Some PDE models in neuroscience

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Introduction and position of the problem

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
- ....

Introduction and position of the problem

Aim : Test the different assumptions made on

- the unit neuron
- the coupling
- memorization effect

to understand the impact on the patterns generated by the network.

Introduction and position of the problem

Model considered : To answer the above questions, we will focus on two models

- The time elapsed model (structured partial differential equation model)
- The nonlinear leaky integrate and fire model (Fokker-Planck equation)

Remarks :

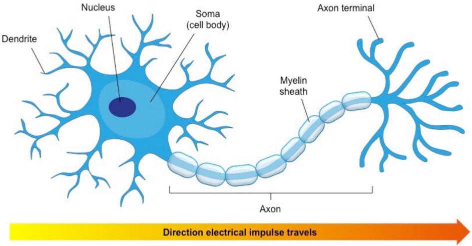
- Those models are not exhaustive and there exists several other PDE's models to describe neural networks
- Very rich dynamics can emerge from those two equations and some of them are easy to tackle theoretically.

Plan of the course

Plan of the course :

- Some classical models for single neuron
- Time elapsed PDE model
- Noisy Leaky Integrate and Fire PDE model

Neural cell.



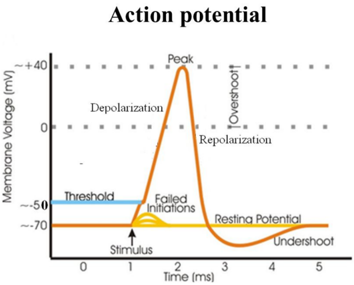
Neuron: specialized cell that

- is electrically excitable
- receive, analyse and transmit signal to other neurons

Neural cell.

Description of a unit neural activity :

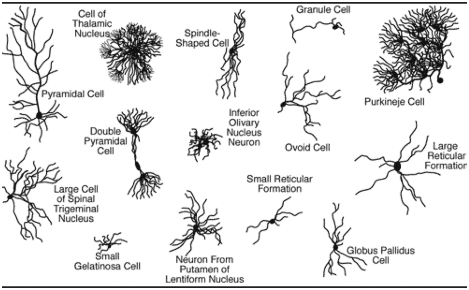
To communicate neurons emit action potential that is also calling ”spike”.



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

Neural cell

Vast spectrum of different types of neurons that can be classified according to their shape, their intrinsic dynamics ...



Model of neural cell

Two aspects of modelling :

- Description via intrinsic mechanisms involved on a unit neuron
- Description via the frequency of ”spikes” of the neuron, omitting the explicit modelling of the intrinsic mechanisms involved on the neuron.

Principal mathematical tools :

- deterministic dynamical systems
- stochastic models.

Description via intrinsic mechanisms on a unit neuron

Intrinsic mechanisms on a unit neuron :

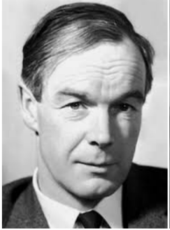
- In the simplest models, the cell is assimilated to an electrical circuit
- In more precise models, for example, propagation of signal along the axon or the impact of dendrites may be included

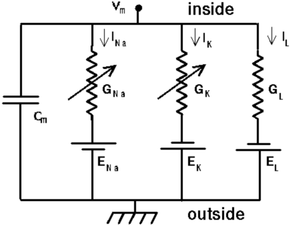
Main electrical circuit model type :

- Hodgkin-Huxley model
- FitzHugh Nagumo model
- Integrate and fire model
- Morris-Lecar model
- ...

Hodgkin-Huxley model

Hodgkin-Huxley model (1952) :





$$C\frac{dV}{dt} = \underbrace{m^3 h g_{Na}(V_{Na} - V(t))}_{\text{Sodium current}} + \underbrace{n^4 g_K(V_K - V)}_{\text{Potassium current}} + \underbrace{g_L(V - V_L)}_{\text{leak current}} + \underbrace{I(t)}_{\text{Input}}$$

$$\tau_n(V)\frac{dn}{dt} = (n_\infty(V) - n),$$ n: probability of potassium channel to be open

$$\tau_m(V)\frac{dm}{dt} = (m_\infty(V) - m)$$ m: probability of Sodium channel to be actif

$$\tau_h(V)\frac{dh}{dt} = (h_\infty(V) - h)$$ h: probability of Sodium channel to be open.

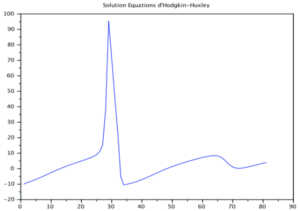
Hodgkin-Huxley model

Hodgkin-Huxley model (1952) :

- 4 coupled equations (one on membrane potential and three on ion channels)
- Allow to reproduce several typical patterns
- Difficult to study mathematically and numerically expensive

Simplified models allowing to well capture several patterns of neurons ?

- Replace some variables by their stationary states (fast variables)
- Do not explicitly model ion channels



FitzHugh-Nagumo model

FitzHugh Nagumo model : Involves two variables

- The membrane voltage v
- The recovery variable w

Equations :

$$\varepsilon v'(t) = v - \frac{v^3}{3} - w + I(t), \quad I(t) : \text{ external current input}$$

$$w'(t) = (v + a - bw).$$

FitzHugh-Nagumo model

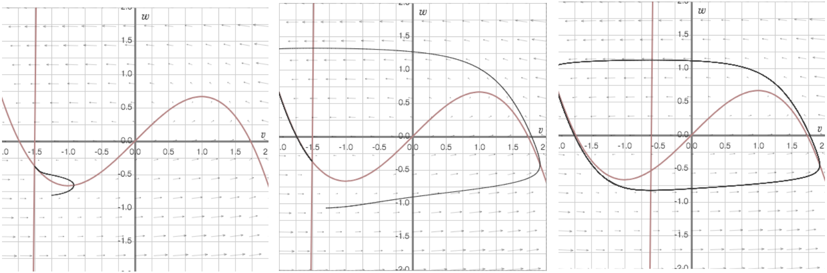
Typical patterns that may capture FitzHugh Nagumo model : Depending of the choice of the parameters (even in the simplest case $I = 0$, $b = 0$)

- Fast convergence to a stationary state
- Excitable case : the neuron emit a spike before coming back to its resting state
- Oscillations and convergence to a periodic solution (limit cycle)

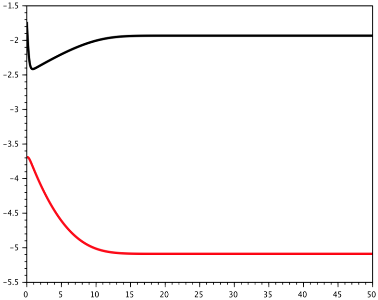
FitzHugh-Nagumo model

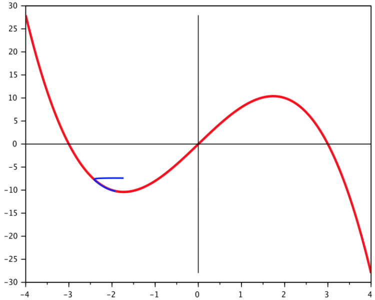
Case $I = cste$, $b = 0$

- Unique stationary state
- Stable if $f' < 0$ and unstable if $f' > 0$.

