

A stochastic model for biological neuronal nets

Antonio Galves Eva Löcherbach

First Workshop of FAPESP's center for Neuromathematics,
NeuroMat Paper
January 20, 2014

Spike trains

- Neurons “talk to each other” by firing sequences of action potentials.

Spike trains

- Neurons “talk to each other” by firing sequences of action potentials.
- One emission of such an action potential is called **spike**.

Spike trains

- Neurons “talk to each other” by firing sequences of action potentials.
- One emission of such an action potential is called **spike**.
- Duration of spikes is very short (about 1 ms) - so : report if in a given time interval (of about 3 ms) there is **presence or absence of spike**.

Spike trains

- Neurons “talk to each other” by firing sequences of action potentials.
- One emission of such an action potential is called **spike**.
- Duration of spikes is very short (about 1 ms) - so : report if in a given time interval (of about 3 ms) there is **presence or absence of spike**. Leads to 0 – 1–valued random variables.

Spike trains

- Neurons “talk to each other” by firing sequences of action potentials.
- One emission of such an action potential is called **spike**.
- Duration of spikes is very short (about 1 ms) - so : report if in a given time interval (of about 3 ms) there is **presence or absence of spike**. Leads to 0 – 1–valued random variables.
- If we report for any neuron the discrete times of appearance of a spike → **spike trains**.

Spike trains

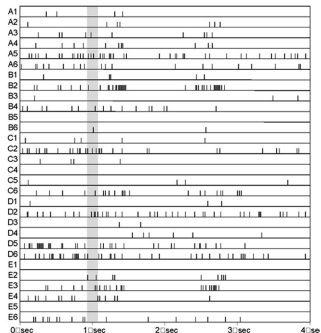


FIG.: Spike trains of several neurons - Picture by W. Maass

Non-exhaustive list of important questions

- How is information encoded in such patterns?
- How can we see an external stimulus in the data?
- Is there appearance of **synchronization**? Synchronized spiking patterns : a huge number of neurons spikes at almost the same time.
- Are successive interspike intervalls independent?

Non-exhaustive list of important questions

- How is information encoded in such patterns?
- How can we see an external stimulus in the data?
- Is there appearance of **synchronization**? Synchronized spiking patterns : a huge number of neurons spikes at almost the same time.
- Are successive interspike intervalls independent?

The model we present is a model in which we will be able to answer such kinds of questions.

Non-exhaustive list of important questions

- How is information encoded in such patterns ?
- How can we see an external stimulus in the data ?
- Is there appearance of **synchronization** ? Synchronized spiking patterns : a huge number of neurons spikes at almost the same time.
- Are successive interspike intervalls independent ?

The model we present is a model in which we will be able to answer such kinds of questions. It is partly inspired by a work done by *Bruno Cessac, A discrete time neural network model with spiking neurons : II : Dynamics with noise. Journal of Mathematical Biology, 62, 2011.*

The model

- Huge system with $N \approx 10^{11}$ neurons that interact. **What I am going to tell you even works in the case where we have an infinite number of neurons.**
- Spike train : for each neuron i and each time $t \in \mathbb{Z}$, we indicate if there is a spike or not.

The model

- Huge system with $N \approx 10^{11}$ neurons that interact. **What I am going to tell you even works in the case where we have an infinite number of neurons.**
- Spike train : for each neuron i and each time $t \in \mathbb{Z}$, we indicate if there is a spike or not.

So we consider a collection of random variables

$$X_t(i) \in \{0, 1\}, X_t(i) = 1 \Leftrightarrow \text{neuron } i \text{ has a spike at time } t .$$

- t is an index of the time window in which we observe the neuron. In the data we considered, the width of this window is typically 3 ms.

The model

Time evolution :

At each time step, **if we know the whole past history of the entire system**, neurons update independently from each other.

The model

Time evolution :

At each time step, **if we know the whole past history of the entire system**, neurons update independently from each other.

Mathematicians say : “Conditionally on the past, neurons update independently.”

The model

Time evolution :

At each time step, **if we know the whole past history of the entire system**, neurons update independently from each other.

Mathematicians say : “Conditionally on the past, neurons update independently.”

