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Controlling Excitable Waves in Cultured Cardio Myocyte

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Motivation

Rotating waves are believed to be responsible for many dangerous cardiac tachyarrhythmias, which are precursors of ventricular fibrillation, causing sudden death. Thus, the controlling of excitable waves in cardiomyocyte culture is an auspicious way to understand the physics of rotating waves in cardiac tissue. In real heart tissue free spiral waves rarely occur because they easily become bound to natural inhomogeneities such as blood vessels. Here we report mutual transformations of free and bound spiral waves (their pinning and unpinning) as well as induced drift of free rotating waves in cardiac tissue.

Methods

Cardiac cells were dissociated from ventricles of 1-day-old rats by using collagenase[1], and plated on $22mm$ in diameter sized cover-slips. After 3 days of incubation in culture medium the cells grow to a full developed network and excitation waves are observable by monitoring calcium transient. The excitation waves were visualized with the aid of calcium sensitive fluorescent dye (fluo-4) by use of a fluorescent microscope and an EM-CCD camera. Spontaneous activity in the cardiomyocyte tissue leads to wave speeds up to $10cms^{-1}$. In order to decrease the speed to a suitable degree we applied heptanol. Application of heptanol also leads to spontaneous origination of free rotating waves with the frequencies of rotation in the order of 1Hz. These rotating waves have slightly different periods each other, so that the ones with lower period force the ones with higher period to drift away. Far-field and point electrode stimulations with applied $1.8V/cm$ and $6V$, respectively, were used for wave initiation. Point stimulation produced waves in the immediate vicinity of the electrode tip; far field stimulation resulted in wave origination at the extended sites usually located near the edge of the coverslip.

Results and Discussion

Figure 1 exemplified the drift of the spiral tip caused by far field stimulation. When paced wave collides with the tip, local refractoriness prevents the spiral from curling into the same area causing a displacement of the wavebreak. Subsequent paced waves continue to displace the tip,

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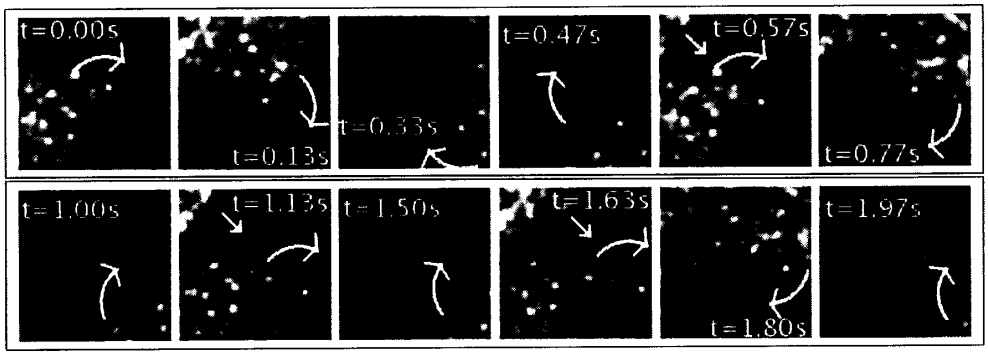

Figure 1: Spiral drift induced by far-field stimulation. Field of view: 2x2 mm

thus causing it to drift[2]. This generic mechanism is also observable in Belousov-Zhabotinsky reactions [3]. Pinning of free rotational waves to obstacles was performed by removing cardiac tissue in the area at the tip of the spiral. Through this method we produced pinned spirals with different rotating frequencies caused by the different obstacle radii. We successfully unpinned spiral waves from obstacles via mono-polar point electrode and far field stimulation. One example of unpinning by stimulation from point electrode is shown in Figure 2. The far field stimulation leads to origination of excited sites as a 'Secondary Source'[4] adjacent to the obstacle, which unpins rotating spiral. Unpinning via point electrode is caused by 'direct' pacing nearby the obstacle. These results indicate that such methods are useful for the elimination of pinned rotating waves. Further studies will give auspicious results, and will lead to deeper understanding of termination of rotating waves in heart tissue.

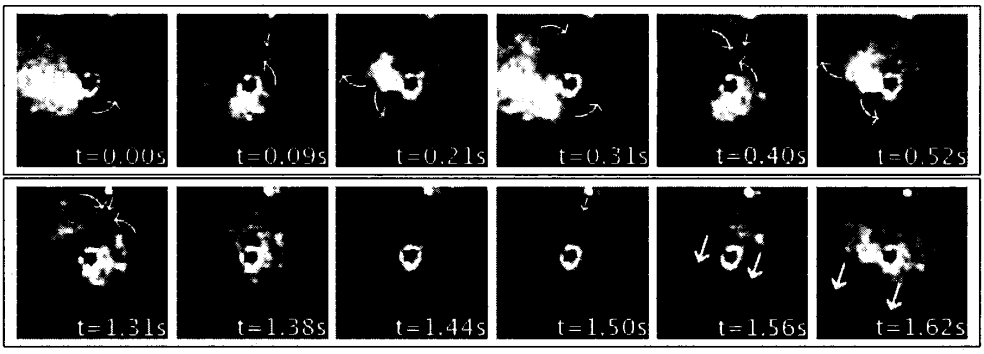

Figure 2: Unpinning of a rotating wave from an obstacle via point stimulation. The first pacing wave creates one more free spiral besides the obstacle via colliding with the rotating wave. The annihilation of pacing wave, free spiral and rotating wave leads to unpinning ($t \approx 1.3s$). The pacing waves can propagate free from the obstacle free. Field of view: 4x4 mm

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