# Two examples of thermodynamic limits in neuroscience

A Random Walk in the Land of Stochastic Analysis and Numerical Probability

in honor of Denis Talay

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INRIA

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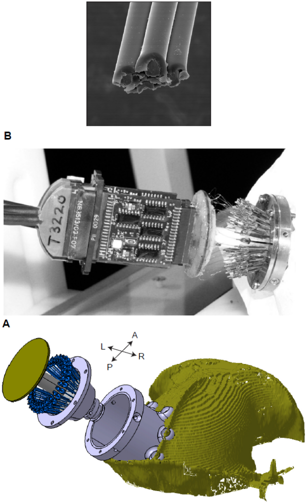
# Outline

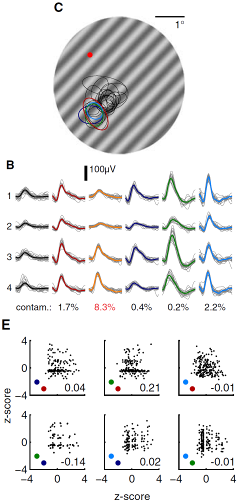
# The neuronal activity in V1: from Ecker et al., Science 2010

- Recording neurons in V1



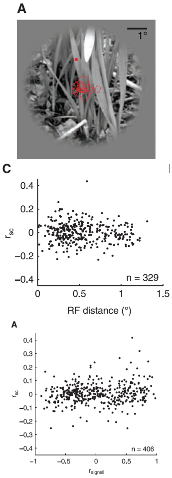
# The neuronal activity in V1: from Ecker et al., Science 2010

- shows that their activity is HIGHLY **decorrelated** for synthetic

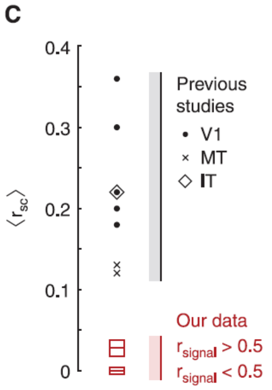


# The neuronal activity in V1: from Ecker et al., Science 2010

- and natural images



## The neuronal activity in V1: from Ecker et al., Science 2010

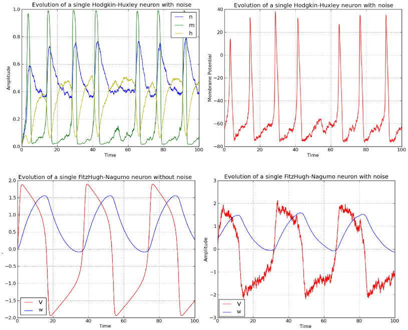



- as opposed to previous results.

# The neuronal activity in V1: from Ecker et al., Science 2010

- Is this a network effect?
- Is this related to the stochastic nature of neuronal computation?

# Networks of continuous spiking neurons



# Networks of continuous spiking neurons

Joint work with M. Bossy and D. Talay

- Hodgkin-Huxley model or one of its 2D reductions.
- Chemical noisy synapses
- Synaptic weights are dynamically changing over time.
- Neurons belong to $P$ different populations (e.g. E and I), noted $\alpha$, $\beta$, $\cdots$. Population $\alpha$ contains $N_\alpha$ neurons.
- Population function $p : \{1, \cdots, N\} \to \mathcal{P} = \{\alpha, \cdots\}$

# Fitzhugh Nagumo model

Stochastic Differential Equation (SDE):

$$\begin{cases} dV_t^i = \left(V_t^i - \frac{(V_t^i)^3}{3} - w_t^i + I_\alpha^{\mathrm{ext}}(t)\right) dt + \sigma_{\mathrm{ext}}^\alpha dW_t^{i,V} \equiv \\ \qquad F_\alpha(t, V^i, w_t^i)dt + \sigma_{\mathrm{ext}}^\alpha dW_t^{i,V} \\ \frac{dw_t^i}{dt} = a_\alpha \left(b_\alpha V_t^i - w_t^i\right) \\ p(i) = \alpha \end{cases}$$

Takes into account an external current noise.

