DY 13: Focus session: Nonlinear Dynamics of the Heart II (organized by Markus Bär, Stefan Luther and Ulrich Parlitz)

Time: Thursday 13:30–16:15 Location: H2

Invited Talk DY 13.1 Thu 13:30 H2

Multi-scale modeling of dyadic structure-function relation in ventricular cardiac myocytes — •Martin Falcke[1], Filippo G. Cosi[2], Wolfgang Giese[1], Wilhelm Neubert[1], Stefan Luther[2], Nagaiah Chmakuri[3], and Ulrich Parlitz[2] — [1]Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany — [2]Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany — [3]IISER Thiruvananthapuram, India

Cardiovascular disease is often related to defects of sub-cellular components in cardiac myocytes, specifically in the dyadic cleft, which include changes in cleft geometry and channel placement. Modeling of these pathological changes requires both spatially resolved cleft as well as whole cell level descriptions. We use a multi-scale model to create dyadic structure-function relationships to explore the impact of molecular changes on whole cell electrophysiology and calcium cycling. This multi-scale 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 calcium and calcium-binding molecules in the cell bulk. We found action potential duration, systolic and diastolic calcium to respond most sensitive to changes in LCC current. The RyR cluster structure inside dyadic clefts was found to affect all biomarkers investigated. The shape of clusters observed in experiments by Jayasinghe et al. and channel density within the cluster showed the strongest correlation to the effects on biomarkers.

DY 13.2 Thu 14:00 H2

Optogenetics control of spiral waves dynamics in cardiac tissue — Sayedeh Hussaini[1], Aidai Mamyraiym kyzy[1], Laura N. Diaz-Maue[1], Johannes Schroeder-Schetelig[1], Vishallini Venkatesan[1], Raul A. Quiñonez Uribe[1], Claudia Richter[1], Vadim Biktashev[2], Rupamanjari Majumder[1], Valentin Krinski[1], and •Stefan Luther[1] — [1]Research Group Biomedical Physics, Max Planck Institute for Dynamics and Self-Organization, G\"ottingen, Germany — [2]Exeter University, Exeter, England, United Kingdom

The heart is an excitable medium. The formation of spiral waves in the heart is the main cause of life-threatening cardiac arrhythmias. Defibrillation is a method to control these abnormal waves. Due to the significant side effects of this method, the development of alternative methods is needed. To do this, we need to deepen our knowledge of the dynamics of spiral waves. For this, Optogenetics has shown its great potential. In this work, using optogenetics we control the dynamics of a spiral wave in a two-dimensional domain of the mouse heart. We apply global and structured illumination patterns at different light intensities. In the sub-threshold regime illumination, we observed the tendency of the spiral wave to drift along the LI gradient. This observation provides us with a new mechanistic insight into optogenetic defibrillation. Global epicardial illumination of the cardiac surface leads to an intramural exponential decay of illumination which may cause the drift of a spiral wave towards the epicardium, where the wave may be terminated with supra-threshold illumination.

DY 13.3 Thu 14:15 H2

Spatiotemporal correlation of cardiac tissue and its variation in response to temperature — •Alessandro Loppini[1], Alessio Gizzi[1], Christian Cherubini[1], Flavio Fenton[2], and Simonetta Filippi[1] — [1]Unit of Nonlinear Physics and Mathematical Modeling, Campus Bio-Medico University of Rome, 00128 Rome, Italy — [2]School of Physics, Georgia Institute of Technology, Atlanta, Georgia, USA

Complex emergent dynamics are at the basis of life-threatening cardiac arrhythmias, including tachycardia and fibrillation. In the past years, a large number of studies have shown that such irregular rhythms in myocardium electrical oscillations are anticipated by cardiac alternans, are supported by nonlinearities, tissue heterogeneity, and anisotropy, and are further shaped by the mechanical and thermal state of the tissue. In this context, a comprehensive understanding of the appearance and development of impaired rhythms, starting from the underlying spatiotemporal dynamics, is required to prevent cardiac failure. In this contribution, we discuss a novel correlation analysis of cardiac activation maps accounting for thermal feedback, showing its application on canine ventricular tissues monitored via optical mapping. Specifically, we define a characteristic length able to describe the emergent synchronization of the tissue and analyze its variations at alternans onset and during their development at different temperatures. Computed results show that the characteristic length is significantly lower in the alternans regime compared to physiological rhythms. Also, we further show that thermal-induced changes in the underlying dynamic result in corresponding variations of the characteristic length.

