

On oscillating systems of interacting neurons

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- Most biological systems are characterized by an **intrinsic periodicity** : $24h$ for the day-night rhythm of most animals, etc....
- In other words, there is some underlying **oscillatory behavior**.
- These oscillations are also observed in the way information is processed in the brain (at least in some sub-systems).

Oscillations

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- In other words, there is some underlying **oscillatory behavior**.
- These oscillations are also observed in the way information is processed in the brain (at least in some sub-systems). **And this is what this talk will be about.**

We will consider large systems of randomly interacting neurons presenting intrinsic oscillations.

- 1 Introduction of the model : Multi class systems of interacting **nonlinear Hawkes processes** : several populations of neurons which interact. Within each population, all neurons behave in the same way.
- 2 Propagation of chaos and associated CLT.
- 3 Study of the oscillatory behavior of the limit system.
- 4 And of the finite size system.

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- 4 And of the finite size system.

The **second part** is deeply based on results of *Delattre, Fournier and Hoffmann (2015)* on high dimensional Hawkes processes (in the one-class frame).

Spike trains modelled by Hawkes processes

- We report for any neuron the times of appearance of a spike (emission of an action potential) \rightarrow spike trains = counting process.
- Neuron i is defined by its counting process

$$Z_i(t) = \text{number of spikes of neuron } i \text{ during } [0, t]$$

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with intensity process $\lambda_i(t)$ defined by

$$P(Z_i \text{ has a jump during }]t, t + dt] | \mathcal{F}_t) = \lambda_i(t) dt.$$

The intensity process

- All we need to know about the process is encoded in its intensity !
- If $\lambda_i(t) \equiv \lambda > 0$, then $Z_i(t)$ is a **Poisson process** with intensity λ . Not really suitable in order to have a good model for spike trains...

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- It is commonly admitted that spike trains should be processes having **infinite memory**.
- Hence $\lambda_i(t)$ is a **stochastic process, depending on the whole history before time t** .

- Hawkes (1971), Hawkes and Oakes (1974), Brémaud and Massoulié (1996) : each past event **triggers** future events : **self-exciting processes**
- Intensity of $Z_i(t)$ of form

$$\lambda_i(t) = f\left(\int_{]0,t]} h(t-s)dZ_i(s)\right).$$

↑ rate fct ↑ leak ↑ past event

- **rate function** $f : \mathbb{R} \rightarrow \mathbb{R}_+$ Lipschitz, increasing.
- **leak term** $h(t-s)$ describes how an event **lying back** $t-s$ **time units in the past** influences the present time t .
- if h is not of compact support, then : truly infinite memory process.

- Questions like : Existence and stability, longtime behavior etc have been answered in the literature (Brémaud and Massoulié 1996)
- We are interested here in a **large system of interacting Hawkes processes**, describing each a spiking neuron.
- This system is made of **several populations** $k = 1, \dots, n$.
- Each population k consists of N_k **neurons** described by their spike train- counting processes

$$Z_{k,i}(t), 1 \leq i \leq N_k.$$

- Within a population, all neurons behave in the same way. **This is a mean-field assumption.**

- Intensity of i -th neuron belonging to population k :

$$\lambda_{k,i}(t) = f_k \left(\sum_{l=1}^n \frac{1}{N_l} \sum_{1 \leq j \leq N_l} \int_{]0,t[} h_{kl}(t-s) dZ_{l,j}(s) \right).$$

- f_k = spiking rate function of population k ; *supposed to be Lipschitz continuous.*
- h_{kl} = synaptic weight function of a typical neuron of population l on a typical neuron of population k ; *supposed to be in $L^2_{loc}(\mathbb{R}_+, \mathbb{R})$.*

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- We are in a **mean field frame** : population l influences population k only through its empirical measure.

Mean field limit

- What happens in the large system size limit ?
- I.e. $N = N_1 + \dots + N_n$ total number of neurons $\rightarrow \infty$ such that for each population

$$\lim_{N \rightarrow \infty} \frac{N_k}{N} > 0.$$

- Remember the intensity

$$\lambda_{k,i}(t) = f_k \left(\sum_{l=1}^n \int_{]0,t[} h_{kl}(t-s) \left[\frac{1}{N_l} \sum_{1 \leq j \leq N_l} dZ_{l,j}(s) \right] \right)$$

$$\uparrow \text{ LLN} \rightarrow d\mathbb{E}(\bar{Z}_l(s)),$$

where \bar{Z}_l is the counting process of a typical neuron belonging to population l in the $N \rightarrow \infty$ -limit.