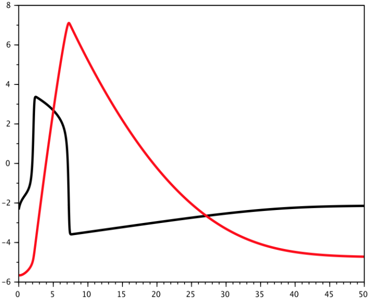


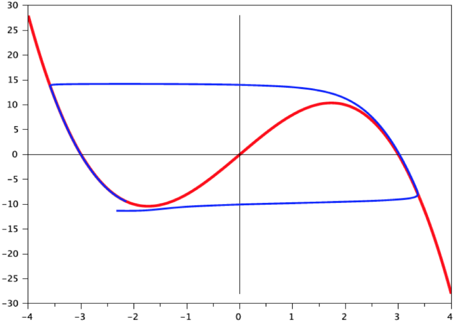
FitzHugh-Nagumo model



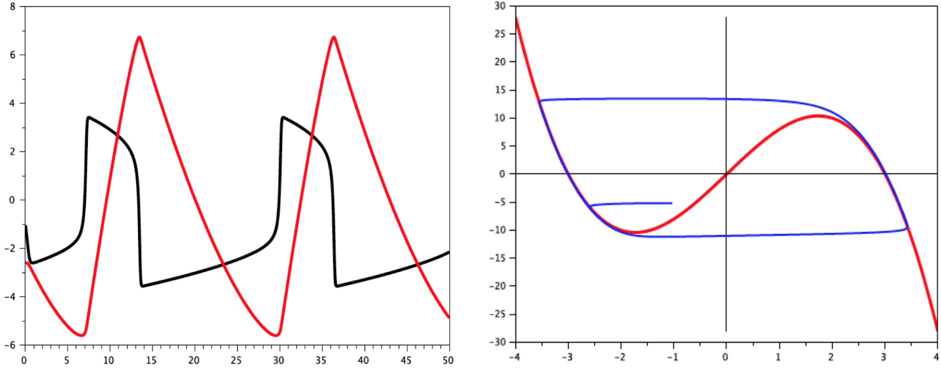


FitzHugh-Nagumo model





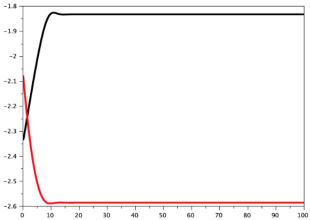
FitzHugh-Nagumo model

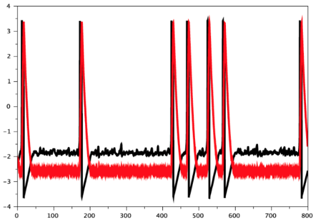


FitzHugh-Nagumo model, role of noise

$$\varepsilon v'(t) = v - \frac{v^3}{3} - w + I(t), \quad I(t): \text{ external current input}$$

$$w'(t) = (v + a - bw) + \frac{dB(t)}{dt}.$$





Leaky Integrate and Fire Model (from Lapicque,1907).

Leaky Integrate and Fire Model :

$$\tau V'(t) = -V(t) + RI(t), \quad V(t) < V_F, \qquad I\text{: external input}$$

$$V(t_-) = V_F \Rightarrow V(t_+) = V_R, \quad V_R < V_F.$$

- V_F is the value of the action potential
- V_R is the reset potential
- We may add some noise : $\tau d_t V = (-V(t) + RI(t))dt + \sigma dW(t), \; V(t) < V_F.$

Very simple structure :

- Linear differential equation on the potential V (if $V < V_F$)
- Spiking modelled via a threshold V_F and jump of V to a given value V_R.

Leaky Integrate and Fire Model (from Lapicque,1907).

FIGURE 4 | Fitting spiking models to electrophysiological recordings. (A) The response of a cortical pyramidal cell to a fluctuating current (from the INCF competition) is fitted to various models: MAT (Kobayashi et al., 2009), adaptive integrate-and-fire, and Izhikevich (2003). Performance on the training data is indicated on the right as the gamma factor (close to the proportion of predicted spikes), relative to the intrinsic gamma factor of the neuron (i.e., proportion of common spikes between two trials). Note that the voltage units for the models are irrelevant (only spike trains are fitted). **(B)** The response of an anteroventral cochlear nucleus neuron (brain slice made from a P12 mouse, see Methods in Magnusson et al., 2008) to the same fluctuating current is fitted to an adaptive exponential integrate-and-fire [Brette and Gerstner, 2005; note that the responses do not correspond to the same portion of the current as in **(A)**]. The cell was electrophysiologically characterized as a stellate cell (Fujino and Oertel, 2001). The performance was $\Gamma = 0.39$ in this case (trial-to-trial variability was not available for this recording).

From C. Rossant et al, Frontiers in Neuroscience (2011)

Wilson-Cowan model.

Wilson-Cowan model : models probability of a neuron to spike at time t, typically

$$u'(t) = -u(t) + S(u(t)),\ \text{where } S \text{ is a sigmoidal function.}$$

Several useful extention/application

- Including inhibitory/excitatory neurons
- Extension to spatial models leading to neural fields equations

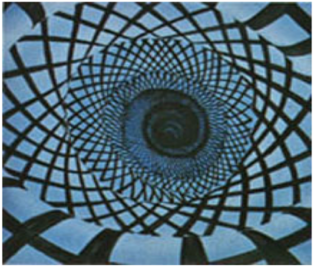
$$u'(t,x) = -u(t,x) + S(\int w(x,y)u(t,y)dy) + I(t,x).$$

- Application in epilepsy in visual cortex

Wilson-Cowan model.

Feature

- multiple steady states and bifurcation theory (S. Amari, Bressloff-Golubitsky, Chossat-Faugeras-Faye)
- Interpretation of visual illusions and visual hallucinations (Klüver, Oster, Siegel...)



Stochastic processes

Ponctual processes/counting processes :

- homogeneous Poisson processes
- inhomogeneous Poisson processes
- Renewal processes
- Hawkes processes
- ...

Homogeneous Poisson processes

Homogeneous Poisson processes : Given a parameter $\lambda > 0$ and a time interval I of size T,

$$P(\text{Neuron discharge } n \text{ times on } I) = \frac{(\lambda T)^n}{n!} e^{-\lambda T}.$$

Main properties

- Time independent
- No dependance with respect to the past
- Probability of a neuron that has not yet discharge at time t : $e^{-\lambda t}$

Inhomogeneous Poisson processes

Inhomogeneous Poisson processes : Given a function $\lambda > 0$ and a time interval $I = [a, b]$,

$$P(\text{Neuron discharge } n \text{ times on } I) = \frac{(\int_a^b \lambda(s)ds)^n}{n!} e^{-(\int_a^b \lambda(s)ds)}.$$

Main properties

- Time dependent
- No dependance with respect to the past
- Probability of a neuron that has not yet discharge at time t : $e^{-\int_0^t \lambda(s)ds}$.

