COMSOL CONFERENCE 2009

OCTOBER 14-16 2009, MILAN, ITALY

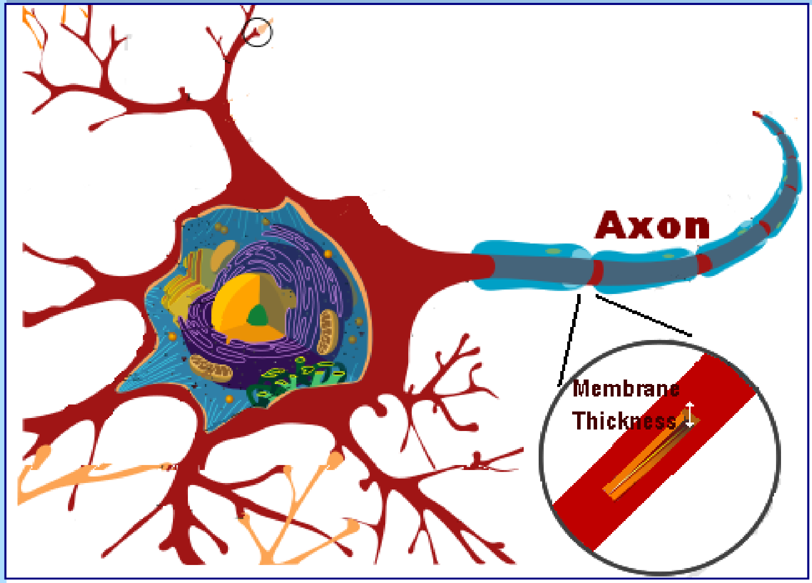
A Finite Element Model for The Axon of Nervous Cells

S. Elia, P. Lamberti, and V. Tucci,
Dept. of Electrical and Information Engineering, University of Salerno,
via Ponte don Melillo, Fisciano, (SA), Italy, **selia@unisa.it**

Outline

- **Introduction**
- **Adopted FEM models**
- **Results**
    - Differences between the two models
    - Temperature Dependence
    - Propagation Effect
- **Conclusions and Future Works**

Introduction

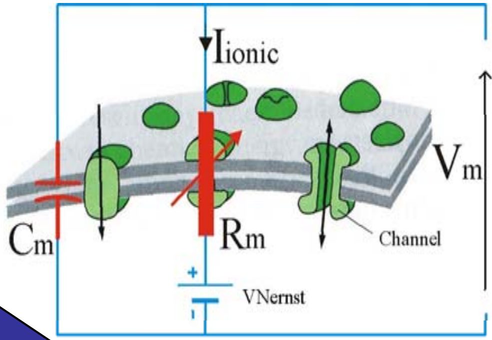


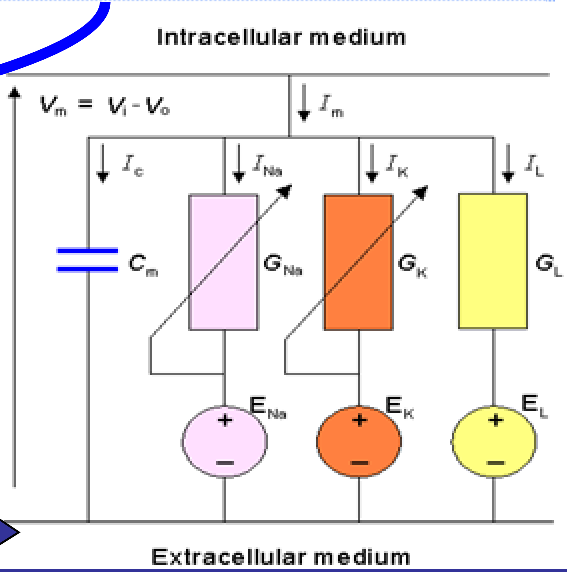
Transmission of signals in the nervous system: fast **fluctuations of the electric potential** across neurons external “coating”: its membrane.

