Nonlinear coupling of Poisson-Nernst-Planck equations with Discrete Duality Finite Volumes : Application to Dendritic spines.

CIRM 2022

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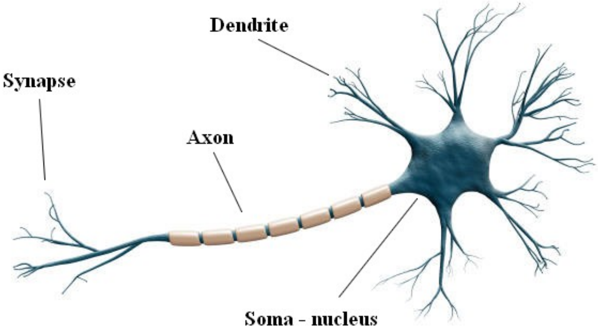
18 October 2022

Context of the study

- Nerve cell specializing in information processing

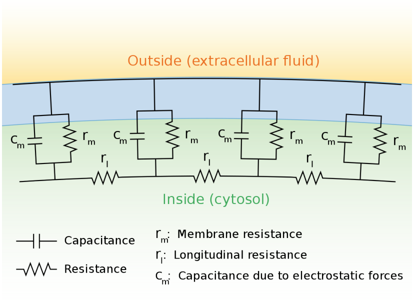


Source : Neuron-bank-istockphoto.com

Cable Theory

→ 1D equation with the Cable Theory (1850s)

- V the electric potential



Source : Wikipedia

Nodal rule (Kirchhoff)

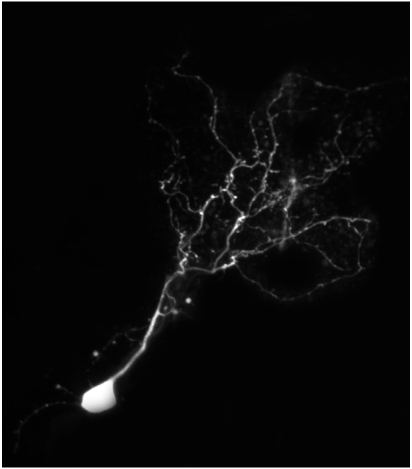
$$i_m = i_c + i_r$$

Following Model

$$\frac{1}{r_l}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + \frac{V}{r_m}$$

Limits of the model and interest on a new model

- Dendritic spine diameter $\sim 0.1\mu m$



Calcium imaging from the Haas Lab (Brain Research Center, UBC, Vancouver)

General system of equations

Poisson-Nernst-Planck (PNP) system for i ionic species on domain Ω and with T_f a finite time (+B.Cs on $\partial\Omega$ and I.Cs)

- Ionic concentration of i species c_i with $z_i = \pm 1$
- Electric potential V

$$
\begin{aligned}
\mathbf{div}(\nabla V) &= -\sum_i A z_i c_i, && \text{in } \Omega \times (0, T_f), \\
\frac{\partial c_i}{\partial t} - \mathbf{div}(D_i \nabla c_i + \Lambda D_i z_i c_i \nabla V) &= 0, && \text{in } \Omega \times (0, T_f).
\end{aligned}
$$

- $c_i(\boldsymbol{x}, t)$ and $V(\boldsymbol{x}, t)$ unknowns of the system
- $A = \dfrac{F}{\epsilon\epsilon_0}$, $\Lambda = \dfrac{F}{RT_\theta}$ and D_i physical parameters

PNP system in 1D for $i = 1$

PNP system for a cation on Ω (+B.Cs on $\partial\Omega$ and I.Cs)

- Ionic concentration of a cation c_P with $z_P = +1$
- Electric potential V

$$
\begin{aligned}
&\frac{\partial^2 V}{\partial x^2} = -A c_P, && \text{in } \Omega \times (0, T_f),\\
&\frac{\partial c_P}{\partial t} - \frac{\partial}{\partial x}\left(D_P \frac{\partial c_P}{\partial x} + \Lambda D_P c_P \frac{\partial V}{\partial x}\right) = 0, && \text{in } \Omega \times (0, T_f).
\end{aligned}
$$

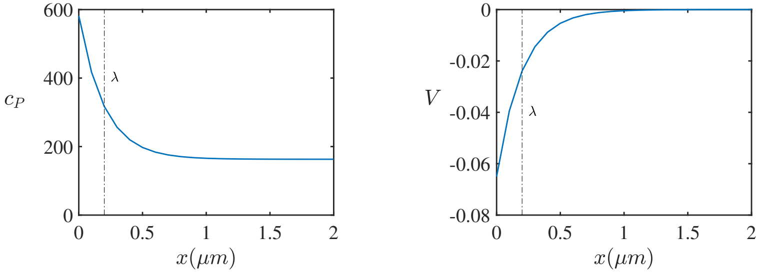
♦ Behaviours of $c_P(x,t)$ and $V(x,t)$?

