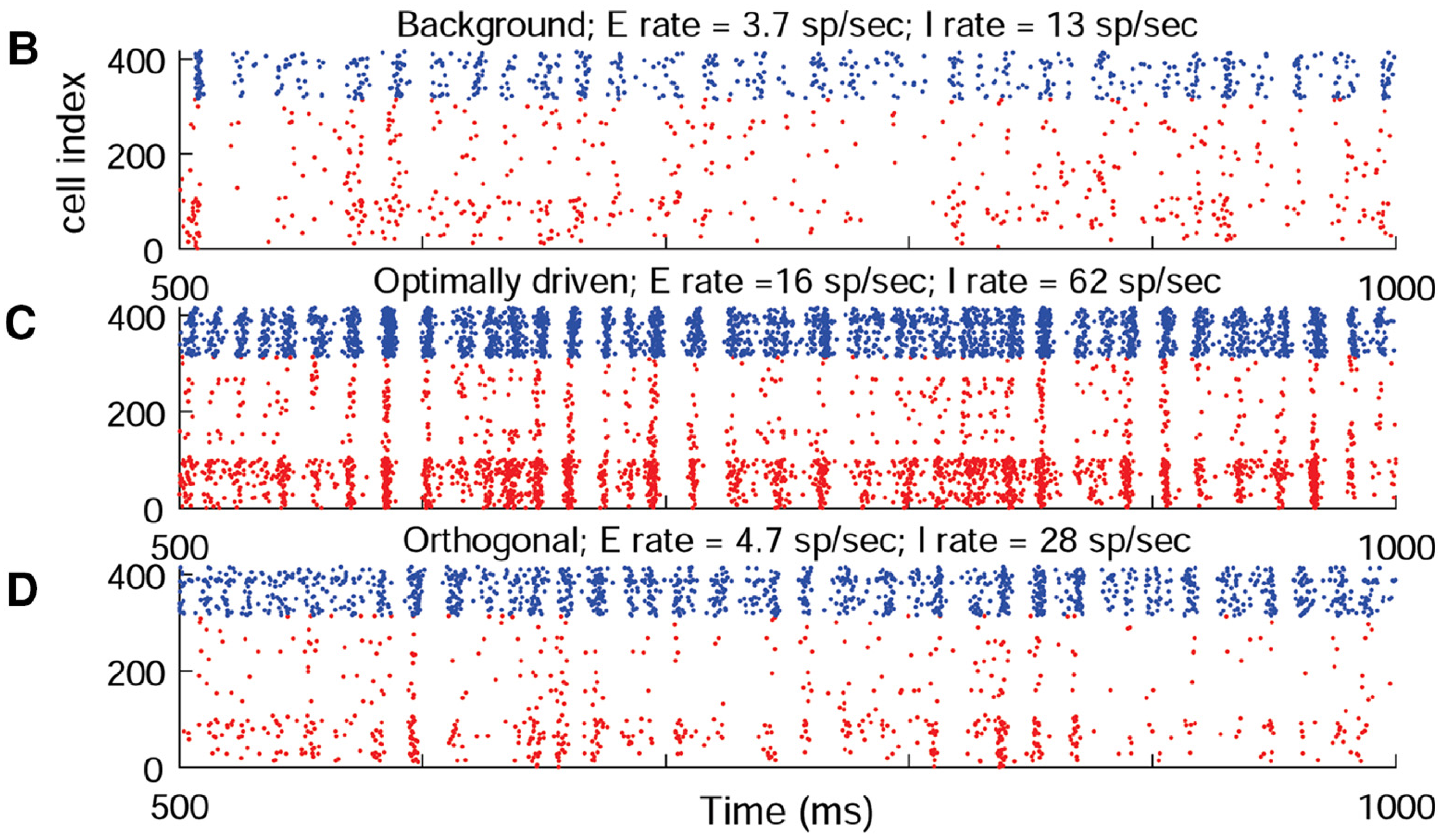

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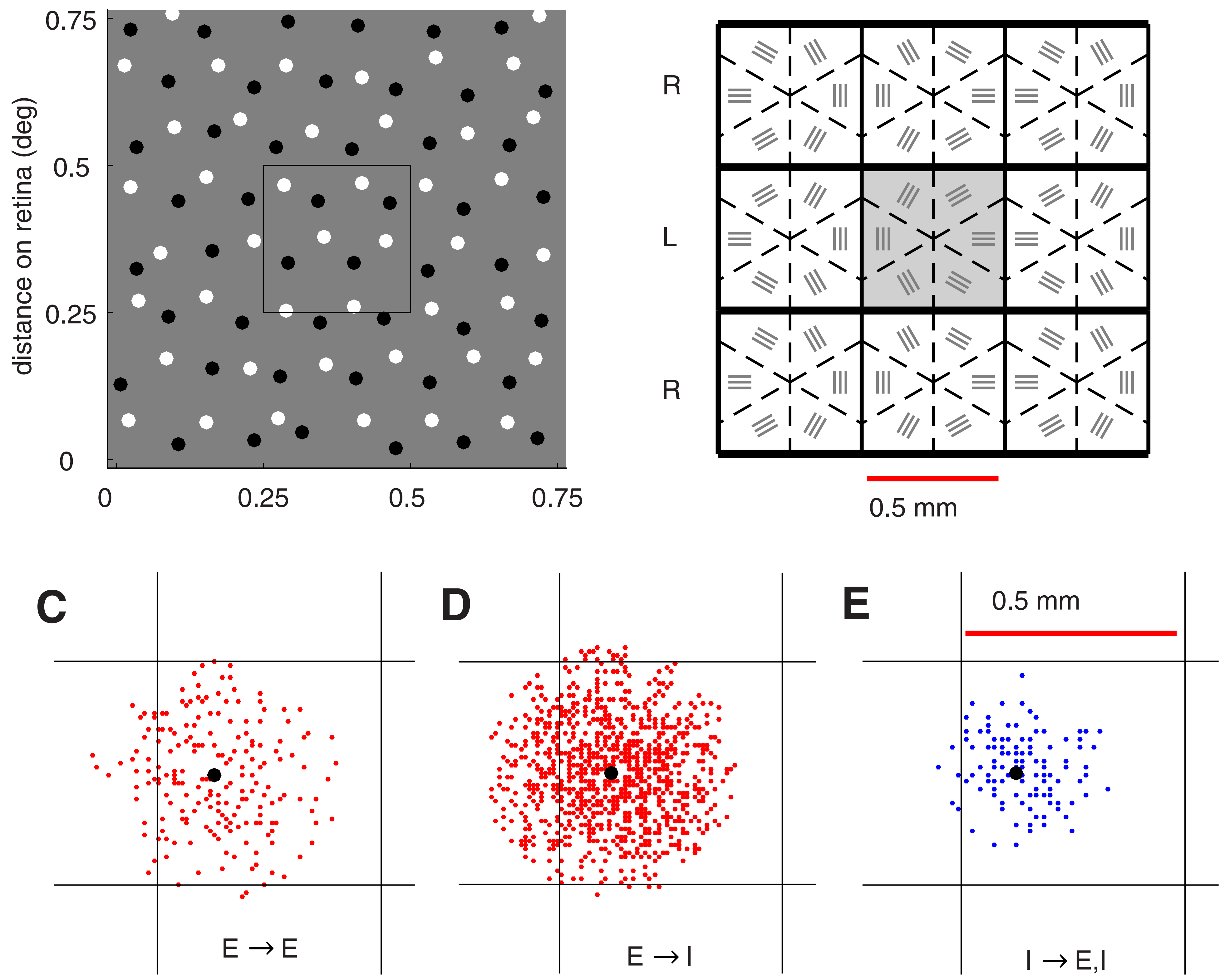

