

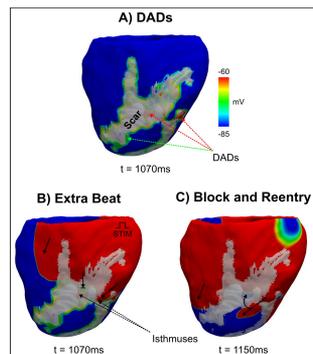
Calcium-mediated Delayed Afterdepolarizations form a Substrate for Conduction Block in the Post-infarction Heart

Fernando O. Campos, Yohannes Shiferaw, John Whitaker, Mark O'Neill, Reza Razavi, Gernot Plank, Martin J. Bishop

School of Biomedical Engineering and Imaging Sciences, King's College London
London, United Kingdom

Background: delayed afterdepolarizations (DADs) due to spontaneous calcium release (SCR) events have been implicated in a variety of arrhythmias. While the role of DADs in forming ectopic beats has been characterized, the arrhythmogenic potential of subthreshold DADs in the infarcted border zone (BZ) remains unknown. **Objective:** to use computational modelling to investigate whether subthreshold DADs may form a substrate for conduction block and reentry in the infarcted BZ. **Methods:** a computational model of the porcine post-infarction heart was constructed based on MRI data. The heart model was pre-paced (1 Hz) at the base followed by a 1500 ms-pacing pause to see whether DADs would emerge. DADs in the BZ were evoked according to a phenomenological model of SCR events. An extra beat with different coupling intervals (CIs) was then applied. Sodium channel loss-of-function due to a 5 mV negative-shift in the steady-state channel inactivation was also simulated to assess its arrhythmogenic potential when combined with DADs.

Results: Figure A shows DADs arising in the BZ 1070 ms after the last paced beat. Next, extra beats with different CIs were simulated. In the control electrophysiological setup, simulations with extra beats did not result in block. However, when combined with a 5 mV-shift in sodium channel inactivation, block and reentry at the larger transmural isthmus were detected for an extra beat with CI = 925 ms (see Figure B-C). **Conclusions:** under physiological conditions, subthreshold DADs are unlikely to provide a substrate for block. However, under conditions of decreased excitability, they can cause conduction block and reentry in the infarcted region.



DAD-mediated conduction block and reentry.