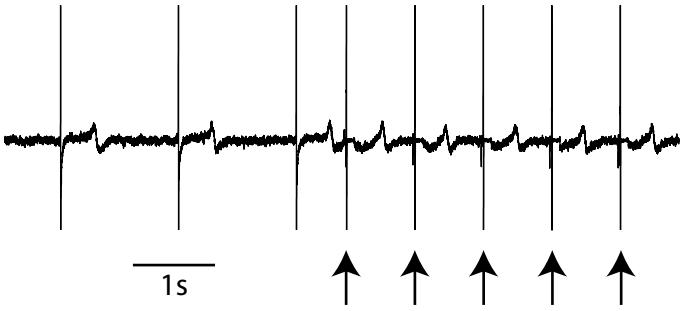
Pacing with iCell® Cardiomyocytes

Pacing is now possible with the Maestro™

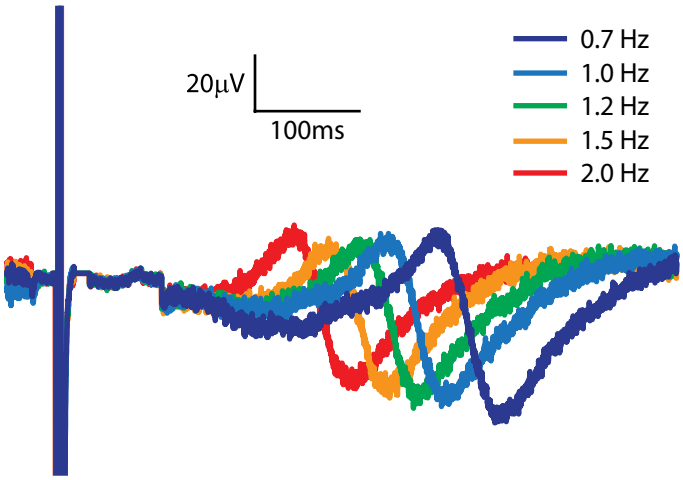
Axion's multiwell MEA platform rapidly evaluates the cardiac safety risk of compounds using stem cell-derived cardiomyocytes. Electrical parameters such as repolarization timing and spontaneous action potential rate are interdependent, complicating the interpretation of drug effects. Experimentally controlling electrical activity through pacing removes this interdependence, increases the accuracy of the measured endpoints, and improves the information content of the assay.

The Advantage

- Specify the beat rate of stem cell-derived cardiomyocyte cultures
- Establish well-to-well consistency for more reliable results
- Perform accurate rate corrections for spontaneously beating cultures
- Differentiate between primary and secondary drug effects
- Directly assess pro-arrhythmic indicators, such as reverse use-dependence of repolarization timing
- Utilize quiescent experimental preparations



Pacing stimuli (arrows) control beat rate.

