Hodgkin-Huxley Model with Fractional Differentiation Displays Spike Time Adaptation

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Introduction

Non-Markovian dynamics of action potential conductances

The spiking activities of neurons are modulated by the dynamics of gating variables of ion channels. These dynamics are typically described using Markovian approach and with fixed time constants. However, recent studies have shown that diffusion through spiny dendrite is anomalous [1], and the diffusion of ions through the channels is fractional [2], which are non Markovian processes, and display multiple timescale or scale free dynamics.

Power law and fractional derivative

The spike time adaptation of pyramidal neurons has been described with fractional order derivatives [3, 4]. Using the Hodgkin–Huxley model, we have developed a fractional model such that the dynamics of the gating variables are governed by the fractional order derivative with long-term memory trace, where the order (exponent) of the derivative is between 0 and 1. The weight of the memory trace increases when the fractional exponent decreases from 1, and this affects the spiking and dynamical properties of the model.

Method

The Hodgkin–Huxley model with fractional gating variables is given by

$$C_m \frac{dV}{dt} = -g_L(V - V_L) - g_{Na}(V)(V - V_{Na}) - g_K(V)(V - V_K) + I_{inj}$$

$$g_{Na}(V) = \bar{g}_{Na} m^3(V) h(V)$$
$$g_K(V) = \bar{g}_K n^4(V)$$
$$0 \le m, n, h \le 1$$

The fractional order dynamics of the gating variables are given by

$$\frac{d^\eta X}{dt^\eta} = \alpha_X(V)(1 - X) - \beta_X(V) X$$

α = opening rate and β = closing rate
X represents the gating variables n, m, or h.

For $0 < \eta < 1$ the fractional derivative is defined as

$$\frac{d^\eta X}{dt^\eta} = \underbrace{\frac{1}{\Gamma(1-\eta)}}_{\text{Gamma function}} \int_0^t \underbrace{\frac{X'(\tau)}{(t-\tau)^\eta}}_{\text{Memory trace}} d\tau$$

$$X(t_N) \approx (dt)^\eta \Gamma(2-\eta)[\alpha_X(V)(1-X) - \beta_X(V)X] + X(t_{N-1}) - \left[\sum_{k=0}^{N-2} [X(t_{k+1}) - X(t_k)][(N-k)^{(1-\eta)} - (N-1-k)^{(1-\eta)}]\right]$$

$$\boxed{X = \textit{Markov term} - \textit{Memory trace of } X}$$

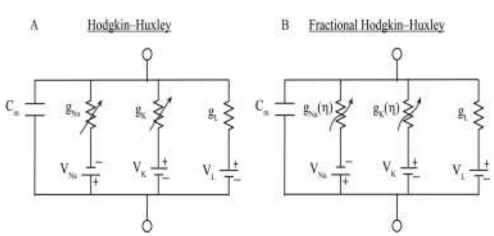


Fig. 1. Schematic circuit diagrams for the classical and fractional Hodgkin-Huxley model.

1. Spiking modes as a function of fractional gating variable to constant input

The Hodgkin–Huxley model with fractional gating variables produces phasic spiking, tonic spiking, Mixed mode oscillations, and bursting oscillations that strongly depends on the exponent of the fractional dynamics. These different spiking modes are produced in response to a constant input.

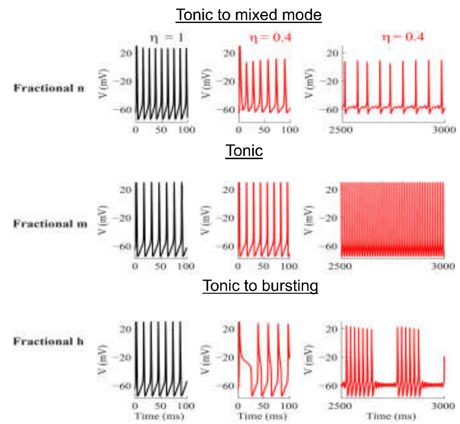


Fig. 2. The spiking activity of the Hodgkin-Huxley model with fractional gating variables n with I_{inj}= 18 μA, m with I_{inj}= 10 μA , and h with I_{inj}= 11 μA .

2. The fractional sodium inactivation gating variable (h) produces oscillatory activity to constant input

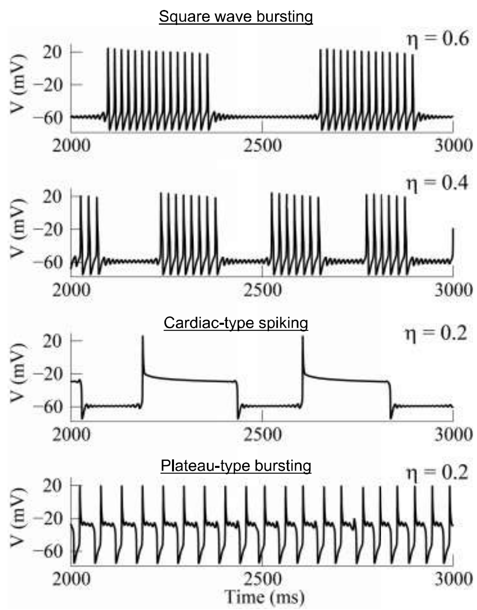
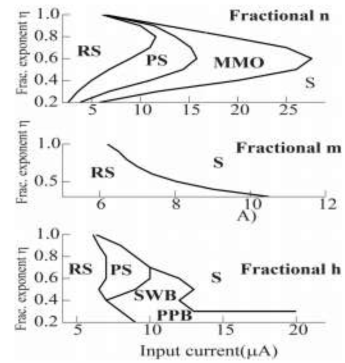


Fig. 3. Fractional gating variable h causes square wave bursting when η = 0.6 or 0.4 (I_{inj}= 11 μA). However, it causes cardiac-type spiking (I_{inj}= 11 μA) or plateau-type bursting (I_{inj}= 12 μA) when η = 0.2.