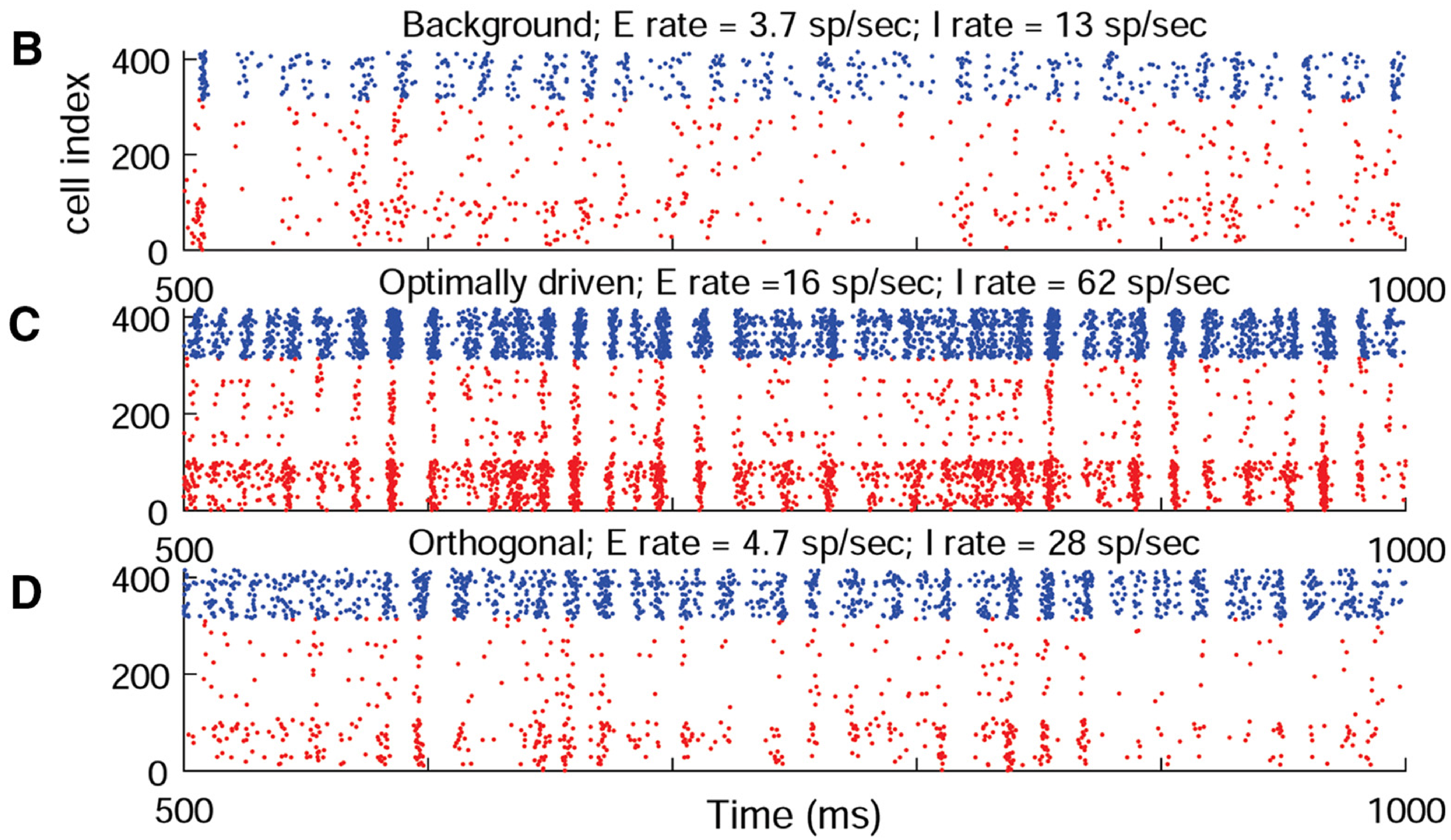

"Background" state

- spontaneous fluctuations
- E-I balance
- Wide range of correlated activity

Small patch of layer 4Cα

- 3×3 hypercols
- 1 layer
- ~36,000 cells
- Focus on ~7 parameters

$$
\begin{aligned}
g_i^E(t) = {} & \underbrace{S^{Q\mathrm{lgn}} \sum_{k=1}^{\infty} G_{\mathrm{ampa}}(t - t^{i,\mathrm{lgn}}(k))}_{\text{(I) LGN}} \;+\; \underbrace{S^{Q\mathrm{amb}} \sum_{k=1}^{\infty} G_{\mathrm{ampa}}(t - t^{i,\mathrm{amb}}(k))}_{\text{(II) ambient}} \\
& + \underbrace{S^{Q\mathrm{L6}} \sum_{k=1}^{\infty} \left[\rho_{\mathrm{ampa}}^{Q} G_{\mathrm{ampa}}(t - t^{i,\mathrm{L6}}(k)) + \rho_{\mathrm{nmda}}^{Q} G_{\mathrm{nmda}}(t - t^{i,\mathrm{L6}}(k))\right]}_{\text{(III) Layer 6}} \\
& + \underbrace{S^{QE} \sum_{j \in N_{4\mathrm{C},E}(i)} \sum_{k=1}^{\infty} \left[\rho_{\mathrm{ampa}}^{Q} G_{\mathrm{ampa}}(t - t^{j}(k)) + \rho_{\mathrm{nmda}}^{Q} G_{\mathrm{nmda}}(t - t^{j}(k))\right]}_{\text{(IV) Layer 4}}
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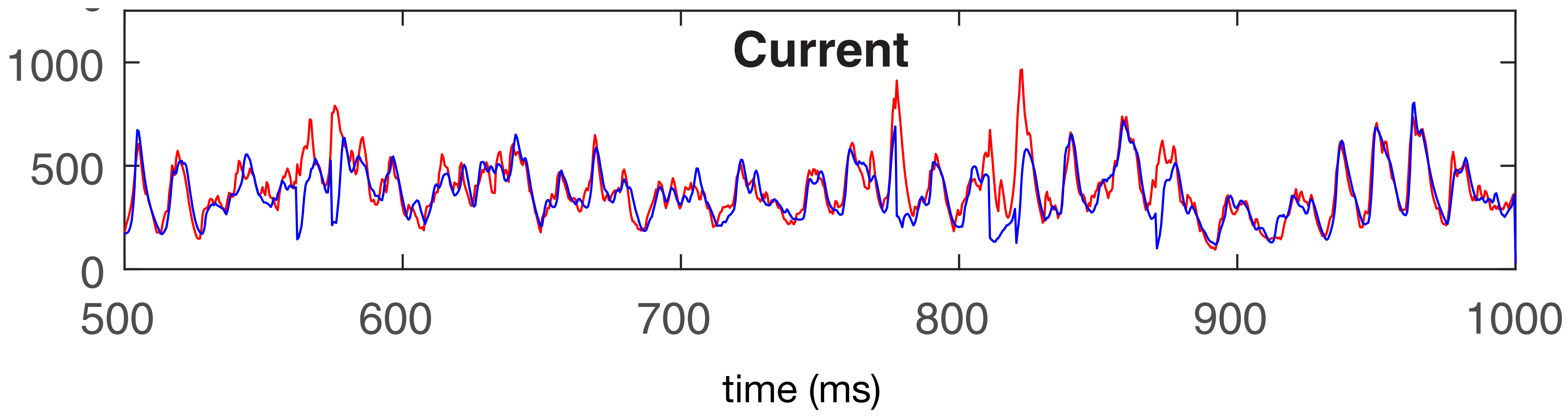

