Conductance Based Neuron Models

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UPMC - LPMA

Workshop PDMP

Rennes 2013

Plan

Conductance Based Neuron Models: a Biological Description

Plan

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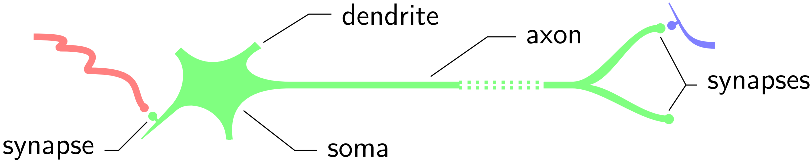
Plan

This talk is inspired by:

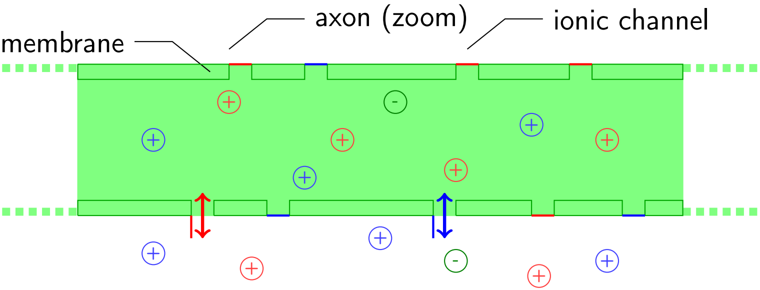
- *Reduction of stochastic conductance-based neuron models with time-scales separation*, J. of Comp. Neuro. (2011) G. Wainrib, M. Thieullen, K. Pakdaman.
- *Averaging and large deviation principles for fully-coupled piecewise deterministic Markov processes*, Markov Proc. Rel. Fields (2009) A. Faggionato, D. Gabrielli and M. Ribezzi Crivellari.
- *Averaging for a Fully-Coupled Piecewise Deterministic Markov Process in Infinite Dimensions*, Adv. in App. Proba. (2012) A. G. and M. Thieullen.
- *An exact stochastic hybrid model of excitable membranes including spatio-temporal evolution*, J. Math. Bio. (2011) E. Buckwar and M. Riedler.
- *Limit theorems for infinite-dimensional piecewise deterministic Markov processes. Applications to stochastic excitable membrane models*, Elect. J. Prob. (2012), M. Riedler, M. Thieullen and G. Wainrib.

The neural cell



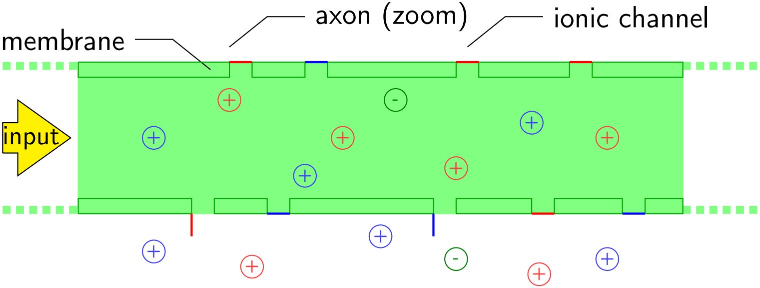
- the soma contains the 'organs' of the cell body;
- the dendrites where the neural cell receives inputs from other neurons or muscles or peripheral organs;
- the axon responsible for transmitting neural information, that is the inputs, to interconnected target neurons;
- the synapses at the interfaces of axon terminals with target cells.

The nerve impulse



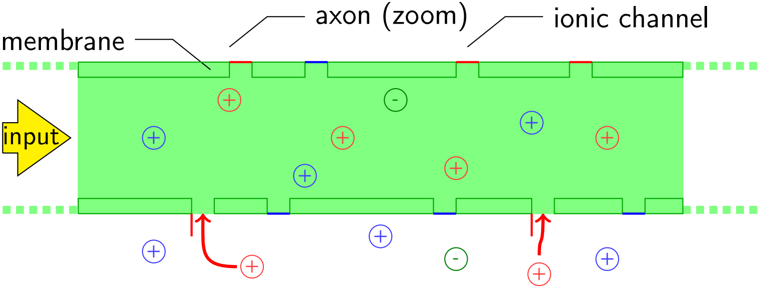
- K^+: potassium.
- Na^+: sodium.
- Cl^-: chloride.

