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## ICMNS 2018-ANTIBES

# Synchronization of stochastic mean field networks of Hodgkin-Huxley neurons with noisy channels 

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## The model

According to the Hodgkin-Huxley model, the dynamics of a neuron's voltage is the result of the passage of ions through its membrane. This ion flux occurs through specific proteins which act as gated channels.

## Single Neuron Model

$V_{t}$ is the voltage of the neuron, $m_{t}, h_{t}, n_{t} \in[0,1]$, are the proportions of open: activation Sodium channels, deactivation Sodium channels and activation Potassium channels respectively

$$
\begin{aligned}
d V_{t} & =F\left(V_{t}, m_{t}, n_{t}, h_{t}\right) d t \\
d x_{t} & =\left[\rho_{x}\left(V_{t}\right)\left(1-x_{t}\right)-\zeta_{x}\left(V_{t}\right) x_{t}\right] d t
\end{aligned}
$$

where, here and in the sequel, $x$ generically represents the $m, n, h$ components and $F: \mathbb{R} \times[0,1]^{4} \rightarrow \mathbb{R}$, defined by
$F(V, m, n, h)=I-g_{\mathrm{K}} n^{4}\left(V-V_{\mathrm{K}}\right)-g_{\mathrm{Na}} m^{3} h\left(V-V_{\mathrm{Na}}\right)$ $-g_{\mathrm{L}}\left(V-V_{\mathrm{L}}\right)$,
represents the effect on the voltage of the ionic channels and of an external current $I$ (assumed constant for simplicity)

## Interaction: Synapses

We consider a population of $N$ neurons $\{1$ two type of interactions:

Chemical Synapses: A neurotransmitter is released to the intercellular media from a pre-synaptic neuron to the post-synaptic one through synaptic channels.

With each neuron $j$ we associate a new variable $y^{(j)} \in[0,1]$ which represents its proportion of open synaptic channels at each time.
Chemical synapses coming from neuron $j$ induce on the voltage $V^{(i)}$ of the neuron $i$ an instantaneous variation at time $t$ of

$$
-\frac{J_{\mathrm{ch}}{ }^{y} y^{(j)}\left(V_{t}^{(i)}\right)}{\left(V_{\mathrm{eve}}\right),}
$$

where $J_{\mathrm{Ch}} \geq 0$ is the chemical conductance.
Electrical Synapses: Neurons directly connected with each other through an intercellular channel called gap junction.

Pre-synaptic neuron $j$ contributes to the variation of the voltage of post-synaptic neuron $i$ by the amount

$$
-\frac{J_{E}\left(v_{3}^{(i)}\right.}{\left.()_{s}^{(j)}\right),}
$$

where $J_{\mathrm{E}} \geq 0$ is the electrical conductance.

## Noise

To consider the intrinsic noise present in the ion and neurotransmitter channels we add a noise to the dynamic of the channels:

$$
d x_{t}=\rho_{x}\left(V_{t}\right)\left(1-x_{t}\right)-\zeta_{x}\left(V_{t}\right) x_{t} d t+\sigma_{x}\left(V_{t}, x_{t}\right) d W_{t}^{x},
$$

where $W^{x}, x=m, n, h, y$ are independent Brownian motions.
For the specific form of $\sigma_{x}$ we refer to Pakdaman et al. [2] and the references therein, where the authors obtain a similar dynamic for the channels as the fluctuations of a Piecewise Deterministic Markov Process.

