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# 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.

$$\begin{aligned} dV_t &= F(V_t, m_t, n_t, h_t) dt \\ dx_t &= [\rho_x(V_t)(1 - x_t) - \zeta_x(V_t)x_t] dt \end{aligned}$$

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

$$F(V, m, n, h) = I - g_K n^4 (V - V_K) - g_{Na} m^3 h (V - V_{Na}) - g_L (V - V_L), \quad (1)$$

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  $\{1, \dots, i, \dots, j, \dots, N\}$ , and 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

$$-\frac{J_{Ch}}{N} y_t^{(j)} (V_t^{(i)} - V_{rev}),$$

where  $J_{Ch} \geq 0$  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

$$-\frac{J_E}{N} (V_s^{(i)} - V_s^{(j)}),$$

where  $J_E \geq 0$  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:

$$dx_t = \rho_x(V_t)(1 - x_t) - \zeta_x(V_t)x_t dt + \sigma_x(V_t, x_t) dW_t^x,$$

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  $i = 1, \dots, N$  will be represented by  $X_t^{(i)} = (V_t^{(i)}, m_t^{(i)}, n_t^{(i)}, h_t^{(i)}, y_t^{(i)})$ , and we denote by

$$\bar{V}_t^N = \frac{1}{N} \sum_{i=1}^N V_t^{(i)}, \quad \bar{y}_t^N = \frac{1}{N} \sum_{i=1}^N y_t^{(i)},$$

the empirical means for the voltage and the proportion of open neurotransmitter channels respectively.

The dynamics will be:

$$\begin{aligned} V_t^{(i)} &= V_0^{(i)} + \int_0^t F(V_s^{(i)}, m_s^{(i)}, n_s^{(i)}, h_s^{(i)}) ds \\ &\quad - \int_0^t J_E (V_s^{(i)} - \bar{V}_s^N) - J_{Ch} \bar{y}_s^N (V_s^{(i)} - V_{rev}) ds, \\ x_t^{(i)} &= x_0^{(i)} + \int_0^t \rho_x(V_s^{(i)})(1 - x_s^{(i)}) - \zeta_x(V_s^{(i)})x_s^{(i)} ds \\ &\quad + \int_0^t \sigma_x(V_s^{(i)}, x_s^{(i)}) dW_s^{x,i}, \end{aligned} \quad (2)$$

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

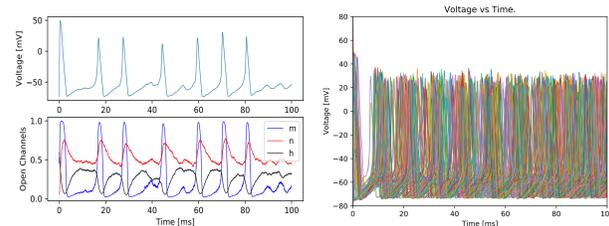


Figure 1: *Left:* The evolution of the Voltage and Channels for one neuron. *Right:* The evolution of the Voltage of 100 neurons  $J_E$  small.

## Emergence of Synchrony

Numerical simulations show when increasing  $J_E$ , 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.

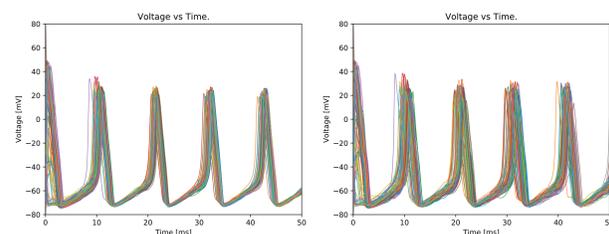


Figure 2: Trajectories for the Voltage of 100 neurons under strong interaction and different level of noise: *Left:*  $\sigma = 0.5$ . *Right:*  $\sigma = 1$ .

As a measure of the synchronicity of the network we compute the empirical variance of Voltage of the system (2):  $N^{-1} \sum_{i=1}^N (V_t^{(i)} - \bar{V}_t^N)^2$ , 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  $\sigma$ .

