Mathematical Models in Biology.

C.O. Tărniceriu

Interdisciplinary Research Department
Field Science

Interspike Interval Distribution. ("Spiking Neuron Models", W. Gerstner and W.M. Kistler)

Consider a single neuron that is stimulated by a known current input and an unknown noise source; what is the probability that, given the last firing time $\hat{t}$, the neuron will emit a spike in $[t, t+\Delta t]$? For $\Delta t \longrightarrow 0$, the answer is given by the *probability density of firing* $P_I(t/\hat{t})$.

$$\int_{t_1}^{t_2} P_I(t/\hat{t})\,\mathrm{d}t = \text{the probability to find a spike in an interval } [t_1, t_2]$$

Interspike Interval Distribution. ("Spiking Neuron Models", W. Gerstner and W.M. Kistler)

Normalization:

$$\int_{\hat{t}}^{\infty} P_I(t/\hat{t})\,\mathrm{d}t = 1 - P_I^{inact},$$

- for excitatory inputs and a sufficient amount of noise, the neuron will always emit further spikes: $P_I^{inact} = 0$

$$\int_{\hat{t}}^{\infty} P_I(t/\hat{t})\,\mathrm{d}t = 1.$$

Survivor function and hazard.("Spiking Neuron Models", W. Gerstner and W.M. Kistler)

The *survivor function* - the probability that the neuron stays quiescent between $\hat{t}$ and t:

$$S_I(t/\hat{t}) = 1 - \int_{\hat{t}}^{t} P_I(t'/\hat{t})\,\mathrm{d}t'$$

Initial value

$$S_I(\hat{t}/\hat{t}) = 1$$

The rate of decay of $S_I(t/\hat{t})$:

$$\rho(t/\hat{t}) = -\frac{\frac{\mathrm{d}}{\mathrm{d}t} S_I(t/\hat{t})}{S_I(t/\hat{t})}$$

$\rho(t/\hat{t})$ - *age-dependent death rate*.

Interconnected neurons. Population density function for Integrate and Fire neurons.

For $N \to \infty$, the fraction of neurons having the membrane's potential in $[v_0, v_0 + \delta v]$ is:

$$\lim_{N\to\infty} \frac{\textit{neurons with } v_0 \leq v(t) \leq v_0 + \Delta v}{\Delta v} = \int_{v_0}^{v_0+\Delta v} p(t, v')\,\mathrm{d}v'$$

- p(t,v) - membrane potential density

How does the membrane potential density function evolves in time?

Normalization:

$$\int_{v_r}^{\eta} p(t, v)\,\mathrm{d}v = 1.$$

Interconnected neurons. Population density function.

The population activity is defined as the fraction of the neurons that "flow" across the threshold, i.e.

$$r(t) = J(t, \eta)$$

Reinjection of neurons:

$$J(t, v_r) = J(t, \eta)$$

The flux is supposed to consists of two parts:

$$J(t, v) = J_{drift}(t, v) + J_{jump}(t, v)$$

Population density models for Integrate and Fire neurons

In the case of Integrate-and fire neurons, the drift flux is given by:

$$J_{drift}(t,v) = [-\gamma v + I]p(t,v)$$

It is supposed next that, every time a neuron of the population receives a signal, will have a jump in potential of magnitude h. Denoting by σ the average reception rate of a neuron, the jump-flux is given by:

$$J_{jump} = \sigma \int_{v-h}^{v} p(t,v')\,\mathrm{d}v'$$

The evolution in time of the density function is dictated by:

$$\frac{\partial}{\partial t}p(t,v) = -\frac{\partial}{\partial v}J(t,v)$$

Population density models for Integrate and Fire neurons

A population density model for integrate and fire neurons:

L. Sirovich

$$\begin{cases} \frac{\partial}{\partial t}p(t,v) + \frac{\partial}{\partial v}\left((-\gamma v)p(t,v)\right) = \sigma\left(p(t,v-h) - p(t,v)\right) \\ +\delta(v - v_r)r(t) \\ p(t,1) = 0 \\ r(t) = \sigma \int_{1-h}^{1} p(t,v)\,\mathrm{d}v = \frac{I}{h}\int_{1-h}^{1} p(t,v)\,\mathrm{d}v \\ p(0,v) = p_0(v). \end{cases}$$

Age-structure in neuronal populations

The repartition of the membrane potential between two spikes is given by:

$$\begin{cases} \frac{\partial}{\partial a} q(a,v) - \gamma \frac{\partial}{\partial v}[vq(a,v)] = \sigma[q(a,v-h) - q(a,v)] \\ q(a,1) = 0 \\ q(0,\cdot) = \delta(v - v_r) \end{cases}$$

- $a = t - \hat{t}$ is the so called "age"; $\hat{t}$ is the last firing time.

