Qualitative properties on a Fokker-Planck equation in neurosciences

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from collaborations with M. Caceres, J.-A. Carrillo, K. Ikeda, B. Perthame, P. Roux, R. Schneider, D. Smets.

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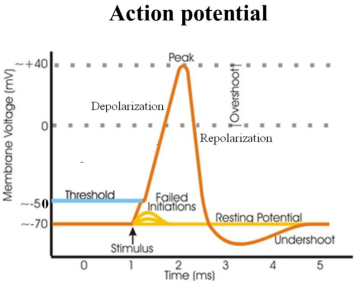
General problematic : How collective neuronal dynamics can emerges from individual neuron ?

It may depends on several aspects as :

- Intrinsic dynamic of each neuron
- Type of coupling between neuron
- Memory effects
- delay of transmission
- ....

Description of a unit neural activity :

To communicate neurons emit action potential that is also calling ”spike”.



This phenomenon involves several complex processes including: opening and closing of various ion channels.

Leaky Integrate and Fire model :

- Neuron describe via its membrane potential $v \in (-\infty, V_F)$
- When the membrane potential reach the value V_F, the neuron spikes
- After a spike, the neuron, instantly, reset at the value V_R.

Model chosen (Brunel, Hakim) :

$$\frac{\partial p}{\partial t}(v,t) + \underbrace{\frac{\partial}{\partial v}\left[\left(-v + bX(t)\right)p(v,t)\right]}_{\text{Leaky Integrate and Fire}} - \underbrace{a\frac{\partial^2 p}{\partial v^2}(v,t)}_{\text{noise}} = \underbrace{N(t)\delta(v - V_R)}_{\text{neurons reset}}, \qquad v \leq V_F\,,$$

$$p(V_F,t) = 0, \quad p(-\infty,t) = 0, \quad p(v,0) = p^0(v) \geq 0 \quad N(t) := -a\frac{\partial p}{\partial v}(V_F,t) \geq 0\,.$$

- $p(v,t)$: density of neurons at time t with a membrane potential $v \in (-\infty, V_F)$
- b : strength of interconnexions.
- $N(t)$: Flux of neurons which discharge at time t.
- $X(t)$: Amplitude of stimulation of that receives the network at time t

Several choices for $X(t)$

- Instantaneous transmission $X(t) = N(t)$ (with Carrillo, Perthame, Smets)(2015)
- Delay transmission $X(t) = N(t - d)$. (with Caceres, Roux, Schneider) (2018) (and with K. Ikeda, P. Roux, D. Smets) (2019)

$$\frac{\partial p}{\partial t}(v,t) + \underbrace{\frac{\partial}{\partial v}\left[\left(-v + bN(t)\right)p(v,t)\right]}_{\text{Leaky Integrate and Fire}} - \underbrace{a\frac{\partial^2 p}{\partial v^2}(v,t)}_{\text{noise}} = \underbrace{N(t)\delta(v - V_R)}_{\text{neurons reset}}, \qquad v \leq V_F\,,$$

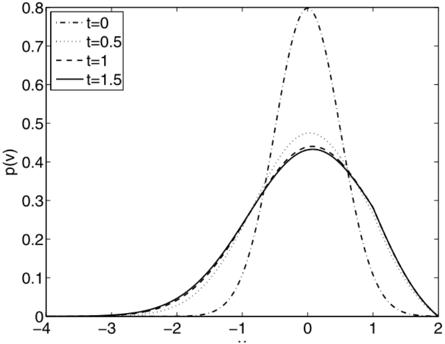
$$p(V_F,t) = 0, \qquad p(-\infty,t) = 0, \qquad p(v,0) = p^0(v) \geq 0\,.$$

$$N(t) := -a\frac{\partial p}{\partial v}(V_F,t) \geq 0\,.$$

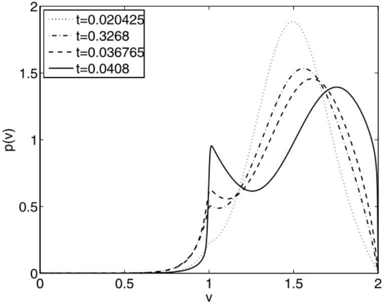
Well posedness of the solution ?

