Synchronized Oscillations and Chaos in Coupled Genetic Repressilators

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Abstract Living organisms are complex, and are typically composed of many interacting subsystems. In order to understand the complex genetic networks present in the whole cell, it is of crucial importance to first understand the dynamic behavior of modular genetic circuits. Recently a few subsystems on the genetic level, namely, genetic repressilators or oscillators, and bi-stable gene circuits, have been constructed and manipulated. In the former case, while mathematical model predicts simple oscillations, it has been observed that period varies from one oscillation to another considerably. Realizing that laboratory biochemical experiments take place in space in a distributed way, we study coupled repressilators. Let the repressilator of Elowitz and Leibler [1] be described by the following set of 6 ordinary differential equations:

$$\frac{dm_i}{dt} = -m_i + \frac{\alpha}{1+p_j^n} + \alpha_0, \quad \frac{dp_i}{dt} = -\beta(p_i - m_i) \tag{1}$$

where p_i, $i = 1,2,3$ for lacI, tetR, cI, denote three repressor-protein concentrations, while m_i are their corresponding mRNA concentrations. The index j corresponding to $i = 1,2,3$ (for lacI, tetR, cI) is 3,1,2 (for cI, lacI, tetR), respectively. One type of coupled repressilators is obtained by modifying one equation in repressilator–1 by

$$\frac{dx_{m_3}}{dt} = -x_{m_3} + \frac{\alpha}{1+(x_{p_2}+\gamma y_{p_2})^n} + \alpha_0,$$

and the corresponding equation in repressilator–2 by

$$\frac{dy_{m_3}}{dt} = -y_{m_3} + \frac{\alpha}{1+(y_{p_2}+\gamma x_{p_2})^n} + \alpha_0,$$

where the parameter γ is the coupling strength. Several different types of coupling are considered, and similar results found. We find that synchronized oscillations may occur between nearly

Proceedings of the 2004 IEEE Computational Systems Bioinformatics Conference (CSB 2004)
0-7695-2194-0/04 $20.00 © 2004 IEEE

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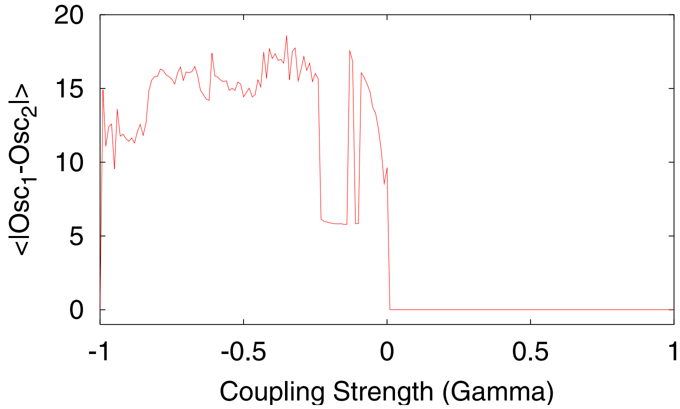

Figure 1: The time-averaged distance between the two coupled oscillators where $\text{Osc}_1 = \vec{x}$ and $\text{Osc}_2 = \vec{y}$. Total synchronization occurs when this quantity is zero.

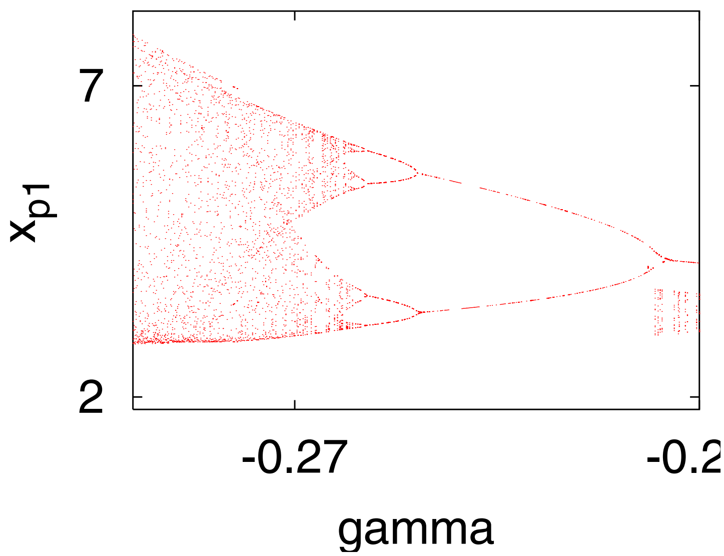

Figure 2: The bifurcation diagram showing a Poincare section composed of the values of x_{p_1}, where $x_{m_1} = x_{p_1}$. From right to left a period doubling bifurcation can clearly be seen.

matched oscillators. See Fig. 1. It is also found that chaos can occur via period doubling route. See Fig. 2. This work thus naturally explains why the periods of the repressilators observed in the experiments vary so considerably. It is further discussed that the feature of period doubling might have occurred experimentally.

Reference Elowitz, M. B. & Leibler, S. (2000) Nature 403, 335-338.

Proceedings of the 2004 IEEE Computational Systems Bioinformatics Conference (CSB 2004)
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