3. Phase plane analysis reveals transitions of spiking activity



RS = Resting State
PS = Phasic Spiking
MMO = Mixed-Mode Oscillations
S = Spiking
SWB = Square Wave Bursting
PPB = Plateau-type Bursting

Fig. 4. The phase plane analysis shows different neuronal spiking regions as the function of the fractional exponent and input strength.

4. Upward and downward spike time adaptation in response to constant input

The fractional activation variable (n) of potassium channel causes downward spike time adaptation, but the fractional activation variable (m) of the sodium channel facilitates spiking and causes upward spike time adaptation. The adaptations are caused by the negative contributions of the memory traces to the activation variables that decrease over time.

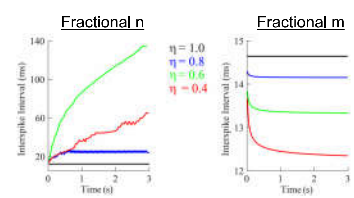


Fig. 5. Left: For fractional gating variable n (I_{inj}= 18 μA) the interspike intervals increase with time and as the fractional exponent decreases. Right: For fractional gating variable m (I_{inj}= 10 μA) the interspike intervals decrease as the expoenent decreases.

5. Variable spike thresholds are caused by fractional gating dynamics

For the fractional gating variables n and h the spike threshold dynamics show significant changes that strongly depend on the fractional exponent η. The moving spike threshold shows adaptation correlated to the spike time adaptation.

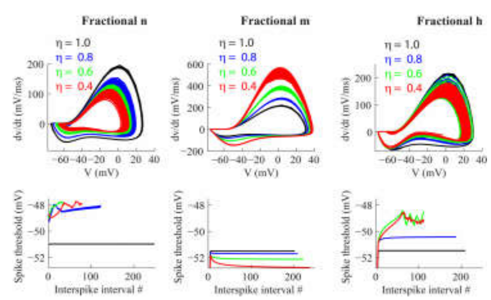


Fig. 6. Spike threshold phase planes and traces.

6. Mixed-mode oscillations are due to canards caused by fractional dynamics

The model with fractional gating variable n or h produces spiking modes with subthreshold oscillations (mixed-mode oscillations). In the phase plane analysis these mixed-mode oscillations correspond to canard trajectories. Canards are typically observed in multiple time scale dynamics and evolve along the attracting and repelling branches of the system. The fractional exponent might trigger time scale separation by making n and h much slower variables.

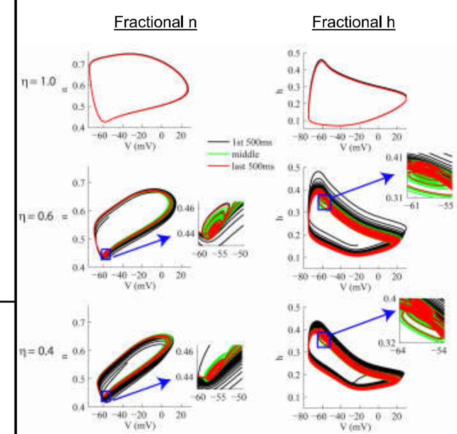


Fig. 7. Time dependent canard trajectories produced from the fractional gating variable of n (left, I_{inj}= 18 μA) and h (right, I_{inj}= 11 μA). Since gating variable m has very fast time scale, there are no canard trajectories from fractional m.

Conclusions

- The Hodgkin–Huxley model with fractional gating variables produces spike time adaptation in response to constant input as a function of the fractional order. This is caused by the memory trace that increases as the fractional exponent decreases.
- The spike threshold dynamics also depends on the fractional exponent.
- The results suggest that models with fractional derivatives can be effective methods to study the long-term correlation of ion channels and its effect on spiking activity. Fractional derivatives can also be effective methods to describe multiple timescale process of biological systems.
- The fractional exponent η may represent the complexity in the ion channel dynamics.

Bibliography

[1] Santamaria et al. (2006) Anomalous diffusion in Purkinje cell dendrites caused by spines. Neuron 52: 635–648.
[2] Goychuk et al. (2004) Fractional diffusion modeling of ion channel gating. Phys Rev E 70: 051915.
[3] Lundstrom et al. (2008) Fractional differentiation by neocortical pyramidal neurons. Nat Neurosci 11: 1335–1342.
[4] Teka et al. (2014) Neuronal Spike Timing Adaptation Described with a Fractional Leaky Integrate-and-Fire Model. PLoS Comput Biol 10(3): e1003526.

Acknowledgments

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