Single-cell stochastic model

(A) Intensity-based model

The neuron state-variable is its instantaneous rate of firing formally defined as a stochastic intensity:

$\lambda(t)$ = function of the past history, which includes neural inputs and the neuron's own spiking history

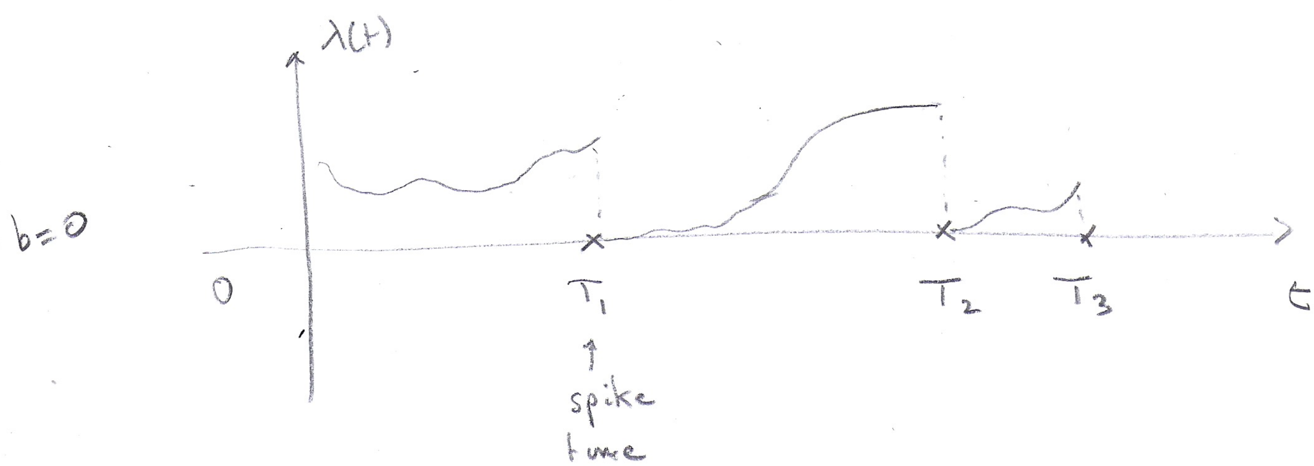
Central example: Markovian neuron with reset, whose dynamics is defined by the following stochastic equation:

$$\lambda(t) = \int_{T(t)}^{t} \alpha(\lambda(s), s)\, ds$$

$T(t) \leftarrow$ last spiking time

$\alpha(\lambda(s),s)$: continuous drift, e.g.,

$$\alpha(\lambda, s) = \underbrace{-\frac{\lambda}{\tau}}_{\text{relaxation}} + \underbrace{I(s)}_{\text{input}} + \underbrace{b}_{\text{base rate}}$$