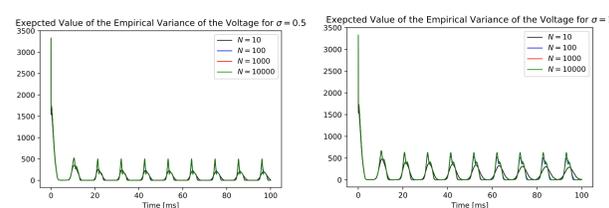


Figure 3: Time evolution of the expected empirical variance of the Voltage for different level of noise: *Left:*  $\sigma = 0.5$ . *Right:*  $\sigma = 1$ .

**Partial Conclusion:** The numerical evidence shows that for big enough  $J_E$  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)

1.  $\rho_x$  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

$$\sigma_x(v, z) = \sigma \sqrt{|\rho_x(v)(1 - z) + \zeta_x(v)z|} \chi(z),$$

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  $(m_0^{(i)}, n_0^{(i)}, h_0^{(i)}, y_0^{(i)}) \in [0, 1]^4$  a.s.

4. The initial voltages are bounded uniformly in  $N$ :

$$\sup_{i=1, \dots, N} |V_0^{(i)}| \leq V_0^{\max} \quad a.s.$$

## Reduce Synchronized Dynamics

For  $t_1 \geq 0$ , let  $(\hat{X}_t^{t_1} : t \geq t_1)$  denote the solution of the ordinary differential equation

$$\begin{aligned} d\hat{V}_t &= [F(\hat{V}_t, \hat{m}_t, \hat{n}_t, \hat{h}_t) - J_{Ch} \hat{y}_t (\hat{V}_t - V_{rev})] dt, \\ d\hat{x}_t &= [\rho_x(\hat{V}_t)(1 - \hat{x}_t) - \zeta_x(\hat{V}_t)\hat{x}_t] dt \end{aligned} \quad (3)$$

### Empirical Case

We denote  $(\hat{X}_t^{t_1, E} : t \geq t_1)$  the solution of (3) with random initial condition  $\hat{X}_t^{t_1, E} = \bar{X}_t^N := (\bar{V}_t^N, \bar{m}_t^N, \bar{n}_t^N, \bar{h}_t^N, \bar{y}_t^N)$ .

### Mean Field Case

For  $(\mu_t : t \geq 0) \in C([0, \infty), \mathcal{P}_1(\mathbb{R} \times [0, 1]^4))$  we denote by  $(\hat{X}_t^{t_1, \infty} : t \geq t_1)$  the solution of (3) with deterministic initial condition  $\hat{X}_t^{t_1, \infty} = \langle \mu_{t_1} \rangle$ , where  $\langle \mu_{t_1} \rangle$  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.

a) **Synchronization.** There exist constants  $J_E^0 > 0$ ,  $C_{\zeta, \rho}^0 > 0$  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  $J_E > J_E^0$  the solution  $X$  of (2) satisfies, for every  $t \geq t_0$  and each  $i \in \{1, \dots, N\}$ :

$$\mathbb{E}(|X_t^{(i)} - \bar{X}_t^N|^2) \leq \mathbb{E}(|X_{t_0}^{(i)} - \bar{X}_{t_0}^N|^2) e^{-\lambda^0(t-t_0)} + \sigma^2 \frac{C_{\zeta, \rho}^0}{\lambda^0}.$$

In particular,  $\limsup_{t \rightarrow \infty} \mathbb{E}(|X_t^{(i)} - \bar{X}_t^N|^2) \leq \sigma^2 \frac{C_{\zeta, \rho}^0}{\lambda^0}$ .

b) **Synchronized dynamics.** Assume  $J_E > J_E^0$ . Then, there are constant  $K_0, K_0' > 0$  depending only on the parameters of the voltage dynamics in (1) and, for each  $\delta \geq 0$ , constants  $K_\delta, K_\delta' > 0$  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  $i \in \{1, \dots, N\}$ :

$$\begin{aligned} &\sup_{t_1 \leq t \leq t_1 + \delta} \mathbb{E}(|X_t^{(i)} - \hat{X}_t^{t_1, E}|^2) \\ &\leq K_0 \wedge 2 \left[ \left( K_0' e^{-\lambda^0(t-t_0)} + \sigma^2 \frac{C_{\zeta, \rho}^0}{\lambda^0} \right) (1 + \delta K_\delta) + \delta K_\delta' \frac{\sigma^2}{N} C_{\zeta, \rho}^0 \right]. \end{aligned}$$