The axon (myelinated or not):

- long cylindrical structure
- surrounded by a complex structured membrane
- physical support for nervous pulses propagation

Circuit parameter equivalent model of the **axon membrane (Hodgkin-Huxley Model):** a capacitance in parallel with several ionic gating channels, whose equivalent conductance depends on Vm (the voltage across the membrane itself).





EQS Implementation of a FEM Model (A) for an Axon Segment

A Transient Analysis of a Quasi Static Electric formulation for Maxwell Equations is adopted to define the current continuity equation on the various domains.

EM Settings Over the Domains

- **All media (but membrane)** are **linear**, **homogeneous**, **isotropic**.
- **Membrane** domain is modelled performing a translation of Hodgkin Huxley (HH) lumped-circuit quantities into parameters adapt to a field solution study:

– σ_m
(highly non-linearly depending on voltage across membrane)

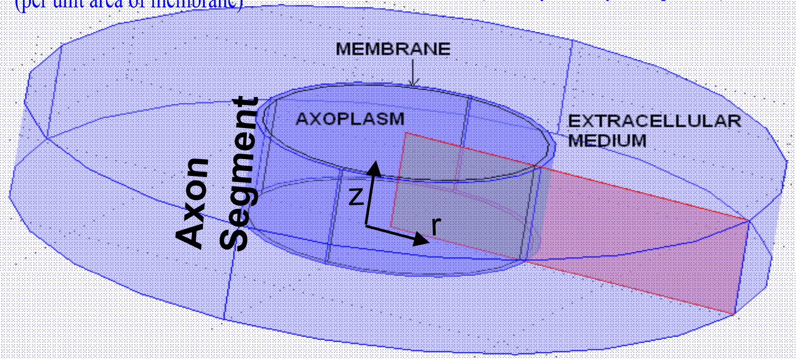
– ε_m
(derived from the capacitance value measured by H&H)

– J_{ext}
(an external impressed current density, also depending on voltage across membrane).

From HODGKIN-HUXLEY CIRCUITAL MODEL
(per unit area of membrane)

➡

To the 3D FIELD MODEL
(axial symmetry is exploited)



*(Dependent Variable: Electric Potential **V**)*

$$\nabla\cdot\frac{\partial\left(\varepsilon_i\nabla V\right)}{\partial t}+\nabla\cdot\left(\sigma_i\nabla V-\overline{J}_{ext}\right)=0$$

$$i\in\left\{D_{ax},D_m,D_{ext}\right\}$$

$$\overline{J}_{ext}=\begin{cases}Je(V_m)\cdot\hat{r} & over\ D_m\\ 0 & elsewhere\end{cases}$$

EQS Implementation of a FEM Model (A) for an Axon Segment

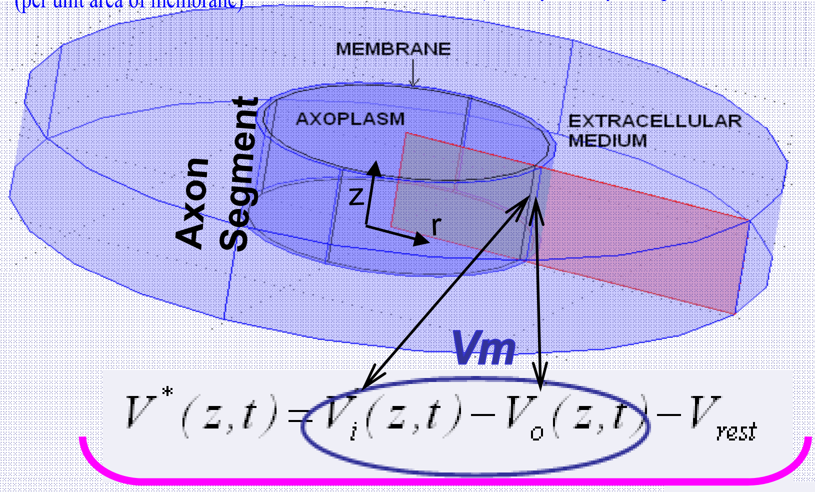
H-H Membrane Total Current

$$I_m = \boxed{C_m}\frac{dV_m}{dt} + V_m \boxed{G_m}(V_m) + \boxed{\sum_{i\in\{Na,K,l\}} -G_i E_i}$$

$$\varepsilon_m = \frac{C_m d_m}{\varepsilon_0} \qquad \sigma_m = G_m \cdot d_m \qquad J_{ext}$$

