Neuronal Network: overarching framework and examples

S. Mischler

(Paris-Dauphine)

CIMPA Summer Research School on "Mathematical modeling in Biology and Medicine" Santiago de Cuba, 8-17 June, 2016

- M., Quiñinao, Touboul, On a kinetic FitzHugh-Nagumo model of neuronal network, Comm. Math. Phys. 2016
- M., Weng, *Relaxation in time elapsed neuron network models in the weak connectivity regime*, arXiv 2015
- M., Quiñinao, Touboul, A survey on kinetic models and methods for neuronal networks, in progress
- Weng, General time elapsed neuron network model: well posedness and strong connectivity regime, in progress

Introduction

- Goal: understand the qualitative (= long time) behaviour of several nonlinear evolution PDEs modeling neuronal network
- More precisely: identify some regimes (e.g. the weak connected regime) for which solutions converge to a (unique) steady state.
- But: neuroscientists look for (observe) periodic behaviour!
- First motivation: understand the different neuronal network modeling by nonlinear evolution PDEs. What is the interest of each one? In which sense are they different? The issue is still not clear for me!
- Second motivation: Develop some efficient mathematical tool to answer about the stability issue for general PDEs: accurate and robust spectral analysis of operators which enjoy suitable splitting

$$\Lambda = \mathcal{A} + \mathcal{B}, \quad \mathcal{A} \preceq \mathcal{B}.$$

Not a a completely new idea since it goes back to Hilbert (1912, applications to Boltzmann equation) and Weyl (1910, 1912, applications to parabolic and integral equations). But a new impluse has been given since Mouhot's work (2006, about Boltzmann equation).

S.Mischler (CEREMADE)

Neuronal Network

Outline of the talk



Overarching framework for Neuronal Network statistical equations

- Modeling
- Qualitative analyze and weak connectivity regime
- 2 List of models
 - > Relaxation in time elapsed neuron network model
 - A variable: refractory time (or kernel) model
 - Noisy leaky integrate and fire model
 - The Hodgkin- Huxley equation
 - > FitHugh-Nagumo statistical model
 - Voltage-Conductance statistical equation

Relaxation in time elapsed neuron network models

- Coming back to the equation and results
- Sketch of the proof : a spectral analysis argument

Outline of the talk



Overarching framework for Neuronal Network statistical equations

- Modeling
- Qualitative analyze and weak connectivity regime

2 List of models

- > Relaxation in time elapsed neuron network model
- A variable: refractory time (or kernel) model
- Noisy leaky integrate and fire model
- The Hodgkin- Huxley equation
- ▷ FitHugh-Nagumo statistical model
- Voltage-Conductance statistical equation

3 Relaxation in time elapsed neuron network models

- Coming back to the equation and results
- Sketch of the proof : a spectral analysis argument

 $z \simeq$ electrical state variable of a neuron (membrane potential, elapsed time since last discharge, ...), **Z** the set of states $\subset \mathbb{R}^d$.

The state $Z_t \in \mathbf{Z}$ of one neuron is a time dependent random variable and evolves accordingly to the SDE

(1)
$$dZ_t = F(Z_t, M_t, d\mathcal{L}_t),$$

 $M_t :=$ given neuron network activity, $d\mathcal{L}_t :=$ Levy noise process (Brownian, Poissonian)

• The neuronal network environment is here known and then one neuron evolves according to a general Markov (no autonomous) process.

• (1) is modeling the evolution of the electrical activity = spikes (electrical discharges) possibly due to (random noise) excitation

Problem 1. Mathematical analyse of equation (1). That is a job for probabilists. But Krein-Rutman theorem makes the job.

N-neuron network

Consider an finite assembly $(Z^1, ..., Z^N)$ of neurons in interaction. The evolution equation for each neuron Z_t^i is exactly the same

(2a)
$$dZ_t^i = F(Z_t^i, M_t, d\mathcal{L}_t^i),$$

excepted that the neuronal network activity M_t is determined by the electric activity of every neurons:

(2b)
$$M_t = \mathcal{M}\left[\frac{1}{N}\sum_{i=1}^N \delta_{Z^i_{[0,t]}}\right]$$

and \mathcal{L}_t^i are independent stochastic noise processes.

 \Rightarrow Neurons are indistinguishable. Simple and quite weak interaction (possibly with delay) between neurons through a same quantity M(t)

Problem 2. Mathematical analyse of equation (2) is really a job for probabilists. We will not consider that issue here.

