Biological modeling of neural networks miniproject: Single neuron models - From Hodgkin-Huxley to AdEx

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0 Introduction

Part 1 missing

In the second part of this project, an Adaptive Exponential Integrate and Fire (AdEx) will be fitted to a Hodgkin-Huxley (HH) adaptive neuron model using an experimentally realistic procedure.

1 Exploration of Hodgkin Huxley neurons

1.1 Getting started

Part 1 missing

1.2 Rebound spike?

Part 1 missing

1.3 Adaptation

Part 1 missing

2 From HH to AdEx

2.1 Passive properties

The passive properties of an AdEx model can be estimated from a single neuronal stimulation. First, let us recall the ordinary differential equations (ODEs) guiding the dynamics of the AdEx model:

$$\begin{aligned} \tau_m \frac{dV}{dt} &= -(V - E_l) + \Delta_T \exp\left(\frac{V - \theta_{rh}}{\Delta_T}\right) - Rw + RI_{ext} \\ \tau_w \frac{dw}{dt} &= a(V - E_l) - w \end{aligned} \tag{1}$$

Additionally, the voltage V and the variables w are updated once the potential reaches a threshold V_T:

$$\begin{aligned} V &\leftarrow V_{Reset} \\ w &\leftarrow w + b \end{aligned} \tag{2}$$

Starting from the resting state, with a current small enough to not generate a spike, the variable w is never updated and remains at 0. Additionally, the exponential term is small as $V - \theta_{rh} < 0$. Ignoring these two terms, we get:

$$\tau_m \frac{dV}{dt} \approx -(V - E_l) + RI_{ext}. \tag{3}$$

Under a step current I_{ext} of amplitude I_0 in $[t_1, t_2]$ and 0 elsewhere, the voltage curve is then given by:

$$V(t) \approx E_l + RI_0 \left[\exp\left(-\frac{t-t_1}{\tau_m}\right) - \exp\left(-\frac{t-t_2}{\tau_m}\right)\right]. \tag{4}$$

Therefore, to extract the parameters, the following protocol can be used. First, stimulate the target

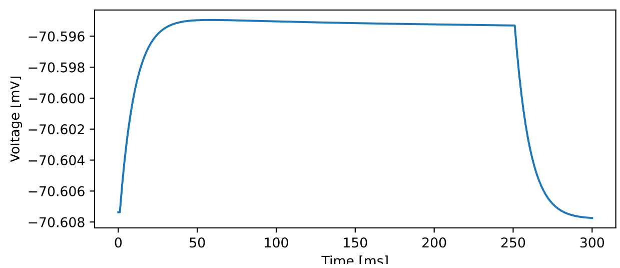

Figure 1: Voltage curve of the *adpative* model under a step current of $1.3nA$ between 1 and 250 ms.

neuron (*adaptive*) with a step current with $I_0 = 1.3nA$, $t_1 = 1ms$ and $t_2 = 250ms$, resulting in the membrane potential evolution show in figure 1. Let $V(t)$ be the voltage curve, the parameters are given by:

$$\begin{aligned}
\tau_m &\approx \left(1 - \frac{1}{e}\right) \arg\max_t [V(t)] = 37.971ms \\
E_l &\approx V(t = 0ms) = -70.607mV \\
R &\approx \frac{\max_t[V(t)] - E_l}{I_0} = 9.923k\Omega \\
g_l &= \frac{1}{R} = 100.779\mu S \\
C &= \frac{\tau_m}{R} = 3.827\mu F
\end{aligned} \tag{5}$$

2.2 Exponential Integrate and Fire

In this section, the parameters θ_{rh} and Δ_T are extracted from neuron stimulation observations. Let $f(V)$ be the membrane dynamics function without adaptation current:

$$f(V) = C\frac{dV}{dt} = -g_l(V - E_l) + g_l \Delta_T \exp\left(\frac{V - \theta_{rh}}{\Delta_T}\right) + I_{ext}. \tag{6}$$

Note that this formulation is equivalent to equation 1 and was obtained by dividing both sides by R.