## Model for a Network

We consider the model for a network fully connected studied by Bossy et al. in [1]. The state of the neuron $i=1, \ldots, N$ will represented by $X_{t}^{(i)}=\left(V_{t}^{(i)}, m_{t}^{(i)}, n_{t}^{(i)}, h_{t}^{(i)}, y_{t}^{(i)}\right)$, and we denote by

$$
\vec{V}_{t}^{N}=\frac{1}{N} \sum_{i=1}^{N} V_{i}^{(i)}, \overrightarrow{\bar{U}_{i}^{W} \mathrm{~N}}=\frac{1}{N} \sum_{i=1}^{N} y_{i}^{(i)},
$$

the empirical means for the voltage and the proportion of open neurotransmitter channels respectively.
The dynamics will be:

$$
\begin{aligned}
V_{t}^{(i)}=V_{0}^{(i)} & +\int_{0}^{t} F\left(V_{s}^{(i)}, m_{s}^{(i)}, n_{s}^{(i)}, h_{s}^{(i)}\right) d s \\
& -\int_{0}^{t} J_{\mathrm{E}}\left(V_{s}^{(i)}-\bar{V}_{s}^{N}\right)-J_{\mathrm{Ch}} \overline{\mathrm{y}}_{s}^{N}\left(V_{s}^{(i)}-V_{\mathrm{rev}}\right) d s, \\
x_{t}^{(i)}=x_{0}^{(i)}+ & \int_{0}^{t} \rho_{x}\left(V_{s}^{(i)}\right)\left(1-x_{s}^{(i)}\right)-\zeta_{x}\left(V_{s}^{(i)}\right) x_{s}^{(i)} d s \\
& +\int_{0}^{t} \sigma_{x}\left(V_{s}^{(i)}, x_{s}^{(i)}\right) d W_{s}^{x_{s}^{, i},},
\end{aligned}
$$

where ( $W^{x, i}: i \in \mathbb{N}, x=m, n, h, y$ ) are one dimensional Brownian motions independent of each other and independent of the initial condition.

Simulating the Model



Figure 1: Left: The evolution of the Voltage and Channels for one neuron. Right: The evolution of the Voltage of 100 neurons $J_{\mathrm{E}}$ small.

## Emergence of Synchrony

Numerical simulations show when increasing $J_{\mathrm{E}}$, the neurons synchronize. This phenomenon is independent of the number of neurons and the phase difference is only affected by the size of the noise.

## Lum Lum

Figure 2: Trajectories for the Voltage of 100 neurons under strong inter action and different level of noise: Left: $\sigma=0.5$. Right: $\sigma=1$.

As a measure of the synchronicity of the network we compute the empirical variance of Voltage of the system (2): $N^{-1} \sum_{i=1}^{N}\left(V_{t}^{(i)}-\bar{V}_{t}^{N}\right)^{2}$, and to obtain statistically meaningful information, we perform Monte Carlo simulations to estimate the evolution of the expected value of this quantity for different values of $N$ and $\sigma$


Figure 3: Time evolution of the expected empirical variance of the Voltage for different level of noise: Left: $\sigma=0.5$. Right: $\sigma=1$

Partial Conclusion: The numerical evidence shows that for big enough $J_{\mathrm{E}}$ the neurons get synchronized, meaning that the empirical variance becomes small in mean. This phenomena seems independent of the size of the network

## Hypothesis (H)

$\rho_{x}$ and $\zeta_{x}$ are strictly positive, locally Lipschitz continuous functions on $\mathbb{R}$. The function $\sigma_{x}: \mathbb{R}^{2} \rightarrow \mathbb{R}$ are given by

$$
\sigma_{x}(v, z)=\sigma \sqrt{\left|\rho_{x}(v)(1-z)+\zeta_{x}(v) z\right|} \chi(z)
$$

with $\chi: \mathbb{R} \rightarrow[0,1]$ a Lipschitz continuous function with support contained in $[0,1]$ and $\sigma \geq 0$
2. The leak conductance $g_{L}$ is strictly positive.
3. One has $\left(m_{0}^{(i)}, n_{0}^{(i)}, h_{0}^{(i)}, y_{0}^{(i)}\right) \in[0,1]^{4}$ a.s.
4. The initial voltages are bounded uniformly in $N$

$$
\sup _{i=1, \ldots, N}\left|V_{0}^{(i)}\right| \leq V_{0}^{\max } \quad \text { a.s. }
$$

