Workshop on Computational Physiology

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Graduate Program in Computational Modeling
Universidade Federal de Juiz de Fora, Brazil
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Organization: Prof. Dr. Rodrigo Weber dos Santos and Prof. Dr. Marcelo Lobosco
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Support:
Universidade Federal de Juiz de Fora. Pós-Graduação em Modelagem Computacional. Instituto de Ciências Exatas. Faculdade de Engenharia. CAPES. FAPEMIG. CNPq.

Place: Anfiteatro Escadinha – Faculdade de Engenharia - UFJF

Program

10:00-11:00

Prof. Dr. Anders Nygren, University of Calgary, Canada

Lateralization of Connexins and Reduced Conduction Reserve in the Diabetic Rat Heart: Insights from Experimental Observations and Computer Simulations

Conduction velocity in the heart is dependent on two main factors: intercellular electrical coupling and cellular electrical excitability. There is significant redundancy, “conduction reserve”, in these parameters such that significant reduction in the conduction velocity of the action potential requires either a large change in one of these parameters or combined changes in both. We have used optical mapping to measure conduction velocity in hearts from streptozotocin-induced diabetic rats. Our results show little change in baseline conduction velocity in diabetic hearts compared to controls. However, both the gap junction uncoupler heptanol (0.5-1 mM), and elevated extracellular potassium (9 mM) produced a significantly greater reduction of conduction velocity in diabetic hearts than in controls. Immunofluorescent labeling of connexin-43 showed significant gap junction reorganization in diabetic hearts, such that an abnormally large fraction of the Cx-43 fluorescence was observed along the sides of the cells. We hypothesize that this process, known as lateralization of connexins, results in reduced intercellular coupling. Depending on whether the lateralized connexins are functional or not, this process may also result in changes in the anisotropy of conduction in the ventricular tissue.

This presentation will illustrate how computer modeling approaches have been used to gain insight into these experimental observations. To gain a better understanding of the reduction of conduction reserve, a rat ventricle myocyte model was used to simulate propagation along a strand of cells. Simulations were performed to assess the effect of reduction of intercellular conductance on the conduction velocity. Consistent with our experimental results, the relationship between conduction velocity and intercellular coupling became steeper with decreasing coupling, such that conduction velocity became increasingly sensitive to further uncoupling. However, the computer simulations also highlighted areas in which our understanding of the experimental results is incomplete. Three-dimensional simulations of action potential propagation have also been used to determine how lateralization of connexins can be expected to affect action potential propagation, as observed by surface recordings using optical mapping. These results demonstrate that while lateralization of connexins does alter the anisotropy ratio of conduction, these effects are difficult to interpret due to rotation of cardiac fiber directions through the wall thickness. This project thus illustrates the important contributions that simulations can make in evaluating experimental observations and guiding further experimental studies.

11:00-11:30

Msc. Ricardo Silva Campos, UFJF, Brazil

An electro-mechanical cardiac simulator based on cellular automata and mass-spring models

The mechanical behavior of the heart is guided by the propagation of an electrical wave, called action potential. Many diseases have multiple effects on both electrical and mechanical cardiac physiology. To support a better understanding of the multiscale and multiphysics processes involved in physiological and pathological cardiac conditions, a lot of work has been done in developing computational tools to simulate the electro-mechanical behavior of the heart. In this work, we propose a new user-friendly and efficient tool for the electro-mechanical simulation of the cardiac tissue that is based on cellular automata and mass-spring models. The proposed tool offers a user-friendly interface that allows one to interact with the simulation on-the-fly. In addition, the simulator is parallelized with CUDA and OpenMP to further speedup the execution time of the simulations.

11:30-12:00

Prof. MSc. Rafael Sachetto de Oliveira, UFSJ/UFMG, Brazil

Efficient solvers based on manycore computers and adaptive techniques for cardiac modeling

Computer models have become valuable tools for the study and comprehension of the complex phenomena of cardiac electrophysiology. However, the high complexity of the biophysical processes translates into complex mathematical and computational models. In this paper we evaluate different parallel and numerical techniques to accelerate these simulations. At tissue level we have used mesh adaptivity and finite volume method, which is a very attractive approach since the spreading electrical wavefront corresponds only to a small fraction of the cardiac tissue. Usually, the numerical solution of the partial differential equations that model the phenomenon requires very fine spatial discretization to follow the wavefront. Therefore, the use of uniform meshes leads to high computational costs. In this sense, the tests reported in this work show that simulations of two-dimensional models of cardiac tissue have been accelerated by 250 times when using an adaptive mesh algorithm together with a time step adaptive algorithm. In addition, we have started to parallelize this new numerical schemes for manycore computers using OpenMP and CUDA. Preliminary results show that these adaptive techniques together with parallel algorithms for manycore computers are a powerful combination for solvers of cardiac models that reduce the execution time of the simulations without significant loss in accuracy.

