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Stochastic Phase Oscillators and Circadian Bioluminescence Recordings

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Abstract

Cultured circadian oscillators from peripheral tissues were recently shown to be both cell autonomous and self-sustained. Therefore the dominant cause for amplitude reduction observed in bioluminescence recordings of cultured fibroblasts is desynchronization rather than the damping of individual oscillators. We propose a generic model for quantifying luminescence signals from biochemical oscillators, based on noisy phase oscillators. Our model incorporates three essential features of circadian clocks: the stability of the limit cycle, fluctuations, and inter-cellular coupling. The model is then used to analyze bioluminescence recording from immortalized and primary fibroblasts. Fits to population recordings allow to simultaneously estimate the stability of the limit cycle (or equivalently the stiffness of individual frequencies), the period dispersion, and the interaction strength between cells. Consistently with other work, coupling is found to be weak and insufficient to synchronize cells. Interestingly we find that frequency fluctuations remain correlated for longer than one clock cycle, which is confirmed from individual cell recordings. We discuss how to link the generic model with more microscopic models, which suggests mechanisms by which circadian oscillators resist fluctuations and maintain accurate timing in the periphery.