- Integrate and fire models : Each neuron’s membrane potential accumulates stimuli coming from the other neurons. The neuron spikes depending on the height of its membrane potential, this height depends on the accumulated stimuli of the other neurons.
- When a neuron has spiked, its membrane potential is reset to a resting potential. Then the neuron restarts accumulating potentials coming from other neurons.

The probability that neuron i spikes at time t is a **function of its membrane potential** and of the time elapsed since the last spike of neuron i .

The probability that neuron i spikes at time t is a **function of its membrane potential** and of the time elapsed since the last spike of neuron i .

The membrane potential of neuron i is **the sum of**

- 1 spikes of other neurons j that occurred since the **last spike time of neuron i before time t**

The probability that neuron i spikes at time t is a **function of its membrane potential** and of the time elapsed since the last spike of neuron i .

The membrane potential of neuron i is **the sum of**

- 1 spikes of other neurons j that occurred since the **last spike time of neuron i before time t** → this introduces a **variable memory structure**

The probability that neuron i spikes at time t is a **function of its membrane potential** and of the time elapsed since the last spike of neuron i .

The membrane potential of neuron i is **the sum of**

- 1 spikes of other neurons j that occurred since the **last spike time of neuron i before time t** \rightarrow this introduces a **variable memory structure**
- 2 these spikes are weighted by the synaptic weight $W_{j \rightarrow i}$ of neuron j on neuron i

The probability that neuron i spikes at time t is a **function of its membrane potential** and of the time elapsed since the last spike of neuron i .

The membrane potential of neuron i is **the sum of**

- 1 spikes of other neurons j that occurred since the **last spike time of neuron i before time t** \rightarrow this introduces a **variable memory structure**
- 2 these spikes are weighted by the synaptic weight $W_{j \rightarrow i}$ of neuron j on neuron i
- 3 they are also weighted by an aging factor which describes the loss of potential since the appearance of the spike of neuron j and the present time t .

The model II

Here is the formula

$$P(\text{neuron } i \text{ spikes at time } t \mid \text{history before time } t) = f(U_t^i, t - L_t^i),$$

where

$$\begin{aligned} U_t^i &= \text{membrane potential of neuron } i \text{ at time } t \\ &= \sum_j W_{j \rightarrow i} \sum_{s=L_t^i}^{t-1} g(t-s) X_s(j). \end{aligned}$$

In the above formula :

- $W_{j \rightarrow i} \in \mathbb{R}$: **synaptic weight** of neuron j on i .
- L_t^i last spike time before time t in neuron i .
- $g : \mathbb{N} \rightarrow \mathbb{R}_+$ describes an aging effect. If there is no aging, then $g \equiv 1$.

Excitatory versus inhibitory influence

Neurons who have a direct influence on i are those belonging to

$$\mathcal{V}_{\rightarrow i} := \{j : W_{j \rightarrow i} \neq 0\} :$$

Excitatory versus inhibitory influence

Neurons who have a direct influence on i are those belonging to

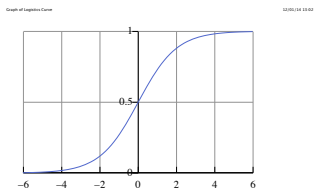
$$\mathcal{V}_{\rightarrow i} := \{j : W_{j \rightarrow i} \neq 0\} :$$

Either excitatory : $W_{j \rightarrow i} > 0$.

Or inhibitory : $W_{j \rightarrow i} < 0$.

Example

The function f is called **firing rate**, it is an **increasing** function.
It can have a logistic shape.



Or it can be a Heaviside function.

$$f(U) = 0 \text{ iff } U \leq K, \quad f(U) = 1 \text{ else.}$$

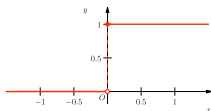
Spiking appears only if the membrane potential U is bigger than the threshold K .

Or it can be a Heaviside function.

$$f(U) = 0 \text{ iff } U \leq K, \quad f(U) = 1 \text{ else.}$$

Spiking appears only if the membrane potential U is bigger than the threshold K .

