MECHANO-ELECTRIC FEEDBACK AND INITIATION OF CARDIAC ARRHYTHMIAS.

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ABSTRACT. The heart beat is controlled by electrical waves of excitation which propagate through the heart and initiate cardiac contraction. Contraction of cardiac tissue also affects the process of wave propagation resulting in a complex global feedback phenomenon known as mechano-electrical feedback. Mechano-electrical feedback has been studied in electrophysiology for well over a century and may have both pro-arrhythmic and arrhythmogenic consequences. Reently we have developed an approach to model the phenomenon of mechano-electrical feedback as coupled reaction-diffusion-mechanics system, which combines the parabolic reactiondiffusion equations with the elliptic equations of finite elasticity[1,2]. For electrophysiological tissue properties we use models of cardiac tissue either low dimensional of the FitzHugh Nagumo type, or detailed ionic model for human ventricular cells developed in our group. We couple our models with the nonlinear stress equilibrium equations that govern tissue mechanics. For representation of mechanics we either use a finite element approach [1], or a discrete framework which employs a mass-lattice model, that undergoes finite deformations [4].

We report on studies of several mechanisms which may underly formation of spiral waves in cardiac tissue due to the phenomenon of the mechano-electric feedback:

- (1) In certain cases, mechano-electric feedback can induce breakup of a single spiral wave into complex fibrillatory patterns. We discuss the mechanism of this process based on the accommodation phenomenon. We also show that this effect is present in low dimensional and ionic molds of cardiac tissue and also in simple geometries and in anatomical model of the heart [2,3].
- (2) We find a new mechanism of spiral wave initiation in the contracting excitable medium [5]. In particular, we show that deformation alters the "classical vulnerable zone," and forms a new vulnerable zone at longer coupling intervals. This mechanically caused vulnerable zone results in a new mechanism of spiral wave initiation, where unidirectional conduction block and rotation directions of the consequently initiated spiral waves are opposite compared to the mechanism of spiral wave initiation due to the "classical vulnerable zone."
- (3) We also study and classify mechanisms of spiral wave initiation in excitable tissue with heterogeneity in passive and in active mechanical properties [6]. We find that selfsustaining spiral wave activity emerges for a wide range of mechanical parameters of the inhomogeneity via five mechanisms. We classify these mechanisms, relate them to parameters of the inhomogeneity, and discuss how these results can be applied to understand the onset of cardiac arrhythmias due to regional mechanical heterogeneity.

Keywords: cardiac dynamics, continuum mechanics, spiral waves, cardiac arrhythmias

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References

- [1] M.P. Nash, and A.V. Panfilov. Electromechanical model of excitable tissue to study re-entrant cardiac arrhythmias. *Progress in Biophysics and Molecular Biology*, 85:501-522,2004
- [2] A.V. Panfilov, and R.H. Keldermann, and M.P. Nash. Drift and breakup of spiral waves in reaction-diffusionmechanics systems. Proc. Natl. Acad. Sci. USA,104:7922-7926,2007
- [3] R.H. Keldermann, and M.P. Nash, and H. Gelderblom, and V.Y. Wang, and A.V. Panfilov. Electromechanical wavebreak in a model of the human left ventricle. Am J Physiol., Heart Circ Physiol, 299:H134-143, 2010
- [4] L.D. Weise, and A.V. Panfilov. New mechanism of spiral wave initiation in a reaction-diffusion-mechanics system PLoS One,6(11):e27264/1- e27264/9,2011

[5] L.D. Weise, and A.V. Panfilov. Emergence of spiral wave activity in a mechanically heterogeneous reactiondiffusion-mechanics system. *Phys Rev Lett.*, 108:228104/1-228104/5, 2012

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