Neuronal population inference reveals how neuromodulation reshapes conductance space

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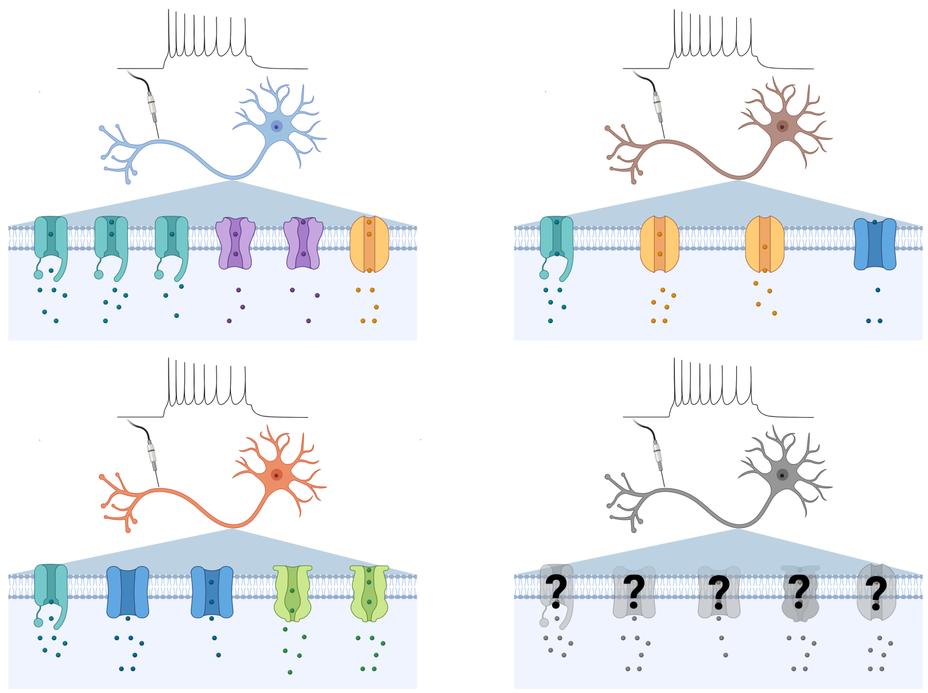
Neurons are degenerate

Neuronal firing patterns are easy to record, but not the underlying ion channel compositions. Many different compositions can produce the same pattern (Marder et al. 2006).



Conductance-based models are mechanistic models

They describe membrane voltage by modeling ion channels as voltage-dependent conductances that generate ionic currents:

$$C\frac{dV}{dt} + g_{\text{leak}}(V - E_{\text{leak}}) = -\sum_{i\in\mathcal{I}} \bar{g}_i m_i^{p_i} h_i^{q_i}(V - E_i) + I_{\text{ext}}$$

The maximum conductance vector $\bar{g}$ directly reflects ion channel densities. Degeneracy means a single recorded pattern x is compatible with many conductance vectors:

