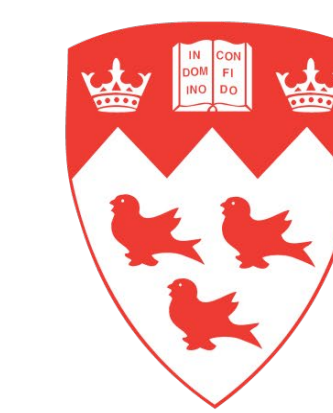


Investigating mechanisms of heterogeneities in sensory neural responses

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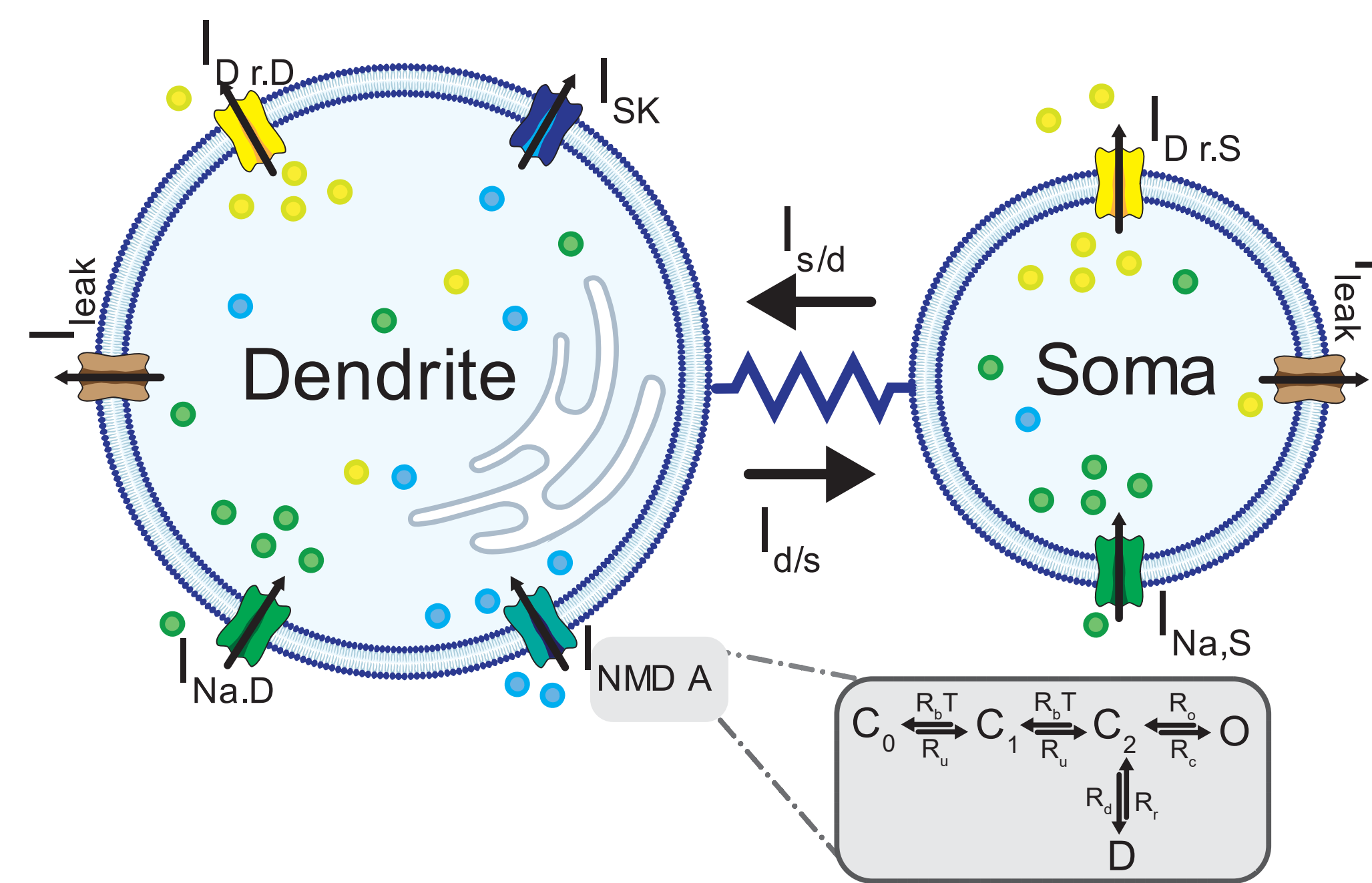
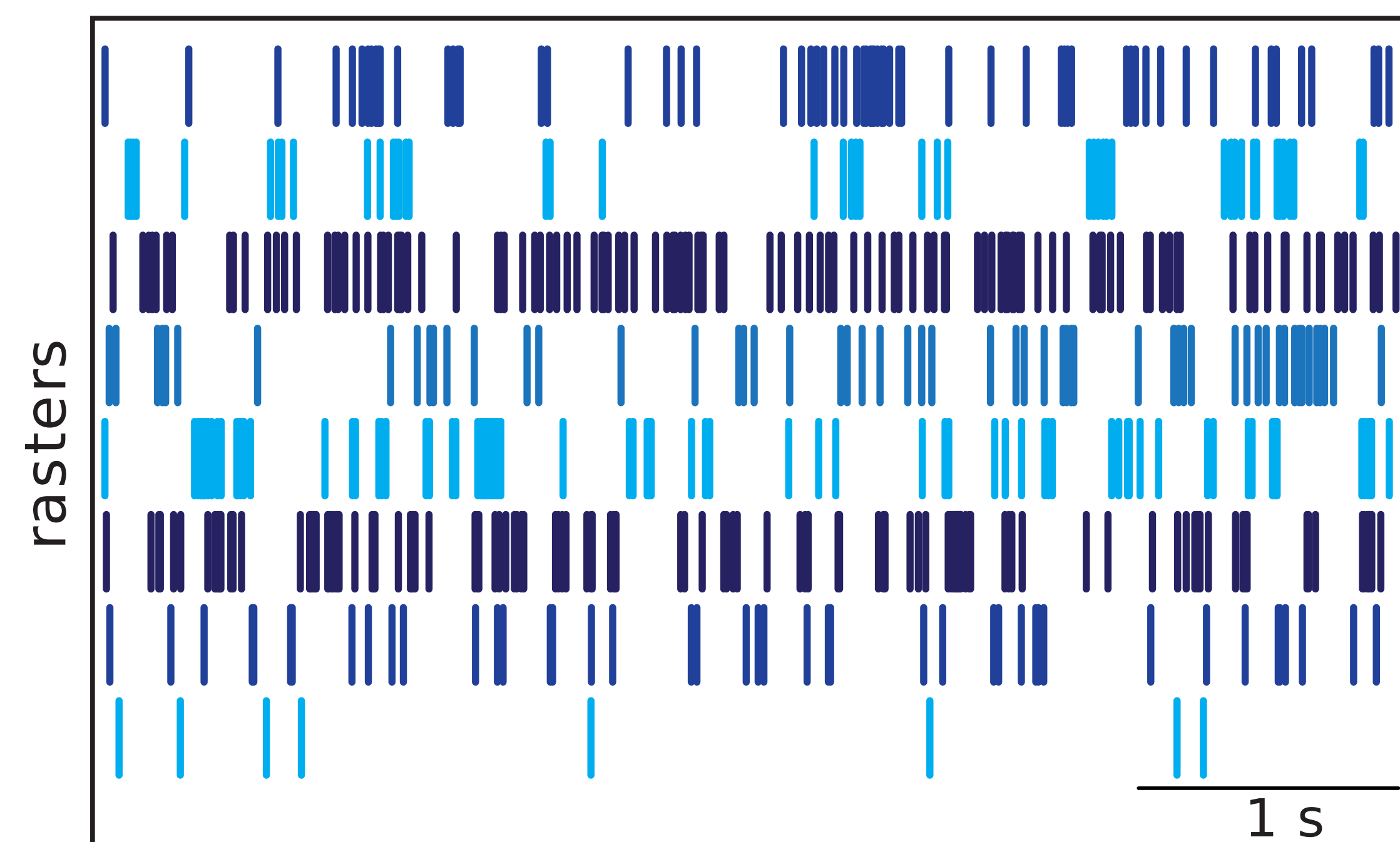
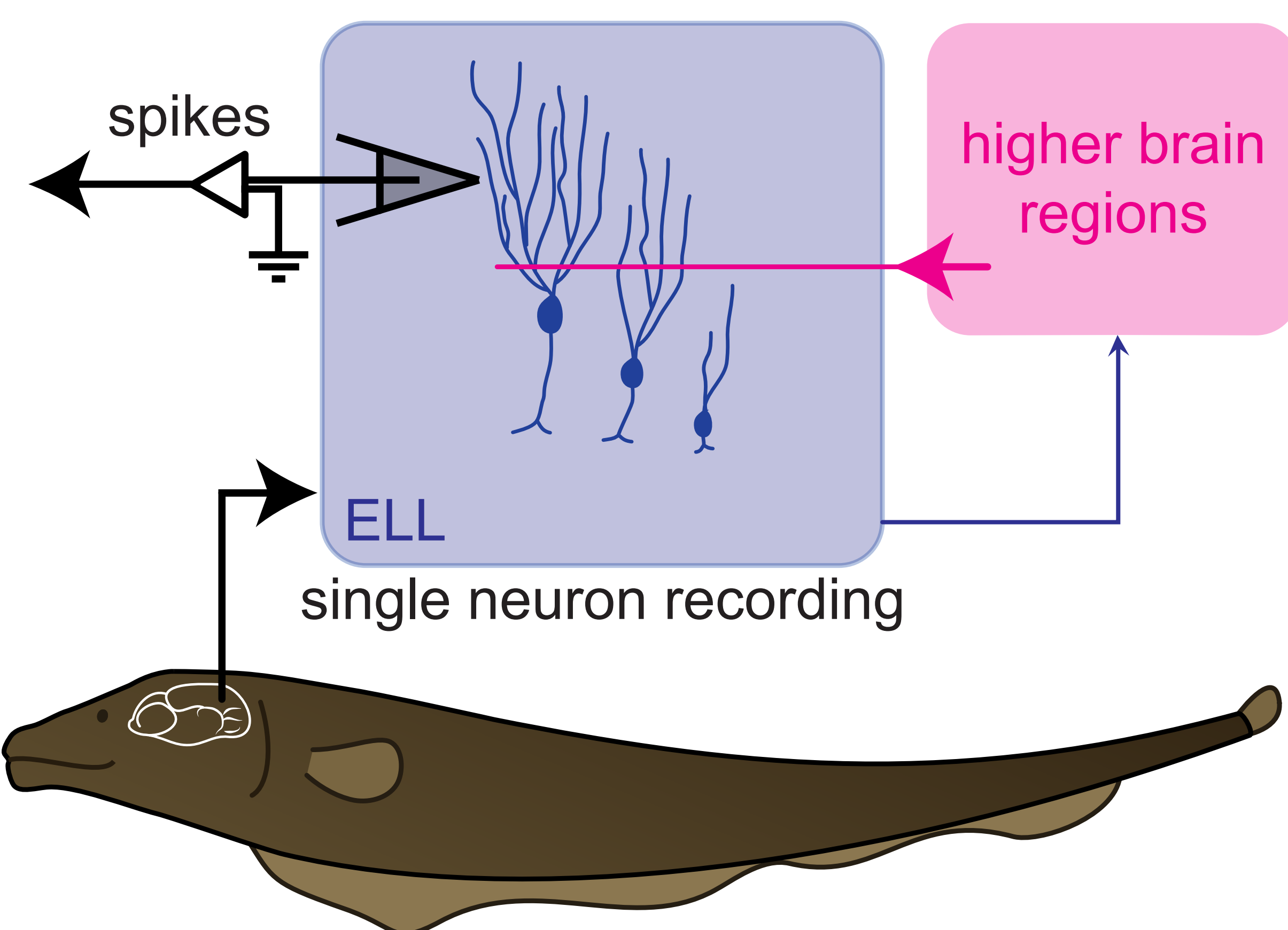
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Understanding how neurons process incoming sensory information that gives rise to perception and behavior remains a central problem in systems neuroscience