E-I balance: sensitivity • correlations

$$g_i^E(t) = \underbrace{S^{Q\mathrm{lgn}} \sum_{k=1}^{\infty} G_{\mathrm{ampa}}(t - t^{i,\mathrm{lgn}}(k))}_{\text{(I) LGN}} + \underbrace{S^{Q\mathrm{amb}} \sum_{k=1}^{\infty} G_{\mathrm{ampa}}(t - t^{i,\mathrm{amb}}(k))}_{\text{(II) ambient}}$$

$$+ \underbrace{S^{Q\mathrm{L6}} \sum_{k=1}^{\infty} \left[\rho^Q_{\mathrm{ampa}} G_{\mathrm{ampa}}(t - t^{i,\mathrm{L6}}(k)) + \rho^Q_{\mathrm{nmda}} G_{\mathrm{nmda}}(t - t^{i,\mathrm{L6}}(k))\right]}_{\text{(III) Layer 6}}$$

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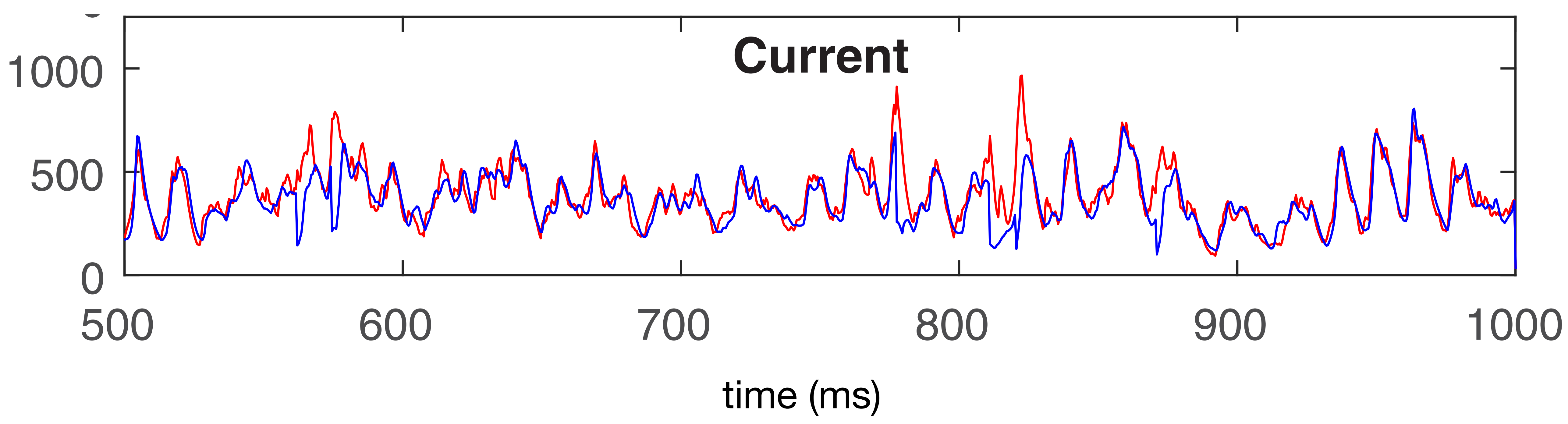

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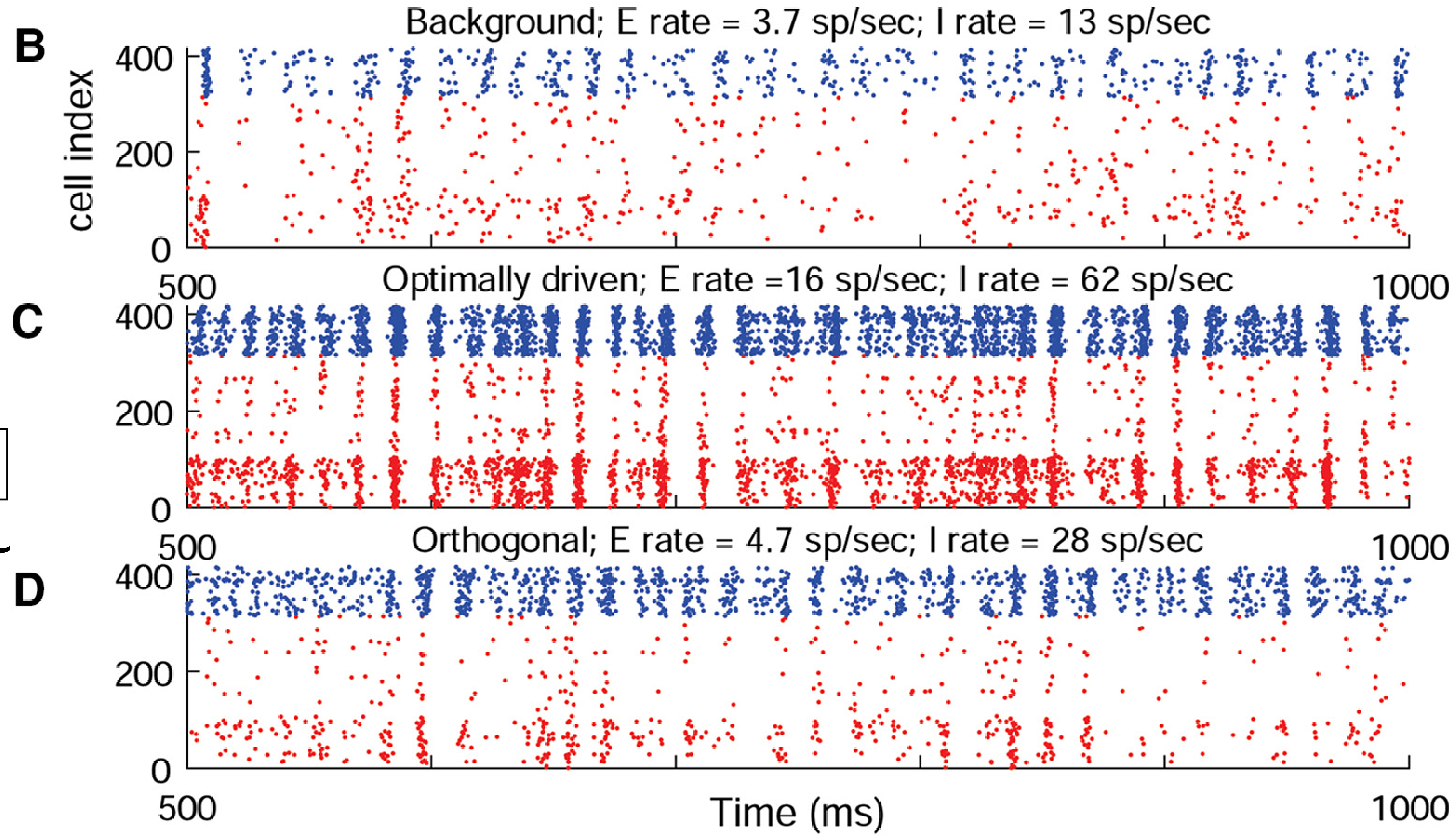

