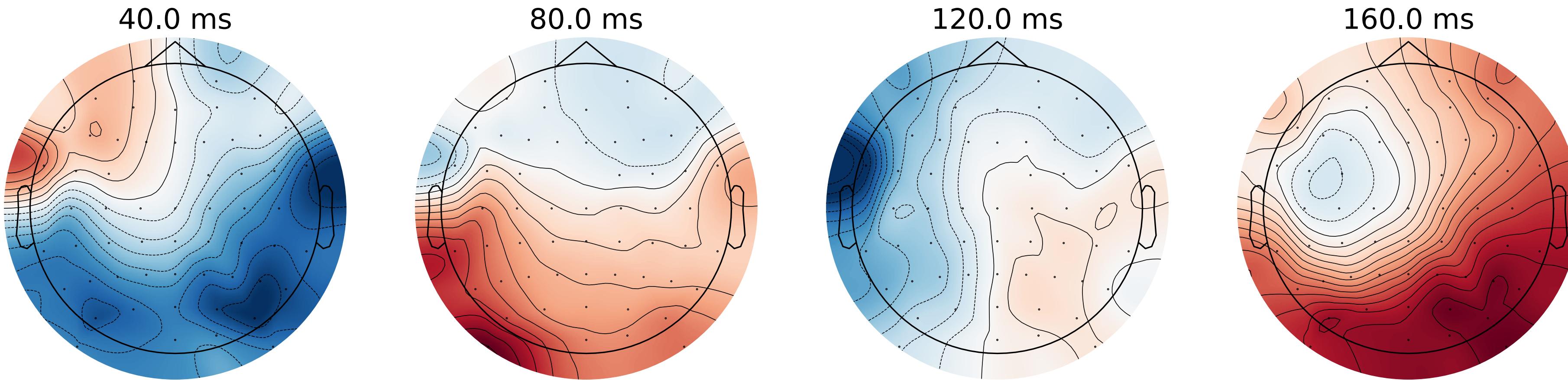


# Modelling Connectivity: DCM for EEG



Nikola Jajcay

National Institute of Mental Health, CZ & Institute of Computer Science, CAS, CZ





## #Normative models

What the answer to the problem should be?

*What* the brain is trying to do?



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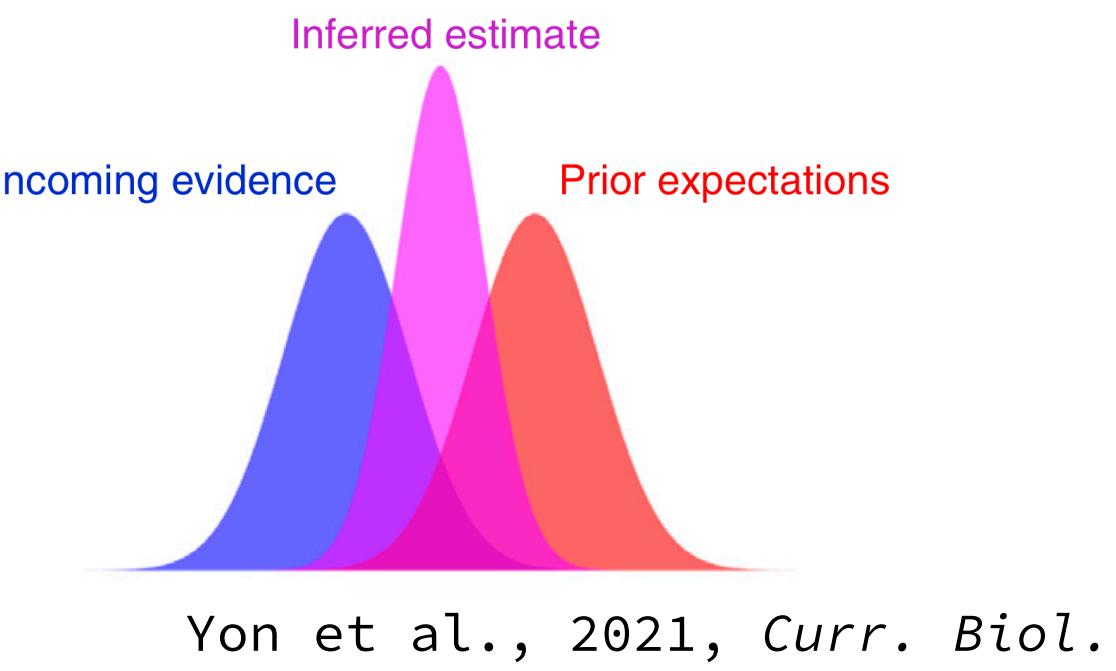
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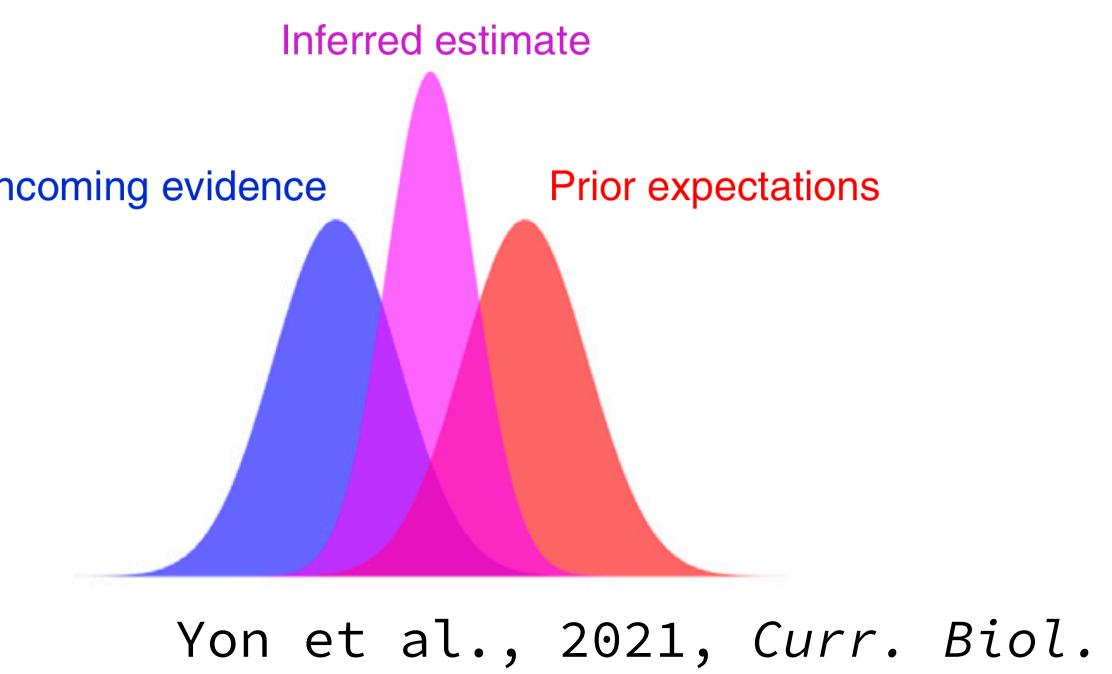


The Bayesian brain  
& Predictive coding

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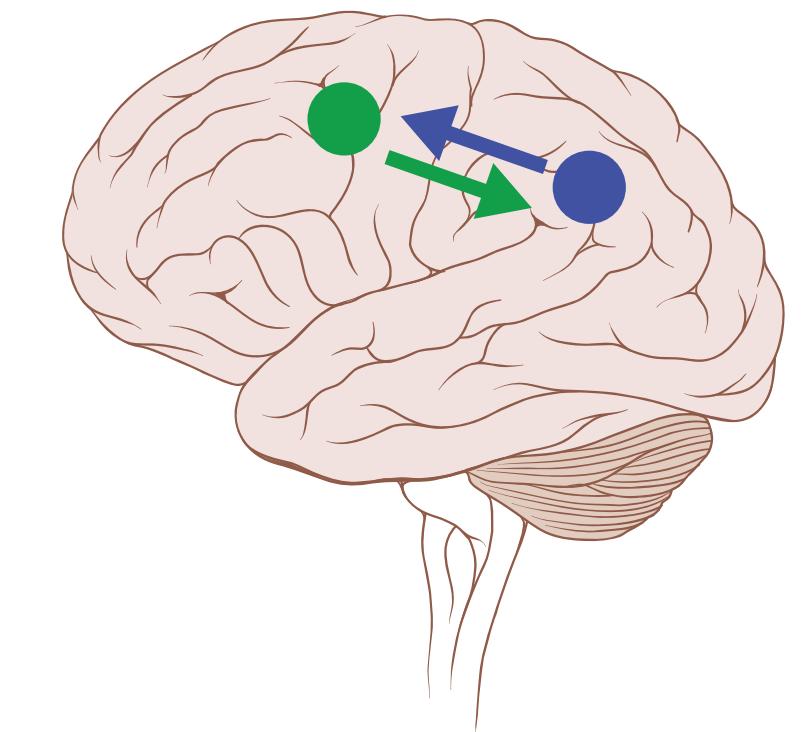
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DCM & Brain connectivity

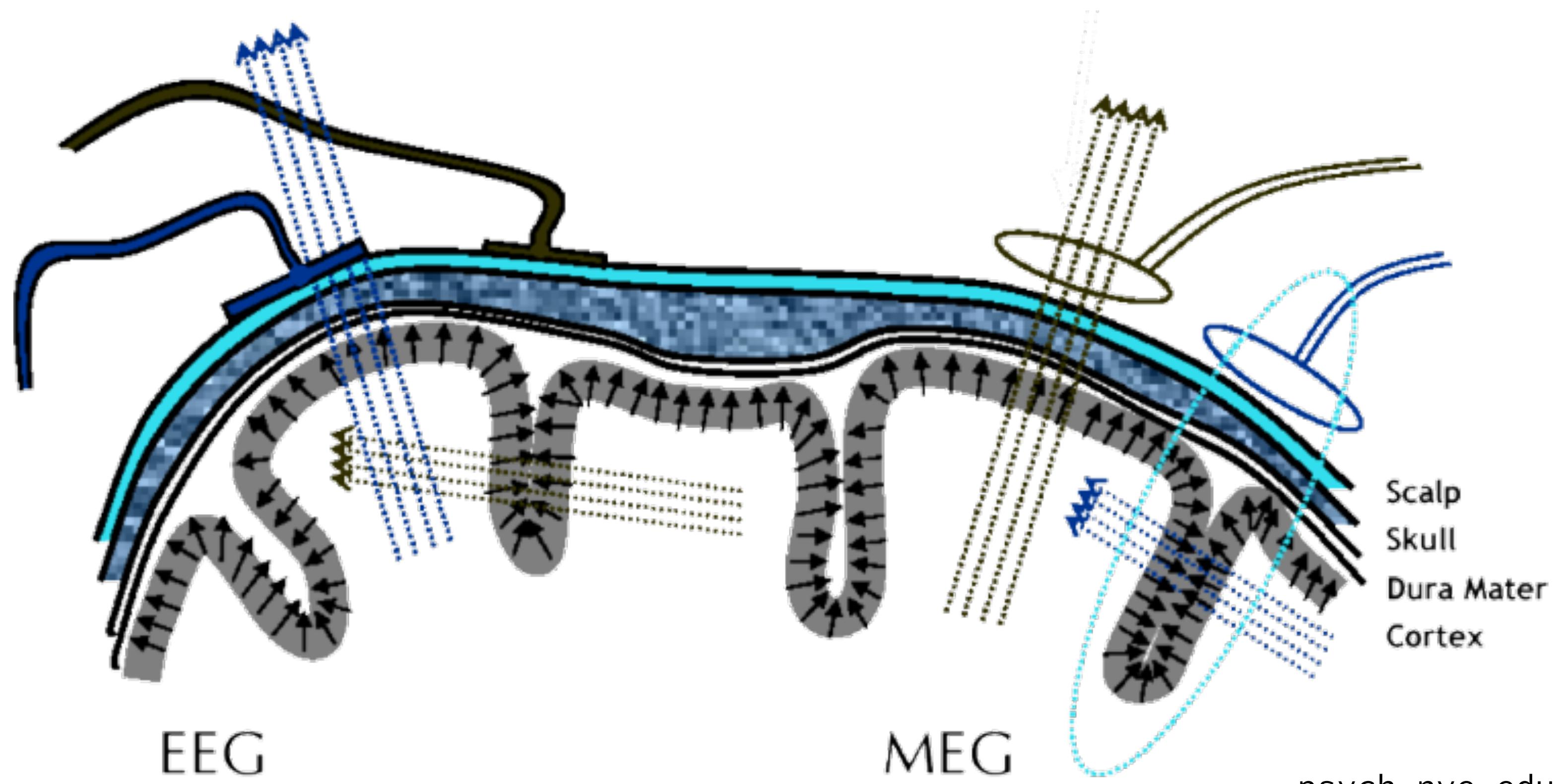
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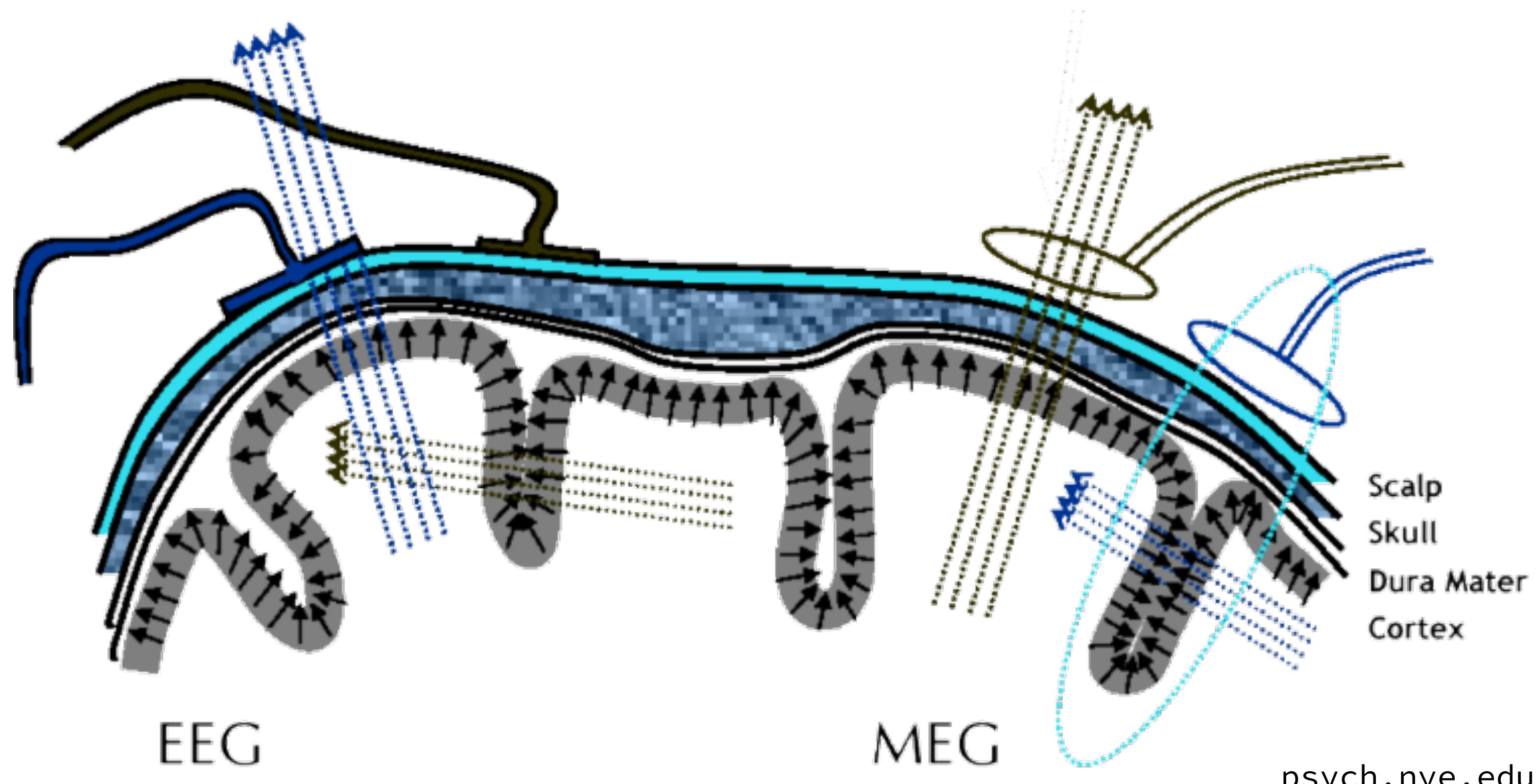
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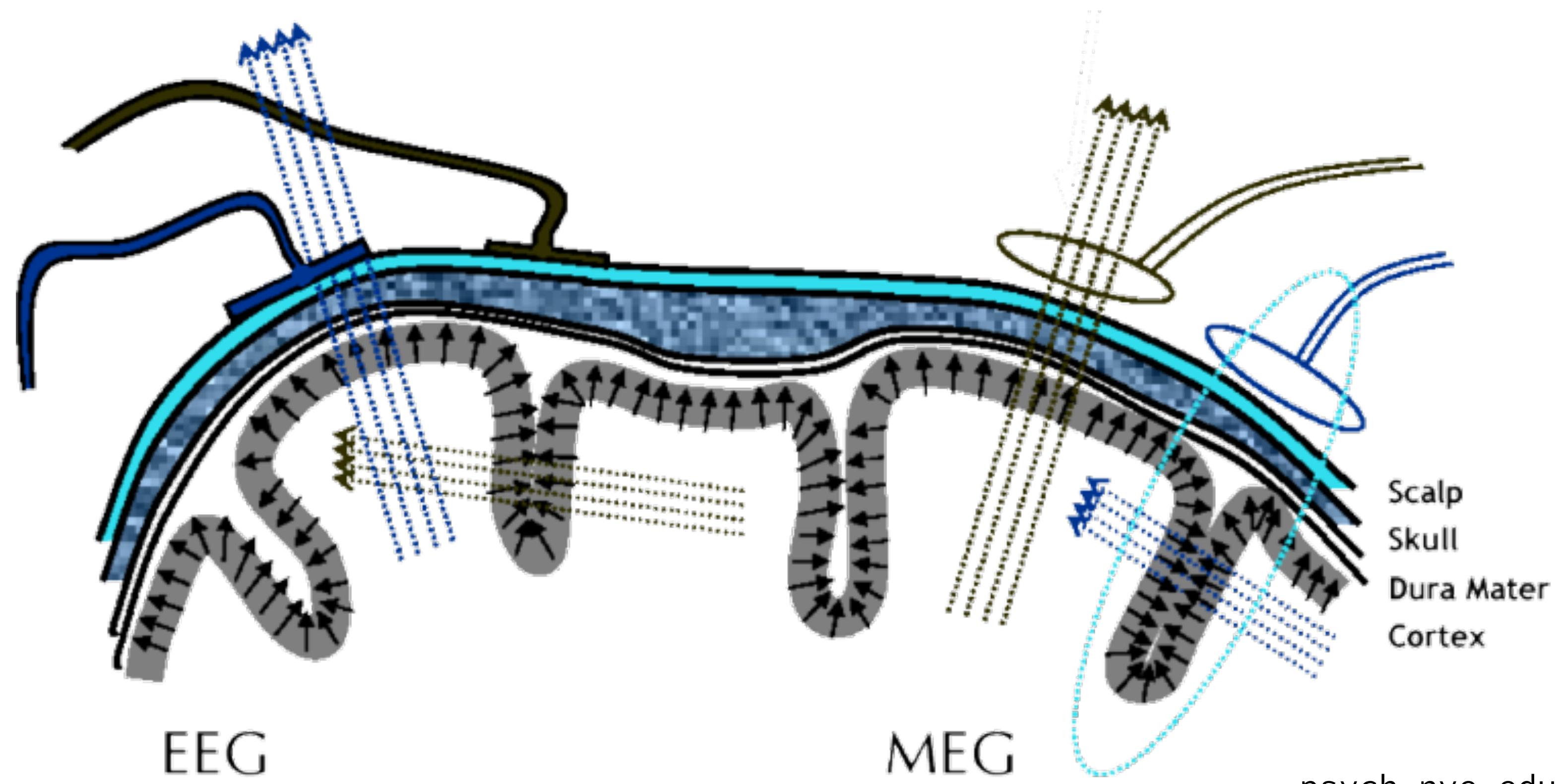
# #Data: M/EEG

- ▶ direct measure: measures electric activity
  - ▶ EEG: extracellular current (dendrites)



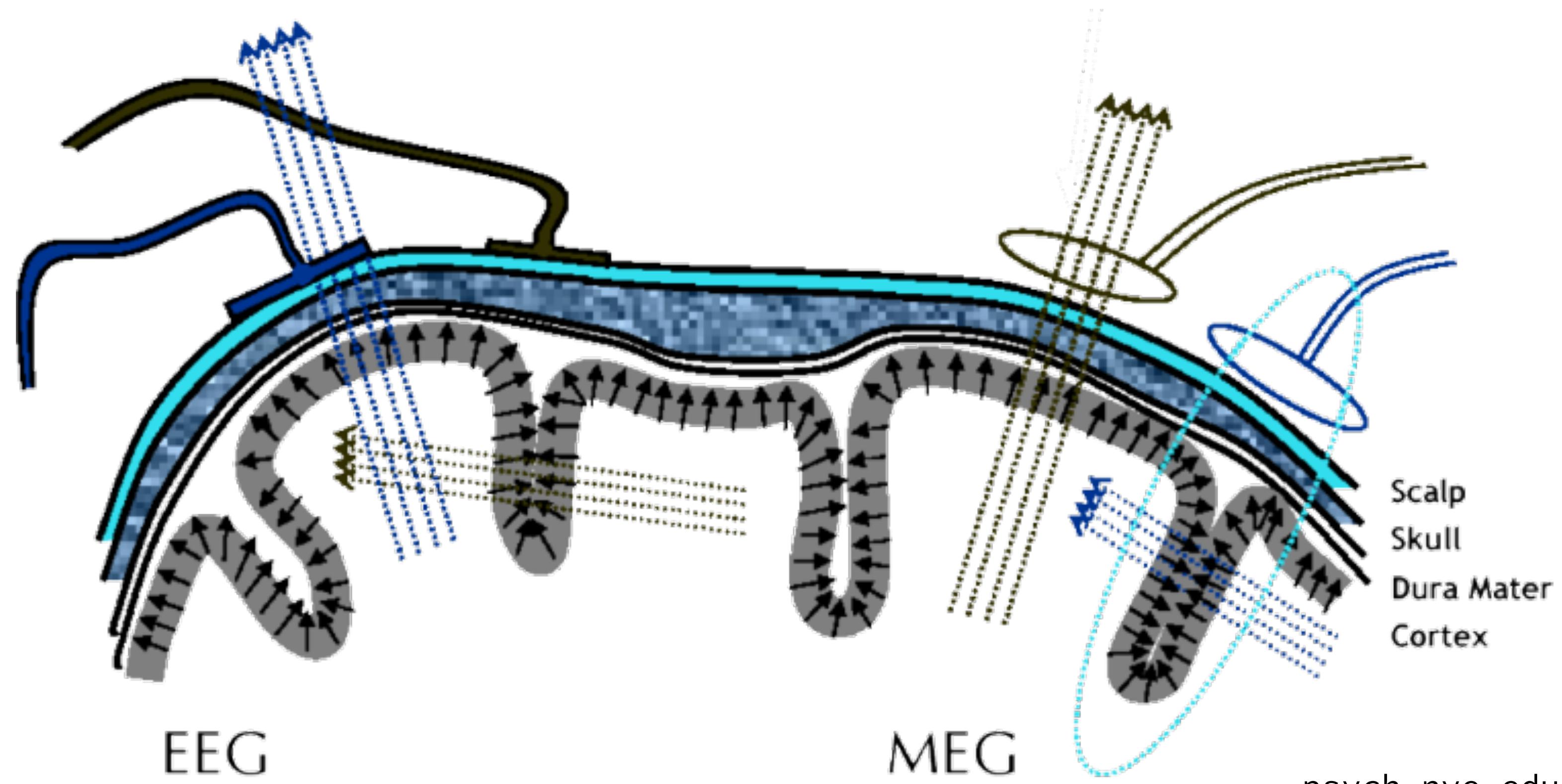
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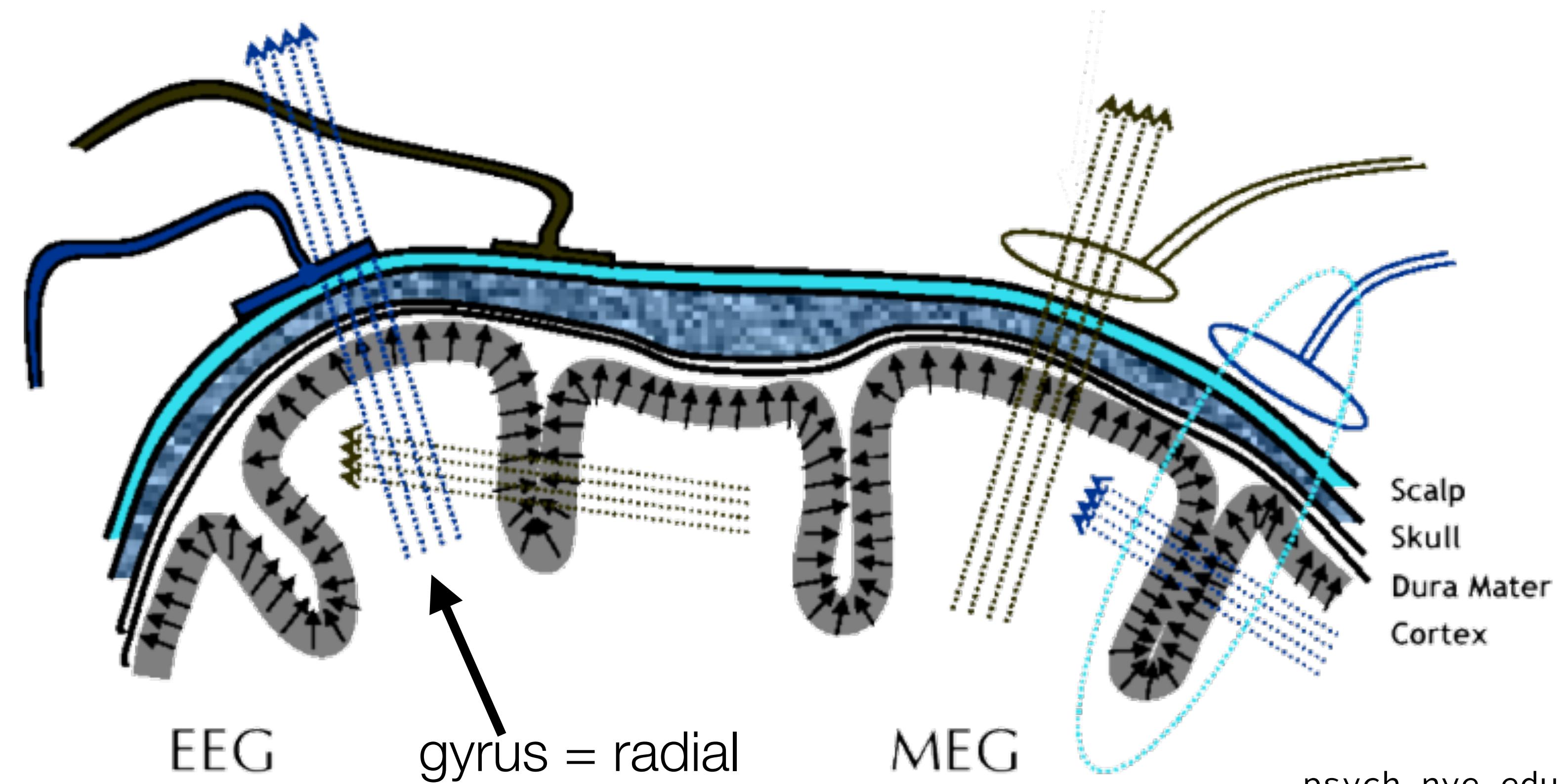
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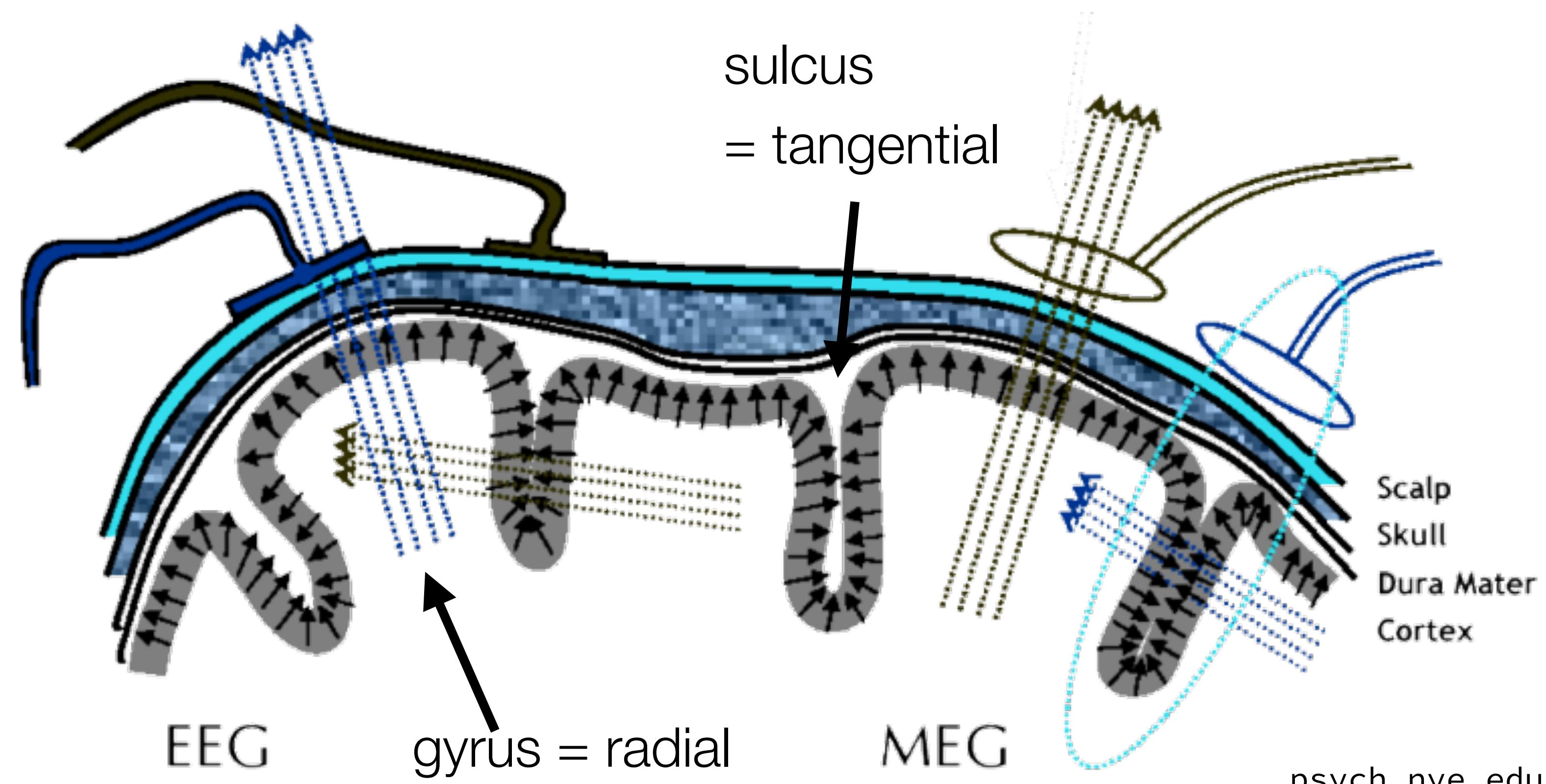
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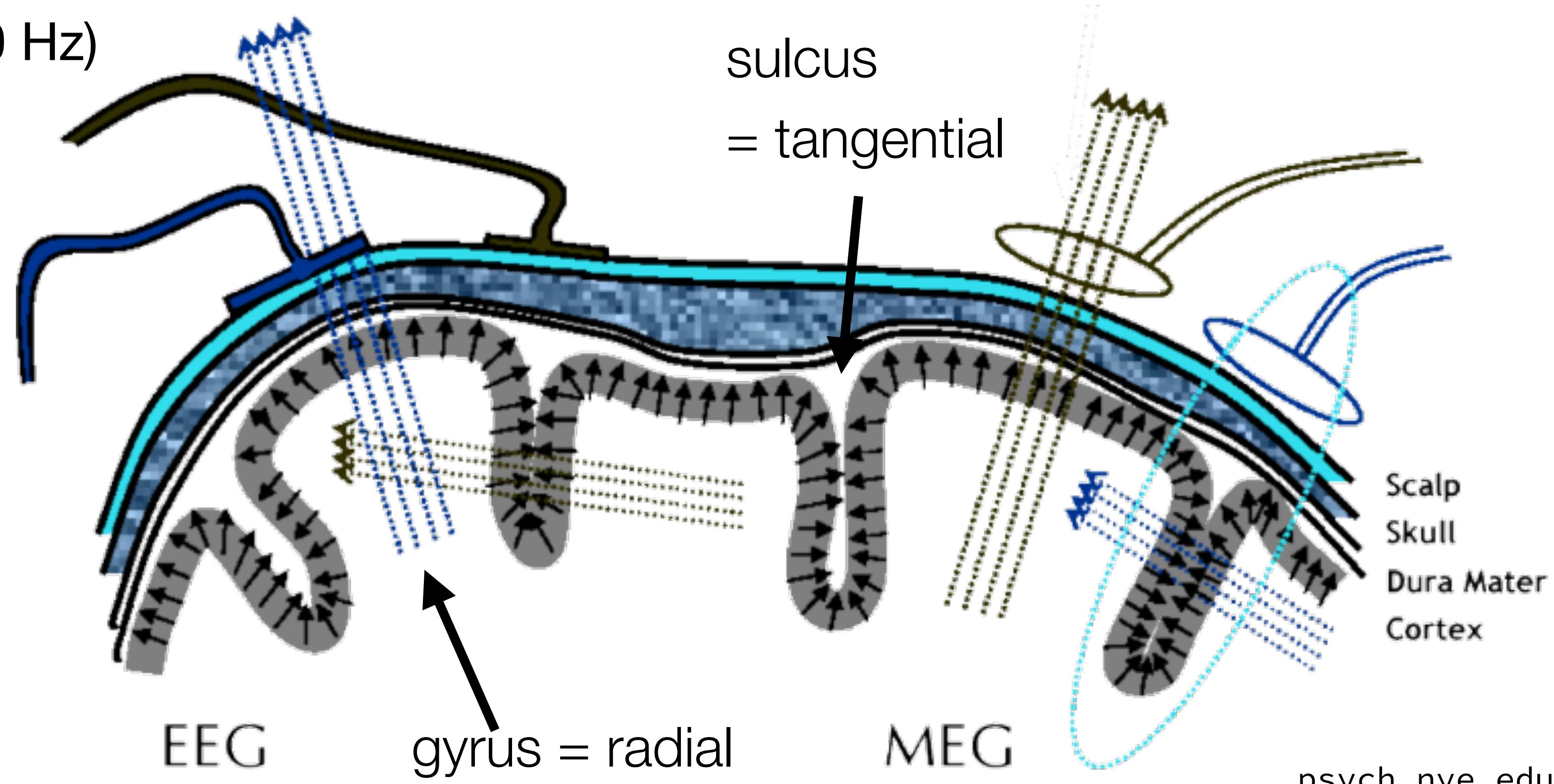
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# #Dynamic Causal Modelling: general approach

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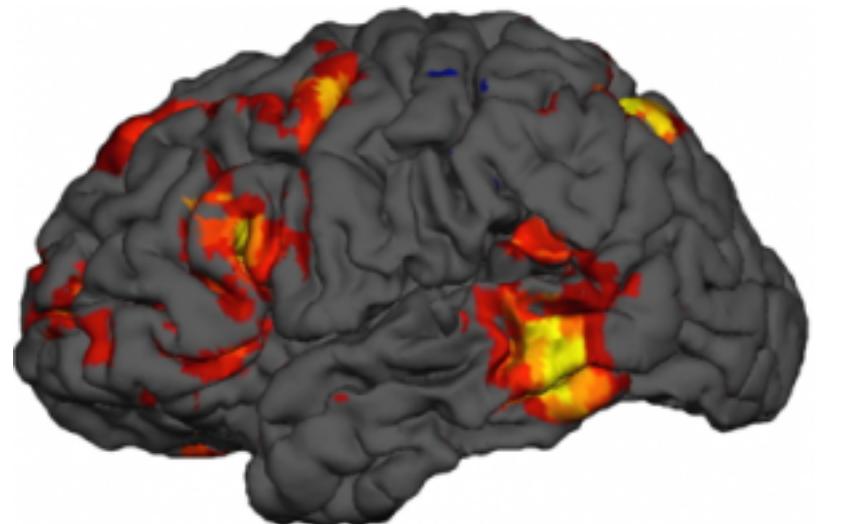


$$\frac{dx}{dt} = F(x, u, \theta)$$

neural state equations

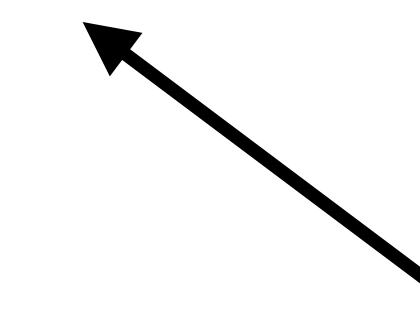
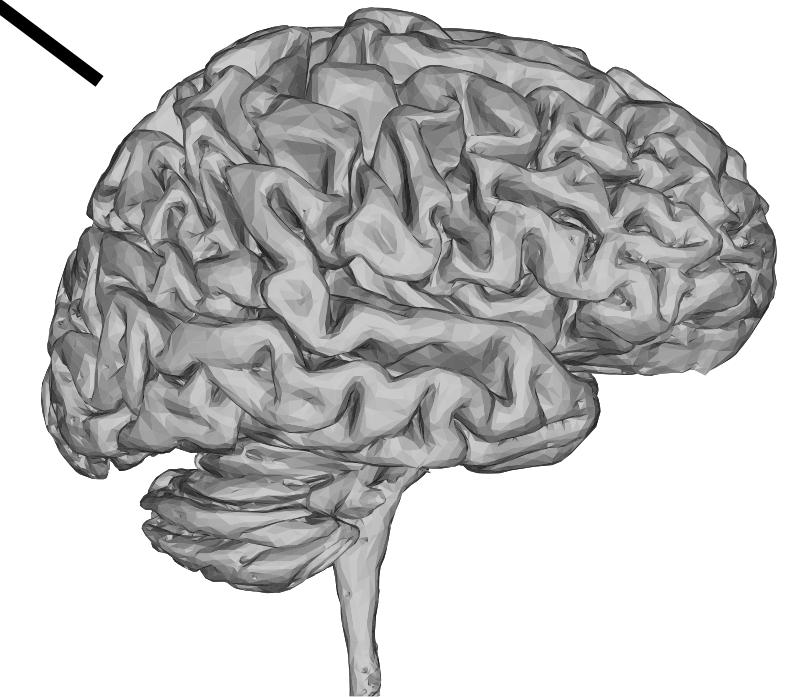
# #Dynamic Causal Modelling: general approach

- ▶ haemodynamic forward model: BOLD



[biopac.com](http://biopac.com)