While it is generally agreed that perception is determined by the activities of large neural populations, understanding how these activities are combined is complicated by the fact that neurons display strong heterogeneities in their responses to sensory input

Pyramidal cells show different patterns of action potentials (e.g., clusters of bursts) that tend to be synchronized).



Methods

We developed a mathematical model to study how intrinsic properties of neural circuits affect the firing patterns of action potentials and how these are interpreted to give rise to perception and behavior.

Two – compartmental Ca^{2+} Based Hodgkin – Huxley model

$$C_m \frac{dV_s}{dt} = I_{Na,S} + I_{Dr,S} + I_{leak} + I_{s/d}$$

$$C_m \frac{dV_d}{dt} = I_{Na,D} + I_{Dr,D} + I_{leak} + I_{d/s} + I_{SK} + I_{NMDA} + I_{Syn}$$

$$\frac{dx}{dt} = \frac{x_{\infty}(V) - x}{\tau_x(V)}$$

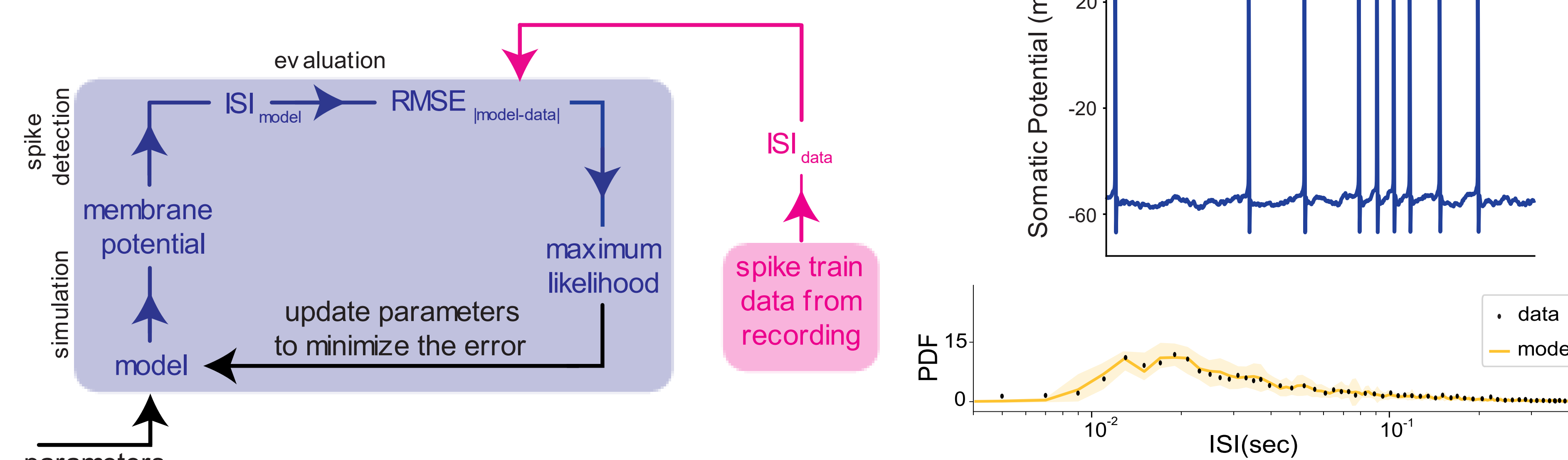
$$\frac{dCa_c^{2+}}{dt} = f_{Ca^{2+}}(J_{NMDA} + J_{Serca} + J_{PMCA} - J_{IP3} + J_{leak})$$

$$\frac{dCa_{ER}^{2+}}{dt} = f_{ERY}(J_{IP3} + J_{leak} + J_{Serca} + J_{PMCA})$$

