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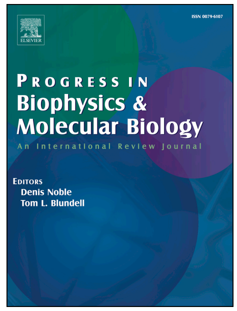

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Olga Solovyova, Leonid B. Katsnelson, Peter Kohl, Alexander V. Panfilov, Andrey K. Tsaturyan, Pavel B. Tsyvian

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MECHANO-ELECTRIC HETEROGENEITY OF THE MYOCARDIUM AS A PARADIGM OF ITS FUNCTION

Solovyova Olga, [1,2] o.solovyova@iip.uran.ru, 1) Institute of Immunology and Physiology, Ural Branch of the Russian Academy of Sciences, Ekaterinburg, Russia, 2) Ural Federal University, Ekaterinburg, Russia;
Katsnelson Leonid B.,[1,2] leonidkatsnelson51@gmail.com 1) Institute of Immunology and Physiology, Ural Branch of the Russian Academy of Sciences, Ekaterinburg, Russia, 2) Ural Federal University, Ekaterinburg, Russia;
Kohl Peter,[3,4] kohl@imperial.ac.uk 3) Research Centre for Cardiovascular Medicine, University of Freiburg, Germany, 4) National Heart and Lung Institute, Imperial College of London, UK;
Panfilov Alexander V.,[5] Alexander.Panfilov@UGent.be 5) Department of Physics and Astronomy, Ghent University, Ghent, Belgium;
Tsaturyan Andrey K.,[6] andrey.tsaturyan@gmail.com 6) Institute of Mechanics of Moscow State University, Russia;
Tsyvian Pavel B.[7] pavel.tsyvian@gmail.com 7) Ural State Medical University, Ekaterinburg, Russia

In memory of Professor Vladimir Semionovich Markhasin, 23/04/1941-11/04/2015

"…So we have to make guesses in order to give any utility at all to science. In order to avoid simply describing experiments that have been done, we have to propose laws beyond their observed range. "
("Messenger Lectures", Richard Phillips Feynman, 1967)

Abstract

Myocardial heterogeneity is well appreciated and widely documented, from sub-cellular to organ levels. This paper reviews significant achievements of the group, led by Professor Vladimir S. Markhasin, Russia, who was one of the pioneers in studying and interpreting the relevance of cardiac functional heterogeneity.

Keywords

Cardiomyocyte, myocardial tissue, heart, gradients in the cellular electrical and mechanical properties, myocardial heterogeneity, muscle duplex, slow force response, cardiac modeling, wet and dry experiment

Introduction: the Myocardial Heterogeneity Challenge

Myocardial heterogeneity reveals itself at different spatial scales, ranging from the molecular to the organ level. Cardiac anatomy and histo-architecture are extremely complex, allowing the heart to effectively function as a pump. The complex geometry of myocardial tissue is associated with heterogeneity in regional stress and strain distributions. Differences in coronary vasculature and energy demand give rise to heterogeneity in regional metabolic conditions. Locally prevailing cell orientation (generally called 'fibre orientation') and organization into mechanically reinforced layers ('sheetlets') underlie significant anisotropy in electrical and mechanical properties of the tissue. In addition, there is spatio-temporal heterogeneity in electrical activation of different cardiac tissue regions, and non-homogeneity in active and passive deformation of tissue within the four cardiac chambers.

In the 1920s, Carl Wiggers was the first to focus on regional features of left ventricular (LV) wall motion during the contractile cycle. He found that the iso*volumic* phase of ventricular contraction is not 'iso*metric*'. In particular, he observed that just before the onset of ejection, apical myocardium contracts, stretching basal myocardium that is activated later. He called this the 'entrant phase' of contraction and suggested that it may increase mechanical efficiency (Wiggers, 1927). Current experimental techniques have reconfirmed and characterized in more detail, the heterogeneity in spatio-temporal patterns of mechanical activation in different layers and regions of the LV wall (Ashikaga et al., 2007; Bogaert and Rademakers, 2001; Sengupta et al., 2006).

A corner-stone paper, published by Arnold and Phyllis Katz, summed up the key concept (and apparent inherent contradiction) of modern myocardial heterogeneity research, in highlighting the emergence of "Homogeneity out of