Mean field limit: to a Boltzmann's like statistical description

We are not interested by the electrical activity of one neuron in particular, but by the neuronal network activity \simeq the activity of neurons in the mean. When N becomes very large, in the mean field limit, we expect that the system simplifies. More precisely, we expect

$$\mathcal{L}aw(Z_s^i) \underset{N \to \infty}{\longrightarrow} f_s$$
, same limit,

 $\mathcal{L}\textit{aw}(Z^i_s,Z^j_s) \underset{N \rightarrow \infty}{\longrightarrow} f_s \otimes f_s, \quad \text{asymptotic independence (chaos)},$

and

$$\frac{1}{N}\sum_{i=1}^N \delta_{Z_s^i} \underset{N \to \infty}{\longrightarrow} f_s, \quad \text{functional law of large numbers.}$$

As a consequence,

$$f_t = \mathcal{L}aw(Z_t) =$$
law of a typical neuron

and Z_t evolves according to the same (but now nonlinear) SDE

Mean field limit: to a Boltzmann's like statistical description

In the mean field limit

$$\frac{1}{N}\sum_{i=1}^N \delta_{Z_{\lfloor [0,t]}^i} \to f_{\rfloor [0,t]} := \mathcal{L}aw(Z_{\lfloor [0,t]}) = \mathsf{law} \text{ of a typical neuron}$$

where Z_t evolves according to the mean field SDE

(3)
$$dZ_t = F(Z_t, M_t, d\mathcal{L}_t), \quad M_t = \mathcal{M}\Big[f_{|[0,t]}\Big].$$

Problem 3. Establish the mean field limit $N \to \infty$. That is a large number law + the proof of asymptotic independence between pairs of neurons (using a propagation of chaos argument). That can be done using several strategies

- BBGKY method (BBGKY, ...)
- Semigroup method (Kac, McKean, Grünbaum, ...)
- Coupling method (Tanaka, Sznitman, ...)
- Nonlinear Martingale method (Sznitman, ...)

 \rhd For the first (elapsed time) model: see the recent papers by Fournier, Löcherbach, Quiñinao, Robert, Touboul, Caceres et al.

S.Mischler (CEREMADE)

Neuronal Network

Mean field PDE

For any test function $\varphi:\mathbf{Z}\to\mathbb{R}$ and from Itô formula, one deduces

$$\mathbb{E}[\varphi(Z_t)] - \mathbb{E}[\varphi(Z_0)] = \int_0^t \mathbb{E}[(\Lambda_{M_s}^* \varphi)(Z_s)] \, ds,$$

for a suitable integro-differential linear operator Λ_m^* .

As a consequence, the law $f := \mathcal{L}aw(Z)$ is a solution to an evolution PDE

(4)
$$\partial_t f = \Lambda_{M(t)} f, \quad M(t) = \mathcal{M}(f_{|[0,t]}), \quad f(0,\cdot) = f_0.$$

We insist again on the fact that Λ_m is a linear operator for any m. Nonlinearity is due to the coupling with neuronal activity M(t).

Other possible definition/equation on the network activity are

$$M(t,x) = \mathcal{M}(f_{|[0,t]},x), \quad M(t) = \mathcal{M}(f_{|[0,t]},M(t)).$$

Problem 4. Well-posedness of equation (4) and perform a qualitative analyze of the solutions. At a formal level fall in that class of problems:

Existence and uniqueness of solutions

From the fact that Z_t is a stochastic process, we find

$$\langle f_t \rangle := \int_{\mathbf{Z}} f_t = \mathbb{E}[1] \equiv 1, \quad \forall t \ge 0.$$

Number of neurons is conserved (that is good!) and it is the only general available qualitative information on the solutions.

Under general and mild assumptions on the operators ${\it F}$ and ${\it M}$

Theorem 1. For any $0 \le f_0 \in L^1 \cap L^p$, there exists (at least) one global solution $f \in C([0,\infty); L^1) \cap L^{\infty}(0,\infty,L^p)$ to the PDE (4).

 \rhd Be careful with Noisy Leaky Integrate and Fire model for which blow up can occur

Theorem 2. There exists (at least) one stationary solution $0 \le G \in L^1 \cap L^\infty$ to the evolution PDE (4), that is

(5)
$$0 = \Lambda_M G, \quad M = \mathcal{M}(G, M).$$

 \triangleright proof: intermediate value theorem or Brouwer fixed theorem

S.Mischler (CEREMADE)
--------------	-----------

No connectivity regime \simeq one-neuron model

We introduce a small parameter $\varepsilon > 0$ corresponding to the strength of the connectivity of neurons with each other, and thus to the nonlinearity of the model:

$$(4_{\varepsilon}) \qquad \partial_t f = \Lambda_{\varepsilon M(t)} f, \quad M(t) = \mathcal{M}_{\varepsilon}(f_{|[0,t]}, M(t)), \quad f(0, \cdot) = f_0.$$

In the not connected regime $\varepsilon = 0$, the equation is linear

(4₀)
$$\partial_t f = \Lambda_0 f, \quad f(0, \cdot) = f_0.$$

The equation is furthermore sign and mass preserving. The operator enjoys suitable splitting.