14:00-14:30

MSc. Bárbara de Melo Quintela, UFJF, Brazil

On the integration of two models of the immune system

The development of mathematical models of the immune response allows a better understanding of the multifaceted mechanisms of this defense system. The main purpose of this work is to establish a general meta-modeling scheme for coupling distinct models of different scales and aspects of the immune system. As an example, we propose a new model where the local tissue inflammation processes are simulated with Partial Differential Equations (PDEs) whereas a system of Ordinary Differential Equations (ODEs) is used as a model for the systemic response. The simulation of different scenarios allows the analysis of the dynamics of different immune cells in the presence of a bacteria. The proposed meta-model demonstrated to be a very promising technique to couple different models of the immune system. The software SI3D is available under request.

14:30-15:00

MSc. Alexandre Bittencourt Pigozzo, UFJF, Brazil

Computational modeling of microabscess formation

Bacterial infections can be of two types: acute or chronic. The chronic bacterial infections are characterized by being a large bacterial infection and/or a infection where the bacteria grows rapidly. In these cases the immune response is not capable of completely eliminating the infection which may lead to the formation of a pattern known as microabscess (or abscess). The microabscess is characterized by an area comprising fluids, bacteria, immune cells (mainly neutrophils) and many types of dead cells. This distinct pattern of formation can only be numerically reproduced and studied by models that capture the spatio-temporal dynamics of the human immune system (HIS). In this context, our work aims to develop and implement an initial computational model to study the process of microabscess formation during a bacterial infection.

15:00-15:30
Coffee Break

15:30-16:00

Bruno Gouvêa de Barros, UFJF, Brazil

Simulations of complex and microscopic models of cardiac electrophysiology powered by multi-gpu platforms

Key aspects of cardiac electrophysiology, such as slow conduction, conduction block and saltatory effects, have been the research topic of many computational modeling studies since they are strongly related to cardiac arrhythmia, reentry, fibrillation or defibrillation. However, to reproduce these phenomena the numerical models need to use sub-cellular discretization for the solution of the Partial Differential Equations and to consider nonuniform, heterogeneous tissue electric conductivity. Due to the high computational costs of simulations that reproduce the fine microstructure of cardiac tissue, previous studies have considered tissue experiments of small or moderate sizes and used simple cardiac cell models. In this paper we develop a cardiac electrophysiology model that captures the microstructure of cardiac tissue by using a very fine spatial discretization (8um) and uses a very modern and complex cell model based on Markov Chains for the characterization of ion channel's structure and dynamics. To cope with the computational challenges, the model was parallelized using a hybrid approach: cluster computing and GPGPUs (General-purpose computing on graphics processing units). Our parallel implementation of this model using a Multi-GPU platform was able to reduce the execution times of the simulations from more than 6 days (on a single processor) to 21 minutes (on a small 8-node cluster equipped with 8 GPUs, i.e. 1 GPU per node). We believe that this new parallel implementation paves the way for the investigation of many open questions associated to the complex and discrete propagation nature of action potentials on cardiac tissue.

16:00-16:30

Johnny Moreira Gomes, UFJF, Brazil

Coupling cellular metabolism, electrophysiology and mechanical contraction models for cardiac myocytes: challenges of a multiphysics and a multiple time scale problem

Complex biological in-silico models involve multiple physics and scales to address the interactions between the different subsystems that affect a given phenomenon. An example of a challenging multiscale and multiphysics problem in cardiac cell modeling is the in-silico reproduction of a ischemic event, which involves different but coupled subsystems, such as cellular metabolism, mechanics and electrophysiology. Metabolic models for cardiac myocytes reproduce phenomena of interest after minutes of simulation, whereas electrophysiological and mechanical models for these cells operate on the scale of milliseconds. In this work we present the coupling of a metabolic model with an electromechanical model. Finally, we also present a combination of numerical methods that significantly reduces the execution time of the simulations of these particular important multiplysics and multiscale problem of cardiac myocyte modeling.

16:30-17:00

Gustavo Montes Novaes, UFJF, Brazil

Parallel computing and metamodels applied to an inverse problem in cardiac electrophysiology

This project has as main goal the evaluation of a Genetic Algorithm (GA) based methodology that aims to automatically adjust electrophysiology cellular models to experimental data. These inverse problems are extremely expensive in terms of computation time. Therefore, we evaluate the combination of two techniques to accelerate the GA: parallel computing and metamodels. The GA was parallelized using the Master-Salve model. In addition, we implemented a metamodel that replaces the evaluation of a candidate fitness by a cheaper estimation based on previous evaluations. The metamodel is dynamically created by the algorithm and has a historic with all the evaluated candidate finesses. This historic, or database, was implemented in two different ways: via an ordered-array and by a structure named Kd-Tree. The GA parallel execution in 20 cores were twice faster than the execution with 10 cores. The Kd-Tree structure accelerate the storage and search functions in 4000 times when compared with the ordered-array implementation. With this implementation, it was possible to estimate the fitness of up to 40% of the candidates by the metamodel without loosing the parameter adjust quality, which reduced the total execution time of 3 hours (without metamodel) to 2 hours.