Hodgkin-Huxley Models of V1 and PFC Neurons Reveal Cell-Type and Area-Specific Differences in Intrinsic Membrane Properties

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1. Introduction

Background

Cortical neurons exhibit **diverse firing patterns**[1]. Intrinsic properties contribute to diversity in action potential (AP) waveform and firing frequency[1].

- Fast spiking inhibitory neurons → narrow APs[2]
- Excitatory pyramidal neurons → broad APs[2]

Research Question

What underlies the functional specialization of the primary visual cortex (V1) and prefrontal cortex (PFC) in primates?

Hypothesis

Intrinsic properties of single neurons differ across areas and support area specific functional specialization in the primate brain[3].

Strategy

Use Hodgkin-Huxley-type models to identify intrinsic differences between cell types and across areas. Bifurcation and slow-fast analyses of these models allow investigation of underlying dynamics.

2. Methods

Data

Data were collected by the Martinez-Trujillo lab at Western University, and the Staiger and Andreas labs at the University of Göttingen:

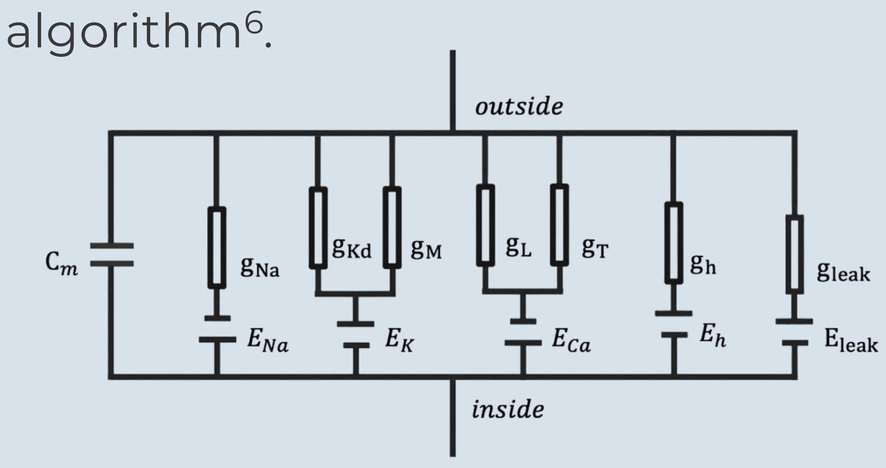
- **Whole cell current-clamp** recordings in marmoset V1 and PFC slices
- One-second square current steps

Mathematical Model

A **Hodgkin-Huxley**-type model[4,5] was fit to voltage traces:

$$C_m \frac{dV}{dt} = -I_{leak} - I_{Na} - I_{Kd} - I_M - I_T - I_L - I_h$$

Multi-objective fitting based on electrophysiological features was performed using an evolutionary algorithm[6].



Classification

Neurons were classified as **narrow** or **broad spiking.**

- **Area-specific threshold:** narrowest spike among confirmed spiny neurons.