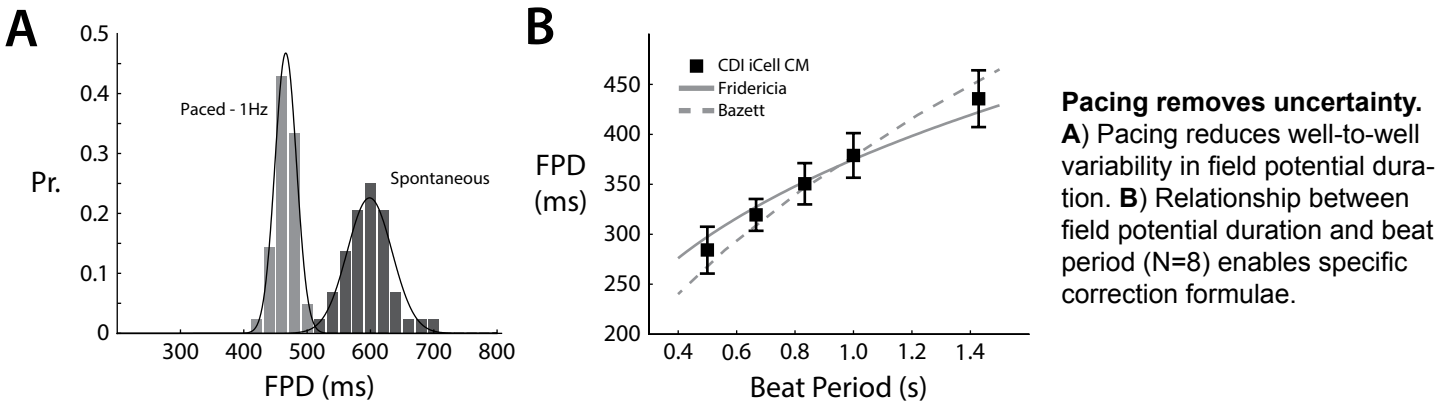


Field potential duration changes with pacing rate.

Take control of your experiment!

First, improve the quality and accuracy of your results...

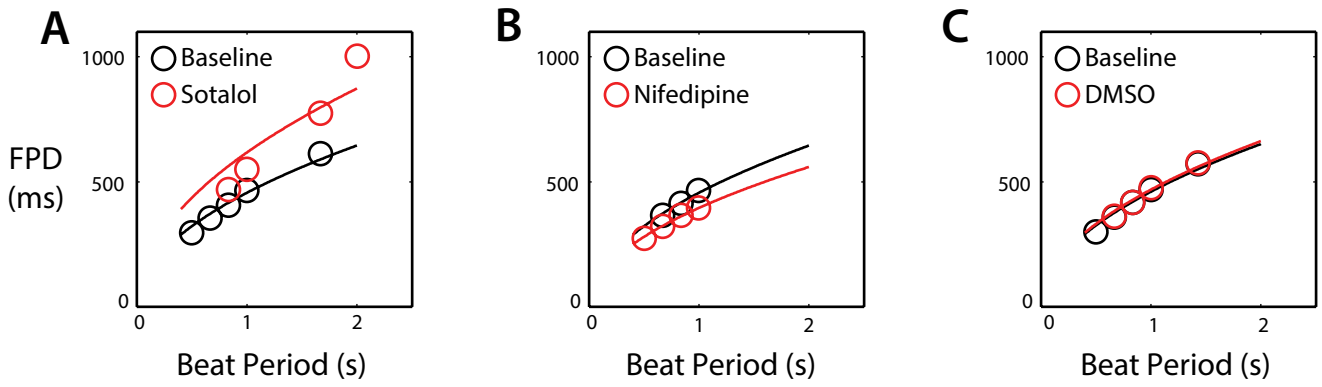
Field potential duration is directly related to the frequency of the cardiac action potentials (beat rate), such that pharmacological manipulations often change both endpoints. The interdependence of these processes obscures the mechanism of change in spontaneously beating cardiomyocytes. Although clinical correction factors reconcile the QT interval and heart rate measured in the ECG, the relevance of these correction factors to *in vitro* preparations has not been established. Electrical pacing of stem cell-derived cardiomyocytes controls the beat rate across wells, increasing the reliability of the measurements while also separating intertwined physiology.



Pacing removes uncertainty. **A**) Pacing reduces well-to-well variability in field potential duration. **B**) Relationship between field potential duration and beat period (N=8) enables specific correction formulae.

Then add depth to your assay

Many compounds exhibit use-dependent effects. Reverse use-dependence occurs when a compound produces a greater effect at slower beat rates. Reverse use-dependence of repolarization timing is an important pro-arrhythmic indicator, as it will manifest under bradycardiac conditions. Pacing is required to directly assess reverse use-dependence by measuring the relationship between beat rate and field potential duration. Thus, electrical pacing with human cardiomyocytes significantly increases the information content of the experiment to aid pro-arrhythmic prediction.



Pacing uncovers reverse use-dependence.
Relationship between field potential duration and beat period before and after dosing with **A**) sotalol, **B**) nifedipine, and **C**) DMSO in paced iCell cultures. Sotalol displays reverse use-dependent prolongation of repolarization.

For more information:

Axion BioSystems, Inc
1819 Peachtree Road NE
Suite 350
Atlanta, GA 30309

info@axionbio.com
www.axionbiosystems.com