The nerve impulse



- Increasing the voltage of the axon membrane produces a large, but transient, flow of positive charge carried by Na^{+} ions flowing into the cell: inward current.
- This transient inward current is followed by a sustained flow of positive charge out of the cell, the outward current carried by a sustained flux of K^{+} ions moving out of the cell.

The nerve impulse



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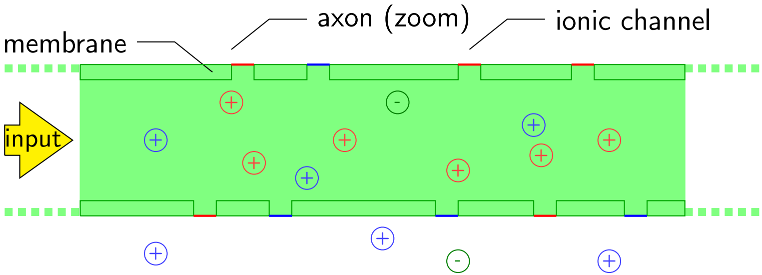

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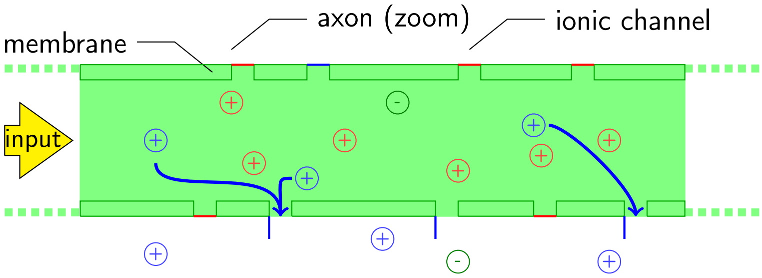

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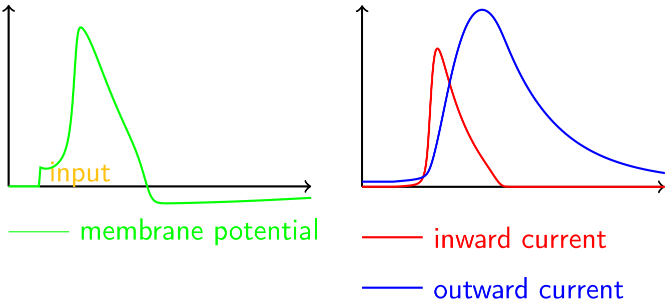
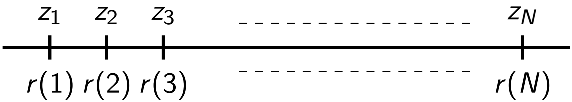


Action potential in the pointwise Hodgkin-Huxley model.

Mathematical model

A membrane with N ionic channels and an axon considered as a segment I.



Generation and propagation of an action potential:

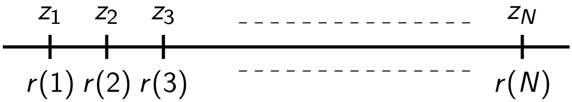
$$C_m \partial_t v_t = \frac{a}{2R} \partial_{xx} v_t + \frac{1}{N} \underbrace{\sum_{i=1}^{N}}_{\text{sum over the channels}} \underbrace{\underbrace{c_{r_t(i)}}_{\text{conductance}} \underbrace{\left(v_{r_t(i)} - v_t(z_i)\right)}_{\text{difference of potential}}}_{\text{current intensity of channel at } z_i \text{ in state } r_t(i)} \underbrace{\delta_{z_i}}_{\text{Dirac mass}}$$

with initial and boundary conditions.