From HODGKIN-HUXLEY CIRCUITAL MODEL
(per unit area of membrane)

To the 3D FIELD MODEL
(axial symmetry is exploited)



$$V^*(z,t) = V_i(z,t) - V_o(z,t) - V_{rest}$$

Boundary Expressions & Extrusion

HH Model Parameters Definition:

$$G_m = G_{Na} + G_K + G_l$$

$$G_{Na} = G_{Na\,max} m^3 h$$

$$G_K = G_{K\,max} n^4$$

$$\frac{dx}{dt} = \alpha_x \cdot (1-x) - \beta_x \cdot x \quad \text{With } x \in \{m,n,h\}.$$

$\alpha_n = 1000\frac{0.1-0.01V^*}{e^{(1-0.1V^*)}-1}$	$\beta_n = 1000\frac{0.125}{e^{0.0125V^*}}$
$\alpha_m = 1000\frac{2.5-0.1V^*}{e^{(2.5-0.1V^*)}-1}$	$\beta_m = 1000\frac{4}{e^{(V^*/18)}}$
$\alpha_h = 1000\frac{0.07}{e^{0.05V^*}}$	$\beta_h = 1000\frac{1}{e^{(3-0.1V^*)}+1}$

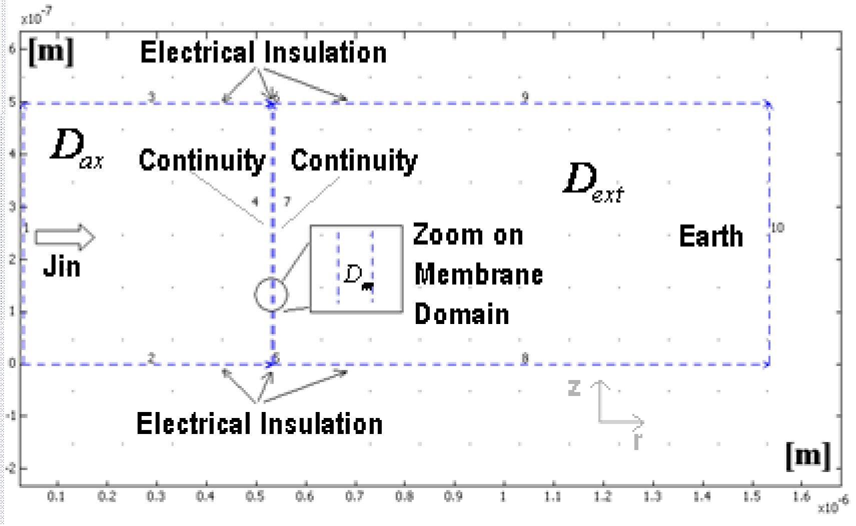
EQS Implementation of a FEM Model (A) for an Axon Segment

H-H Membrane Total Current

$$I_m = \boxed{C_m} \frac{dV_m}{dt} + V_m \boxed{G_m}(V_m) + \boxed{\sum_{i \in \{Na, K, l\}} -G_i E_i}$$

$$\varepsilon_m = \frac{C_m d_m}{\varepsilon_0} \qquad \sigma_m = G_m \cdot d_m \qquad J_{ext}$$