**fMRI**

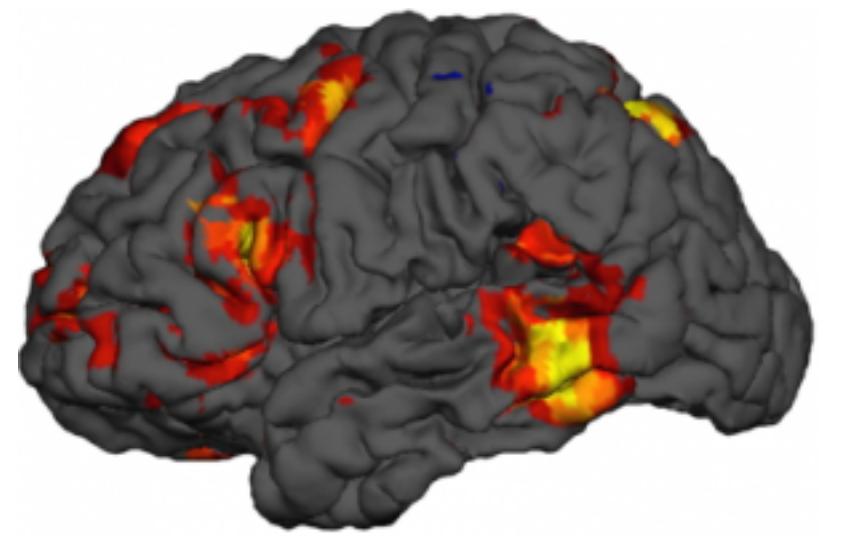


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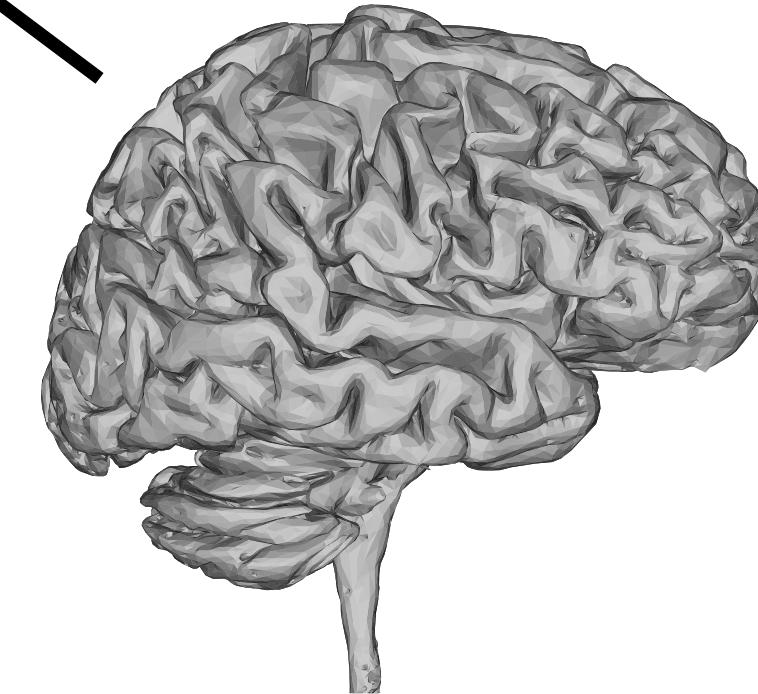
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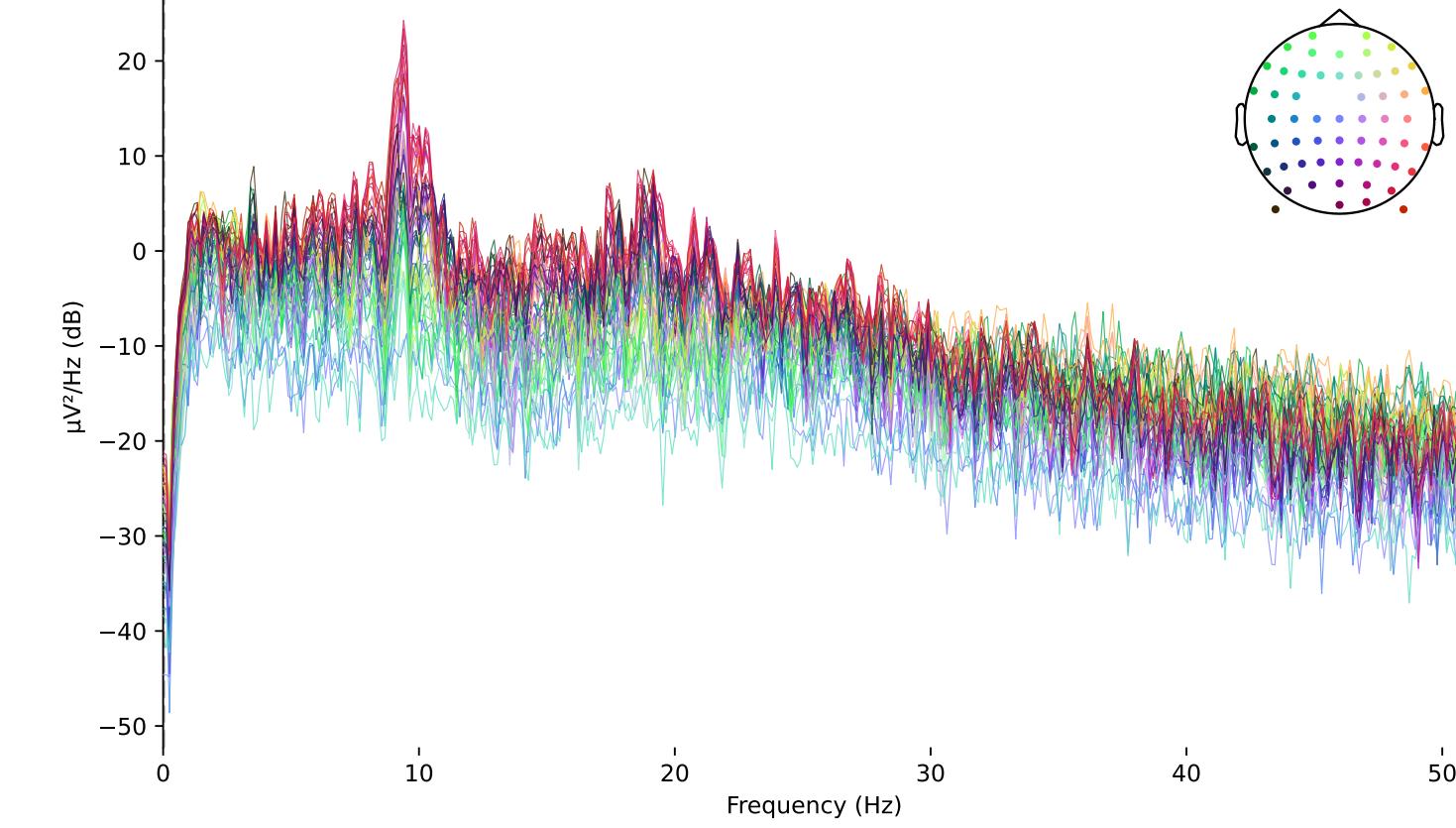
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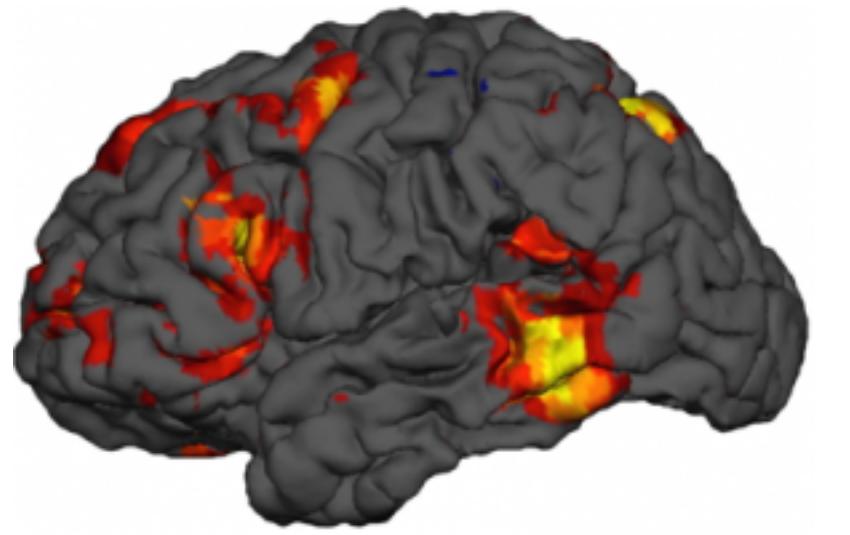
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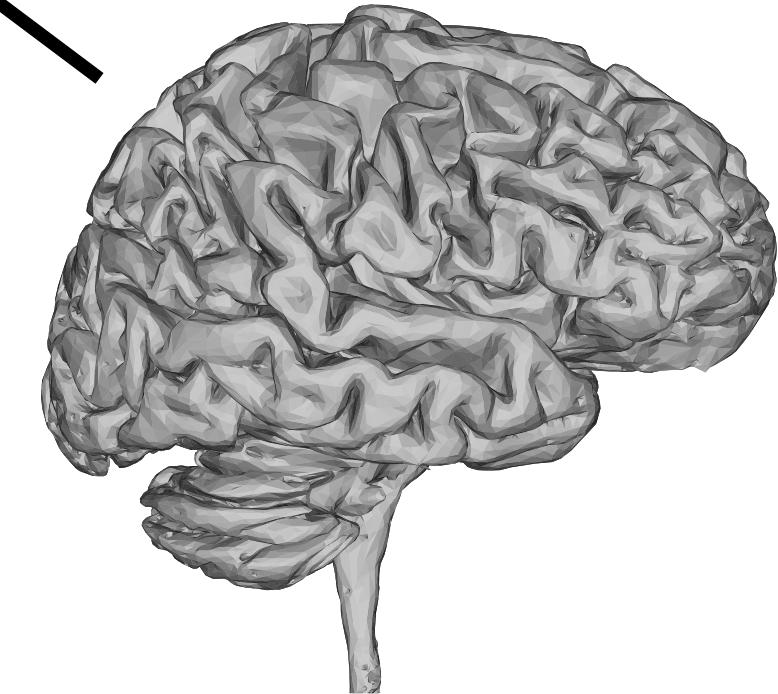
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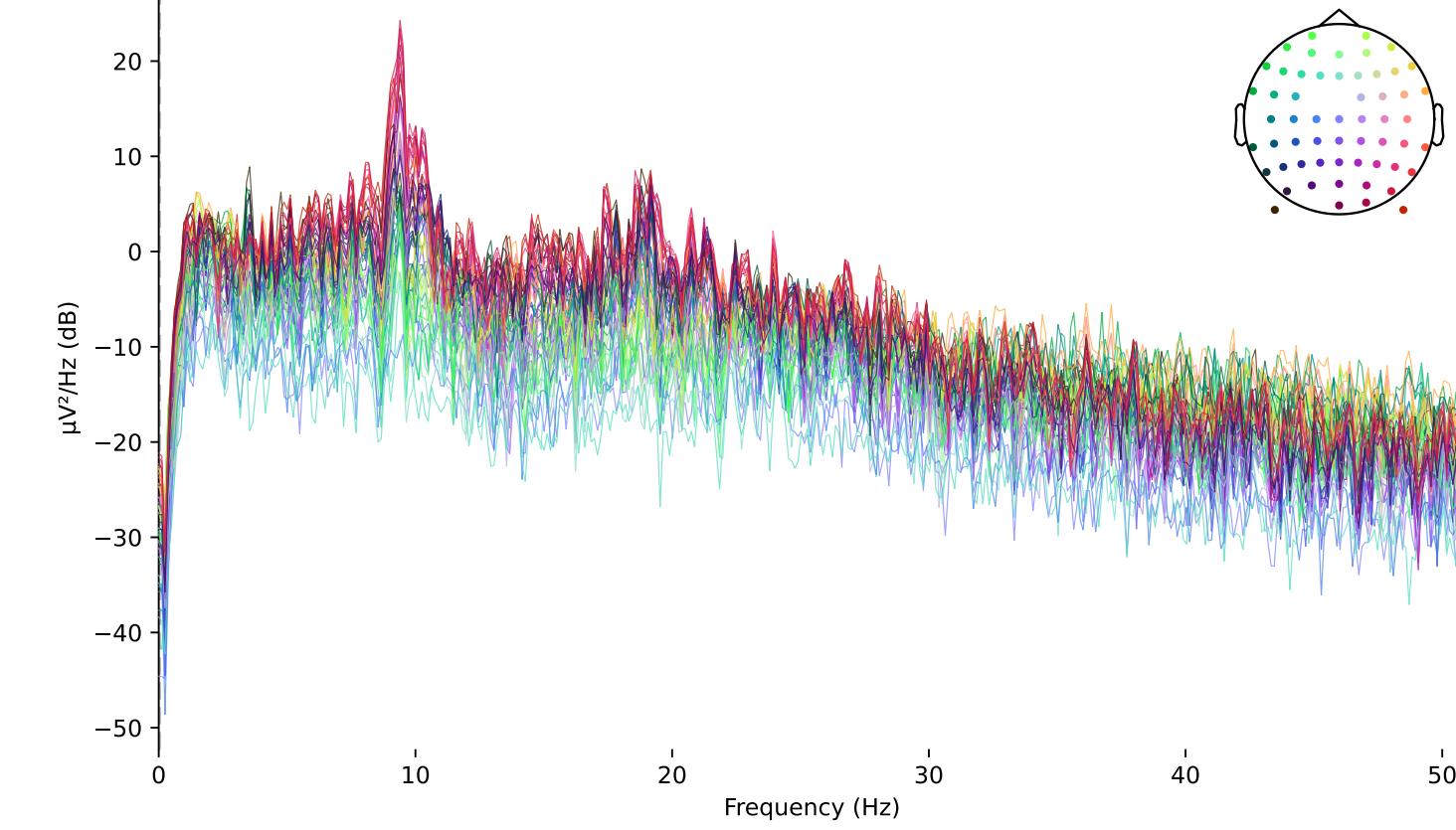
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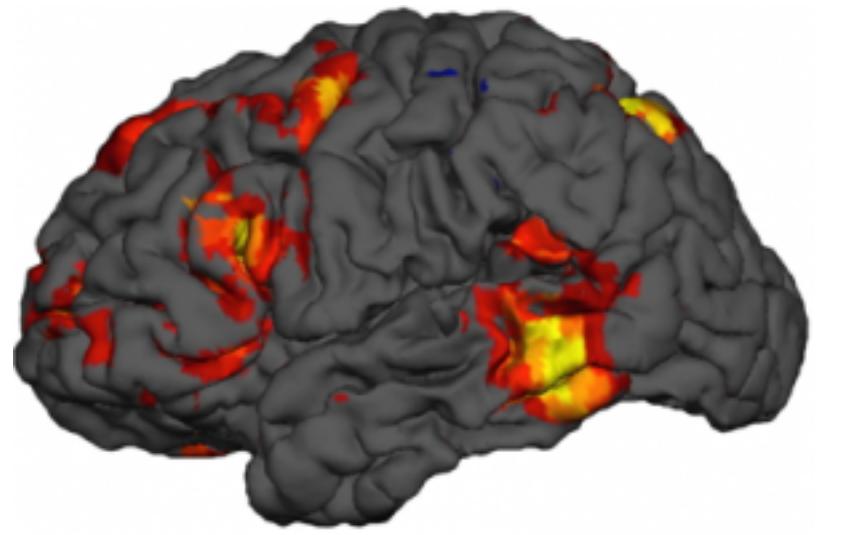


**M/EEG**

$$y = G(x, \theta) + \epsilon$$

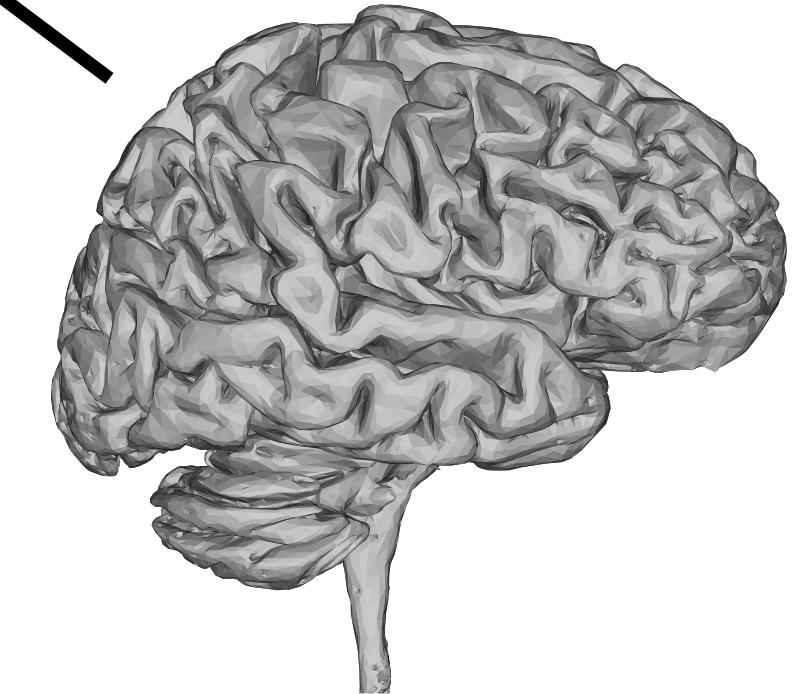
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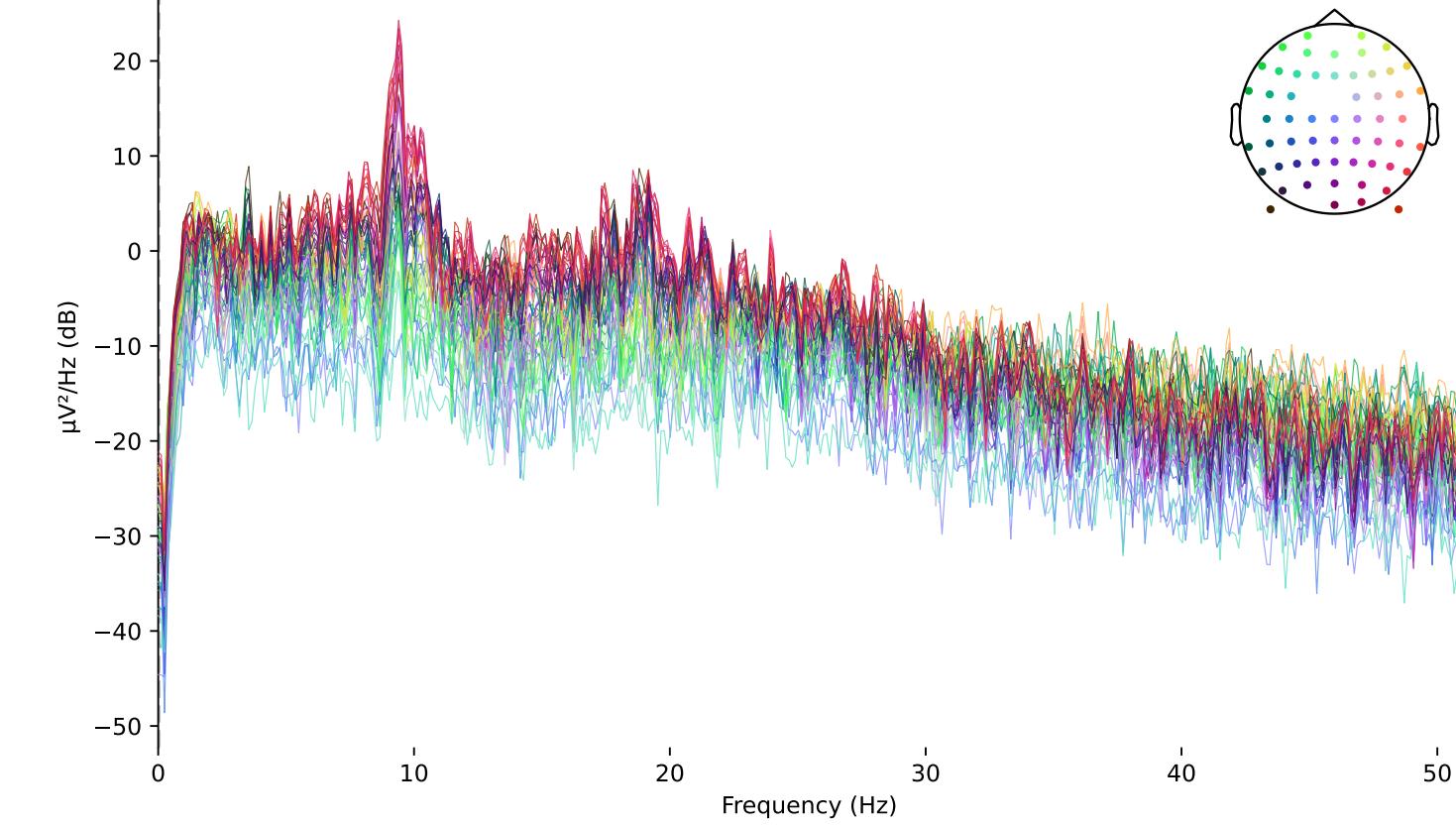
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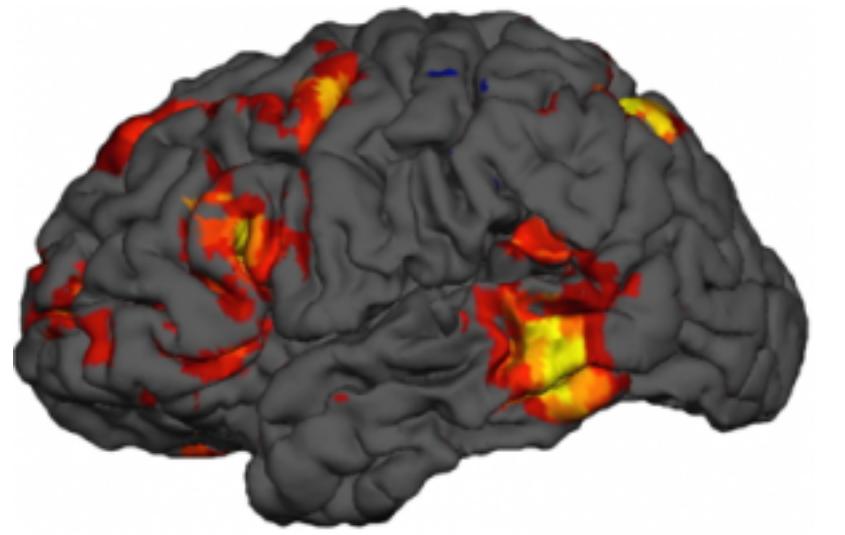
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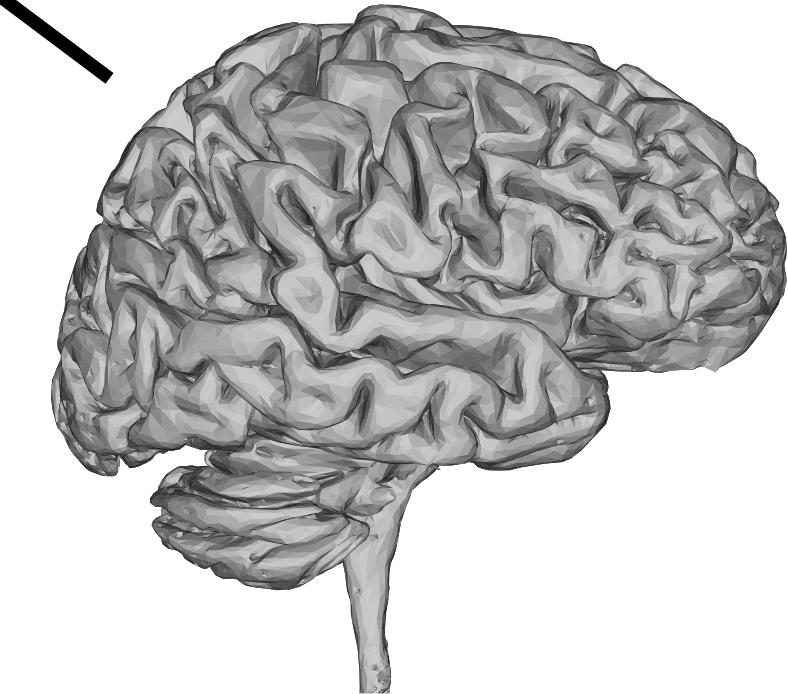
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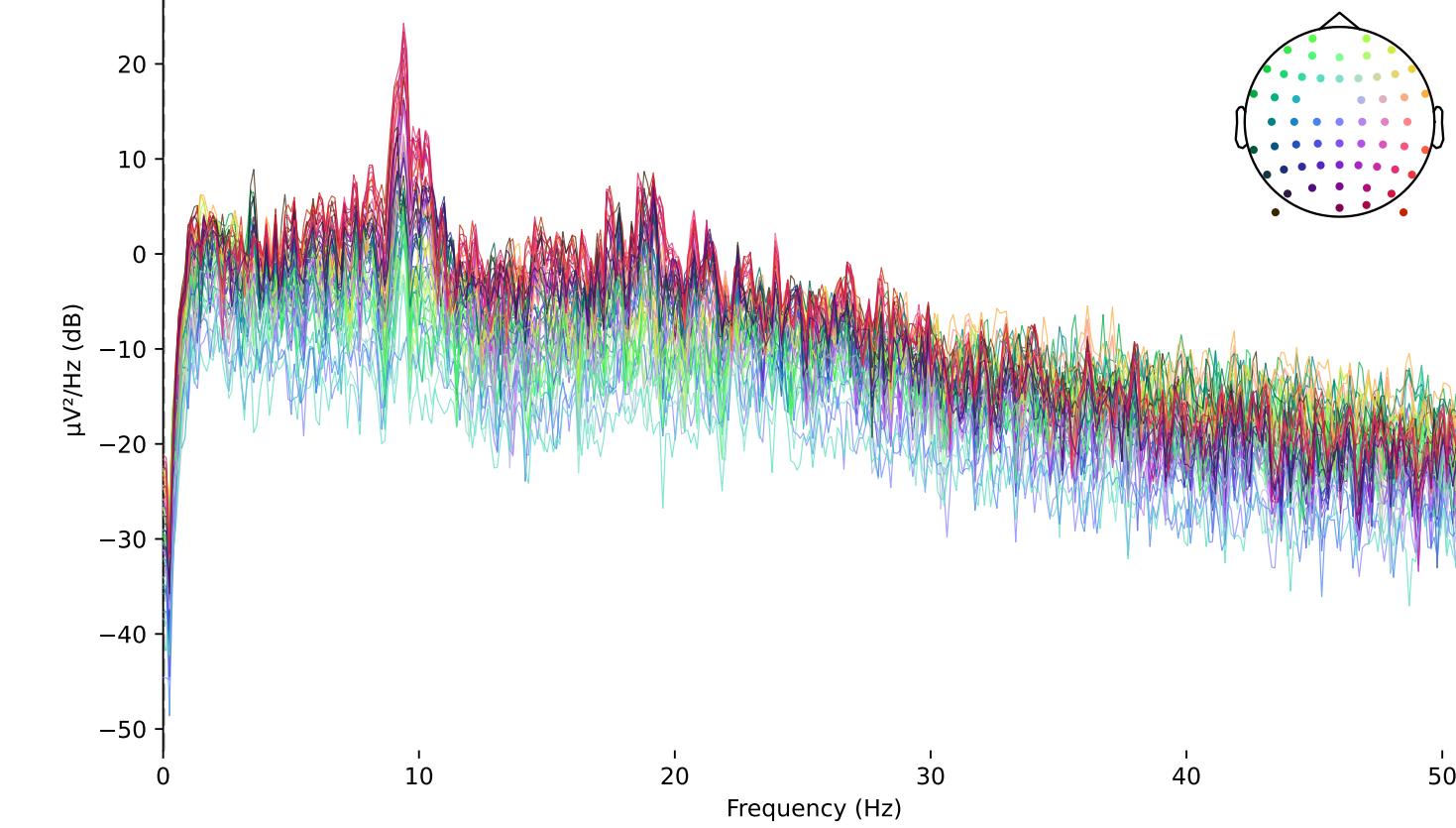
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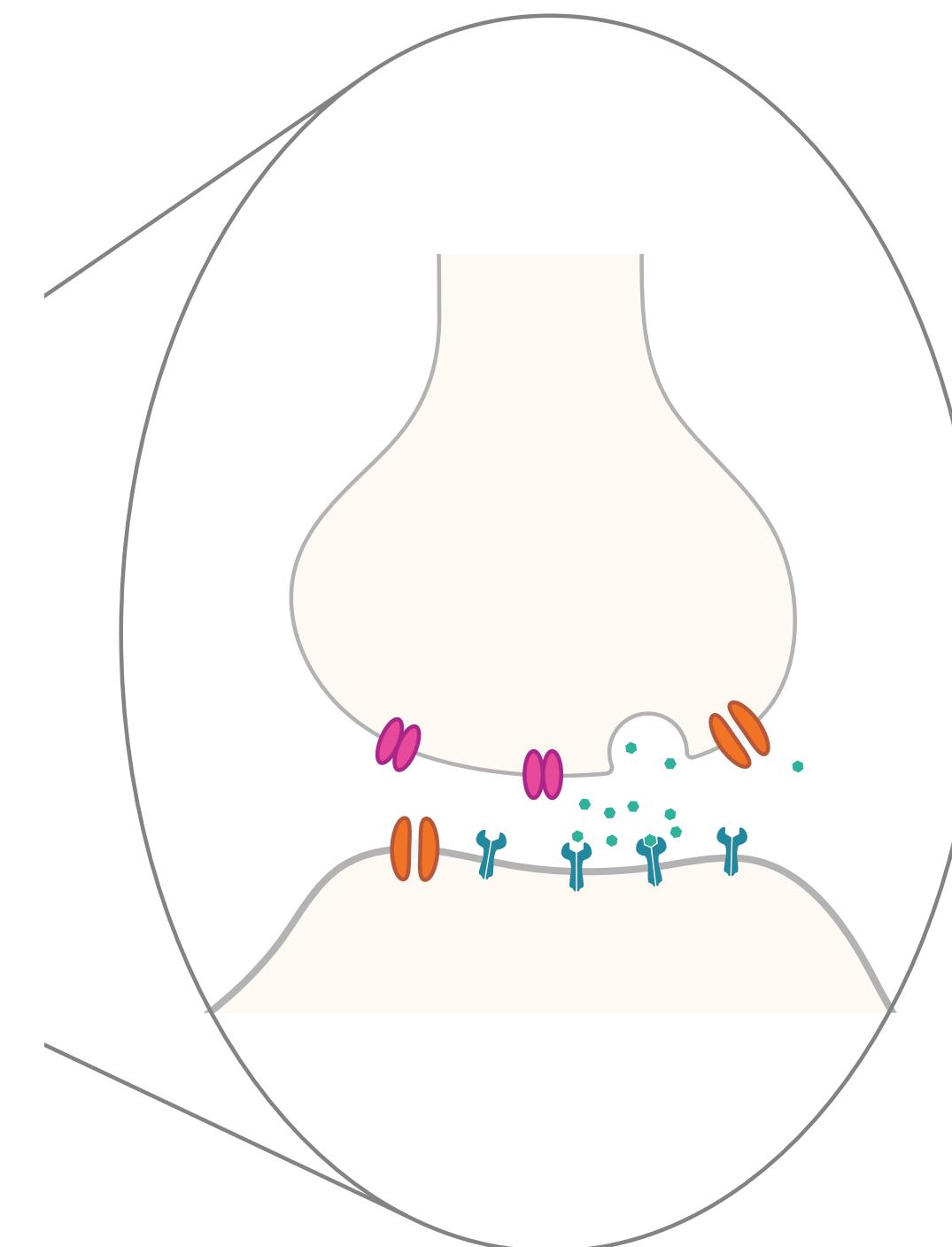


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$$\text{parameter estimates: } \hat{\theta} = E[\theta|y, m]$$

# #Neuronal models: modelling the hierarchy

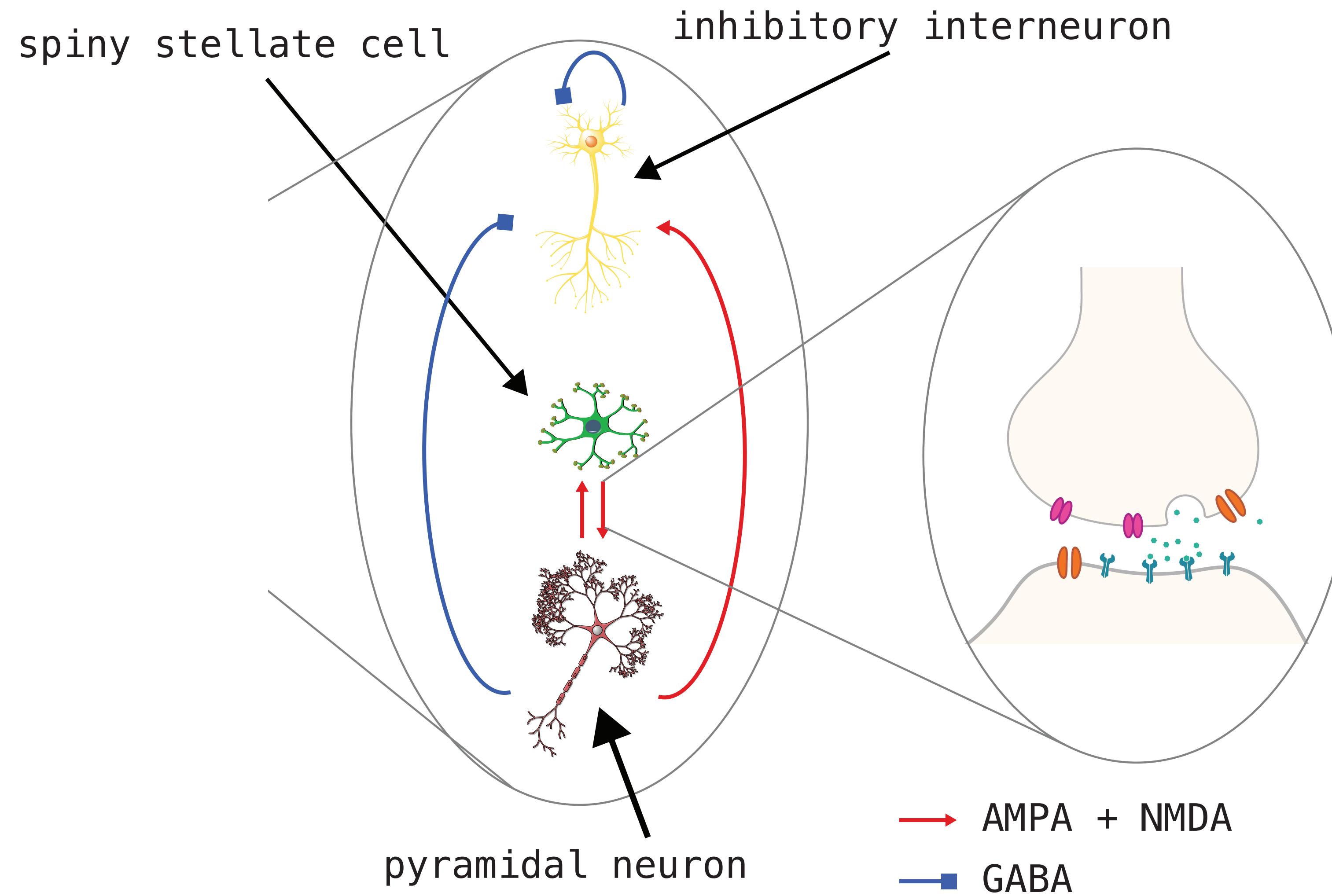
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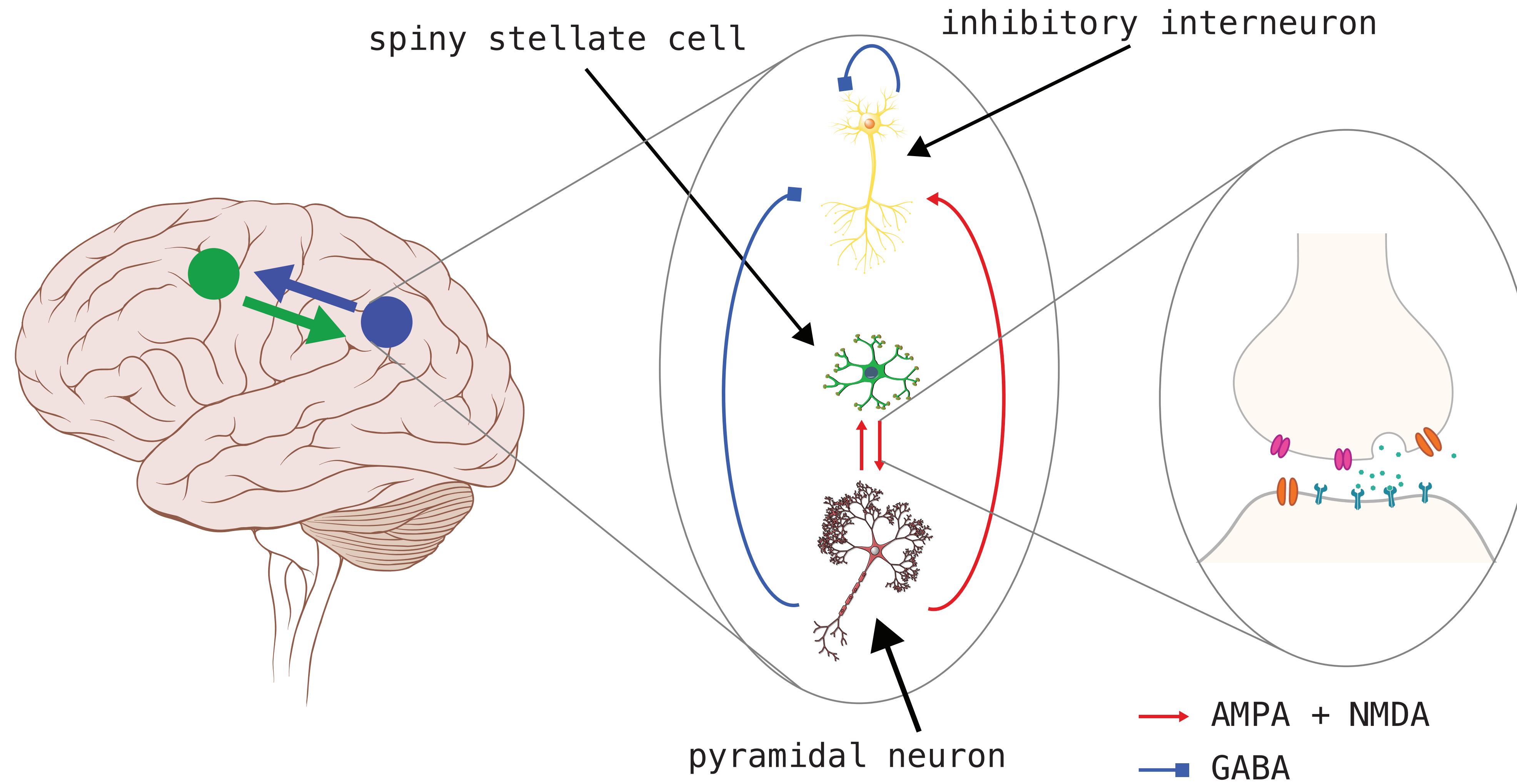
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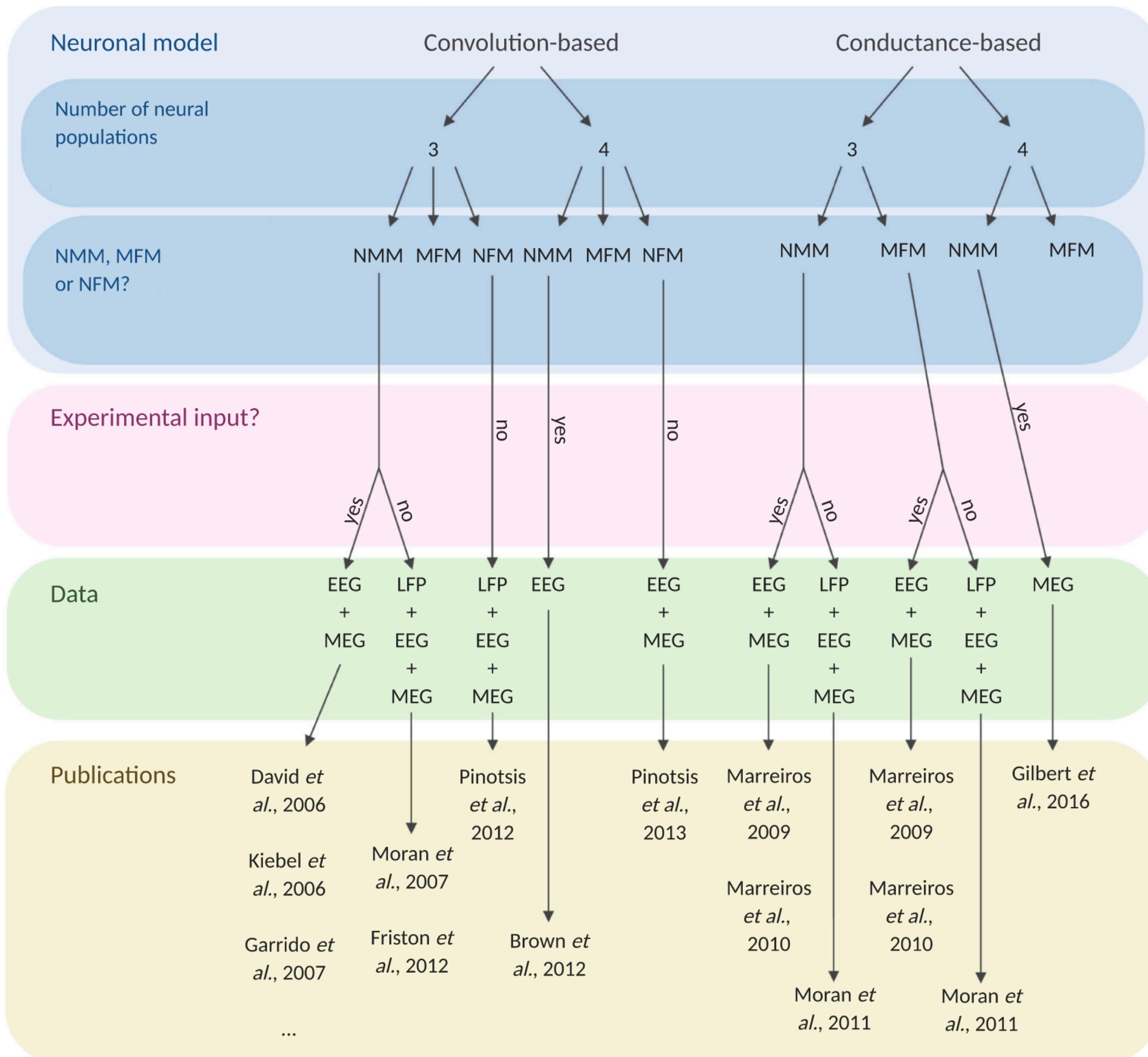
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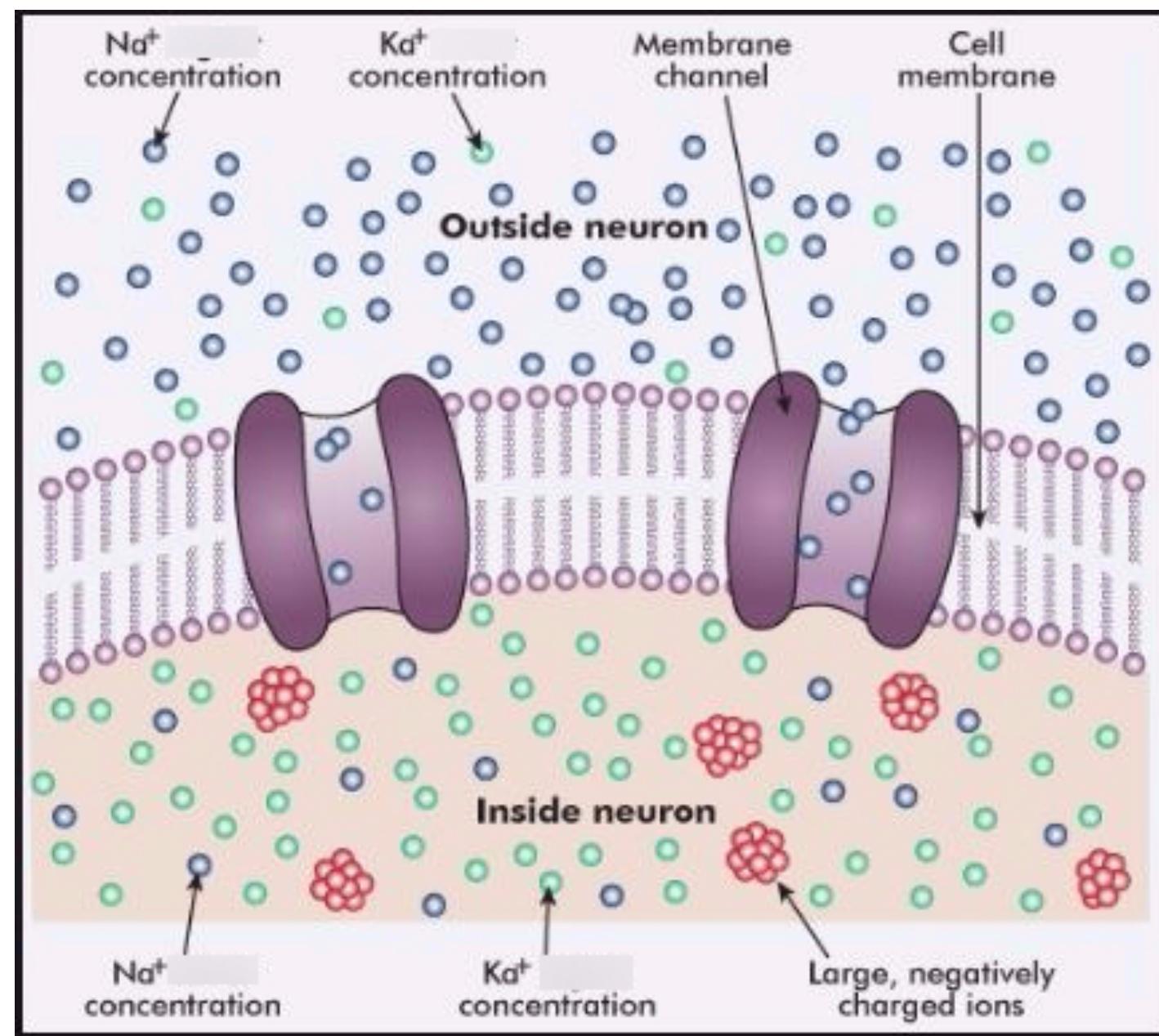
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# #Building a model: electrophysiology