B) Integrate-and-fire model

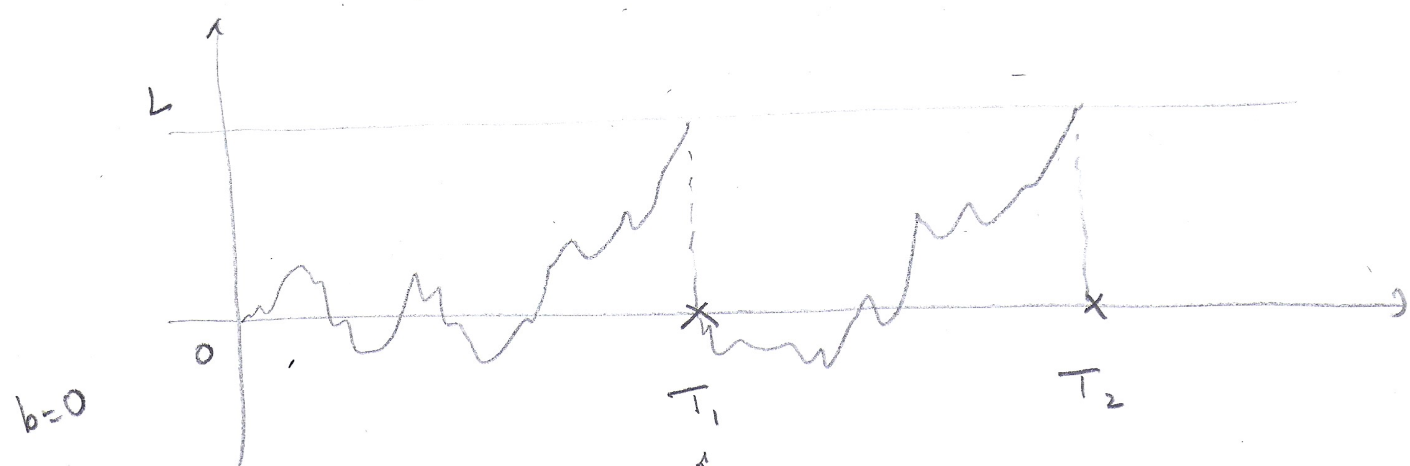
The neuron state variable is a diffusive random variable X_t representing the membrane voltage. The neuron spike whenever the voltage reaches a given threshold L, the resets to base level. $b<L$.

Central example: Linear integrate-and-fire neuron whose dynamics is defined by the following stochastic equation.

subthreshold dynamics $\longrightarrow$ $$dX_t = \left(-\frac{X_t}{\tau} + I(t)\right)dt + \sigma\, dW_t\,, \quad X_0 = b$$

↑ Gaussian white noise

reset mechanism $\longrightarrow$
$$T_i = \inf_t \{X_t \geq L \mid T_i > T_{i-1}\}\,, \quad T_0 = 0$$
$$X_{T_i^+} = b$$



↑ spike time = first-passage time (FPT)

Stochastic equations for reset models

(A) $$\lambda(t) = \lambda(0) + \underbrace{\int_0^t \alpha(\lambda(s), s)\, ds}_{\text{continuous part}} + \underbrace{\int_0^t (b - \lambda(s))\, dN_s}_{\text{reset part}}$$

spiking point process with intensity function $\lambda(t)$

$\mathbb{E}[N(t, t+dt)] = \lambda(t) dt$

(B) $$X_t = X_0 + \underbrace{\int_0^t \alpha(X_s, s)\, ds}_{\text{drift part}} + \underbrace{\int_0^t \sigma(X_s, s)\, dW_s}_{\text{diffusive part}} + \underbrace{\int_0^t (b - X_s)\, dN_s}_{\text{reset part}}$$

$$N_t = \int_0^T \delta(X_s = L)\, ds = \sum_i \mathbb{1}_{\{T_i < t\}} \leftarrow \text{process counting spiking event}$$

The above equation are integral equations for the dynamics
For deterministic systems:

$$\dot{x} = F(x) \iff x(t) = x(0) + \int_0^t F(x) \quad (*)$$

For deterministic systems, the function f defines a vector field which locally define the dynamics. This vector field is the "infinitesimal generator" of the dynamics.

For random dynamics, the direct equivalent of vector fields become stochastic and trajectories depend on the noise realization. One can recover relations akin to $(*)$ by averaging over random trajectories and by introducing test functions $g : \Omega \times \mathbb{R} \longrightarrow \mathbb{R}$.

$$g : \underset{\substack{\uparrow \\ \text{domain}}}{\Omega} \times \underset{\substack{\uparrow \\ \text{time dependence}}}{\mathbb{R}} \longrightarrow \mathbb{R}$$