Boundary Conditions



HH Model Parameters Definition:

$$G_m = G_{Na} + G_K + G_l$$

$$G_{Na} = G_{Na\,\max} m^3 h$$

$$G_K = G_{K\,max} n^4$$

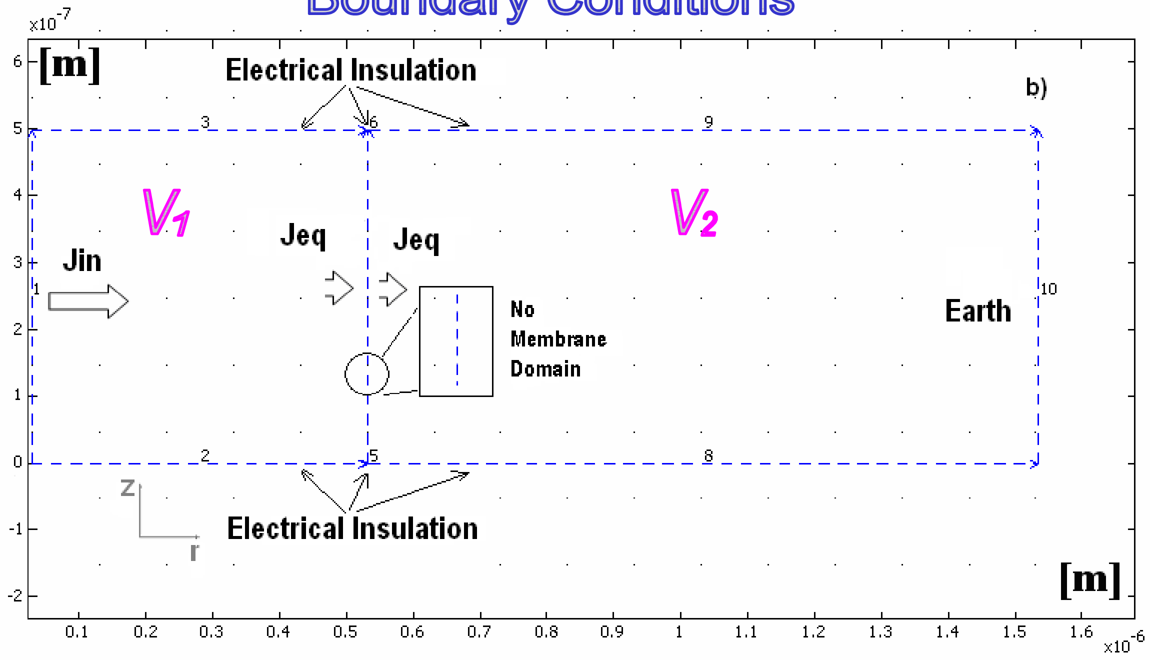
$$\frac{dx}{dt} = \alpha_x \cdot (1 - x) - \beta_x \cdot x$$

With $x \in \{m, n, h\}$ PDE Packet (general form)

$\alpha_n = 1000 \frac{0.1 - 0.01V^*}{e^{(1-0.1V^*)} - 1}$	$\beta_n = 1000 \frac{0.125}{e^{0.0125\,V^*}}$
$\alpha_m = 1000 \frac{2.5 - 0.1V^*}{e^{(2.5-0.1V^*)} - 1}$	$\beta_m = 1000 \frac{4}{e^{(V^*/18)}}$
$\alpha_h = 1000 \frac{0.07}{e^{0.05\,V^*}}$	$\beta_h = 1000 \frac{1}{e^{(3-0.1V^*)} + 1}$

Thin Layer Approximated Model (B)

Boundary Conditions



Alternative model, performing a **thin layer approximation** for the membrane.

Membrane is **substitued by a discontinuity surface** on which an equivalent current density J_{eq} is imposed to account membrane electrophysiological effects.

HH parameters defined only on membrane boundary.

