Non-Linear dynamics of beating cardiomyocytes

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Recent experiment by the group of Tzlil [1] have shown that nearby cardiac cells seeded ($\sim$ 100 micrometers apart) on an elastic gel, synchronize their beating phase and frequency even without direct contact. By introducing an inert probe that induced periodic elastic deformations in the substrate, the experiments showed that one can pace beating cardiac cells that are relatively far from the probe. The time required to pace the cell was on the order of $\sim$ 15 min, and the cell maintained the new beating frequency for as long as $\sim$ 1 hr after the probe was removed. These long time scales are in complete contrast to the very short time scales ($\sim$ 1 sec) that characterize relaxation after electrical stimulation is removed [1].

We predict and compare with experiment [1] the dynamical states and persistence time of a beating cardiomyocyte, using a non-linear oscillator model motivated by acto-myosin dynamical contractility [2, 3]. This model was recently applied to hair cells in the ear, where the effect of varying the amplitude of an oscillating signal (sound wave) on these cells was examined. It was shown that the non-linear mechanical response is crucial in for the excitation of hair bundles due to specific tone frequencies [4, 5, 6].

Our findings relate to the coupled beating of two nearby cells, or a cell paced by a nearby mechanical probe. We begin in Sec. **??** with a simple, analytical treatment of the deterministic dynamics that predicts spontaneous, entrained beating (with the probe frequency) and "bursting" (short periods of entrainment to the probe separated by quiescence) of paced cells, and predict how these depend on the probe amplitude and frequency, in agreement with experiment [1]. We further consider the interesting effects of small noise on the non-linear oscillator model of the beating cell [7], and show how it affects the coherence of beating. Finally, we predict the dependence of time required for a cell to transition from spontaneous to entrained beating once the probe is applied as well as its dependence on the probe amplitude. We account for the origin of the much longer time scale (minutes) required to entrain spontaneously beating cells by considering biological adaptation (which delays the response of the cell to the external signal).

References

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