Stationary solutions of c_P and V

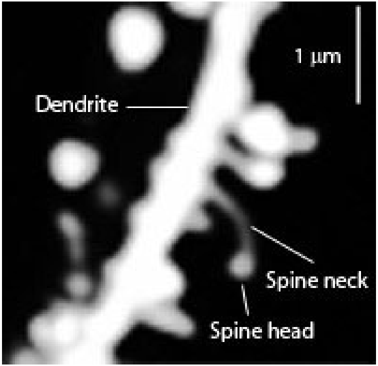
▶ Asymptotic development → Electric boundary layer (λ the Debye layer)

⇝ Approximated solutions of c_P and V

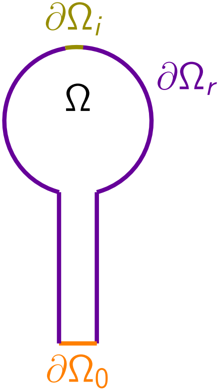
$$c_P = c_0 e^{-\frac{F}{RT_\theta} V} \quad \text{and } V \approx V_0 e^{-\frac{x}{\lambda}} \quad \text{with } \lambda^2 = \frac{\epsilon \epsilon_0 R T_\theta}{F^2 C_P}.$$



Dendritic spine



Imaging of dendritic spine (Wikipedia).



Spine representation with Ω domain and boundaries $\partial\Omega = \partial\Omega_i \cup \partial\Omega_r \cup \partial\Omega_o$.

Configuration of PNP system on dendritic spine domain

- Ionic concentration of a cation c_P with $z_P = +1$
- Ionic concentration of an anion c_N with $z_N = -1$
- Electric potential V

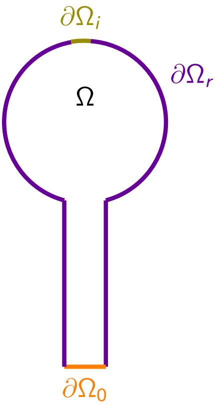
$$
\begin{aligned}
&\mathbf{div}(\nabla V) = -A(c_P - c_N), && \text{in } \Omega \times (0, T_f),\\
&\frac{\partial c_P}{\partial t} - D_P\, \mathbf{div}(\nabla c_P + \Lambda c_P \nabla V) = 0, && \text{in } \Omega \times (0, T_f),\\
&\frac{\partial c_N}{\partial t} - D_N\, \mathbf{div}(\nabla c_N - \Lambda c_N \nabla V) = 0, && \text{in } \Omega \times (0, T_f).
\end{aligned}
$$

♦ $c_P(\boldsymbol{x}, t)$, $c_N(\boldsymbol{x}, t)$ and $V(\boldsymbol{x}, t)$ unknowns of the system

Boundary conditions of dendritic spine domain

On $\partial\Omega_o \times (0, T_f)$

- $V = 0$,
- $c_P = {c_P}^0$,
- $c_N = {c_N}^0$.



- ${c_P}^0$, ${c_N}^0$ initial ionic concentrations.

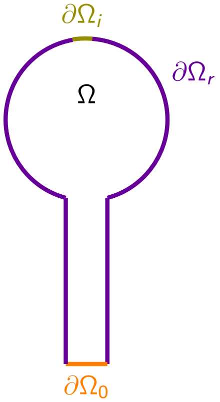
Boundary conditions of dendritic spine domain

On $\partial\Omega_i \cup \partial\Omega_r \times (0, T_f)$

- $\frac{\partial c_N}{\partial \mathrm{n}} - \Lambda c_N \frac{\partial V}{\partial \mathrm{n}} = 0.$

On $\partial\Omega_r \times (0, T_f)$

- $\frac{\partial c_P}{\partial \mathrm{n}} + \Lambda c_P \frac{\partial V}{\partial \mathrm{n}} = 0.$