Mathematical model

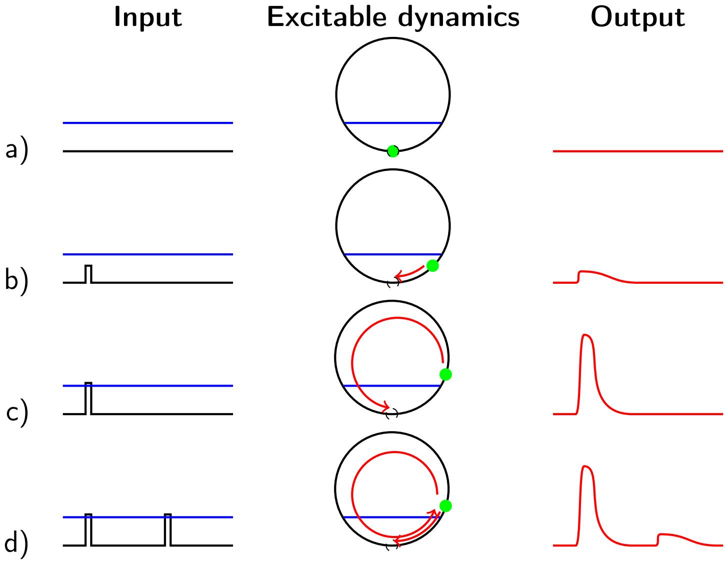
Dynamic of ionic channels (voltage-dependent):

$$\mathbb{P}(r_{t+h}(i) = \zeta | r_t(i) = \xi) = \underbrace{\alpha_{\xi\zeta}(v_t(z_i))}_{\text{rate of jump}} h + \mathrm{o}(h)$$



- $r_t(i) \in E$ state of the channel at locus z_i at time t.
- State space: $r = (r(i), i = 1, \dots, N) \in E^N$.

An excitable system



A class of switching PDEs

An evolution equation:

$$C_m \partial_t v_t = \frac{a}{2R} \partial_{xx} v_t + \frac{1}{N} \sum_{i=1}^{N} c_{r_t(i)} (v_{r_t(i)} - v_t(z_i)) \delta_{z_i}$$

with coefficient $r = (r(i), i = 1, \ldots, N)$ updated at voltage dependent rates:

$$q_{r\tilde{r}}(v) = \begin{cases} 0 & \text{if } r \text{ and } \tilde{r} \text{ differ from more than one component,} \\ \frac{\alpha_{r(i)\tilde{r}(i)}(v(z_i))}{\alpha_{r(i)}(v(z(i)))} & \text{if } r(i) \neq \tilde{r}(i) \text{ and all the other components agree.} \end{cases}$$

A PDMP !

A class of switching PDEs

Remarks on the evolution equation :

- Smoothed choice:

$$C_m \partial_t v_t = \frac{a}{2R}\partial_{xx} v_t + \frac{1}{N}\sum_{i=1}^{N} c_{r_t(i)}(v_{r_t(i)} - (v_t, \phi_{z_i}))\phi_{z_i},$$

- Compartment type models:

Infinitesimal generator:

$$\mathcal{A}f(v,r) = \mathcal{C}(r)f(\cdot,r)(v) + \mathcal{J}(v)f(v,\cdot)(r)$$

Macroscopic generator and microscopic generator:

$$\mathcal{C}(r)f(\cdot,r)(v) =< f_v(v,r), \frac{a}{2R}\Delta v + \frac{1}{N}\sum_{i=1}^{N} c_{r(i)}(v_{r(i)} - v(z_i))\delta_{z_i} >$$

$$\mathcal{J}(v)f(v,\cdot)(r) = \sum_{i=1}^{N}\sum_{\zeta\in E}[f(v, r_{r(i)\to\zeta}) - f(v,r)]\alpha_{r(i),\zeta}(v(z_i))$$

When N goes to infinity

- At a fixed N:

$$
\begin{cases}
\partial_t v_t = \partial_{xx} v_t + \frac{1}{N}\sum_{i=1}^{N} c_{r_t(i)}(v_{r_t(i)} - (v_t(z_i))\delta_{z_i}, \\
\mathbb{P}(r_{t+h}(i) = \zeta | r_t(i) = \xi) = \alpha_{\xi\zeta}(v_t(z_i))h + \mathrm{o}(h).
\end{cases}
$$

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- Deterministic limit:

$$\begin{cases} \partial_t v_t = \partial_{xx} v_t + \sum_{\xi \in E} c_\xi (v_\xi - v_t), \\ \partial_t p_{\xi,t} = \sum_{\zeta \neq \xi} p_{\zeta,t}\alpha_{\zeta\xi}(v_t) - p_{\xi,t}\alpha_{\xi\zeta}(v_t). \end{cases}$$