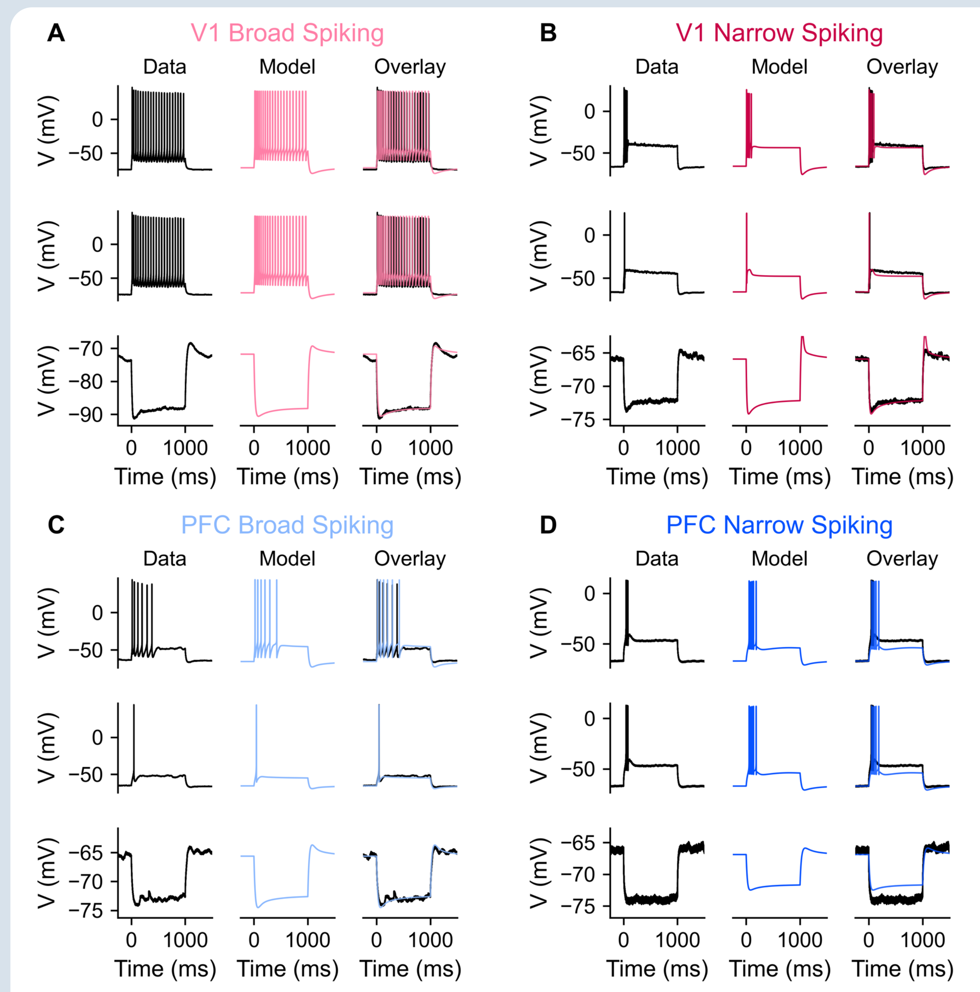


Figure 1. ***Hodgkin-Huxley model fits to example neuron voltage traces.*** Model fits are shown for broad (A) and narrow (B) spiking neurons in V1 and for broad (C) and narrow (D) spiking neurons in PFC. Experimental data is shown on the left column, simulation on the middle column, and their overlap on the right column. Top two rows show voltage traces in response to depolarizing current injections, while bottom row shows a trace in response to a hyperpolarizing injection.

3. Results: Bifurcation Analysis

Bifurcation analysis:
Study changes in the structure of solutions of a dynamical system that occur with perturbations in parameters[7].

Bifurcation analysis was performed using the **applied current** as a bifurcation parameter.