2.2.1 Extraction of θ_{rh}

When the membrane dynamics function is strictly greater than zero, the voltage always increases, eventually yielding to the emission of a spike. However, as Δ_T and θ_{rh} are unknown yet, estimating the required current only from $f(V)$ is unrealistic. Therefore, we apply again the bisection method to approximate the smallest current that generates a spike using a 3 seconds step current. This method yields an intensity of $1.4042\mu A$. Using $\Delta_T = 30mV$ and $\theta_{rh} = -40mV$ as first guesses, the function $f(V)$ is indeed greater than zero, with a minimum at around $1.343\mu A$. By definition, the rheobase voltage corresponds to the potential after which the dynamics of membrane changes to the spike emission phase. As we ensured the minimum of $f(V)$ is close to zero, the derivative of the voltage curve should be very close to zero but still positive. At some point, it will reach the rheobase potential and the derivative will grow quickly until the spike is emitted. The rheobase voltage can therefore be found by estimating the time t_{rh} at which $V(t)$ and $dV(t)/dt$ start changing significantly. As shown in figure 2, $t_{rh} \approx 107.4ms$. Evaluating $V(t_{rh})$ yields:

$$\theta_{rh} \approx V(t = 107.4ms) \approx -46.197mV \tag{7}$$

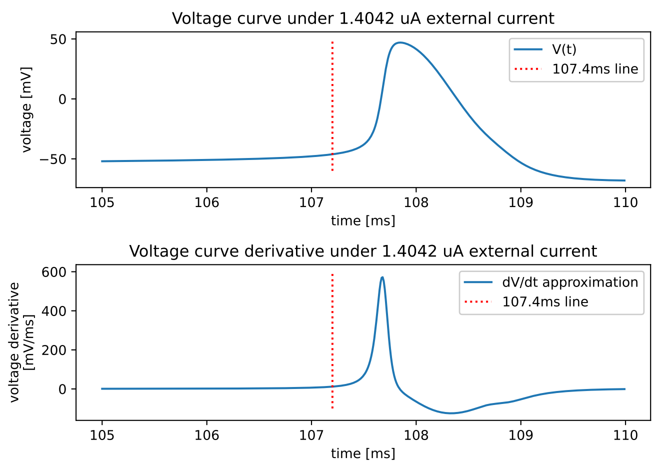

Figure 2: Voltage and voltage discrete derivative curves under a step current of intensity of $I = 1.4042\mu A$.

2.2.2 Extraction of Δ_T

In this section, we estimate Δ_T by looking at the zeros of $f(V)$. Indeed, $f(V)$ has two zeros, the first one approximately at E_l and the second one at V_S. for $V \in [-\infty, V_S[$, the membrane potential will always be brought back to E_l but for $V > V_S$, it increases to emit a spike. Therefore, if the neuron is stimulated with a current that almost creates a spike it means that the maximum potential achieved is almost V_S. As V_S is a zero of $f(V)$, this can be used to solve the equation $f(V_S) = 0$ for Δ_T numerically. Using the bisection method, we find that an input pulse current of $I = 1.954267501mA$ during $1\mu s$ almost creates a spike. Simulating the target neuron with that input value gives a maximum voltage of $V_S \approx -69.972mV$. Solving $f(V_S) = 0$ for Δ_T gives:

$$\Delta_T \approx 9.970mV \tag{8}$$

2.3 Subthreshold adaptation

This section aims at estimating the adaptation voltage coupling coefficient of the adaptation current, a in equation 1. When the dynamics are slow and far from threshold, the $dV/dt \approx 0$, $dw/dt \approx 0$ and $\exp((V - \theta_{rh})/\Delta_T) \approx 0$. Plugging these approximation in equations 1 and combining them allows to extract a linear dependence between the external current and the membrane potential:

$$\begin{aligned} 0 &\approx -g_l(V - E_l) + 0 - w + I_{ext} \\ 0 &\approx a(V - E_l) - w \\ \implies I_{ext} &\approx (g_l - a)(V - E_l). \end{aligned} \tag{9}$$

Stimulating the target neuron with a current respecting the assumptions above allow for straightforward extraction of the parameter a. A ramp current from $0\mu A$ to $1.2\mu A$ during $10s$ is used to generate the voltage trace. Figure 3 shows the resulting I-V curve. We observe that the linear approximation seems to hold between $5\mu A$ and $10\mu A$. Let m be such that $V \approx mI$, then, using equations 9:

$$\begin{aligned} V \approx mI \implies I \approx \frac{1}{m}V \implies g_l - a \approx \frac{1}{m} \implies a \approx g_l - \frac{1}{m} \\ \implies a \approx 100.779\mu S - \frac{10\mu A - 5\mu A}{V(I = 10\mu A) - V(I = 5\mu A)} \approx -1.693S \end{aligned} \tag{10}$$

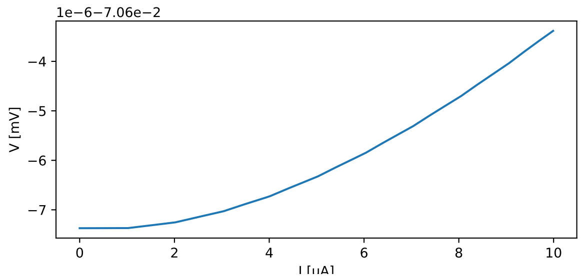

Figure 3: I-V curve under a ramp current from 0 to $1.2\mu A$ during $10s$.

