A Combinatorial Algorithm to Detect Higher-Order Dynamics in Cardiac Signals

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Introduction: Repolarization alternans is one of the mainstays of theoretical cardiac electrophysiology and provides a link between cellular dynamics and fibrillation. Action potential duration (APD) alternans is the beat-to-beat (period-2) oscillation in the APD and is the simplest quantifier of repolarization dynamics. However, cardiac dynamics is complex and does not stop at period-2. In particular, excitation-contraction coupling can generate higher-order periodicities that are precursors to chaotic rhythms. Detection of APD alternans is relatively easy. It is even applicable to clinical ECG (e.g., T-wave Microvolt Alternans). However, higher-order dynamics tends to be transient, of low amplitude, and spatially heterogeneous; hence, the standard algorithms used for period-2 alternans fail to detect them. As a result, higher-order periods have been experimentally elusive and only detected in a few cases. We present a combinatorial algorithm to detect higher-order periodicities in experimental and clinical cardiac signals.
Methods: The key idea of the algorithm is to set up a weighted-directed graph, where the vertices correspond to the action potentials (beats) in the input sequence, and the links are assigned according to the distance metric function between the beats (see Figure). The shortest path between the first and last beats in the graph determines the optimal periodicity of each beat.
Results: We applied the algorithm to optical-mapping signals recorded using voltage-sensitive fluorescent dyes from ex-vivo swine (n=4) and human (n=6; from heart transplantation recipients) hearts. We detected and visualized stable islands of period-4 and areas of transient period-5 and period-6. Furthermore, the detection of period-5 and period-6 strongly suggests the existence of chaotic regimes in the heart.
Conclusion: Our graph-based algorithm is a valuable tool to probe the complex dynamics of cardiac tissue by looking beyond classic alternans, especially at fast rates and before the transition to chaotic fibrillation.