An algorithm for proving global entrainment and synchronization of biological systems

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INTRODUCTION

When an autonomous system is driven by an external periodic input, entrainment is often expected as an outcome, i.e. for all system solutions to align themselves with the external source. A typical example of this phenomenon in biology is that of endogenous circadian systems that adapt in period and phase to light.

Another important issue is to determine under what conditions multiple coupled biological oscillators align their solutions, i.e. they all synchronize onto some common asymptotic evolution. Synchronization is indeed a fundamental mechanism in biological networks; examples include networks of neurons in the circadian pacemaker and the insulin-secreting cells of pancreas.

Here, we derive a novel set of analytical conditions for analysing/constructing networks of genetic biological circuits that can be entrained by an exhogenous signal and/or synchronize.

METHODS AND RESULTS

Results are obtained using Contraction Theory, an extremely useful tool from the theory of nonlinear dynamical systems [1]. Specifically, we present here an algorithmic procedure to derive analytical conditions on the parameters/topology of the circuit of interest ensuring entrainment by a periodic system and/or synchronization (if the oscillators are coupled).

The use of the algorithm is then illustrated on two representative examples:

- tuning the parameters of a synthetic biological circuit in order to obtain synchronization [2];

- analyze the behavior of transcriptional modules, showing that they can be entrained to an external periodic input.

CONCLUSIONS

A new, completely general, algorithmic procedure is presented giving algebraic conditions guaranteeing convergence of systems trajectories towards each other. Easy-to-satisfy biological guidelines are proposed stemming from a rigorous mathematical derivation. The effects of noise and parameter mismatches are also investigated.

[1] On Contraction Analysis for Nonlinear systems, W. Lohmiller J. Slotine, Automatica, Vol. 34, pp 683-696

[2] How to synchronize biological clocks, G. Russo M. di Bernardo, Int. Journal of Computational Biology, Vol. 16, pp. 379-393