Picture is like this (where O has to be replaced by the firing threshold K)



<http://upload.wikimedia.org/wikipedia/commons/2/2e/Heaviside...>

This is a new class of non Markovian processes having a countable number of interacting components.

This is a new class of non Markovian processes having a countable number of interacting components.

- It extends in a non trivial way Spitzer's interacting particle systems

This is a new class of non Markovian processes having a countable number of interacting components.

- It extends in a non trivial way Spitzer's interacting particle systems (which are Markovian).

This is a new class of non Markovian processes having a countable number of interacting components.

- It extends in a non trivial way Spitzer's interacting particle systems (which are Markovian).
- It also extends Rissanen's stochastic chains with memory of variable length

This is a new class of non Markovian processes having a countable number of interacting components.

- It extends in a non trivial way Spitzer's interacting particle systems (which are Markovian).
- It also extends Rissanen's stochastic chains with memory of variable length (it is only **locally** of variable length).

This is a new class of non Markovian processes having a countable number of interacting components.

- It extends in a non trivial way Spitzer's interacting particle systems (which are Markovian).
- It also extends Rissanen's stochastic chains with memory of variable length (it is only **locally** of variable length).
- It is a chain of infinite order with a non countable state space.

This is a new class of non Markovian processes having a countable number of interacting components.

- It extends in a non trivial way Spitzer's interacting particle systems (which are Markovian).
- It also extends Rissanen's stochastic chains with memory of variable length (it is only **locally** of variable length).
- It is a chain of infinite order with a non countable state space.

So it is an interesting mathematical object....

- The discrete time frame is not important – a continuous time description is analogous, and my PhD-student Pierre Hodara has just proven the existence of such a kind of process in continuous time.

- The discrete time frame is not important – a continuous time description is analogous, and my PhD-student Pierre Hodara has just proven the existence of such a kind of process in continuous time.
- Our model is a version in discrete time of the so-called **Hawkes process** (see Brémaud& Massoulié 1991) – but : with an infinity of components and, locally, a structure of variable memory.

Basic mathematical questions that have been answered in our paper

- Does a chain with the above dynamics exist and if so, is it unique ?

Basic mathematical questions that have been answered in our paper

- **Does a chain with the above dynamics exist and if so, is it unique?**

Yes - under some conditions - this is the first result of our paper.

Basic mathematical questions that have been answered in our paper

- **Does a chain with the above dynamics exist and if so, is it unique ?**

Yes - under some conditions - this is the first result of our paper.

- **Are neighboring inter-spike intervals correlated ?**

This is both a mathematical and a biological question,

Basic mathematical questions that have been answered in our paper

- **Does a chain with the above dynamics exist and if so, is it unique ?**

Yes - under some conditions - this is the first result of our paper.

- **Are neighboring inter-spike intervals correlated ?**

This is both a mathematical and a biological question, and there are experimental facts that we have to explain...

What about the independence of successive Interspike intervals (ISI's) ?

Goldberg et al. (1964) in their article “Response of neurons of the superior olivary complex of the cat to acoustic stimuli of long duration” observe :

In many experimental setups the empirical correlation between successive inter-spike intervals is very small –

What about the independence of successive Interspike intervals (ISI's) ?

Goldberg et al. (1964) in their article “Response of neurons of the superior olivary complex of the cat to acoustic stimuli of long duration” observe :

In many experimental setups the empirical correlation between successive inter-spike intervals is very small –

“indicating that a description of spiking as a **stationary renewal process** is a good approximation” (Gerstner and Kistler 2002).

In the same direction :

The statistical analysis of the activity of several (but not all!) neurons in the hippocampus selects as best model a

renewal process.

- *Data registered by Sidarta Ribeiro (Brain Institute UFRN), in 2005.*
- *Data analyzed by Karina Y. Yaginuma, using the SMC (smallest maximiser criterion).*

HOWEVER :

Nawrot et al. (2007) in their article “Serial interval statistics of spontaneous activity in cortical neurons in vivo and in vitro”

find statistical evidence that **neighboring inter-spike intervals are correlated**, having negative correlation !!!