# Synapses

Synaptic current from the $j$th to the $i$th neuron:

$$I_{ij}^{\mathrm{syn}} = -g_{ij}(t)(V^i - V_{\mathrm{rev}}^{\alpha\gamma}) \quad p(i) = \alpha,\ p(j) = \gamma$$

Conductance:

$$g_{ij}(t) = J_{ij}(t)y^j(t)$$

# Synapses

The function $y^j$ denotes the fraction of open channels and satisfies a SDE.

$$dy_t^j = \left(a_r^\gamma S_\gamma(V^j)(1 - y^j(t)) - a_d^\gamma y^j(t)\right)\, dt + \sigma_\gamma(V^j, y^j)\, dW_t^{j,y}$$

where (Langevin approximation of a PDMP, Wainrib 2010)

$$\sigma_\gamma(V^j, y^j) = \sqrt{|a_r^\gamma S_\gamma(V^j)(1 - y^j) + a_d^\gamma y^j|}\chi(y^j),$$

and the function $S$:

$$S_\gamma(V^j) = \frac{T_{\max}^\gamma}{1 + e^{-\lambda_\gamma(V^j - V_T^\gamma)}}$$

# Maximum conductances

The maximum conductances (synaptic weights) are affected by dynamical random variations:

$$J_{i\gamma}(t) = \frac{\bar{J}_{\alpha\gamma}}{N_\gamma} + \frac{\sigma^J_{\alpha\gamma}}{N_\gamma}\xi^{i,\gamma}(t),$$

Advantage : simplicity

Disadvantage : an increase of the noise level increases the probability that the sign of $J_{ij}(t)$ is different from that of $\bar{J}_{\alpha\gamma}$.
This can be fixed (Cox-Ingersoll-Ross model)

# Putting everything together

Each neuron $i$ ($p(i) = \alpha$) is represented by a state vector of dimension 3:

$$
(P) \begin{cases}
dV_t^i & = F_\alpha(t, V_t^i, w_t^i)dt \\
& \quad - \sum_{\gamma\in\mathcal{P}}(V_t^i - V_{\text{rev}}^{\alpha\gamma})\frac{\bar{J}_{\alpha\gamma}}{N_\gamma}\left(\sum_{j=1}^N \mathbb{1}(p(j)=\gamma)y_t^j\right)dt \\
& \quad - \sum_{\gamma\in\mathcal{P}}(V_t^i - V_{\text{rev}}^{\alpha\gamma})\frac{\sigma_{\alpha\gamma}^J}{N_\gamma}\left(\sum_{j=1}^N \mathbb{1}(p(j)=\gamma)y_t^j\right)dB_t^{\gamma,i} \\
& \qquad + \sigma_{\text{ext}}^\alpha dW_t^{i,V} \\
\frac{dw_t^i}{dt} & = a_\alpha\left(b_\alpha V_t^i - w_t^i\right) \\
dy_t^i & = (a_r^\alpha S_\alpha(V_t^i)(1-y_t^i) - a_d^\alpha y_t^i)dt + \sigma_\alpha(V_t^i, y_t^i)dW_t^{i,y}
\end{cases}
$$

# The limit equations

$$(M)\begin{cases} dV_t^\alpha & = F_\alpha(t, V_t^\alpha, w_t^\alpha)dt - \sum_{\gamma\in\mathcal{P}}(V_t^\alpha - V_{\rm rev}^{\alpha\gamma})\bar{J}_{\alpha\gamma}\mathbb{E}[y_t^\gamma]dt \\ & \quad -\sum_{\gamma\in\mathcal{P}}(V_t^\alpha - V_{\rm rev}^{\alpha\gamma})\sigma^J_{\alpha\gamma}\mathbb{E}[y_t^\gamma]dB_t^{\gamma,\alpha} + \sigma_{\rm ext}^\alpha dW_t^{\alpha,V} \\ \frac{dw_t^\alpha}{dt} & = a_\alpha\left(b_\alpha V_t^\alpha - w_t^\alpha\right) \\ dy_t^\alpha & = (a_r^\alpha S_\alpha(V_t^\alpha)(1-y_t^\alpha) - a_d^\alpha y_t^\alpha)dt + \sigma_\alpha(V_t^\alpha, y_t^\alpha)dW_t^{\alpha,y} \end{cases}$$

# Hypotheses

I) Ion channels models: $\chi$ is bounded Lipschitz continuous with compact support included in (0, 1).