The total activity of the network $N(t)$ acts instantly on the network.

1. For all $b > 0$, by well choosing the initial data, we have blow-up (Caceres, Carrillo, Perthame)
2. As soon $b \leq 0$, the solution is globally well defined (Carrillo, González, Gualdani, Schonbek, Delarue, Inglis, Rubenthaler, Tanré, Carrillo, Perthame, Salort, Smets).



From Carrillo, Caceres, Perthame



t=0.020425
t=0.3268
t=0.036765
t=0.0408
p(v)
v
0
0.5
1
1.5
2

Stationary states (Caceres, Carrillo, Perthame)

Implicit formula

$$p_\infty(v) = \frac{N_\infty}{a} e^{-\frac{(v-bN_\infty)^2}{2a}} \int_{\max(v,V_R)}^{V_F} e^{\frac{(w-bN_\infty)^2}{2a}} dw$$

with the constraint on N_∞

$$\int_{-\infty}^{V_F} p_\infty(v)dv = 1.$$

1. There exists $C > 0$ such that, if $b \leq C$, there exists a unique stationary state
2. for intermediate b and some range of parameters (V_R, V_F, a), there exists at least two stationary states
3. If b is big enough, there is no stationary states.

Asymptotic qualitative dynamic if $b = 0$: (no interconnexions) solutions converge to a stationary state (Caceres, Carrillo, Perthame)

Idea of the proof :

- Entropy inequality with $G(x) = (x-1)^2$

$$\frac{d}{dt}\int_{-\infty}^{V_F} p_\infty(v) G\left(\frac{p(v,t)}{p_\infty(v)}\right) dv \leq -2a \int_{-\infty}^{V_F} p_\infty(v) \left[\frac{\partial}{\partial v}\left(\frac{p(v,t)}{p_\infty(v)}\right)\right]^2 dv.$$

- Poincaré estimates

$$\int_{-\infty}^{V_F} \frac{(p-p_\infty)^2}{p_\infty} dv \leq C \int_{-\infty}^{V_F} p_\infty \left(\nabla\left(\frac{p-p_\infty}{p_\infty}\right)\right)^2 dv.$$

What happens if we add interconnexions ? (Carrillo, Perthame, Salort, Smets) (in 2015)

Inhibitory case (entropy methods and upper-solutions) :

- Uniform estimates on the flux of neurons N with respect to b and the initial data (assuming t large enough)
- Exponential convergence to the stationary state if $|b|$ small enough (global attractor)

Exitatory case (combining entropy methods and some kind of supersolutions) :

- Estimates on N, depending on the initial data and b.
- Exponential convergence to a unique stationary state for sufficiently weak interconnections with respect to the initial data (not global attractor)

Existence of periodic solutions ?

- Not numerically observed

Theorem :

Inhibitory case :

- There exists a constant C, such that for all initial data and $b \leq 0$, there exists $T > 0$ such that for all $I \subset [T, +\infty)$,

$$\int_I N(t)^2 dt \leq C(1 + |I|).$$

- Assume the initial data in L^∞. Then, for all $b \leq 0$, there exists $C > 0$ such that

$$\|N\|_{L^\infty} \leq C.$$

Excitatory case :

- Given an initial data and $b > 0$ small enough, $\exists\ C > 0$ such that for all interval I,

$$\int_I N(t)^2 dt \leq C(1 + |I|)$$

Theorem :

Inhibitory case :

- Let $b \leq 0$. $\exists\, C, \mu > 0$ such that for all $0 \leq -b \leq C$ and all initial data

$$\int_{-\infty}^{V_F} p_\infty \left(\frac{p - p_\infty}{p_\infty}\right)^2 (t, v)dv \lesssim e^{-\mu t} \int_{-\infty}^{V_F} p_\infty \left(\frac{p - p_\infty}{p_\infty}\right)^2 (0, v)dv.$$

Excitatory case :

- Given an initial data, if $b > 0$ is small enough, then $\exists\, \mu > 0$ such that

$$\int_{-\infty}^{V_F} p_\infty \left(\frac{p - p_\infty}{p_\infty}\right)^2 (t, v)dv \lesssim e^{-\mu t} \int_{-\infty}^{V_F} p_\infty \left(\frac{p - p_\infty}{p_\infty}\right)^2 (0, v)dv.$$