- Limit system : family of counting processes $\bar{Z}_k(t), 1 \leq k \leq n$ (one for each population), solution of an **inhomogeneous equation**

$$\bar{Z}_k(t) = \int_0^t \int_{\mathbb{R}_+} \mathbf{1}_{\{z \leq f_k(\sum_{l=1}^n \int_0^s h_{kl}(s-u) d\mathbb{E}(\bar{Z}_l(u))\}} N^k(ds, dz),$$

N^k i.i.d. PRM on $\mathbb{R}_+ \times \mathbb{R}_+$ with intensity $d\mathbf{s}d\mathbf{z}$.

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N^k i.i.d. PRM on $\mathbb{R}_+ \times \mathbb{R}_+$ with intensity $dudz$.

- Taking expectations yields : $m_t^k = \mathbb{E}(\bar{Z}_k(t)), 1 \leq k \leq n$, solves

$$m_t^k = \int_0^t f_k \left(\sum_{l=1}^n \int_0^s h_{kl}(s-u) dm_u^l \right) ds.$$

Convergence to limit system

- Existence of a pathwise unique solution of the limit system standard ; follows ideas of Delattre, Fournier and Hoffmann (2015) in the one-population case.
- Convergence of the finite size system (of the **collection of empirical measures of each population**) to the limit as well.
- Multi-population frame : reminiscent of Graham (2008), see also Graham and Robert (2009), who has invented the notion of “multi-chaoticity” .
- Note that in the limit the different populations are independent.

What is the speed of convergence in the above limit theorem ?

Theorem

Under suitable assumptions : For any fixed $l_1 \leq N_1, \dots, l_n \leq N_n$,

$$\left(\left(\frac{Z_{1,i}(t) - m_t^1}{\sqrt{m_t^1}} \right)_{1 \leq i \leq l_1}, \dots, \left(\frac{Z_{n,i}(t) - m_t^n}{\sqrt{m_t^n}} \right)_{1 \leq i \leq l_n} \right) \xrightarrow{\mathcal{L}} \mathcal{N}(0, I_{l_1 + \dots + l_n})$$

as $N, t \rightarrow \infty$.

Remark

1) *Result similar to the one obtained by Delattre, Fournier and Hoffmann (2015), but extension to the non-linear case (the rate functions f_k are not supposed to be linear) : we have to use old results on **matrix renewal equations** obtained by Crump (1970) and Athreya and Murthy (1976).*

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- 2) *Rate of convergence given by $\sqrt{m_t^k}$, $1 \leq k \leq n$.*
- 3) Main difficulty : We do not dispose of equivalents of m_t^k as $t \rightarrow \infty$.
- 4) Result only holds assuming that m_t^k is at least of linear growth, within all populations. (*In other words, within each population, there is always some minimal strictly positive spiking intensity* - we will come back to this point later).

Remark

1) Main assumption is on the spectral properties of the “upper” offspring matrix Λ given by

$$\Lambda_{ij} = L \int_0^\infty |h_{ij}|(t) dt, 1 \leq i, j \leq n.$$

Here, L is the Lipschitz constant of the rate functions f_1, \dots, f_n .

2) In the subcritical case, nothing has to be imposed on the way $N, t \rightarrow \infty$. Main ingredient of the proof in this case is

$$\mathbb{E}(|Z_{k,i}(t) - \bar{Z}_k(t)|) \leq CtN^{-1/2}.$$

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3) Supercritical case more difficult, in this case

$$\mathbb{E}(|Z_{k,i}(t) - \bar{Z}_k(t)|) \leq Ce^{\alpha t} N^{-1/2},$$

and we have to suppose that $t, N \rightarrow \infty$ in such a way that $e^{\alpha t} N^{-1/2} \rightarrow 0$.

Oscillations of the limit system

- CLT shows that the finite size system is close to $(m_t^1, \dots, m_t^n) =$ system of the integrated intensities within each population.
- Oscillations????
- We consider this question in the frame of a **monotone cyclic feedback system** in the sense of **Mallet-Paret and Smith 1990** - which is somehow the oscillatory system “per se”.
 - Cyclic means : population k is only influenced by population $k + 1$, for all k .
 - Feedback means : population n is only influenced by population 1.
 - Monotone : we suppose that all rate functions f_k are non-decreasing.

Erlang kernels for the synaptic weight functions

- “Cyclic” : Intensity of the i -th neuron belonging to population k is given by

$$\lambda_{k,i}(t) = f_k \left(\int_{]0,t[} h_k(t-s) \frac{1}{N_{k+1}} \sum_{j=1}^{N_{k+1}} dZ_{k+1,j}(s) \right).$$

- Erlang kernel :

$$h_k(t) = c_k \frac{t^{m_k}}{(m_k)!} e^{-\nu_k t}, \nu_k > 0, m_k \in \mathbb{N}_0, c_k \in \mathbb{R}.$$

- If $c_k > 0$, then population $k + 1$ is excitatory for population k .
Else : inhibitory.
- Put $\delta := \prod_{k=1}^n c_k$. If $\delta > 0$, the system is of **positive feedback**, else, it is of **negative feedback**.