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- Langevin approximmation:

$$\begin{cases} v_t^{(N)} \simeq v_t + \frac{1}{\sqrt{N}} V_t, \\ \frac{1}{N}\sum_{i=1}^{N} 1_\xi(r_t(i))\delta_{z_i} \simeq p_{\xi,t} + \frac{1}{\sqrt{N}} P_{\xi,t}. \end{cases}$$

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Introduction of two time scales

The model with **two time scales**:

$$\begin{cases} \partial_t v_t^{\varepsilon} = \partial_{xx} v_t^{\varepsilon} + \frac{1}{N}\sum_{i=1}^{N} c_{r_t^{\varepsilon}(i)}(v_{r_t^{\varepsilon}(i)} - v_t^{\varepsilon}(z_i))\delta_{z_i} \\ \mathbb{P}(r_{t+h}^{\varepsilon}(i) = \zeta | r_t^{\varepsilon}(i) = \xi) = \alpha_{\xi\zeta}^{\varepsilon}(v_t^{\varepsilon}(z_i))h + \mathrm{o}(h) \end{cases}$$

with l different **classes**: $E = E_1 \sqcup \cdots \sqcup E_l$.

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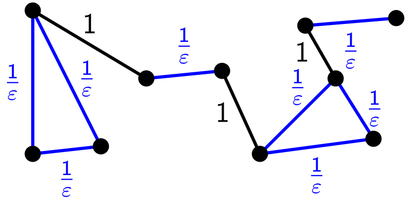

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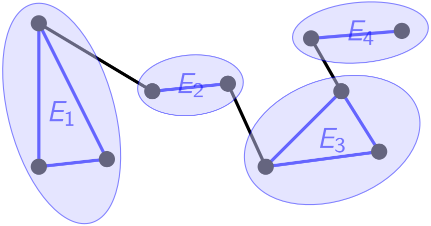

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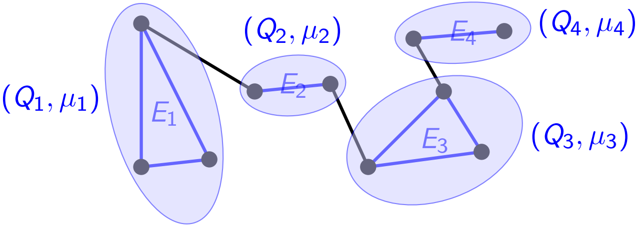
with l different **classes**: $E = E_1 \sqcup \cdots \sqcup E_l$. The **aggregated** process:

$$\bar{r}_t^\varepsilon(i) = j \text{ iff } r_t^\varepsilon(i) \in E_j$$

When v is held fixed...



Let v held fixed and $i = 1, \ldots, N$, $\overline{r}^{\varepsilon}(i)$ converges weakly toward the Markov process $\overline{r}(i)$ with generator:

$$\overline{\mathcal{J}}[v]f(\overline{r}(i)) = \sum_{j=1}^{l} 1_j(\overline{r}(i)) \sum_{k=1, k\neq j}^{l} (f(k) - f(j)) \underbrace{\sum_{\xi\in E_k} \sum_{\zeta\in E_j} \alpha_{\zeta,\xi}(v(z_i))\mu_j(v(z_i))(\zeta)}_{\text{averaged jump's rate from } E_j \text{ to } E_k}$$

When ε goes to zero

- When ε is held fixed:

$$\begin{cases} \partial_t v_t^\varepsilon = \partial_{xx} v_t^\varepsilon + \frac{1}{N} \sum_{i \in \mathcal{N}} c_{r_t^\varepsilon(i)} (v_{r_t^\varepsilon(i)} - v_t^\varepsilon(z_i)) \delta_{z_i} \\ \mathbb{P}(r_{t+h}^\varepsilon(i) = \zeta | r_t^\varepsilon(i) = \xi) = \alpha_{\xi\zeta}^\varepsilon(v_t^\varepsilon(z_i)) h + \mathrm{o}(h) \end{cases}$$