Entropy estimate

Classical entropy estimates : Let $G(x) = (x-1)^2$, then

$$\frac{d}{dt}\int_{-\infty}^{V_F} p_\infty(v) G\left(\frac{p(v,t)}{p_\infty(v)}\right) dv =$$

$$\underbrace{-N_\infty\left[G\left(\frac{N(t)}{N_\infty}\right) - G\left(\frac{p(V_R,t)}{p_\infty(V_R)}\right) - \left(\frac{N(t)}{N_\infty} - \frac{p(V_R,t)}{p_\infty(V_R)}\right) G'\left(\frac{p(V_R,t)}{p_\infty(V_R)}\right)\right]}_{\leq 0 \text{ because } G \text{ convex}}$$

$$-2a\int_{-\infty}^{V_F} p_\infty(v)\left[\frac{\partial}{\partial v}\left(\frac{p(v,t)}{p_\infty(v)}\right)\right]^2 dv$$

$$\underbrace{+2b(N-N_\infty)\int_{-\infty}^{V_F} p_\infty\left[\partial_v\left(\frac{p(v,t)}{p_\infty(v)}\right)\left(\frac{p(v,t)}{p_\infty(v)} - 1\right) + \partial_v\left(\frac{p(v,t)}{p_\infty(v)}\right)\right] dv.}_{\text{non linear part}}$$

Strategy to obtain uniform estimates (inhibitory case)

Introduction of a fictif stationary state associated to a parameter $b_1 > 0$ different from $b \leq 0$.

For all convex function G regular,

$$\frac{d}{dt} p^1_\infty(v) G\left(\frac{p(v,t)}{p^1_\infty(v)}\right) =$$

$$-N^1_\infty \delta_{v=V_R} \left[G\left(\frac{N(t)}{N^1_\infty}\right) - G\left(\frac{p(v,t)}{p^1_\infty(v)}\right) - \left(\frac{N(t)}{N_\infty} - \frac{p(v,t)}{p^1_\infty(v)}\right) G'\left(\frac{p(v,t)}{p^1_\infty(v)}\right)\right]$$

$$-a p^1_\infty(v)\; G''\left(\frac{p(v,t)}{p^1_\infty(v)}\right)\; \left[\frac{\partial}{\partial v}\left(\frac{p(v,t)}{p^1_\infty(v)}\right)\right]^2$$

$$+(bN(t) - b_1 N^1_\infty) \frac{\partial}{\partial v} p^1_\infty(v) \left[G\left(\frac{p(v,t)}{p^1_\infty(v)}\right) - \frac{p(v,t)}{p^1_\infty(v)} G'\left(\frac{p(v,t)}{p^1_\infty(v)}\right)\right].$$

Idea of proof for uniform estimates.

We choose $G(x) = x^2$, $b_1 > 0$ given, we multiply by a function γ supported on $(V_R, V_F]$, to have

$$\frac{d}{dt}\int_{-\infty}^{V_F} p_\infty^1 \left(\frac{p}{p_\infty^1}\right)^2 (t,v)\gamma(v)dv =$$

$$\int_{-\infty}^{V_F} (-v + bN(t))p_\infty^1 \left(\frac{p}{p_\infty^1}\right)^2 (t,v)\gamma'(v)dv - \frac{N^2(t)}{N_\infty^1}(t)\gamma(V_F)$$

$$-2a\int_{-\infty}^{V_F} p_\infty^1 \left(\partial_v\left(\frac{p}{p_\infty^1}\right)\right)^2 \gamma(v)dv + a\int_{-\infty}^{V_F} p_\infty^1 \left(\frac{p}{p_\infty^1}\right)^2 (t,v)\gamma''(v)dv$$

$$-\left(bN(t) - b_1 N_\infty^1\right)\int_{-\infty}^{V_F} \gamma(v)\partial_v p_\infty^1 \left(\frac{p}{p_\infty^1}\right)^2 dv.$$

Conclusion of instantaneous LIF model

- Equation ill posed as soon $b > 0$ if the initial data is well chosen.
- If $b > 0$ is small enough and the initial data well chosen, exponential convergence to the unique stationary state.
- In the inhibitory case, uniform estimates on $N(t)$ and exponential convergence for $|b|$ small enough.
- Question of proof of convergence to the unique stationary state open, for the inhibitory case and $|b|$ large
- Question of periodic solution is totally open.