Infinitesimal generator

A $\quad \Omega = \mathbb{R}, \quad g : \mathbb{R} \to \mathbb{R}$

probability no spike in $(t, t+dt]$

continuous drift

$$\mathbb{E}\left[g(\lambda(t+dt)) \mid \lambda(t)\right] = (1 - \lambda(t)dt)\, g\left(\lambda(t) + \alpha(\lambda(t), t)\, dt\right)$$

$$+ \lambda(t)dt \; g(b + O(dt)) \quad + o(dt)$$

probability one spike in $(t, t+dt]$ $\quad$ post spike reset

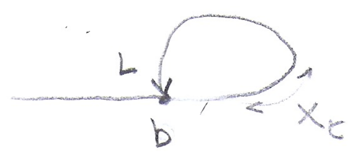
$$\mathcal{L}[g](\lambda, t) = \lim_{dt \to 0} \frac{\mathbb{E}\left[g(\lambda(t+dt)) \mid \lambda(t) = \lambda\right] - g(\lambda)}{dt}$$

infinitesimal generator

$$= \alpha(\lambda, t)\, \partial_\lambda g \; + \lambda\left(g(b) - g(\lambda)\right) \quad \leftarrow \text{linear operator}$$

jump size enforcing reset

B $\quad \Omega = (-\infty, L), \quad g : \Omega \to \mathbb{R}$ such that $g(L) = g(b)$



no FPT

$$\mathbb{E}\left[g(X_{s+ds}) \mid X_s = x\right] = (1 - \lambda(t)dt)\, \mathbb{E}\, g\left(x + \alpha(x,s)\, ds + \sigma(x,s)\, dW_s\right)$$

diffusive dynamics

$$+ \lambda(t)\, dt\; \mathbb{E}\, g(b + O(dt))$$

post spike reset

one FPT

Ito lemma : $\quad g(x + \alpha(x,s)\, ds + \sigma(x,s)\, dW_s)$

$$= g(x) + \partial_x g\, (\alpha\, ds + \sigma\, dW_s) + \frac{\partial_{xx} g}{2} (\alpha\, ds + \sigma\, dW_s)^2$$

$$= g(x) + \partial_x g\, (\alpha\, ds + \sigma\, dW_s) + \frac{\partial_{xx} g}{2} \sigma^2\, ds + o(ds)$$

$$\mathbb{E}\, g(x + \alpha(x,s)\, ds + \sigma(x,s)\, dW_s) = g(x) + \alpha(x,s)\, \partial_x g + \frac{\sigma^2(x,s)}{2} \partial_{xx} g + o(ds)$$

$$\mathcal{L}[g](x,s) = \lim_{ds\to 0} \frac{\mathbb{E}[g(X_{s+ds}) \mid X_s = x]}{ds}$$

infinitesimal generator

$$= \alpha(x,s)\,\partial_x g + \frac{\sigma^2(x,s)}{2}\,\partial_{xx} g$$

same linear operator as that of the free diffusion in $\mathbb{R}$ (without reset). ⚠ $\neq$ test functions $g(L) = g(b)$ ⚠

These calculations generalize to time dependent test function: the infinitesimal generator is then $\mathcal{A}[g] = \partial_t g + \mathcal{L} g$.

Dynkin's formula: $\mathbb{E}[g(X_t,t) \mid X_s = x] - g(x,s)$

similar to (*)

$$= \int_s^t \underbrace{\mathbb{E}\left[\mathcal{A}[g](X_\tau,\tau) \mid X_s = x\right]}_{\sim \text{ vector field}} d\tau$$

Dynkin's formula allows one to derive straightforwardly the backward and forward Kolmogorov equations for the dynamics, which are partial differential equation (PDE) characterization.