$$\bar{g} \in \mathcal{G}^*(x) \subset \mathcal{G}$$

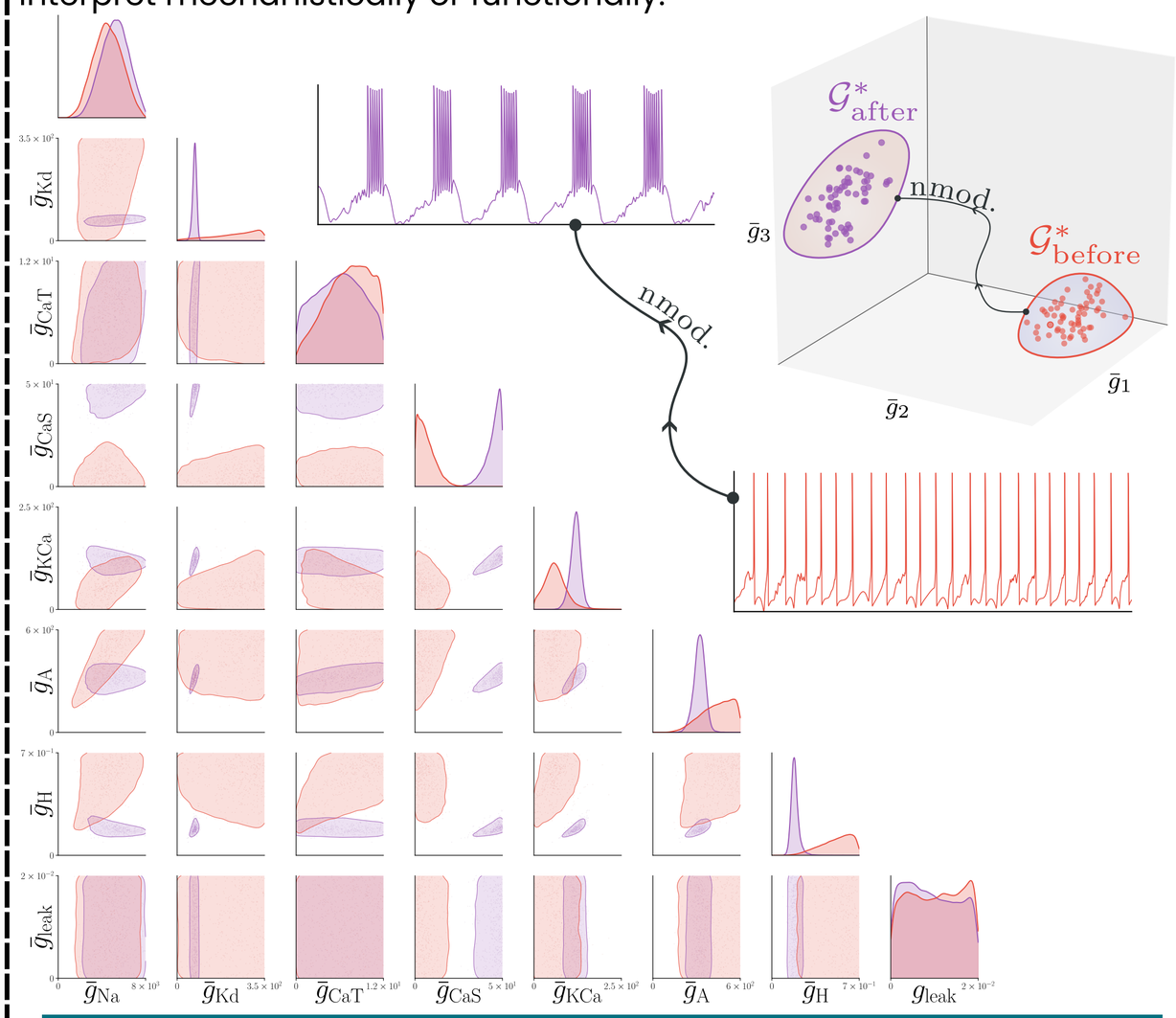
Studying neurons and neuromodulation demands a degeneracy-aware framework.

Simulation-Based Inference quantifies degeneracy but lacks mechanistic interpretation

SBI trains neural networks to solve the nonlinear, high-dimensional inverse problem of inferring conductances from recorded patterns:

$$q_\phi(\bar{g} \mid x) \approx p(\bar{g} \mid x)$$

This captures the degenerate set, but the posterior remains hard to interpret mechanistically or functionally.



