Consistent Analysis of Action Potential Parameters for Various Types of Cardiomyocytes

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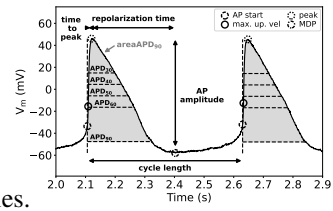
Introduction: Analyzing cardiac action potential (AP) properties has been a crucial tool in arrhythmia research and drug development for decades. In recent years, human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) have become an emerging field in cardiovascular research. The spontaneous electrical activity of hiPSC-CMs allows to simultaneously investigate parameters from both individual APs and the collective recording of multiple APs such as beating frequency or arrhythmogenicity *in vitro*. However, due to the diverse morphologies of hiPSC-CM APs, manual extraction of standard AP parameters is time-consuming and depends on the operator's subjective judgment which hampers reproducible, quantitative comparisons between various types of CMs. Here, we introduce a consistent, fast, reproducible and operator-independent algorithm, which extracts quantitative AP parameters from recordings of various CM types.

Methods: Given the variability and noise in hiPSC-CM AP recordings, classical mathematical tools or thresholding cannot be directly applied. Instead, APs are identified as sequences characterized by a potential rise exceeding 20 mV within a time frame of 25 ms. Markers for the start of an AP, maximum upstroke velocity, peak potential and maximum diastolic potential are derived automatically (for further details, see https://gitlab.kit.edu/kit/ibt-public/analysis-of-ap-parameters). The analyzed AP parameters are complemented by the AP duration (APD), AP amplitude, cycle length, frequency, area of APD_{90} and APD corrected by Bazett's formula for varying beating frequencies.



Results: The algorithm was tested on 1607 AP recordings from hiPSC-CMs, isolated native CMs, HL-1 cells and computational electrophysiological simulations. In absence of a ground truth, our algorithm was validated against manual expert inspection. The markers placed by the algorithm were considered correct in over 99% of cases, computed in 0.4 s for a 60 s AP recording.

Conclusion: This algorithm enables standardized, reproducible and operator-independent high-throughput analyses of diverse AP recordings, facilitating quantitative comparisons of electrophysiological properties in various CM types.