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- Averaged model:

$$\begin{cases} \partial_t v_t = \\ \partial_{xx} v_t + \frac{1}{N}\sum_{i=1}^{N}\sum_{j=1}^{l} 1_{E_j}(\overline{r}_t(i)) \sum_{\xi\in E_j} \mu_j(v_t(z_i))(\xi) c_\xi(v_\xi - v_t(z_i))\delta_{z_i} \\ \mathbb{P}(\overline{r}_t(i) = l_2 | \overline{r}_t(i) = l_1) = \overline{\alpha}_{l_1 l_2}(v_t(z_i))h + \mathrm{o}(h) \end{cases}$$

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- Langevin approximation:

$$\begin{cases} dv_t^\varepsilon = [\partial_{xx} v_t^\varepsilon + F_{\overline{r}_t}(v_t^\varepsilon)]dt + \sqrt{\varepsilon} B_{\overline{r}_t}(v_t^\varepsilon) dW_t \\ \mathbb{P}(\overline{r}_t(i) = l_2 | \overline{r}_t(i) = l_1) = \overline{\alpha}_{l_1 l_2}(v_t(z_i))h + \mathrm{o}(h) \end{cases}$$

- Averaged model:

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Another multiscale model

What happens if the potential is also fast?

$$\begin{cases} \partial_t v_t = \frac{1}{\varepsilon}\left[\partial_{xx} v_t + \frac{1}{N}\sum_{i=1}^{N}\sum_{k=1}^{2} c_{r_t^k(i)}(v_{r_t^k(i)} - (v_t, \phi_{z_i}))\phi_{z_i}\right] \\ \mathbb{P}(r_{t+h}^{(1)}(i) = \zeta | r_t^{(1)}(i) = \xi) = \frac{1}{\varepsilon}\alpha_{\xi\zeta}^{(1)}((v_t, \phi_{z_i}))h + \mathrm{o}(h) \\ \mathbb{P}(r_{t+h}^{(2)}(i) = \zeta | r_t^{(2)}(i) = \xi) = \alpha_{\xi\zeta}^{(2)}((v_t, \phi_{z_i}))h + \mathrm{o}(h) \end{cases}$$

In this case, the fast part of the process is a still a PDMP...

Another multiscale model

Fix $r^{(2)}$ and consider the PDMP:

$$\begin{cases} \partial_t v_t = \partial_{xx} v_t + \frac{1}{N} \sum_{i=1}^{N} \sum_{k=1}^{2} c_{r_t^k(i)} (v_{r_t^k(i)} - (v_t, \phi_{z_i})) \phi_{z_i} \\ \mathbb{P}(r_{t+h}^{(1)}(i) = \zeta | r_t^{(1)}(i) = \xi) = \alpha_{\xi\zeta}^{(1)}((v_t, \phi_{z_i}))h + o(h) \end{cases}$$

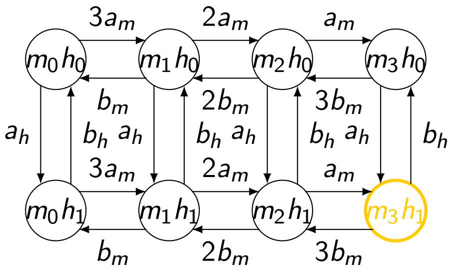
There exists a unique invariant measure $\mu_{r^{(2)}}$.

Remark: one can show that the speed of convergence towards the invariant measure is exponential in Wasserstein distance.

Averaged model: a CTMC $\bar{r}^{(2)}$ with rates:

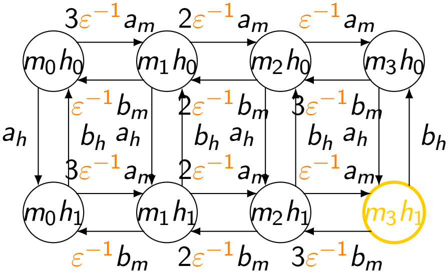
$$\bar{q}_{r\tilde{r}}^{(2)} = \int_{L^2(I)\times E^1} q_{r\tilde{r}}^{(2)}((v, \phi_{z_i}))\mu_r(dv, dr^1)$$

Example: ε goes to zero



$$\partial_t v_t^\varepsilon = \nu \partial_{xx} v_t^\varepsilon + \frac{1}{N} \sum 1_{m_3 h_1}(r_t^\varepsilon(i)) c_{\mathrm{Na}} (v_{\mathrm{Na}} - v_t^\varepsilon(z_i)) \delta_{\frac{i}{N}}$$