II) Chemical synapse model: $S_\alpha$ is a sigmoid, $a_r^\alpha$ and $a_d^\alpha$ are positive

III) Membrane model: The $F_\alpha(t, v, w)$ are continuous, one-sided Lipschitz wrt $v$ and Lipschitz wrt $w$.

IV) Initial conditions: $V_0^i$, $y_0^i$, $w_0^i$, $J_0^{i\gamma}$ are i.i.d. r.v. with the same law as $V_0^\alpha$, $y_0^\alpha$, $w_0^\alpha$, $J_0^{\alpha\gamma}$ when $p(i) = \alpha$. $V_0^\alpha$ and $J_0^{\alpha\gamma}$ have moments of any order.

# Well-posedness of the $N$-neuron model

## Proposition

Under Hypotheses I-IV, the system $(P)$ has a unique pathwise solution on all time intervals $0 \leq t \leq T$. In addition the components of the processes $y_t^i$ take values in $(0, 1)$.

# Well-posedness of the mean-field limit models

## Proposition

Under Hypotheses I-IV, the system $(M)$ has a unique pathwise solution on all time intervals $0 \leq t \leq T$. In addition the components of the processes $y_t^\alpha$ take values in $(0, 1)$.

## Proof.

Slight extension of the fixed point method developed in Sznitman 1989 and arguments found in Luçon-Stannat 2014. □

Let $\mathbb{P}$ be the law of its solution.

# Convergence and propagation of chaos

1. $(R_t) = (R_t^\alpha, \alpha \in \mathcal{P}) = (V_t^\alpha, (J_t^{\alpha\gamma}, \gamma \in \mathcal{P}), y_t^\alpha, w_t^\alpha; \alpha \in \mathcal{P})$ the solution to $(M)$
2. $(R_t^{i,N}, i = 1, \cdots, N) = (V_t^i, (J_t^{i\gamma}, \gamma \in \mathcal{P}), y_t^i, w_t^i; i = 1, \cdots, N)$ the solution to $(P)$
3. The coupling $(\tilde{R}_t^i)$: all $N_\alpha$ indices $i$ such that $p(i) = \alpha$ are such that $(\tilde{R}_t^i)$ are independent copies of $(R_t^\alpha)$

# Convergence and propagation of chaos

## Proposition

Assume that for all $\gamma \in \mathcal{P}$, the proportion $N_\gamma / N$ is nonzero and independent of $N$. Then for all set of $P$ indexes $(i_\alpha, \alpha \in \mathcal{P})$ in $\{1, \cdots, N\}$ with $p(i_\alpha) = \alpha$. the vector process $(R^{i_\alpha, N} - \tilde{R}_t^{i_\alpha})$ satisfies

$$\sqrt{N}\mathbb{E}\left[\sup_{0 \leq t \leq T} \sum_{\alpha \in \mathcal{P}} |R^{i_\alpha, N} - \tilde{R}_t^{i_\alpha}|^2\right] \leq C$$

# Convergence and propagation of chaos

The law of any subsystem of size $k$

$$((R_t^{1_\alpha,N}, \alpha \in \mathcal{P}) \cdots (R_t^{k_\alpha,N}, \alpha \in \mathcal{P})) \quad p(i_\alpha) = \alpha$$

converges to $\mathbb{P}^{\otimes k}$ when the $N_\alpha$s tend to infinity

# Convergence and propagation of chaos

## Proof.

The proof follows and adapts Sznitman 1989 and Méléard 1996. □

Difficulty: some of the coefficients are not globally Lipschitz continuous. The drift $f$ is of the form

$$f\left(t, v, w, j, \frac{1}{N}\sum_{i=1}^{N} y^i\right) = F_\alpha(t, v, w) - j(v - \bar{V}^{\alpha\gamma})\left(\frac{1}{N}\sum_{i=1}^{N} y^i\right)$$

