Synchronization of Cell Cycle Oscillator by Multi-pulse Chemical Perturbations

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Oscillators underlie biological rhythms in various organisms and provide a timekeeping mechanism. Cell cycle oscillator, for example, controls the progression of cell cycle stage and drives cyclic reproduction in both prokaryotes and eukaryotes. The understanding of the underlying nonlinear regulatory network allows experimental design of external perturbations to interact and control cell cycle oscillation. We have previously demonstrated in experiment and in simulation that the cell cycle coherence of a model bacterium can be progressively tuned by the level of a histidine kinase. Here, we present our recent effort to synchronize the division of a population of bacterium cells by external pulsatile chemical perturbations. We were able to synchronize the cell population by phase-locking approach: the external oscillator (i.e. periodic perturbation) entrains the internal cell cycle oscillator which is in analogous to the phase-locking of circadian clock to external light/dark oscillator. We explored the ranges of frequencies for two external oscillators of different amplitudes where phase-locking occurred. To our surprise, non-periodic chemical perturbations could also cause synchronization of a cell population, suggesting a Markovian cell cycle oscillation dynamics.