Renewal processes/Hawkes processes

Renewal processes : include models with memory of the preceding spike and therefore useful to integrate the refractory period.

Main properties

- The delay between two consecutive spikes are independent
- The delay between two consecutive spikes are identically distributed

Hawkes processes : More complex processes that allows to model synaptic integration (see Caceres, Chevallier, Doumic, Reynaud-Bouret)

From the microscopic to macroscopic scale ?

Macroscopic scale via mean field assumptions leading to PDE's :

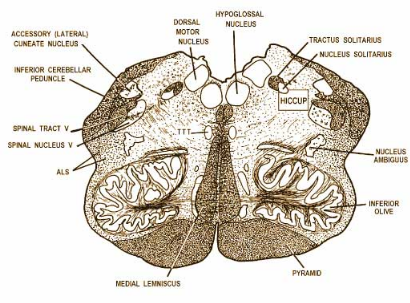
- Infinitely many neurons
- Homogeneous interconnexions
- Each neuron receive the mean activity of the network

Many PDE models obtain via this paradigm

- time-elapsed model
- Leaky-integrate and fire type models (Fokker-Planck model)
- oscillators (Kuramoto equation)
- ...

Biological motivation and setting

Biological motivation and setting : From Pham, Pakdaman, Champagnat, Vibert



http://www.neuroanatomy.wisc.edu/virtualbrain/BrainStem/11Solitarius.html

- Networks at the Nucleus Tractus Solitarius (NTS) responsible of basic rhythms.
- NTS contains neural circuits with only excitatory connections displaying a spontaneous activity.
- No pacemaker neurons responsible for the spontaneous activity.
- Simple partial differential equation model to explore the possible mechanisms of spontaneous activity generation ?

First studies

First studies :

- Simulation of several computational models adjusted to the experiments revealed that the network could sustain regular rhythmic activity in some parameter ranges
- Phenomenon of spontaneous activity persists in networks with diverse connectivity.

Conclusion

- That the phenomenon can be observed in many models suggests that the fine details of the model may not be at the core of the mechanism, and that to get the gist of the phenomena, one may focus on a few features of neural dynamics.
- We have proposed a simple mathematical model where neurons are describe via the time elapsed since the last discharge to obtain theoretically this phenomenon of spontaneous activity observed.

Elapsed time model

Main assumptions on the model.

Dynamic on each neuron :

- The neurons are excitatory
- Even without stimulations, the neurons have an activity
- Neurons discribe via the time elapsed sinc the last discharge
- When a neuron discharge, it's new intrinsic dynamic may depends on it's past activity

Interconnexions :

The amplitude of stimulation $X(t)$ is homogeneous with

$$X(t) = \int_0^t \alpha(s) N(t-s) ds$$

where $N(t)$ is the flux of neurons which discharge at time t. To simplify, we take here $X(t) = N(t)$.

Time elapsed model

$$\underbrace{\frac{\partial n(s,t)}{\partial t} + \frac{\partial n(s,t)}{\partial s}}_{\text{aging neurons}} + \underbrace{p(s, N(t))n(s,t)}_{\text{death of the neurons}} = \underbrace{\int_0^{+\infty} K(s,u)p(u, N(t))n(u,t)du,}_{\text{Redistribution in age of the death neurons}}$$

$$N(t) := \int_0^{+\infty} p(s, N(t))\, n(s,t)ds, \quad n(s=0,t) = 0.$$

- $n(s,t)$: density of neurons at time t such that the time elapsed since the last discharge is s.
- $N(t)$: flux of neurons which discharge at time t
- $p(s,u)$: firing rate of the neurons of age s which discharge when they are submitted to an amplitude of stimulation $u \geq 0$.
- $K(s,u)$: Positive measure allowing to give the repartition of neurons which discharge at the state u and which reset at the state s.

Assumptions on p and K.

The function $p(s, u)$:

- The probability for a neuron to survive up to the age t :

$$P(s \geq t) = e^{-\int_0^t p(s,u)ds}.$$

- The account of refractory period

$$\partial_s p \geq 0 \text{ and } p \equiv 0 \text{ for } s \text{ small enough.}$$

- Excitatory neurons :

$$\partial_u p \geq 0.$$

- Interconnexions between the neurons :

$$\text{modeled via } \partial_u p, \quad \text{if no interconnexions } \partial_u p = 0.$$

Assumptions on p and K.

The kernel fragmentation $K(s,u)$:

- For each $u \geq 0$, $K(s,u)$ models the measure of probability for a neuron which has discharge at the age u to reset in the new state s.
- $K(s,u) = 0$ for $s > u$: all the neurons which discharge at an age u, reset at an age s smaller than u
- $\int_0^u K(s,u)ds = 1$, and so $\int_0^{+\infty} n(s,t)ds = 1, \quad \forall t \geq 0.$

Assumptions on p and K

The kernel fragmentation $K(s,u)$:

We also introduce the two following quantities :

- $0 \leq f(s,u) := \int_0^s K(s,u)ds \leq 1$ which is the probability for a neuron which discharge at the state u reset to an age smaller than s.
- $-\partial_u f := \Phi(s,u) \geq 0$ which implies that the bigger u is, the smaller the probability that a neuron which has discharge at the age u reset to a state smaller than s is small.

We assume that

$$\int_0^{+\infty} \Phi(s,u)ds = \theta < 1;$$

and

$$\int_0^u sK(s,u)ds \leq \theta u$$

i.e. the expected value of the new state of a neuron which has discharge at age u is smaller or equal to θu.

Main questions

Main questions : What is the impact of the strength of interconnections on the dynamic of the neural network ?

- 1. When the interconnections are low or inexistant, intuitively, we expect that the solution converges to a stationary state.
- 2. For hight interconnections, we expect the apparition of more complex patterns as periodic solutions.

Methods to tackle the problem

Case 1: dynamic ”almost linear” :

- Spectral methods ($K = \delta_{s=0}$) (Mischler, Weng)
- With entropy generalized methods, inspired by Laurençot and Perthame where we search decreasing functional by multiply the Equation by judicious test functions.

Case 2 : Situation more complex :

- Many different patterns and periodic solutions numerically observed.
- By well choosing p and K, explicit of infinitely many periodic solutions.

Plan of study without interconnexions.

Plan of study without interconnexions

- Existence and uniqueness of stationary state (Krein Rutman Theorem)
- Entropy type inequality
- Proof of convergence to a stationary state

Case without interconnections.

Stationary states Is there existence and unicity of the solution of Equation

$$\partial_s A + p(s)A = \int_0^{+\infty} K(s,u)p(u)A(u)du,$$

$$A(0) = 0, \quad A > 0, \int_0^{+\infty} A(s)ds = 1.$$

Krein-Rutman Theorem :

Let $T > 0$ and

$$C = \{f \in \mathcal{C}([0,T]) \text{ such that } f \geq 0\}.$$

Let T be a compact operator strictly positif on C. Then, the spectral radius of T is a simple eigenvalue of T and there exists a unique normalized eigenvector in $\mathring{C}$.

