Master thesis - Project description

Title: *Characterization of cardiac cellular dynamics using Physics-Informed Neural Networks*

Background:

The heart is a complex, dynamic organ consisting of billions of individual cells working electro-mechanically in concert. Key to this is that these cells that are excitable, able to generate an electrical action potential, which in turn triggers contraction and ultimately pumping of blood to the rest of the body. These are incredibly all studied systems, and the electrical behavior of individual cells can be accurately modeled using systems of ordinary differential equations (ODEs) describing the flow of keys ions through the cell and its surroundings,

$$\frac{\partial s}{\partial t} = F(s;t).$$

where s is a vector of state variables and t is time.

A promising new technology known as “heart on chip” systems opens up the possibility to study these heart cells in an environment that is similar to the environment inside the body. Using these systems, consisting of microfluidically controlled cardiac cells derived from human induced pluripotent stem cells (hIPSCs), we are able to measure properties that can be used to fit biophysical mathematical models.

Recently, scientists have developed so called *Physics-informed neural networks (PINN)* models[1, 6] which allow for regularizing a deep learning framework using some physical laws. For example we could say that we want to approximate the whole state vector s by a neural network $s(t) \approx \mathcal{N}(t)$ and now formulate a loss function based on partial observations[2]. Another approach is to model parts of the ODE system as a Neural network [3] assuming that we know the dynamics of the remaining system.

Goal

We want to study PINN models in the context for cardiac cellular dynamics. More specifically we would like to measure the performance of these PINN models when using simulated data.

Outline of project

1. The student should learn about modeling heart cells at the cellular level and learn methods for solving the governing equations.
2. The student should learn about Physics-informed neural networks models and implement some basic model to learn the concept. This includes implementing a neural network in python using a suitable library.
3. The student should apply and investigate the performance of Physics-informed neural networks models using simple cell models [4]
4. The student should apply and investigate the performance of Physics-informed neural networks models using more complex cardiac cell models [5]
5. The student should should investigate how sensitive the model is to noise in the input data.

Possible directions for the project

Depending on the students interests, the project can take different directions.

Reconstructing cell model using sparse data

All state variables in a cell model are seldom possible to measure experimentally. In particular, it is currently only possible to estimate membrane potential and intracellular calcium concentrations using these heart-on-chip systems. Therefore it is of interest to see if it is possible to learn cellular dynamics based only on a sparse selection of the data. If this direction is taken we could also test this framework using real experimental data.

Characterizing different dynamics of the cell model

Instead of approximating the whole state vector in the ODE system the student can try to only approximate parts of the system, i.e approximating only a subset of the state variables.-

Extending modeling framework to a collection of cells

One possibility is to extend the project to study conduction properties in a collection of cells. The flow of current through the tissue can futhermore be described by a PDE known as the Bidomain model,

$$\frac{\partial v}{\partial t} - \nabla \cdot (M \nabla v) = I_s - I_{ion},$$

$$\frac{\partial s}{\partial t} = F(s; v, t).$$

The student could be to look at characterization of the conduction using a PINN model for the cellular part.

References

[1] Raissi, Maziar, Paris Perdikaris, and George E. Karniadakis. "Physics-informed neural networks: A deep learning framework for solving forward and inverse problems involving nonlinear partial differential equations." Journal of Computational Physics 378 (2019): 686-707.

[2] Ayed, Ibrahim, et al. "Learning dynamical systems from partial observations." arXiv preprint arXiv:1902.11136 (2019).

[3] Nascimento, Renato G., Kajetan Fricke, and Felipe AC Viana. "A tutorial on solving ordinary differential equations using Python and hybrid physics-informed neural network." Engineering Applications of Artificial Intelligence 96 (2020): 103996.

[4] Izhikevich, Eugene M., and Richard FitzHugh. "Fitzhugh-nagumo model." Scholarpedia 1.9 (2006): 1349.

[5] Jæger, Karoline Horgmo, et al. "Improved computational identification of drug response using optical measurements of human stem cell derived cardiomyocytes in microphysiological systems." Frontiers in pharmacology 10 (2020): 1648.

[6] Willard, Jared, et al. "Integrating physics-based modeling with machine learning: A survey." arXiv preprint arXiv:2003.04919 (2020).