Theorem 3 (Krein-Rutman).

- There exists a unique normalized and positive stationary state G_0 to the evolution PDE (4₀), that is $\Lambda_0 G_0 = 0$.
- G_0 is stable for the associated semigroup: $\exists a < 0, C \ge 1$,

$$\|S_{\Lambda_0}(t) f_0 - \langle f_0 \rangle G_0\| \leq C e^{at} \|f_0\|, \quad \forall t \geq 0, \ \forall f_0.$$

 \triangleright proof: KR $\Rightarrow \exists ! G_0 \ge 0$, $\langle G_0 \rangle = 1$, $\Lambda_0 G_0 = \lambda G_0$, but $\lambda = 0$ because $\Lambda_0^* 1 = 0$ (mass conservation) or because of Theorem 2.

Small connectivity regime = a perturbative regime

Theorem 4.1. There exists $\varepsilon_0 > 0$ such that the normalized and positive stationary state G_{ε} is unique for any $\varepsilon \in (0, \varepsilon_0)$.

 $ightarrow \Lambda_0^{-1}$ exists and use (half of the) implicit function theorem

Theorem 4.2. There exists $\varepsilon_1 > 0$ such that G_{ε} is exponentially linearly stable for the associated semigroup: $\exists a < 0, C \ge 1$,

$$\|S_{\Lambda_{\varepsilon}}(t)f_0 - \langle f_0 \rangle G_{\varepsilon}\| \leq C e^{at} \|f_0\|, \quad \forall t \geq 0, \ \forall f_0, \ \forall \varepsilon \in (0, \varepsilon_1).$$

 $\triangleright \Sigma(\Lambda_{\varepsilon}) \cap \Delta_a = \{0\}$ for $\varepsilon > 0$ small by a perturbation trick and then use the spectral mapping theorem.

Theorem 4.3. There exists $\varepsilon_2 > 0$ such that G_{ε} is exponentially nolinearly stable : $\exists a < 0, C \ge 1$,

$$\|f(t)-\langle f_0\rangle G_{\varepsilon}\|\leq C_{f_0}\,e^{at},\quad \forall\,t\geq 0,\;\forall\,f_0,\;\forall\,\varepsilon\in(0,\varepsilon_2).$$

• Whatever is the complexity of the model: asynchronous spiking holds in the small connectivity regime. Synchronization comes from nonlinearity?

S.Mischler (CEREMADE)

Neuronal Network

June 13, 2016 12 / 31

Outline of the talk

- Overarching framework for Neuronal Network statistical equations
 - Modeling
 - Qualitative analyze and weak connectivity regime
- 2 List of models
 - > Relaxation in time elapsed neuron network model
 - A variable: refractory time (or kernel) model
 - Noisy leaky integrate and fire model
 - The Hodgkin- Huxley equation
 - > FitHugh-Nagumo statistical model
 - Voltage-Conductance statistical equation

3 Relaxation in time elapsed neuron network models

- Coming back to the equation and results
- Sketch of the proof : a spectral analysis argument

Relaxation in time elapsed neuron network model - PPS 2010, 2013

• Dynamic of the neuron network: (age structured) evolution equation

$$\partial_t f = -\partial_x f - a(x, m(t))f, \quad f(t, 0) = p(t)$$

on the density number of neurons $f = f(t, x) \ge 0$.

- $a(x, m) \ge 0$: firing rate for neurons in state x in network activity $m \ge 0$.
- p(t): total density of neurons undergoing a discharge at time t given by

$$p(t) := \int_0^\infty a(x, m(t)) f(t, x) \, dx$$

• m(t): network activity at time $t \ge 0$ resulting from earlier discharges given by

$$m(t):=\int_0^\infty p(t-y)b(dy),$$

b delay distribution taking into account the persistence of electric activity

14 / 31

- Case without delay, when $b = \delta_0$ and then m(t) = p(t).
- Case with delay, when $b = \delta_{y=\tau}$ or $b = \tau^{-1} e^{-\tau^{-1}y} dy$, $\tau > 0$
- Total density of neurons conserved because of the flux condition
 S.Mischler (CEREMADE) Neuronal Network June 13, 2016

A variant : variable refractory time (or kernel) model - PPS 2014

• Dynamic of the density number of neurons $f = f(t, x) \ge 0$

$$\partial_t f + \partial_x f + a(x, M(t)) f = \mathcal{K}[f, M(t)] \quad f(t, 0) = 0,$$

where the kernel \mathcal{K} and the function a are defined by

$$\mathcal{K}[f,m] = \int_0^\infty k(x',x,m) f(x') dx', \quad a(x,m) := \int_0^\infty k(x,x',m) dx',$$

and the network activity function M(t) and the total density of spiking neurons N(t) are defined as before.