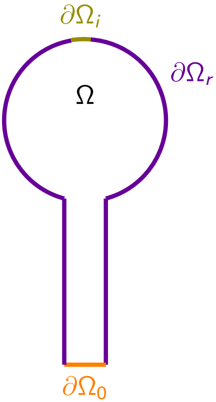


Boundary conditions of dendritic spine domain

On $\partial\Omega_i \cup \partial\Omega_r \times (0, T_f)$

- $\dfrac{\partial V}{\partial \mathrm{n}} = -\dfrac{\rho}{\epsilon\epsilon_0}.$

- ρ the charge density.



On $\partial\Omega_i \times (0, T_f)$

- $\dfrac{\partial c_P}{\partial \mathrm{n}} + \Lambda c_P \dfrac{\partial V}{\partial \mathrm{n}} = I.$

- I the injected synaptic current.

Dendritic spine coefficients

- Injected synaptic current from [Cartailler and al.2018]
  - $I = \dfrac{I_{stim}(t)}{\pi r_i^2 F D_P}$ with $I_{stim}(t) = I_{max} \dfrac{t}{\tau} exp(-\dfrac{t}{\tau} + 1)$
  - I_{max} the maximal current
  - τ the decay time constant
  - r_i the radius of $\partial\Omega_i$

- Initial conditions

$$
\begin{aligned}
V(\cdot, 0) &= 0, && \text{in } \Omega,\\
c_P(\cdot, 0) &= {c_P}^0, && \text{in } \Omega,\\
c_N(\cdot, 0) &= {c_N}^0, && \text{in } \Omega.
\end{aligned}
$$

Key property

▶ Reformulation in non-linear form [Cancès and al.2018]

$$\frac{\partial c_P}{\partial t} = D_P \, \mathbf{div}(c_P \nabla(\log c_P + \Lambda V))$$

$$\frac{\partial c_N}{\partial t} = D_N \, \mathbf{div}(c_N \nabla(\log c_N - \Lambda V)).$$

$\Rightarrow$ Positivity of c_P,c_N

⬩Solving PNP system with the non-linear term using Discrete Duality Finite Volume (DDFV) method.

DDFV notations

- $\mathcal{T}$ the set of primal and dual meshes $\mathcal{T} = (\mathcal{M}, \mathcal{M}^*)$
- $\mathfrak{D}$ the diamond mesh

Discrete solutions : $\rightsquigarrow u_{\mathcal{T}} = (u_{\mathcal{M}}, u_{\mathcal{M}^*}) \in \mathbb{R}^{\mathcal{T}}$

- $\mathrm{div}^{\mathcal{T}}(\xi^{\mathfrak{D}})$ the discrete divergence operator
- $\nabla^{\mathfrak{D}}(u_{\mathcal{T}})$ the discrete gradient operator

- $\mathcal{K}$ and its neighbour $\mathcal{L}$, centers in $\mathcal{M}$
- $\mathcal{K}^*$ and its neighbour $\mathcal{L}^*$, vertices in $\mathcal{M}^*$

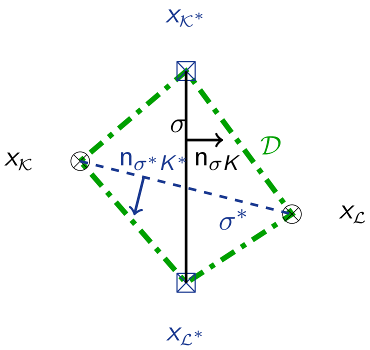
PNP scheme

- DDFV scheme for $(c_{P\mathcal{T}}^{n+1}, c_{N\mathcal{T}}^{n+1}, V_{\mathcal{T}}^{n+1})$ (+B.Cs and I.Cs)