Age-structure in neuronal populations

A description of a population of connected neurons structured by its *age a*:

$$\begin{cases} \frac{\partial}{\partial t} n(t,a) + \frac{\partial}{\partial a} n(t,a) + \rho(a) n(t,a) = 0 \\ r(t) = \int_0^\infty \rho(a) n(t,a) \, \mathrm{d}a \\ n(t,0) = r(t) \\ n(0,a) = n_0(a) \end{cases}$$

where ρ is the hazard function introduced above.

An integral transformation. (G. Dumont - Ph.D. thesis)

If the initial distributions n_0 and p_0 satisfy:

$$p_0(v) = \int_0^\infty \frac{q(a,v)}{\int_0^1 q(a,w)\,\mathrm{d}w} n_0(a)\,\mathrm{d}a$$

then the corresponding solutions satisfy

$$p(t,v) = \int_0^\infty \frac{q(a,v)}{\int_0^1 q(a,w)\,\mathrm{d}w} n(t,a)\,\mathrm{d}a.$$

An integral transformation. Open questions - in working progress.

- The inverse transformation?
- Uniqueness of the above presented transformation?

Importance:

- Age-structured systems have been intensively studied over the last decades; in particular, qualitative results on the solutions, asymptotic behavior, control problems have been analyzed. Being to able to write the evolution of repartitions of neurons with respect to the "age", meaning the time between two consecutive spikes, will help giving answers to numerous problems such as those quoted above.

Population density models for connected neurons

The population density models for connected neurons are based on few modeling assumptions:

- The population of neurons is homogeneous, i.e. all the neurons have the same characteristics; in particular they are all supposed to emit spikes at the same threshold value and are reset to the same given reset value.
- they all receive the same input from the rest of the population

Adding some variability in the model. Escape rate model

In order to introduce some heterogeneity in the population, one may assume that the neurons do not emit a spike at a fix threshold potential value. An idea to model this is given by the *escape rate* or *hazard function* introduced by W. Gerstner and W.M. Kistler. The strict firing threshold is replaced by a stochastic firing criterion; spikes occur at any time with a probability density

$$\rho = f(u - \eta) \quad \text{with} \quad f \longrightarrow 0 \quad \text{as} \quad u \longrightarrow -\infty$$

Escape rate model

The escape rate depends on the momentary distance of the potential from the threshold; the neuron can emit a spike when its membrane potential is in a certain interval.
The sharp threshold is obtained for:

$$f(u-\eta) = \begin{cases} 0, & u < \eta \\ \Delta^{-1}, & u \geq \eta \end{cases}$$

Escape rate model

In population density formalism, taking into account this assumption will lead to introduction of a "mortality rate" in the partial differential equation that gives the evolution of the neurons' density in the phase space:

- the firing rate will no longer be the flux through the fix threshold, but is given by

$$r(t) = \sigma(t) \int_0^{+\infty} \rho(v - \eta) \int_v^{v-h} p(t, w)\, dw\, dv$$

- σ - the average reception rate and ρ- the escape rate

Escape rate model

$$\begin{cases} \frac{\partial}{\partial t} p(t,v) - \frac{\partial}{\partial v}(vp(t,v)) + \rho(v-\eta)\sigma(t) \int_v^{v-h} p(t,w)\,dw = \\ = \sigma(t)\left(p(t,v-h) - p(t,v)\right) + \delta(v-v_r)r(t) \quad \text{for} \quad v \in (0;+\infty) \\ p(t,\eta) = 0 \end{cases}$$

- ρ is the equivalent of a "mortality rate" in age-structured systems

Variability of the reset potential

- Since we assumed variability in the firing threshold of neurons of the population, it seems natural to assume the same variability in the reset potential
- Neurons of the population will not be re-injected in a fix reset potential value. Then $\delta(v - v_r)r(t)$ that expresses the re-injection of the neurons that fired in the reset potential value will be replaced by a term $\int_0^1 k(v, v')p(t, v')\,\mathrm{d}v'$
- we shall consider the diffusion limit, i.e., the second order approximation of the integral $\int_{v-h}^{v} p(t, w)\,\mathrm{d}w$.

Variability of the reset potential. Open questions.

- finding k such that the equation is a conservation law;
- finding appropriate boundary conditions; an idea is to use the dynamic boundary conditions used in size- structured models (Farkas).
- analysis of the solution of the model.