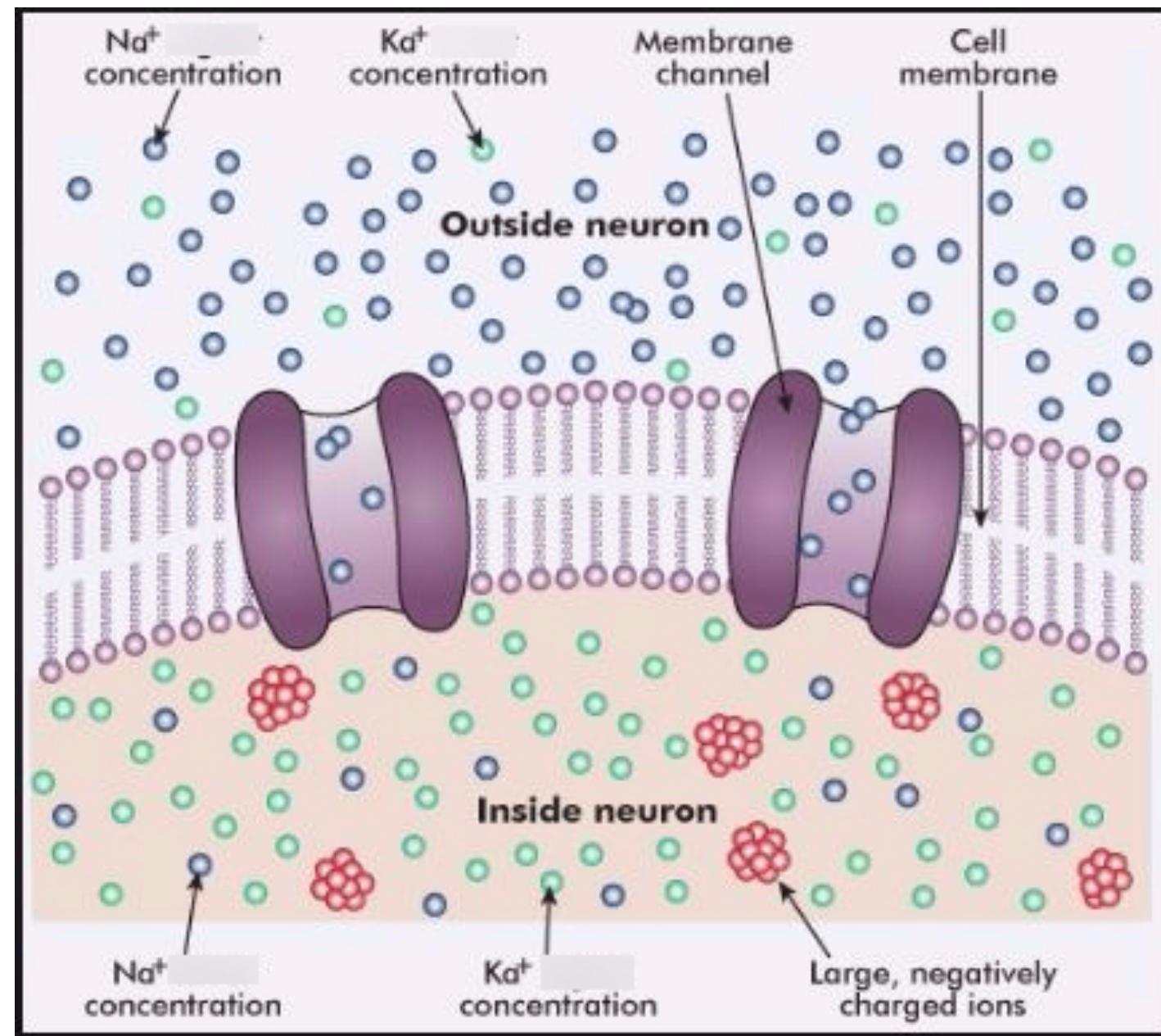
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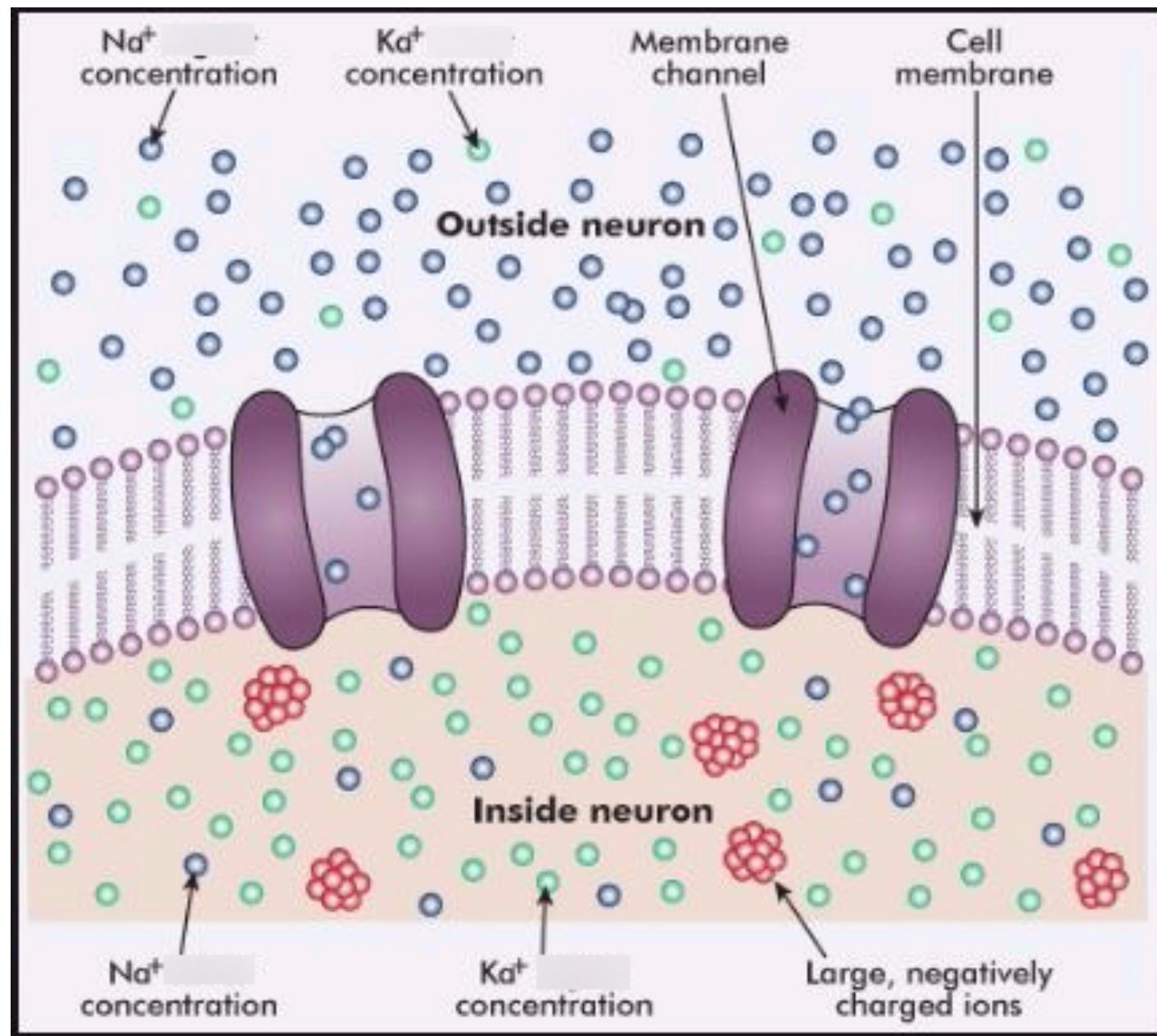
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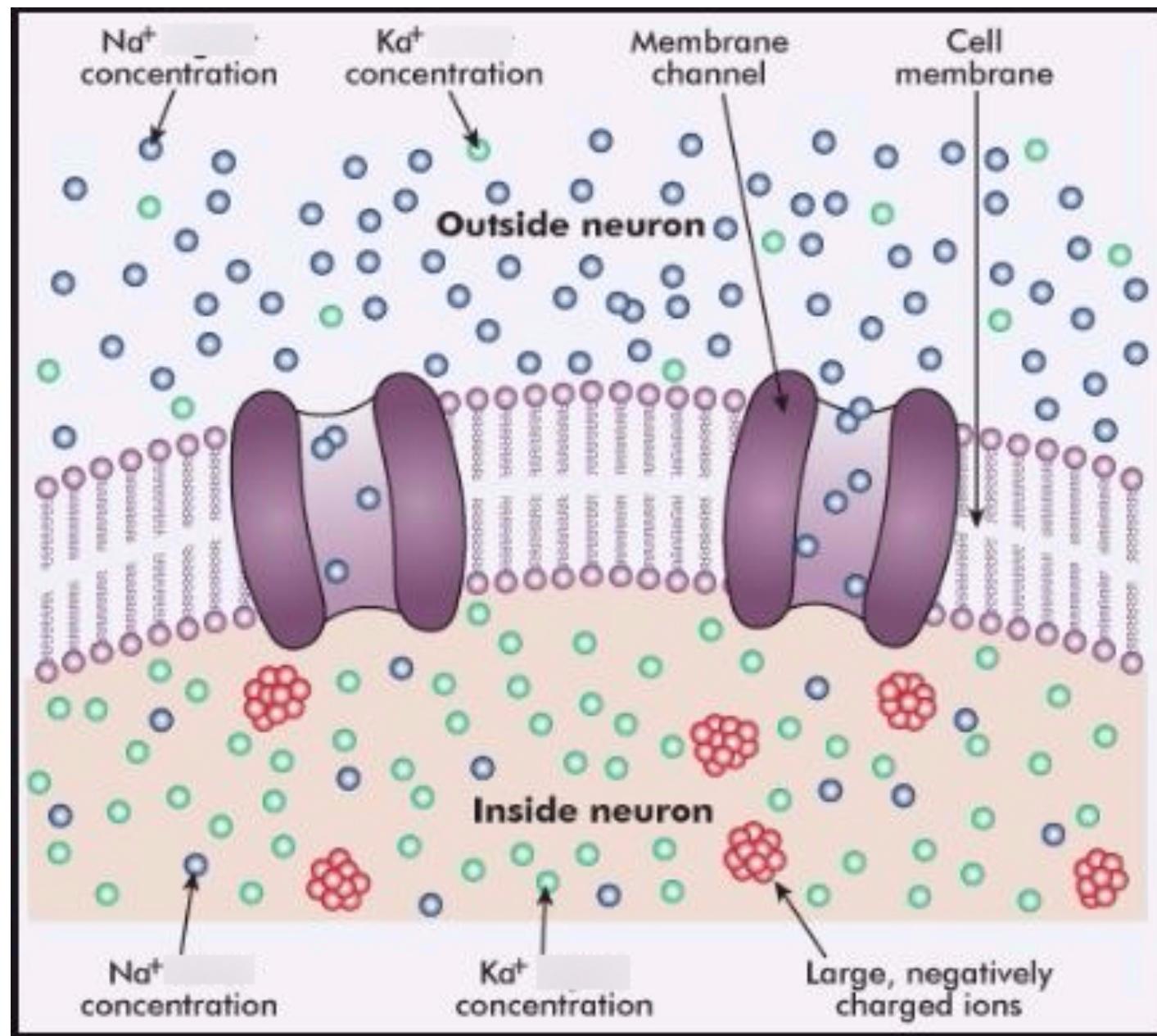
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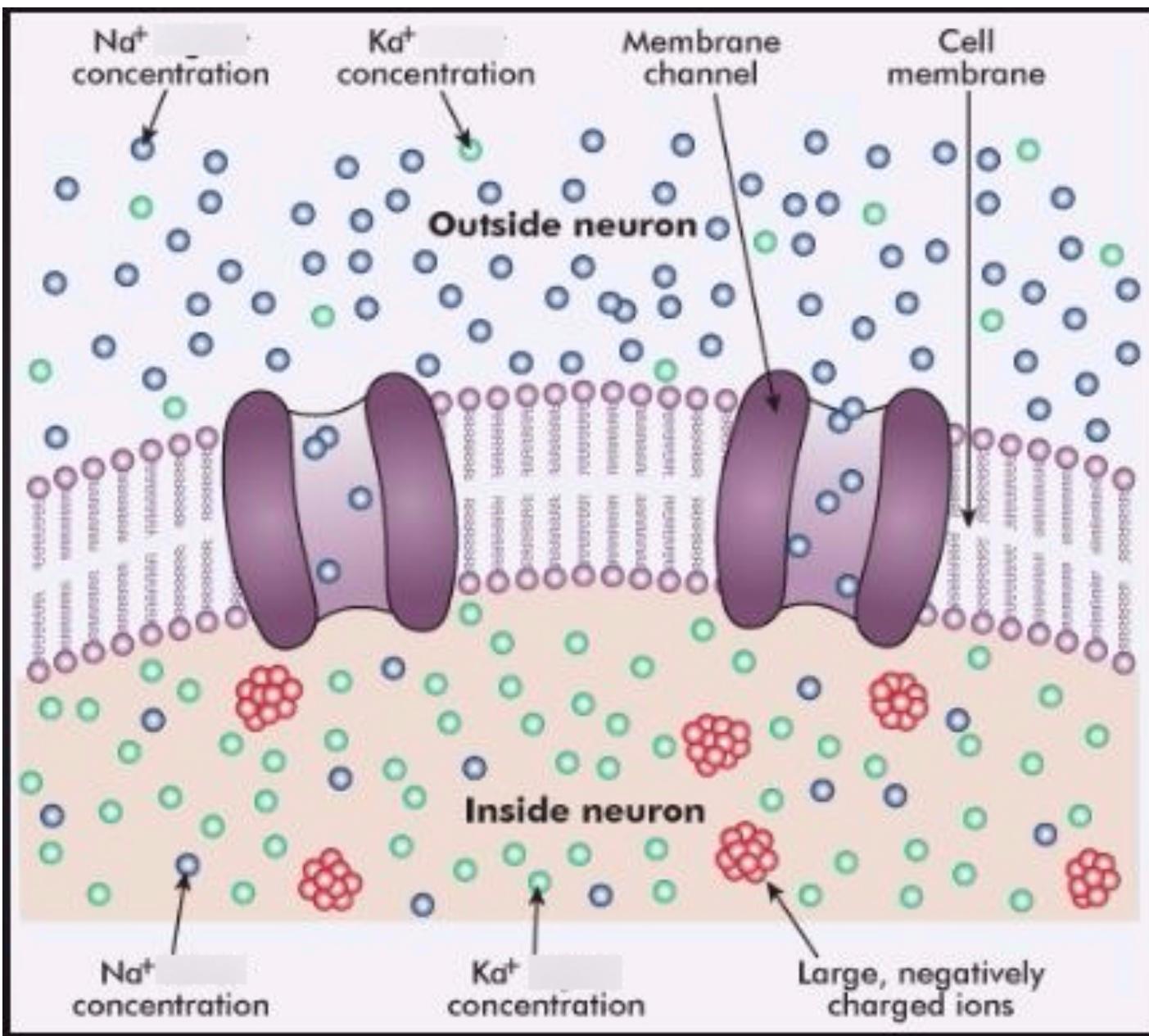
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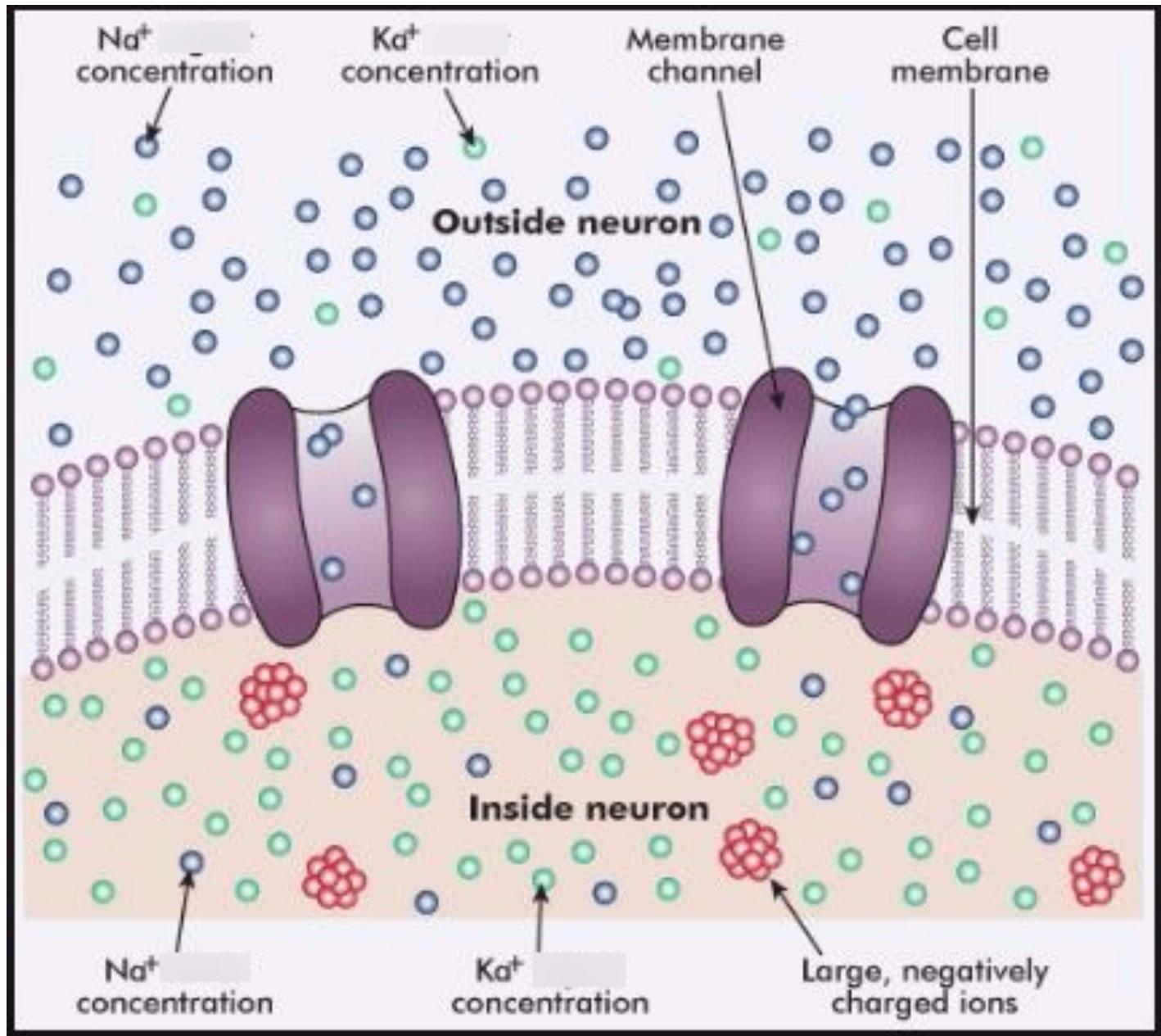


ionic current

$$I_X = g_X (V - E_X)$$

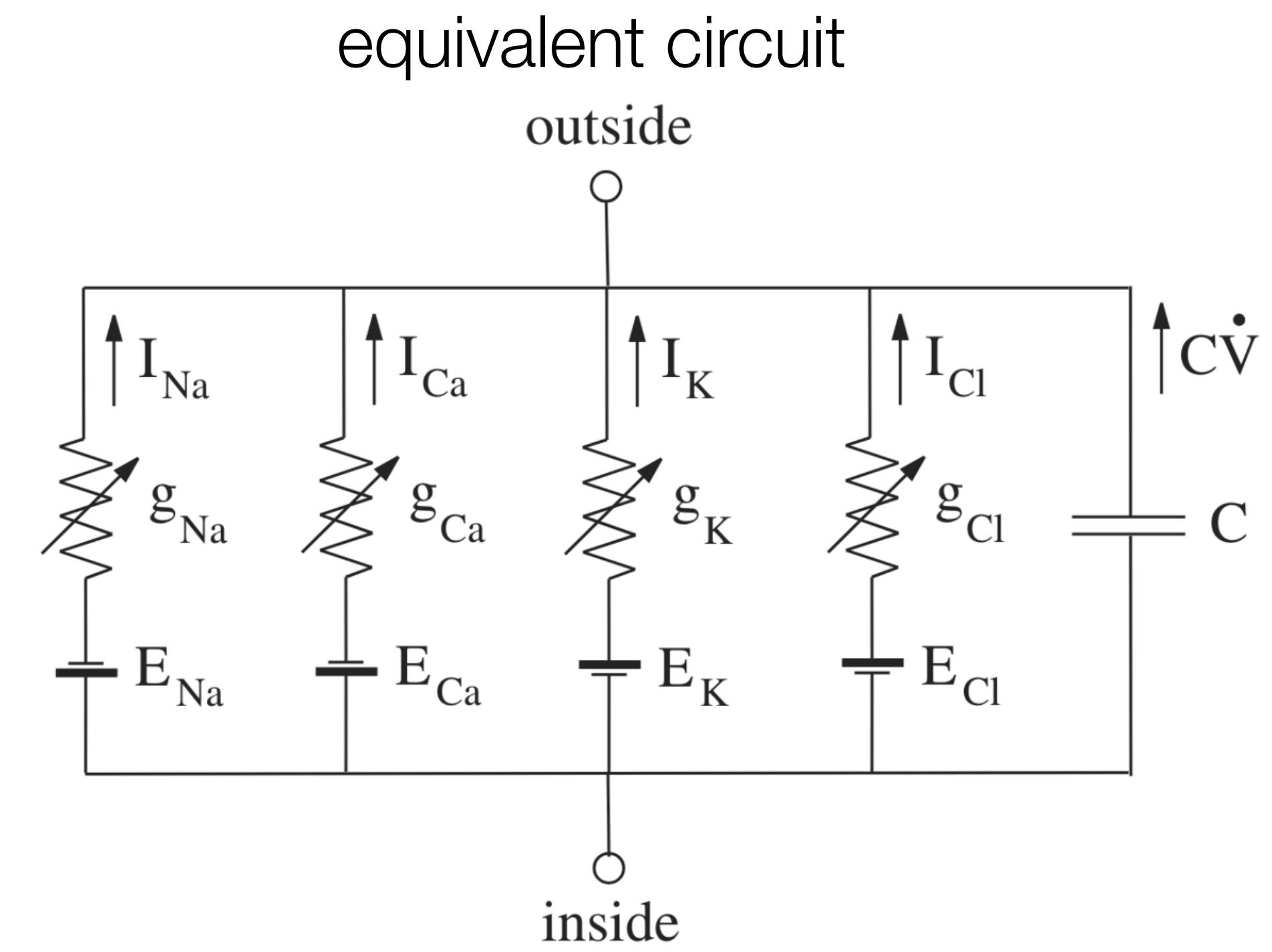
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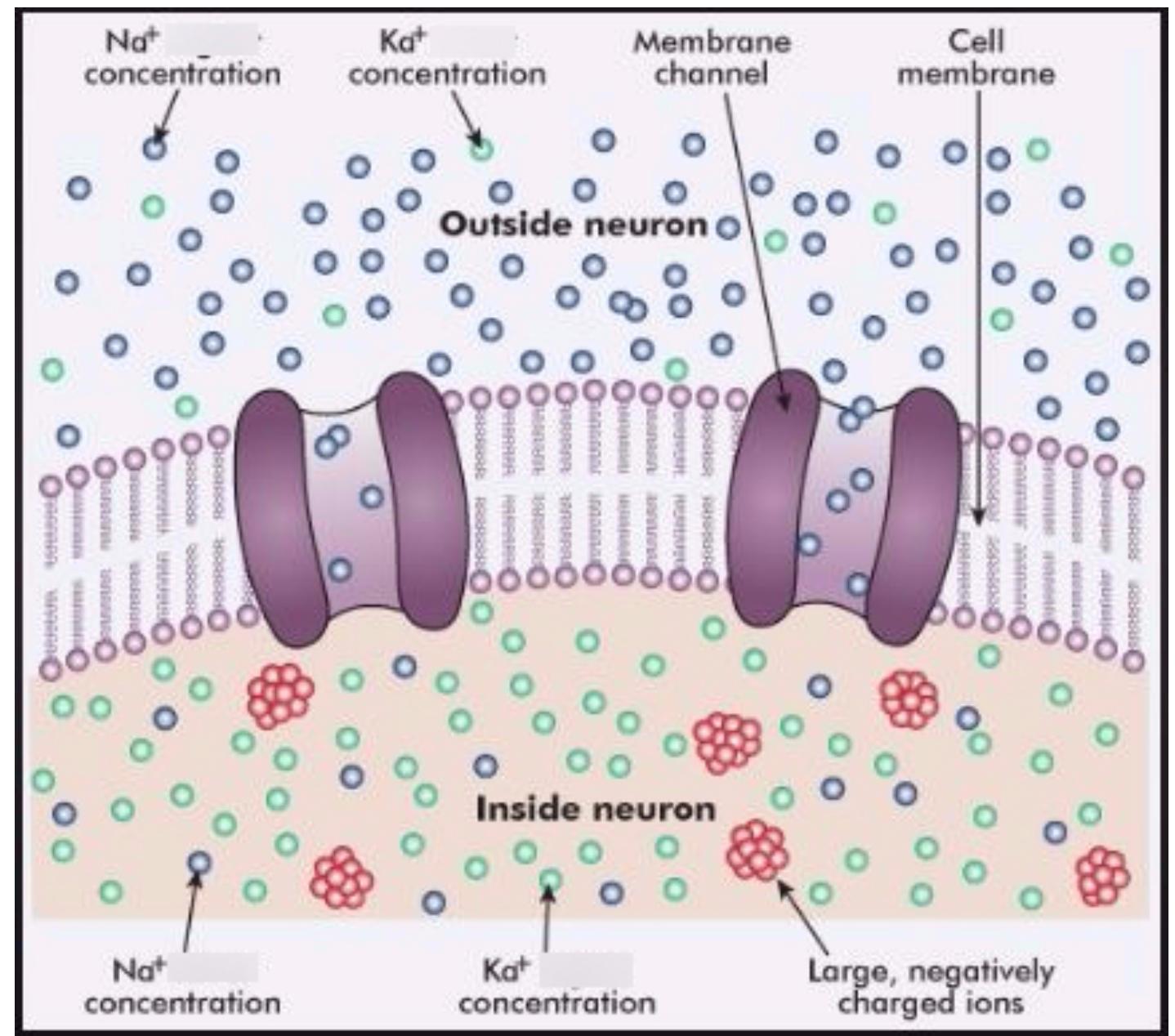
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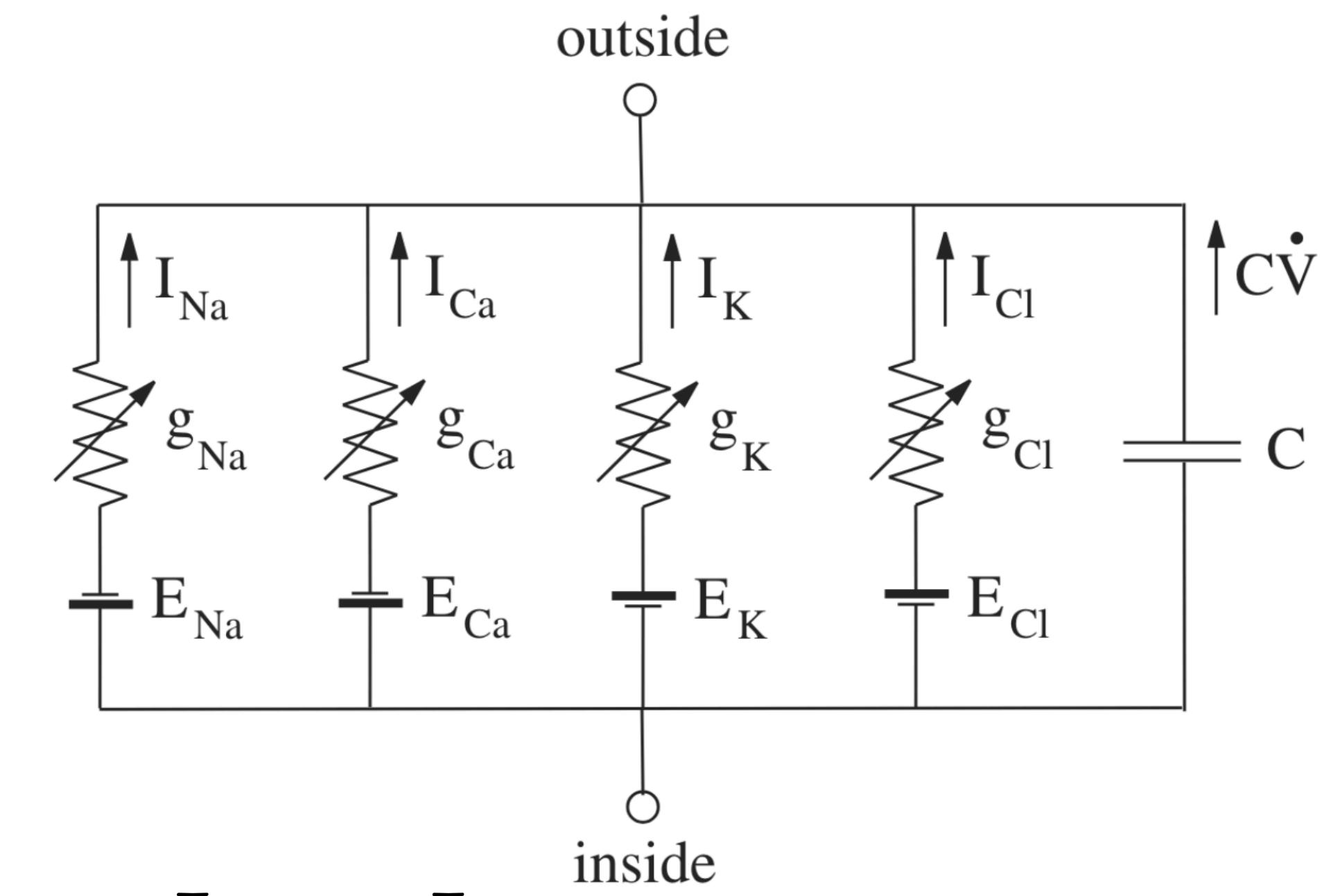
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equivalent circuit

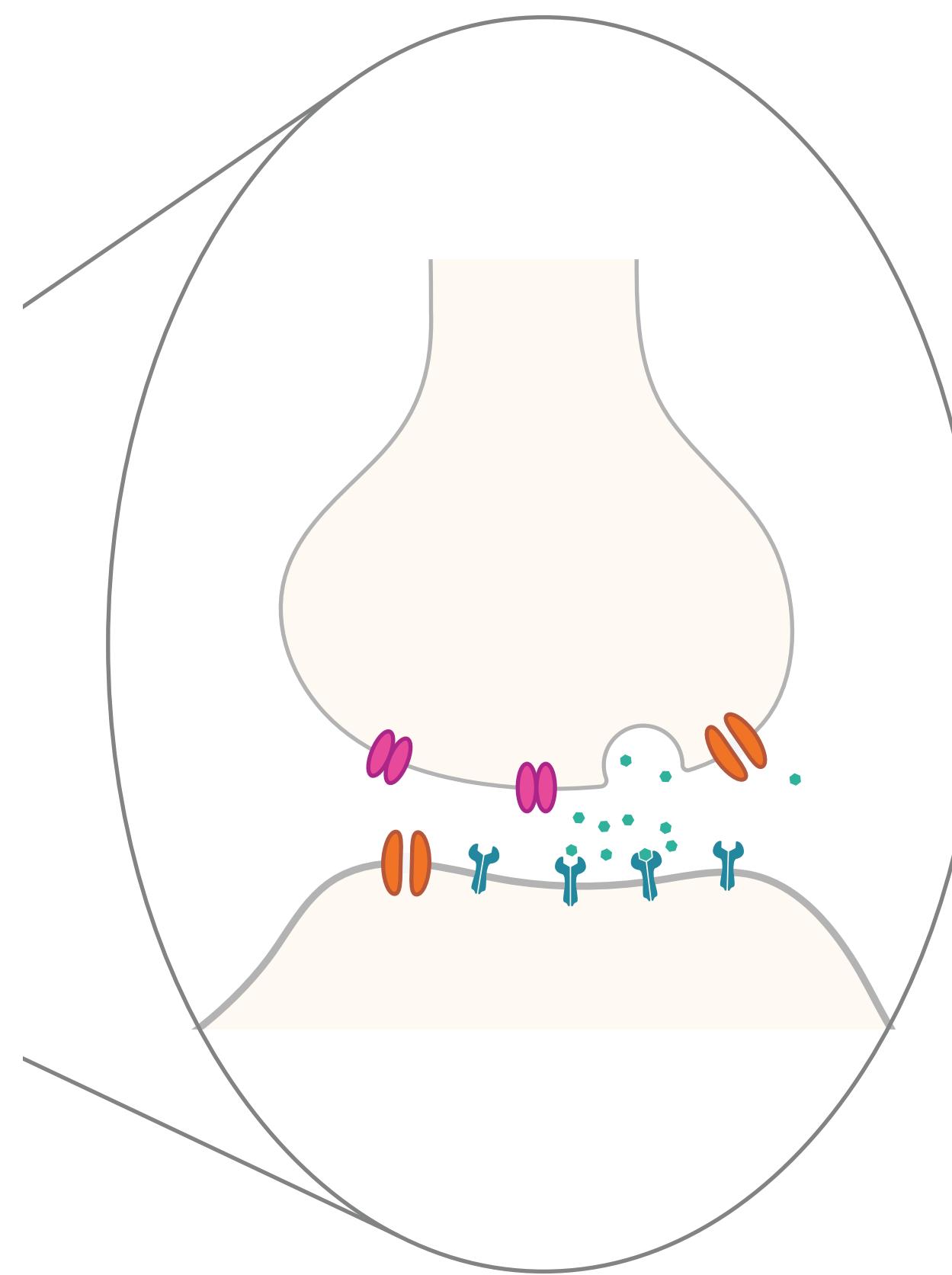


$$I = C \frac{dV}{dt} + I_{\text{Na}} + I_{\text{Ca}} + I_K + I_{\text{Cl}}$$

adapted from Izhikevich, 2006, MIT Press

# #Building a model: conductance-based single cell

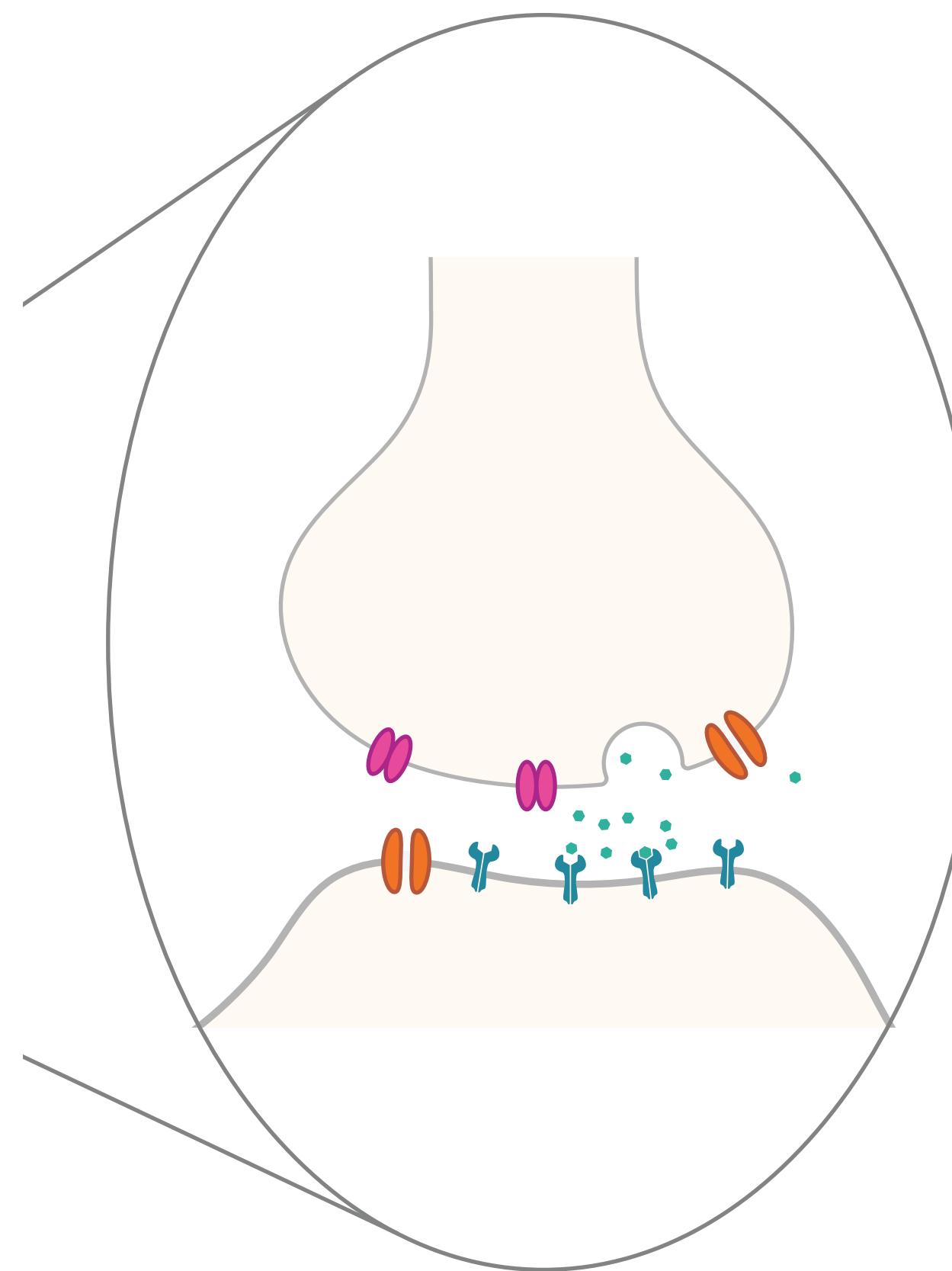
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→ AMPA + NMDA

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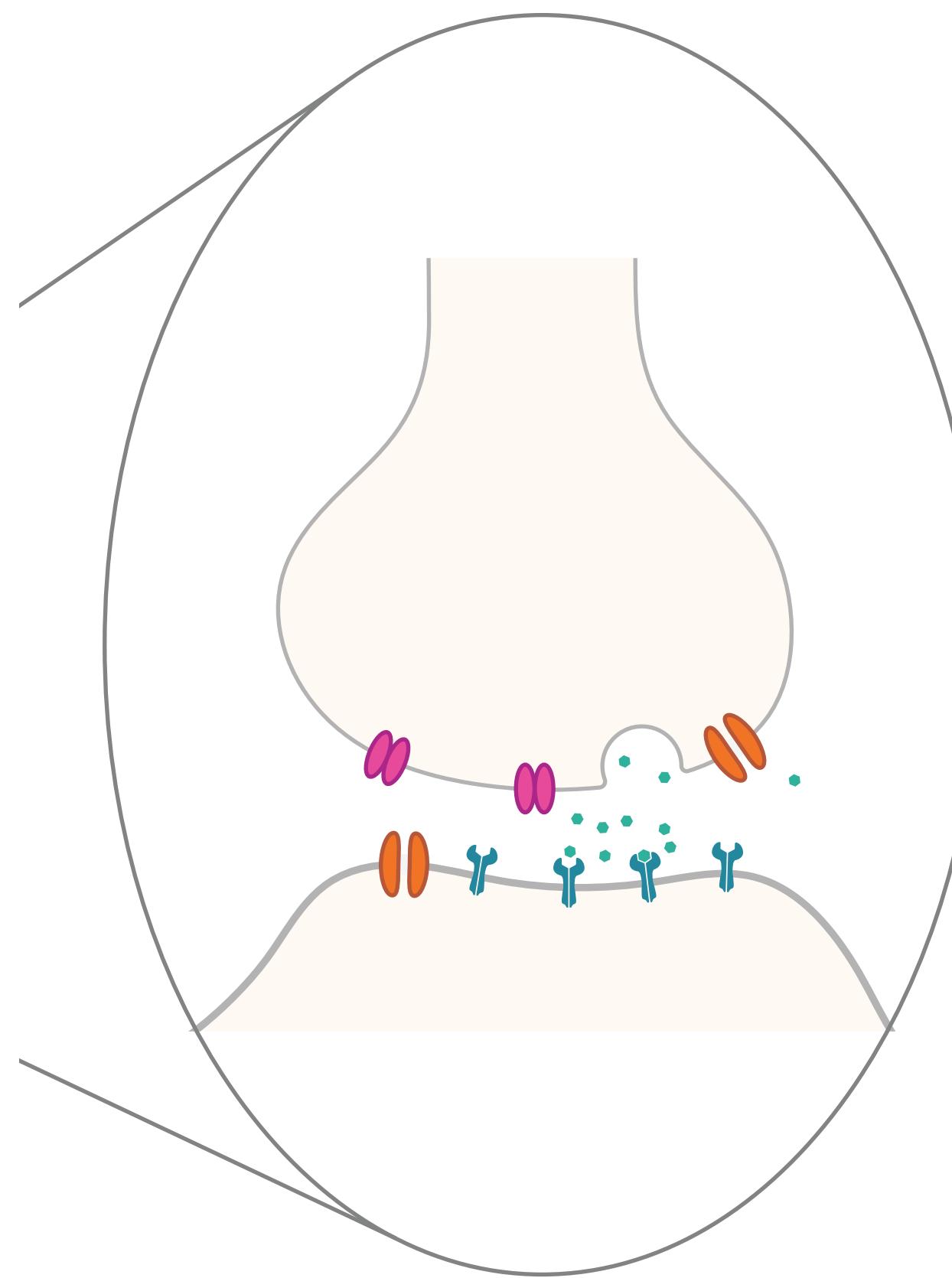


$$C\dot{V} = \left( \sum_k g_k (V_k - V) \right) + g_{NMDA} \cdot m(V) \cdot (V_{NMDA} - V) + \xi_V$$