Two Different EQS Packets(Dep. vars: V_1, V_2)

$$\boxed{J_{eq} = \sigma_m \frac{(V_2 - V_1)}{d_m} + J_{ext} + \frac{\varepsilon_m \varepsilon_0}{d_m} \frac{\partial (V_2 - V_1)}{\partial t}}$$

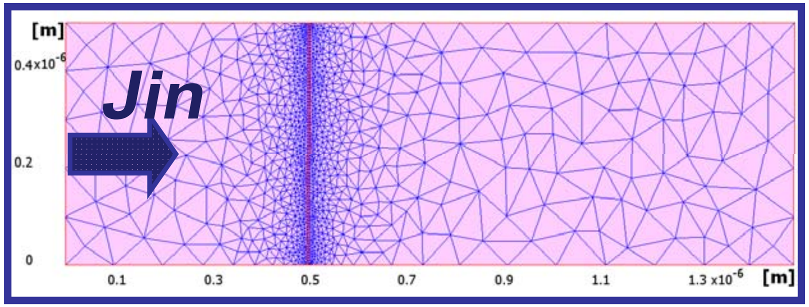
PDE Packet (weak form for boundaries)

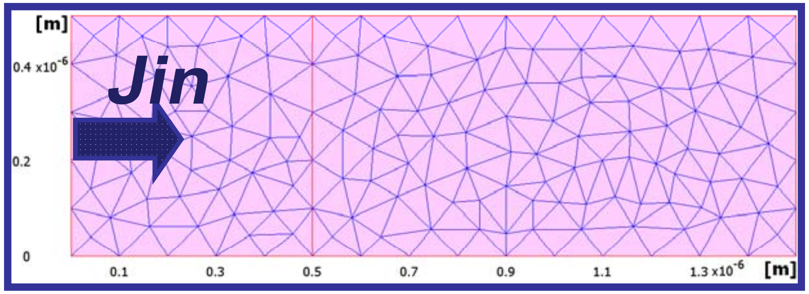
Hps:

1) Membrane conductivity is lower than those of the other two;
2) Lateral boundaries are insulated (null net flux);
3) Current density φ and z components are negligible with respect to transversal one.

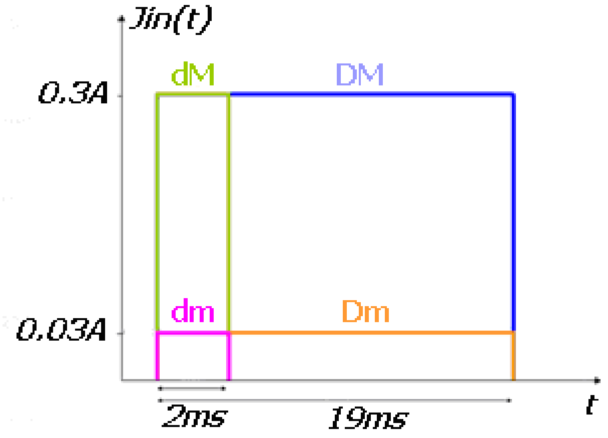
COMSOL Multiphysics Reference Manual, *Thin Film Resistance* application example

Comparison between the two models





Considerable advantage in terms of calculus time and memory usage.