Parameters: a conundrum

- **Dynamics sensitive:** 1-4% $\Longrightarrow$ unrealistic response

Group	Parameter	Meaning	Value	Bounds
within L4	S^{EE}	E-to-E synaptic weight	0.024	(-3%, 1%)
	S^{II}	I-to-I synaptic weight	0.120	(-4%, 1%)
	S^{EI}	I-to-E synaptic weight	0.0362	(-1%, 3%)
	S^{IE}	E-to-I synaptic weight	0.0176	(-1%, 3%)
LGN to L4	$S^{E\mathrm{lgn}}$	lgn-to-E synaptic weight	0.048	(-5%, 3%)
	$S^{I\mathrm{lgn}}$	lgn-to-I synaptic weight	0.096	(-6%, 9%)
	$F^{E\mathrm{lgn}}$	total # lgn spikes/s to E	80 Hz	(-7%, 4%)
	$F^{I\mathrm{lgn}}$	total # lgn spikes/s to I	80 Hz	(-9%, 11%)
L6 to L4	$S^{E\mathrm{L6}}$	L6-to-E synaptic weight	0.008	(-16%, 11%)
	$S^{I\mathrm{L6}}$	L6-to-I synaptic weight	0.0058	(-19%, 30%)
	$F^{E\mathrm{L6}}$	total # L6 spikes/s to E	250 Hz	(-16%, 10%)
	$F^{I\mathrm{L6}}$	total # L6 spikes/s to I	750 Hz	(-16%, 29%)
amb to L4	S^{amb}	ambient-to-E/I synaptic wt.	0.01	(-8%, 6%)
	$F^{E\mathrm{amb}}$	rate of ambient to E	500 Hz	(-7%, 5%)
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Yet: biological networks are robust & CHSY could tune model by hand

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Yet: biological networks are robust & CHSY could tune model by hand

Approach

- **Mean field reduction of realistic data-driven model**
  - *Eq free [Kevrekidis et al], HMM [E, Vanden-Eijnden, …]*
- **Coordinates matter**
  - *geometry of cortical space*
- ***Constrain E & I rates***

MF+v: *data-informed mean field*

$$\tau\dot{v}_i(t) = -g^L(v(t) - V_{rest}) - g_i^E(t)(v_i(t) - v^E) - g_i^I(t)(v_i(t) - v^I)$$

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↓ **Time average** [Wilson-Cowan, Bressloff, ...]

Firing rate $f_i \approx (1 - f_i \cdot \tau_{\text{ref}}) \times \left[-g_R \bar{v}_i + \bar{g}_i^E (V^E - \bar{v}_i) + \bar{g}_i^I (V^I - \bar{v}_i) \right]$ $(\star)$

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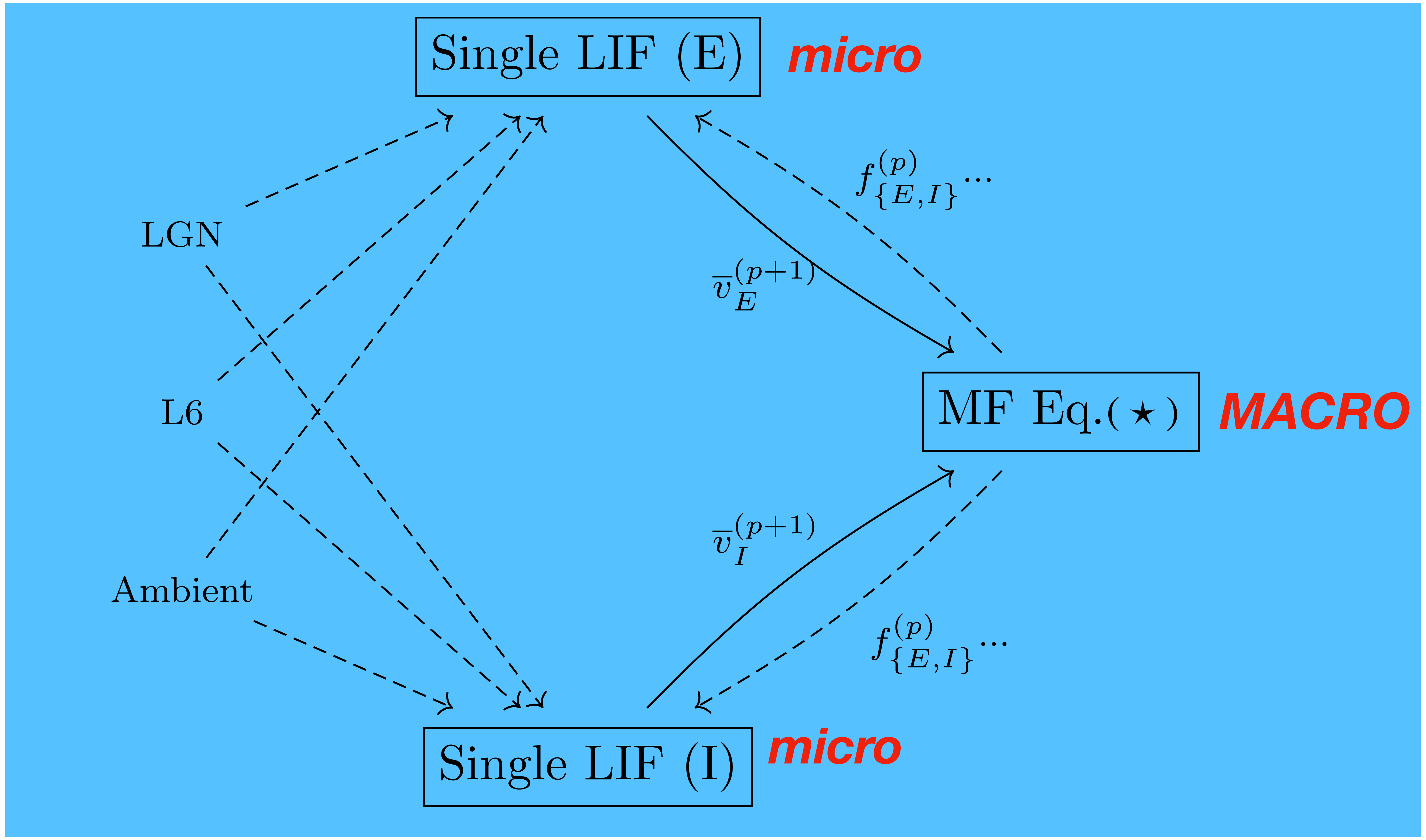
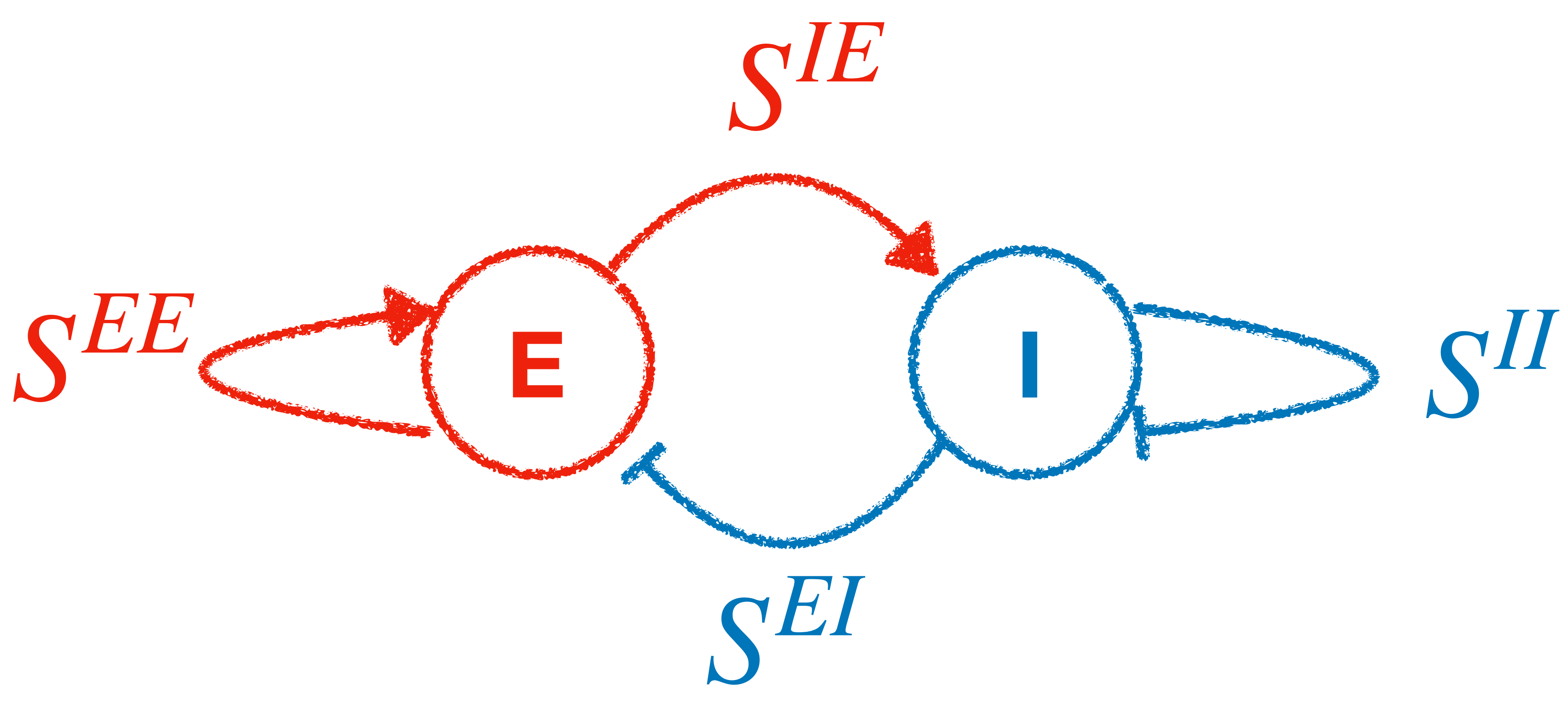