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- Put $\delta := \prod_{k=1}^n c_k$. If $\delta > 0$, the system is of **positive feedback**, else, it is of **negative feedback**. We will consider the **negative feedback case**.

Monotone cyclic feedback system

- Deriving successively the Erlang kernel functions with respect to time, it is possible to develop the above system into a **high dimensional ODE** of dimension $\kappa := n$ (number of populations) + $\sum_{k=1}^n m_k$ (memory length).
- This is a **monotone cyclic negative feedback system** as considered by *Mallet-Paret and Smith (1990)*, see also *Benaïm and Hirsch (1999)*.

Under the condition that $\delta < 0$ (negative feedback) and that the f_k are bounded Lipschitz functions :

Theorem (Mallet-Paret and Smith)

- 1) $\exists!$ equilibrium point x^* of the above system.
- 2) \exists easily verifiable condition implying that x^* is unstable. In this case, there exists at least one non constant periodic orbit which is attracting.

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- 2) \exists easily verifiable condition implying that x^* is unstable. In this case, there exists at least one non constant periodic orbit which is attracting.
- 3) If the dimension of the system is 3, then there exists a globally attracting invariance surface, and x^* is a repellor for the system.
The theorem of Poincaré-Bendixson implies that in this case, any solution will be attracted to a non constant periodic orbit.

Remark

1) So here they are, the oscillations (not for the m_t^k , but for the intensities)!

2) In particular, $\liminf_{t \rightarrow \infty} \frac{m_t^k}{t} > 0$, which was one of the conditions for the CLT.

- In which sense are these oscillations also felt by the finite size system?

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- In which sense are these oscillations also felt by the finite size system?
- First answer is given by the CLT.
- But the very specific structure of the Erlang kernels allows adopt a **Markovian description** of the Hawkes processes via its intensities

$$X_k(t) := \frac{1}{N_{k+1}} \sum_{j=1}^{N_{k+1}} \int_0^t h_k(t-s) dZ_{k+1,j}(s).$$

- Deriving successively the Erlang kernel functions with respect to time, it is possible to complete the above system of intensities

$$X_k(t) = \frac{1}{N_{k+1}} \sum_{j=1}^{N_{k+1}} \int_0^t h_k(t-s) dZ_{k+1,j}(s), 1 \leq k \leq n,$$

to a **high dimensional system** of PDMP's of dimension $\kappa := n + \sum_{k=1}^n m_k$.

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to a **high dimensional system** of PDMP's of dimension $\kappa := n + \sum_{k=1}^n m_k$.

- What we did : **Study of an associated diffusion approximation** Y (noise is easier to handle!)

Diffusion approximation

- To simplify : suppose that synaptic weight kernels are *exponential* :

$$h_k(t) = c_k e^{-\nu_k t}.$$

- Then $X_k(t), 1 \leq k \leq n$, is a PDMP.
- Diffusion approximation of the system of PDMP's $X_k(t)$:

$$\left\{ \begin{array}{l} dY_k(t) = -\nu_k Y_k(t)dt + c_k f_{k+1}(Y_{k+1}(t))dt \\ \quad + \frac{c_k}{\sqrt{N_{k+1}}} \sqrt{f_{k+1}(Y_{k+1}(t))} dB_t^{k+1} \end{array} \right\},$$

$$1 \leq k \leq n.$$

- We have the control

$$\|P_t^X \varphi - P_t^Y \varphi\|_\infty \leq Ct \frac{\|\varphi\|_{4,\infty}}{N^2}.$$

- This diffusion is hypo-elliptic (even in the case of higher order memory kernels, when noise appears only in a few components, it is shown to satisfy the weak Hörmander condition).
- Hence it is strong Feller (*Ichihara and Kunita 1974*).

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- Hence it is strong Feller (*Ichihara and Kunita 1974*).
- Using a convenient Lyapunov-function and the control theorem (and ideas inspired by the work we did with Michèle Thieullen and Reinhard Höpfner) , we obtain the following theorem.

Theorem

Let Γ be a non constant periodic orbit of the limit system which is asymptotically orbitally stable. Then for all $\varepsilon > 0$ and for all $T > 0$, for all starting configurations x , P_x -almost surely,

$Y(\cdot)$ visits $B_\varepsilon(\Gamma)$ during a time period of length T ,

infinitely often.

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Hence the diffusion approximation visits the oscillatory region infinitely often.

The same result should hold true for the original PDMP (the intensities of the system, plus the developments of the memory) - but we did not yet prove this (we have a control on the weak approximation error when replacing the PDMP by the diffusion, but only on finite time horizon).