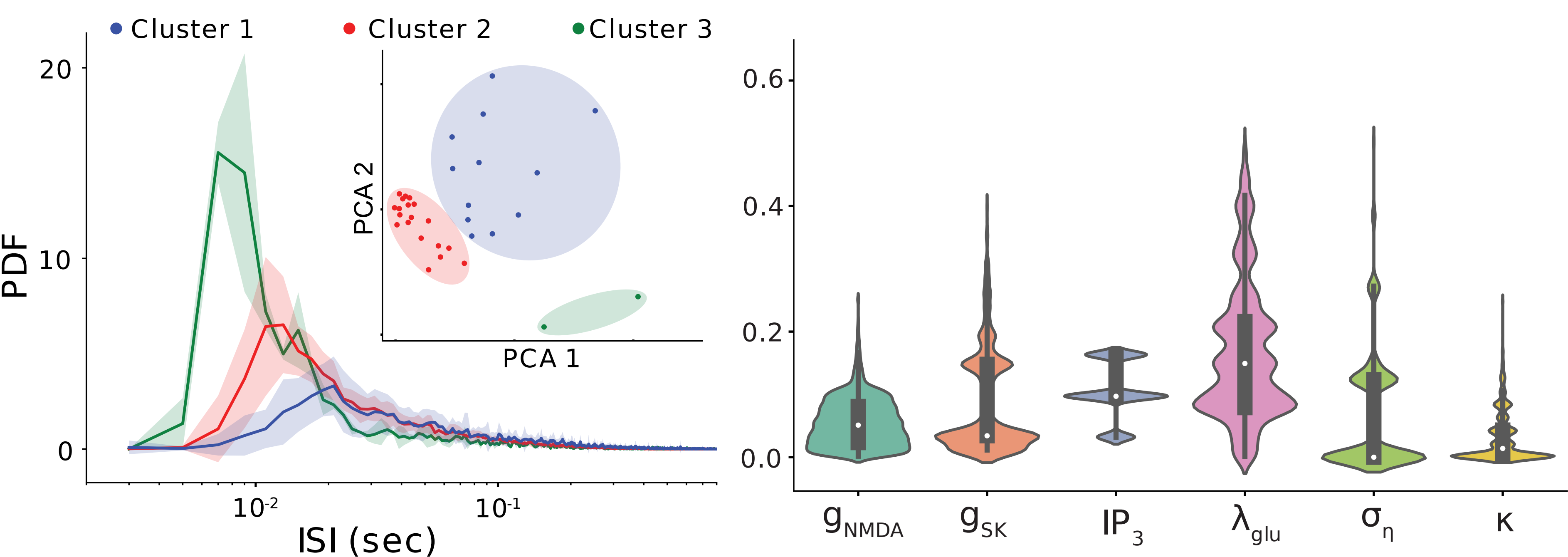
$$x_{\infty}(V) = \frac{1}{1 + \exp\left(\frac{V_x - V}{S_x}\right)}$$

Where x denotes activation/inactivation gating variables

Simulating the model and fitting neural responses with the extracellular recording for each cell identified the functional role of ionic channels and extrinsic inputs in the behavior of pyramidal cells.