→ AMPA + NMDA

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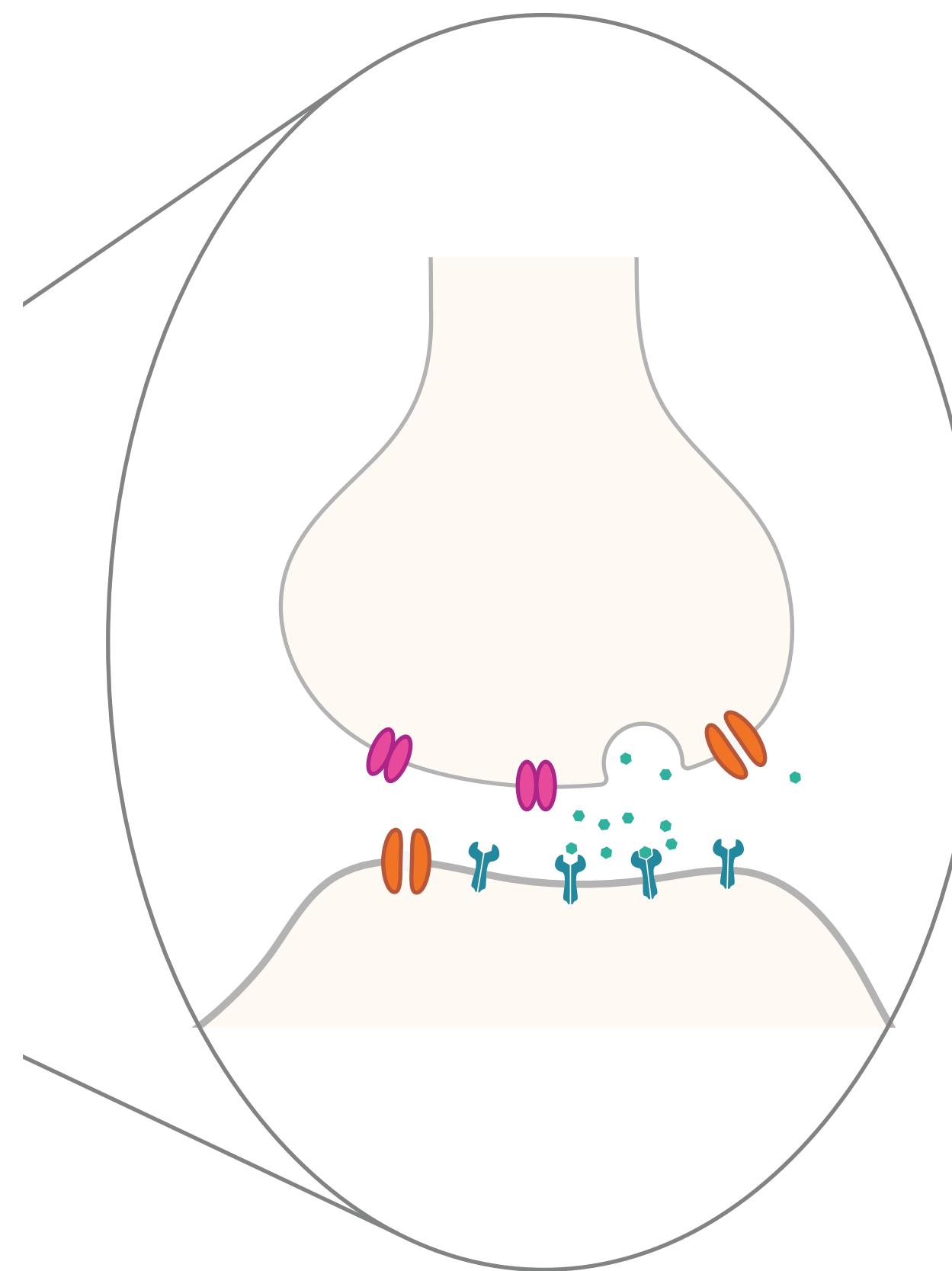
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$k = \text{leak, AMPA, GABA}$

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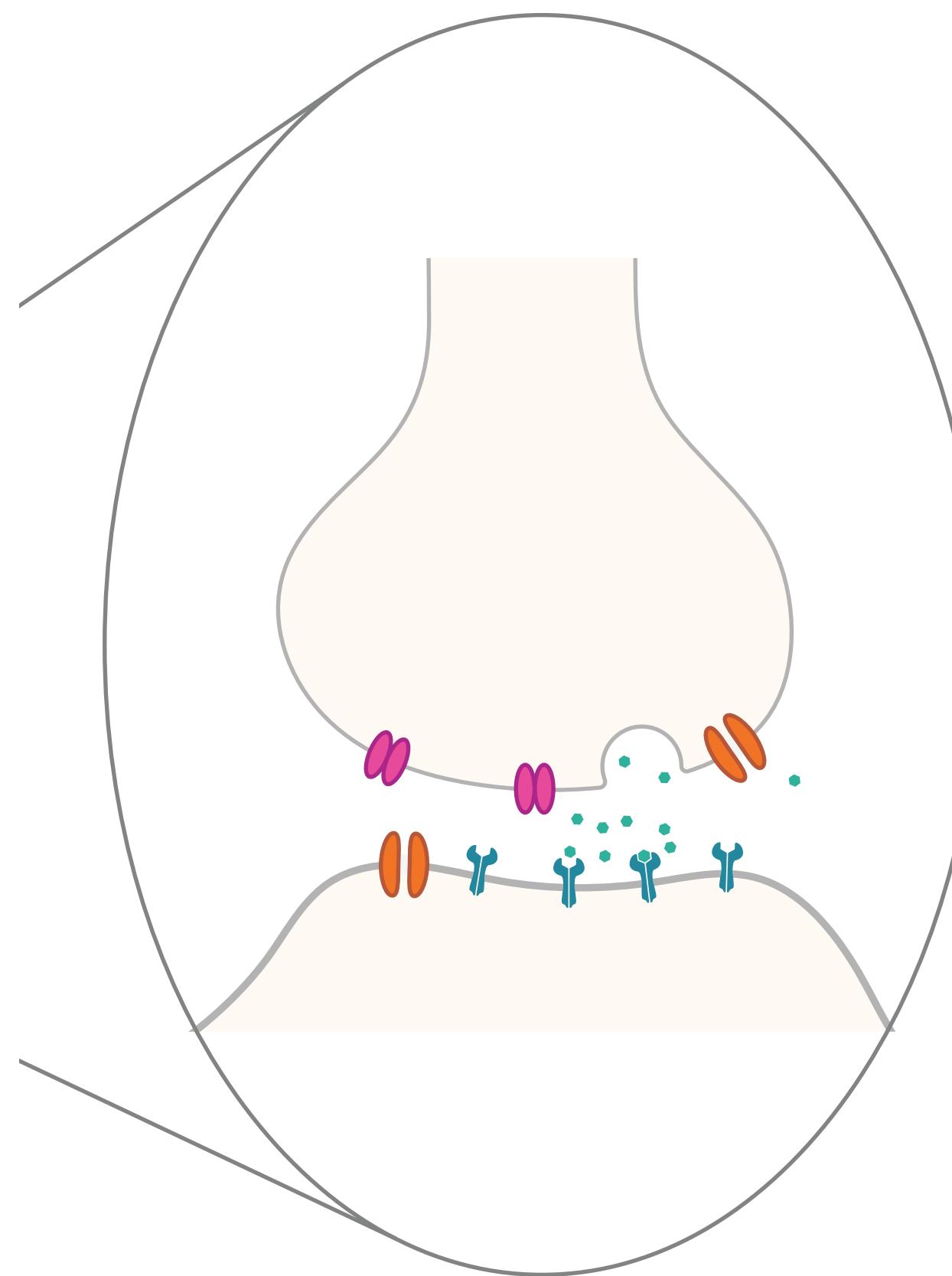
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$$\dot{g}_k = \kappa_k \cdot (\zeta_k - g_k) + \xi_g$$

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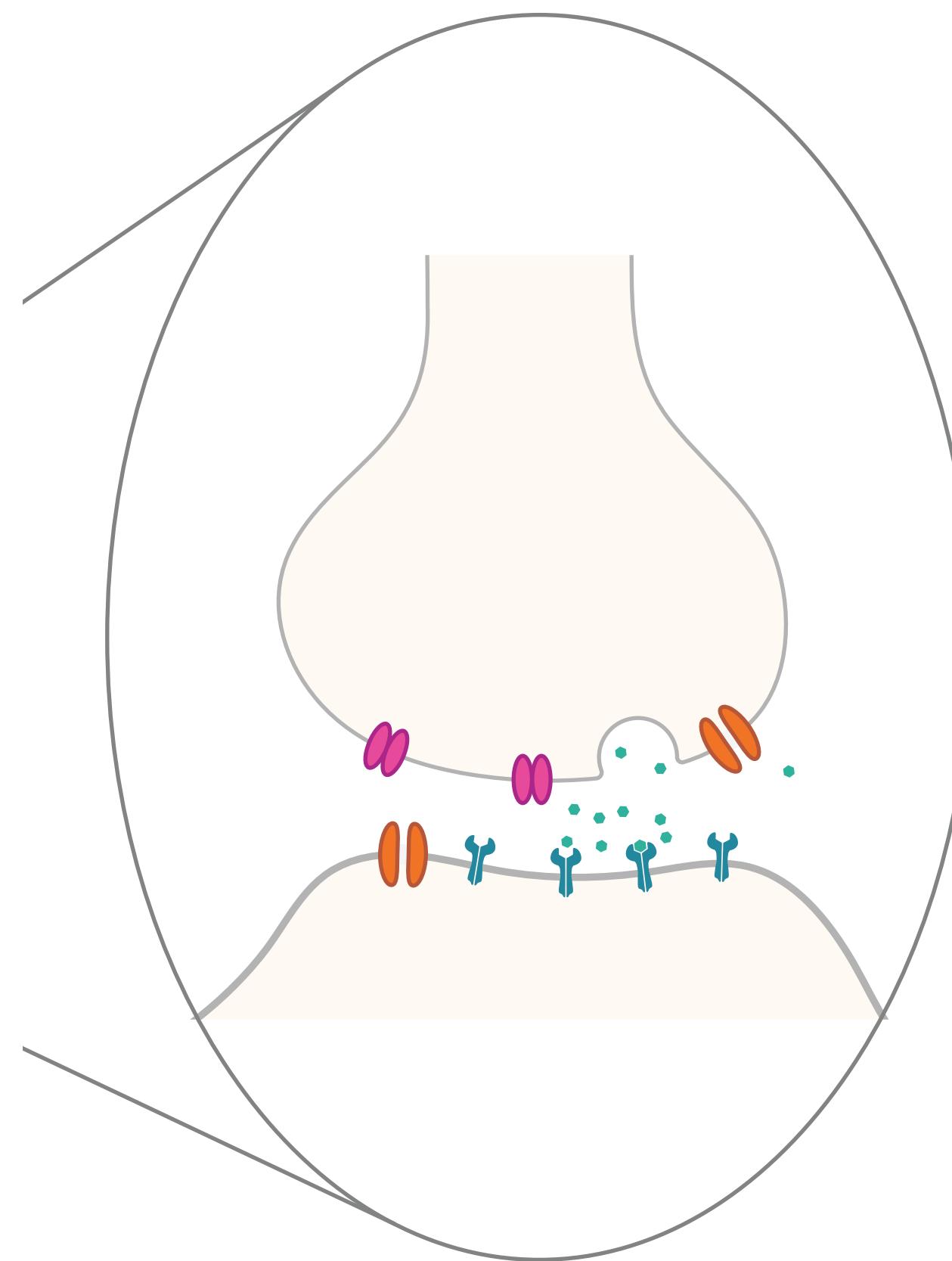
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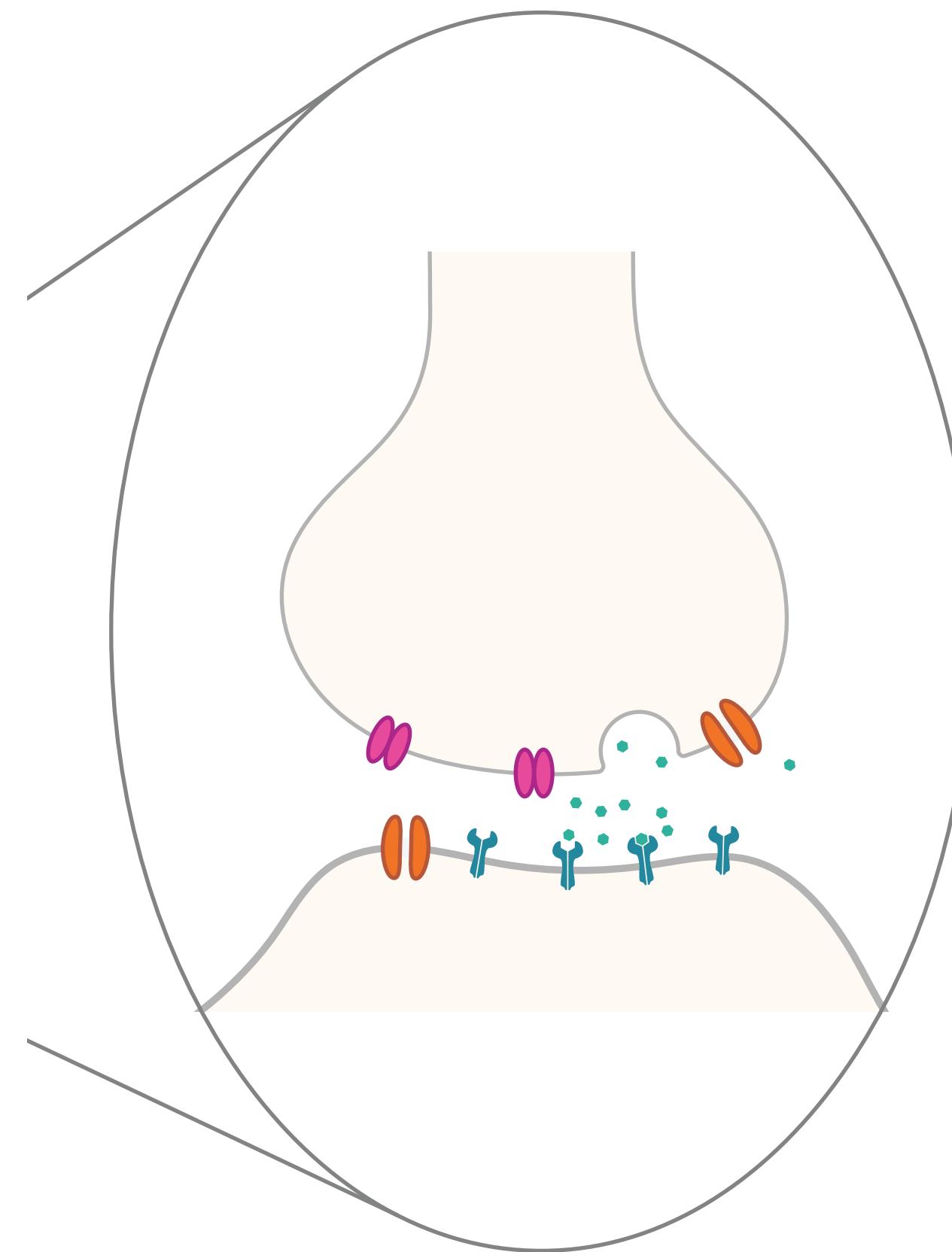
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$$m(V) = \frac{\alpha_{\text{scale}}}{1 + \alpha_{\text{slope}} \exp(-\alpha_{\text{sens}} \cdot V)}$$

→ AMPA + NMDA

— GABA

# #Building a model: conductance-based single cell



$$C\dot{V} = \left( \sum_k g_k(V_k - V) \right) + g_{NMDA} \cdot m(V) \cdot (V_{NMDA} - V) + \xi_V \quad k = \text{leak, AMPA, GABA}$$

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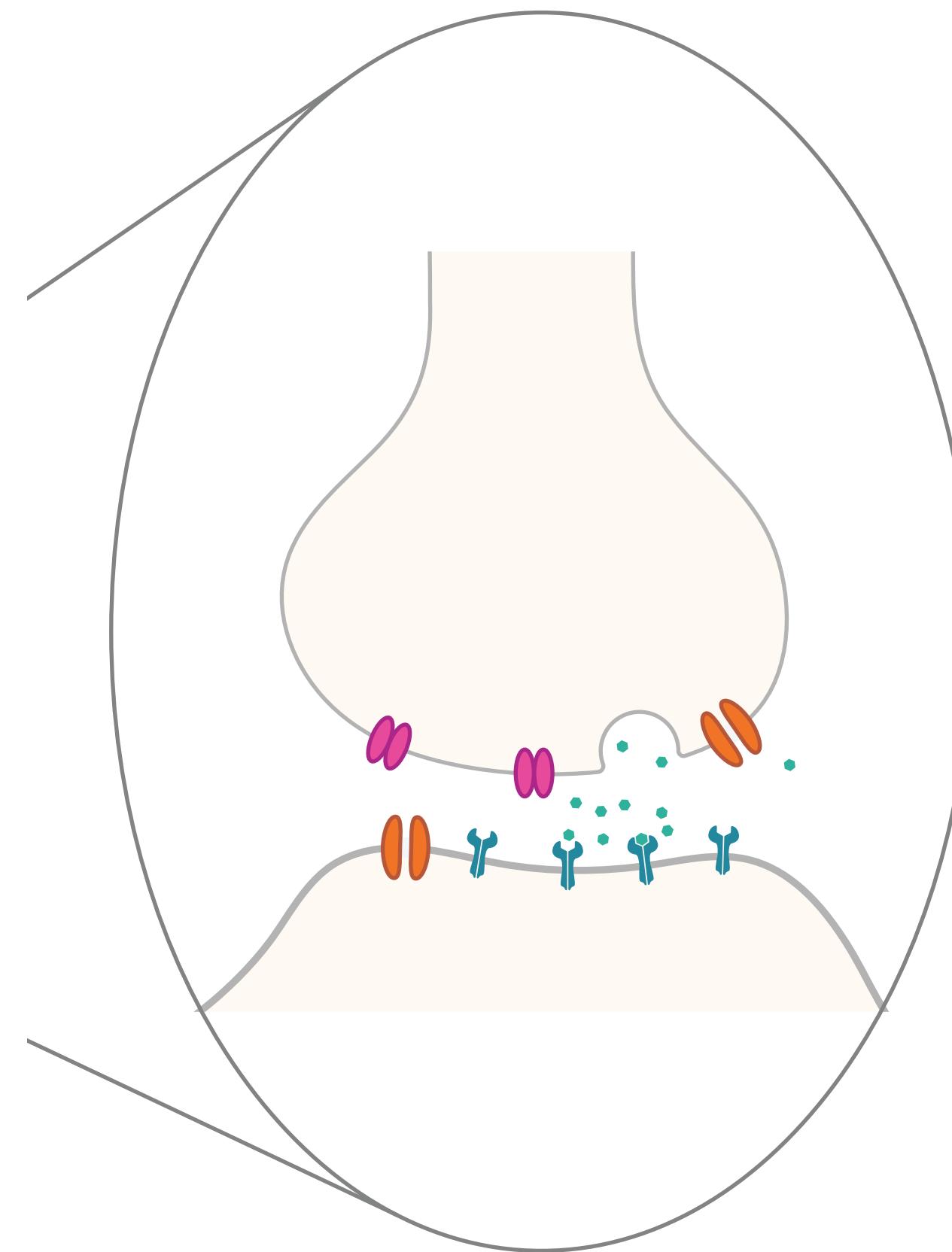
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Fokker - Planck with Laplace approximation

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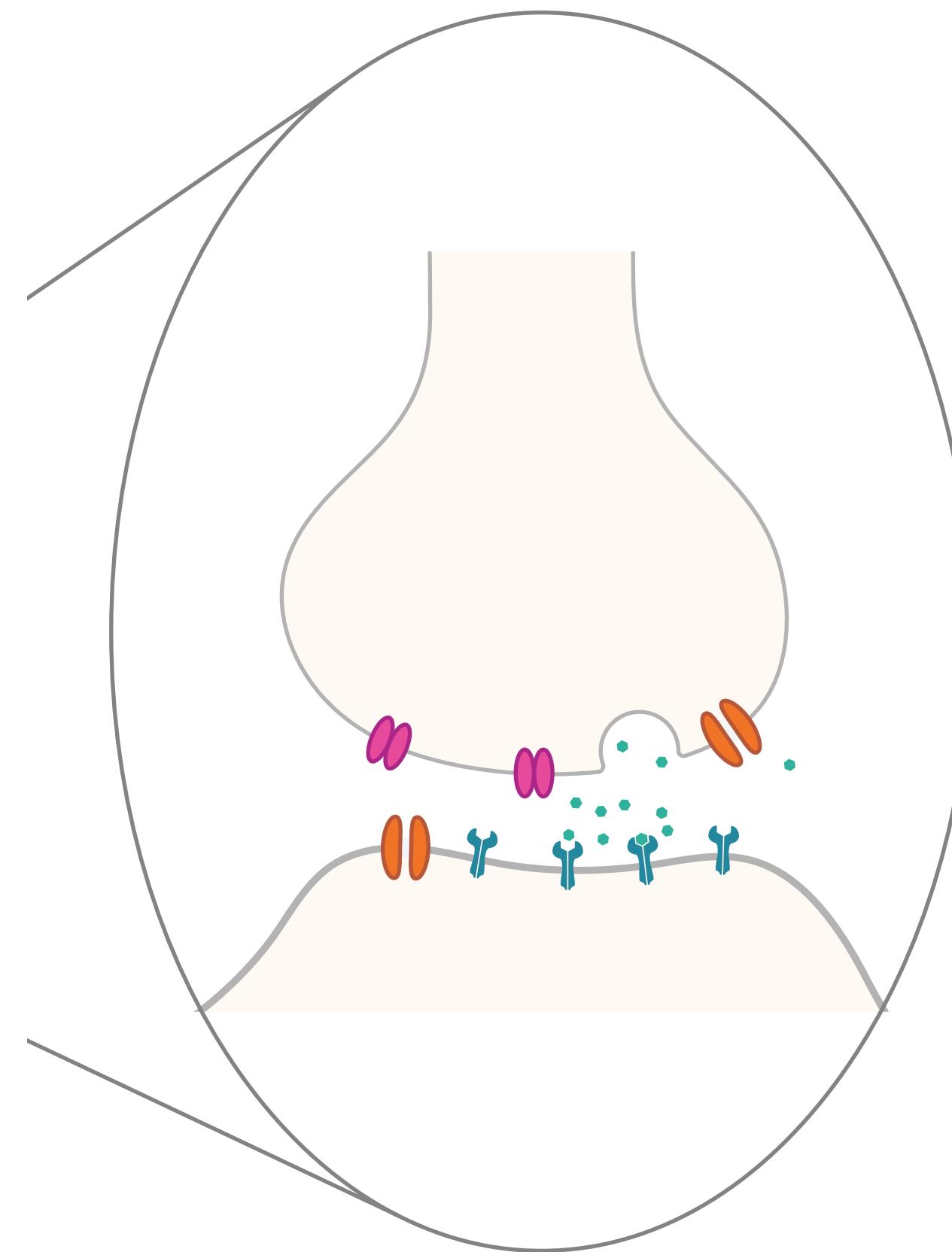
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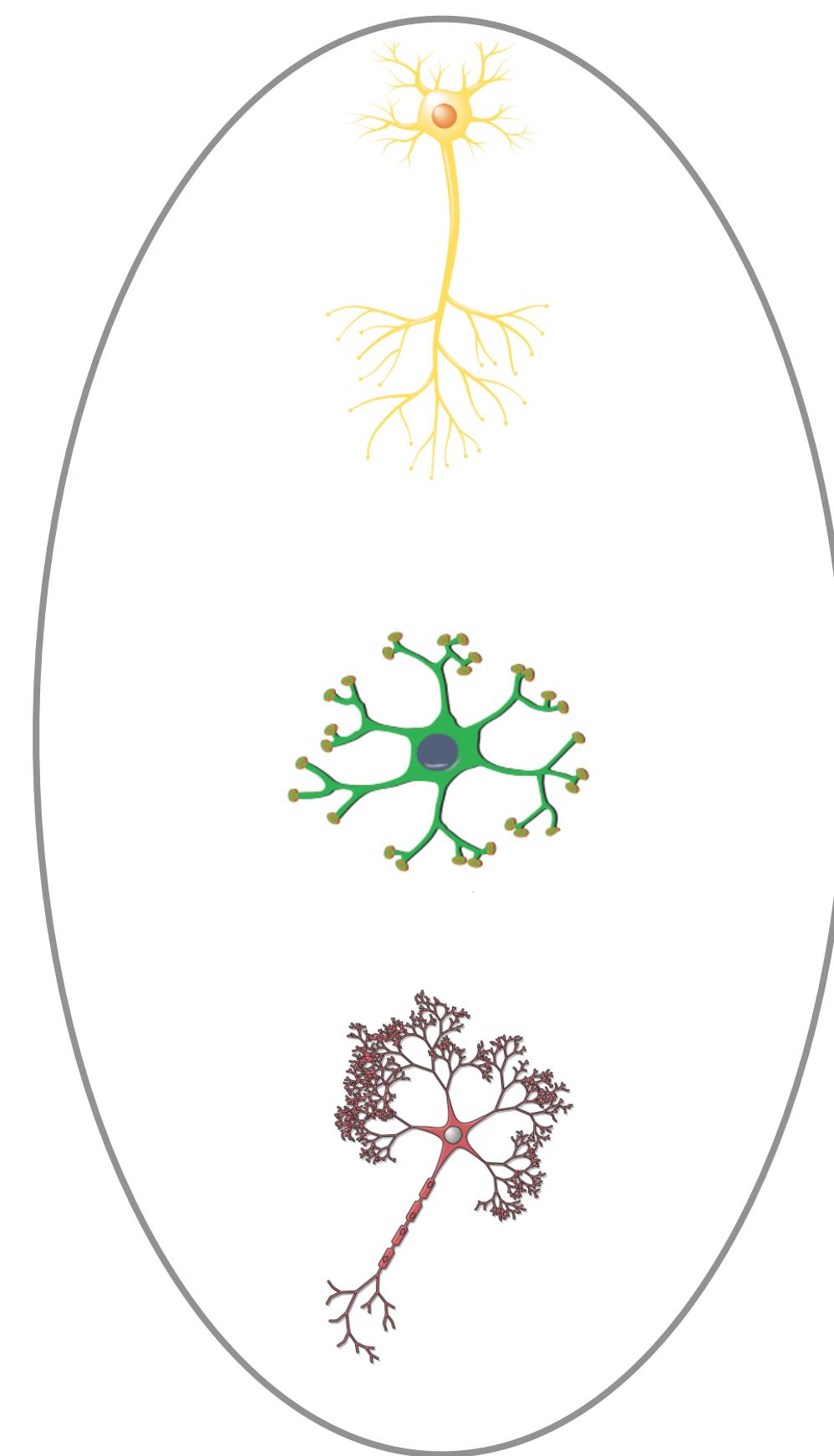
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$$\zeta_k^{(j)} = \sum_i \gamma_k^{(j,i)} \sigma(\mu_V^{(i)} - V_R, \Sigma^{(i)})$$

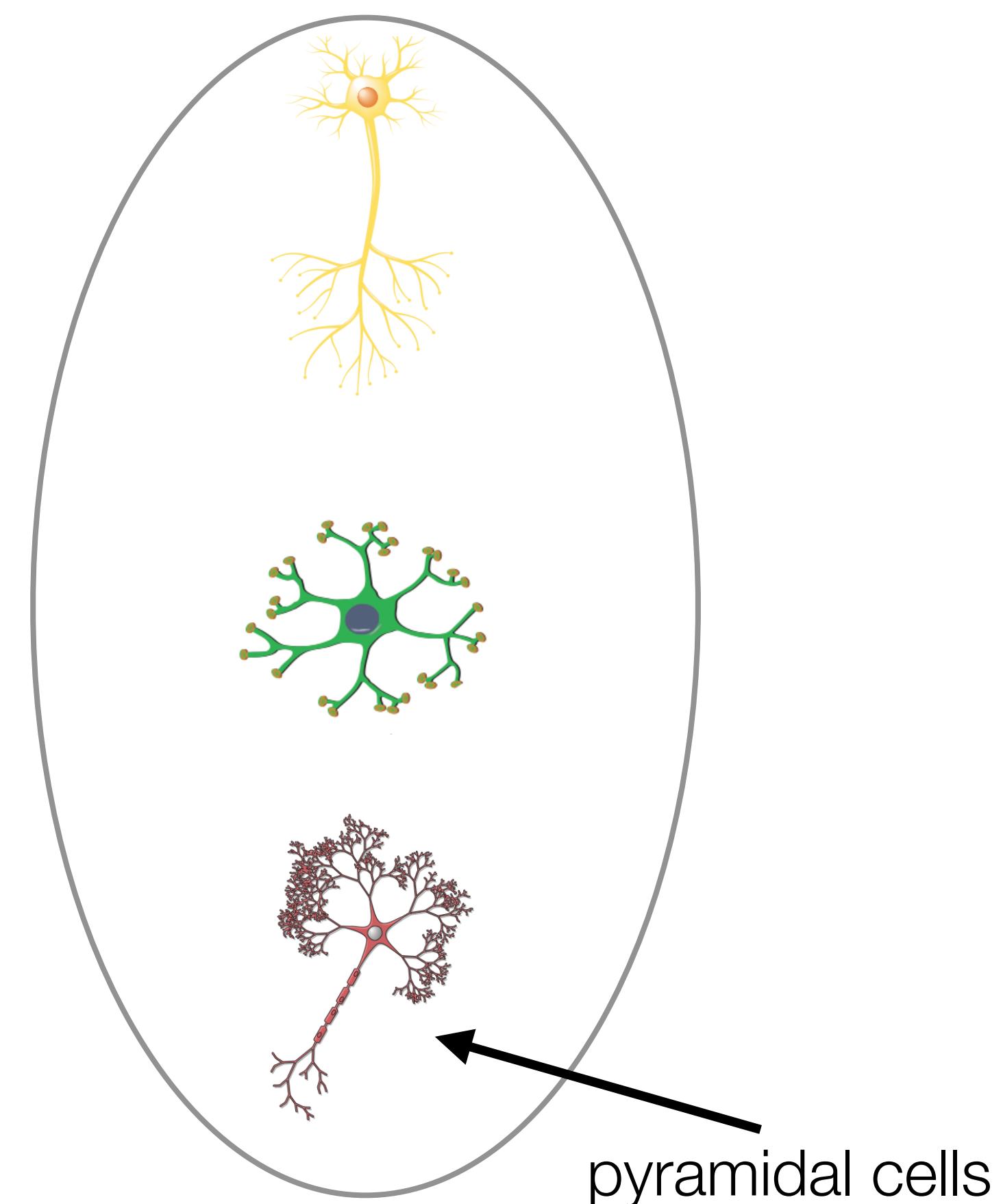
# #Building a model: cortical column

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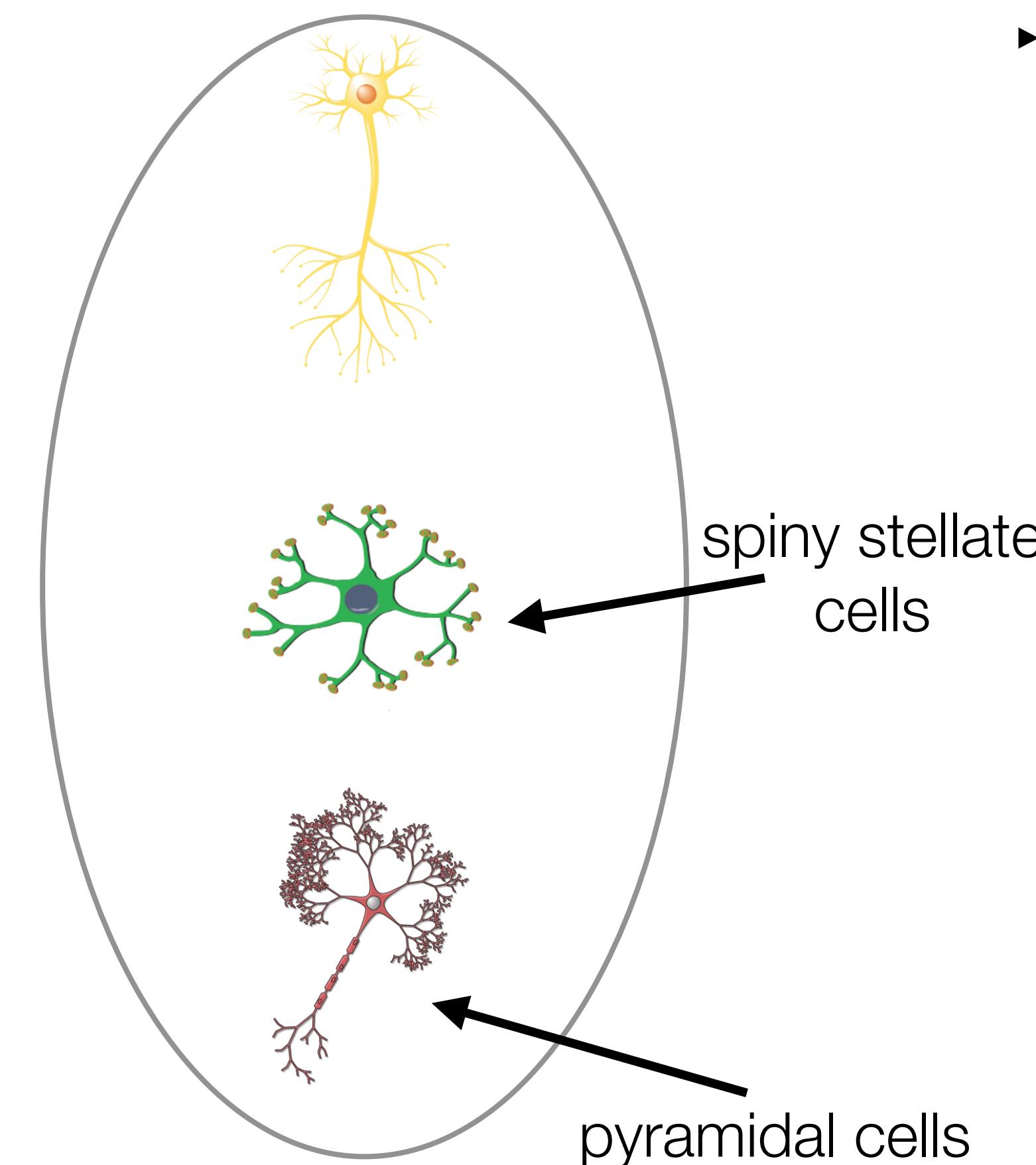
► *3-population model:*

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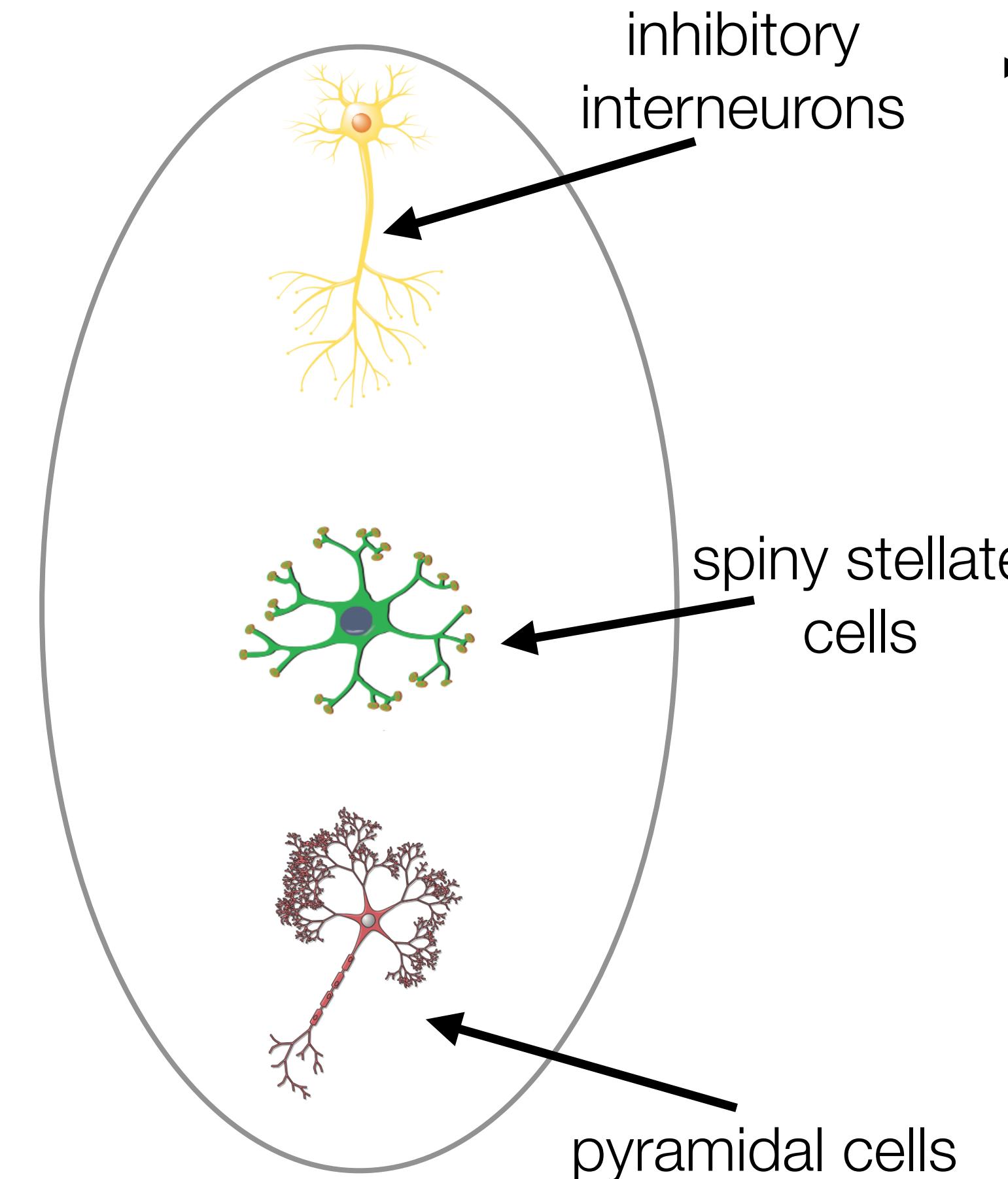
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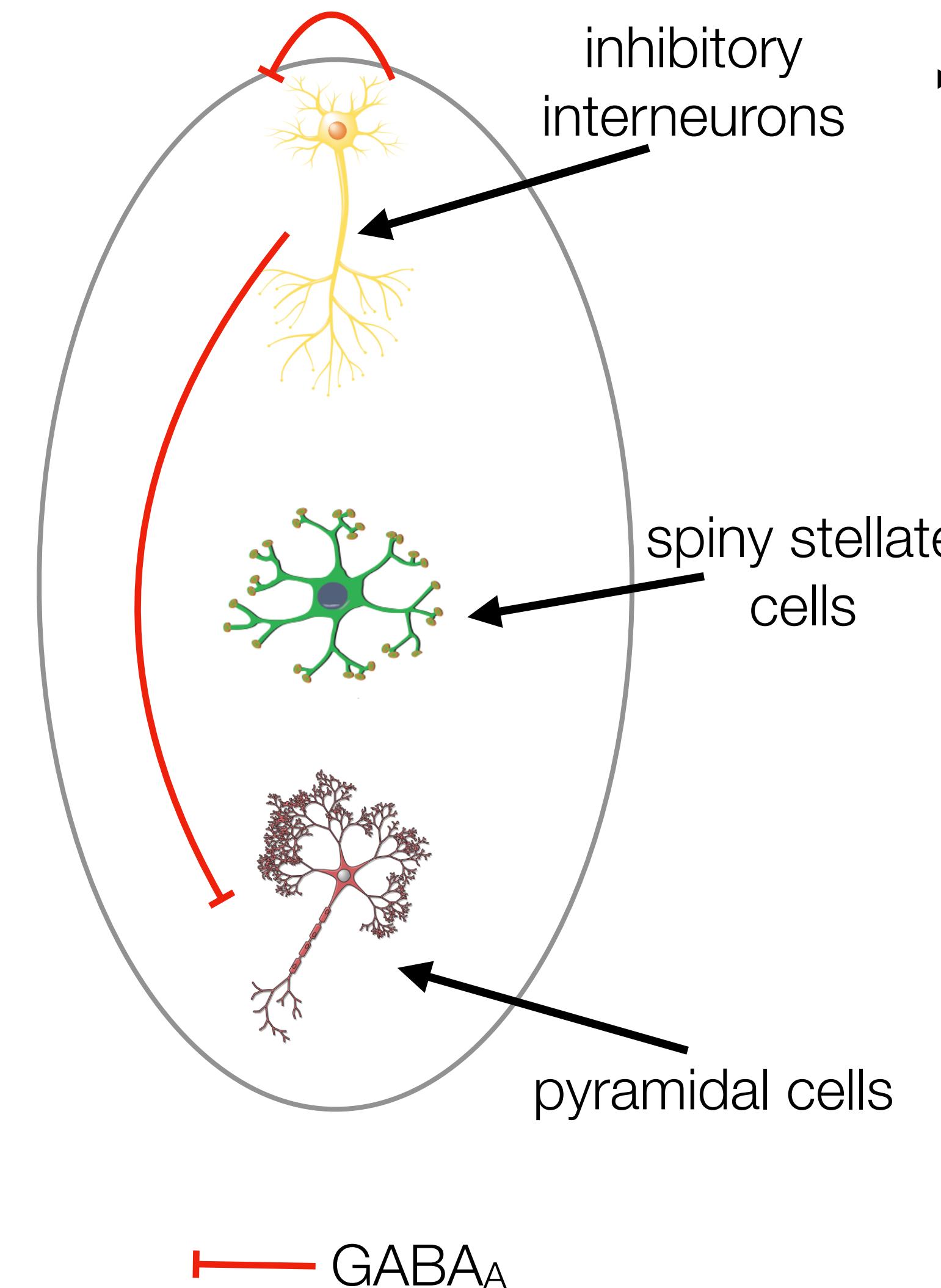
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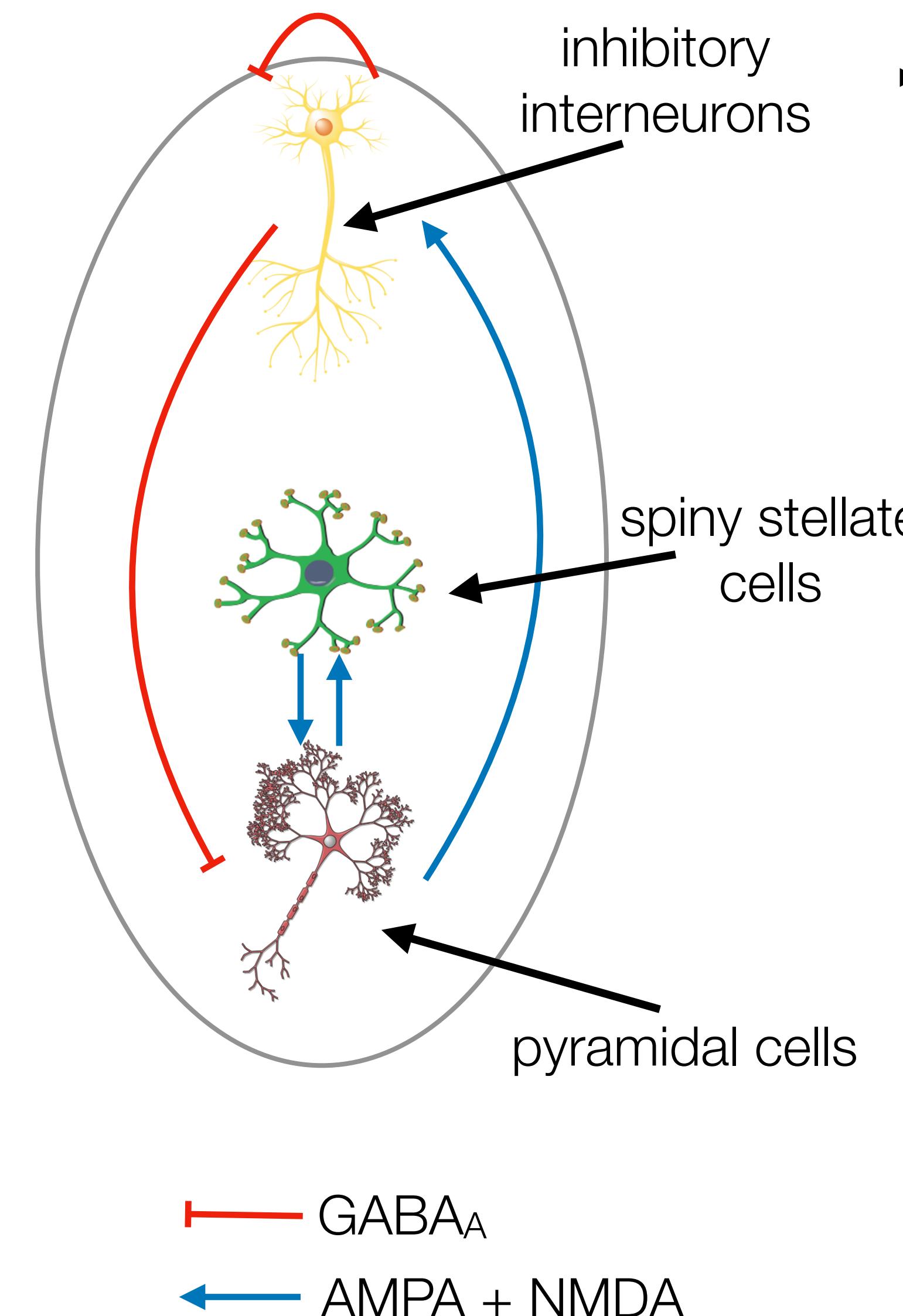
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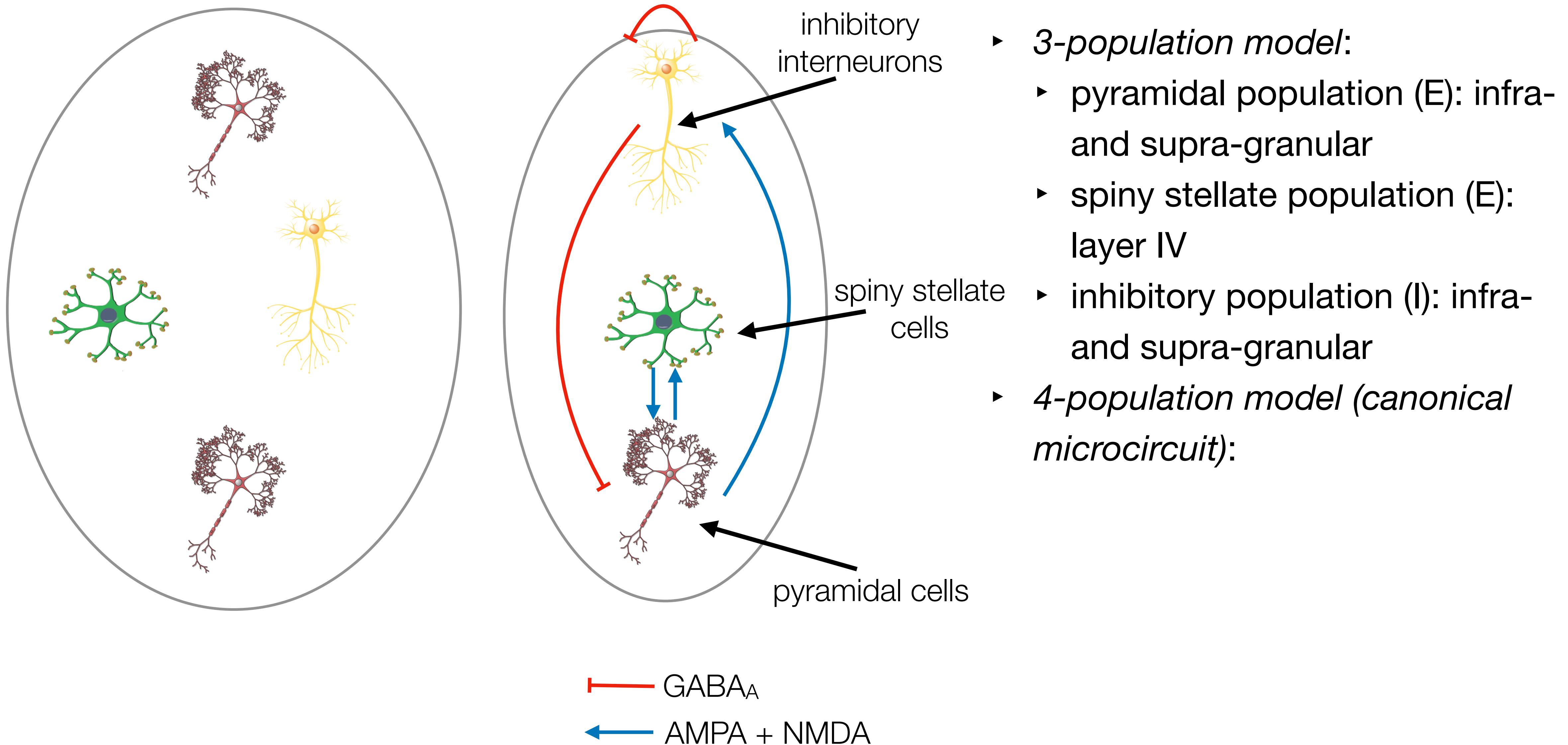
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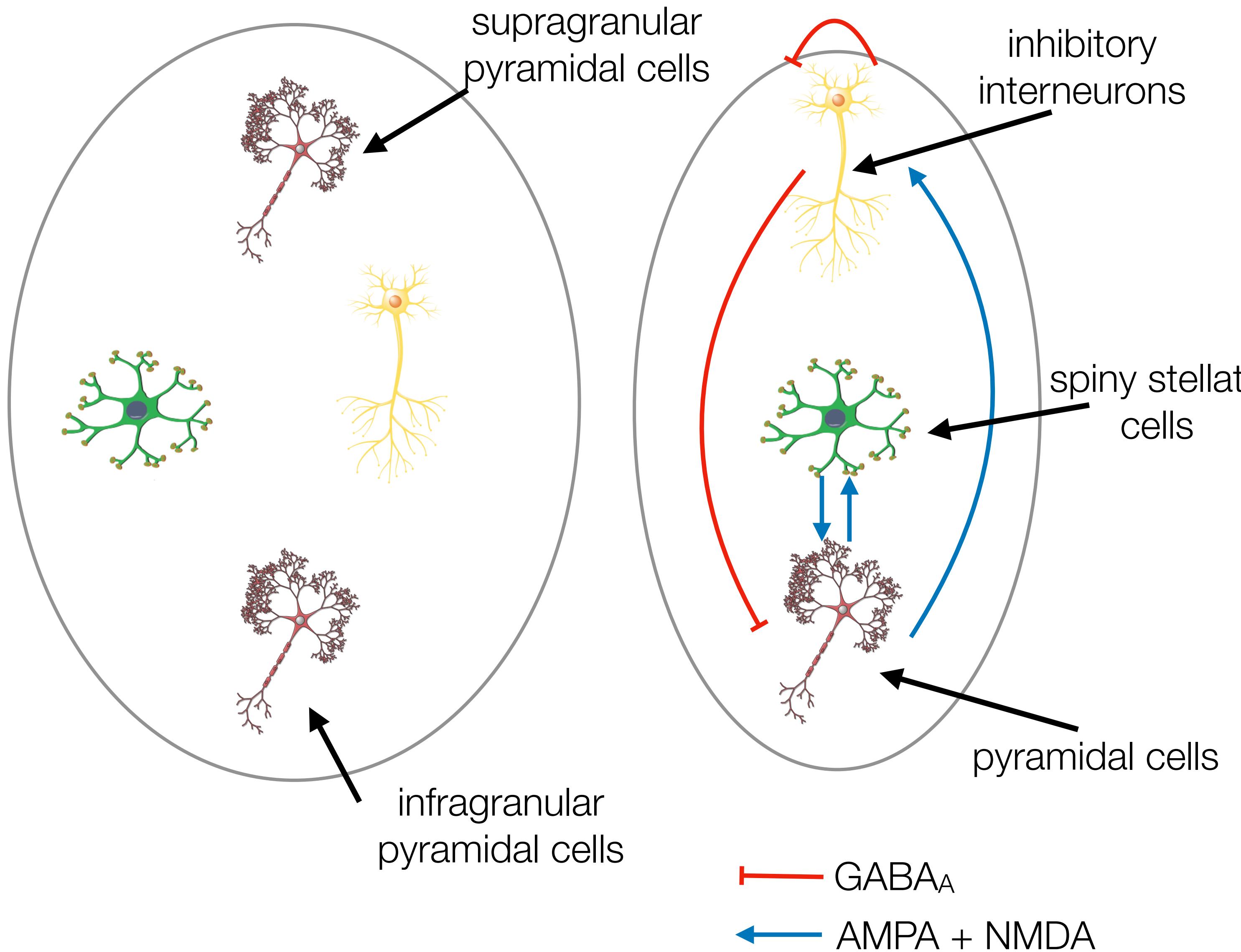