Geometry of cortical space:

slice by "inhibition planes"



Geometry of cortical space:

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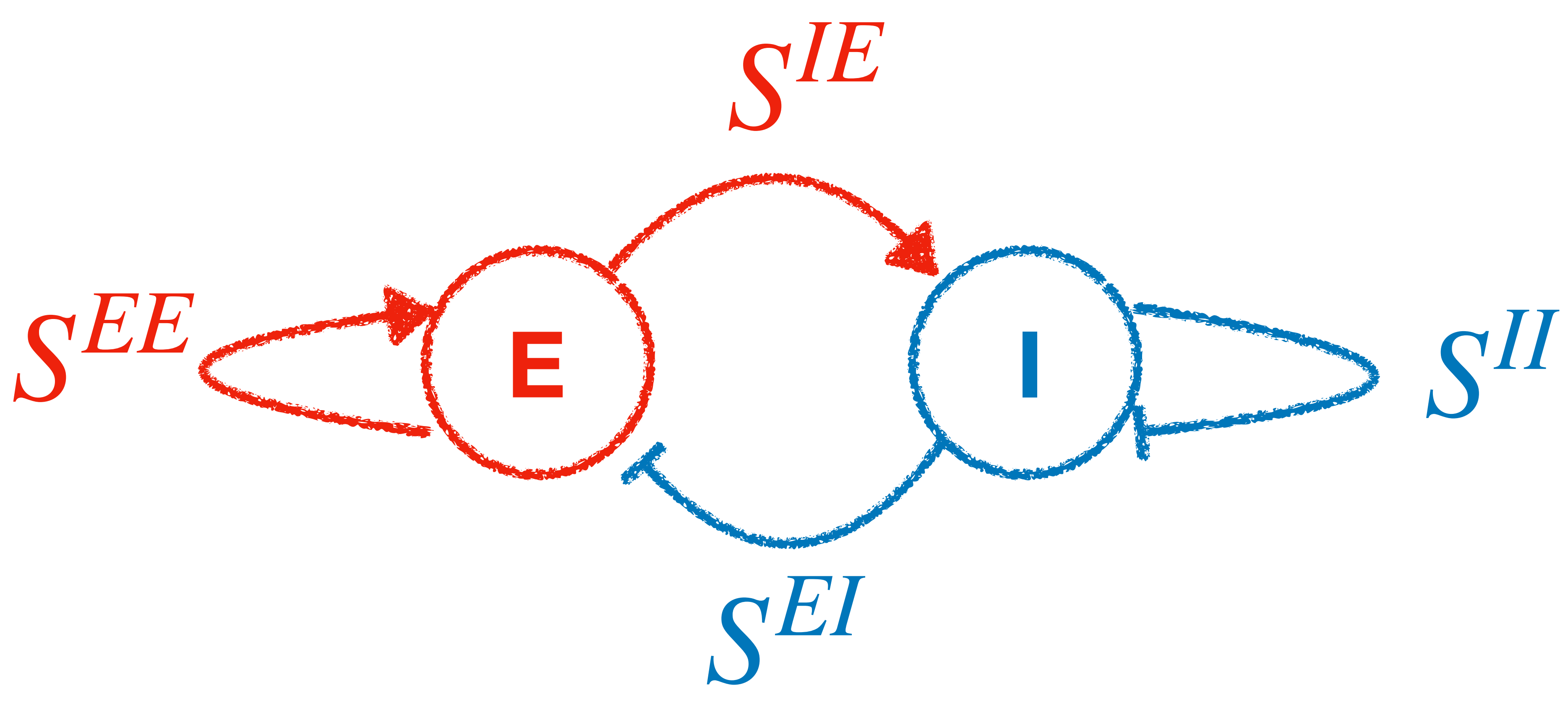