• k(x', x, m) = rate for a neuron in state x to jump to the state x'. When

$$\mathsf{supp} k(x', x, m) \subset \{x' \leq x_0 < x_1 \leq x\}$$

the model takes into account a possible variable refractoty time (time during a neuron does not spike).

The previous age structured model corresponds to $k(x, x', m) := a(x, m) \delta_{x'=0}$. Total density number of neurons is conserved because

$$\frac{d}{dt}\int_0^\infty f(t,x)\,dx = \int_0^\infty \mathcal{K}[f,M(t)]\,dx - \int_0^\infty \mathcal{K}(x,M(t))\,f(t,x)\,dx = 0.$$

Noisy leaky integrate and fire model - I

The state $x := membrane \ potential \in (-\infty, x_1)$ where $x_1 \in (0, \infty)$ is a threshold (firing voltage) or where $x_1 = +\infty$. Density of neurons $f = f(t, x) \ge 0$ evolves

$$\partial_t f + \partial_x [a(x, M(t)) f] - \sigma(M(t)) \partial_{xx}^2 f + \phi(x, M(t)) f = Q(t) \delta_{x=x_0}$$

with the boundary conditions

$$f(t, -\infty) = f(t, x_1) = 0$$
 and $x_0 < x_1$.

The amplitude of stimulation of the network M(t) and the density of neurons leaving the refractory period Q(t) are defined by

$$M(t) := \int_0^t N(t-y) b(dy)$$
 and $Q(t) = \int_0^t N(t-z) k(dz)$

for some probability measures b and k. The discharges flux N(t) is defined by

$$N(t) = -\sigma(M(t)) \partial_x f(t, x_1)$$
 or $N(t) = \int_0^\infty \phi(x, M(t)) f(t, x) dx$

depending whether $x_1 < +\infty$ (and $\phi = 0$) or $x_1 = +\infty$ (and $\phi \not\equiv 0$)

Noisy leaky integrate and fire model - II

• $x_1 = 1$, $\phi = 0$, $x_0 = 0$, and Q(t) = M(t) = N(t) is considered in Caceres, Carrillo, Perthame 2011

• $x_1 = 1$, $\phi = 0$, $x_0 = 0$ and M(t) = N(t) is considered in Caceres, Perthame 201? ($k := \tau^{-1} e^{-y/\tau} dy$) and in Brunel 2000 ($k := \delta_{y=\tau}$)

• $x_1 = +\infty$, $\phi = \phi(x) \ge 0$, $\phi \not\equiv 0$, M(t) = N(t) and $k := \tau^{-1} e^{-y/\tau} dy$ is considered in Caceres, Perthame 201?

Introducing the primitive function K and the quantity R(t) defined by

$$K(y) := \int_y^\infty k(dy'), \quad R(t) := \int_0^t N(s) \, K(t-s) \, dy,$$

we observe that

$$R'(t)=N(t)-Q(t),$$

and we deduce the following generalized mass conservation

$$\frac{d}{dt}\Big(\int_{-\infty}^{x_1}f(t,x)\,dx+R(t)\Big)=0.$$

4d ODE/SDE for dynamics of the nerve cell membrane

$$\begin{cases} \dot{v} \simeq x^4 (v - V_K) - y^3 z (v - V_{Na}) - (v - V_L) \\ dx = [\rho_x(v) (1 - x) - \zeta_x(v) x] dt + \sigma_x(v, x) dW_t^x \\ dy = [\rho_y(v) (1 - y) - \zeta_y(v) y] dt + \sigma_y(v, y) dW_t^y \\ dz = [\rho_z(v) (1 - z) - \zeta_z(v) z] dt + \sigma_z(v, z) dW_t^z \end{cases}$$

where

- v : membrane potential;
- x : voltage-gated persistent K^+ (Potassium) current;
- y : voltage-gated transient Na^+ (Sodium) current;
- z : Ohmic leak current (mostly Cl^{-} ions).