$$
\begin{aligned}
&-\mathrm{div}^{\mathcal{T}}(\nabla^{\mathfrak{D}} V_{\mathcal{T}}^{n+1}) + A(c_{N\mathcal{T}}^{n+1} - c_{P\mathcal{T}}^{n+1}) = 0,\\
&\frac{c_{P\mathcal{T}}^{n+1} - c_{P\mathcal{T}}^{n}}{\Delta t} + D_P\, \mathrm{div}^{\mathcal{T}}({J_{\mathfrak{D}}}^{n+1}) = 0,\\
&\frac{c_{N\mathcal{T}}^{n+1} - c_{N\mathcal{T}}^{n}}{\Delta t} + D_N\, \mathrm{div}^{\mathcal{T}}({G_{\mathfrak{D}}}^{n+1}) = 0,\\
&{J_{\mathfrak{D}}}^{n+1} = -r^{\mathfrak{D}}(c_{P\mathcal{T}}^{n+1})\nabla^{\mathfrak{D}}(\log c_{P\mathcal{T}}^{n+1} + \Lambda V_{\mathcal{T}}^{n+1}),\\
&{G_{\mathfrak{D}}}^{n+1} = -r^{\mathfrak{D}}(c_{N\mathcal{T}}^{n+1})\nabla^{\mathfrak{D}}(\log c_{N\mathcal{T}}^{n+1} - \Lambda V_{\mathcal{T}}^{n+1}).
\end{aligned}
$$

DDFV operator

RECONSTRUCTION OPERATOR



$r^{\mathfrak{D}}$ constant on each diamond cell

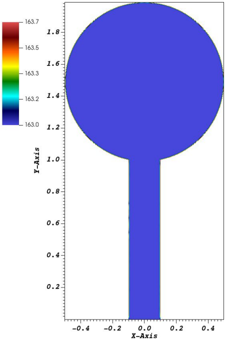
$$\forall \mathcal{D} \in \mathfrak{D},$$

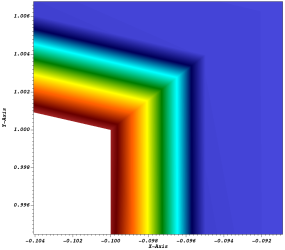
$$r^{\mathcal{D}} u_{\mathcal{T}} = \frac{1}{4}(u_{\mathcal{K}} + u_{\mathcal{L}} + u_{\mathcal{K}^*} + u_{\mathcal{L}^*}).$$

Numerical results

- Application to ionic and voltage dynamics in a dendritic spine

c_P simulation (left) and zoom simulation of the junction head-neck (right) on Ω with $T_f = 0.5$s.





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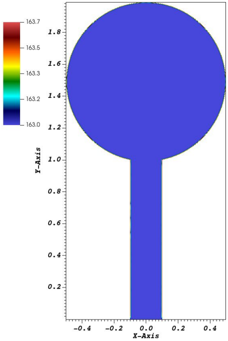
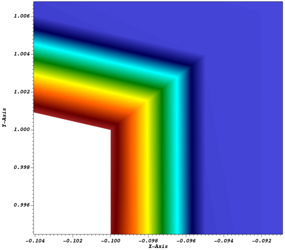
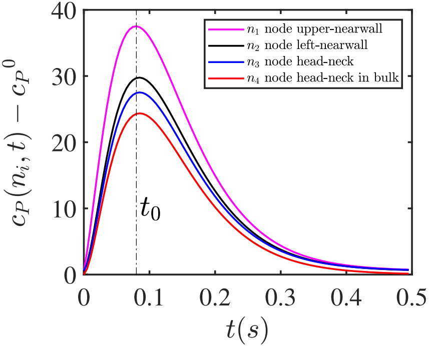
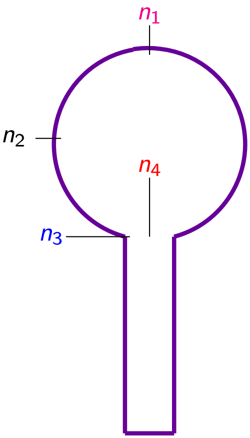




Numerical results

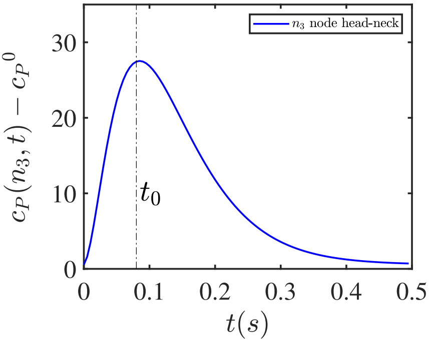
c_P simulations at different locations on Ω

