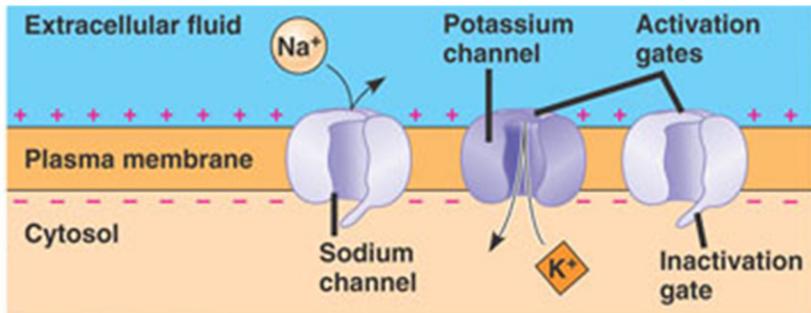


*Supplementary information*

## **Approaches to Parameter Estimation from Model Neurons and Biological Neurons**

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1. Nine-ion channel conductance model used to infer the parameters of the songbird neuron in Figure 1.
2. Links to parameter inference software



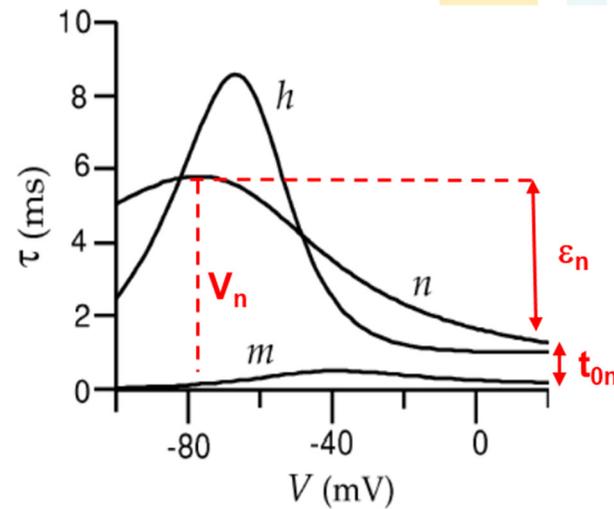
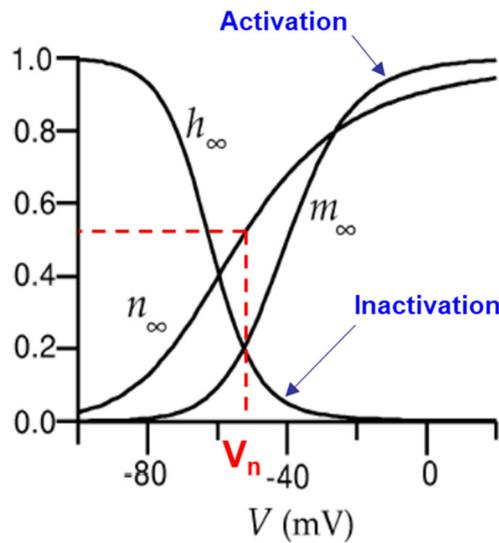
**Dynamics of the Potassium-activation gate:**

$$\frac{dn(t)}{dt} = \frac{n_{\infty}(V) - n(t)}{\tau_n(V)}$$

$$n_{\infty}(V) = \frac{1}{2} \left[ 1 + \tanh\left(\frac{V - V_n}{dV_n}\right) \right]$$

$$\tau_n(V) = t_{0n} + \epsilon_n \left[ 1 - \tanh^2\left(\frac{V - V_n}{dV_n}\right) \right]$$

5 model parameters



**Sodium activation and inactivation gates:**

10 model parameters

**Figure S1:** The generic rate equation of a gate variable, here  $n(t)$ .  $V_n$  is the threshold of the sigmoidal activation.  $dV_n$  is the width of the transition from the open to the closed state of the gate.  $dV_n > 0$  gives an activation curve;  $dV_n < 0$ , inactivation. The recovery time  $\tau_n(V)$  of most gate variables has a Bell-shaped curve defined by 3 parameters:  $V_n, t_{0n}, \epsilon_n$ . This dependence describes all activation gates and almost all inactivation gates the exception being the K2 and CaT inactivation recovery times which exhibit a rectifying behaviour and a biexponential dependence respectively.