FitHugh-Nagumo: microscopic description

• As a simplification of the Hodgkin-Huxley 4d ODE, FitzHugh-Nagumo 2d ODE describes the electric activity of one neuron and writes

$$\dot{v} = v - v^3 - x + l_{ext} = -B_0 + l_{ext}$$
$$\dot{x} = bv - ax = -A,$$

with $I_{ext} = i(t) + \sigma \dot{W}$ exterior input split as a deterministic part + a stochastic noise. We assume $i(t) \equiv 0$.

• For a network of N coupled neurons, the associated model writes for the state $\mathcal{Z}_t^i := (\mathcal{X}_t^i, \mathcal{V}_t^i)$ of the neuron labeled $i \in \{1, ..., N\}$

$$d\mathcal{V}^{i} = [-B_{0}(\mathcal{X}^{i}, \mathcal{V}^{i}) - \sum_{j=1}^{N} \varepsilon_{ij} (\mathcal{V}^{i} - \mathcal{V}^{j})]dt + \sigma d\mathcal{W}^{i}$$
$$d\mathcal{X}^{i} = -A(\mathcal{X}^{i}, \mathcal{V}^{i})dt$$

where $\varepsilon_{ij} > 0$ corresponds to the connectivity between the two neurons labeled *i* and *j*. The model takes into account an intrinsic deterministic dynamic + mean field interaction + stochastic noise.

S.Mischler (CEREMADE)

Neuronal Network

June 13, 2016 19 / 31

We assume $\varepsilon_{ij} := \varepsilon/N$, $(\mathcal{Z}_0^1..., \mathcal{Z}_0^N)$ are i.i.d. random variables with same law f_0 and we pass to the limit $N \to \infty$. $(\mathcal{Z}_t^1, ..., \mathcal{Z}_t^N)$ is chaotic and $\mathcal{Z}_t^i \to \overline{\mathcal{Z}}_t = (\overline{\mathcal{X}}_t, \overline{\mathcal{Y}}_t)$ solution to the nonlinear SDE

$$\begin{aligned} \bar{\mathcal{V}} &= [-B_0(\bar{\mathcal{X}},\bar{\mathcal{V}}) - \varepsilon \left(\bar{\mathcal{V}} - \mathbb{E}(\bar{\mathcal{V}})\right)] dt + \sigma \, d\mathcal{W} \\ \bar{\mathcal{X}} &= -A(\bar{\mathcal{X}},\bar{\mathcal{V}}) dt. \end{aligned}$$

From Ito calculus, the law $f(t, x, v) := \mathcal{L}aw(\bar{\mathcal{X}}_t, \bar{\mathcal{V}}_t)$ satisfies

$$\partial_t f = \partial_x (Af) + \partial_v (Bf) + \partial_{vv}^2 f \quad \text{on } (0,\infty) \times \mathbb{R}^2$$

where

$$\begin{cases} A = A(x, v) = ax - bv, & B = B(x, v; \mathcal{J}_f) \\ B(x, v; \mu) = v^3 - v + x + \varepsilon (v - \mu), & \mathcal{J}_f := \int_{\mathbb{R}^2} v f(x, v) \, dv dx \end{cases}$$

Outline of the talk

- Overarching framework for Neuronal Network statistical equations
 - Modeling
 - Qualitative analyze and weak connectivity regime
- 2 List of models
 - > Relaxation in time elapsed neuron network model
 - A variable: refractory time (or kernel) model
 - Noisy leaky integrate and fire model
 - The Hodgkin- Huxley equation
 - ▷ FitHugh-Nagumo statistical model
 - Voltage-Conductance statistical equation

Relaxation in time elapsed neuron network models

- Coming back to the equation and results
- Sketch of the proof : a spectral analysis argument

Relaxation in time elapsed neuron network models

- State of a neuron: local time (or internal clock) $x \ge 0$ corresponding to the elapsed time since the last discharge;
- Dynamic of the neuron network: (age structured) evolution equation

$$\partial_t f = -\partial_x f - a(x, \varepsilon m(t))f =: \mathcal{L}_{\varepsilon m(t)}f, \quad f(t, 0) = p(t)$$

on the density number of neurons $f = f(t, x) \ge 0$.

• $a(x, \varepsilon \mu) \ge 0$: firing rate of a neuron in the state x for a network activity $\mu \ge 0$ and a network connectivity parameter $\varepsilon \ge 0$.