Case without interconnections.

- we set $\varepsilon > 0$, $R > 0$ and consider the operator $T : (C([0,R]) \to \mathcal{C}([0,R])$ which to f associate the solution

$$\partial_s A + (\mu + p(s))A - \int_0^R K(s,u)p(u)A(u)du = f, \quad A(0) = \varepsilon \int_0^R A(s)ds.$$

- For μ big enough $\varepsilon > 0$ small enough, T well defined and compact and we have $f > 0 \Rightarrow T(f) > 0$.

Conclusion

By Krein-Rutman Theorem, there exists $\lambda_{R,\varepsilon}$ and $A > 0$ such that

$$\partial_s A + (p(s) + \lambda_{R,\varepsilon})A = \int_0^R K(s,u)p(u)A(u)du, \quad A(0) = \varepsilon, \quad A > 0, \int_0^R A(s)ds = 1.$$

Case without interconnections.

Limit $R \to +\infty$, $\varepsilon \to 0$

- Compactness obtained via assumption (mass do not goes at the limit to infinity)

$$\int_0^u sK(s,u)ds \le \theta u, \quad \theta < 1.$$

Hence, at the limit $\int_0^{+\infty} A(s)ds = 1$.

- More precisely, for ε small enough and $R > 0$ big enough,

$$\varepsilon - \frac{2}{R} \le \lambda_{\varepsilon,R} \le \varepsilon, \quad (1-\theta)\int_0^R sA_{\varepsilon,R}(s)ds \le C, \quad \|A_{\varepsilon,R}\|_{L^\infty} + \|\partial_x A_{\varepsilon,R}\|_{L^1} \le C.$$

Case without interconnections : asymptotic analysis.

Convergence to the stationary state

- Setting $m(s,t) = n(s,t) - A(s)$, we find by linearity that m is solution of Equation

$$\partial_t m + \partial_s m + p(s)m = \int_0^{+\infty} p(u)K(s,u)m(u,t)du, \quad \int_0^{+\infty} m(s,t)ds = 0.$$

- For all $\alpha(s) \in \mathbb{R}$,

$$\int_0^{+\infty} p(u)K(s,u)m(u,t)du = \int_0^{+\infty} p(u)K(s,u)m(u,t) - \alpha(s)m(u,t)du.$$

Case without interconnections : asymptotic analysis.

with fragmentation term : If the kernel fragmentation ”mixed everything”, the above strategy will give nothing.

Strategy for general kernel fragmentation

- We consider the following new quantity

$$B(s,t) = \int_0^s n(u,t)du$$

  which models the probability for a neuron that the time elapsed since its last discharge is smaller than s.

- We search an entropy inequality on

$$M(s,t) := \int_0^s n(u,t) - A(u)du.$$

Case without interconnections : asymptotic analysis.

Equation on M : closed equation

$$\frac{\partial M(s,t)}{\partial t} + \frac{\partial M(s,t)}{\partial s} + p(s)M(s,t) = -\int_{u=s}^{\infty} \frac{\partial p(u)}{\partial u} f(s,u)M(u,t)du + \int p(u)\Phi(s,u)M(u,t)du.$$

By setting the absolute values

$$\frac{\partial |M(s,t)|}{\partial t} + \frac{\partial |M(s,t)|}{\partial s} + p(s)|M(s,t)| \leq \int_{u=s}^{\infty} |p'(u)||f(s,u)|M(u,t)|du + \int p(u)\Phi(s,u)|M(u,t)|du.$$

Case without interconnections : asymptotic analysis.

- if $p = cst > 0$, then, with

$$\int_0^{+\infty} \Phi(s,u)ds \le \theta,$$

We directly obtain that

$$\frac{d}{dt}\int |M(s,t)|ds \le (-1+\theta)\int p|M(u,t)|du.$$

- Else, we multiply Equation on M by a judicious test function P solution of

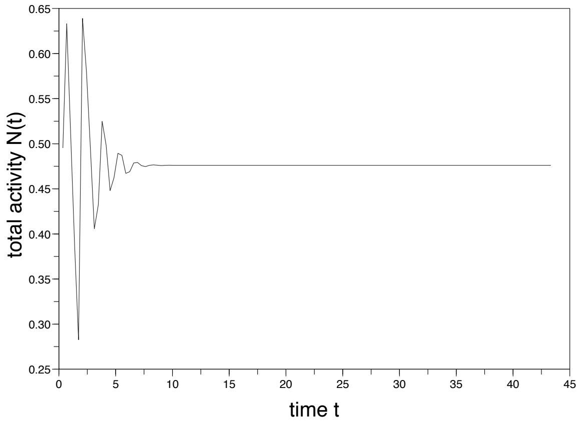
$$-\frac{\partial P(s)}{\partial s} + (\lambda + p(s))P(s) \ge \int_0^s \left[|p'(s)|f(u,s) + p(s)\Phi(u,s)\right] P(u)du.$$

- We then have

$$\frac{d}{dt}\int_0^{+\infty} P(s)|M(s,t)|ds \le \lambda \int_0^{+\infty} P(s)|M(s,t)|ds$$

- Exponential decreased for $|M|$ as soon $\lambda < 0$ and $P \ge C > 0$.
- As M and $\partial_t M$ are solution of the same Equation, we obtain exponential decrease of m in L^1.

Numerical simulation



Case of strong interconnections.

The study of periodic solution is complex. Numerically, we observe many periodic solutions when the strength of interconnections is strong enough.

Aim of this part : Explicitly construct many different periodic solutions in a particular case where the solution of the equation can be reduced to a time delay Equation on the flux of neurons $N(t)$.

Assumptions : We assume that $p(s,u) = \mathbb{I}_{s \geq \sigma(u)}$, where σ is a decreasing function, and $K(s,u) = \delta_{s=0}$.

Case of strong interconnections.

Reduction to a delay equation on N. Assume that we have a solution of our transport Equation and that

$$\frac{d}{dt}(\sigma(N(t)) \leq 1$$

Then, by using the mass conservation law, we have for all $t \geq \sigma^+$,

$$N(t) + \int_{t-\sigma(N(t))}^{t} N(s)ds = 1.$$

Proof

With the mass conservation, for all $t \geq \sigma^+$ we have

$$\int_0^{+\infty} n(s,t)ds = \int_0^{\sigma(N(t))} n(s,t)ds + \int_{\sigma(N(t))}^{+\infty} n(s,t)ds = \int_0^{\sigma(N(t))} n(s,t)ds + N(t).$$

Now, as $\frac{d}{dt}(\sigma(N(t)) \leq 1$, for $s \leq \sigma(N(t))$, we deduce that

$$n(s,t) = N(t-s).$$

Case of strong interconnections.