Reduce Synchronized Dynamics
For $t_{1} \geq 0$, let $\left(\widehat{X}_{t}^{t_{1}}: t \geq t_{1}\right)$ denote the solution of the ordinary differential equation

$$
\begin{aligned}
& d \widehat{V}_{t}=\left[F\left(\widehat{V}_{t}, \widehat{m}_{t}, \widehat{n}_{t}, \widehat{h}_{t}\right)-J_{\mathrm{Ch}} \widehat{y}_{t}\left(\widehat{V}_{t}-V_{\mathrm{rev}}\right)\right] d t \\
& d \widehat{x}_{t}=\left[\rho_{x}\left(\widehat{V}_{t}\right)\left(1-\widehat{x}_{t}\right)-\zeta_{x}\left(\widehat{V}_{t}\right) \widehat{x}_{t}\right] d t
\end{aligned}
$$

## Empirical Case

We denote ( $\widehat{X}_{t}^{t_{1}, E}: t \geq t_{1}$ ) the solution of (3) with random initial condition $\hat{X}_{t_{1}}^{t_{1}, E}=\bar{X}_{t_{1}}^{N}:=\left(\bar{t}_{t_{1}}^{N}, \bar{m}_{t_{1}}^{N}, \bar{n}_{t_{1}}^{N}, \bar{h}_{t_{1}}^{N}, \bar{y}_{t_{1}}^{N}\right)$.

## Mean Field Case

For $\left(\mu_{t}: t \geq 0\right) \in C\left([0, \infty), \mathcal{P}_{1}\left(\mathbb{R} \times[0,1]^{4}\right)\right)$ we denote by
$\left(\widehat{X}_{t}^{t_{1}, \infty}: t \geq t_{1}\right)$ the solution of (3) with deterministic initial condition $\widehat{X}_{t_{1}}^{t_{1}, \infty}=\left\langle\mu_{t_{1}}\right\rangle$, where $\left\langle\mu_{t_{1}}\right\rangle$ is the vector of means of $\mu_{t_{1}}$.

## Main Results

## Theorem 1: Synchronization

Assume (H) and that the initial condition is an exchangeable random vector.

## ) Synchronization. There exist constants $J_{\mathrm{E}}^{0}>0, C_{\zeta, \rho}^{0}>0$ and

$\lambda^{0}>0$ not depending on $N \geq 1, \sigma \geq 0$ or $X_{0}$, and there exists a time $t_{0} \geq 0$ not depending on $N \geq 1$ or $\sigma \geq 0$, such that for each $J_{\mathrm{E}}>J_{\mathrm{E}}^{0}$ the solution $X$ of (2) satisfies, for every $t \geq t_{0}$ and each $i \in\{1, \ldots, N\}$ :

Synchronized dynamics. Assume $J_{\mathrm{E}}>J_{\mathrm{E}}^{0}$. Then, there are constant $K_{0}, K_{0}^{\prime}>0$ depending only on the parameters of the voltage dynamics in (1) and, for each $\delta \geq 0$, constants $K_{\delta}, K_{\delta}^{\prime}>0$ depending on the coefficients in (2) and on $\delta$ (increasingly) but not on $N$, such that for every $t_{1} \geq t_{0}$ and each $i \in\{1, \ldots, N\}$ :

$$
\begin{aligned}
& \sup _{t_{1} \leq t \leq t_{1}+\delta} \mathbb{E}\left(\left|X_{t}^{(i)}-\widehat{X}_{t}^{t_{1}, E}\right|^{2}\right) \\
& \leq K_{0} \wedge 2\left[\left(K_{0}^{\prime} e^{-\lambda_{0}\left(t_{1}-t_{0}\right)}+\sigma^{2} \frac{C_{\zeta, \rho}^{0}}{\lambda^{0}}\right)\left(1+\delta K_{\delta}\right)+\delta K_{\delta}^{\prime} \frac{\sigma^{2}}{N} C_{\zeta, \rho}^{0}\right] .
\end{aligned}
$$