Equation with delay

$$\frac{\partial p}{\partial t}(v,t) + \underbrace{\frac{\partial}{\partial v}\left[\left(-v + bN(t-d)\right)p(v,t)\right]}_{\text{Leaky Integrate and Fire}} - \underbrace{a\frac{\partial^2 p}{\partial v^2}(v,t)}_{\text{noise}} = \underbrace{N(t)\delta(v - V_R)}_{\text{neurons reset}}, \qquad v \le V_F\,,$$

$$p(V_F,t) = 0, \qquad p(-\infty,t) = 0, \qquad p(v,0) = p^0(v) \ge 0\,.$$

$$N(t) := -a\frac{\partial p}{\partial v}(V_F,t) \ge 0\,.$$

Principal properties (with Caceres, Roux et Schneider) (see also Delarue, Inglis, Rubenthaler, Tanré)

- No more blow-up
- Existence and uniqueness of a global classical solution
- Exponential convergence to a unique stationary state as soon $|b|$ small enough (with same assumption as in the case without delay).

Idea of proof for global existence :

- Via a change of variable, we obtain an implicit equation on the flux N.
- Via a fix point argument, we obtain local existence
- We construct a super solution to obtain uniform estimates and conclude to global existence

Construction of the supersolution for a given input N^0 :

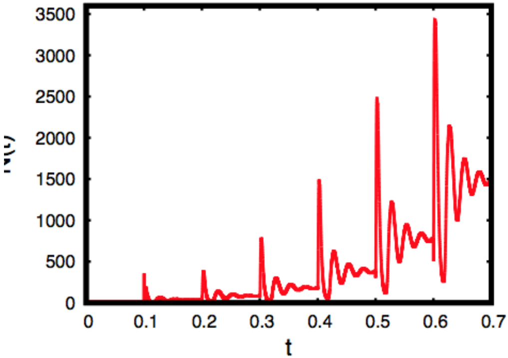
$$\bar{\rho}(v,t) = e^{\xi t} f(v), \qquad \xi \text{ large enough}$$

Construction of f

1. Let $\varepsilon > 0$ with $\frac{V_F+V_R}{2} + \varepsilon < V_F$ and let $\psi \in C_b^\infty(\mathbb{R})$ satisfying $0 \leq \psi \leq 1$ and
$$\psi \equiv 1 \text{ on } (-\infty, \frac{V_F+V_R}{2}) \text{ and } \psi \equiv 0 \text{ on } (\frac{V_F+V_R}{2} + \varepsilon, +\infty).$$
2. Let $B > 0$ such that
$$\forall t \geq 0, \forall v \in (V_R, V_F), \quad |-v + bN^0(t)| \leq B$$
and $\delta > 0$ such that $a\delta - B \geq 0$.
3. We chose
$$f \equiv 1 \text{ on } (-\infty, V_R]$$
$$f(v) = e^{V_R - v}\psi(v) + \frac{1}{\delta}(1-\psi(v))(1 - e^{\delta(v-V_F)}) \text{ on } (V_R, V_F].$$

What about periodic solutions in the excitatory case ?

Still no periodic solutions if we add a delay in the excitatory case

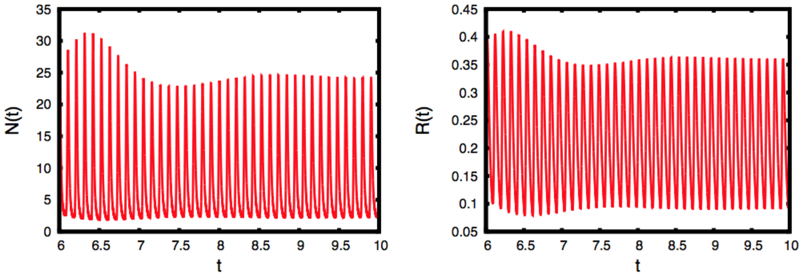


from Caceres Schneider

$$\frac{\partial p}{\partial t}(v,t) + \underbrace{\frac{\partial}{\partial v}\left[\left(-v + bN(t-d)\right)p(v,t)\right]}_{\text{Leaky Integrate and Fire}} - \underbrace{a\frac{\partial^2 p}{\partial v^2}(v,t)}_{\text{noise}} = \underbrace{\frac{R(t)}{\tau}\delta(v - V_R)}_{\text{neurons reset}}, \qquad v \leq V_F\,,$$