Construction of periodic solutions : We take the "inverse" problem : Given a periodic function $N(t)$ of period T, we consider the following Equation

$$\begin{cases} \frac{\partial n(s,t)}{\partial t} + \frac{\partial n(s,t)}{\partial s} + p(s,N(t))\; n(s,t) = 0, \qquad t \in \mathbb{R},\; s \geq 0, \\ n(s=0,t) = N(t). \end{cases}$$

As we look forward periodic solution n in time, we do not need initial data and the method of characteristics gives the solution

$$n(t,s) = N(t-s)e^{-\int_0^s p(u,N(u+t-s))du} \text{ if } t-s \geq 0.$$

By periodicity of n, we obtain that for all $s \leq kT$, $k \in \mathbb{N}$, we must have

$$n(t=0,s) = N(kT-s)e^{-\int_0^s p(u,N(u+kT-s))du}.$$

Hence finding periodic flux $N(t)$ of our Equation can reduced to find conditions on N such that the solution of the above Equation is also solution of the initial transport Equation; that is we must have

$$N(t) = \int_{\sigma(N(t))}^{+\infty} n(s,t)ds \text{ and } \int_0^{+\infty} n(s,t)ds = 1.$$

Case of strong interconnections.

Proposition (Criteria linking σ and N)

Let $\sigma(\cdot)$ be a decreasing function and let N be a T periodic function such that

$$\frac{d}{dt}\sigma\big(N(t)\big) \leq 1, \qquad 1 = N(t) + \int_0^{\sigma(N(t))} N(t-s)ds.$$

Assume that

$$p(s, N) = \mathbb{I}_{s>\sigma(N)}.$$

Then the solution of our Equation with N given is also solution of the non linear transport Equation.

Proof. We observe that, as $\frac{d}{dt}\sigma\big(N(t)\big) \leq 1$, then, for $s \in (0, \sigma(N(t)))$, we have $n(s,t) = N(t-s)$. We deduce, by setting $M(t) = \int_0^{+\infty} n(s,t)ds$, that

$$\frac{d}{dt}M(t) + M(t) = 1$$

and as M is periodic, we have $M = 1$, which proves the Proposition.

Case of strong interconnections.

Explicit construction of periodic solutions : We can construct infinitely many periodic solutions. The simplest example is the following

Let $\alpha > 0$, we set

$$0 < Nm(\alpha) := \frac{1}{2e^{\alpha} - 1} < Np(\alpha) := \frac{e^{\alpha}}{2e^{\alpha} - 1} < 1, \tag{1}$$

and we assume that

$$\sigma(x) = \begin{cases} 2\alpha & \text{on } [0, Nm(\alpha)], \\ \alpha - \ln(x) + \ln(Np(\alpha)) & \text{on } [Nm(\alpha), Np(\alpha)], \\ \alpha & \text{on } [Np(\alpha), \infty). \end{cases} \tag{2}$$

We can remark that, in this system, there exists a unique stationary state.

Then, the function N, α periodic defined by

$$N(t) = Np(\alpha)e^{-t}, \quad t \in (0, \alpha)$$

satisfies the assumptions of the Proposition.

Case of strong interconnections

Let

$$\sigma(x) = \begin{cases} \sigma_0 - \ln(Nm) + \ln(Np) & \text{on } [0, Nm], \\ \sigma_0 - \ln(x) + \ln(Np) & \text{on } [Nm, Np], \\ \sigma_0 & \text{on } [Np, \infty). \end{cases}$$

Proposition

Let $n \geq 0$ be an integer and $(\alpha_i)_{i \leq n+1}$ be an increasing sequence with $\alpha_0 = 0$. Define

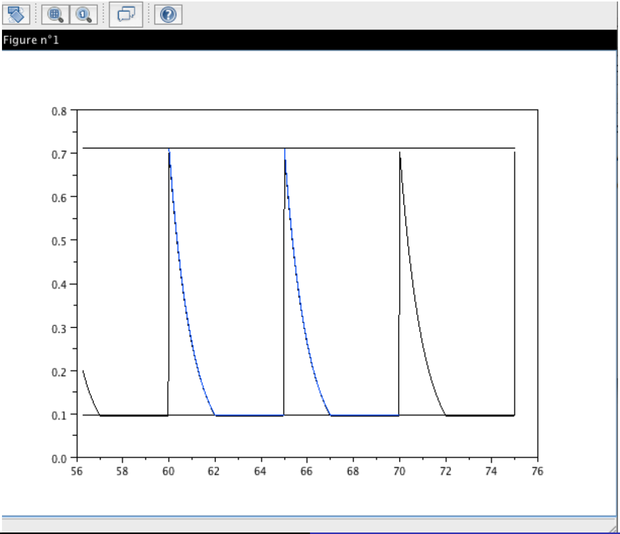
$$\begin{cases} Nm := \frac{1}{1+\sum_{i=1}^{n-1}(e^{\alpha_{i+1}-\alpha_i}-1)+\alpha_{n+1}-\alpha_n}, & N_n^+ := Nm, \\ N_i^+ := e^{\alpha_{i+1}-\alpha_i}\ Nm,\ i \in \{0, ..., n-1\}, & Np := \sup_{0 \leq i \leq n} N_i^+. \end{cases}$$

We consider the function σ given above with $\sigma_0 = \alpha_{n+1} - \alpha_1 + \ln(N_0^+/Np)$. Then, the α_{n+1}-periodic function N defined as

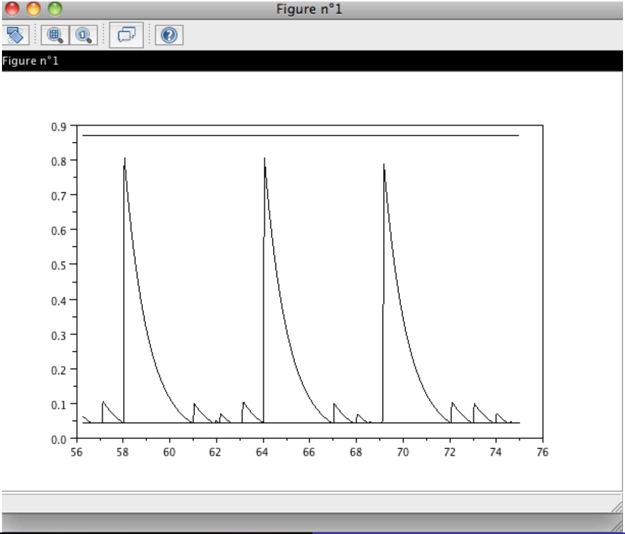
$$N(t) = N_i^+ e^{\alpha_i - t} \quad \text{for } t \in (\alpha_i, \alpha_{i+1}),\ 0 \leq i \leq n-1, \qquad N(t) := Nm = N_n^+ \quad \text{for } t \in (\alpha_n, \alpha_{n+1}),$$

