Cardiac electrical simulations at the microscopic scale

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Context

- Microscopic alterations of the heart tissue (fat, fibre invasion, fibre crossing responsible of non-anisotropic behavior) are responsible of alterations of the electric wave propagation.
- It leads to macroscopic heart diseases.

Purpose

- Get a better understanding on the consequences of microscopic alterations in the heart.
- Provide a usable microscopic model for electric wave propagation.
- Simulate this model efficiently by solving Domain Decomposition issue.

State of the art

1. The biological process involved in electrical activity of human heart are known.
2. Bidomain model (microscopic version).
   (a) Mathematical model which describes simultaneously the intracellular and the extracellular domains.
   (b) Does not implement complex gap junction representation.
   (c) Practically not used in 3D representations.
3. Bidomain model (macroscopic version).
   (a) Mathematical model which describes simultaneously the intracellular and the extracellular domains.
   (b) Values are averaged on an important amount of cells which makes the tissue look periodic.
   (c) Specifically used for simulation of arrhythmia.
4. Monodomain model (fully macroscopic).
   (a) Assumption: anisotropic ratios are the same for intracellular and extracellular medium.
   (b) The mathematical model is reduced to only one equation.
   (c) Values are averaged on an important amount of cells which makes the tissue look periodic.
   (d) Useful to simulate a heart without extracellular applied current.

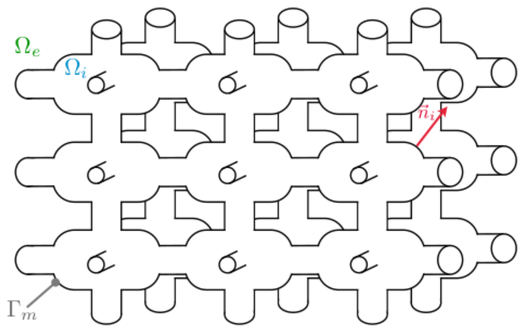

Figure 1: *Basic representation of a 3D tissue in a mathematical point of view*

Development of a microscopic model

- Homogenization do not allow to take non-linear behavior of gap junctions between cells into account.
- Malfunctions in gap junctions may lead from differed signal propagation to no signal propagation at all.
- The microscopic version of the bidomain could be adapted and implemented in scientific computing codes.
- This leads to algorithmic problems as mathematical ones in order to have a high performance computing code.

Initial schedule

- Get a first set of equations for ”microscopic model”.
- Adapt CEPS code to the requirements of this model.
- Design a simulation process.
- Check the simulation results regarding medical and mathematical expectations.

Mathematics equations for bidomain and monodomain models

In the following, σ_i is the intracellular conductivity, as σ_e is the extracellular conductivity. u_i and u_e respectively are the intracellular and extracellular potential. Also, I_{ion}^{tot} is the ionic current over the membrane per unit of area, and C_m is the electrical capacitance of the membrane per unit of area. Finally, $V_m = u_i - u_e$.

Bidomain model

$$\begin{aligned} \nabla \cdot (\sigma_i \nabla V_m) + \nabla \cdot (\sigma_i \nabla u_e) &= \chi \left(C_m \frac{\partial V_m}{\partial t} + I_{tot}^{ion} \right) \\ \nabla \cdot (\sigma_i \nabla V_m) + \nabla \cdot ((\sigma_i + \sigma_e) \nabla u_e) &= 0 \end{aligned} \tag{1}$$

Monodomain model

Anisotropic ratio is the same for intracellular and extracellular medium : the two equations combine in one.

$$\frac{\lambda}{1+\lambda} \nabla \cdot (\sigma_i \nabla V_m) = \chi \left(C_m \frac{\partial v}{\partial t} + I_{\text{ion}} \right) \tag{2}$$

A first microscopic mathematical model

Deduced from the physical laws ruling the electrical activity of the cardiac cells.

$$\begin{aligned} \nabla \cdot (\sigma_i \nabla u_i) &= 0 & \Omega_i \\ \nabla \cdot (\sigma_e \nabla u_e) &= 0 & \Omega_e \\ \sigma_i \nabla u_i \cdot n_i &= \sigma_e \nabla u_e \cdot n_i & \Gamma_m \\ -\sigma_i \nabla u_i \cdot n_i &= C_m \frac{\partial V_m}{\partial t} + I_{ion}^{tot} & \Gamma_m \end{aligned} \tag{3}$$

Modelling gap junctions

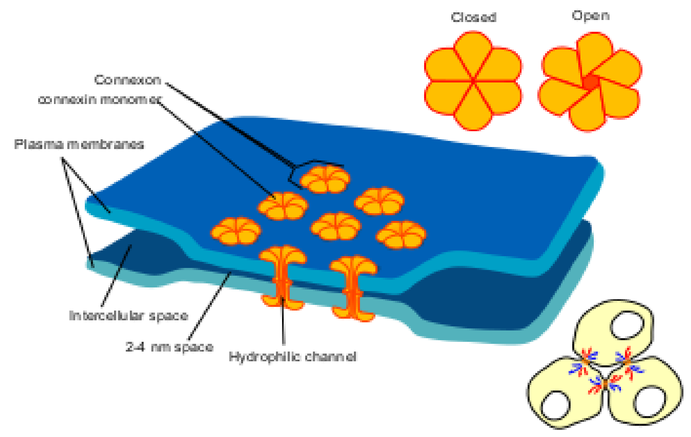

Figure 2: *A representation of gap junctions. Credit: Mariana Ruiz, 2006*

Gap junctions have a different conductivity. The last equation can be slightly modified to take this into account.

$$-\sigma_{i1} \vec{\nabla}_{\vec{x}} u_{i1} \cdot \vec{n}_{i1} = \sigma_g \frac{\partial V_g}{\partial t} + I_g I_{ion}^{tot} \quad \text{Gap}$$

σ_g being the conductivity of the gap junction, $V_g = u_{i1} - u_{i2}$ the tension between the two cells at the gap junction, I_g a one or zero operator modelling the open/closed state of the gap junction.

On a first step, gap junctions will be assumed having a linear conductivity.

CEPS : Cardiac ElectroPhysiology Simulator

- Reaction-diffusion model.
- The equations are currently solved with a P1 Lagrange finite elements method.
- CARMEN team develops its own numerical methods (discretisation in space and time) in the CEPS code.
- CEPS uses PETSc and Parmetis (soon using Scotch, an equivalent developed at INRIA) to operate matrix decomposition. One of the goals is to implement domain decomposition features.

CEPS is designed to simulate any cardiological model.

Figure 3: Maison de la simulation *is a lab with expertise in High Performance Computing*

Work with CEPS

- Discretize equation system mathematically.
- Describe a finite element method to compute a solution.
- Ensure the algorithm is eager to scale on big amount of data, and is compatible with domain decomposition methods.
- Test simple solvers on CEPS.
- Implement this method in CEPS.

Perspectives

- Have a working basic simulation to be able to run tests.
- Run these tests on the clusters at bigger scales to identify scaling issues.
- Develop gap junction complex models in collaboration with medical teams.
- Compare macroscopic bi-domain and monodomain model to homogenization-based methods achieved in CARMEN.