• p(t): total density of neurons undergoing a discharge at time t given by

$$p(t) := \mathcal{P}_{\varepsilon}[f(t); m(t)], \quad \mathcal{P}_{\varepsilon}[g, \mu] := \int_{0}^{\infty} a(x, \varepsilon \mu) g(x) \, dx.$$

• m(t): network activity at time $t \ge 0$ resulting from earlier discharges given by

$$m(t) := \int_0^\infty p(t-y)b(dy),$$

- b delay distribution taking into account the persistence of electric activity
 - Case without delay, when $b = \delta_0$ and then m(t) = p(t).
 - Case with delay, when b is a smooth function.

Existence result

Monotony (and smoothness) assumptions

$$\partial_x a \ge 0, \quad a' = \partial_\mu a \ge 0,$$

$$0 < a_0 := \lim_{x \to \infty} a(x, 0) \le \lim_{x, \mu \to \infty} a(x, \mu) =: a_1 < \infty,$$

$$examples : a \in W^{2, \infty}(\mathbb{R}^2_+) \quad \text{or} \quad a(x) = \mathbf{1}_{x \ge \sigma(\mu)},$$

$$b = \delta_0 \quad \text{or} \quad \exists \delta > 0, \quad \int_0^\infty e^{\delta y} \left(b(y) + |b'(y)| \right) dy < \infty.$$

Theorems 1,2. For any $0 \le f_0 \in L^1$, there exists (at least) one global solution $f \in C([0,\infty); L^1) \cap L^{\infty}(0,\infty; L^p)$. There exists (at least) one normalized and positive stationary solution $G_{\varepsilon} \in L^1 \cap L^{\infty}$:

$$\mathcal{L}_{\varepsilon M_{\varepsilon}} G_{\varepsilon} = -\partial_x G_{\varepsilon} - a(x, \varepsilon M_{\varepsilon}) G_{\varepsilon} = 0, \quad G_{\varepsilon}(0) = M_{\varepsilon},$$

$$M_{\varepsilon} = \mathcal{P}_{\varepsilon}[G_{\varepsilon}; M_{\varepsilon}] = \int_{0}^{\infty} a(x, \varepsilon M_{\varepsilon}) G_{\varepsilon}(x) dx.$$

Small connectivity regime

Theorems 3, 4. $\exists \varepsilon_1 > 0$ such that for any $\varepsilon \in (0, \varepsilon_1)$ the stationary solution G_{ε} is unique and exponentially stable for the associated linear semigroup.

Extends Pakdaman, Perthame, Salort results to the case with delay.

▷ About the proof: The linearized equation for the variation

$$(g, n, q) = (f, m, p) - (G_{\varepsilon}, M_{\varepsilon}, M_{\varepsilon})$$

around a stationary state $(G_{\varepsilon}, M_{\varepsilon}, M_{\varepsilon})$ writes

$$\partial_t g = -\partial_x g - a(x, \varepsilon M_\varepsilon)g - n(t) \varepsilon (\partial_\mu a)(x, \varepsilon M_\varepsilon)F_\varepsilon, \ g(t, 0) = q(t),$$

with a delay term at the boundary

$$\begin{split} q(t) &= \int_0^\infty a(x, \varepsilon \, M_\varepsilon) g \, dx + n(t) \, \varepsilon \int_0^\infty (\partial_\mu a)(x, \varepsilon M_\varepsilon) F_\varepsilon \, dx \\ n(t) &:= \int_0^\infty q(t-y) b(dy). \end{split}$$

Intermediate evolution equation for incoding the delay term

We introduce an intermediate evolution equation

$$\partial_t \mathbf{v} + \partial_y \mathbf{v} = 0, \quad \mathbf{v}(t,0) = q(t), \quad \mathbf{v}(0,y) = 0,$$

where $y \ge 0$ represent the local time for the network activity. That last equation can be solved with the characteristics method

$$\mathbf{v}(t,y) = \mathbf{q}(t-y)\mathbf{1}_{0 \le y \le t}$$

The equation on the variation n(t) of network activity writes

$$n(t) = \mathcal{D}[\mathbf{v}(t)], \quad \mathcal{D}[\mathbf{v}] := \int_0^\infty \mathbf{v}(y) b(dy),$$

and the equation on the variation q(t) of discharging neurons writes

$$q(t) = \mathcal{O}_{\varepsilon}[g(t), \mathbf{v}(t)],$$

with

$$\mathcal{O}_{\varepsilon}[g, \mathbf{v}] := \mathcal{N}_{\varepsilon}[g] + \kappa_{\varepsilon} \mathcal{D}[\mathbf{v}],$$
$$\mathcal{N}_{\varepsilon}[g] := \int_{0}^{\infty} a_{\varepsilon}(M_{\varepsilon})g \, dx, \quad \kappa_{\varepsilon} := \int_{0}^{\infty} a_{\varepsilon}'(M_{\varepsilon})G_{\varepsilon} \, dx.$$

