BP 34: Nonlinear Dynamics of the Heart II (joint session DY/BP)

Time: Thursday 14:00–15:45 Location: ZEU 118

Invited Talk BP 34.1 Thu 14:00 ZEU 118

Dyadic structure-function relationships in ventricular cardiac myocytes: from sparks to action potentials — •Martin Falcke[1,2], Filippo G. Cosi[3], Wolfgang Giese[1], Wilhelm Neubert[1], Stefan Luther[3], and Ulrich Parlitz[3] — [1]Max Delbrück Center, Berlin — [2]Dept. of Physics, Humboldt University Berlin — [3]MPI for Dynamics and Self-Organization, Göttingen

Cardiovascular disease is often related to defects in molecular and subcellular components in cardiac myocytes, specifically in the dyadic cleft, which include changes in cleft geometry and channel placement. Modelling of these pathological changes requires both spatially resolved cleft as well as the whole cell level descriptions. We use a multiscale model to create dyadic structure-function relationships in order to explore the impact of molecular changes on whole cell electrophysiology and calcium cycling. This multiscale model incorporates stochastic simulation of individual L-type calcium channels (LCC) and ryanodine receptor channels (RyRs), spatially detailed concentration dynamics in dyadic clefts, rabbit membrane potential dynamics, and a system of partial differential equations for myoplasmic and lumenal free Ca^{2+} and Ca^{2+}-binding molecules in the bulk of the cell.

We create models with varying dyadic cleft properties including RyR and LCC clustering, stochastic opening and closing rates as well as changes in LCC and RyR calcium currents. We investigate biomarkers describing action potential, Ca^{2+} transient and Ca^{2+} spark dynamics. We quantify sensitivity and parameter uncertainty and derive cellular functional implications from molecular level properties.

BP 34.2 Thu 14:30 ZEU 118

Multiscale modeling of dyadic structure-function relation in ventricular cardiac myocytes — •Filippo Cosi[1,4,5], Wolfgang Giese[2], Wilhelm Neubert[2], Stefan Luther[1,4,5], Nagaiah Chamakuri[3], Ulrich Parlitz[1,4,5], and Martin Falcke[2,5] — [1]Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany — [2]Max Delbrück Center for Molecular Medicine in the Helmholtz association, Berlin, Germany — [3]Institute of Applied Mathematics, University of Hohenheim, Stuttgart, Germany — [4]Georg-August-Universität Göttingen, Institute for the Dynamics of Complex Systems, Göttingen, Germany — [5]DZHK (German Center for Cardiovascular Research), Partnersites Göttingen and Berlin, Germany

Understanding how defects in the subcellular components of single cardiomyocytes affect the calcium cycling in single cells can help to pin down the origin of cardiovascular disease. A multiscale model is used, which combines the stochastic nature of subcellular components (as Ryanodine Receptors, RyR or L-type Calcium Channels, LCC), their spatial arrangement as well as spatio-temporal calcium and buffer gradients at the whole-cell level. Recent findings regarding the geometrical clustering of RyRs and LCCs inspired us to include the physiological description of it into our mathematical model. The included structure modifications showed a dramatic effect on the model's outputs; in detail the arrangement of RyRs has a strong impact on cell functions. Our study aims to lay a quantitative fundament for the analysis of defect cardiomyocytes under physiologically conditions to deepen the understanding of how diseased heart tissue might be treated.

BP 34.3 Thu 14:45 ZEU 118

Simple mechanism for low-energy antifibrillation pacing — Pavel Buran, Thomas Niedermayer und •Markus Bär — Physikalisch-Technische Bundesanstalt (PTB), Berlin

Rotating excitation waves and electrical turbulence in cardiac tissue are associated with arrhythmias such as life-threatening ventricular fibrillation. Experimental studies have shown that a sequence of low-energy electrical far-field pulses is able to terminate fibrillation with less energy than a single large energy shock [1]. Previous theoretical approaches to understand this low-energy antifibrillation pacing (LEAP) have often focused on unpinning and removal of a small number of rotating spirals in quasi-two-dimensional situations. These theories, however, cannot explain the defibrillation of spatiotemporal chaos. Based on a systematic simulation study, we present an alternative mechanism for the success of LEAP in two dimensions, which explains both, the termination of stable spirals as well as spatiotemporal chaos. It turns out that actually each pulse during LEAP annihilates all excitation fronts, however, that new fronts could arise at the borders between refractory and excitable parts of the tissue. The success probability of each individual pulse can thus be simply interpreted as the probability that no new front arises. Furthermore, we will show that the success probability depends exponentially on the total length of these refractory boundaries and that successful LEAP is characterized by pulses causing a gradual decrease of this length simultaneously increasing the success probability of subsequent pulses until complete defibrillation.
[1] Luther et al., Nature **475**, 235-239 (2011)