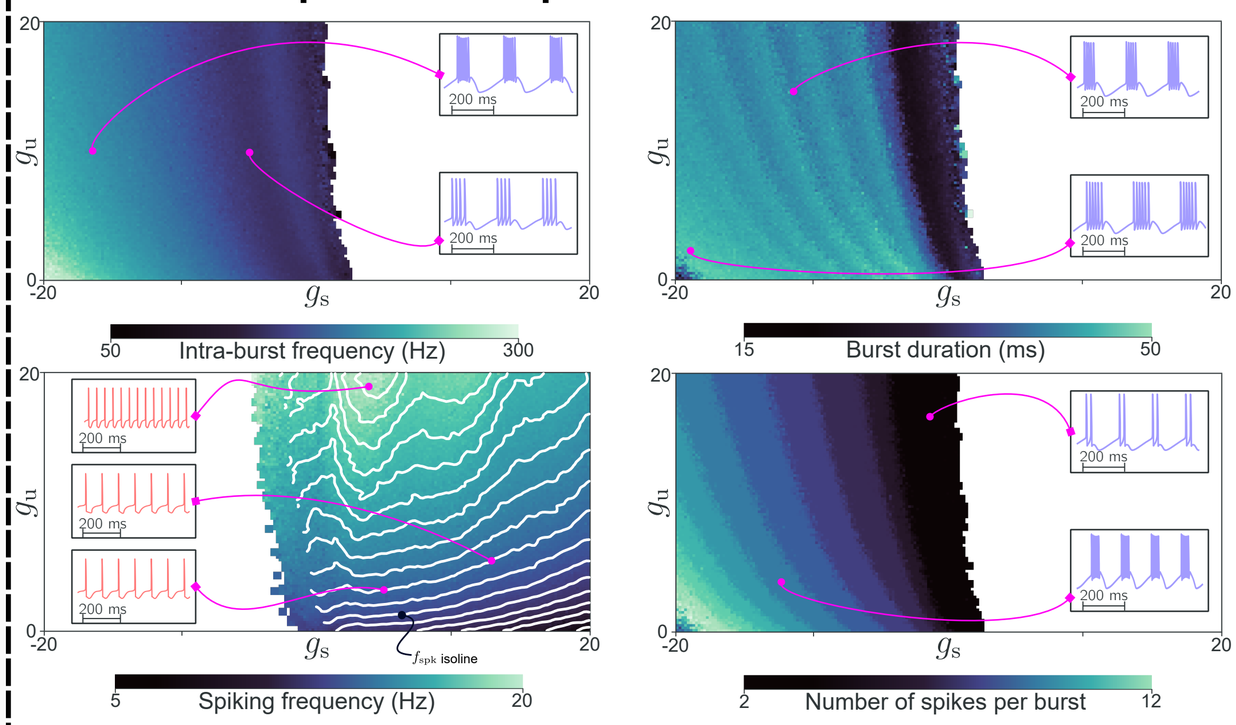
How does neuromodulation robustly shift neurons from one regime to another? The posterior alone cannot tell.

Dynamic Input Conductances compress degeneracy into interpretable structure

DICs aggregate ion channel contributions into net effective feedback gains across timescales (Drion et al. 2015), evaluated at threshold V_{th} :

$$g_{\text{DICs}}(V_{\text{th}}) = S(V_{\text{th}}) \cdot \bar{g} = \begin{bmatrix} g_{\text{s}}(V_{\text{th}}) \\ g_{\text{u}}(V_{\text{th}}) \end{bmatrix}$$