HOWEVER :

Nawrot et al. (2007) in their article “Serial interval statistics of spontaneous activity in cortical neurons in vivo and in vitro”

find statistical evidence that **neighboring inter-spike intervals are correlated**, having negative correlation !!!

Can we account for these apparently contradictory facts with our model ?

Random synaptic weights

We must describe in a more precise way the **directed graph defined by the synaptic weights** :

Random synaptic weights

We must describe in a more precise way the **directed graph defined by the synaptic weights** :

Vertices = neurons.

Random synaptic weights

We must describe in a more precise way the **directed graph defined by the synaptic weights** :

Vertices = neurons.

There is a directed edge from neuron i to neuron j iff $W_{i \rightarrow j} \neq 0$.

Random synaptic weights

We must describe in a more precise way the **directed graph defined by the synaptic weights** :

Vertices = neurons.

There is a directed edge from neuron i to neuron j iff $W_{i \rightarrow j} \neq 0$.

In what follows this graph will be a realization of a **critical directed Erdős-Rényi graph**. In such a graph there is a unique giant cluster, and we work in this giant cluster.

Critical directed Erdős-Rényi random graph

- Large but finite system of neurons with $N \approx 10^{11}$ neurons.

Critical directed Erdős-Rényi random graph

- Large but finite system of neurons with $N \approx 10^{11}$ neurons.
- **Random synaptic weights** :
 $W_{i \rightarrow j}, i \neq j$, are independent Bernoulli random variables taking values 0 or 1 with

$$P(W_{i \rightarrow j} = 1) = 1 - P(W_{i \rightarrow j} = 0) = p.$$

Critical directed Erdős-Rényi random graph

- Large but finite system of neurons with $N \approx 10^{11}$ neurons.
- **Random synaptic weights** :
 $W_{i \rightarrow j}, i \neq j$, are independent Bernoulli random variables taking values 0 or 1 with

$$P(W_{i \rightarrow j} = 1) = 1 - P(W_{i \rightarrow j} = 0) = p.$$

- Here, $p = \lambda/N$ and $\lambda = 1 + \vartheta/N, \vartheta > 0$.

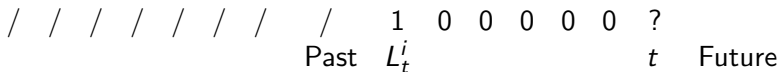
Critical directed Erdős-Rényi random graph

- Large but finite system of neurons with $N \approx 10^{11}$ neurons.
- **Random synaptic weights** :
 $W_{i \rightarrow j}, i \neq j$, are independent Bernoulli random variables taking values 0 or 1 with

$$P(W_{i \rightarrow j} = 1) = 1 - P(W_{i \rightarrow j} = 0) = p.$$

- Here, $p = \lambda/N$ and $\lambda = 1 + \vartheta/N$, $\vartheta > 0$.
- Observe that $W_{i \rightarrow j}$ and $W_{j \rightarrow i}$ are distinct and independent : being influenced by neuron i is different from influencing neuron i

Does the past before the last spike of a neuron influence the future?

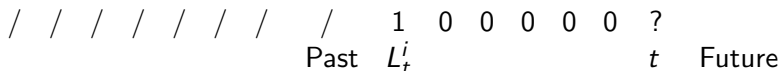


Does the past before the last spike of a neuron influence the future?

/ / / / / / / / 1 0 0 0 0 0 ?
 Past L_t^i t Future

Does it affect the future whether the last spike before L_t^i took place immediately before L_t^i or whether it took place many steps before?

Does the past before the last spike of a neuron influence the future ?



Does it affect the future whether the last spike before L_t^i took place immediately before L_t^i or whether it took place many steps before ?