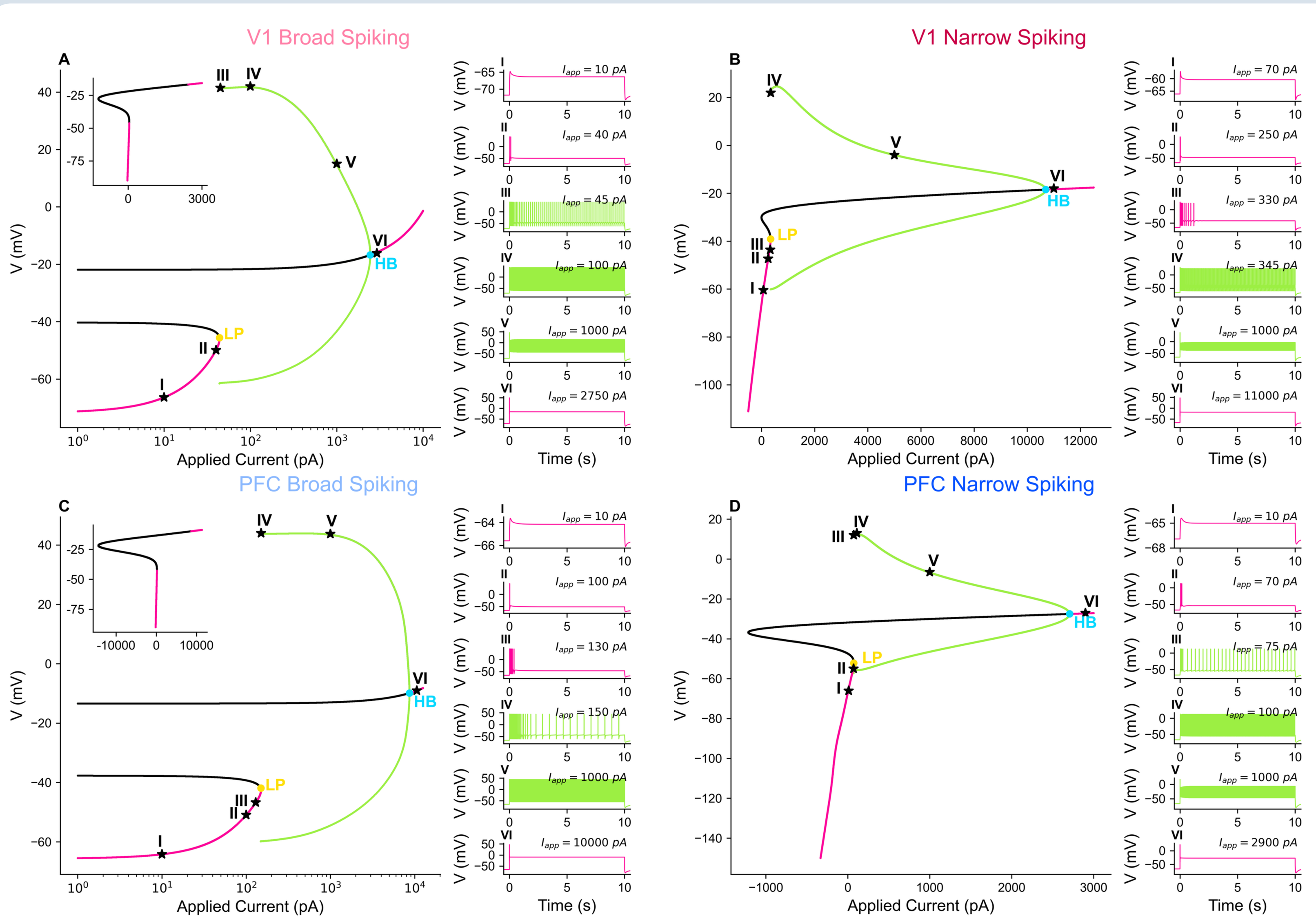


Figure 2. ***Bifurcation diagrams of example neuron models, with the applied current as a bifurcation parameter.*** Current-voltage bifurcation diagrams are shown for broad (A) and narrow (B) spiking neurons in V1 and for broad (C) and narrow (D) spiking neurons in PFC. Pink curves indicate stable solutions, black unstable solutions, and green periodic solutions. Labeled points (I-VI) correspond to example voltage traces shown to the right for the indicated applied currents. HB = Hopf bifurcation, LP = Saddle node bifurcation.

All four models exhibit transient responses and can produce oscillatory behavior. Models differ mainly in the range of their oscillatory regimes and in the range of negative applied current over which the unstable solution persists.

4. Results: Slow-Fast Analysis

Slow-fast analysis:

i. Identify variables that evolve on slower timescales[8].
ii. Treat these variables as bifurcation parameters to perform bifurcation analysis on the fast subsystem[8].

Slow fast analysis was performed using the $\mathbf{h_2}$ component of the **hyperpolarization-activated current** as a bifurcation parameter.