Example: ε goes to zero



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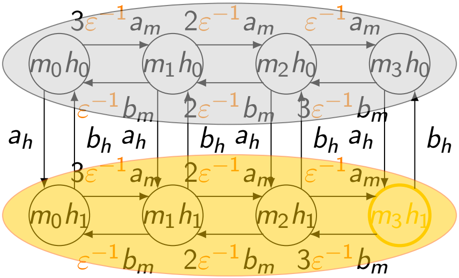

$$\partial_t v_t^\varepsilon = \nu \partial_{xx} v_t^\varepsilon + \frac{1}{N} \sum \mathbf{1}_{m_3 h_1}(r_t^\varepsilon(i)) c_{\mathrm{Na}} (v_{\mathrm{Na}} - v_t^\varepsilon(z_i)) \delta_{\frac{i}{N}}$$

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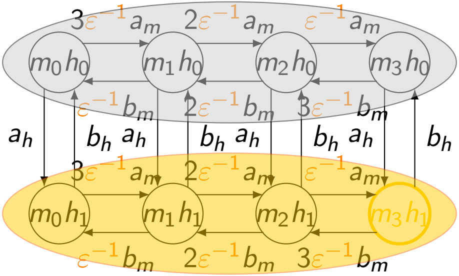
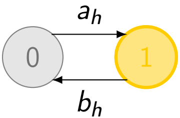


$$\partial_t v_t^\varepsilon = \nu \partial_{xx} v_t^\varepsilon + \frac{1}{N} \sum 1_{m_3 h_1}(r_t^\varepsilon(i))\, c_{\mathrm{Na}}(v_{\mathrm{Na}} - v_t^\varepsilon(z_i))\, \delta_{\frac{i}{N}}$$



$$\partial_t v_t = \nu \partial_{xx} v_t + \frac{1}{N} \sum 1_1(\bar{r}_t(i))\, \mu_1(v_t(z_i))(m_3 h_1)\, c_{\mathrm{Na}}(v_{\mathrm{Na}} - v_t(z_i))\, \delta_{\frac{i}{N}}$$

Example

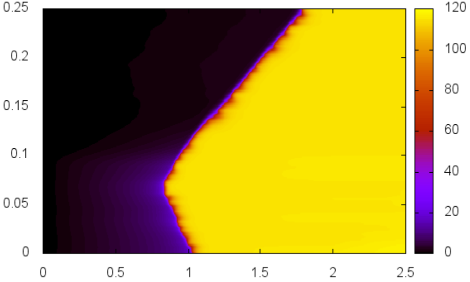
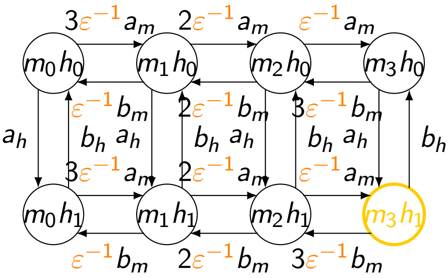


Figure: Simulation of the averaged model with $N = 250$

Example: N goes to infinity, ε held fixed



$$\partial_t v_t^\varepsilon = \partial_{xx} v_t^\varepsilon + \frac{1}{N} \sum 1_{m_3 h_1}(r_t^\varepsilon(i)) c_{\mathrm{Na}}(v_{\mathrm{Na}} - v_t^\varepsilon(z_i))\delta_{\frac{i}{N}}$$

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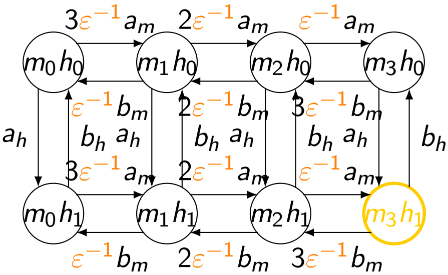