## Theorem 2: Mean Field Limit

Assume (H) and that for all $N \geq 1$ the initial condition are i.i.d. random vectors with (compactly supported) common law $\mu_{0} \in \mathcal{P}(\mathbb{R} \times$ $[0,1]^{4}$ ) not depending on $N$
Consider the notations:
$\Phi(w, z, v, u):=F\left(v, u_{m}, u_{n}, u_{h}\right)-J_{\mathrm{E}}(v-w)-J_{\mathrm{Ch}} z\left(v-V_{\text {rev }}\right)$
$b_{x}(v, u):=\rho_{x}(v)\left(1-u_{x}\right)-\zeta_{x}(v) u_{x}$
$a_{x}(v, u):=\left(\rho_{x}(v)\left(1-u_{x}\right)+\zeta_{x}(v) u_{x}\right) \chi\left(u_{x}\right)$
$\langle\mu\rangle:=\left(\left\langle\mu^{V}\right\rangle,\left(\left\langle\mu^{x}\right\rangle\right)_{x=m, n, h, y}\right)$
a) There exists $\left(\mu_{t}: t \geq 0\right)$ in $C\left(\mathbb{R}^{+} ; \mathcal{P}_{2}\left(\mathbb{R} \times[0,1]^{4}\right)\right)$ a global solution (in the sens of distribution) of the non linear McKean-Vlasov Fokker Planck equation
with initial condition $\mu_{0}$.
) For each $T>0$, the process of empirical measures of the system (2) $\left(\mu_{t}^{N}=N^{-1} \sum_{i=1}^{N} \delta_{X_{t}^{(i)}}: t \in[0, T]\right)$ converges in law on $C\left([0, T] ; \mathcal{P}_{2}\left(\mathbb{R} \times[0,1]^{4}\right)\right)$, when $N$ tends to infinity, to a deterministic and uniquely determined flow of probability measures ( $\mu_{t}: t \in[0, T]$ ) defined on part a).
There is a constant $C(T)>0$ depending on $V_{0}^{\max }, T>0$ and on the coefficients of system (2), but not on $N$, such that

$$
\sup _{t \in[0, T]} \mathbb{E}\left(\mathcal{W}_{2}^{2}\left(\mu_{t}^{N}, \mu_{t}\right)\right) \leq C(T) N^{-2 / 5},
$$

where $\mathcal{W}_{2}$ is the Wasserstein distance of order 2.

## Synchronization + Mean Field Limit

Under the assumptions of Theorem 2 and for the same constants as in Theorem 1, whenever $J_{\mathrm{E}}>J_{\mathrm{E}}^{0}$ we have:
a) For every $t \geq t_{0}$,

$$
\mathcal{W}_{2}^{2}\left(\mu_{t}, \delta_{\left(\mu_{t}\right)}\right) \leq \mathcal{W}_{2}^{2}\left(\mu_{t_{0},}, \delta_{\left(\mu_{t_{0}}\right)}\right) e^{-\lambda^{0}\left(t-t_{0}\right)}+\sigma^{2} \frac{C_{\frac{\zeta, p, p}{0}}^{\lambda^{0}} .}{} .
$$

In particular, lim sup $\sin _{\rightarrow \infty} \mathcal{W}_{2}^{2}\left(\mu_{t}, \delta_{\left(\mu_{t}\right)}\right) \leq \sigma^{2} \frac{C_{\rho}^{0}}{\lambda^{0}}$.
b) For every $t_{1} \geq t_{0}$ and $\delta \geq 0$ we have:
$\sup _{t_{1} \leq t \leq t_{1}+\delta} W_{2}^{2}\left(\mu_{t}, \delta_{\tilde{X}_{t}^{\tilde{x}_{t}^{1, x}}}\right.$

$$
\leq K_{0} \wedge 2\left[\left(K_{0}^{\prime} e^{-\lambda_{0}\left(t_{1}-t_{0}\right)}+\sigma^{2} \frac{C_{\zeta}^{0}, f}{\lambda^{0}}\right)\left(1+\delta K_{\delta}\right)\right]
$$

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