For the new unknown (g, v) the equation writes

$$\partial_t(g, v) = \Lambda_{\varepsilon}(g, v) = \mathcal{A}_{\varepsilon}(g, v) + \mathcal{B}_{\varepsilon}(g, v),$$

where the operator $\Lambda_{\varepsilon}=(\Lambda_{\varepsilon}^1,\Lambda_{\varepsilon}^2)$ is defined by

$$\begin{split} \Lambda^1_\varepsilon(g,v) &:= -\partial_x g - a_\varepsilon g - a'_\varepsilon F_\varepsilon \mathcal{D}[v] + \delta_{x=0} \mathcal{O}_\varepsilon[g,v], \\ \Lambda^2_\varepsilon(g,v) &:= -\partial_y v + \delta_{y=0} \mathcal{O}_\varepsilon[g,v], \end{split}$$

 $\triangleright \mathcal{B}_{\varepsilon}$ is dissipative;

 $arphi (S_{\mathcal{B}_{\varepsilon}}\mathcal{A}_{\varepsilon})^{(*2)}$ has a smoothing effect in M^1 when a is smooth

▷ We may apply the spectral theory in general Banach space (Weyl's Theorem, spectral mapping Theorem, Krein-Rutman Theorem, perturbation Theorem) developped by M., Scher, Tristani.

Linear stability when the spiking rate is a step function - I

We consider
$$\mathcal{B}f := -\partial_x f - \mathbf{1}_{x \ge 1} f \simeq -\partial_x f - f,$$

 $\mathcal{A}f := \delta_0 \mathcal{K}[f], \quad \mathcal{K}[f] := \int_0^\infty \mathbf{1}_{z \ge 1} f(z) dz.$

$$\begin{split} & \succ S_{\mathcal{B}} : L^{p} \to L^{p} \text{ as } \mathcal{O}(e^{-t}). \\ & \Rightarrow \mathcal{A}S_{\mathcal{B}} : L^{p} \to \mathbb{C}\delta_{0} \text{ as } \mathcal{O}(e^{-t}). \\ & \mathsf{Proof} : S_{\mathcal{B}}(t)f(x) \simeq e^{-t} f(x-t) \mathbf{1}_{x-t \ge 0}. \\ & \succ S_{\mathcal{B}} * \mathcal{A}S_{\mathcal{B}} : L^{1} \to L^{1} \cap L^{p} \text{ as } \mathcal{O}(e^{at}), \forall a > -1. \\ & \Rightarrow S_{\mathcal{B}} * \mathcal{A}S_{\mathcal{B}} : \mathbb{C}\delta_{0} \to L^{1} \cap L^{p} \text{ as } \mathcal{O}(e^{at}), \forall a > -1. \\ & \Rightarrow S_{\mathcal{B}} * (\mathcal{A}S_{\mathcal{B}})^{(*k)} : L^{1} \cap L^{p} \to \mathcal{L}^{1} \cap L^{p} \text{ as } \mathcal{O}(e^{at}), \forall a > -1. \\ & \Rightarrow \mathsf{Proof} : S_{\mathcal{B}} * \mathcal{A}S_{\mathcal{B}}(t)f(x) \simeq e^{-t} \mathbf{1}_{x \le t} \mathcal{K}[f(\cdot - t + x)], \ \mathcal{K}[f] := \int_{0}^{\infty} \mathbf{1}_{z \ge 1} f(z) \, dz. \end{split}$$

 $\triangleright (R_{\mathcal{B}}\mathcal{A})^{2}: L^{1} \cap L^{p} \to L^{1} \cap L^{p} \text{ as } \mathcal{O}(\langle z \rangle^{-1}), \forall z \in \Delta_{a}, \forall a > -1.$ Proof : We write

$$\begin{aligned} (S_{\mathcal{B}}\mathcal{A})^{(*2)}(t)f &= \varphi_t \,\mathcal{K}[f], \quad \varphi_t(x) := e^{-t} \,\mathbf{1}_{x \le t-1}, \\ (R_{\mathcal{B}}(z)\mathcal{A})^2(z)f &= \hat{\varphi}_z \,\mathcal{K}[f], \quad \hat{\varphi}_z(x) = \frac{1}{1+z} \,e^{-(1+z)(x+1)} \end{aligned}$$

Linear stability when the spiking rate is a step function - II

 \triangleright We may adapt the spectral theory in general Banach space (Weyl's Th., spectral mapping Th., Krein-Rutman Th., perturbation Th.) developped by M., Scher, Tristani.