The point is : the last spike of neuron i before time L_t^i affects many neurons – different from i , which in turn affect other neurons and so on. **How long does it take until this influence returns to the starting neuron i ?**

This time is a sort of *recurrence time* in the random graph :

$$C_1^i = \text{all neurons which directly influence } i$$

This time is a sort of *recurrence time* in the random graph :

$$C_1^i = \text{all neurons which directly influence } i = \{j : W_{j \rightarrow i} \neq 0\}.$$

This time is a sort of *recurrence time* in the random graph :

$$C_1^i = \text{all neurons which directly influence } i = \{j : W_{j \rightarrow i} \neq 0\}.$$

Iteratively :

$$\begin{aligned} C_n^i &= \text{all neurons which influence the neurons in } C_{n-1}^i \\ &= \{j : \exists k \in C_{n-1}^i : W_{j \rightarrow k} \neq 0\}. \end{aligned}$$

Then the recurrence time is

$$T_i = \inf\{n : i \in C_n^i\}.$$

Comparing to a branching process \Rightarrow

Proposition

$$P(\text{recurrence time} \leq k) \leq \frac{k}{N} e^{\vartheta k/N}.$$

N = number of neurons, ϑ = parameter appearing in the definition of the synaptic weight probabilities, $Np = 1 + \vartheta/N$.

This implies

Theorem

On a “good set” of random synaptic weights :

$$|\text{Covariance of neighboring inter-spike intervals}| \leq C \frac{1}{\delta^2} N(1-\delta)^{\sqrt{N}}.$$

Here, δ is the spontaneous spiking activity. Moreover,

$$P(\text{good set}) \geq 1 - CN^{-1/2}.$$

This implies

Theorem

On a “good set” of random synaptic weights :

$$|\text{Covariance of neighboring inter-spike intervals}| \leq C \frac{1}{\delta^2} N(1-\delta)^{\sqrt{N}}.$$

Here, δ is the spontaneous spiking activity. Moreover,

$$P(\text{good set}) \geq 1 - CN^{-1/2}.$$

This conciliates the empirical results both of Goldberg et al. (1964) and of Nawrot et al. (2007)!

This paper has appeared in Journal of Statistical Physics 2013 -
you can also find it on arXiv : <http://arxiv.org/abs/1212.5505>!

- Right now, we work together with Anna de Masi and Errico Presutti on the *hydrodynamical limit* of such models.
- N neurons, represented by their membrane potential.
- **Mean field interaction** : the synaptic weights are all of the same order ;

- Right now, we work together with Anna de Masi and Errico Presutti on the *hydrodynamical limit* of such models.
- N neurons, represented by their membrane potential.
- **Mean field interaction** : the synaptic weights are all of the same order ; $W_{i \rightarrow j} = \frac{1}{N}$ for all $i \neq j$.
- We add direct interactions which are due to **gap junctions**.

More precisely :

- Each neuron spikes randomly following a point process with rate $f(U_t^i)$ depending on its membrane potential.

More precisely :

- Each neuron spikes randomly following a **point process with rate $f(U_t^i)$ depending on its membrane potential.**
- At its spiking time, the membrane potential of the spiking neuron is reset to an equilibrium potential 0.

More precisely :

- Each neuron spikes randomly following a **point process with rate $f(U_t^i)$ depending on its membrane potential.**
- At its spiking time, the membrane potential of the spiking neuron is reset to an equilibrium potential 0.
- At the same time, simultaneously, the other neurons, which do not spike, receive an additional $\frac{1}{N}$ which is added to their membrane potential.

More precisely :

- Each neuron spikes randomly following a **point process with rate $f(U_t^i)$ depending on its membrane potential.**
- At its spiking time, the membrane potential of the spiking neuron is reset to an equilibrium potential 0.
- At the same time, simultaneously, the other neurons, which do not spike, receive an additional $\frac{1}{N}$ which is added to their membrane potential.
- **Electrical synapses** occur through *gap-junctions* → attraction between the values of the membrane potentials of the different neurons → drift of the system towards its center of mass.

- Interactions between neurons are very complex –

- Interactions between neurons are very complex – our model only takes into account their **average effect** - by the mean field assumption.

- Interactions between neurons are very complex – our model only takes into account their **average effect** - by the mean field assumption.
- **Hydrodynamical limit** means : We represent the system of N neurons by their associated **empirical measure**.

As the size of the systems gets huge (i.e. $N \rightarrow \infty$), we prove **convergence in law** of **the empirical measure** (which is random) to a limit measure.

- Interactions between neurons are very complex – our model only takes into account their **average effect** - by the mean field assumption.
- **Hydrodynamical limit** means : We represent the system of N neurons by their associated **empirical measure**.