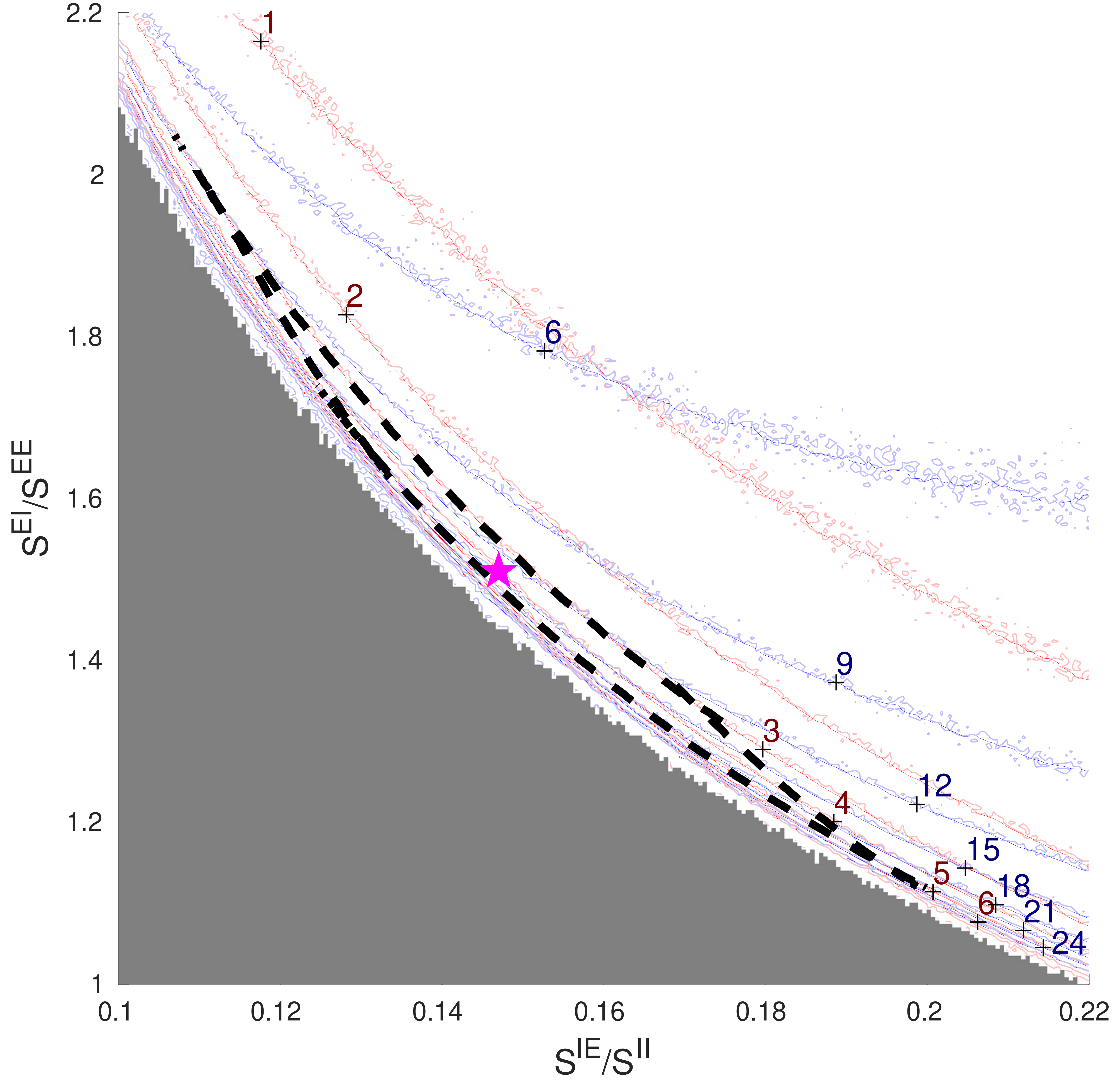

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