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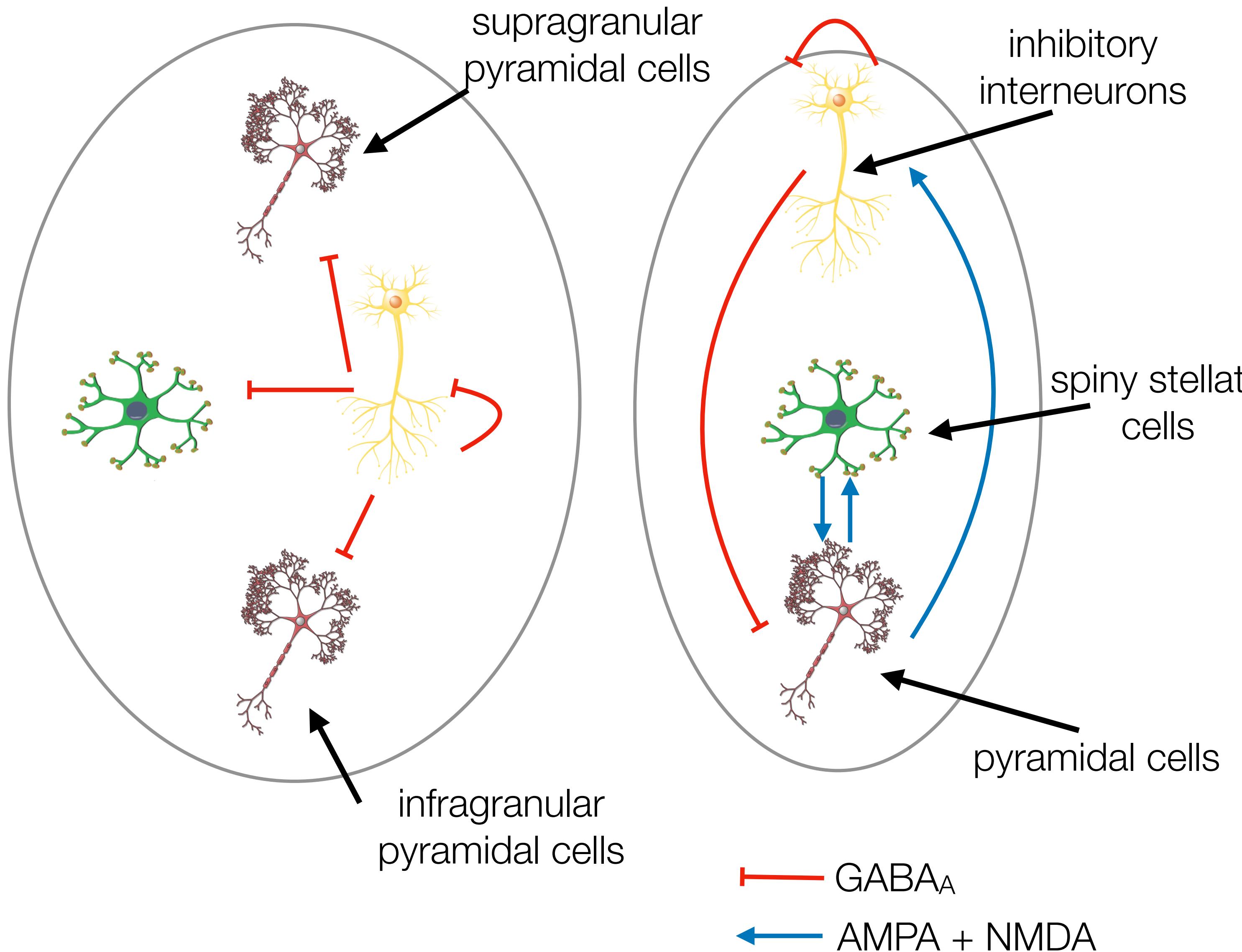


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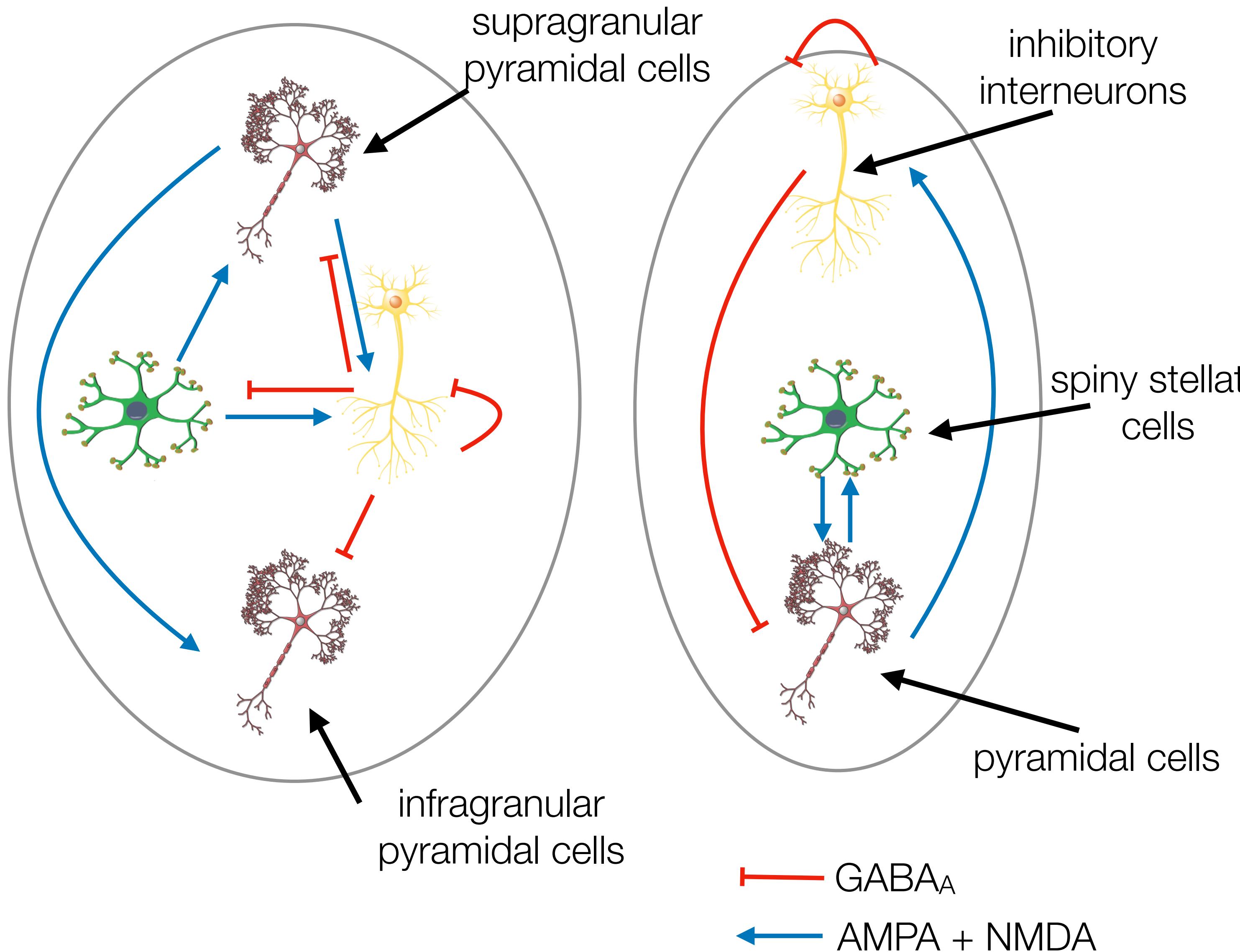
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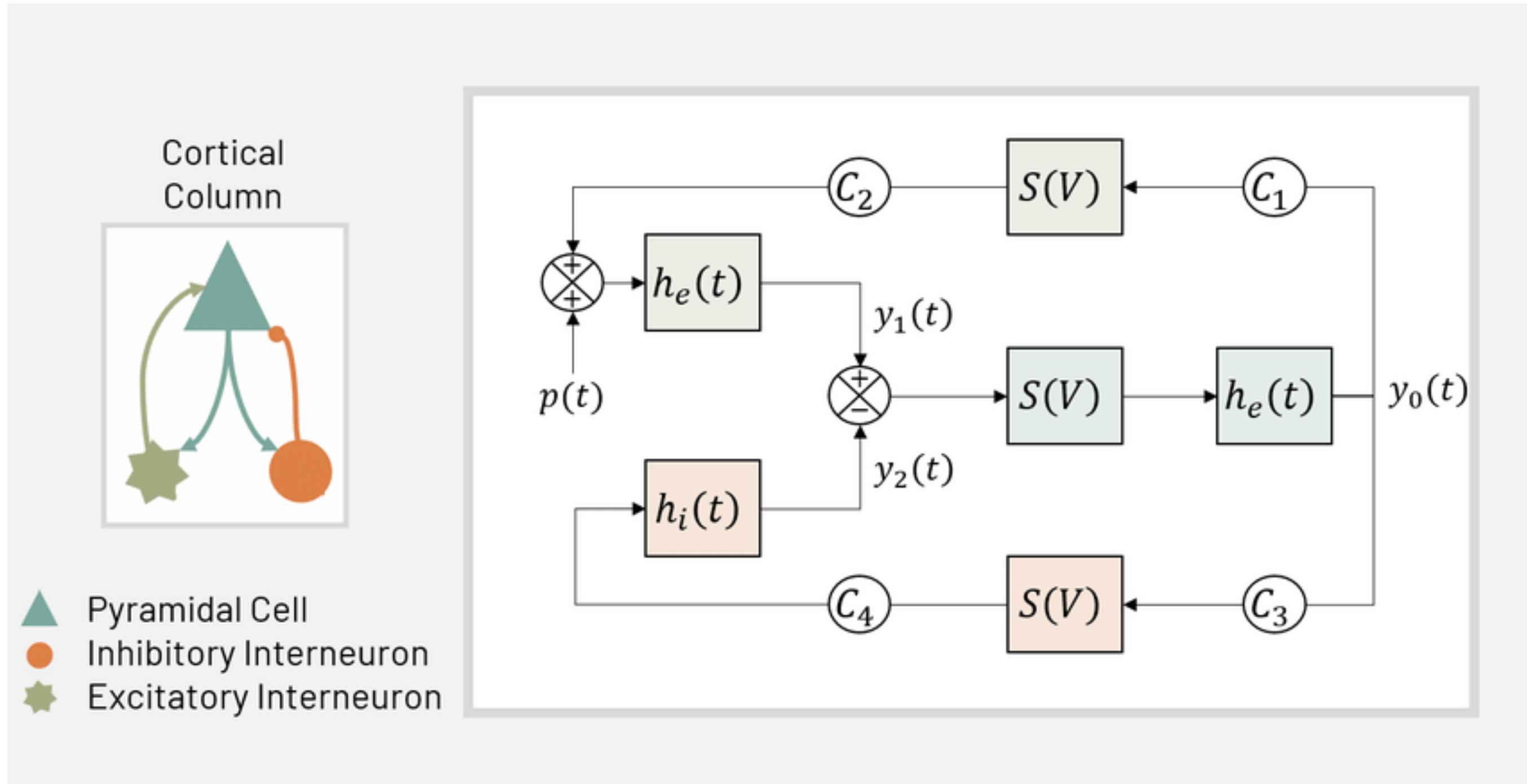
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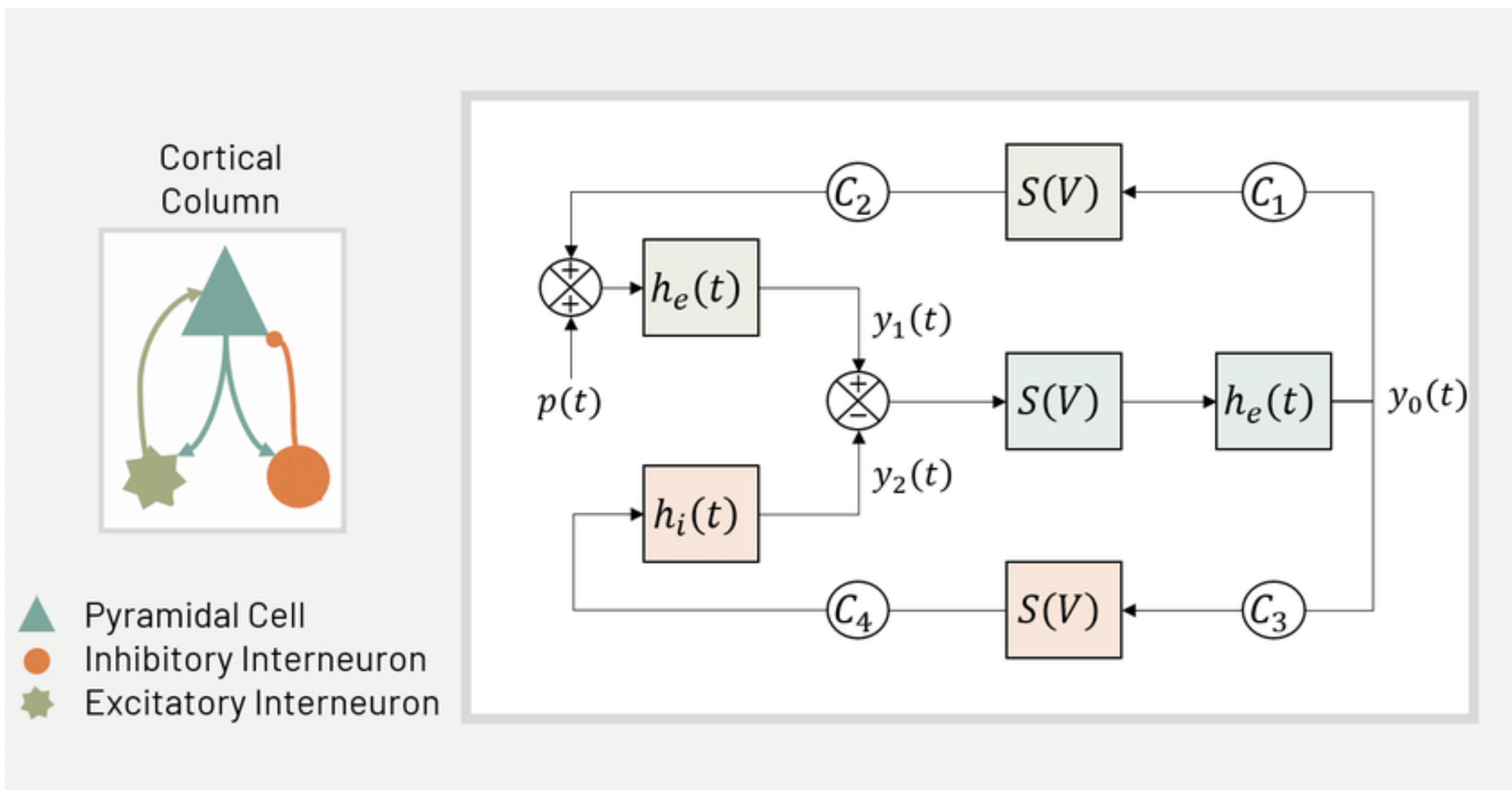
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Sanchez-Todo et al., 2018, *bioRxiv*

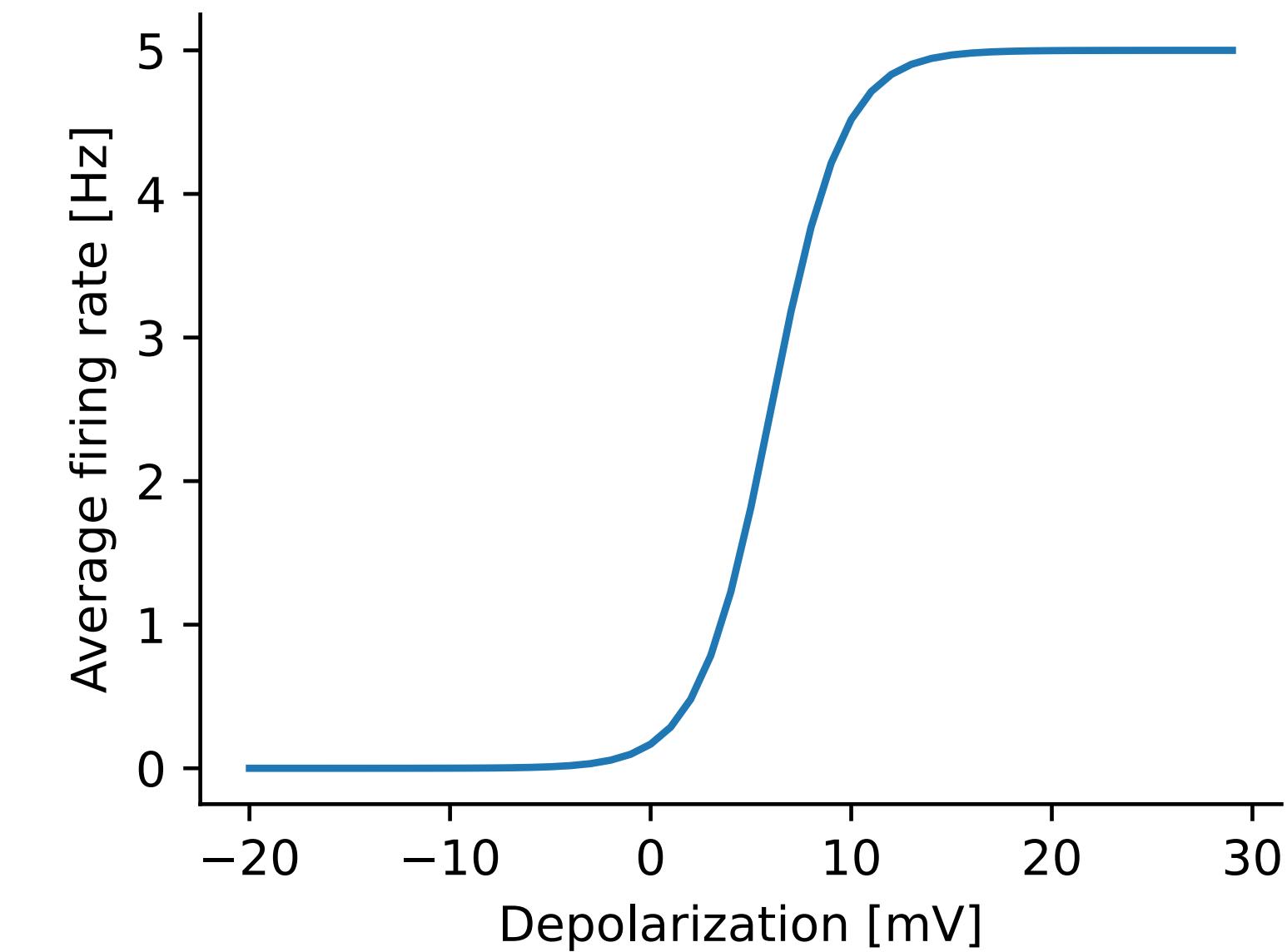
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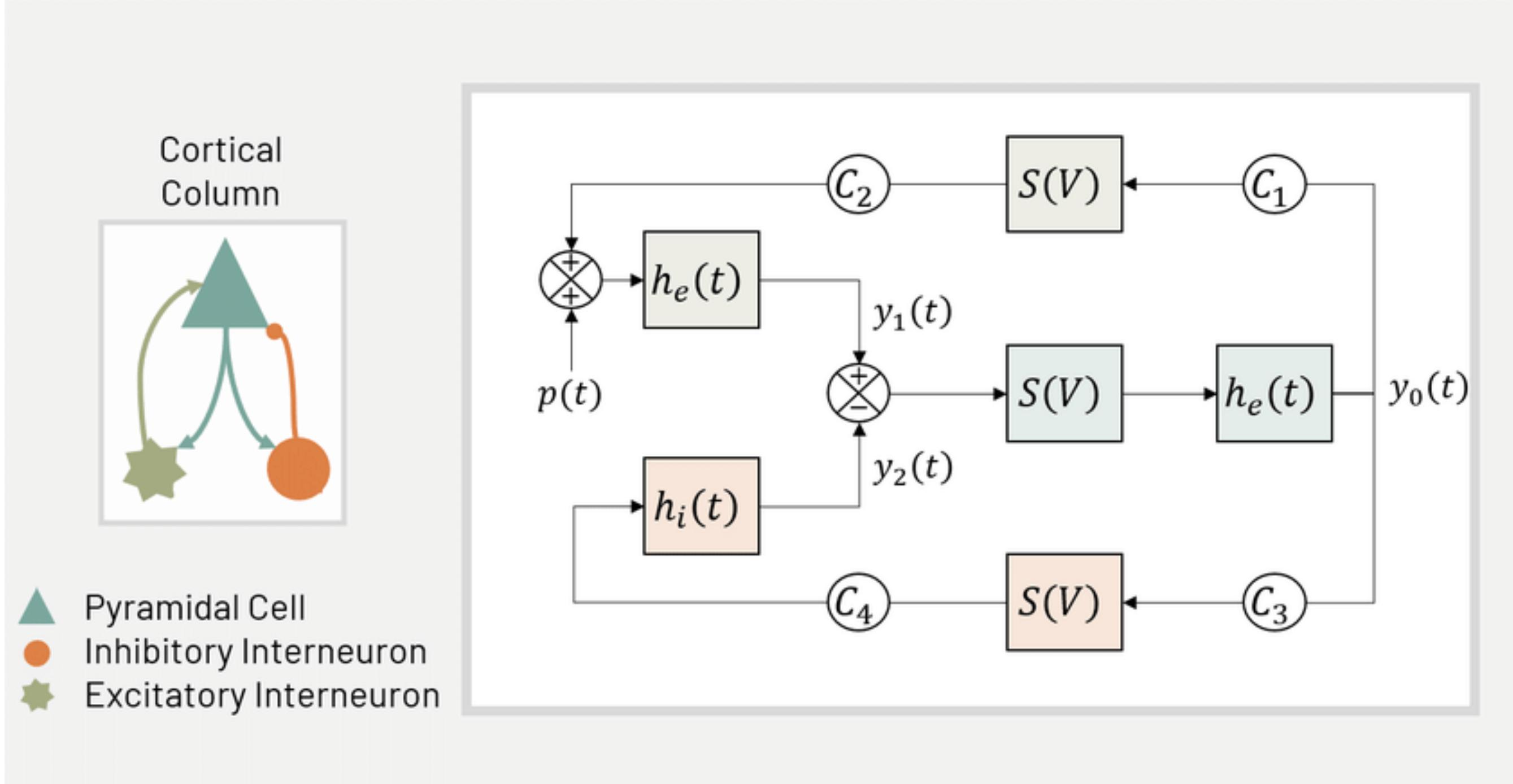
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$$\sigma(v) = \frac{2e_0}{1 + \exp(r(v_0 - v))}$$

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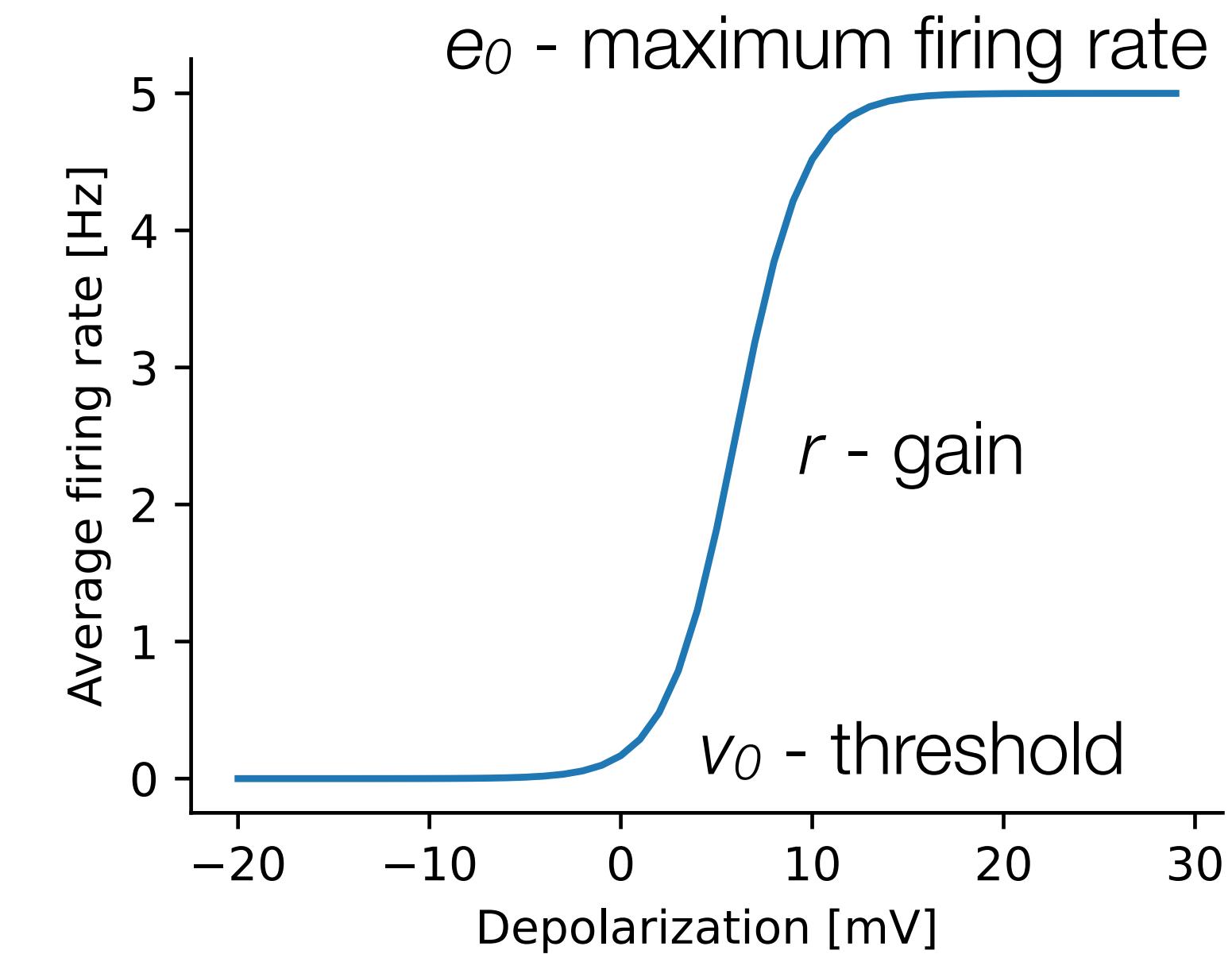
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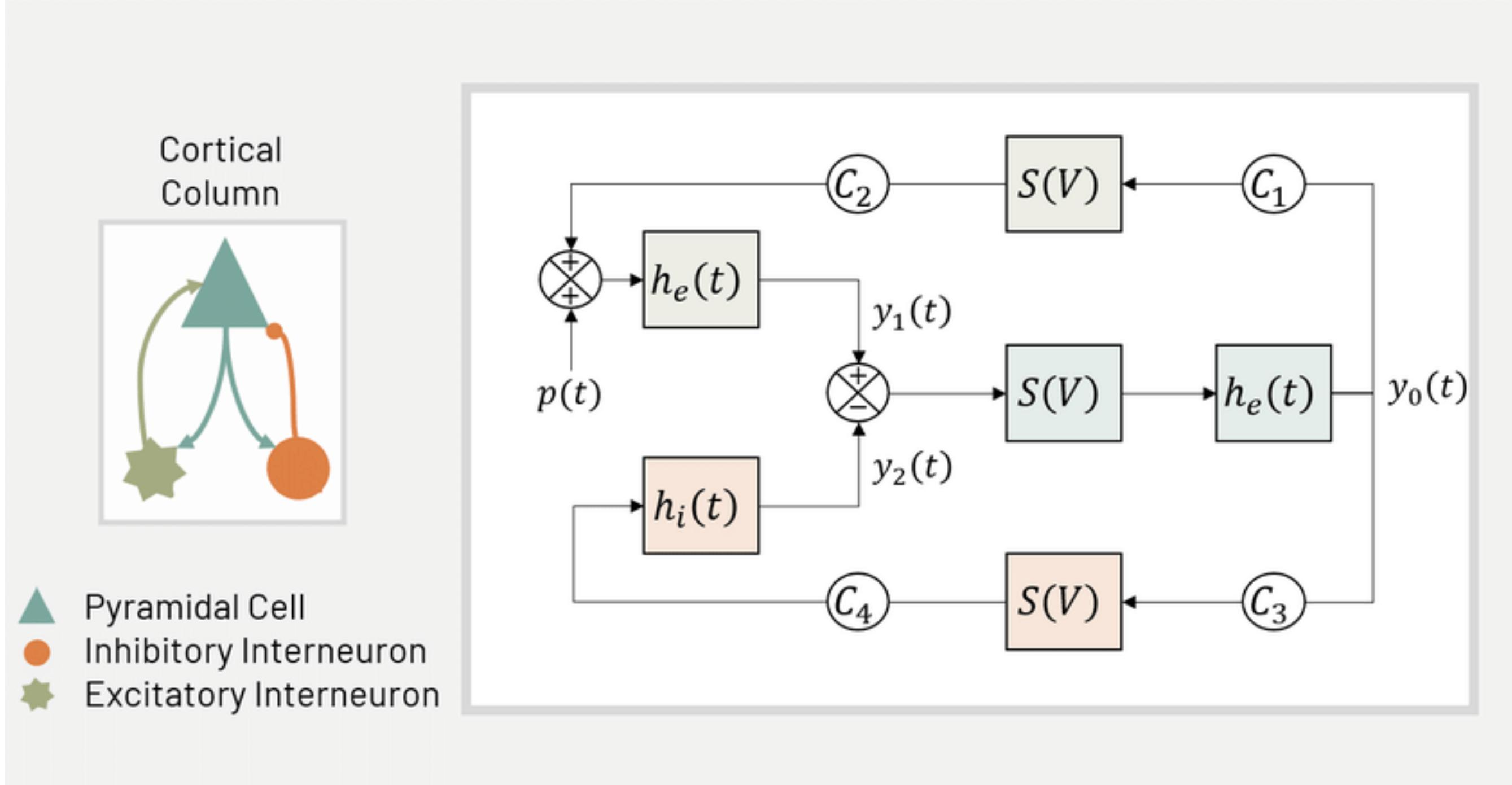
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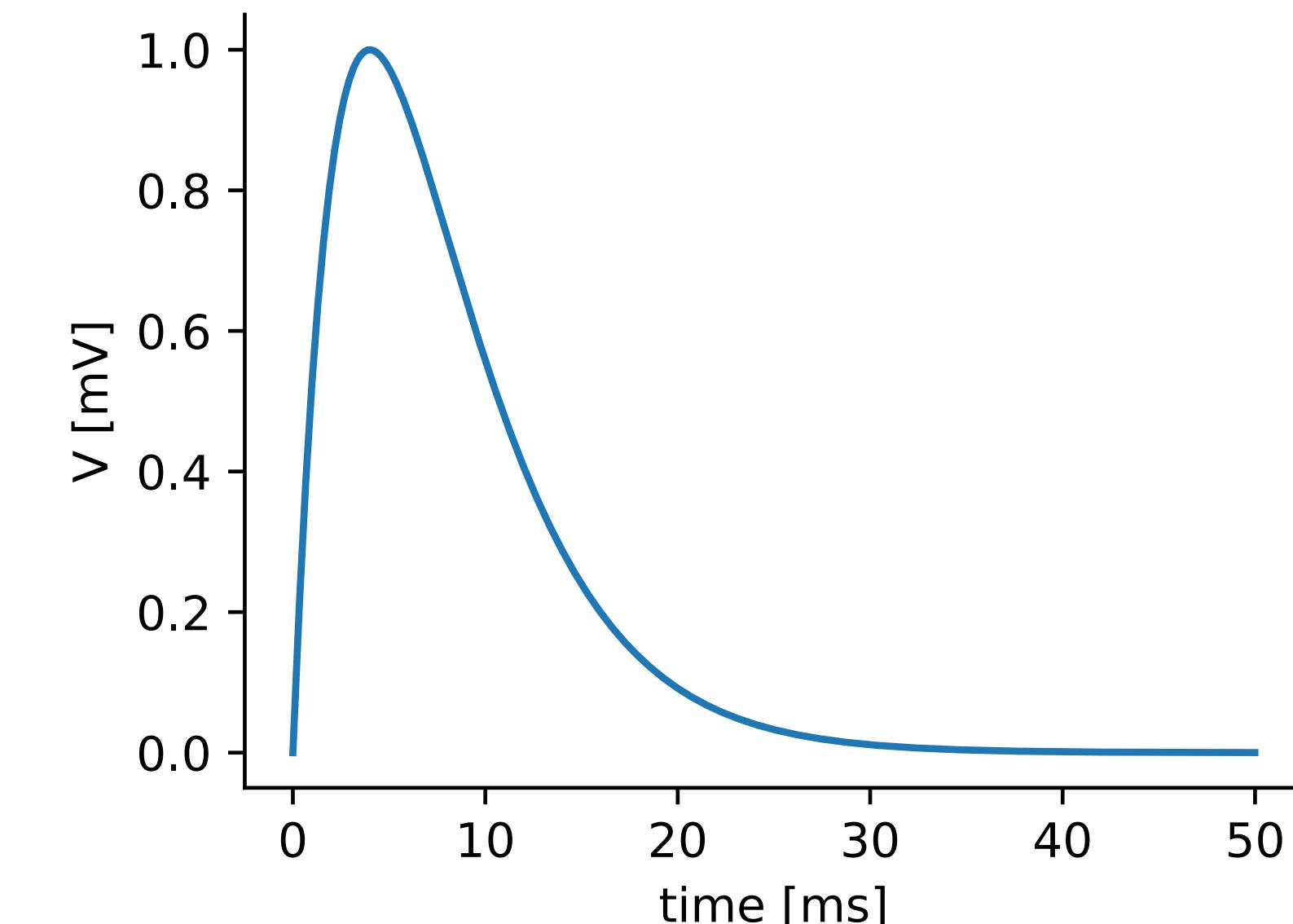
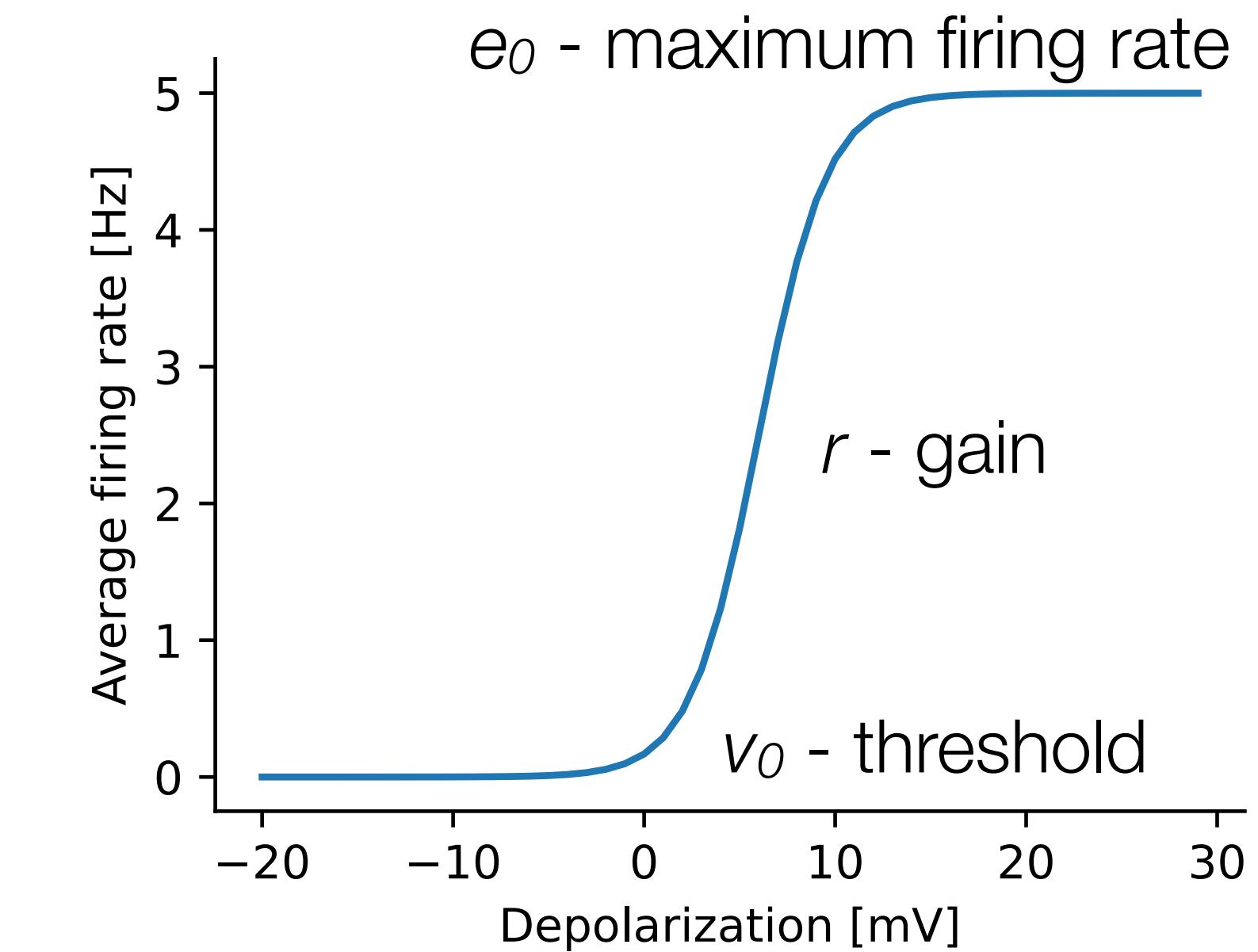