Thanks to

- $F_\alpha$ is one-sided Lipschitz:

$$\begin{aligned}(F_\alpha(t, v, w) - F_\alpha(t, v', w))(v - v') &\leq L(v - v')^2 - M(v, v')(v - v')^2 \quad L, \\ |F_\alpha(t, v, w) - F_\alpha(t, v, w')| &\leq L|w - w'|\end{aligned}$$

- The processes $J_t^{\alpha\gamma}$ are positive

# Convergence and propagation of chaos

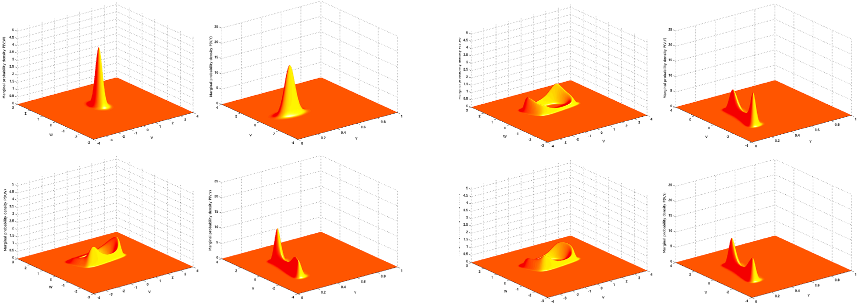
- The processes $y_t^i$ are in $(0, 1)$
- The term $-j(v - \bar{V}^{\alpha\gamma})\left(\frac{1}{N}\sum_{i=1}^{N} y^i\right)$ stabilises the moments of $V_t$

M. Bossy, O.F., D. Talay, Journal Math. Neur., 2015.

# A glimpse of the results

- The 10 millions equations are "summarized" by $P$ describing the stochastic time evolution of $P$ "meta" neuron.

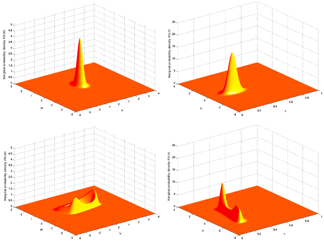
Left $= (V, w)$ - Right $= (V, y)$

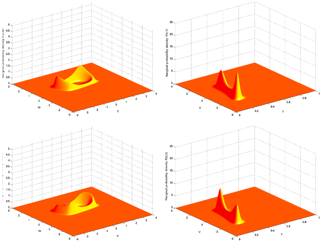


Initial conditions - $T = 30.0$ $\qquad$ $T = 50.0$ - $T = \infty$

J. Baladron, D. Fasoli, O.F., J. Touboul, Journal Math. Neur., 2012.

# Some movies





J. Baladron, D. Fasoli, O.F., J. Touboul, Journal Math. Neur., 2012.

# The mathematical model

After Ben Arous and Guionnet, joint work with Etienne Tanré

# The mathematical model

- Ignore the spikes, consider only the "firing rates"
- Intrinsic dynamics:

$$\mathcal{S} := \begin{cases} dV_t & = & -V_t dt + dB_t, \ 0 \leq t \leq T \\ \text{Law of } V_0 & = & \mu_0, \end{cases}$$

- There is a unique strong solution to $\mathcal{S}$ (Ornstein-Uhlenbeck process):
- Note $P$ its law on the set $\mathcal{T} := \mathcal{C}([0, T]; \mathbb{R})$ of trajectories

# The mathematical model

- $N$ neurons in a completely connected network
- Coupled dynamics

$$\mathcal{S}(J^N) :=$$

$$\begin{cases} dV_t^i & = & (-V_t^i + \sum_{j=1}^N J_{ij}^N f(V_t^j))dt + dB_t^i \\ & & \quad i \in \{1, \cdots, N\} \\ \text{Law of } V_N(0) & = & (V_0^1, \cdots, V_0^N) = \mu_0^{\otimes N} \end{cases}$$

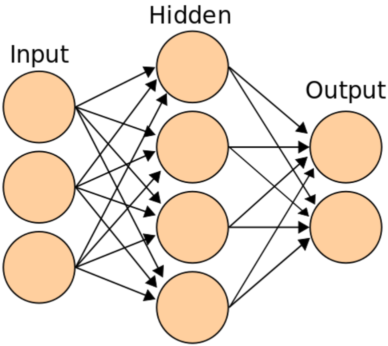
$i \in \{1, \cdots, N\}$.