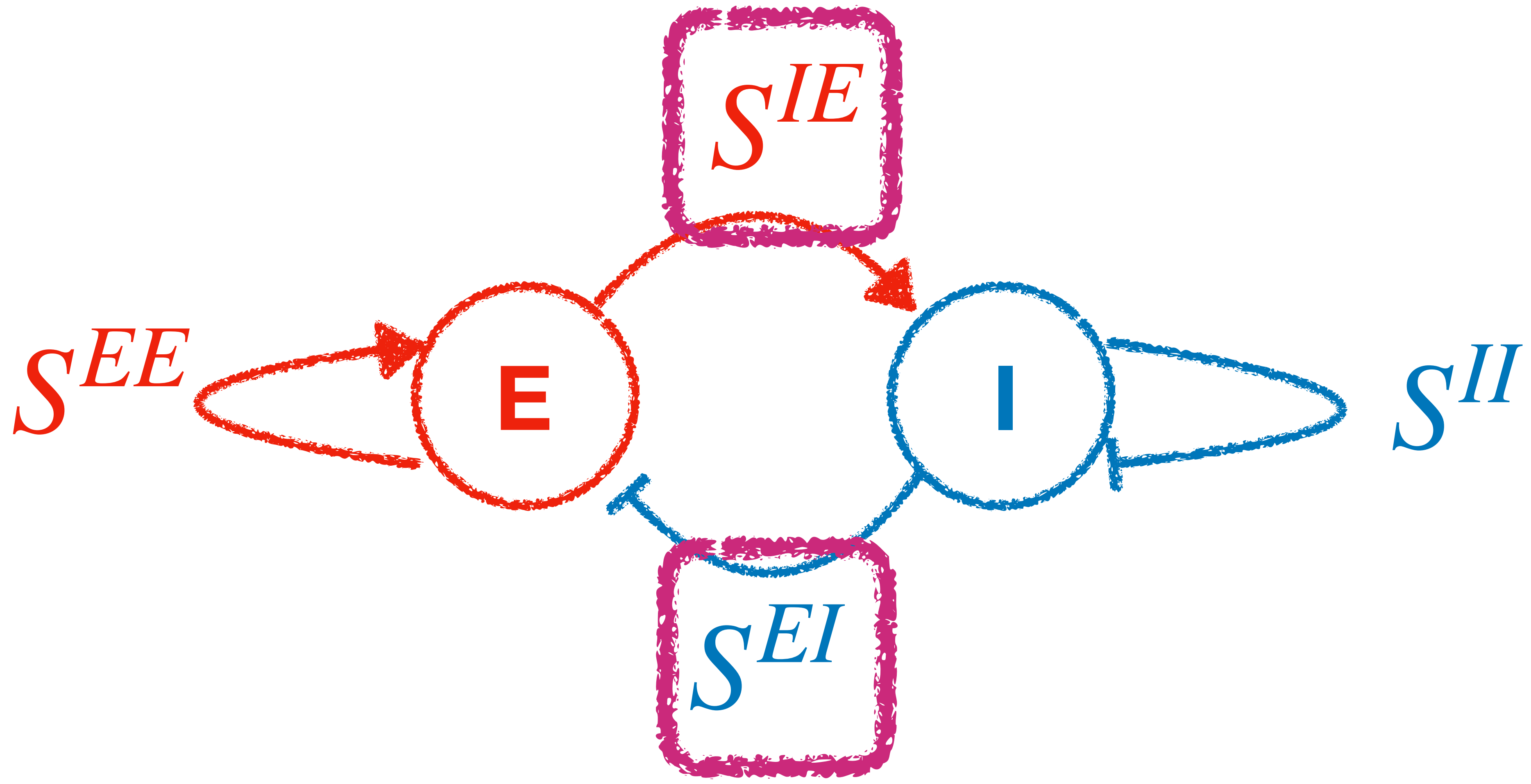
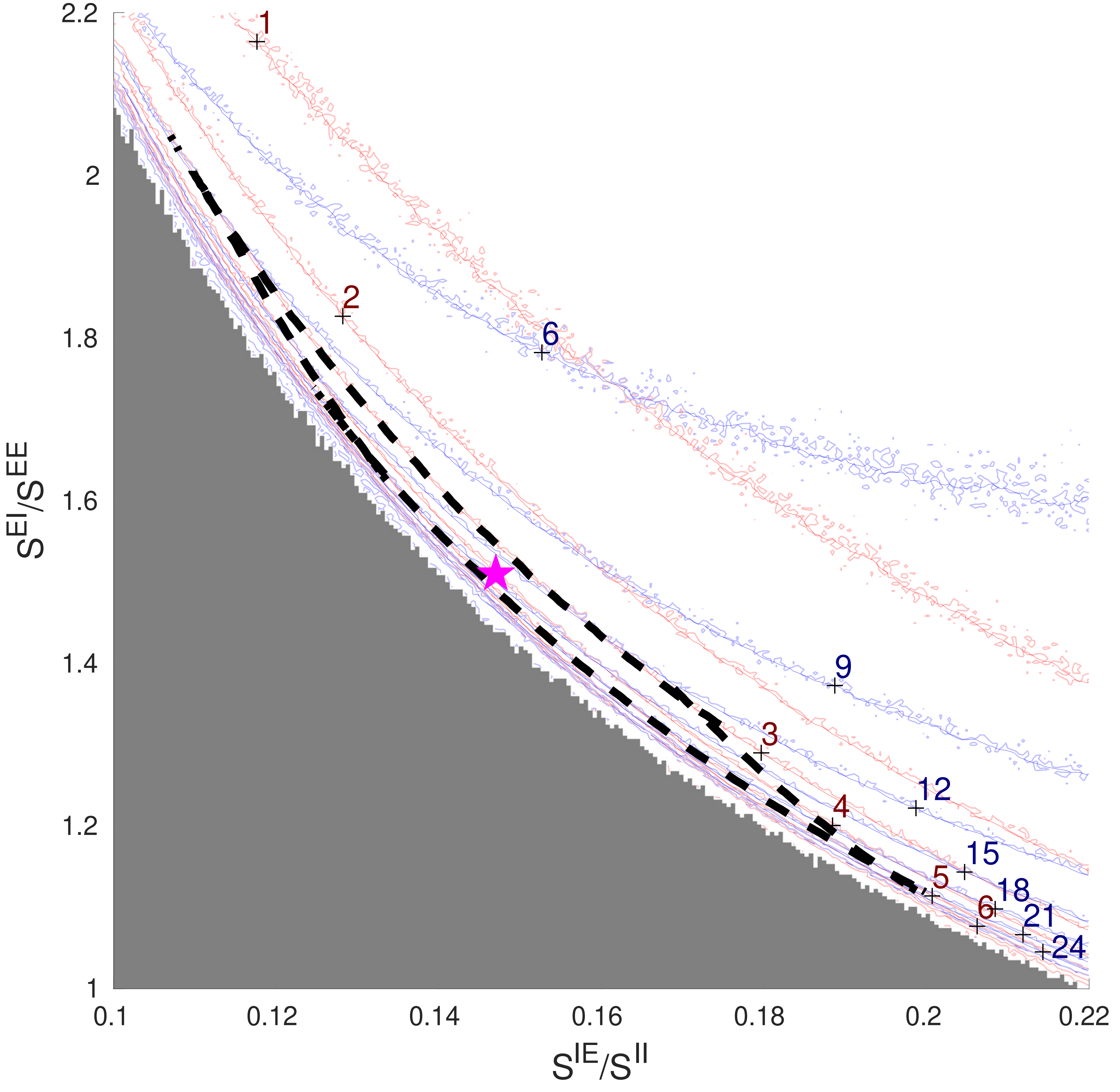
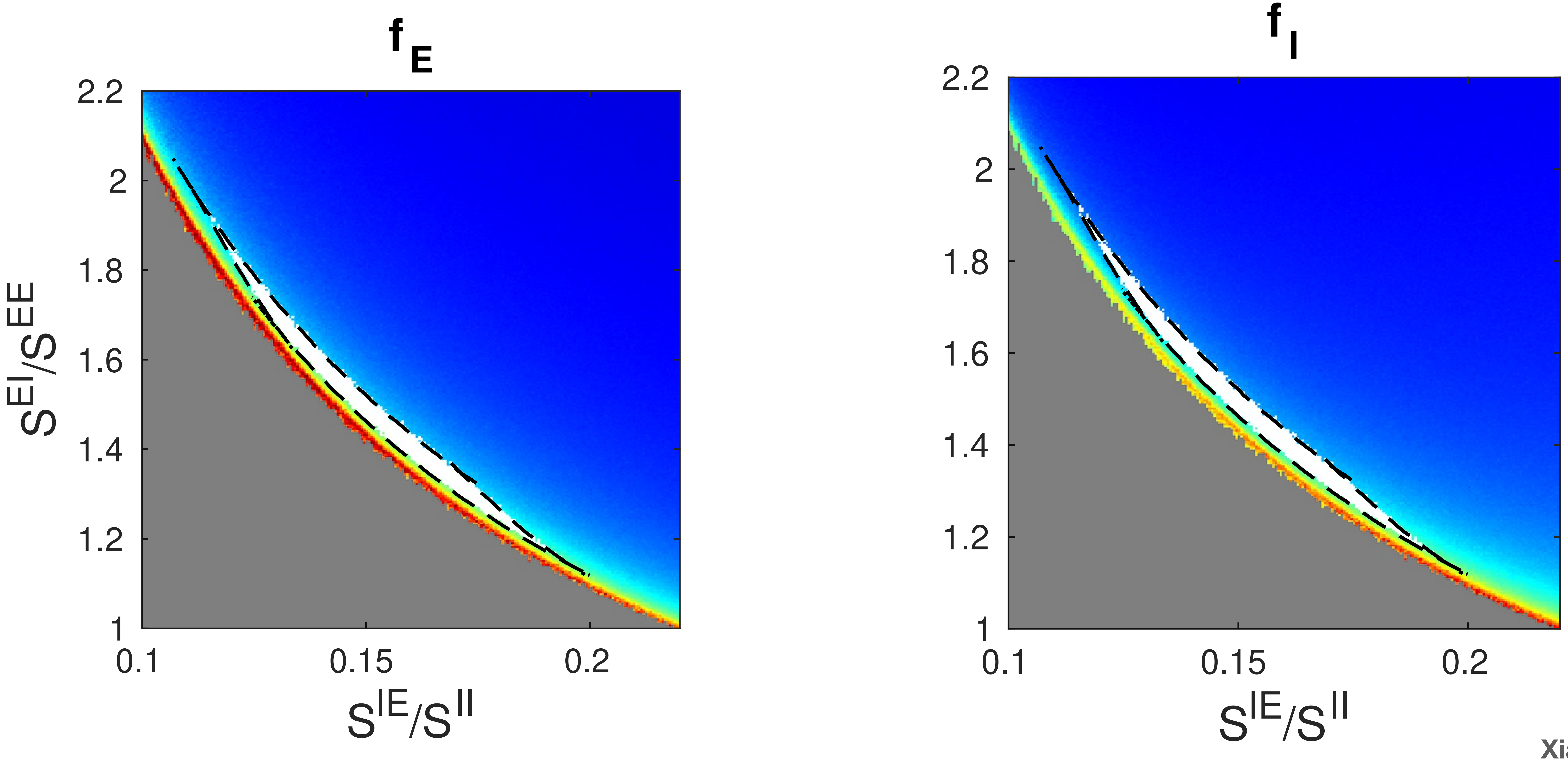