$$R'(t) + \frac{R}{\tau} = N(t)$$

Periodic solutions if b large enough if we add a refractory state



from Caceres Schneider

Conclusion on the preceding results of the NLIF model

- Instantaneous transmission implies often an ill-posed problem and no periodic solutions seems to numerically emerge
- Adding of delay implies global existence and emergence but still no periodic solutions if $b > 0$
- Adding a refractory state, we obtain the emergence of periodic solutions.

Setting : We consider the inhibitory case with delay transmission ($b << 0$, $d = 1$, $V_F = 0$, $a = 1$)

$$\frac{\partial p}{\partial t}(v,t) + \underbrace{\frac{\partial}{\partial v}\left[\left(-v + bN(t-1)\right)p(v,t)\right]}_{\text{Leaky Integrate and Fire}} - \underbrace{\frac{\partial^2 p}{\partial v^2}(v,t)}_{\text{noise}} = \underbrace{N(t)\delta(v - V_R)}_{\text{neurons reset}}, \qquad v \leq 0\,,$$

$$p(0,t) = 0, \quad p(-\infty,t) = 0, \quad p(v,0) = p^0(v) \geq 0 \quad N(t) := -\frac{\partial p}{\partial v}(0,t) \geq 0\,.$$

Theorem (with K. Ikeda, P. Roux, D. Smets) :
The solution of NLIF can be written as

$$p(t,v) = \phi(v - c(t)) + R(v,t), \text{ where } \phi(x) = \frac{1}{\sqrt{2\pi}} e^{-\frac{x^2}{2}}$$

and where R is such that,

$$2e^{-t}\int_0^t e^s \|R(s)\|_{L^2}^2 ds \leq \|U(0)\|_{L^2}^2 e^{-t} + \widetilde{C}e^{-t}\int_0^t e^s N(s)ds - \|U(t)\|_{L^2}^2$$

where

$$U(t) = \int_{-\infty}^{v} R(t,w)dw \text{ and } c'(t) + c(t) = bN(t-1).$$

Can we theoretically tackle emergence of periodic solutions ?

Formal restriction to a delay equation

$$c'(t) + c(t) = bc(t-1)e^{-\frac{c^2(t-1)}{2}}.$$

Theorem (with K. Ikeda, P. Roux, D. Smets)

Assume that $b << 0$ is small enough, then there exists a non trivial periodic solution of Equation

$$c'(t) + c(t) = bc(t-1)e^{-\frac{c^2(t-1)}{2}}.$$

Idea of the proof : Inspired from a proof from K. P. Hadeler and J. Tomiuk.

- Unstable eigenvalues of the linearized problem with a good control of the imaginary part
- Application of a fixed point Browder Theorem via an introduction of an appropriate cone of initial functions where we can obtain useful estimates of the solution of the delay equation.

Thank you

Let $\mathscr{D}$ be a closed subset of a Banach space and $\mathscr{F}: \mathscr{D} \to \mathscr{D}$ a continuous mapping. Let $\bar{x}$ be a fixed point of $\mathscr{F}$ with the following property: There is an open neighborhood $U \ni \bar{x}$, $U \subset \mathscr{D}$, such that for every $x \in U$ with $x \neq \bar{x}$ there is an integer $n = n(x)$ for which $\mathscr{F}^{(n)} x \notin U$. Such point $\bar{x}$ is called an ejective fixed point of $\mathscr{F}$.

Theorem 2 (BROWDER [4]). *Let $\mathscr{D}$ be a closed, bounded, convex set of infinite dimension in a Banach space, and let $\mathscr{F}: \mathscr{D} \to \mathscr{D}$ be continuous and compact. Then $\mathscr{F}$ has a fixed point which is not ejective.*