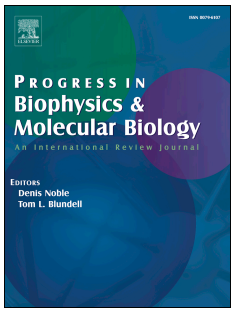
Accepted Manuscript



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PII: S0079-6107(17)30047-0

DOI: 10.1016/j.pbiomolbio.2017.08.008

Reference: JPBM 1253

To appear in: *Progress in Biophysics and Molecular Biology*

Received Date: 22 February 2017

Revised Date: 12 August 2017

Accepted Date: 18 August 2017

Please cite this article as: Timmermann, V., Dejgaard, L.A., Haugaa, K.H., Edwards, A.G., Sundnes, J., McCulloch, A.D., Wall, S.T., An integrative appraisal of mechano-electric feedback mechanisms in the heart, *Progress in Biophysics and Molecular Biology* (2017), doi: 10.1016/j.pbiomolbio.2017.08.008.

An Integrative Appraisal of Mechano-Electric Feedback Mechanisms in the Heart

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Abstract

Mechanically-induced alterations in cardiac electrophysiology are referred to as mechano-electric feedback (MEF), and play an important role in electrical regulation of cardiac performance. The influence of mechanical stress and strain on electrophysiology has been investigated at all levels, however the role of MEF in arrhythmia remains poorly understood. During the normal contraction of the heart, mechano-sensitive processes are an implicit component of cardiac activity. Under abnormal mechanical events, stretch-activated mechanisms may contribute to local or global changes in electrophysiology (EP). While such mechanisms have been hypothesised to be involved in mechanically-initiated arrhythmias, the details of these mechanisms and their importance remain elusive.

We assess the theoretical role of stretch mechanisms using coupled models of cellular electrophysiology and sarcomere contraction dynamics. Using models of single ventricular myocytes, we first investigated the potential MEF contributions of stretch-activated currents (SAC), and stretch-induced myofilament calcium release, to test how strain and fibrosis may alter cellular electrophysiology. For all models investigated, SACs were alone not sufficient to create a pro-arrhythmic perturbation of the action potential with stretch. However,

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