Spatially Heterogeneous Ionic Remodelling Promotes Wavefront Instability in Simulated Atrial Tissue

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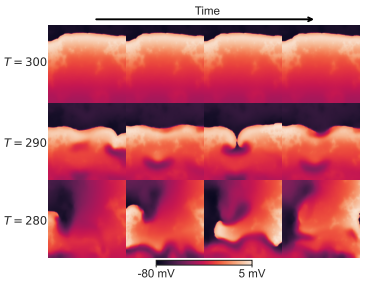
Electrical remodelling is a hallmark of atrial fibrillation (AF), yet it is typically modelled as a uniform global change in ionic parameters. Given the inherent heterogeneity of cardiac tissue, remodelling likely develops in a spatially non-uniform manner. This study investigates how the spatial distribution of ionic remodelling affects wavefront stability and the initiation of fibrillatory behaviour.

We developed a 2D computational model of atrial tissue using the Grandi model of atrial action potential. Cells were assigned either "normal" or "remodelled" (based on chronic AF parameters) states. To simulate different structural regimes of remodelling, we distributed these states using a 2D Ising model, varying the coupling strength (K) relative to the critical point (K_c): $K < K_c$ (small interwoven clusters), $K = K_c$ (scale-free regions), and $K > K_c$ (sparse emerging remodelling). Tissue was paced at cycle lengths (T) from 260-300 ms. Wavefront stability was quantified using a cycle-to-cycle distance metric.



AP snapshots over successive beats for $K = K_c$.

At high pacing frequencies ($T \leq 290$ ms), even sparse remodelling ($K = 1.1K_c$) was sufficient to destabilise wavefronts, leading to spatiotemporally chaotic propagation. Sudden rate increases triggered long chaotic transients (up to 1000 beats) as intracellular sodium ($[\mathrm{Na}]_i$) slowly adapted to the new rate. At the critical point ($K = K_c$), we observed a qualitative progression from laminar wavefronts ($T = 300$ ms) to coherent fronts with small wave breaks ($T = 290$ ms), and finally to full turbulence induced by large wave breaks ($T = 280$ ms).

Our results suggest that the non-uniform development of ionic remodelling could create a substrate for fibrillatory behaviour by promoting wave breakup, thereby promoting further remodelling. This provides a mechanistic link to the "AF begets AF" paradigm, wherein AF promotes conditions that favour its own maintenance and progression.