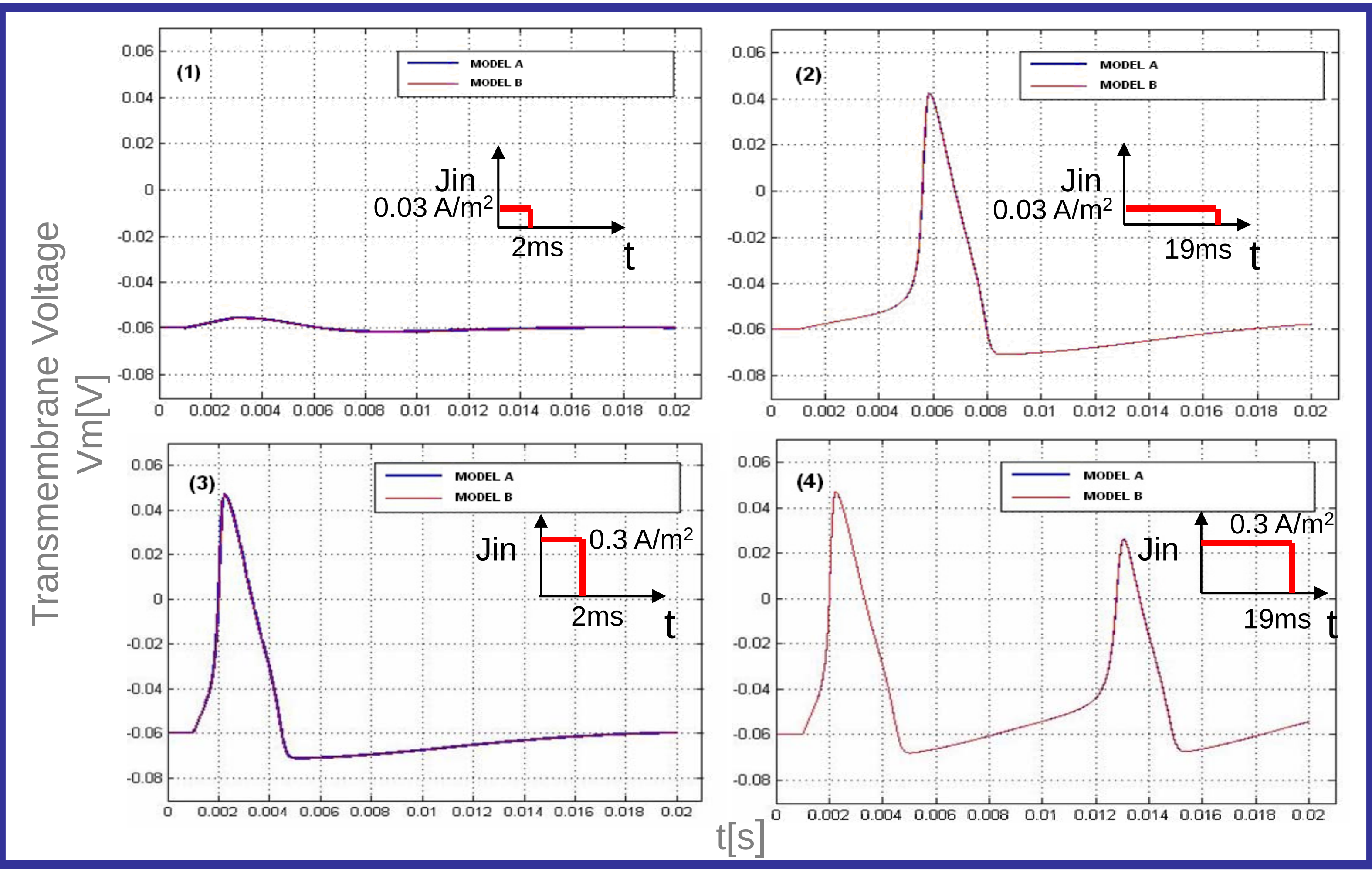
PARAMETER / MODEL	A	B
Degrees of freedom	7086	685
Number of boundary sides	220	45
Number of elements	2378	300
Minimum quality level	0.5867	0.5666

Simulat. Duration [s]

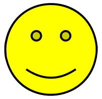
	dm	dM	Dm	DM
Model A	83.64	185.59	119.31	183.71
Model B	19.79	48.96	26.89	42.70