As the size of the systems gets huge (i.e. $N \rightarrow \infty$), we prove **convergence in law** of **the empirical measure** (which is random) to a limit measure.

- The limit measure is deterministic and given by a **probability density** $\rho_t(x)$ = density of neurons having membrane potential x at time t .

- Interactions between neurons are very complex – our model only takes into account their **average effect** - by the mean field assumption.
- **Hydrodynamical limit** means : We represent the system of N neurons by their associated **empirical measure**.

As the size of the systems gets huge (i.e. $N \rightarrow \infty$), we prove **convergence in law** of **the empirical measure** (which is random) to a limit measure.

- The limit measure is deterministic and given by a **probability density** $\rho_t(x)$ = density of neurons having membrane potential x at time t .
- This limit density satisfies a **non-linear** PDE of hyperbolic type.

Theorem

$$\frac{\partial \rho_t(x)}{\partial t} = [\lambda x - \lambda \bar{\rho}_t - \rho_t] \frac{\partial \rho_t(x)}{\partial x} - [f(x) - \lambda] \rho_t(x),$$

Theorem

$$\frac{\partial \rho_t(x)}{\partial t} = [\lambda x - \lambda \bar{\rho}_t - p_t] \frac{\partial \rho_t(x)}{\partial x} - [f(x) - \lambda] \rho_t(x),$$

where λ is the strength of the gap junctions, p_t is the mean firing rate, $\bar{\rho}_t$ the center of mass, i.e.

$$\int_0^\infty f(x) \rho_t(x) dx = p_t \quad \text{and} \quad \int_0^\infty x \rho_t(x) dx = \bar{\rho}_t, \quad \text{for all } t \geq 0.$$

Moreover, the above solution satisfies the initial condition

$$\rho_t(0) = \frac{p_t}{p_t + \lambda \bar{\rho}_t} \quad \text{for all } t \geq 0.$$

Remarks

- Usual way to prove hydrodynamic limits in mean field systems : show that **propagation of chaos** holds, i.e. show that neurons i and j get uncorrelated as the system gets huge.

Remarks

- Usual way to prove hydrodynamic limits in mean field systems : show that **propagation of chaos** holds, i.e. show that neurons i and j get uncorrelated as the system gets huge.
- BUT : each time that another neuron fires, it instantaneously affects both neurons i and j by changing them with an additional amount $1/N$.

Remarks

- Usual way to prove hydrodynamic limits in mean field systems : show that **propagation of chaos** holds, i.e. show that neurons i and j get uncorrelated as the system gets huge.
- BUT : each time that another neuron fires, it instantaneously affects both neurons i and j by changing them with an additional amount $1/N$.
- Thus i and j are correlated, and propagation of chaos comes only by proving first that the firing activity of the other neurons – by propagation of chaos – is essentially deterministic → circular argument!!!

- What we did : We introduced an **auxiliary process** = good approximation of the true process.

This auxiliary process is constant on time intervals $[n\delta, (n + 1)\delta[$.

- What we did : We introduced an **auxiliary process** = good approximation of the true process.

This auxiliary process is constant on time intervals $[n\delta, (n + 1)\delta[$.
... and it is easy to prove the hydrodynamic limit for it

- What we did : We introduced an **auxiliary process** = good approximation of the true process.

This auxiliary process is constant on time intervals $[n\delta, (n+1)\delta[$.

... and it is easy to prove the hydrodynamic limit for it

- We then conclude by letting $\delta \rightarrow 0$.

- What we did : We introduced an **auxiliary process** = good approximation of the true process.

This auxiliary process is constant on time intervals $[n\delta, (n+1)\delta[$.

... and it is easy to prove the hydrodynamic limit for it

- We then conclude by letting $\delta \rightarrow 0$.

Open questions for the moment :

Existence of a stationary solution for the limit equation ?

Does the non-existence of a stationary solution imply **synchronization patterns** ?

Thank you for your attention !
Paper should be on arXiv soon !

Thank you for your attention !

Paper should be on arXiv soon !

The next talks will develop some mathematical, statistical and biological issues suggested by this model