2.4 Remaining parameters

In this section, we tune the last parameters of the AdEx model, namely V_{Reset}, b and τ_w, to match the spike train generated by a $2\mu A$ step current over $1500ms$. The reset potential can easily be extracted by finding to which value the potential is reset after the first spike. This approach returns

$$V_{Reset} \approx -67.570mV. \tag{11}$$

The parameter b does not seem to play an important role in the spike timings. As it is the property we want to approximate, we simply let

$$b \approx 10mV. \tag{12}$$

Finally, τ_w plays an important role. The larger τ_w, the larger the expected interspike distance. Unfortunately, as shown on figure 4, while the firing frequency of the adaptive HH model is almost constant, our AdEx model always exhibits an increasing firing frequency, that is a few spikes at the beginning and many spikes at the end. Therefore, a proper fit is not possible. Trying to fit as many spikes as possible, we settled for

$$\tau_w \approx 10ks. \tag{13}$$

Table 1 shows all the estimated parameters.

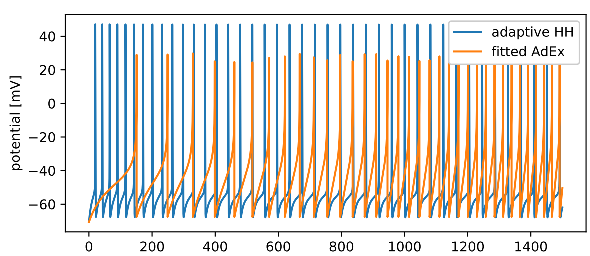

Figure 4: Final fit of the spike train generated by a $1500ms$ step current of amplitude $2\mu A$.

τ_m	R	E_l	V_{Reset}	θ_{rh}	a	b	V_{spike}	Δ_T	τ_w
37.971 ms	9.923 kΩ	-70.607 mV	-67.570 mV	-46.197 mV	-1.693 S	10 pA	30 mV	8.980 mV	10 ks

Table 1: Final parameters

2.5 Testing on random input

In this final section, we evaluate the model by testing it with two random gaussian currents, one with a 500ms during and the other with 2500ms, both sampled from $\mathcal{N}(1\mu A, 15\mu A)$. Figure 5 shows the fitted voltage traces. In general, the accuracy is not great. While the general trend of the voltage curve is quite well approximated, it seems that the estimated rheobase voltage may be too low as the fitted model fires less often than the target HH model. It also seems that the accuracy is greater with the longer stimulation. This may be related to the observation made in the previous section, that is that the fitted neuron increases its firing frequency. This is probably due to the w variable which changes at each spike, therefore, some time may be required to achieve a decent range of values. Hence, the greater accuracy after approximately 1500ms of stimulation.

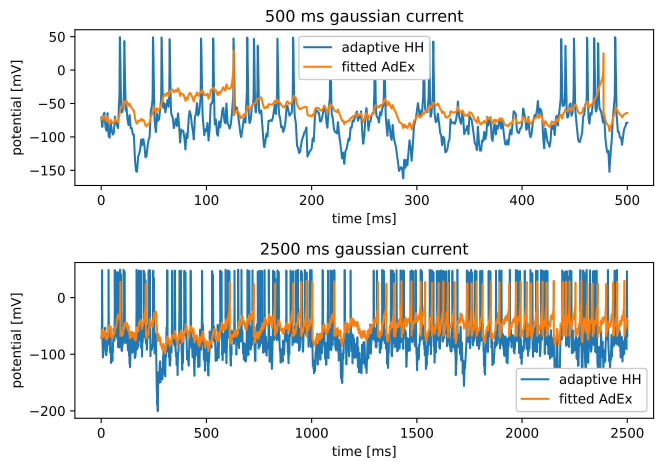

Figure 5: Gaussian random inputs fit

3 Conclusion

Part 1 missing

The fitting procedure used in this project follows an experimentally realistic protocol. However, it often relied on approximations and graphical interpretations which are not accurate. This eventually led to a low accuracy on short random inputs.