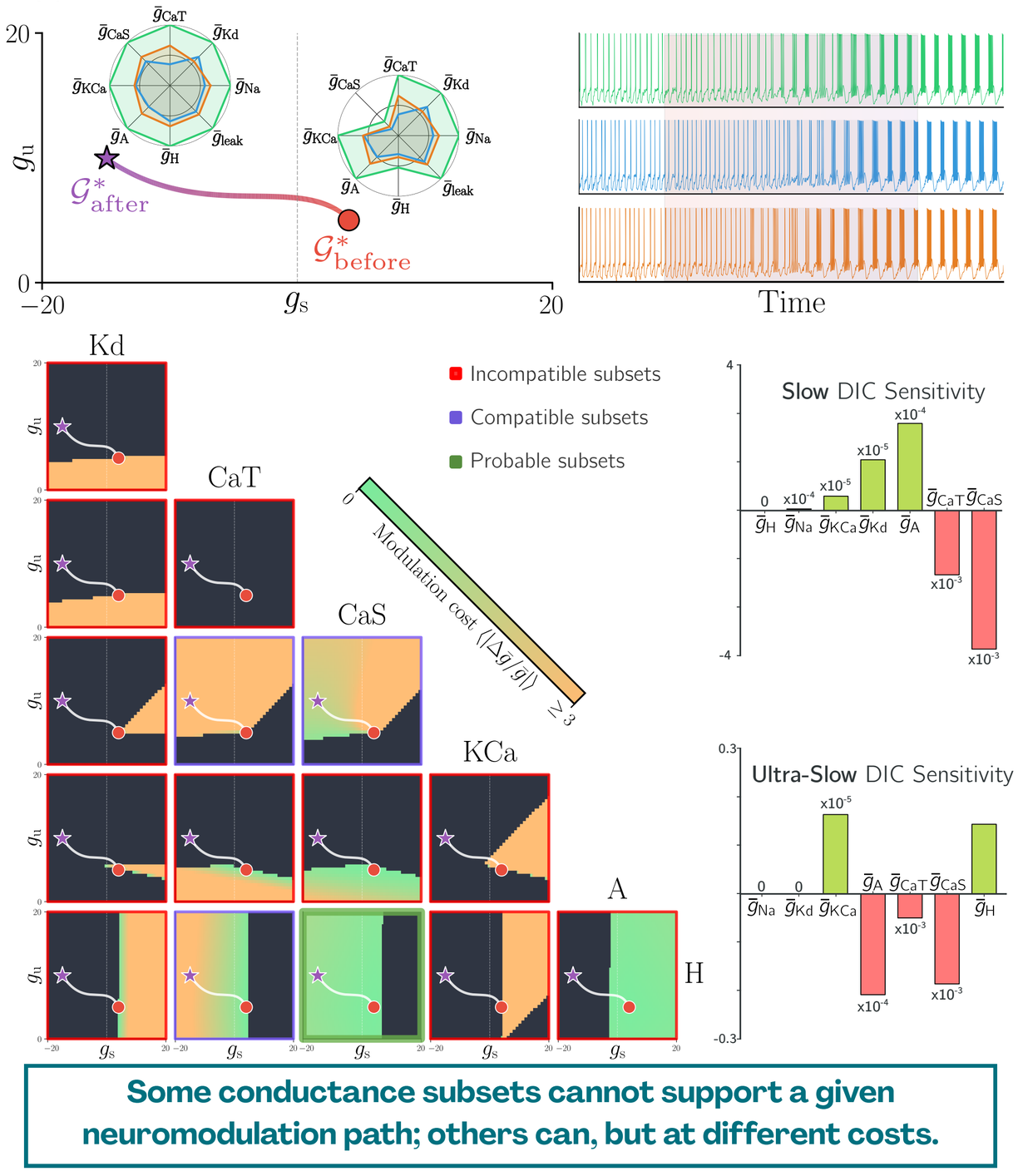
Degenerate conductance vectors sharing the **same activity** collapse onto the **similar points in DIC space**.



DICs provide a degeneracy-aware framework to study how activity is organized and how it changes.

Neuromodulation shifts the degenerate set through DIC space

Two activity regimes map to two points in DIC space. Neuromodulation traces a path between them, shifting entire degenerate populations together. Reachability maps expose which conductance subsets support this transition and at what cost.



Some conductance subsets cannot support a given neuromodulation path; others can, but at different costs.

Can we trace neuromodulatory mechanisms back to specific ion channels from activity recordings alone?

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Computational and Systems Neuroscience (COSYNE) 2026