15 min. break.

Invited Talk DY 13.4 Thu 14:45 H2

Cardiac repolarization dynamics and arrhythmias in healthy and diseased hearts — •Esther Pueyo — University of Zaragoza, Zaragoza, Spain

The electrical activity of the heart is the result of a set of complex nonlinear biophysical and biochemical processes occurring at different scales within the cardiac tissue. The variability arising from these processes translates into variability at the cell, tissue, organ and whole-body levels. The importance of investigating variability in cardiac electrical activity, in general, and in cardiac repolarization (i.e. the return of cells to their resting state after electrical activation), in particular, has been well documented, having shown value for diagnosis, monitoring and treatment of cardiac diseases.

In this talk, I will present studies combining computational, experimental and clinical methods to investigate temporal and spatial variability in cardiac repolarization. I will show the role of stochasticity in contributing to this variability in health and diseased hearts. The link between enhanced repolarization variability and pro-arrhythmia will be described, with emphasis on the role of the autonomic nervous system as a modulator of this link.

DY 13.5 Thu 15:15 H2

Using small perturbations and machine learning for the control of spiral wave chaos — •Thomas Lilienkamp — Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany

The dynamics during life threatening cardiac arrhythmias like ventricular fibrillation is governed by chaotic spiral/scroll wave dynamics. In ex-vivo experiments and numerical simulations, a phenomenon called self-termination can be observed frequently, where the chaotic dynamics terminates by itself without any interaction. We demonstrate what implications this observation has on the structure of the state space, and how this structure can be exploited for an efficient control of the dynamics via small but finite perturbations (localized in space and time). We also discuss, how machine learning algorithms can be used for the control of such systems.

DY 13.6 Thu 15:30 H2

A simulation study of the effects of optogenetics on the human cardiac pacemaker: Prospects of Opto-ATP control. — Afnan Nabizath Mohamed Nazer[1], Sayedeh Hussaini[2,3], Raul A. Quinonez Uribe[2], Stefan Luther[2,3], and •Rupamanjari Majumder[1,2] — [1]University Medical Center Göttingen, 37075 Göttingen, Germany — [2]Max Planck Institute for Dynamics and Self-Organization, Goettingen, Germany — [3]Institute for the Dynamics of Complex Systems, Goettingen University, Goettingen, Germany

High-frequency electric spiral and scroll waves often occur in the heart during lethal cardiac arrhythmias. Treatment of such arrhythmias necessitates removal of these waves. Currently, the most effective approach to eliminating these waves is defibrillation, which involves delivering high-voltage shocks to the heart. However, the technique is accompanied by numerous negative side effects that make it suboptimal.

Optimizing defibrillation primarily requires reducing defibrillation energy. To this end, the approach that works best for tachycardic arrhythmias is anti-tachycardia pacing (ATP). ATP relies on the external application of a series of low-energy, high-frequency electrical pulses that stimulate the heart faster than the arrhythmia. A biological evolution of this approach would be to replace the external energy source with the heart's own pacemaker. But such a step would require

deeper understanding of pacemaker function. Recently, optogenetics has emerged as a powerful tool in cardiac research. Using optogenetic simulations, I explore the possibility to realise ATP in human hearts.

Invited Talk DY 13.7 Thu 15:45 H2

Dynamics of paroxysmal tachycardias — •Gil Bub — McGill University, Montreal, Canada

Reentrant cardiac arrhythmias can start and stop spontaneously, giving rise to paroxysmal bursting rhythms. Experiments and simulations suggest that the dynamics of these paroxysmal reentrant waves may be natural consequences of structural heterogeneity, action potential restitution, and tissue fatigue. Recent experimental studies show that reentrant wave termination is linked to alternans, the beat-to-beat variation in action potential duration and velocity. The impact of alternans on termination was also confirmed using simulations that include restitution curve dynamics. Initiation of these waves, however, is less well understood. Current challenges include the development of imaging technologies that can observe rare spontaneous initiation events in multiple samples to gain mechanistic insights.