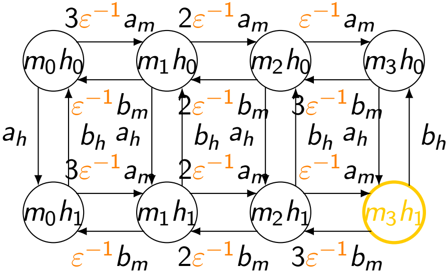
$$\partial_t v_t^\varepsilon = \partial_{xx} v_t^\varepsilon + \frac{1}{N} \sum 1_{m_3 h_1}(r_t^\varepsilon(i)) c_{\mathrm{Na}}(v_{\mathrm{Na}} - v_t^\varepsilon(z_i)) \delta_{\frac{i}{N}}$$

Converges to:

$$\begin{cases} \partial_t v_t^\varepsilon = \partial_{xx} v_t^\varepsilon + p_{m_3 h_1, t} c_{\mathrm{Na}}(v_{\mathrm{Na}} - v_t^\varepsilon) \\ \partial_t p_{\xi,t} = \sum_{\zeta \neq \xi} \alpha^\varepsilon_{\zeta\xi}(v_t^\varepsilon) p_{\zeta,t} - \alpha_{\xi\zeta}(v_t^\varepsilon) p_{\xi,t} \end{cases}$$

for $\xi \in E = \{m_0 h_0, m_1 h_0, m_2 h_0, m_3 h_0, m_0 h_1, m_1 h_1, m_2 h_1, m_3 h_1\}$.

Example: deterministic averaging, $N = \infty$, $\varepsilon \to 0$



$$\begin{cases} \partial_t v_t^\varepsilon = \partial_{xx} v_t^\varepsilon + p_{m_3h_1,t} c_{\mathrm{Na}}(v_{\mathrm{Na}} - v_t^\varepsilon) \\ \partial_t p_{\xi,t} = \sum_{\zeta \neq \xi} \alpha_{\zeta\xi}(v_t^\varepsilon) p_{\zeta,t} - \alpha_{\xi\zeta}(v_t^\varepsilon) p_{\xi,t} \end{cases}$$

for $\xi \in E = \{m_0h_0, m_1h_0, m_2h_0, m_3h_0, m_0h_1, m_1h_1, m_2h_1, m_3h_1\}$.
The model converges to

$$\begin{cases} \partial_t v_t = \partial_{xx} v_t + \left(\frac{a_m(v_t)}{a_m(t)+b_m(v_t)}\right)^3 h_t c_{\mathrm{Na}}(v_{\mathrm{Na}} - v_t), \\ \partial_t h_t = (1 - h_t) a_h(v_t) - b_h(v_t) h_t. \end{cases}$$

Example

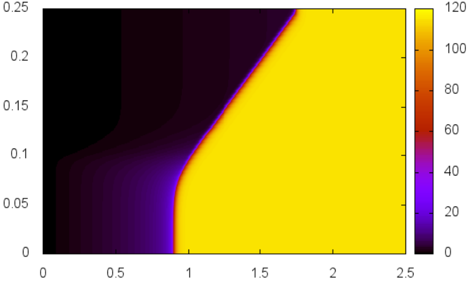
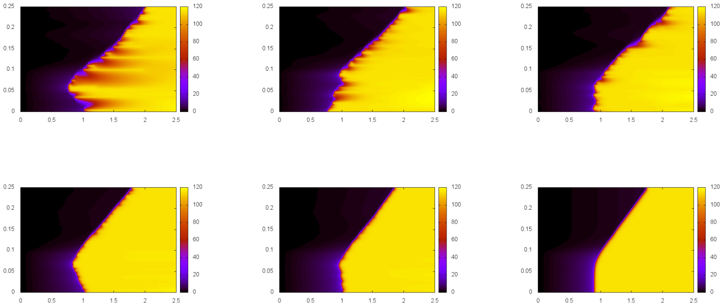


Figure: Simulation of the averaged deterministic model ($N = \infty$)

Simulations for various N.



Remarks: The speed of the deterministic front wave is always greater than the mean speed of the stochastic wave.

The difference for large N is of order $\frac{1}{\sqrt{N}}$.

Concluding remarks

- The joint convergence $(\varepsilon, N) \to (0, \infty)$ need to be clarify.
- Dependence of the model w.r.t. the initial conditions of ionic channels.
- Why, in the presented example, the stochastic celerity is smaller (in mean) than the deterministic one?
- In the model where both the potential and some ionic channels are fast, may we say more about the invariant measure of the fast system?

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Thank you for your attention !