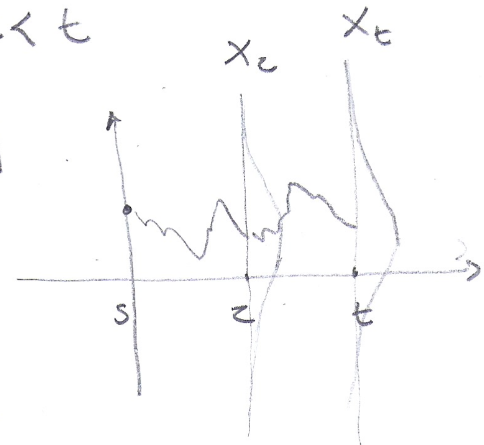
Backward Kolmogorov equation

Consider: $u(x,s) = \mathbb{E}[g(X_t,t) \mid X_s = s]$

By the Markovian property, for $s < z < t$

$$u(x,s) = \mathbb{E}\big[\mathbb{E}[g(X_t,t) \mid X_z] \mid X_s = s\big]$$

$$= \mathbb{E}[u(X_z,z) \mid X_s = s]$$



Thus taking u as a test function in Dynkin's formula yields:

$$0 = \mathbb{E}[u(X_z,z) \mid X_s = s] - u(x,s)$$

$$= \int_s^z \mathbb{E}[\partial_t u + \mathcal{L}u \mid X_s = x]\, dt$$

In particular: $\lim_{z \to s} \frac{1}{z-s} \int_s^z \mathbb{E}[\partial_t u + \mathcal{L}u \mid X_s = x]\, dt = 0$

$$\Leftrightarrow \quad \boxed{\partial_s u + \mathcal{L}u = 0}$$

Backward Kolmogorov. (BK)

Terminal condition: $u(x,t) = g(x,t) \Rightarrow$ solved backward

Forward Kolmogorov: (otherwise known as Fokker Planck)

This is the equation satisfied by the transition kernel $p(y,t\,|\,x,s) = \mathbb{E}\left[\delta_y(X_t)\,|\,x,s\right]$ associated to the dynamics. It is simply obtained from the Dynkin's formula for a time independent test function

$$\mathbb{E}\left[g(X_t)\,|\,X_s = x\right] - g(x) = \int_\Omega g(y)\,p(y,t\,|\,x,s)\,dy$$

$$\overset{\text{Dykin}}{=}$$

$$\int_s^t \mathbb{E}\left[\mathcal{L}[g](X_z,z)\,|\,X_s = s\right] dz$$

$$=$$

$$\int_s^t \int_\Omega \mathcal{L}[g](y,z)\,p(y,z\,|\,x,s)\,dy$$

Differentiating with respect to t yields

dual operator

$$\int_\Omega g(y)\,\partial_t p\,dy = \int_\Omega \mathcal{L}[g]\,p\,dy = \int_\Omega g\,\mathcal{L}^*[p]\,dy$$

wich holds for all g if p is a weak solution of the Forward Kolmogorov equation: $\boxed{\partial_t p = \mathcal{L}^* p}$

depends on Ω

Initial condition $p(y,s\,|\,x,s) = \delta_x(y)$

Conservation of probability

(4) $\Omega = \mathbb{R}$, $g : \mathbb{R} \to \mathbb{R}$, $\mathcal{L}[g](\lambda, t) = \alpha(\lambda, t)\,\partial_\lambda g + \lambda\big(g(b) - g(\lambda)\big)$

$$\int_{\mathbb{R}} \mathcal{L}[g](\lambda,t)\, p(\lambda,t)\, d\lambda = \int_{\mathbb{R}} \left[\alpha\, \partial_\lambda g + \lambda\big(g(b) - g\big)\right] p \, d\lambda$$

integration by parts $\rightarrow$
$$= -\int_{\mathbb{R}} g\, \partial_\lambda(\alpha p)\, d\lambda + \left(\int_{\mathbb{R}} \lambda p \, d\lambda\right) \overbrace{\int_{\mathbb{R}} \underset{\uparrow \text{ Dirac}}{\delta_b}\, g \, d\lambda}^{g(b)} - \int_{\mathbb{R}} \lambda g p \, d\lambda$$

$$= \int_{\mathbb{R}} g \underbrace{\left[-\partial_\lambda(\alpha p) - \lambda p + \left(\int_{\mathbb{R}} \lambda' p \, d\lambda'\right) \delta_b\right]}_{\mathcal{L}^*[p]} d\lambda$$