satisfies the wanted assumptions

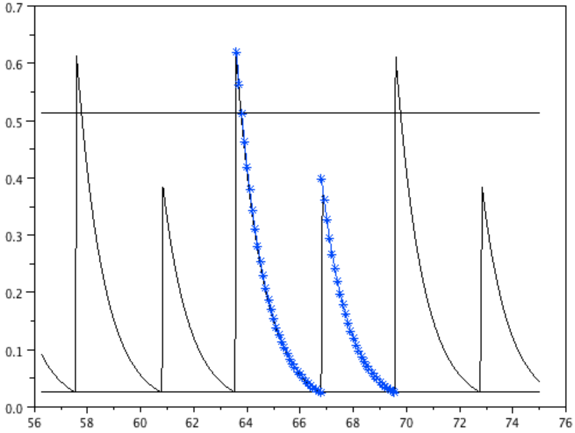
Numerical simulations



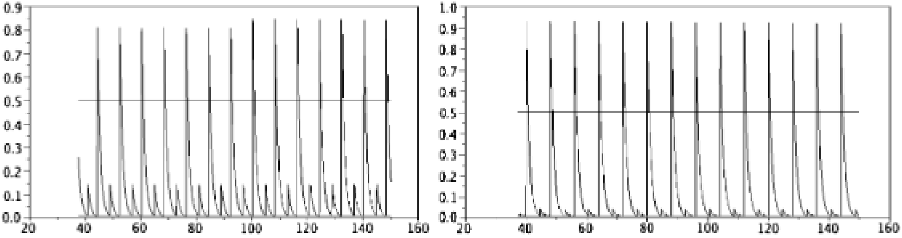
Numerical simulations.



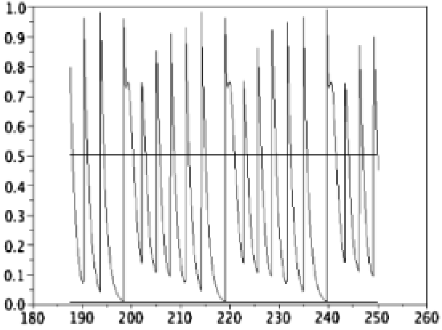
Numerical simulations.

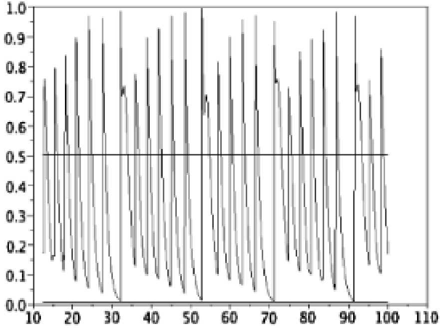


Comparaison with the case with kernel fragmentation.

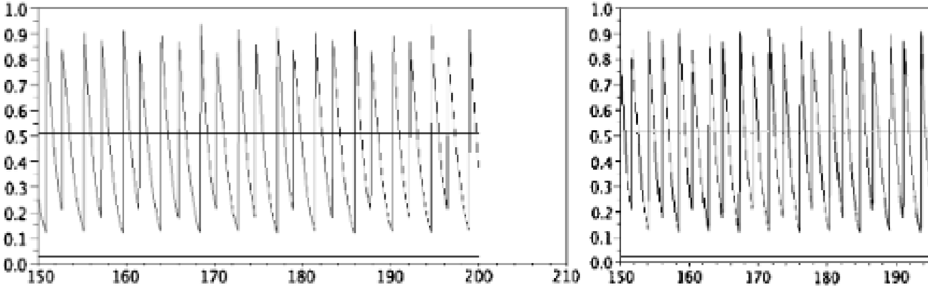


Comparaison with the case with adaptative memory.





Comparaison with the case with adaptative memory.



Finite size model.

For the PDE model, we now chose the following amplitude of stimulation X such that

$$X(t) = \frac{1}{a} e^{-a\cdot} \star N(t)$$

$$\frac{1}{a} X'(t) = -X(t) + N(t).$$

Let us see what happens in the case where there is a finite number K of neurons.

Description of the dynamic.

- We have a neuron which receive an input signal X.
- If the time elapsed since the last discharge s is such that

$$s \leq \sigma(X) \text{ then } p(s, X) = 0, \text{ else } p(s, X) = 1.$$

- If $\sigma(X) < s$, the probability of discharge of a neuron is equal to 0, else it is given by an exponential law of parameter 1.

Finite size model.

Description of the dynamic.

- while there is no discharge X satisfies the Equation

$$X(v) = X(0)e^{-av}.$$

- When there is a discharge, at a time t_1, we have

$$X(t_1) = X(0)e^{-at_1} + a/K$$

To find the time t_1

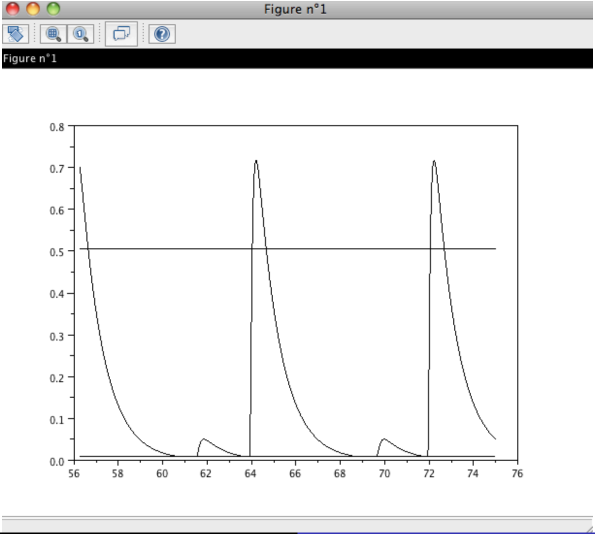
- We chose randomly a Δ which satisfies an exponential low of parameter 1.
- We define μ by

$$\mu(u) = \int_0^u \mathbb{I}_{[s(0)+v>\sigma(X(v))]} dv.$$

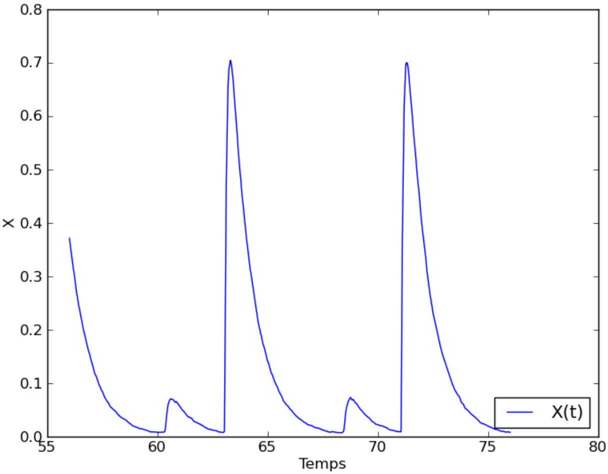
- The time of discharge of the neuron is then given by the time t such that

$$\mu(t) = \Delta.$$

Finite size model.



Finite size model.