- $f$ is bounded, Lipschitz continuous (usually a sigmoid), defining the firing rate
- $B^i$: independent Brownians: intrinsic noise on the membrane potentials

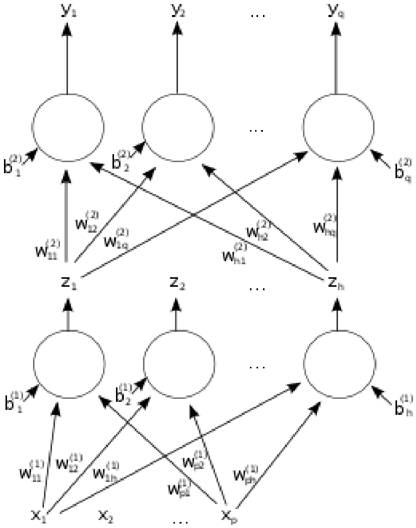
# The mathematical model

- There is a unique strong solution to $\mathcal{S}(J^N)$
- Note $P(J^N)$ its law on the set $\mathcal{T}^N$ of $N$-tuples of trajectories.

# Connection with Neural Networks




Source: Wikipedia



# Modeling the synaptic weights

- The $J_{ij}^N$s are i.i.d. random synaptic weights $\frac{1}{\sqrt{N}}\mathcal{N}(0,1)$
- Even so, hard to guess the limit when $N \to \infty$ of $\mathcal{S}(J^N)$!

# Consequences

- $P(J^N)$ is a random law on $\mathcal{T}^N$
- Consider the law $P^{\otimes N}$ of $N$ independent uncoupled neurons
- Girsanov theorem allows us to compare the law of the solution to the coupled system, $P(J^N)$, with the law of the uncoupled system, $P^{\otimes N}$:

$$\frac{dP(J^N)}{dP^{\otimes N}} = \exp\left\{ \sum_{i=1}^{N} \int_0^T \left( \sum_{j=1}^{N} J_{ij}^N f(V_t^j) \right) dB_t^i - \frac{1}{2} \int_0^T \left( \sum_{j=1}^{N} J_{ij}^N f(V_t^j) \right)^2 dt \right\}$$

# Empirical measure

- Consider the empirical measure:

$$\hat{\mu}^N(V_N) = \frac{1}{N} \sum_{i \in I_n} \delta_{V^i},$$

$$V_N = (V^1, \cdots, V^N)$$

- It defines the mapping

$$\hat{\mu}^N : \mathcal{T}^N \to \mathbf{P}(\mathcal{T})$$

# Empirical measure

- We are interested in the law of $\hat{\mu}^N$ under $P(J^N)$
- Define

$$Q^N = \int_\Omega P(J^N(\omega))\, d\omega,$$

the average of $P(J^N)$ w.r.t. to the "random medium", i.e. the synaptic weights.

- We study the law of $\hat{\mu}^N$ under $Q^N$: annealed results.

# The strategy

- Consider the law $\Pi^N$ of $\hat{\mu}^N$ under $Q^N$: it is a probability measure on $\mathbf{P}(\mathcal{T})$:

$$\Pi^N(B) = \left(Q^N \circ (\hat{\mu}^N)^{-1}\right)(B) = Q^N(\hat{\mu}^N \in B),$$

$B$ measurable set of $\mathbf{P}(\mathcal{T})$

# The strategy

- Establish a Large Deviation Principle for the sequence of probability measures $(\Pi^N)_{N \geq 1}$, i.e.
- Design a rate function (non-negative lower semi-continuous) $H$ on $\mathbf{P}(\mathcal{T})$
- The intuitive meaning of $H$ is the following

$$Q^N(\hat{\mu}^N \simeq Q) \simeq e^{-NH(Q)}$$

- The measures $\hat{\mu}^N$ concentrate on the measures $Q$ such that $H(Q) = 0$.
- If $H$ reaches 0 at a single measure $Q$ then $\Pi^N$ converges weakly toward the Dirac mass $\delta_Q$