Sanchez-Todo et al., 2018, *bioRxiv*

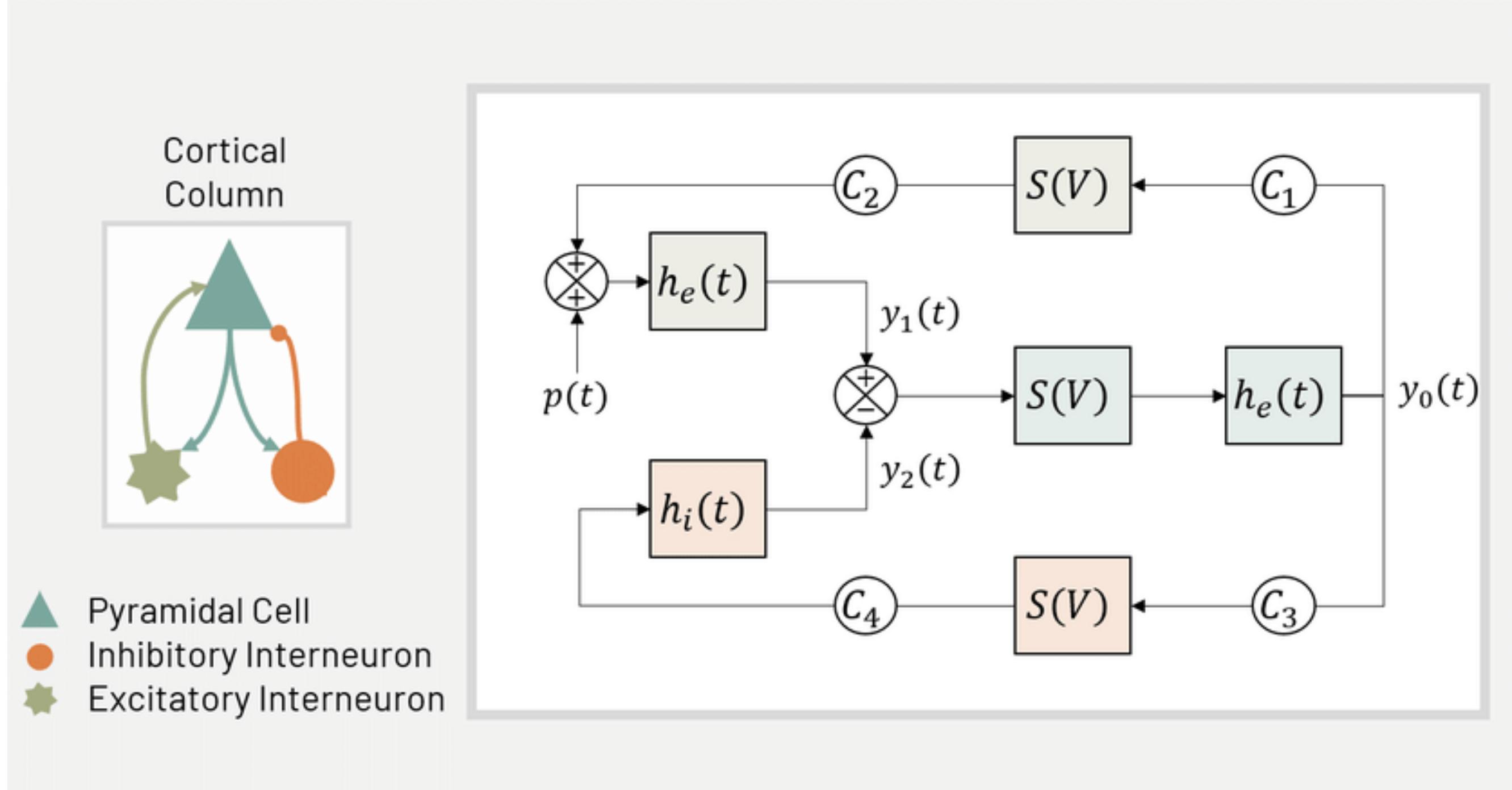
$$v(t) = h(t) \otimes \sigma(t)$$

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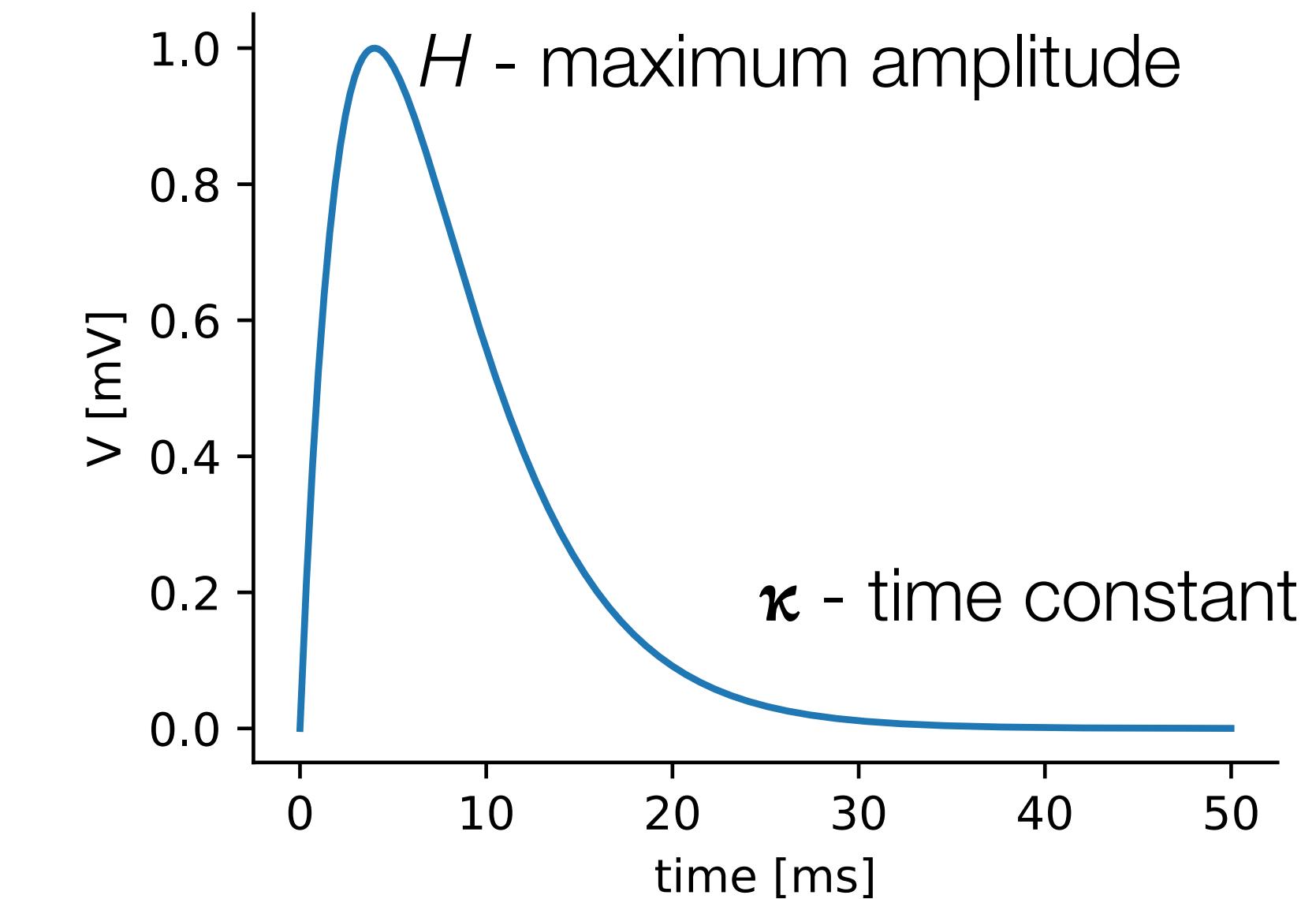
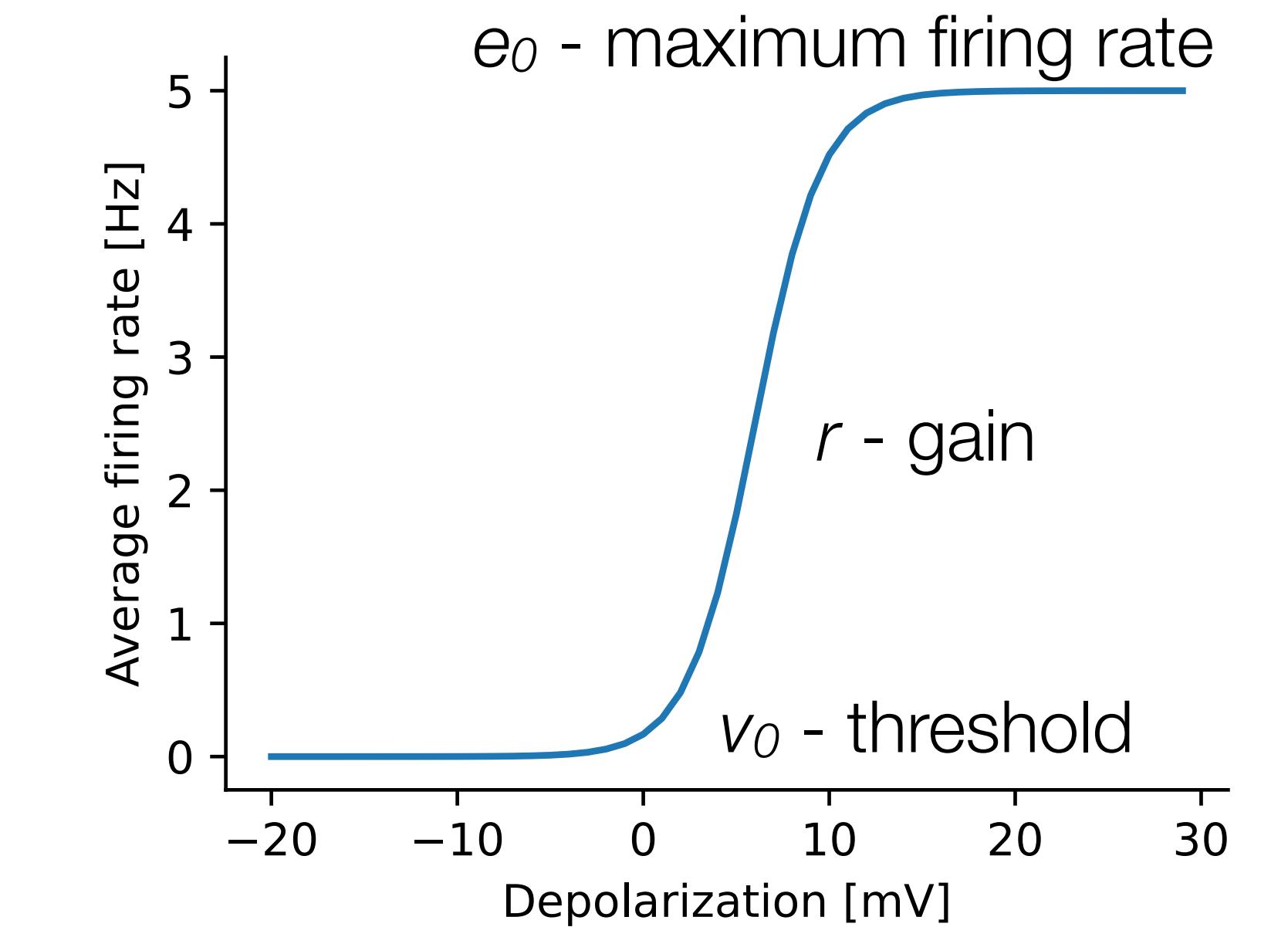
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impulse-response function

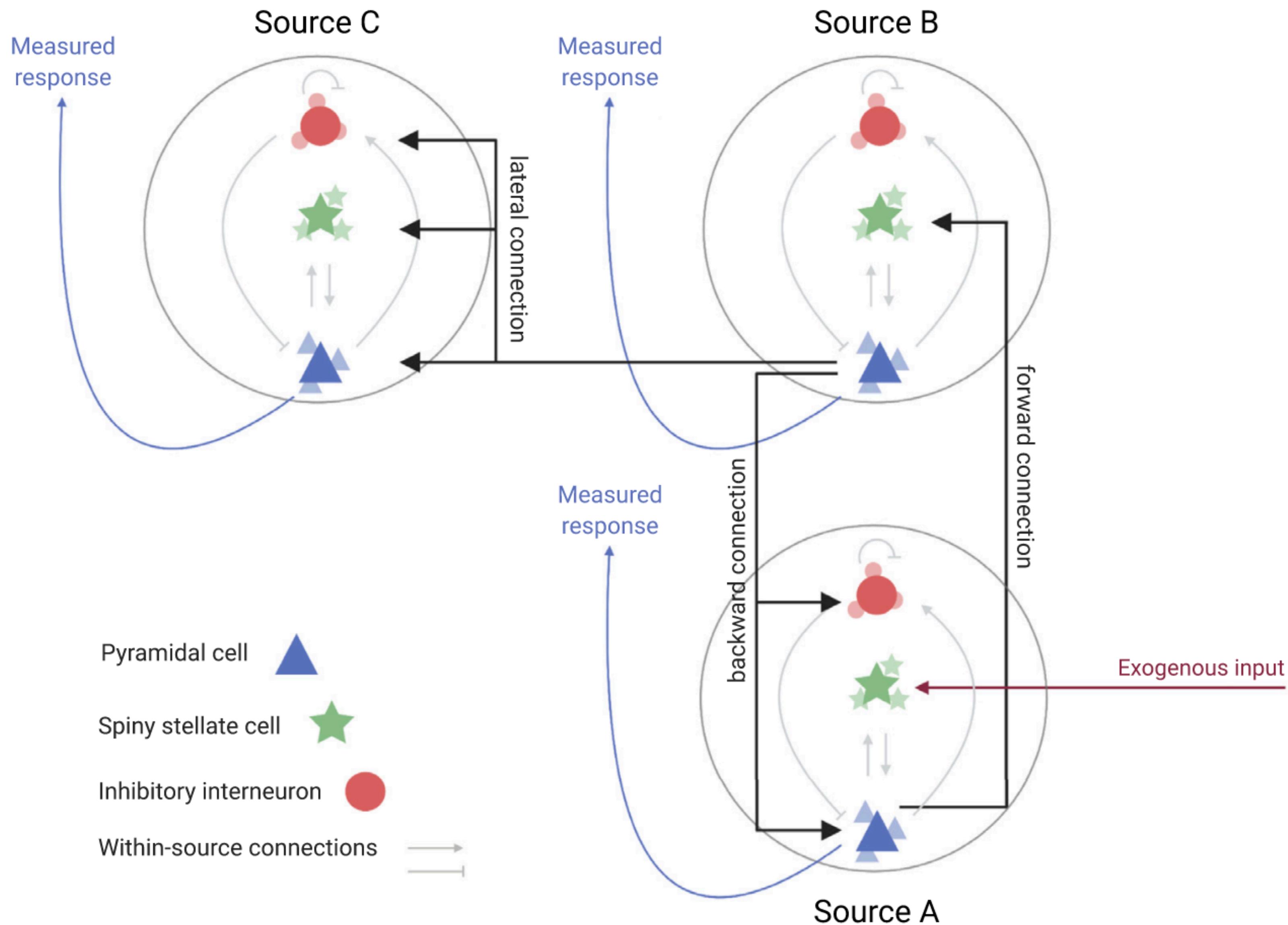
$$h(t) = H\kappa t e^{(-\kappa t)}$$

David et al., 2003, *NeuroImage*



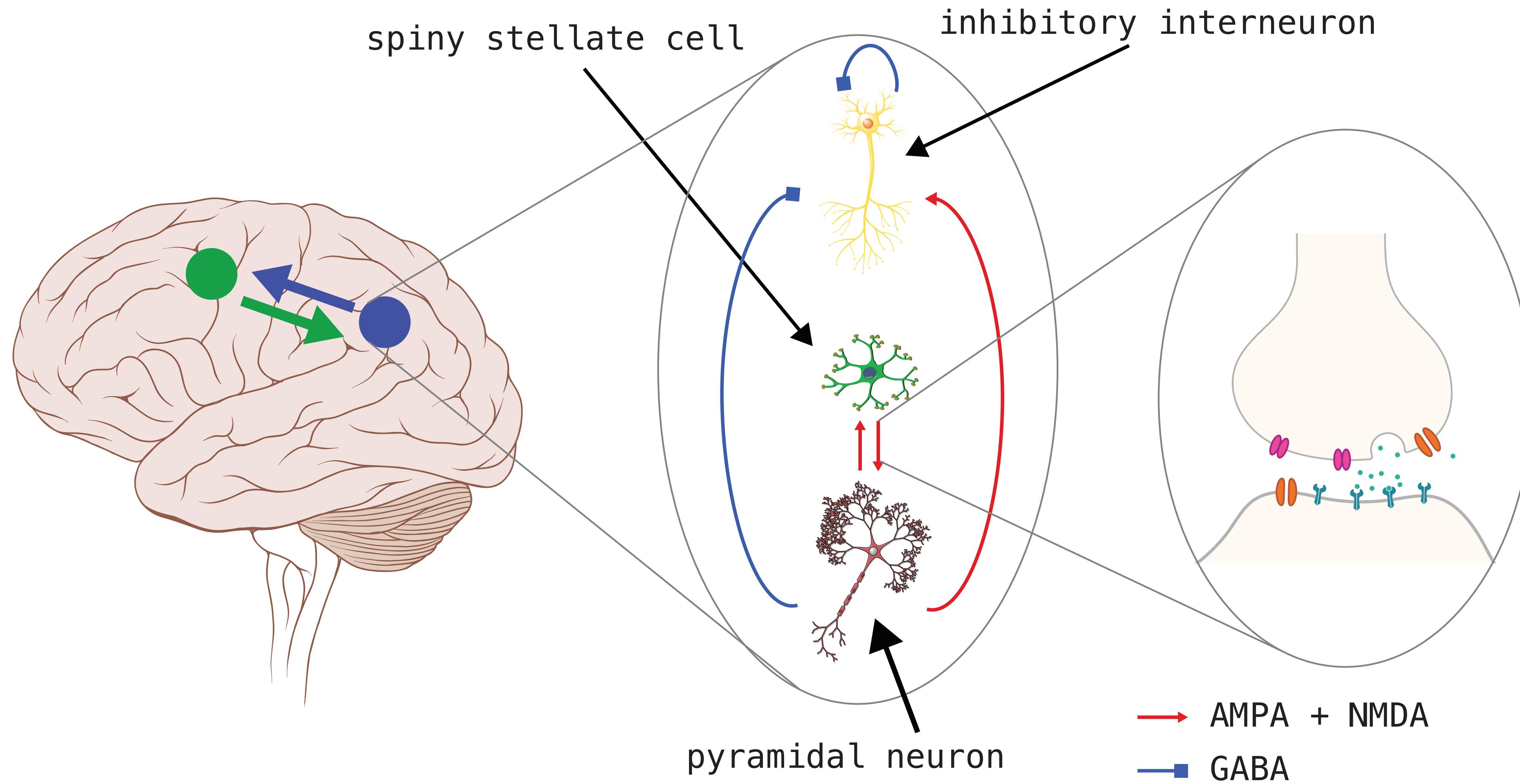
# #Building a model: laminar structure

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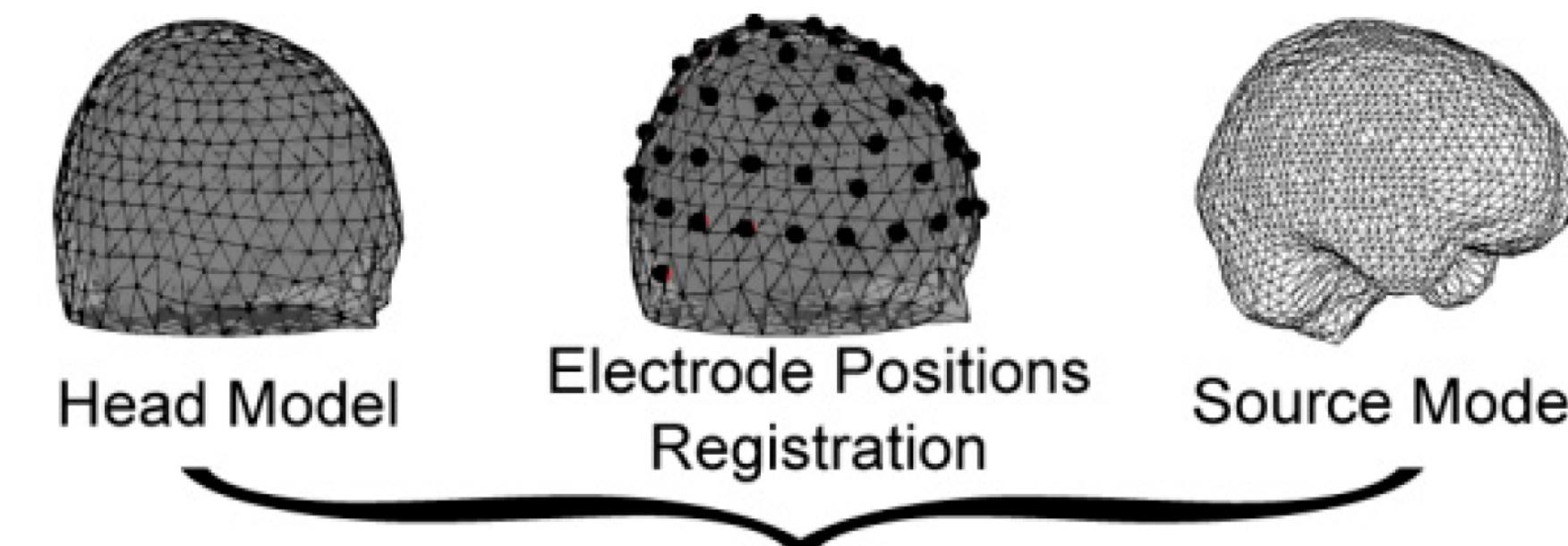
# #Building a model: whole brain

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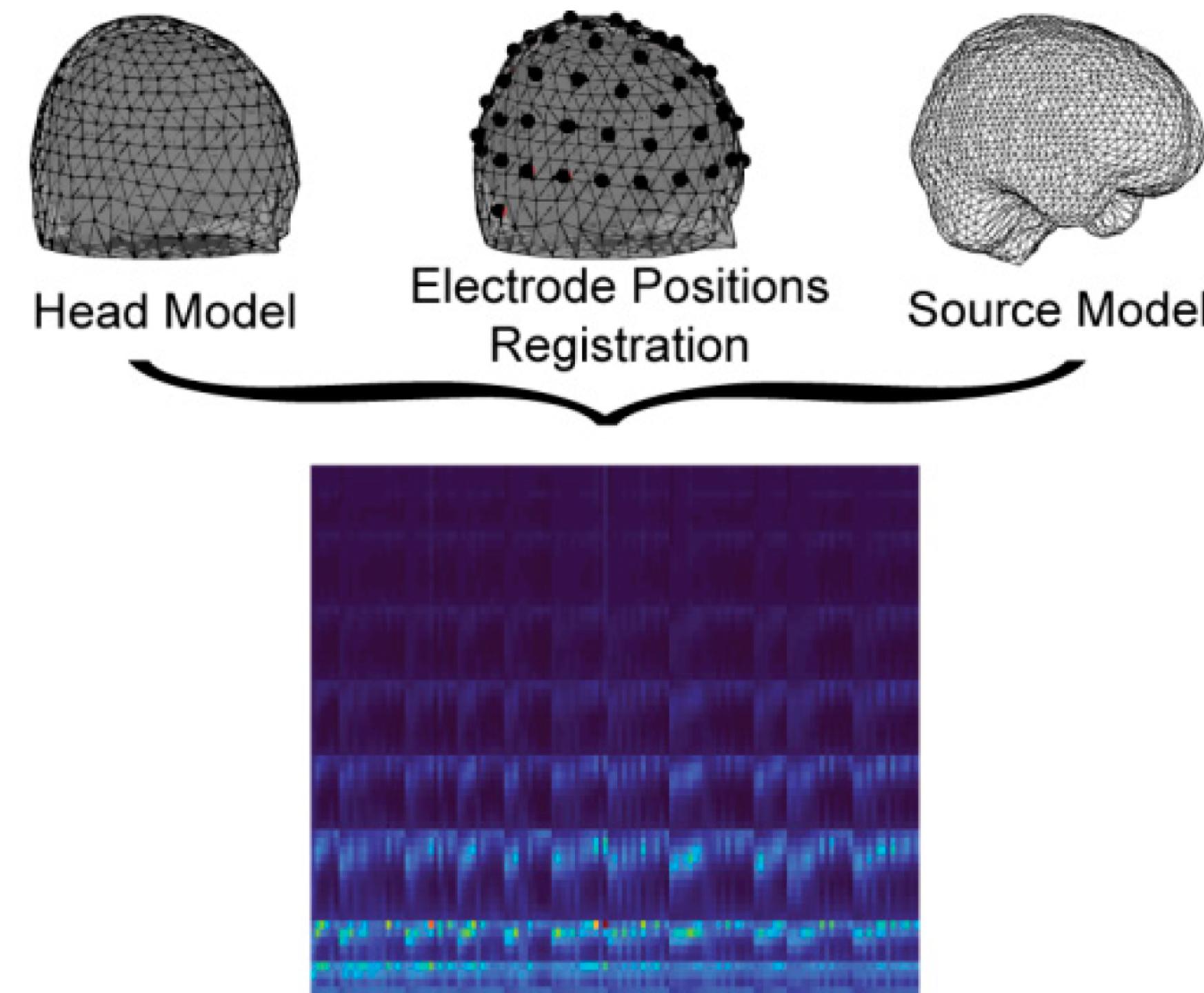


# #Building a model: electromagnetic forward model

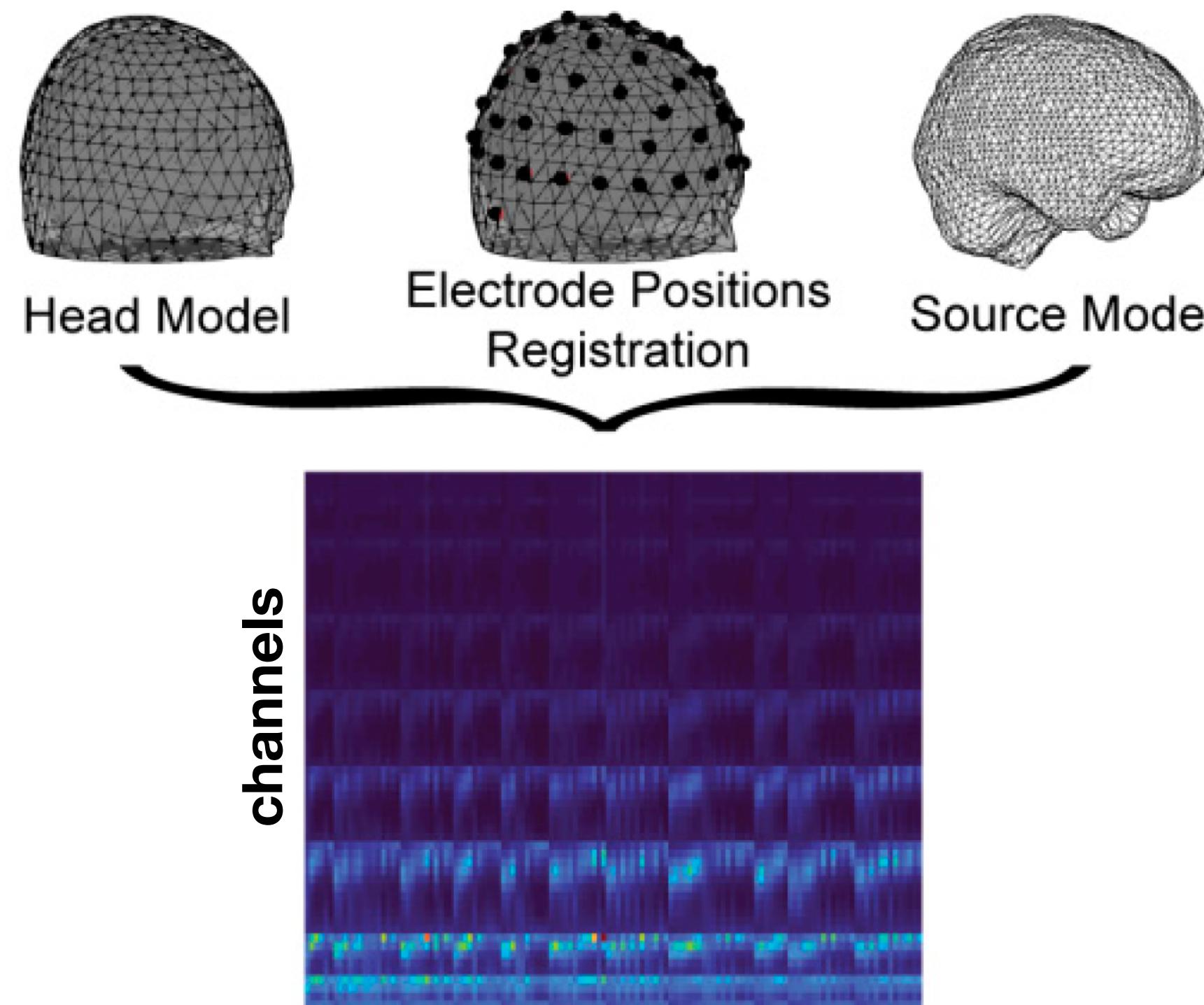
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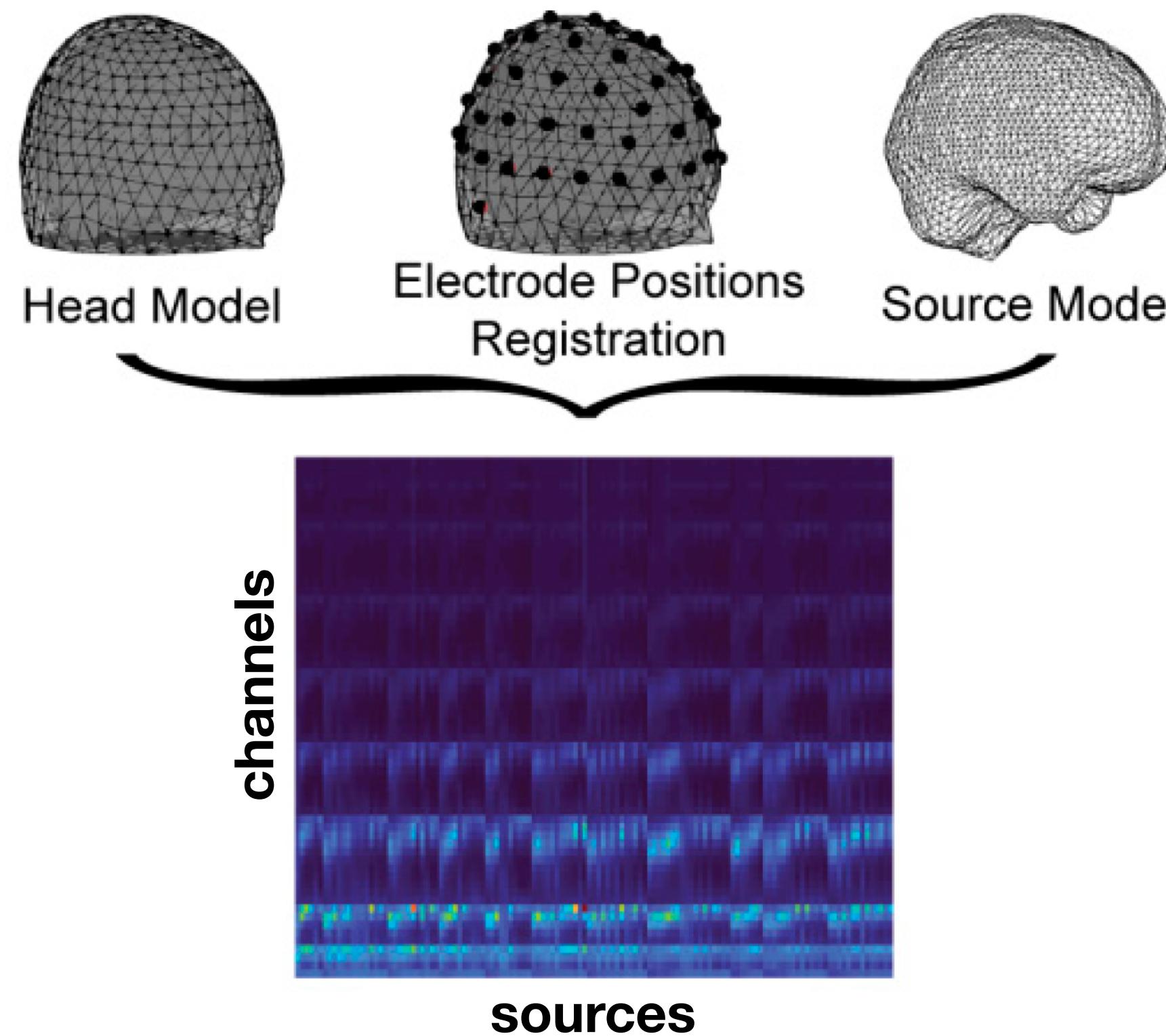
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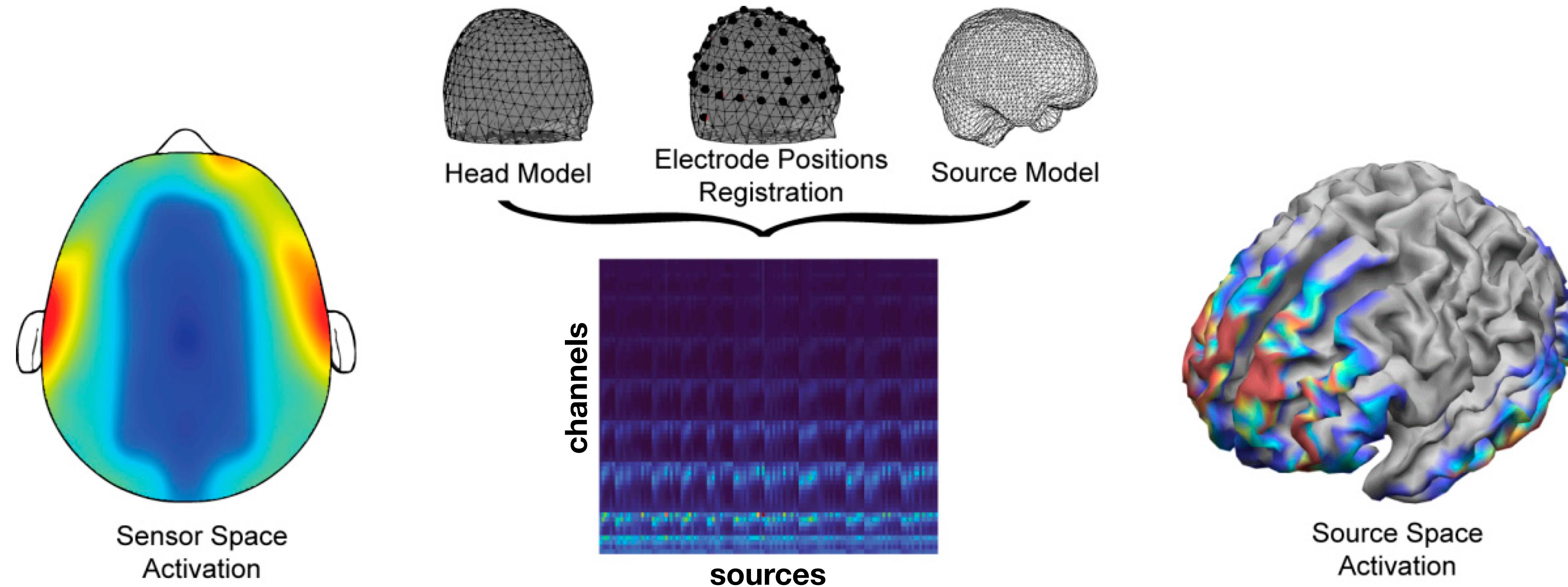
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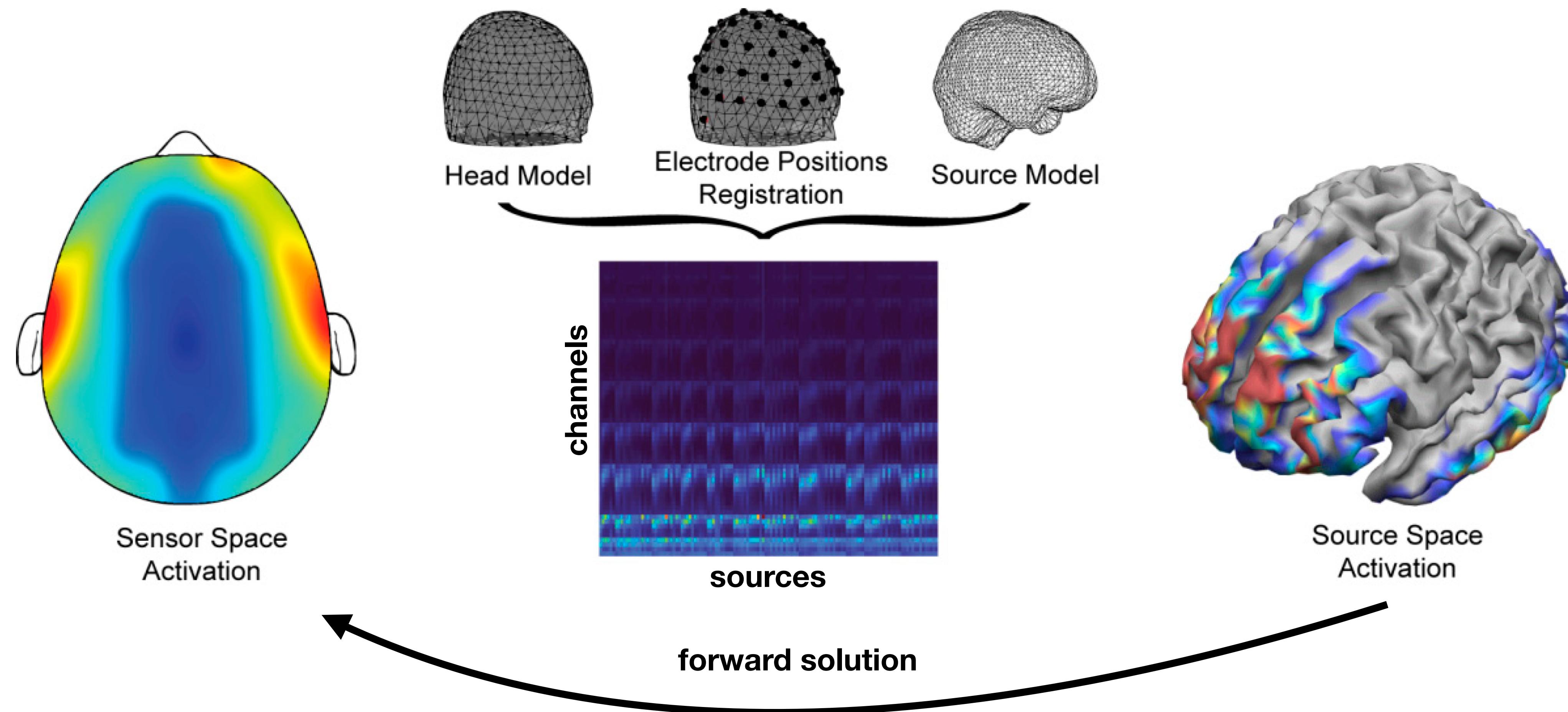
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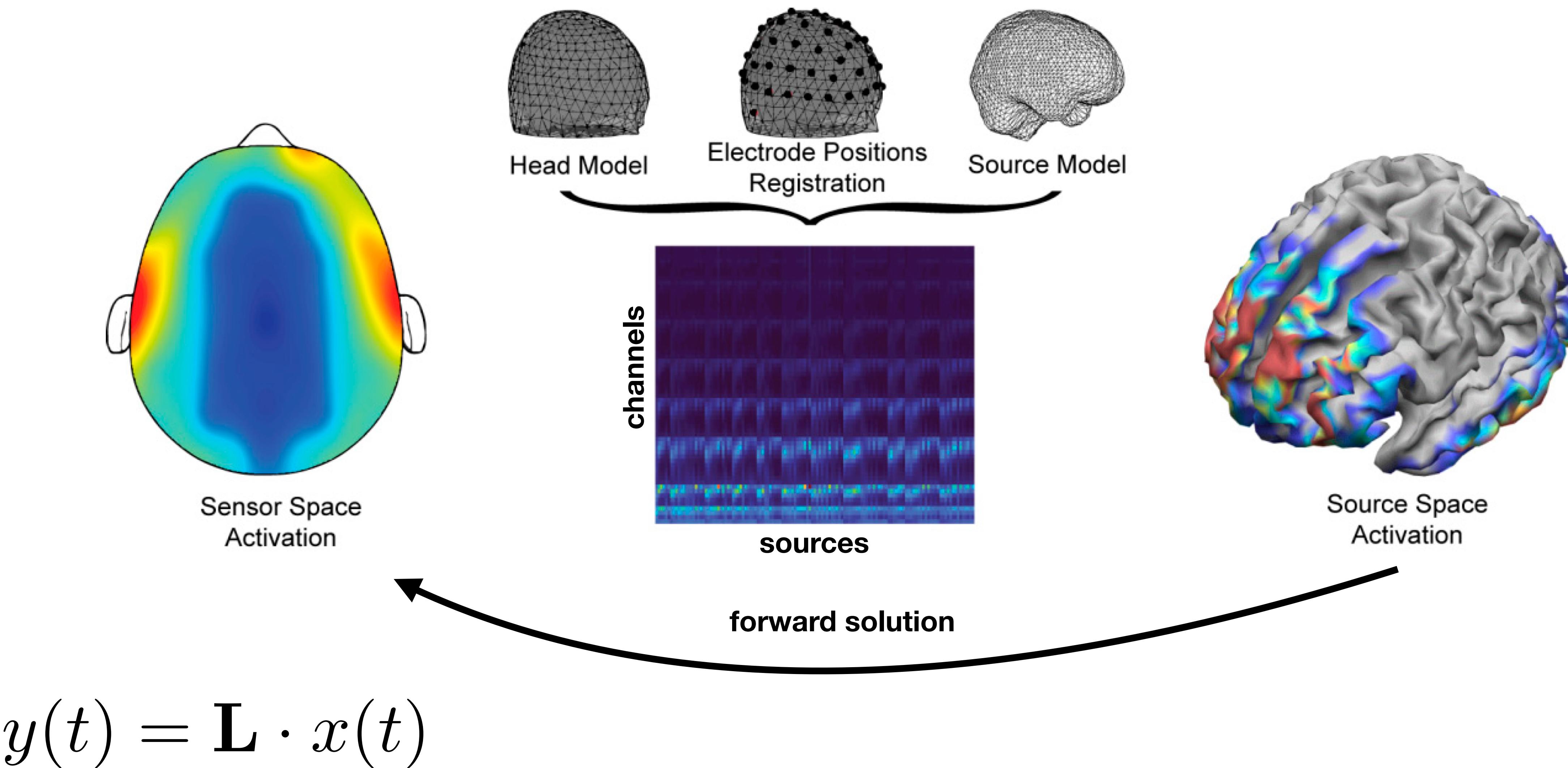
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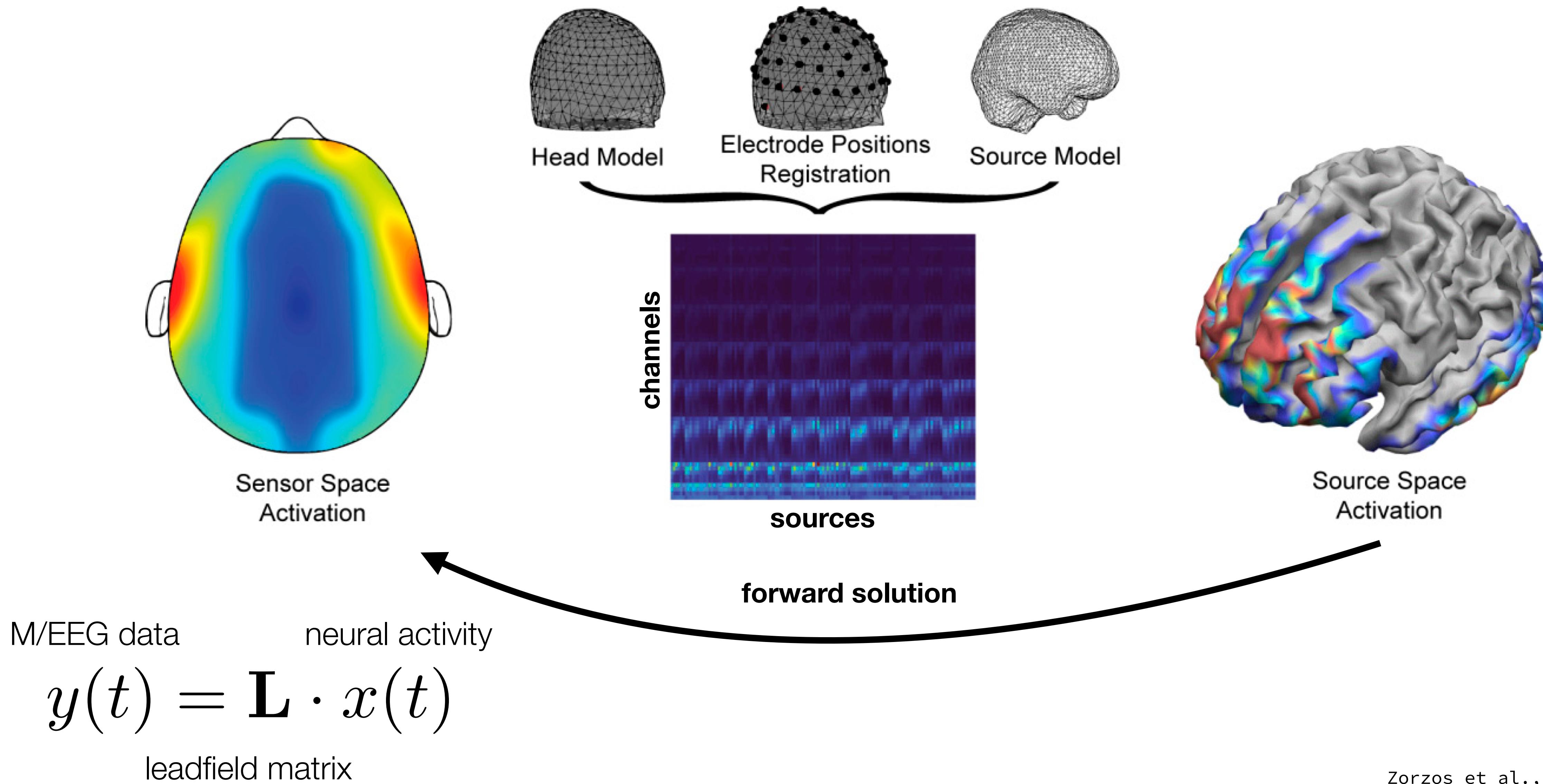
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# #Building a model: data features