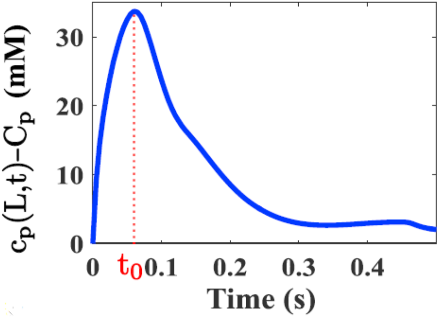




Comparaison with existing results with biological data

c_P simulations : left from our code and right from [Cartailler and al.2018]





Conclusion and Perspectives

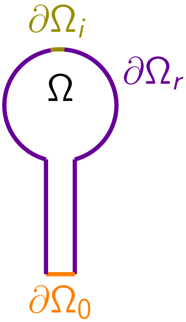
- Numerical scheme with positivity conservation on ionic concentrations

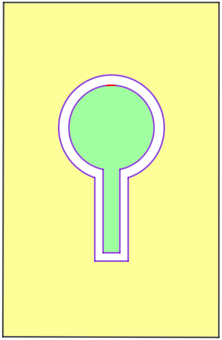
Conclusion and Perspectives

- Numerical scheme with positivity conservation on ionic concentrations

- Is the BC for V on $\partial\Omega_i \cup \partial\Omega_r$ right ?

  - Reminder : $\dfrac{\partial V}{\partial \mathrm{n}} = -\dfrac{\rho}{\epsilon\epsilon_0}$, on $\partial\Omega_i \cup \partial\Omega_r \times (0, T_f)$.





Thank you for your attention

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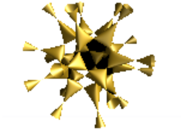


References

- Hodgkin AL, Huxley AF (August 1952). "A quantitative description of membrane current and its application to conduction and excitation in nerve". The Journal of Physiology. 117 (4) : 500–44.

- Kirby, B. J. (2010). "Micro-and nanoscale fluid mechanics : transport in microfluidic devices." Cambridge university press.

- Cartailler, J., Kwon, T., Yuste, R., Holcman, D. (2018). Deconvolution of voltage sensor time series and electro-diffusion modeling reveal the role of spine geometry in controlling synaptic strength. Neuron, 97(5), 1126-1136.

- Cancès, C., Chainais-Hillairet, C., Krell, S. (2018). Numerical analysis of a nonlinear free-energy diminishing discrete duality finite volume scheme for convection diffusion equations. Computational Methods in Applied Mathematics, 18(3), 407-432.

Annexe

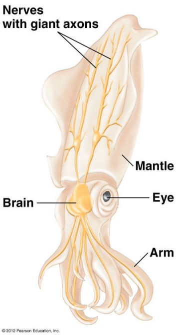
- Scheme for Neumann boundary conditions

$$
\begin{aligned}
\mathrm{m}_\sigma \nabla^{\mathfrak{D}} V_{\mathcal{T}}^{n+1} \cdot \mathsf{n} &= 0, && \forall\ \mathcal{D} \in \mathfrak{D}_{\partial\Omega_i \cup \partial\Omega_r}, \\
\mathrm{m}_\sigma {G_{\mathfrak{D}}}^{n+1} \cdot \mathsf{n} &= 0, && \forall\ \mathcal{D} \in \mathfrak{D}_{\partial\Omega_i \cup \partial\Omega_r}, \\
\mathrm{m}_\sigma {J_{\mathfrak{D}}}^{n+1} \cdot \mathsf{n} &= 0, && \forall\ \mathcal{D} \in \mathfrak{D}_{\partial\Omega_r}, \\
\mathrm{m}_\sigma {J_{\mathfrak{D}}}^{n+1} \cdot \mathsf{n} &= I, && \forall\ \mathcal{D} \in \mathfrak{D}_{\partial\Omega_i},
\end{aligned}
$$

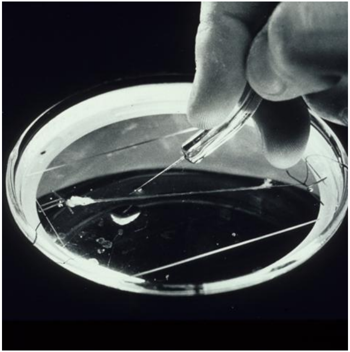
Hodgkin and Huxley model

First mathematical model published by Hodgkin and Huxley in 1952

- Squid Giant Axon with diameter $\sim$ 1mm



Source : Researchgate.com



Source : Wikipedia