# Minimum of $H$

By adapting the results of Ben Arous and Guionnet (1995), Guionnet (1997), and of Moynot and Samuelides (2002) one obtains:

## Theorem

$$H(\mu) = I^{(2)}(\mu; P) - \Gamma(\mu),$$

*where $I^{(2)}(\mu; P)$ is the relative entropy of $\mu$ w.r.t. $P$ and $\Gamma$ is defined by*

$$\frac{dQ^N}{dP^{\otimes N}} = e^{N\Gamma(\hat{\mu}^N)}$$

*$H$ achieves its minimum at a unique point $\mu$ of $\mathbf{P}(\mathcal{T})$.*

**Remark** This result is universal as shown in Dembo, Lubetsky and Zeitouni (2021)

# Minimum of $H$

## Theorem

*$\mu$ is the unique solution to the fixed point problem:*

$$\frac{d\mu}{dP} = \int \exp\left\{ \int_0^T G_t^\mu \, dB_t - \frac{1}{2} \int_0^T (G_t^\mu)^2 \, dt \right\} d\gamma_\mu,$$

*where, under $\gamma_\mu$, $G_t^\mu$ is a centered Gaussian process with covariance*

$$K_\mu(t,s) = \int_{\mathcal{T}} f(v_t) f(v_s) \, d\mu(v),$$

# Stochastic system

## Theorem

*$\mu$ is the law of the solution to a non-linear non-Markovian stochastic system.*

$$\begin{cases} X_t & = & X_0 - \int_0^t X_s \, ds + B_t \\ B_t & = & W_t + \int_0^t \int_0^s \tilde{K}_\mu(s,u) \, dB_u \, ds \\ \text{Law of } X & = & \mu, \quad \mu_{\mathcal{F}_0} = \mu_0 \\ K_\mu(t,s) & = & \int_{\mathcal{T}} f(X_t) f(X_s) \, d\mu(X) \end{cases}$$

- $W_t$ is a Brownian motion under $\mu$.
- $\tilde{K}_\mu^t(t,s)$ is a covariance function which depends nonlinearly upon $K_\mu$:

$$\tilde{K}_\mu^t = K_\mu \circ (\mathrm{Id} + K_\mu)^{-1}$$

- The proof requires a good deal of stochastic and Gaussian calculus

# Stochastic system

- The second equation can be solved with respect to $B$ using the theory of Volterra equations:

$$B_t = W_t + \int_0^t \widetilde{W}_s \, ds + \int_0^t \left( \int_0^s H_\mu^s(s,u) \widetilde{W}_u \, du \right) ds,$$

where

$$\widetilde{W}_t = \int_0^t \tilde{K}_\mu^t(t,s) \, dW_s$$

The function $H_\mu^t$ is defined from $\tilde{K}_\mu^t$ by

$$\bar{H}_\mu^t = (\mathrm{Id} - \bar{\tilde{L}}_\mu^t)^{-1}, \quad \tilde{L}_\mu^t(s,u) = \begin{cases} \tilde{K}_\mu^t(s,u) & \text{if } u \leq s \\ 0 & \text{otherwise,} \end{cases}$$

# Stochastic system

- $K_\mu$ can be estimated by a fixed point procedure based on Monte-Carlo simulations:

## Proof.

The proof is through the use of the solution to the previous Volterra equation. A good deal of stochastic and Gaussian calculus is again needed. □

# Stochastic system

- Extensions to nonzero mean weights and several populations of neurons are possible:

$$\begin{cases} X_t & = & X_0 - \int_0^t X_s\,ds + \int_0^t c_\mu(s)\,ds + B_t \\ B_t & = & W_t + \int_0^t \int_0^s \tilde{K}_\mu^s(s,u)\,dB_u\,ds \\ m_\mu(t) & = & \int f(X_t)\,d\mu(X) \\ c_\mu(t) & = & \left(\mathrm{Id} + \bar{K}_\mu\right)^{-1} \cdot m_\mu(t) \\ K_\mu(t,s) & = & \int f(X_t) f(X_s)\,d\mu(X) \\ \text{Law of } X & = & \mu, \quad \mu_{|\mathcal{F}_0} = \mu_0 \end{cases}$$