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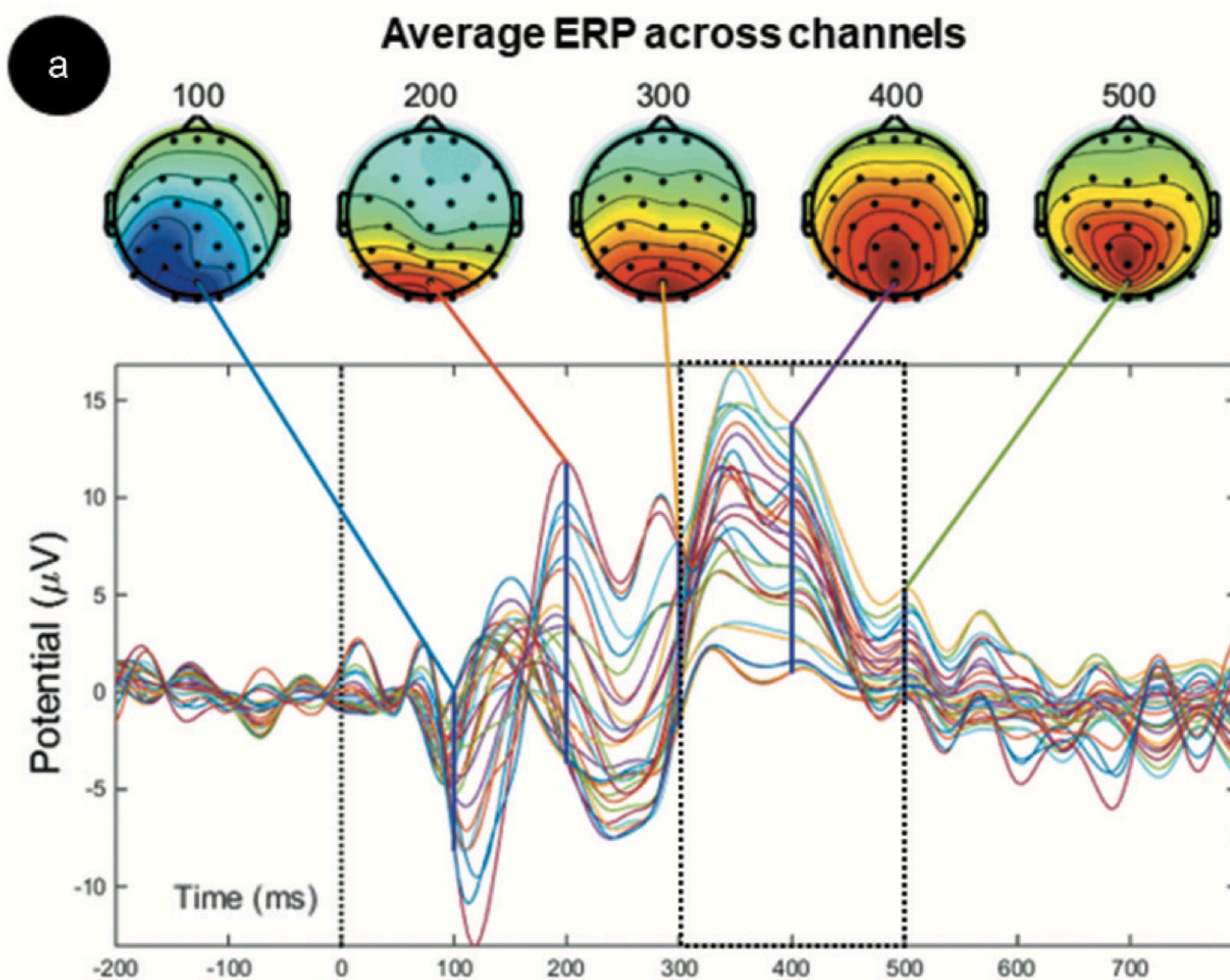
*actual time series*

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- ▶ temporal representation:  
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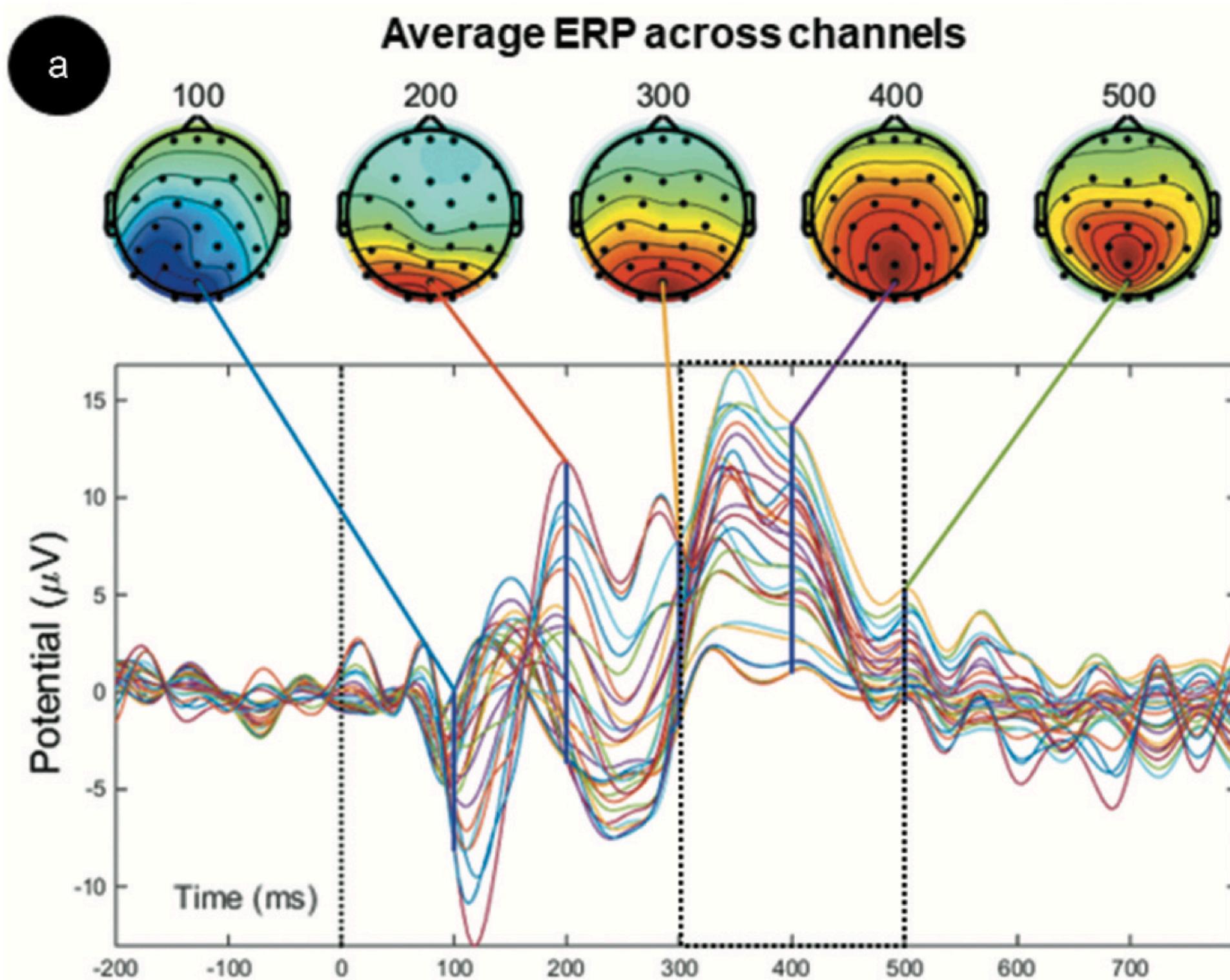
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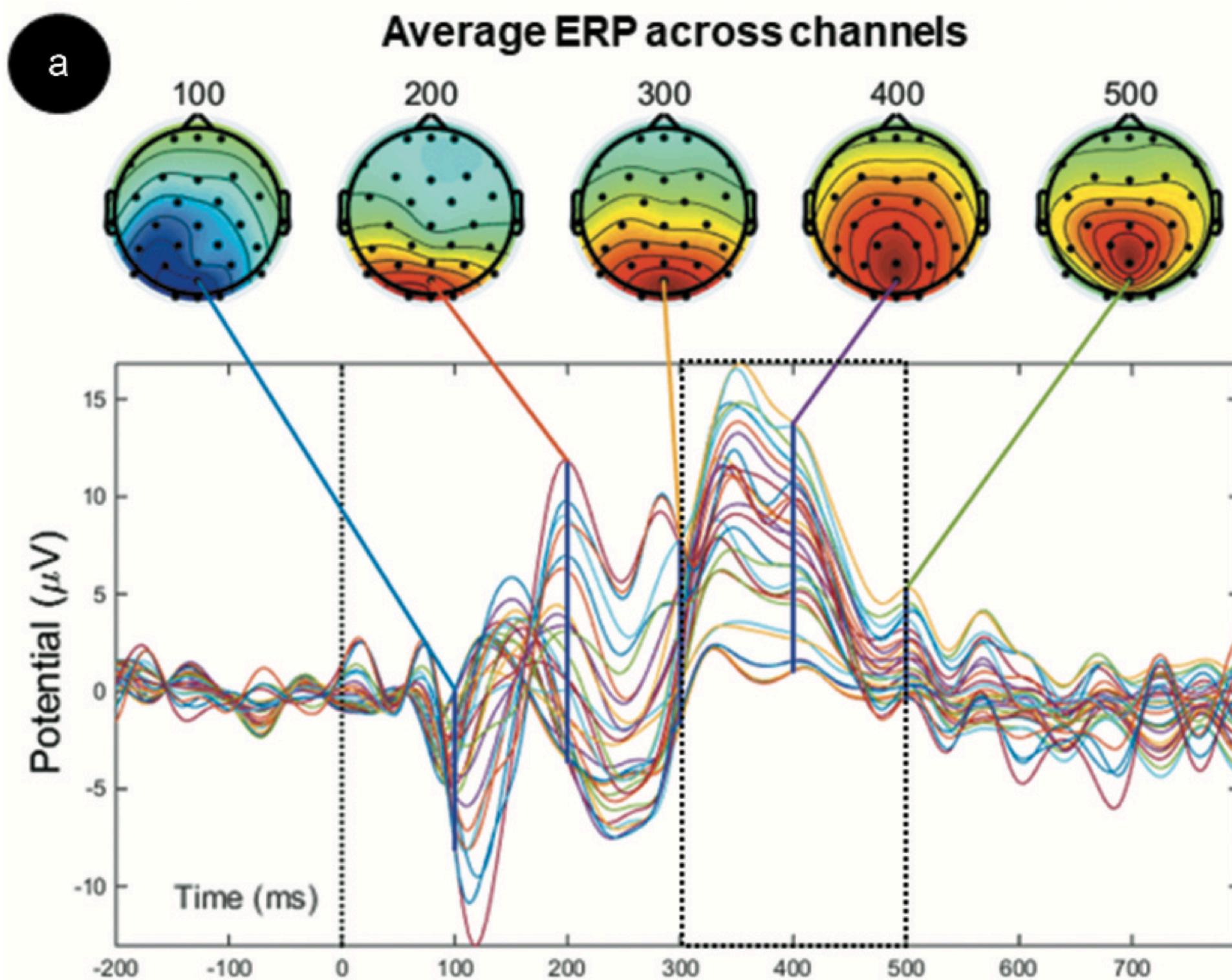
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- ▶ temporal representation:  
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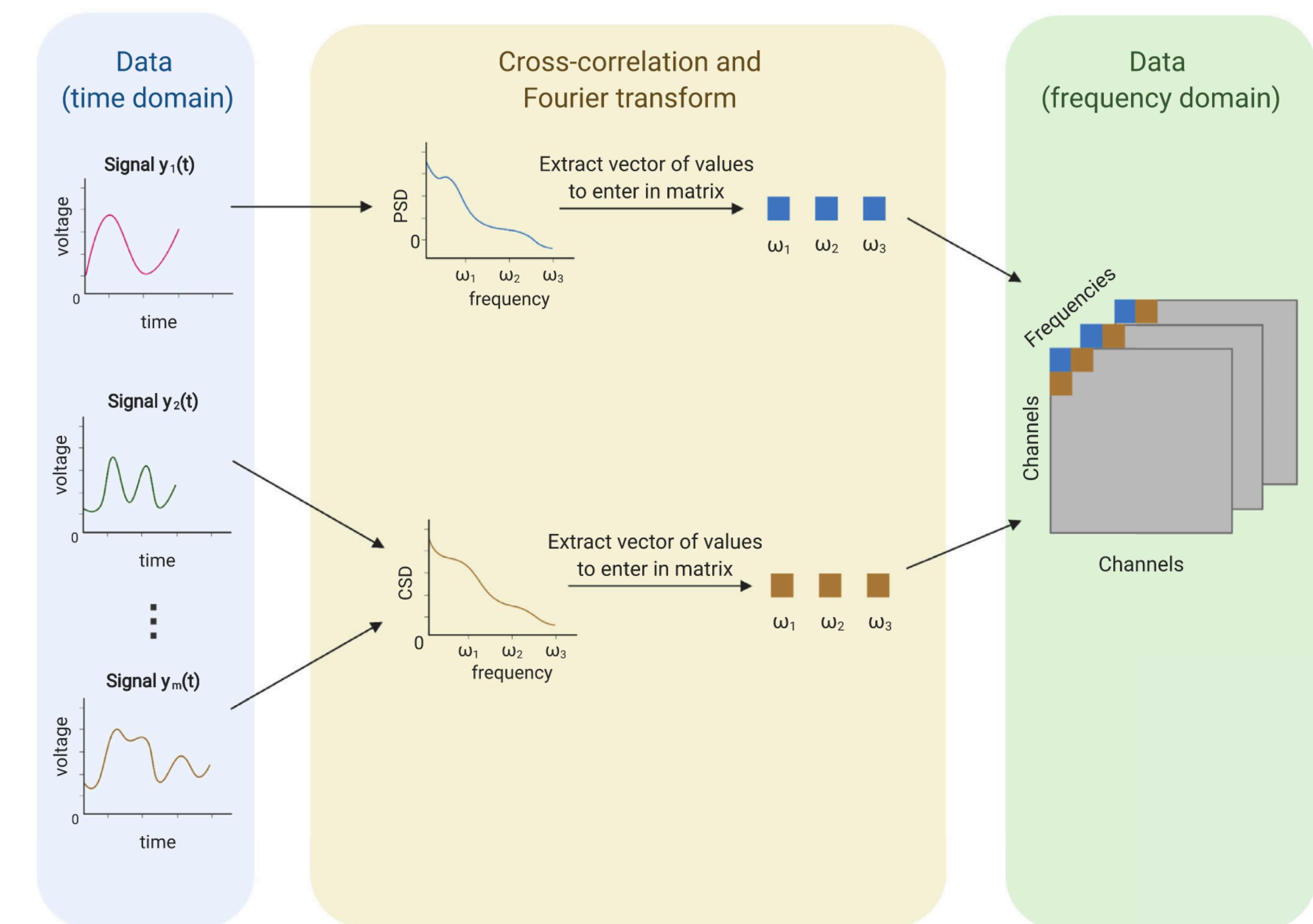
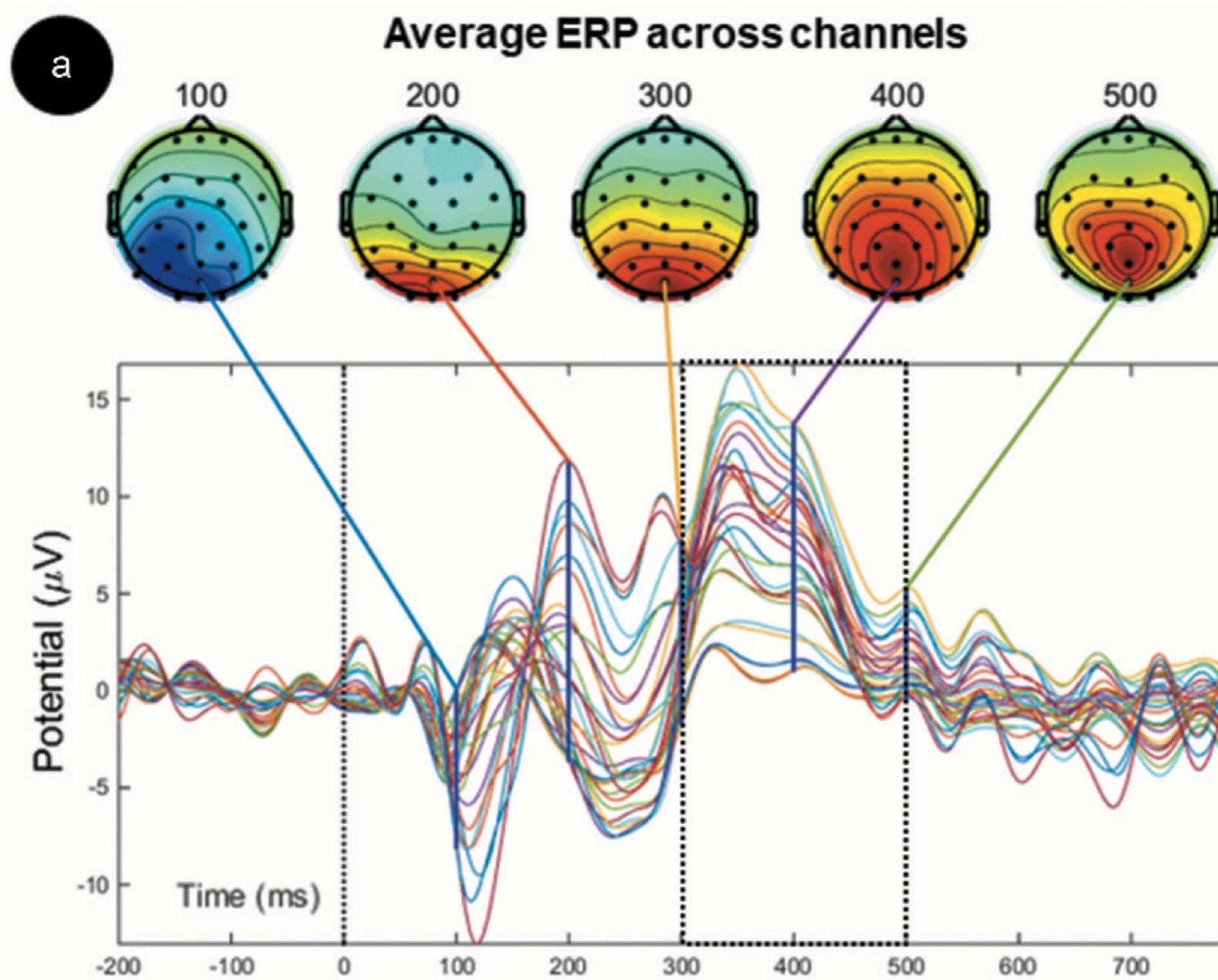
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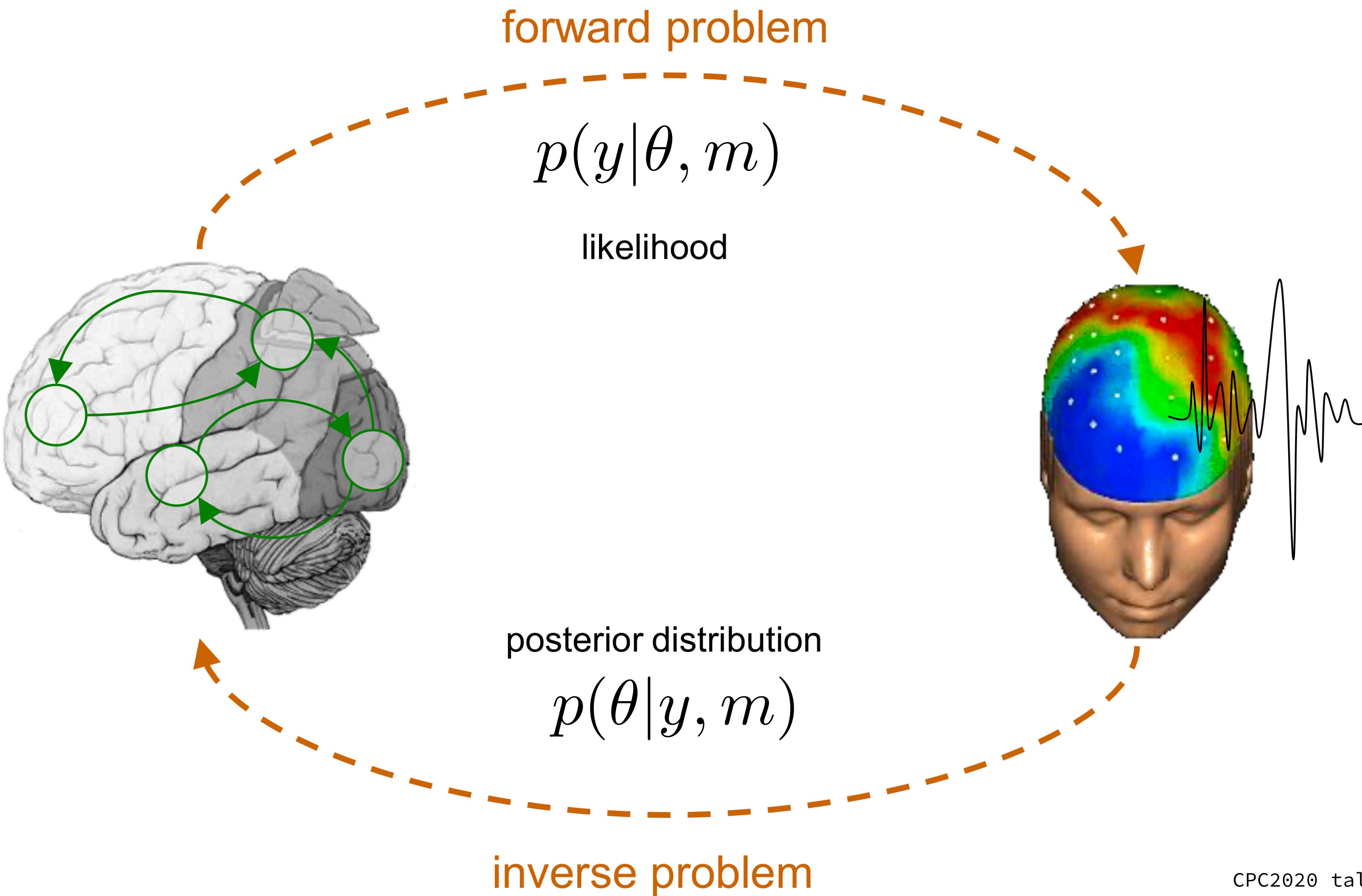
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model evidence

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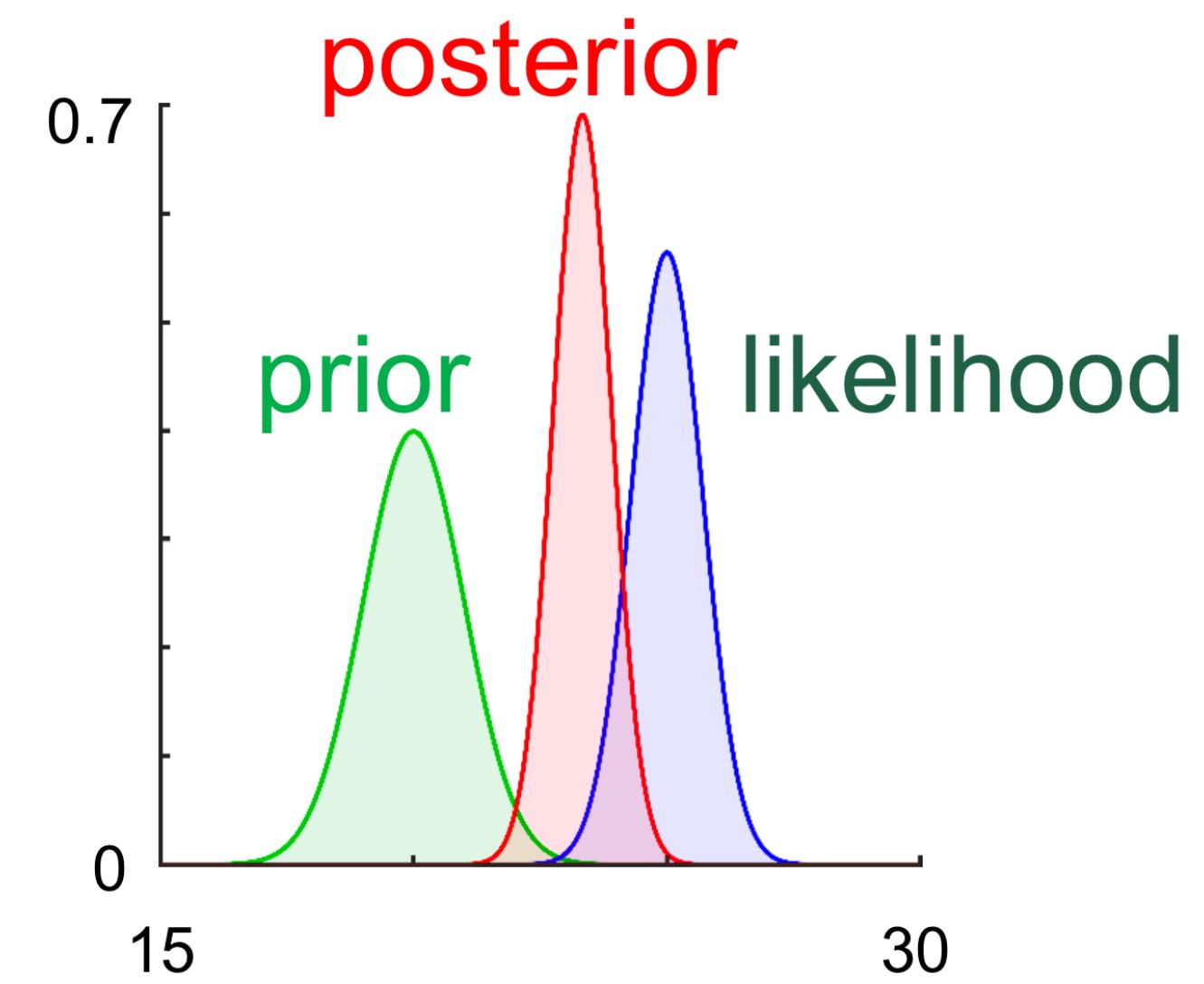
posterior

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$p(y|\theta, m)p(\theta|m)$

likelihood prior

model evidence



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$$y(t) = g(x(t), \theta) + \epsilon$$

$$\epsilon \sim \mathcal{N}(0, \Sigma)$$

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Noise parameters:

- ▶ difficult to set
- ▶ wrong assumptions → wrong explanations

## #Example: NMDA receptor antibody encephalitis

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## Ion channels in EEG: isolating channel dysfunction in NMDA receptor antibody encephalitis

Mkael Symmonds,<sup>1,2,3</sup> Catherine H. Moran,<sup>4</sup> M. Isabel Leite,<sup>1,5</sup> Camilla Buckley,<sup>1</sup> Sarosh R. Irani,<sup>1,5</sup> Klaas Enno Stephan,<sup>6</sup> Karl J. Friston<sup>7</sup> and Rosalyn J. Moran<sup>8,9</sup>

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See Roberts and Breakspear (doi:10.1093/brain/awy136) for a scientific commentary on this article.

Neurological and psychiatric practice frequently lack diagnostic probes that can assess mechanisms of neuronal communication non-invasively in humans. In N-methyl-D-aspartate (NMDA) receptor antibody encephalitis, functional molecular assays are particularly important given the presence of NMDA antibodies in healthy populations, the multifarious symptomology and the lack of radiological signs. Recent advances in biophysical modelling techniques suggest that inferring cellular-level properties of neural circuits from macroscopic measures of brain activity is possible. Here, we estimated receptor function from EEG in patients with NMDA receptor antibody encephalitis ( $n = 29$ ) as well as from encephalopathic and neurological patient controls ( $n = 36$ ). We show that the autoimmune patients exhibit distinct fronto-parietal network changes from which ion channel estimates can be obtained using a microcircuit model. Specifically, a dynamic causal model of EEG data applied to spontaneous brain responses identifies a selective deficit in signalling at NMDA receptors in patients with NMDA receptor antibody encephalitis but not at other ionotropic receptors. Moreover, though these changes are observed across brain regions, these effects predominate at the NMDA receptors of excitatory neurons rather than at inhibitory interneurons. Given that EEG is a ubiquitously available clinical method, our findings suggest a unique re-purposing of EEG data as an assay of brain network dysfunction at the molecular level.

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- ▶ final: 12 minutes, 21-channel sensors