Conclusion of the time elapsed model

Conclusion of the time elapsed model

- Simple model based on the time elapsed since the last discharge
- However, very rich dynamics with several patterns.
- Several possible extentions
- Link between the micro/macroscopic scale by Caceres, Chevallier, Doumic, Reynaud-Bouret
- Add of heterogeneity (with Kang, Perthame).

Leaky Integrate and Fire model

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) :

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

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

- $p(v,t)$: 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.

Model chosen

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

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

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

Questions :

- Qualitative dynamic and existence/uniqueness result (with Carrillo, Perthame, Smets) (see also Caceres, Carrillo, González, Gualdani, Perthame , Schonbek)
- Link between micro and macroscopic model (Delarue, Inglis, Rubenthaler, Tanré)
- Link with time elapsed model ? (Dumont, Henry, Tarniceriu)
- Add of heterogeneity (with B. Perthame and G. Wainrib)

Link with the time elapsed model in the linear case.

Link with the time elapsed model in the linear case with $K(s,u) = \delta_{s=0}$. (Dumont, Henry, Tarniceriu)

Term of discharge $d(s)$ in time elapsed : We compute d of Equation

$$\partial_t n + \partial_s n + d(s) n(s,t) = 0$$

corresponding to the one given by the Fokker-Planck equation.

Steps :

- We consider the function $q(s,v)$ solution of

$$\partial_s q(s,v) + \partial_v(-vq) - \sigma \partial_{vv} q = 0, \quad q(s=0,v) = \delta_{v=V_R}.$$

- d constructed via q using that the probability that a neuron reach the age s without discharge is

$$\mathcal{P}(a \geq s) = \int_{-\infty}^{V_F} q(s,v)dv = e^{-\int_0^s d(a)da}.$$

Link with the time elapsed model in the linear case.

Link kernel K : Density of probability $K(v,s)$ for a neuron to be at the potential v knowing that the time elapsed since its last discharge is $\geq s$,

$$K(v,s) := \frac{q(s,v)}{\int_{-\infty}^{V_F} q(s,v)dv}.$$

Formula of p with respect to n :

$$\text{If } \; p_0(v) := \int_0^{+\infty} K(v,s)n_0(s)ds, \;\text{ then }\; p(v,t) = \int_0^{+\infty} K(v,s)n(t,s)ds$$

is solution of

$$\partial_t p + \partial_v(-vp) - \sigma\partial_{vv}p = \delta_{v=V_R}N(t), \quad N(t) := -\sigma\frac{\partial p}{\partial v}(V_F,t), \quad p(0,v) = p_0.$$

with n solution of

$$\partial_t n + \partial_s n + d(s)n = 0, \quad n(0,s) = n_0(s).$$

Qualitative dynamic

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

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

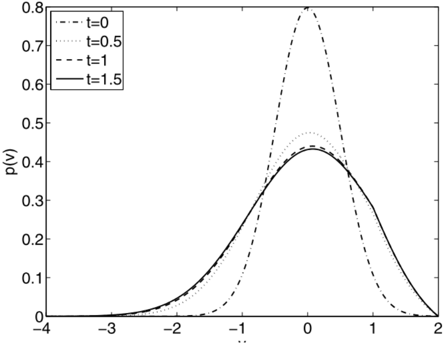
$$N(t) := -\sigma\frac{\partial p}{\partial v}(V_F,t) \geq 0\,.$$

Well posedness of the solution ?

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

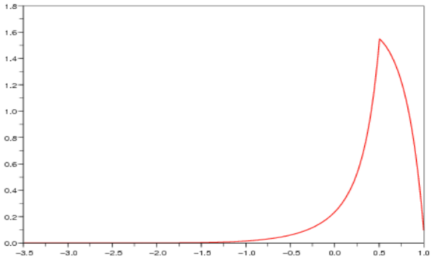
1. With the diffusion, this implies that for all $b > 0$, by well choosing the initial data, we have blow-up (Caceres, Carrillo, Perthame).
2. As soon $b \leq 0$, the solution is globally well defined (Carrillo, González, Gualdani, Schonbek, Delarue, Inglis, Rubenthaler, Tanré).
3. If we add a delay N on the network, the equation is always well posed (with Caceres, Roux, Schneider)

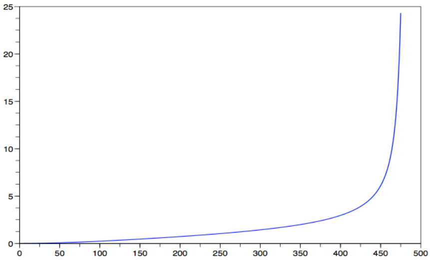
Qualitative dynamic



From Carrillo, Caceres, Perthame

Qualitative dynamic





Qualitative dynamic

Stationary states (Caceres, Carrillo, Perthame)

Implicit formula

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

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, σ), there exists at least two stationary states
3. If b is big enough, there is no stationary states.

Qualitative dynamic

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

Idea of the proof :

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

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

- Poincaré estimates

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

Qualitative dynamic

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

Inhibitory case :

- Inhibitory case : Uniform estimates on N in L^2, independent of b and the initial data,
- Inhibitory case : L^∞ estimates dependent of b and the initial data.

Exitatory case :

- Estimates on N, depending on the initial data and b.
- Convergence to a unique stationary state for sufficiently weak interconnections with respect to the initial data

Existence of periodic solutions ?

- Not numerically observed
- Signification of the blow-up condition ? Is there a way to prolongate the solution after the blow-up ?

A priori estimates on N.

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,

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

Asymptotic dynamic.

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

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

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

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

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

Entropy estimates.

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,

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

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

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

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

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

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

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

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

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

Sursolution methods.

We assume that $b \leq 0$ and that $0 \leq V_R < V_F$.

Definition

Let $b \leq 0$, $V_0 \in [-\infty, V_F)$ and $T > 0$. A function $\bar{p}$ is a universel sur-solution on $[V_0, V_F] \times [0, T]$ if

$$\frac{\partial \bar{p}}{\partial t}(v,t) - \frac{\partial}{\partial v}(v\,\bar{p}(v,t)) - a\frac{\partial^2 \bar{p}}{\partial v^2}(v,t) \geq \bar{N}(t)\delta(v - V_R) \quad (3)$$

on $(V_0, V_F) \times (0, T)$, where $\bar{N}(t) := -a\frac{\partial \bar{p}}{\partial v}(V_F, t) \geq 0$ and

$$\bar{p}(\cdot, t) \text{ is decreasing on } [V_0, V_F] \quad \forall t \in [0, T].$$

Lemma

Let $V_0 \in (-\infty, V_F)$ and $T > 0$. Let $\bar{p}$ be an universal sur-solution on $[V_0, V_F] \times [0, T]$, and assume that

$$\bar{p}(v, 0) \geq p(v, 0) \quad \forall v \in [V_0, V_F] \qquad \text{and that} \qquad \bar{p}(V_0, t) \geq p(V_0, t) \quad \forall t \in [0, T].$$

Then, $\bar{p} \geq p$ on $[V_0, V_F] \times [0, T]$ and if $\bar{p}(\cdot, 0) - p(\cdot, 0)$ non idendically equal to 0, then $\bar{p} > p$ on $(V_0, V_F) \times (0, T)$.