Comparison between the two models

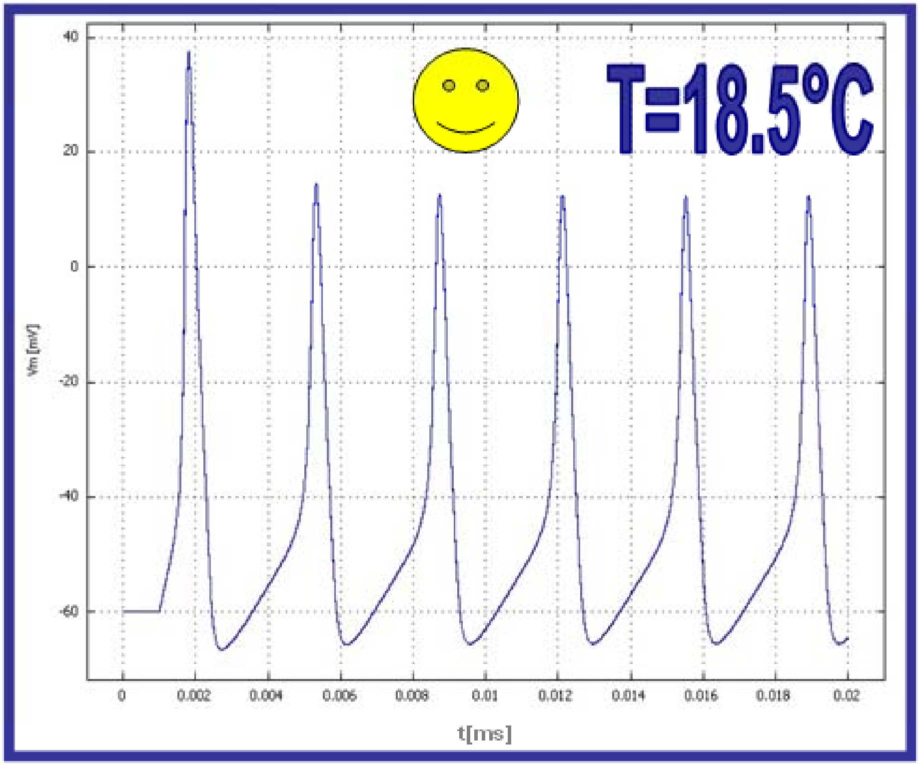
Action Potentials under Four Different Current Density Stimuli



Moulin C. et al., “A new 3D finite element model of extracellular action potentials recording with a microelectrode in a tissue slice”, Conf Proc IEEE Eng Med Biol Soc. 2006;1:603-6.



Temperature Dependence



Burst of faster APs.

$$\frac{dx}{dt} = [\alpha_x(1-x)-\beta_x x]$$

$\text{with} \quad x \in \{m, n, h\}$

$\text{and} \quad \tau_x = \frac{1}{\alpha_x+\beta_x}$

τ(T= 6.3°C)

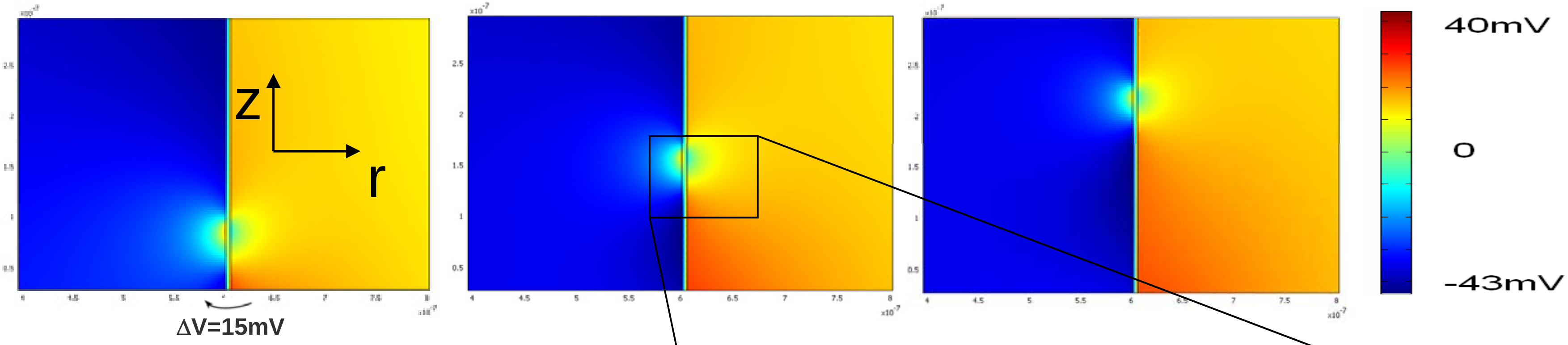
$$\frac{dx}{dt} = [\alpha_x(1-x)-\beta_x x]\cdot 3^{\frac{T-6.3}{10}}$$