We write the factorization formula

$$\begin{array}{rcl} R_{\Lambda} & = & R_{\mathcal{B}} - R_{\Lambda} \mathcal{A} R_{\mathcal{B}} \\ & = & R_{\mathcal{B}} + ... - R_{\mathcal{B}} (\mathcal{A} R_{\mathcal{B}})^3 + R_{\Lambda} (\mathcal{A} R_{\mathcal{B}})^4 =: \mathcal{U} + R_{\Lambda} \mathcal{V} \end{array}$$

and then

$$R_{\Lambda}(I-\mathcal{V})=\mathcal{U}$$

with $\mathcal{U}, \mathcal{V} : \Delta_a \to \mathcal{B}(X)$ holomorphic and $I - \mathcal{V}$ is a compact perturbation of the identity. \triangleright From Ribarič-Vidav-Voigt's version of Weyl's theorem:

$$\Sigma(\Lambda) \cap \Delta_a = \Sigma_d(\Lambda) \cap \Delta_a =$$
discrete set.

 \triangleright From the decay estimate on \mathcal{V} , we get

$$\Sigma(\Lambda) \cap \Delta_a = \Sigma_d(\Lambda) \cap \Delta_a =$$
finite set.

 \triangleright From the positivity of S_{Λ} , we conclude with

 $\exists \ a \in (-1,0) \quad \Sigma(\Lambda_{\varepsilon}) \cap \Delta_a = \{0\}.$

We write the itared Duhamel formula

$$S_{\Lambda} = S_{\mathcal{B}} + ... + S_{\mathcal{B}} * (\mathcal{A}S_{\mathcal{B}})^{(*3)} + S_{\Lambda} * (\mathcal{A}S_{\mathcal{B}})^{(*4)}$$

and deduce

$$\Pi S_{\Lambda} \simeq \Pi \{S_{\mathcal{B}} + ... + S_{\mathcal{B}} * (\mathcal{A}S_{\mathcal{B}})^{(*3)}\} + e^{at} \int_{\uparrow a} \Pi R_{\Lambda} (\mathcal{A}R_{\mathcal{B}})^4 dz.$$

In a similar way, for any solution g to the linear equation

$$\partial_t g = \Lambda_{\varepsilon} g := -\partial_x g - a(\varepsilon M)g + \delta_0 \langle a(\varepsilon M)g \rangle, \quad a(x,\mu) := \mathbf{1}_{x \ge \sigma(\mu)}$$

such that $\langle g_0 \rangle = 0$, we have

$$\frac{d}{dt}\|g\|_{L^1} \lesssim a \|g\|_{L^1}.$$

Nonlinear stability when the spiking rate is a step function

We consider a solution to the nonlinear time elapsed neuron network model

$$\partial_t f = -\partial_x f - a(\varepsilon m)f + \delta_0 \langle a(\varepsilon m)f \rangle, \quad m = \langle a(\varepsilon m)f \rangle, \quad \langle f \rangle = 1,$$

and the associated steady state function

$$0 = -\partial_x G - a(\varepsilon M)G + \delta_0 \langle a(\varepsilon M)G \rangle, \quad M = \langle a(\varepsilon M)G \rangle, \quad \langle G \rangle = 1.$$

We define the variation g := f - G which satisfies

$$\partial_t g = \Lambda_{\varepsilon} g + (a(\varepsilon M) - a(\varepsilon m))f + \delta_0 (a(\varepsilon M) - a(\varepsilon m))f.$$

We compute for $\varepsilon > 0$ small enough

$$\frac{d}{dt} \|g\|_{L^1} \lesssim a \|g\|_{L^1} + 2 \|f\|_{L^{\infty}} |\sigma(\varepsilon M) - \sigma(\varepsilon m)|$$

$$\lesssim a \|g\|_{L^1} + C \varepsilon \|g\|_{L^1}.$$

As a consequence, for $\|g_0\|_{L^1} \leq \eta$ small enough, we have

$$\|f-G\|_{L^1} \lesssim e^{at}, \quad \forall t \ge 0.$$

What about other models? Is it possible to prove exactly the same results for :
 > the couple voltage-conductance model?

 \rhd Hodgkin-Huxley statistical model based on the Hodgkin-Huxley 4d ODE sytem? \vartriangleright ...

What about "larger" connectivity coefficients: ε is not small?
 ▷ unstability of "the" steady state?

 \triangleright periodic solutions? local stability of one of them?

• Is there any model which is more pertinent than the others? Depending of the situation we are insterested in / the accurancy we want?

• What is the next step? Several kinds of neurons? Space dependence?