# Notes on fitting the rEIF model to data from dynamic clamp recordings

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We consider fitting the *refractory exponential integrate and fire* (rEIF) model to data from retinal ganglion cells. We wish to model

$$\frac{dV}{dt} = f(V, t - t_{spike}) + \frac{I_{syn}(t)}{C} \tag{1}$$

where

$$f(V, t - t_{spike}) = \frac{1}{\tau_m}\left(E_L - V + \Delta_T e^{(V - V_T)/\Delta_T}\right) \tag{2}$$

and

$$I_{syn}(t) = -g_{exc}(t)(V - V_{exc}) - g_{inh}(t)(V - V_{inh}) \tag{3}$$

(We use the subscript "syn" because these currents are presumed to result from excitatory and inhibitory synapses). We will assume that the parameters $\tau_m$, $E_L$, $\Delta_T$, and $V_T$ actually depend on the time that has elapsed since the last spike: i.e. $t - t_{spike}$. We are given a long time sequence of voltage and conductance measurements at equally spaced time intervals, $t_n = n\,\delta t$: i.e. $V(n\,\delta t)$, $g_{exc}(n\,\delta t)$ and $g_{inh}(n\,\delta t)$.

Our goal is to infer an appropriate functional form for the parameters $\tau_m$, etc... Furthermore, we must infer the capacitance $C$, voltage reset $V_r$, and voltage threshold $V_{th}$.

## 1 Input data

Our input data is in the form of a MATLAB file (`ON_parasol_dclamp.mat`) which contains:

`exc_high_same`: $1 \times N_t$ array of excitatory conductances
`inh_highc_same`: $1 \times N_t$ array of inhibitory conductances
`highc_same`: $8 \times N_t$ array of voltage values

The voltage array contains data from 8 trials and is in units of volts (V). All of the above were with a high contrast stimulus. Everything is sampled at a rate of 0.1 ms ($10^4$ Hz). (The conductance arrays were normalized: to get the original values, multiply by $A_{exc} = 30$ nS, $A_{inh} = 40$ nS).

Then there are three other arrays, which contain the analogous information for a low contrast stimulus. (`exc_low_same`, `inh_low_same`, `lowc_same`).

## 2 Basic idea

The theoretical underpinning of this fitting is the following (as described in Badel): "basic electrophysiology" provides the following relationship between the capacitive charging current $C\frac{dV}{dt}$, the transmembrane current $I_m$, and the injected current $I_{in}$:

$$C\frac{dV}{dt} + I_m(V,t) + I_{noise}(t) \quad = \quad I_{in}(t) \tag{4}$$

$I_{noise}$ contains current from unmodelled sources. We know $I_{in}$ and $V$ as a function of time, because we have data from an experiment in which $I_{in}$ was injected into a neuron (via dynamic clamp) and $V(t)$ was measured. Our goal is to infer $I_m(V,t)$. We hypothesize that $I_m$ can be written as a function of $V$ and the time since the last spike $t - t_{spike}$: matching Eqn. (4) with Eqn. (1),

$$\frac{I_m(V,t)}{C} = -f(V, t - t_{spike})$$

Badel et al. refers to this relationship as a *dynamic I-V curve.* (It is "dynamic" because it depends on time as well as voltage). Rewriting Eqn. 4,

$$I_m(V,t) + I_{noise}(t) \quad = \quad I_{in}(t) - C\frac{dV}{dt} \tag{5}$$

we assume that for a fixed $V$ and $t - t_{spike}$, we can best estimate $f$ by assuming that $I_{noise}$ has zero mean: therefore

$$f(V,b) \quad \approx \quad Mean[I_m(v,t) + I_{noise}(t)]\Bigg|_{v=V,\, t-t_{spike}=b} \tag{6}$$

Here are what I see as the main steps we will need to take:

1. Find spike times
2. Estimate capacitance $C$.
3. Fit $f(V, t - t_{spike})$: long-time data
   (a) Suggestion: develop and check your procedure with "long time" data: $t - t_{spike} > T_0$.
   (b) First, use low voltage $V < V_0$ to extract $\tau_m$ and $E_L$.
   (c) Then use what remains of $f(V)$ to find $\Delta_T$ and $V_T$.
4. Fit $f(V, t - t_{spike})$: all time windows
5. Decide on $V_r$, $V_{th}$
6. *(and finally...)* to what extent does our new model recreate our original spike trains?

## Step 1: Find spike times

We first need to be able to separate data by the time that has elapsed since the last spike. So, we first need to know when spikes occurred!

**Deliverable:** Function that returns a list of spike times, given: voltage data at equi-spaced time points, time interval width $\delta t$.
**Suggestion:** Use an upward threshold crossing. Try for varying values of $V_{th}$, to check robustness: does it matter which value we choose?

## Step 2: Find capacitance

We hypothesize that capacitance is the quantity $C$ that will minimize the variance of

$$f(V) = \frac{1}{C}\left(I_{syn} - C\frac{dV}{dt}\right)$$

at a specific $V$.

Badel justifies this in their Eqns. 5, 6: rewriting Eqn. (5) by dividing by a *hypothetical*, possibly incorrect capacitance $C_e$:

$$\frac{I_{in}}{C_e} - \frac{dV}{dt} = \frac{I_m}{C} + \left(\frac{1}{C} - \frac{1}{C_e}\right) I_{in} + \frac{I_{noise}}{C} \tag{7}$$

Then

$$\begin{aligned} \mathrm{Var}\left[\frac{I_{in}}{C_e} - \frac{dV}{dt}\right]_V &= \mathrm{Var}\left[\frac{I_m}{C}\right]_V + \mathrm{Var}\left[\left(\frac{1}{C} - \frac{1}{C_e}\right) I_{in}\right]_V + \mathrm{Var}\left[\frac{I_{noise}}{C}\right]_V & (8) \\ &= \mathrm{Var}\left[\frac{I_m}{C}\right]_V + \left(\frac{1}{C} - \frac{1}{C_e}\right)^2 \mathrm{Var}\left[I_{in}\right]_V + \mathrm{Var}\left[\frac{I_{noise}}{C}\right]_V & (9) \end{aligned}$$

assuming that $I_{in}$, $I_m$ and $I_{noise}$ are independent. The subscript $V$ indicates that we should only consider data at a specific value of the voltage $V$. Notice that the only quantity in the last equation that changes as $C_e$ changes is the squared difference between $1/C$ and $1/C_e$; this is minimized precisely when $C = C_e$!

**Deliverable:** Function that returns an estimated capacitance.
**Things to consider:** Must use data at a fixed voltage (or in a small voltage interval $(V - \Delta V, V + \Delta V)$); also only use data for long $t - t_{spike} > T_0$. Try it for different $T_0$: does your answer change? Create plots like Fig. 1C and 1D in Badel to see if you get what you expect.

## Step 3: Preliminary work: establish a procedure to get $g_L$, $E_L$, $\Delta_T$ and $V_T$

Use long time data $t - t_{spike} > T_0$.