BP 34.4 Thu 15:00 ZEU 118

Feedback-based protocol for low-energy defibrillation — •Pavel Buran, Thomas Niedermayer und Markus Bär — Physikalisch-Technische Bundesanstalt (PTB), Berlin

Low-energy antifibrillation pacing (LEAP) is a method where electrical turbulence characteristic for atrial or ventricular fibrillation is suppressed by a series of low energy pulses [1]. Systematic simulation studies show that the choice of the right pacing period is crucial for successful LEAP [2]. However, the range of those successful pacing periods is a priori not known for a given tissue. Methods that efficiently determine the range of successful pacing periods are therefore of high interest. We have found, that termination probability of each individual pulse during LEAP depends exponentially on the total length of the interfaces between refractory and excitable parts of the tissue. Based on this finding, we present a feedback controlled protocol that ensures that pulses are applied in such a way to minimize the mentioned interface length in line with our earlier findings about the mechanism of LEAP. This protocol does not need any a priori information about the system and can thus also be used as an efficient method to determine the optimal pacing period.
[1] Luther et al., Nature **475**, 235-239 (2011)
[2] Buran et al., Chaos **27**, 113110 (2017)

BP 34.5 Thu 15:15 ZEU 118

General equilibrium approach to resolve ventricular calcium homeostais — •Enrique Alvarez-Lacalle[1], Blas Echebarria[1], Angelina Peñaranda[1], Inmaculada R. Cantalapiedra[1], Yohannes Shiferaw[2], and David Conesa[1] — [1]Departament de Física. Universitat Politècnica de Catalunya (UPC-BarcelonaTech), Barcelona, Spain. — [2]Department of Physics. California State University Nortridge, Los Angeles, USA.

The ventricular contraction in the heart is roughly proportional to the amount of calcium released from the Sarcoplasmic Reticulum during systole. The change in the membrane potential triggers the opening of thousands of Ryanodine Receptor clusters in the SR membrane, being the release larger when pre-systolic calcium levels are larger. While it is rather straightforward to measure calcium levels and contractibility under different physiological conditions, the complexity of calcium handling during systole and diastole has made the prediction of its release at steady-state from measurements away from steady-state impossible. In this contribution, we present a general equilibrium framework to understand how homeostasis can be understood and analyzed to make predictions about its level when key properties of ionic channels or buffers (due to phosphorylation, genetic mutation,etc..) involved in calcium handling are changed. This framework should be useful to describe why different animals have such different homeostatic behavior upon changes in the pacing rate and provide a physiological mechanism for SERCA gene therapy failure.

BP 34.6 Thu 15:30 ZEU 118

Synchronization-based reconstruction of electromechanical wave dynamics in elastic excitable media — Jan Lebert[1,2,3] and •Jan Christoph[1,2,3] — [1]University Medical Center Göttingen, Germany — [2]Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany — [3]German Center for Cardiovascular Research, Partnersite Göttingen, Germany

Reconstructing electrical excitation wave dynamics within the heart muscle remains a major scientific challenge. Recently, it was shown using high-resolution 4D ultrasound that it is possible to identify mechanical filament-like phase singularities within the contracting, fibrillating heart wall, suggesting that the tissue mechanics reflect three-dimensional electrical scroll wave dynamics.

Here, we present a mechano-electrical data assimilation approach

with which it is possible to reconstruct electrical excitation wave dynamics, including electrical vortex filaments, within the volume of deformable excitable media. By observing the spatio-temporal deformation patterns, which occur in response to the electrical excitation, the mechanical data is assimilated in a numerical replication of the observed elastic excitable system, and within this replication the data drives the intrinsic excitable dynamics, which then co-evolve and correspond to a reconstruction of the original dynamics. We provide a numerical proof-of-principle and demonstrate the performance of the approach by recovering even complicated three-dimensional scroll wave patterns.