suppression index $:= \dfrac{S^{EI}}{S^{EE}} \times \dfrac{S^{IE}}{S^{II}}$

- (roughly) governs firing rates
- level curves *hyperbolic*

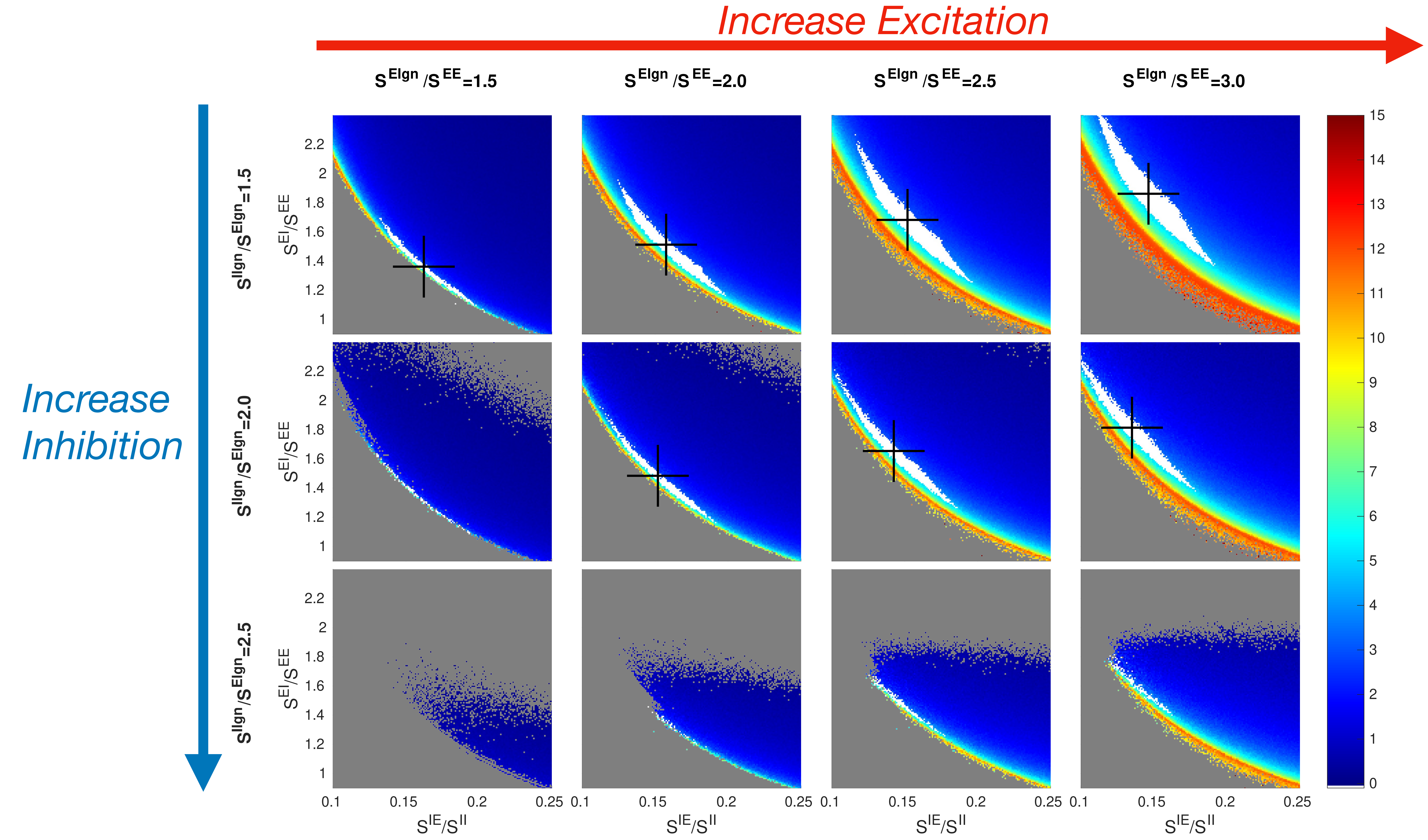


Geometry of viable manifold



Xiao, KL, Young,
PLoS Computat Biol 2022

∼codim-1 • non-generic • sensitivity + **robustness**



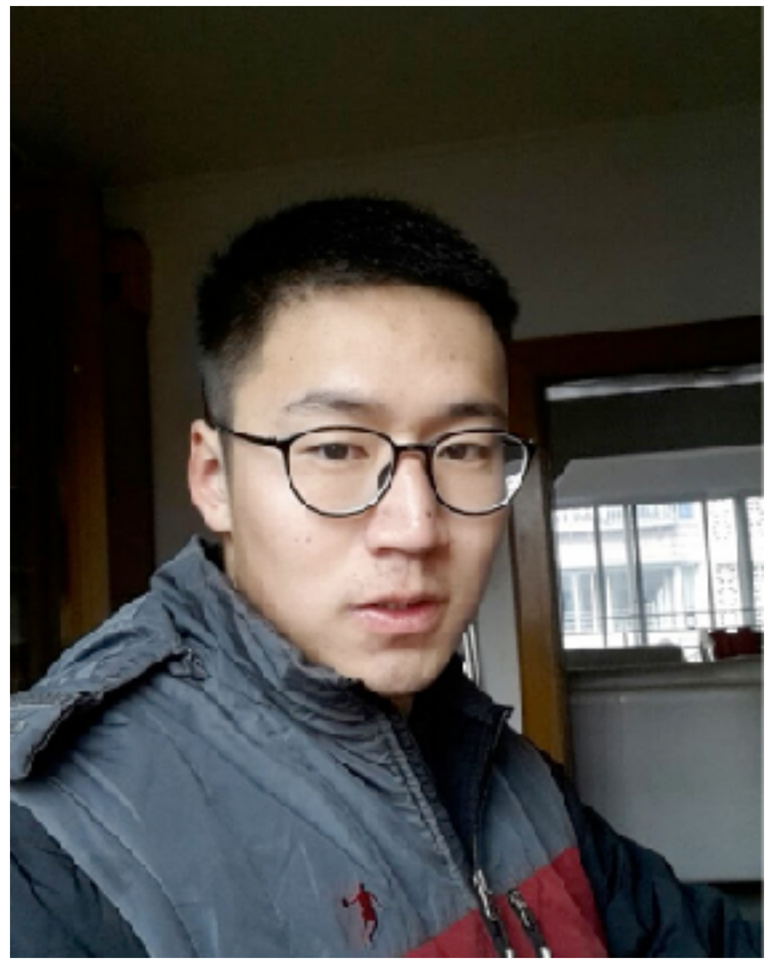
Xiao, KL, Young, *PLoS Computat Biol 2022*

Conclusions

1. *MF+v: efficient & accurate surrogates*
2. *Inhibition planes — conceptualize cortical viable parameters*

Next

- V1 under drive; larger cortical circuits
- Why does MF work?
- *Future:* multi-fidelity "biology-preserving" data driven models?



References

- Z-C Xiao, KKL, L-S Young, *PLoS Comp. Biol. (2022)*

Thanks to NSF, organizers…

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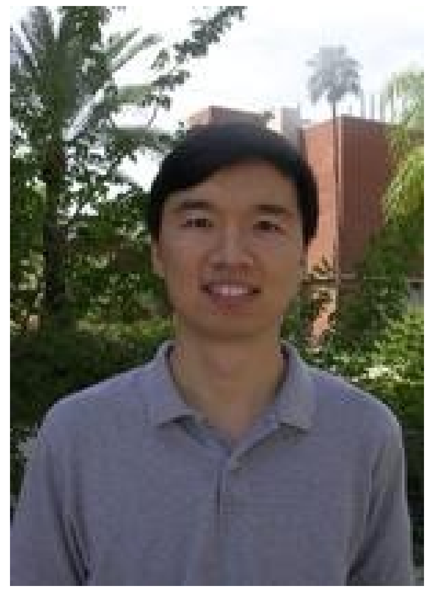
 Ali Bilgin ***Biomed Engr***	 Ning Hao ***Mathematics***	 Leonid Kunyansky ***Math***	 Selena Niu **Mathematics**	 Megha Padi **MCB**
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