Sur-solution method.

We construct two classes of universal sur-solution

- $$P(v,t) = \begin{cases} \exp(t) & \text{pour } v \leq V_R, \\ \exp(t)\,\frac{V_F - v}{V_F - V_R} & \text{pour } V_R \leq v \leq V_F. \end{cases} \qquad (4)$$
- We consider Q_1 and Q_2 solutions of

$$-aQ_1' - vQ_1 = a \quad \text{on } (V_R, V_F), \qquad Q_1(V_F) = 0, \qquad (5)$$
$$-aQ_2' - vQ_2 = 0 \quad \text{on } (0, V_R), \qquad Q_2(V_R) = Q_1(V_R), \qquad (6)$$

We define Q on $[0, V_F]$ equal to Q_1 on $[V_R, V_F]$ and equal to Q_2 on $[0, V_R]$.

Sursolution Method.

Strategy

- Via a change of variable, we reduce our equation to the linear heat equation on a domain which depends on time and this outside the singularity at $v = V_R$.
- We use the 2 universal sur-solutions and the regularizing effect on the heat equation to prove that the solution is under the universal sur-solution βQ for β big enough, where Q is prolongated by $Q(0)$ on $(-\infty, 0)$

Sursolution Method.

Change of variable Let $t_0 \geq 0$ and $T \geq t_0$. We set

$$q(y,\tau) = e^{-(t-t_0)} p(e^{-(t-t_0)} y + \int_{t_0}^{t} bN(s) e^{-(t-s)} ds, t) \text{ et } \tau = \frac{1}{2} e^{2(t-t_0)}.$$

The function q is solution of the heat Equation

$$\partial_t q - a \partial_{yy} q = 0$$

on Ω_{t_0} which is the set of (y,τ) such that

$$\frac{1}{2} e^{-2t_0} \leq \tau \leq \frac{1}{2} e^{2(T-t_0)}, \; y \neq \sqrt{2\tau} V_R - \int_0^{\frac{1}{2}\ln(2\tau)} bN(s+t_0) e^s ds$$

$$\text{and } y < \sqrt{2\tau} V_F - \int_0^{\frac{1}{2}\ln(2\tau)} bN(s+t_0) e^s ds.$$

Sursolution Method.

We arg by a contradiction argument

- Assume that there exists $t_0 \geq 1$ such that for all β big enough (we can chose $v_0 \leq 0$)

$$p(v_0, t_0) = \beta Q(v_0)$$

- Using that, on $[0, t_0]$, Q is a sursolution, we know that N is bounded.
- We show that the cylinder $\Gamma_{v_0,r}$

$$[v_0 - r, v_0 + r, \frac{1}{2} - \frac{r^2}{a}, \frac{1}{2}] \subset \Omega_{t_0}$$

  with

$$r \leq \frac{1}{2}\exp(-\frac{1}{2})V_R \qquad \text{et} \qquad \frac{r^2}{a} \leq \min\left(\frac{1}{2}(1-\exp(-1)), \frac{1}{2}\frac{V_R}{V_R - 2ba\beta}\right).$$

- We use the regularizing effect

$$|q(v_0, \frac{1}{2})| \leq Kar^{-3}\|q\|_{L^1(\Gamma_{v_0,r})}.$$

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 transmission delay

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

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

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

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

Principal properties (Caceres, Perthame)

- Still blow-up
- Existence of odd stationary states for all $b > 0$ and unique stationary state for $b \le C$, $C > 0$ small enough
- Exponential convergence to a unique stationary without connectivity.

Equation with delay

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

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

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

Principal properties (with Caceres, Roux et Schneider)

- 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).

Equation with delay

Idea of proof for global existence :

- Via a change of variable, we obtain the following 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

Equation with delay

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

$$\forall t \geq 0, \forall v \in (V_R, V_F), \quad |-v + bN^0(t)| \leq B$$

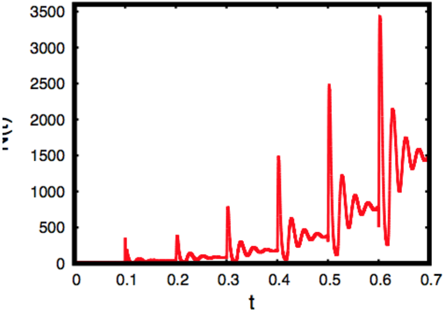
and $\delta > 0$ such that $a\delta - B \geq 0$.

3. We chose

$$f \equiv 1 \text{ on } (-\infty, V_R]$$

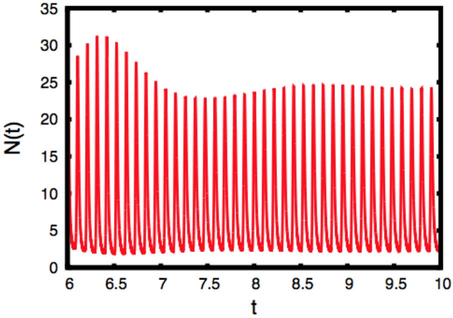
$$f(v) = e^{V_R - v}\psi(v) + \frac{1}{\delta}(1-\psi(v))(1-e^{\delta(v-V_F)}) \text{ on } (V_R, V_F].$$

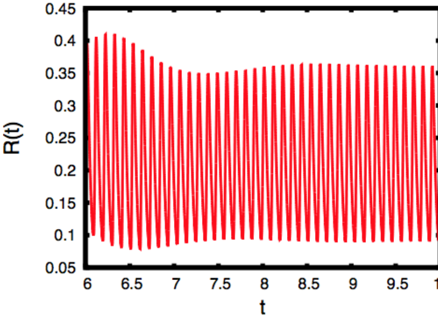
Equation with delay



from Caceres Schneider

Equation with delay





from Caceres Schneider

kinetic model

$$\frac{\partial}{\partial t}p(v,g,t)+\frac{\partial}{\partial v}\left[\left(-v+g(V_E-v)\right)p(v,g,t)\right]+\frac{\partial}{\partial g}\left[\left(b\mathcal{N}(t)-g\right)p(v,g,t)\right]$$

$$-(a+b^2\mathcal{N}(t))\frac{\partial^2}{\partial g^2}p(v,g,t)=0,$$

with

$$N(g,t):=[-g_L V_F+g(V_E-V_F)]p(V_F,g,t)\geq 0, \qquad \mathcal{N}(t):=\int_0^{+\infty}N(g,t)dg.$$

$p(v,g,t)$: density of neurons at time t with membrane potential $v\in(V_R,V_F)$, $V_R\geq 0$, and conductance $g>0$ (Cai, Tao, Shelley, McLaughlin)

Kinetic model

Difficulties of the equation

- Degenerate diffusion.
- no natural entropy which emerges
- A priori estimates on the flux $\mathcal{N}(t)$ (avec B. Perthame)
- Oscillations may appear via simulationw (Caceres, Carrillo, Tao).
- The passage micro/macro is totally open