Upcoming arxiv, O.F., Etienne Tanré, 2023+

# Propagation of chaos

## Theorem

*$Q^N$ is $\mu$-chaotic.*

i.e. for all $m \geq 2$ and $\varphi_i$, $i = 1, \ldots, m$ in $C_b(\mathcal{T})$

$$\lim_{N \to \infty} \int_{\mathcal{T}^N} \varphi_1(v^1) \cdots \varphi_m(v^m)\, dQ^N(v^1, \cdots, v^N) = \prod_{i=1}^{m} \int_{\mathcal{T}} \varphi_i(v)\, d\mu(v)$$

"In the thermodynamic limit ($N \to \infty$) and on average, the neurons in any finite-size group become independent. One observes the propagation of chaos. The neurons become asynchronous."

# Quenched results

These results are marginally useful in practice because we have averaged over the weights **J** but we also have:

**Existence and uniqueness of a quenched limit**
The law of the empirical measure of the quenched system converges to $\delta_\mu$ for almost all **J**s (Theorem 2.7 in Ben Arous and Guionnet (95)).

This of course does not imply a quenched propagation of chaos since the neurons are not exchangeable for almost all interaction but we have

# Quenched results

**Quenched propagation of chaos**

If the initial law $\mu_0$ is symmetric, then for any set of $m$ continuous bounded functions $(\varphi_j)_{m=1,\cdots,m}$ defined on $\mathcal{C}$

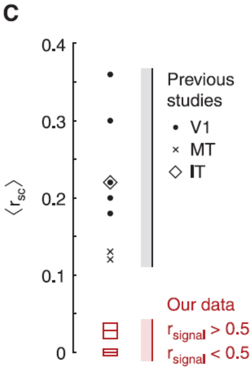
$$\int \prod_{j=1}^{m} \varphi_j(X^j)\, dP^N(\mathbf{J})(X) \xrightarrow{p} \prod_{j=1}^{m} \int \varphi_j(X)\, d\mu(X)$$

This means that for all $\varepsilon > 0$

$$\lim_{N\to\infty} \gamma \left( \omega \, : \left| \int \prod_{j=1}^{m} \varphi_j(X^j)\, dP^N(\mathbf{J})(X) - \prod_{j=1}^{m} \int \varphi_j(X)\, d\mu(X) \right| > \varepsilon \right) = 0$$

# Conclusion

- We did all this technical work because of this biological observation:



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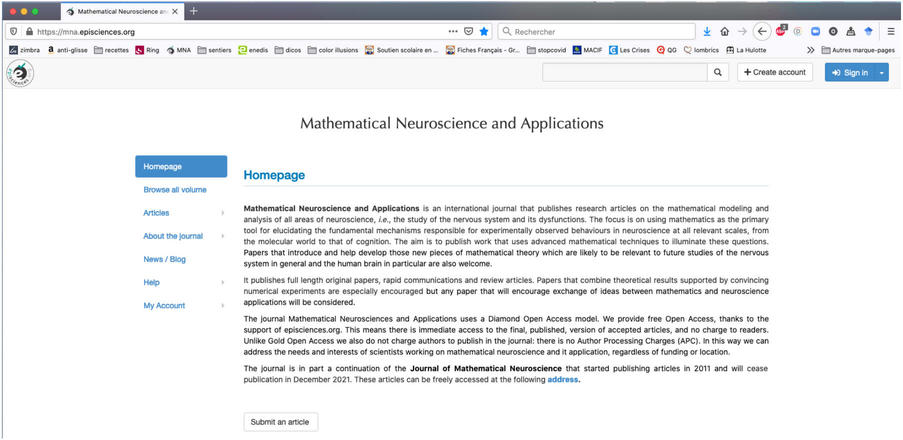


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