$$\boxed{\partial_t p = -\partial_\lambda(\alpha p) - \lambda p + \left(\int \lambda' p \, d\lambda'\right) \delta_b}$$

transport term due to drift — death rate due to spiking — birth rate due to reset at b

$$\partial_t \int_{\mathbb{R}} p = -\underbrace{\int_{\mathbb{R}} \partial_\lambda(\alpha p)\, d\lambda}_{0} - \int_{\mathbb{R}} \lambda p \, d\lambda + \int_{\mathbb{R}} \lambda' p \, d\lambda' \overbrace{\int_{\mathbb{R}} \delta_b}^{1} = 0$$

B $\Omega = (-\infty, L)$, $g : \Omega \to \mathbb{R}$ $\quad g(L) = g(b)$

$$\mathcal{L}[g](x,s) = \alpha(x,s)\,\partial_x g + \frac{\sigma^2(x,s)}{2}\,\partial_{xx} g$$

$$\int_{-\infty}^{L} \mathcal{L}[g](x,s)\,p(x,s)\,dx = \int_{-\infty}^{L} \left[\alpha\,\partial_x g + \frac{\sigma^2}{2}\,\partial_{xx} g\right] p\,dx$$

integration by parts

$$= \Big[\alpha g p\Big]_{-\infty}^{L} - \int_{-\infty}^{L} \partial_x(\alpha p)\,g\,dx$$

$$+ \left[\frac{\sigma^2}{2}\,\partial_x g\,p\right]_{-\infty}^{L} - \int_{-\infty}^{L} \partial_x\left(\frac{\sigma^2}{2} p\right) \partial_x g\,dx$$

F.P.T. $\to$ $p(L) = 0$ absorbing boundary condition !

$$= -\int_{-\infty}^{L} \partial_x(\alpha p)\,g\,dx$$

integration by parts $\to$ $- \left[g\,\partial_x\left(\frac{\sigma^2}{2} p\right)\right]_{-\infty}^{L} + \int_{-\infty}^{L} \partial_{xx}\left(\frac{\sigma^2}{2} p\right) g\,dx$

F.P.T. $\to$ $\partial_x\left(\frac{\sigma^2}{2} p\right)\Big|_L \neq 0$ flux through boundary = spiking rate

$$= \int_{-\infty}^{L} \left[-\partial_x(\alpha p) + \partial_{xx}\left(\frac{\sigma^2}{2} p\right)\right] g\,dx$$

$$- \int_{-\infty}^{L} \partial_x\left(\frac{\sigma^2}{2} p\right)\Big|_{x=L} \delta_b\, g\,dx$$

$\uparrow$ $g(L) = g(b)$

$$\mathcal{L}^*[p] = \underbrace{-\partial_x(\alpha p) + \partial_{xx}\left(\frac{\sigma^2}{2} p\right)}_{\text{Free diffusion Fokker Plank operator}} - \partial_x\left(\frac{\sigma^2}{2} p\right)\Big|_{x=L} \delta_b$$

$\uparrow$ source term in b.

$$\boxed{\partial_t p = -\partial_x(\alpha p) + \partial_{xx}\left(\frac{\sigma^2}{2}p\right) - \partial_x\left(\frac{\sigma^2}{2}p\right)\Big|_{x=L}\delta_b}$$

transport term du to drift

diffusion term due to noise

spike rate = birth rate at b

$$\partial_t \int_{-\infty}^{L} p\,dx = -\underbrace{\int_{-\infty}^{L}\partial_x(\alpha p)\,dx}_{0} + \underbrace{\int_{-\infty}^{L}\partial_{xx}\left(\frac{\sigma^2}{2}p\right)dx}_{\cancel{-\partial_x\left(\frac{\sigma^2}{2}p\right)\big|_{x=L}}} \cancel{-\partial_x\left(\frac{\sigma^2}{2}p\right)\Big|_{x=L}}\overbrace{\int_{-\infty}^{L}\delta_b\,dx}^{1}$$