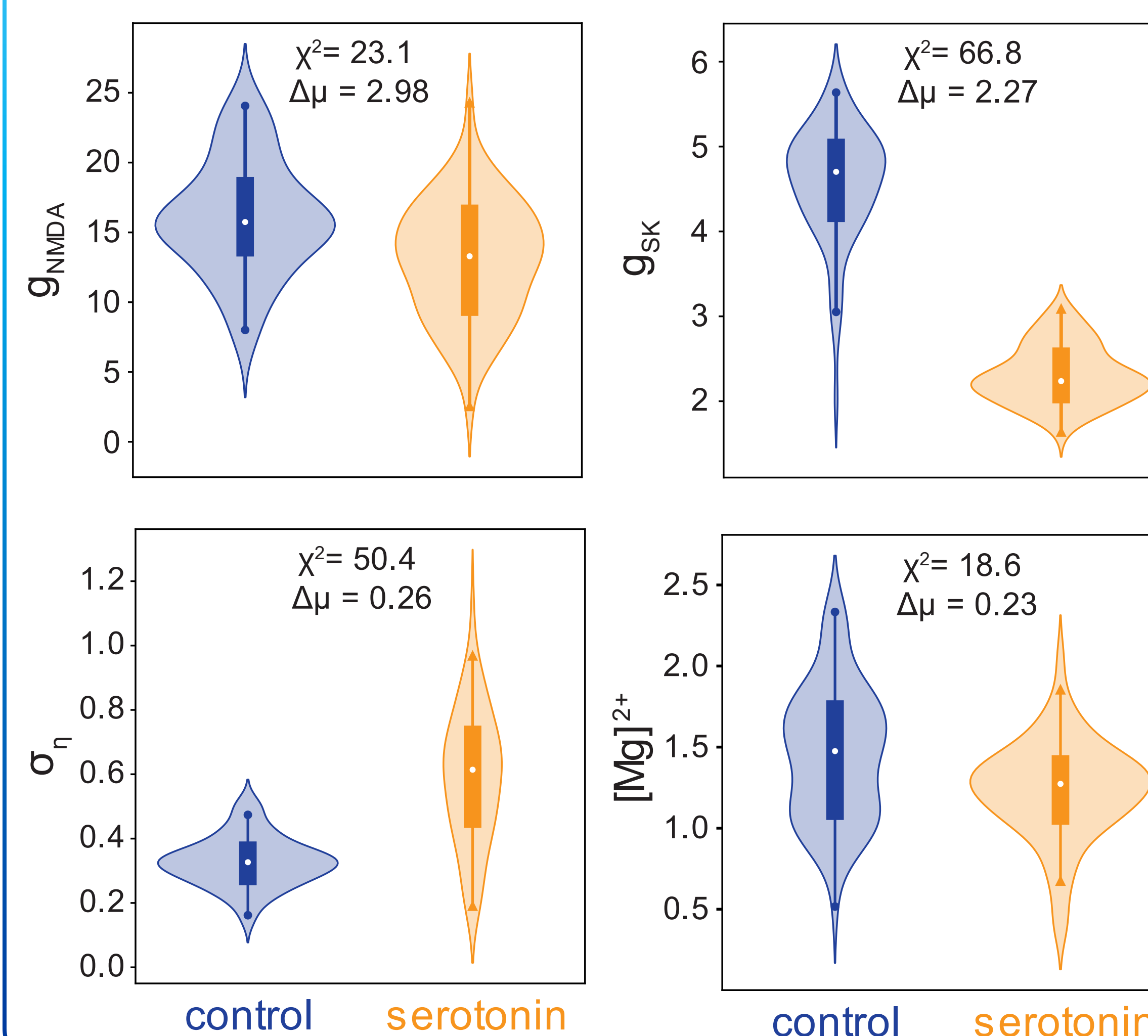
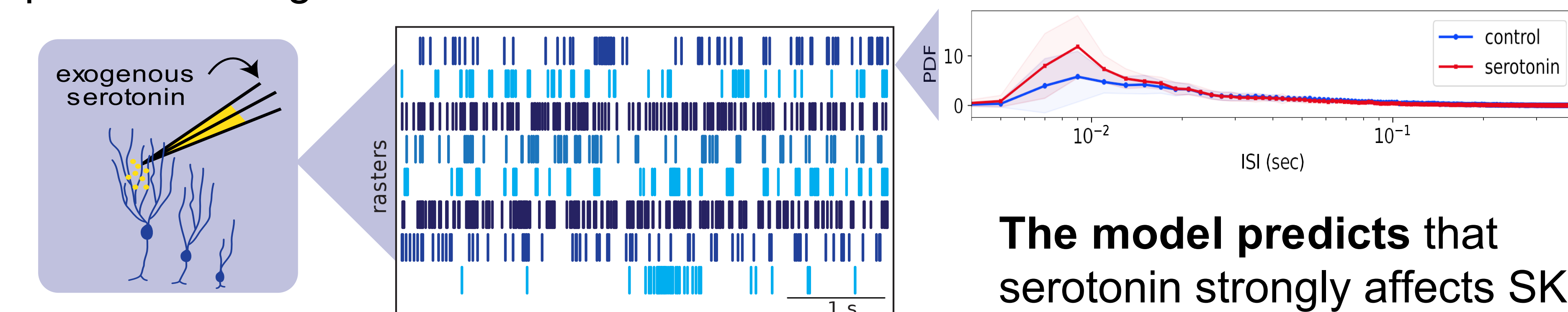


The model shows that maximal conductance of SK channel (g_{SK}), signal to release the glutamate (λ_{glu}) and the synaptic input intensity (σ_{η}) are the most important parameters that causing the heterogeneity.



Studies show that neuromodulatory serotonergic input 5-HT increases burst firing by blocking the SK channel.

To test this and making new predictions, we used the model to fit experimental ISIs after serotonin treatment and quantifying the change in the distribution of parameters against control condition.



The model predicts that serotonin strongly affects SK channels and Calcium dynamics, and these parameters play important role in PC responses.

$$\chi^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

χ^2 = Chi-squared
 O_i = Observed (serotonin)
 E_i = Expected (control)

Our findings align with experiments to explain the downregulatory role of serotonin on SK channel.

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Doiron, B., et al. (2001) *Journal of computational neuroscience*, 12(1), 5-25.
 Marquez, M.M., Chacron, M., (2020). *The Journal of Physiology*, 598(8), 1573-1589.