$$I_h = g_h(fh_1 + (1-f)h_2)(V - E_h)$$

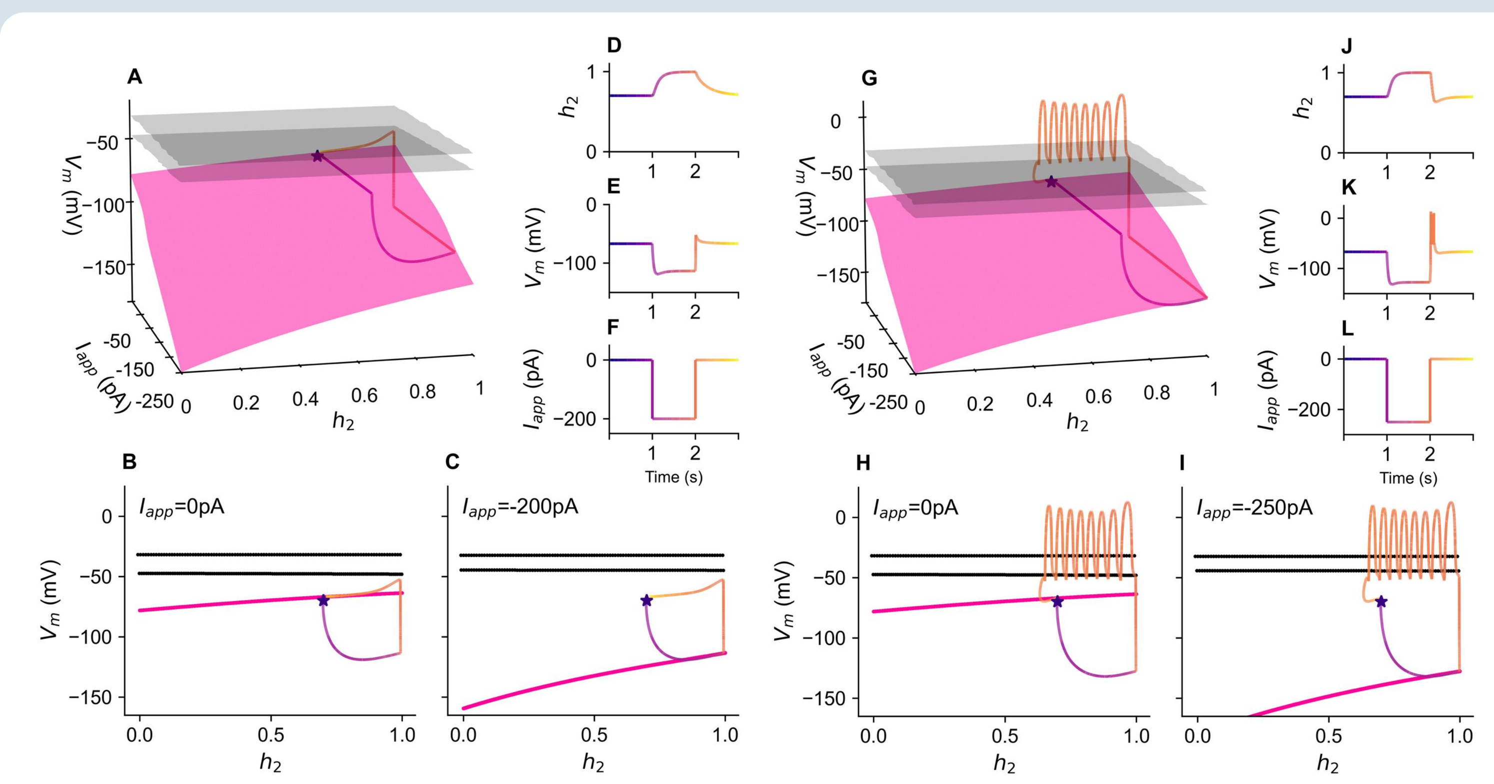


Figure 3. ***Bifurcation diagrams of narrow spiking PFC neuron model, with the h_2 gating variable as a bifurcation parameter.*** h_2-voltage bifurcation diagrams with superimposed voltage traces for −200 pA and −250 pA square current steps are shown across the negative current range (A, G), at zero applied current (B, H), and during the applied square-wave current (C, I). Time courses of the h2 gating variable, membrane voltage, and applied current used in the simulations are shown in panels D–F and J–L, respectively.

Rebound spiking is driven by the slow component of the hyperpolarization-activated current, h_2.

5. Discussion & Conclusions

i. **Bifurcation Analysis:** Oscillatory regime may be more rarely engaged under physiological conditions in some neurons.
ii. **Slow-Fast Analysis:** Rebound firing is driven by the slow component of the hyperpolarization-activated current.

These results suggest that intrinsic membrane properties differ across cell types and cortical areas, potentially contributing to the distinct functional roles of inhibitory and excitatory neurons in V1 and PFC circuits.

6. References & Funding

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