The equation of motion governing the membrane voltage is:

$$C \frac{dV(t)}{dt} = -J_{NaT} - J_{NaP} - J_{K1} - J_{K2} - J_{K3} - J_{CaL} - J_{CaT} - J_{HCN} - J_{Leak} + I_{data}(t)/A, \quad (1)$$

The rate equations for activation and inactivation gates are:

$$\begin{aligned} \frac{dm(t)}{dt} &= \frac{m_{\infty}(V) - m(t)}{\tau_m(V)}, \\ \frac{dh(t)}{dt} &= \frac{h_{\infty}(V) - h(t)}{\tau_h(V)}, \end{aligned} \quad (2)$$

with steady state activation and time delays given by:

$$\begin{aligned} m_{\infty}(V) &= \frac{1}{2} \left( 1 + \tanh \frac{V - V_m}{dV_m} \right), & \tau_m(V) &= t_{0m} + \varepsilon_m \left( 1 - \tanh^2 \frac{V - V_m}{dV_m} \right), \\ h_{\infty}(V) &= \frac{1}{2} \left( 1 + \tanh \frac{V - V_h}{dV_h} \right), & \tau_h(V) &= t_{0h} + \varepsilon_h \left( 1 - \tanh^2 \frac{V - V_h}{dV_h} \right), \end{aligned} \quad (3)$$

The rectifying behaviour of the recovery time constant of the K2 current was formally described in the data assimilation code with the following equation:

$$\tau_h(V) = t_{0h} + \varepsilon_h \left( 1 - \tanh^2 \frac{\delta_h}{dV_{th}} + \frac{1}{2} (1 - \tanh(1 - V_{th} - \delta_h)) \left( \tanh^2 \frac{\delta_h}{dV_{th}} - \tanh^2 \frac{V - V_{th}}{dV_{th}} \right) \right). \quad (4)$$

The bi-exponential dependence of the CaT recovery time constant was described by the following equation:

$$\tau_h(V) = t_{0h} + \varepsilon_h \frac{\left( 1 + \tanh \left( \frac{V - V_h}{dV_{t1}} \right) \right) \left( 1 - \tanh \left( \frac{V - V_h}{dV_{t2}} \right) \right)}{1 + \tanh \left( \frac{V - V_h}{dV_{t1}} \right) \tanh \left( \frac{V - V_h}{dV_{t2}} \right)} \left( (1 - \tanh(V - V_h)) \tanh \left( \left( \frac{1}{dV_{t1}} + \frac{1}{dV_{t2}} \right) (V - V_h) \right) \right) \quad (5)$$

The ionic currents are given in Figure B. Note that no two ionic current have the same mathematical form due to either different gate exponents or gate kinetics.

ID	Channel	Current density	Nominal conductance
<b>NaT</b>	Fast and transient Na <sup>+</sup> current	$J_{NaT} = g_{NaT}m^3h(E_{Na} - V)$	$g_{NaT}=110\text{mS.cm}^{-2}$
<b>NaP</b>	Persistent Na <sup>+</sup> current	$J_{NaP} = g_{NaP}m(E_{Na} - V)$	$g_{NaP}=0.064\text{mS.cm}^{-2}$
<b>K1</b>	Transient depolarization activated K <sup>+</sup> current	$J_{K1} = g_{K1}m^4(E_K - V)$	$g_{K1}=5\text{mS.cm}^{-2}$
<b>K2</b>	Rapidly inactivating K <sup>+</sup> current (A current)	$J_{K2} = g_{K2}m^4h(E_K - V)$	$g_{K2}=12\text{mS.cm}^{-2}$
<b>K3</b>	Ca <sup>2+</sup> activated K <sup>+</sup> current	$J_{K3} = g_{K3}m(E_K - V)$	$g_{K3}=9.1\text{mS.cm}^{-2}$
<b>CaL</b>	High threshold Ca <sup>2+</sup> current	$J_{CaL} = \rho m^2 J_{Ca}$	-
<b>CaT</b>	Low threshold Ca <sup>2+</sup> current	$J_{CaT} = m^2 h J_{Ca}$	-
<b>HCN</b>	Hyperpolarization-activated cation current	$J_{HCN} = g_{HCN}h(E_{HCN} - V)$	$g_{HCN}=0.092\text{mS.cm}^{-2}$
<b>Leak</b>	Leakage channels (K & Na)	$J_L = g_L(E_L - V)$	$g_L=0.066\text{mS.cm}^{-2}$

**Calcium current prefactor:**  $J_{Ca} = \left( \frac{g_{out} - g_m \exp(V/V_T)}{\exp(V/V_T) - 1} \right) \times V$  Goldman-Hodgkin-Katz equation

**12 state variables, 71 parameters**  
**12 coupled non linear differential equations**

**Figure S2:** Mathematical form of the 9 ionic currents used to model the songbird neuron in Figure 1 of the manuscript.

## 2. Links to parameter inference methods online.

- Interior Point Optimization: <https://github.com/coin-or/Ipopt>
- 4DVar: [http://www.met.reading.ac.uk/~darc/training/ecmwf\\_collaborative\\_training/var\\_practice.pdf](http://www.met.reading.ac.uk/~darc/training/ecmwf_collaborative_training/var_practice.pdf)
- Stochastic gradient descent which can be adapted for non convex problems:  
<https://github.com/arseniyturin/SGD-From-Scratch>
- LASSO: <https://github.com/lasso-gmbh>