### 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:

$$\begin{aligned} \Phi(w, z, v, u) &:= F(v, u_m, u_n, u_h) - J_E(v - w) - J_{Ch} z (v - V_{rev}) \\ b_x(v, u) &:= \rho_x(v)(1 - u_x) - \zeta_x(v)u_x \\ a_x(v, u) &:= (\rho_x(v)(1 - u_x) + \zeta_x(v)u_x)\chi(u_x) \\ \langle \mu \rangle &:= (\langle \mu^V \rangle, \langle \mu^x \rangle)_{x=m, n, h, y} \end{aligned}$$

a) There exists  $(\mu_t : t \geq 0)$  in  $C(\mathbb{R}^+; \mathcal{P}_2(\mathbb{R} \times [0, 1]^4))$  a global solution (in the sens of distribution) of the non linear McKean-Vlasov Fokker Planck equation

$$\begin{aligned} \partial_t \mu_t &= \partial_v \left( \Phi(\langle \mu_t^V \rangle, \langle \mu_t^y \rangle, \cdot, \cdot) \mu_t \right) \\ &\quad + \sum_{x=m, n, h, y} \frac{1}{2} \sigma^2 \partial_{u_x}^2 (a_x \mu_t) - \partial_{u_x} (b_x \mu_t) \end{aligned}$$

with initial condition  $\mu_0$ .

b) For each  $T > 0$ , the process of empirical measures of the system (2)  $(\mu_t^N = N^{-1} \sum_{i=1}^N \delta_{X_t^{(i)}} : t \in [0, T])$  converges in law on  $C([0, T]; \mathcal{P}_2(\mathbb{R} \times [0, 1]^4))$ , 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).

c) 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

$$\sup_{t \in [0, T]} \mathbb{E} \left( \mathcal{W}_2^2(\mu_t^N, \mu_t) \right) \leq C(T) N^{-2/5},$$

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  $J_E > J_E^0$  we have:

a) For every  $t \geq t_0$ ,

$$\mathcal{W}_2^2(\mu_t, \delta_{\langle \mu_t \rangle}) \leq \mathcal{W}_2^2(\mu_{t_0}, \delta_{\langle \mu_{t_0} \rangle}) e^{-\lambda^0(t-t_0)} + \sigma^2 \frac{C_{\zeta, \rho}^0}{\lambda^0}.$$

In particular,  $\limsup_{t \rightarrow \infty} \mathcal{W}_2^2(\mu_t, \delta_{\langle \mu_t \rangle}) \leq \sigma^2 \frac{C_{\zeta, \rho}^0}{\lambda^0}$ .

b) For every  $t_1 \geq t_0$  and  $\delta \geq 0$  we have:

$$\begin{aligned} &\sup_{t_1 \leq t \leq t_1 + \delta} \mathcal{W}_2^2(\mu_t, \delta_{\hat{X}_t^{t_1, \infty}}) \\ &\leq K_0 \wedge 2 \left[ \left( K_0' e^{-\lambda^0(t-t_0)} + \sigma^2 \frac{C_{\zeta, \rho}^0}{\lambda^0} \right) (1 + \delta K_\delta) \right]. \end{aligned}$$

## References

- [1] M. Bossy, O. Faugeras, and D. Talay. Clarification and complement to "mean-field description and propagation of chaos in networks of Hodgkin-Huxley and Fitzhugh-Nagumo neurons". *The Journal of Mathematical Neuroscience (JMN)*, 5(1):1-23, 2015.
- [2] K. Pakdaman, M. Thieullen, and G. Wainrib. Fluid limit theorems for stochastic hybrid systems with application to neuron models. *Adv. in Appl. Probab.*, 42(3):761-794, 09 2010.