$$\frac{dx}{dt} = [\alpha'_x(1-x)-\beta'_x x]$$

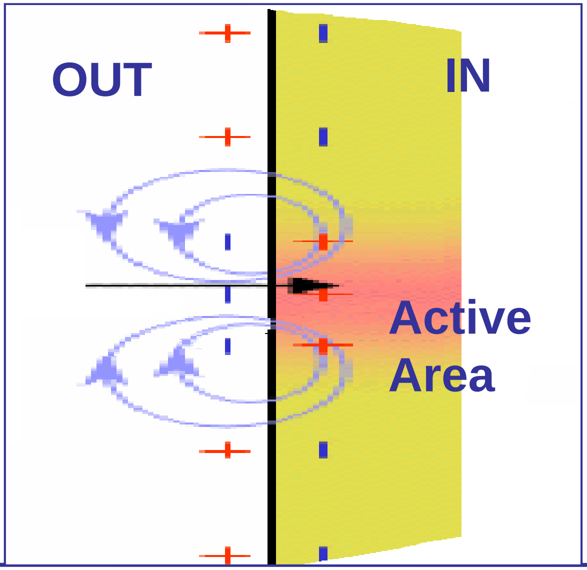
$$\tau'_x = \frac{1}{\alpha'_x+\beta'_x} = \frac{\tau_x}{3^{\frac{T-6.3}{10}}}$$

τ(T= 18.5°C)

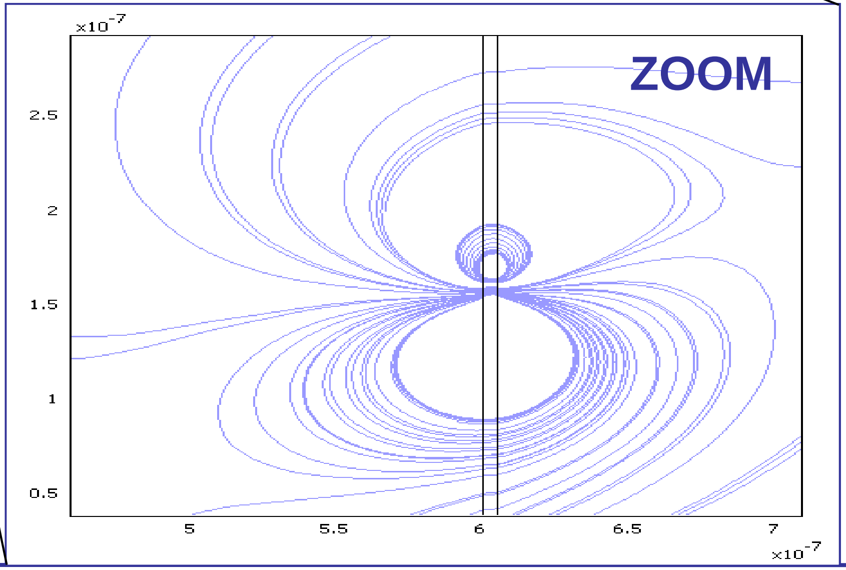
Propagation Effect



Theoretical Current Density Fluxes Lines,
in the Active Area



Simulated Current Density Fluxes Lines,
in the Active Area



Conclusions and Future Works

- **The described FEM models allow:**
  - to simulate the electrophysiological behaviour of a portion of nervous cell axon (under-threshold and active dynamic behaviour),
  - to reproduce accurately action potentials with an efficient approach,
  - to simulate a whole non-myelinated fibre and to introduce soma, dendrites, etc…
- **Work in progress: neurostimulation with nano-electrodes.**

Thank you for your attention!