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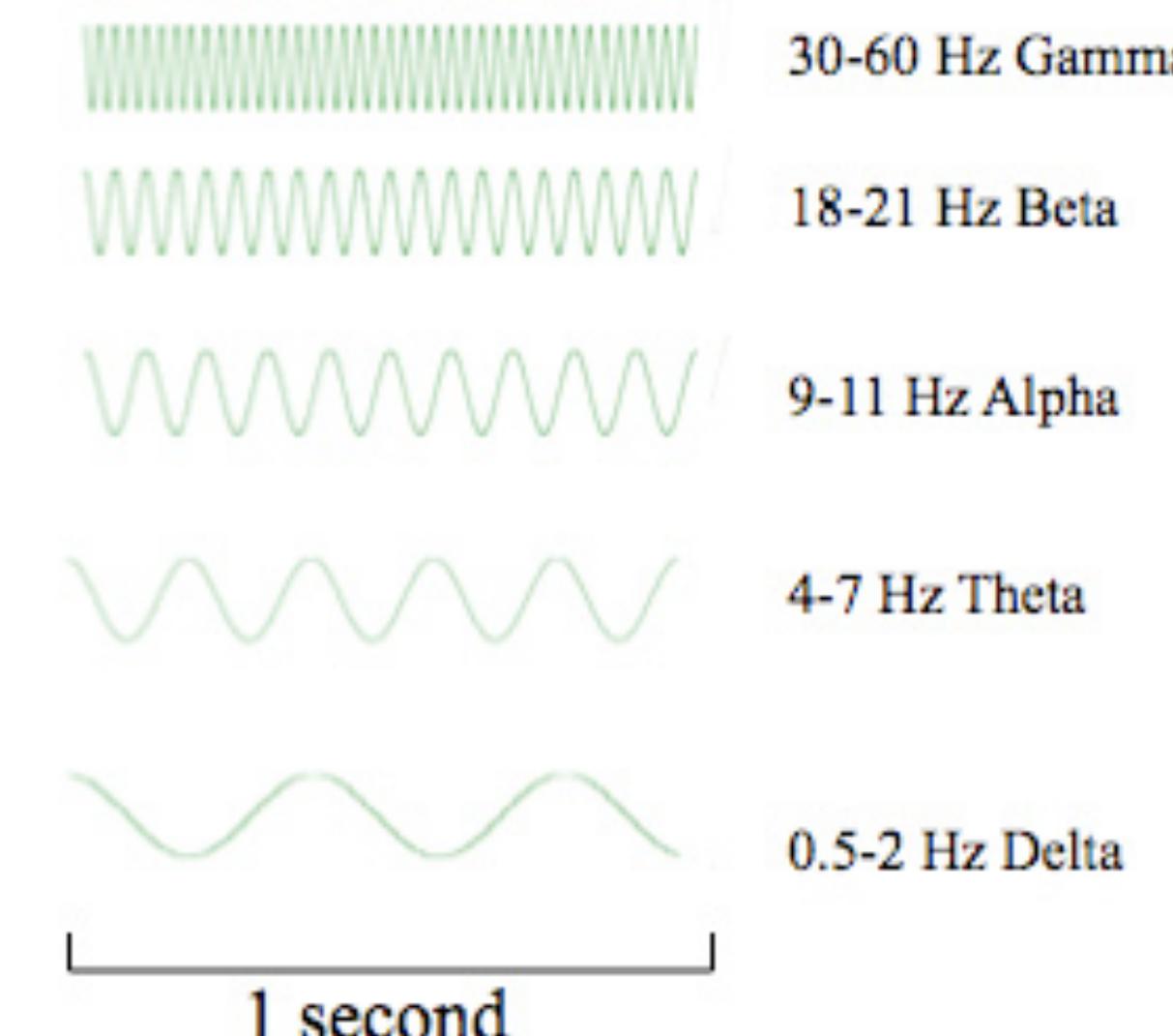
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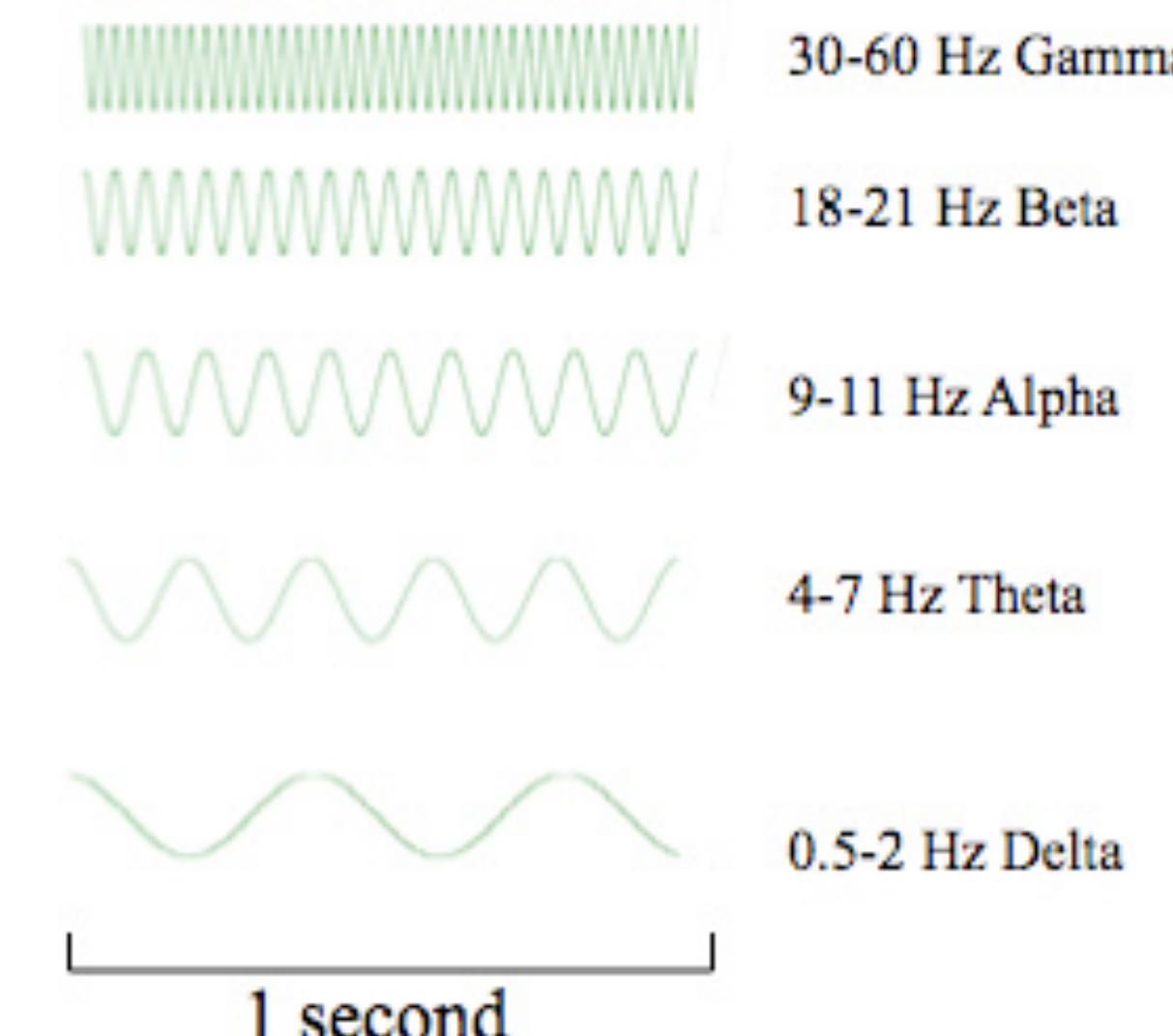
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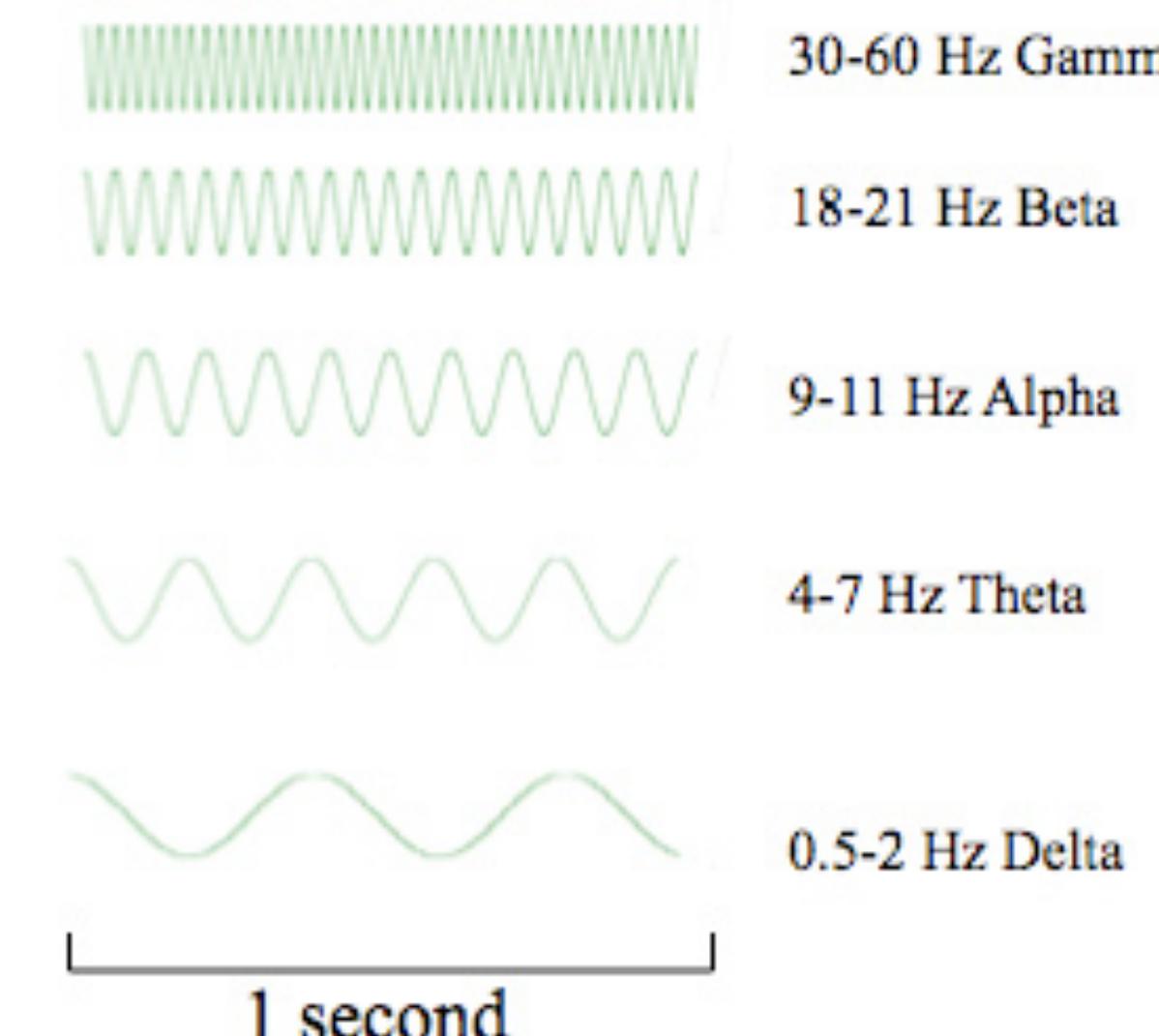
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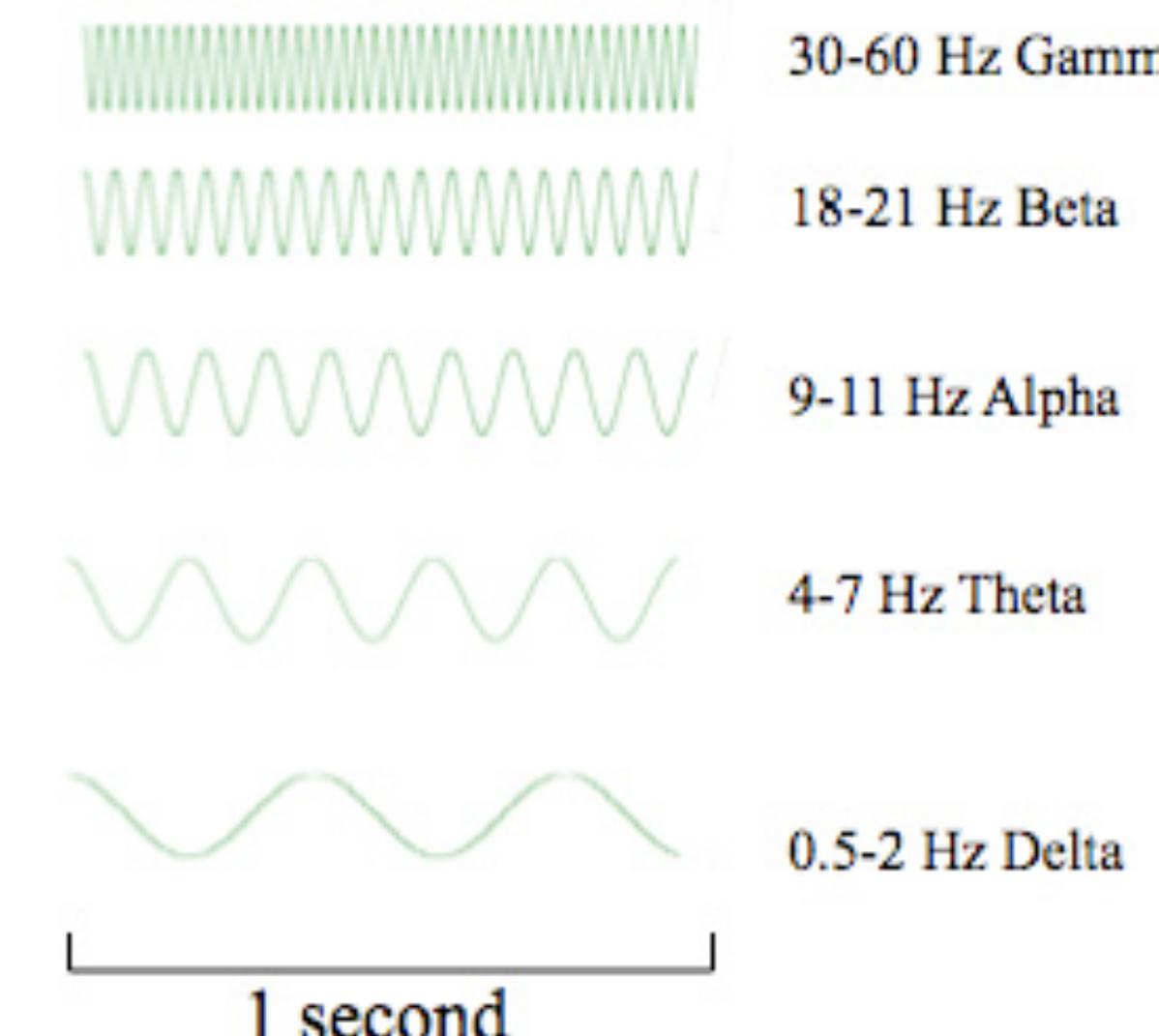
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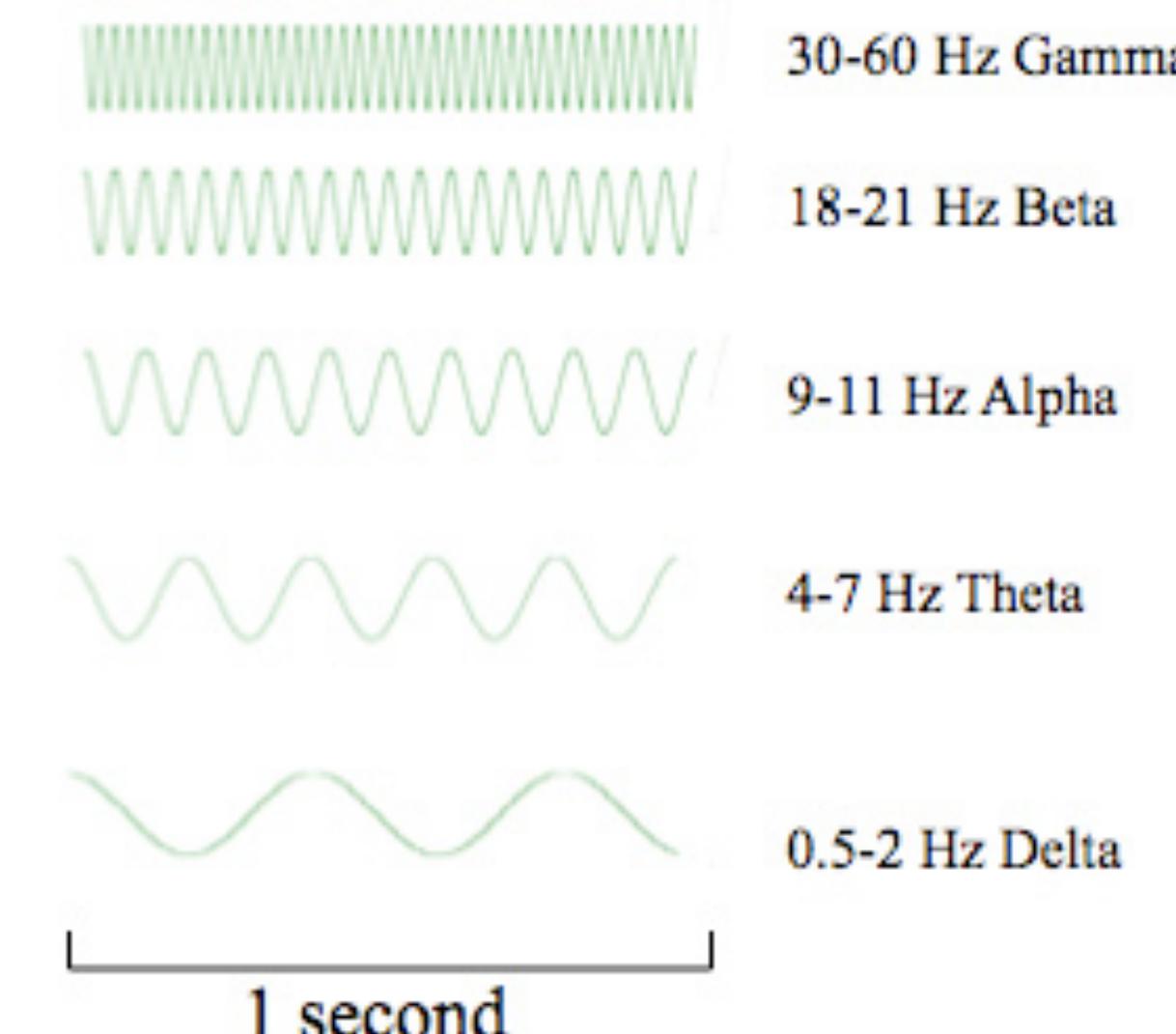
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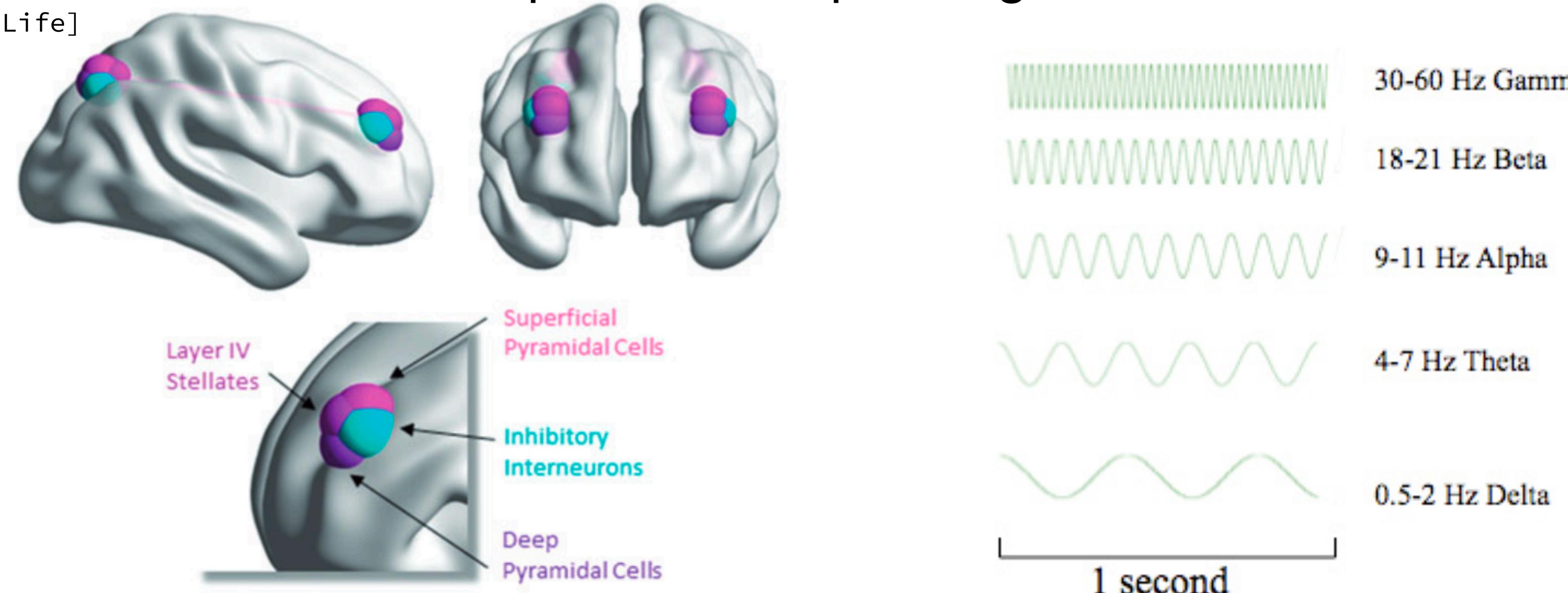
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Symmonds et al., 2018, *Brain*

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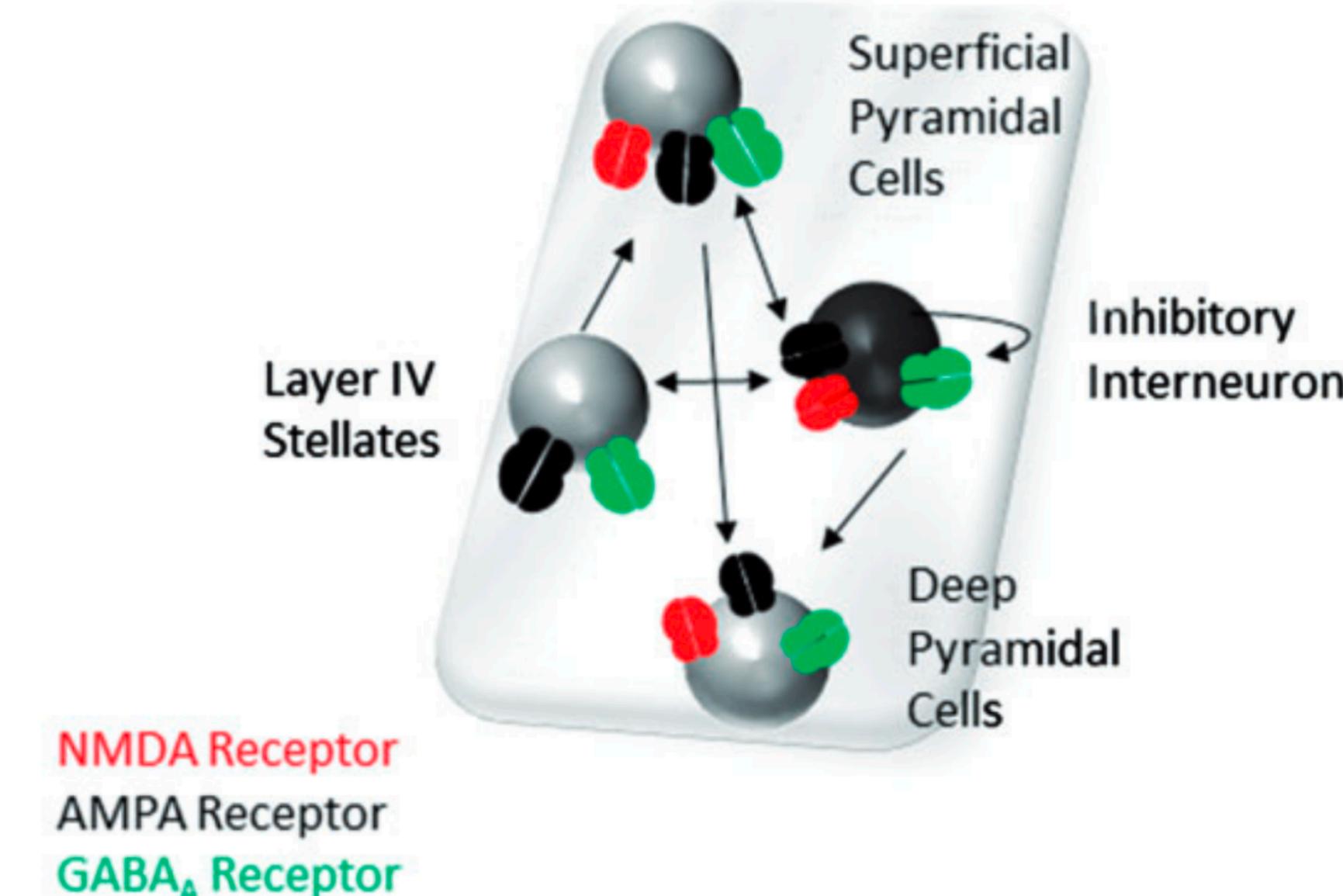
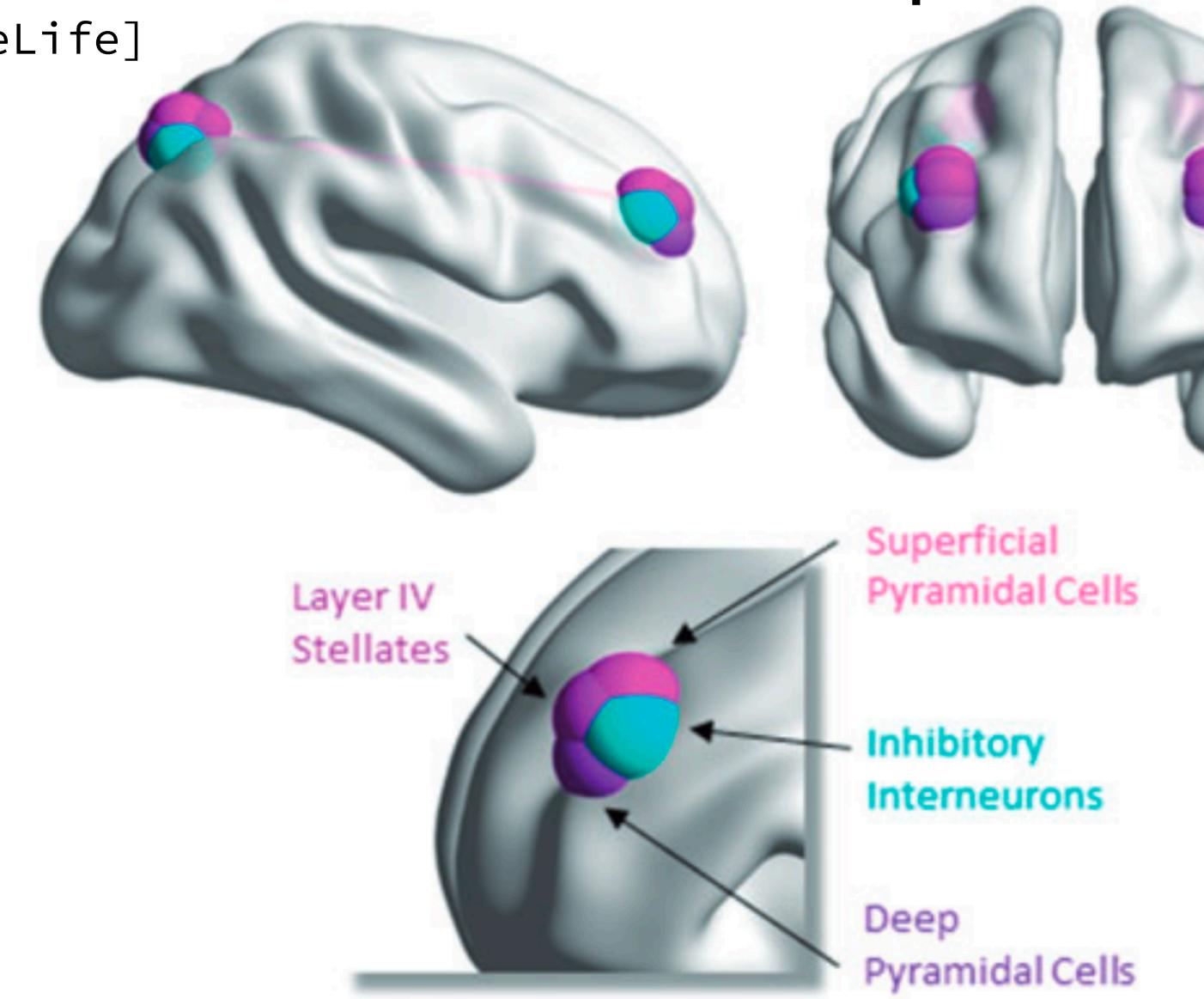
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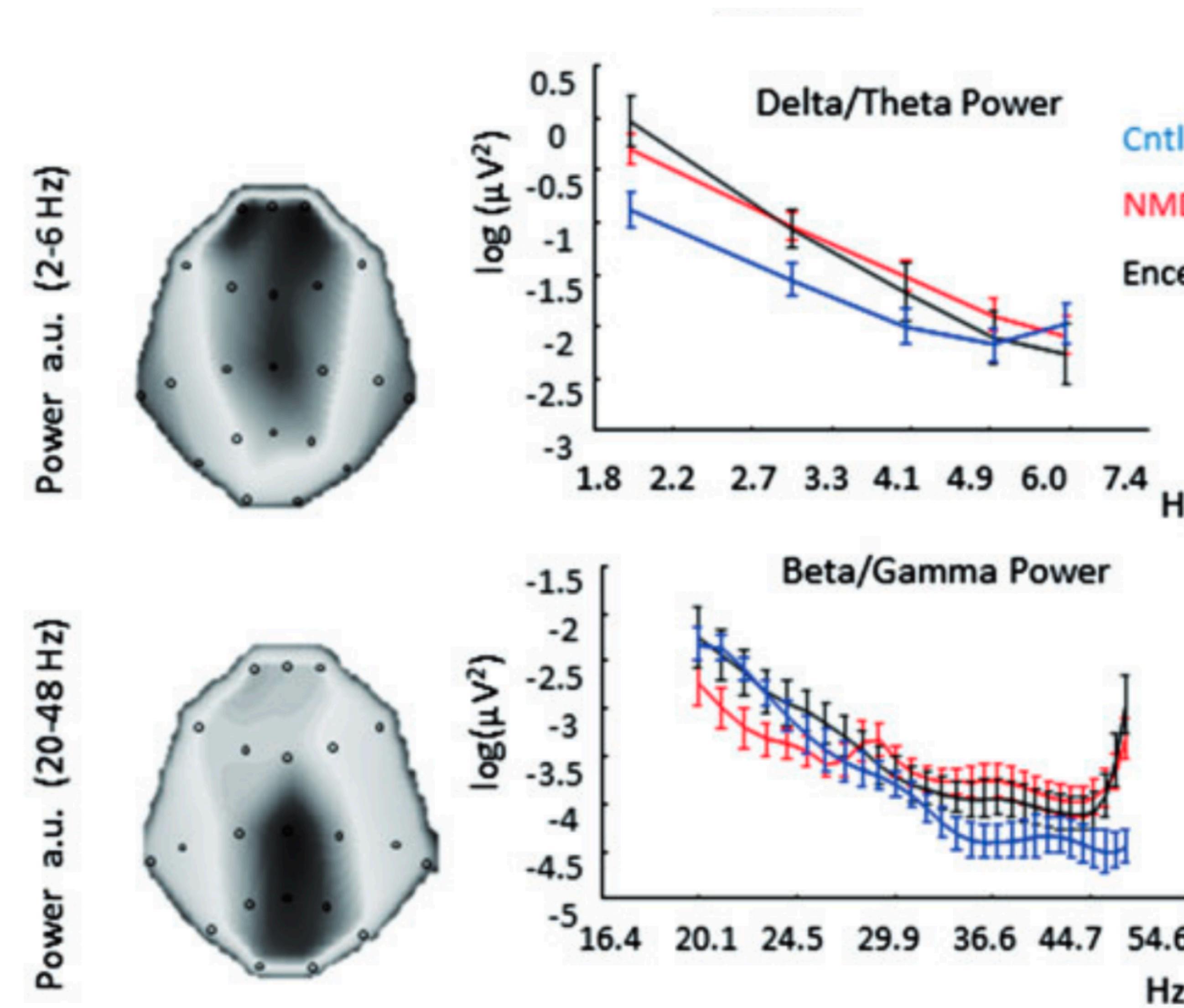
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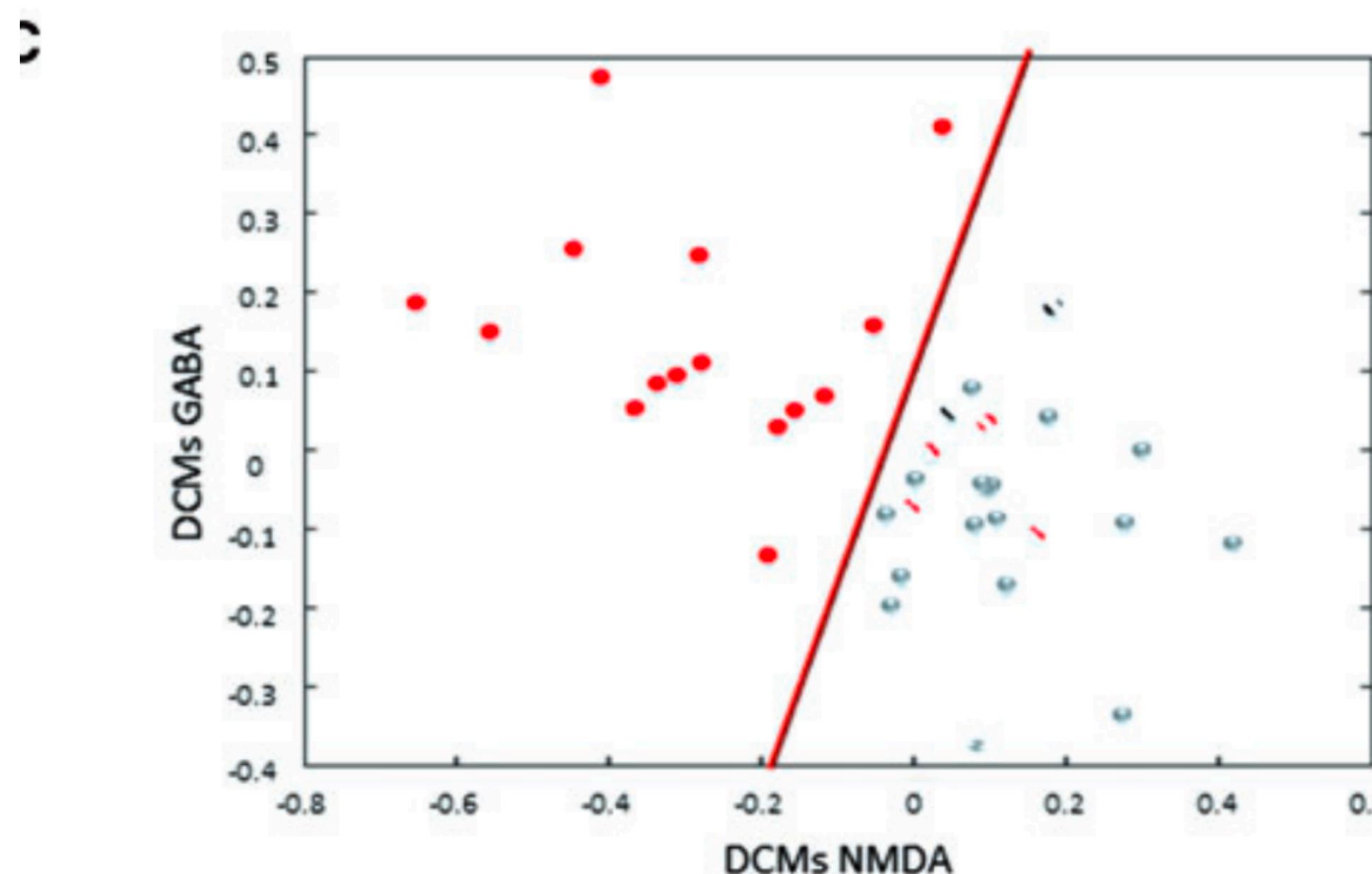
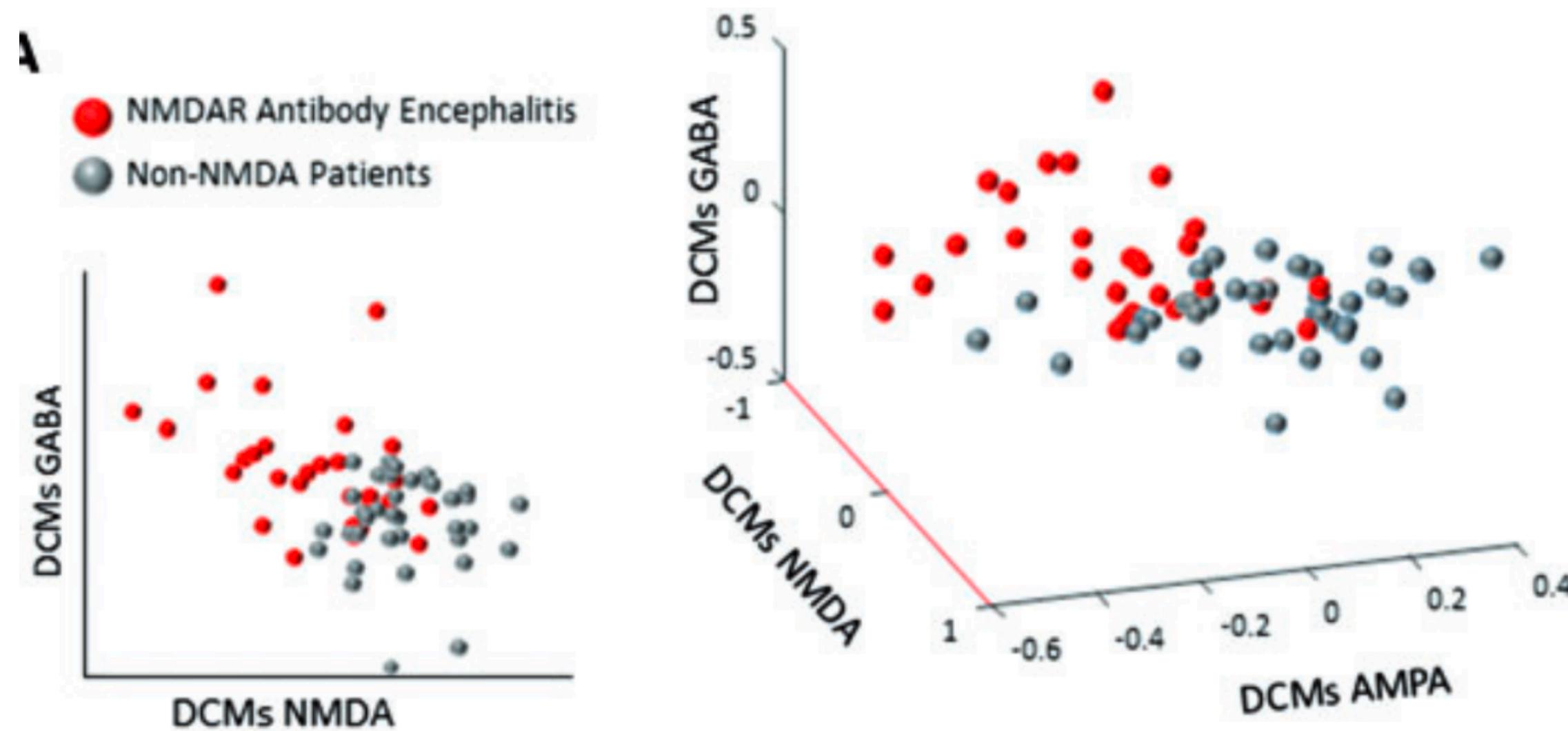
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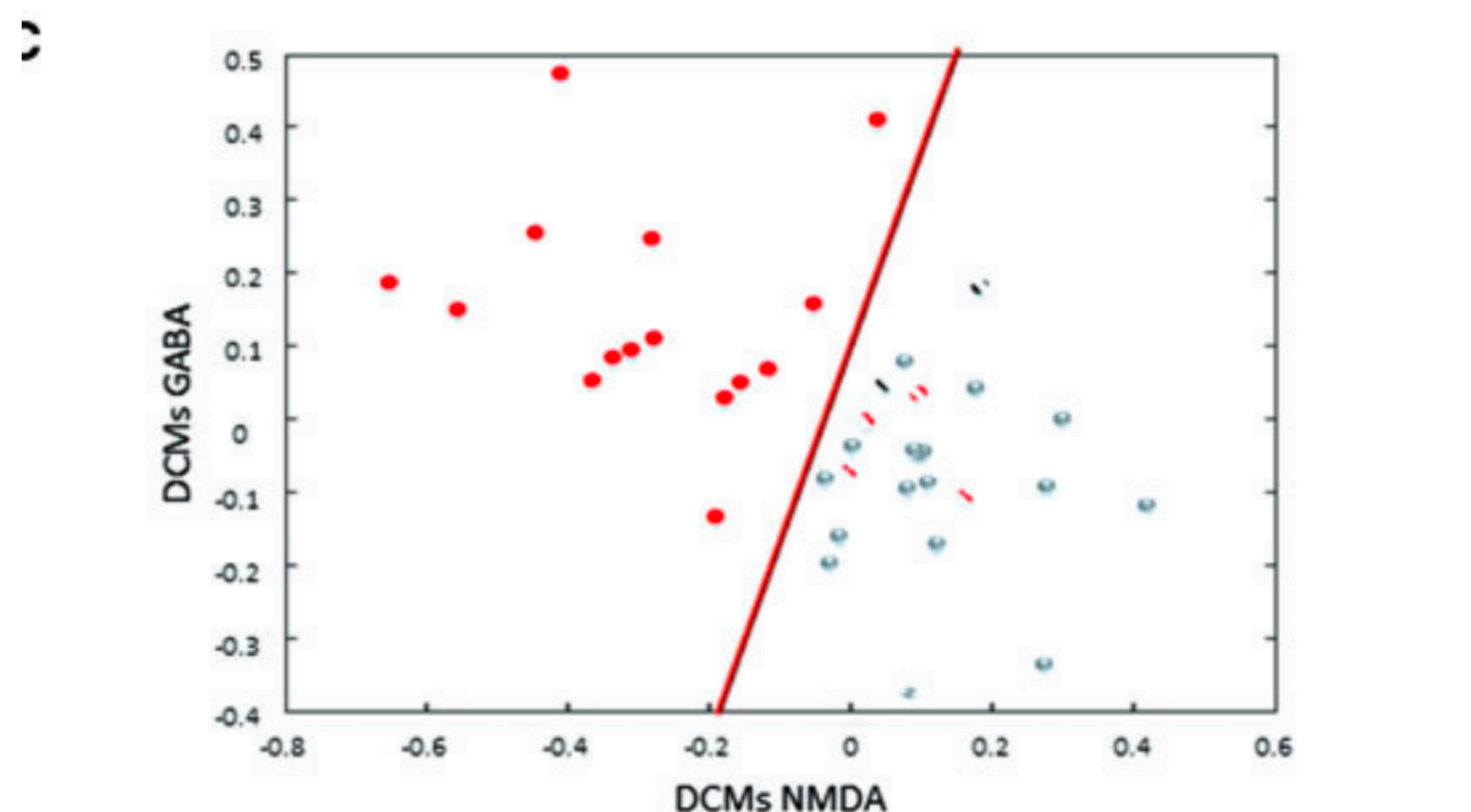
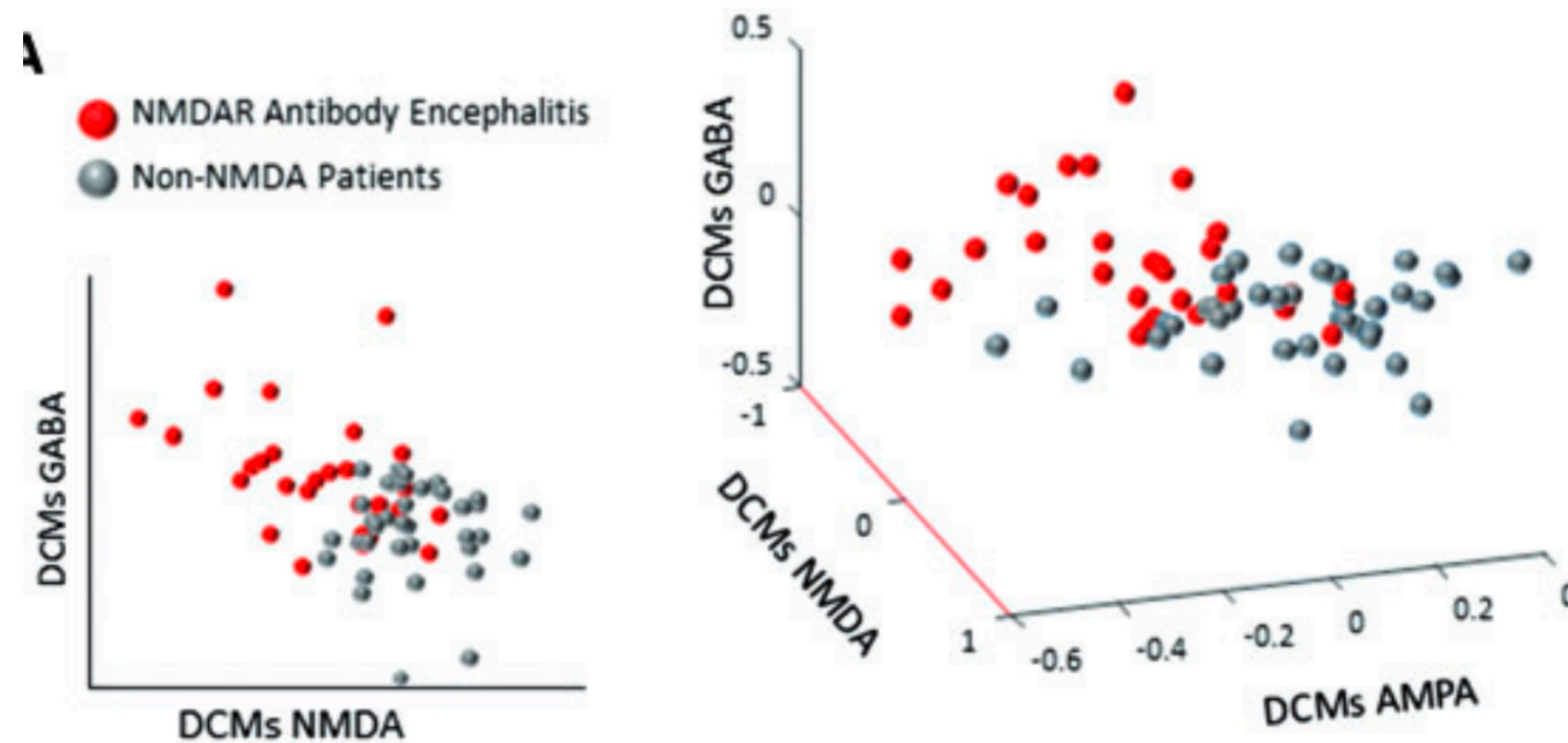


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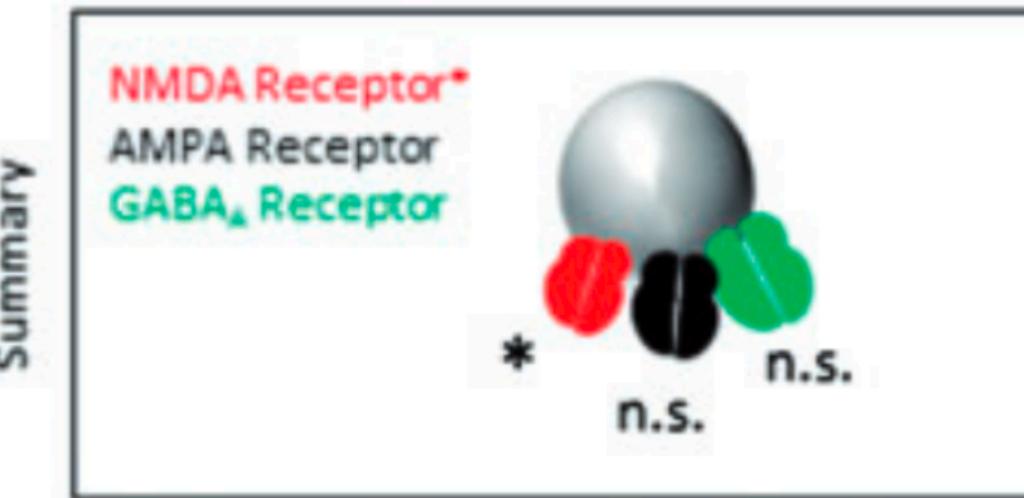
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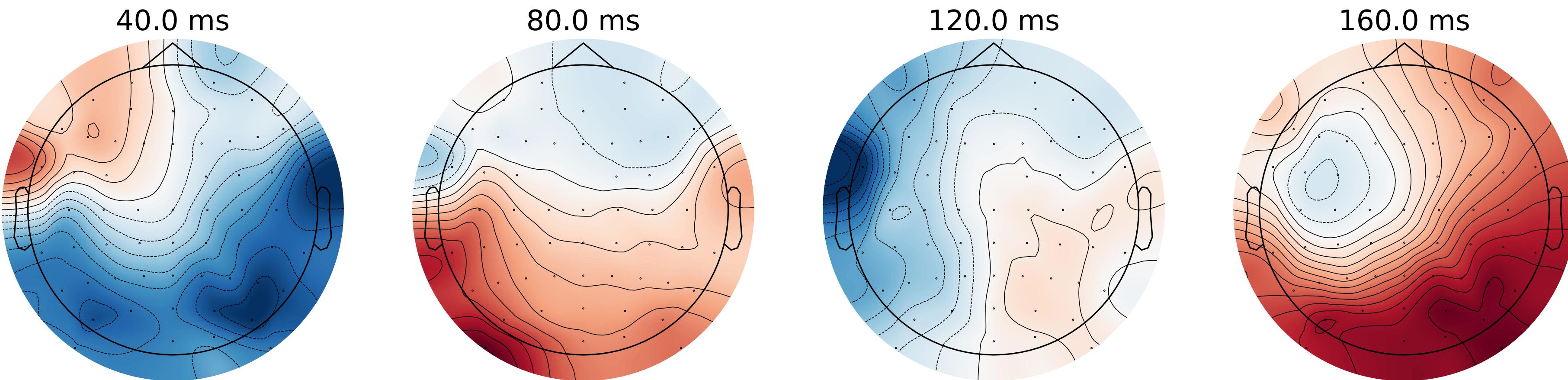
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# Thank you for your attention!



Many thanks to Inês Pereira, Rosalyn Moran, Jean Daunizeau, Jakob Heinzle, and Klaas Enno Stephan  
for slides, ideas, and comments!

