

Oral presentation

Noise characteristics of interlocked repressilators

Martin Hemberg* and Mauricio Barahona

Address: Department of Bioengineering, Imperial College London, Exhibition Road, London SW7 2AZ, UK

Email: Martin Hemberg* - martin.hemberg@imperial.ac.uk

* Corresponding author

from BioSysBio 2007: Systems Biology, Bioinformatics and Synthetic Biology
Manchester, UK. 11–13 January 2007

Published: 8 May 2007

BMC Systems Biology 2007, 1(Suppl 1):S7 doi:10.1186/1752-0509-1-S1-S7

This abstract is available from: <http://www.biomedcentral.com/1752-0509/1?issue=S1>

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Oscillators are important components of biological systems. Biochemical networks that exhibit oscillatory behavior are used at the molecular level for essential time-keeping in the cell. In many cases, these networks involve transcriptional circuits that are intrinsically noisy. In a seminal paper from 2000, Elowitz and Leibler presented the repressilator: a synthetic oscillator implemented in *E. coli* using three mutually repressive genes [1]. Through experiments, stochastic and deterministic simulations they showed that the system is indeed oscillatory but extremely noisy due to the low number of molecules involved in the reactions.

We use a recently developed extension of Gillespie's algorithm (DCFTP-SSA) [2], which guarantees sampling from the stationary distribution, to characterize the noise in the fully stochastic version of the repressilator. Furthermore, we develop a robust algorithm which allows us to fit the distribution of the period lengths and the amplitudes to a generalized Gamma distribution. Inspired by the structure of circadian oscillators found in natural systems, we construct simple extensions of this circuit by interlocking two or more repressilators. We find that the noise characteristics of the resulting circuits differ from the isolated one. This is an indication that simple modifications of the topology could be a useful strategy for tuning the characteristics of synthetic oscillators as opposed to modifying their parameters. Most importantly, we find that some of the proposed topologies exhibit reduced levels of noise for both the period and the amplitude.

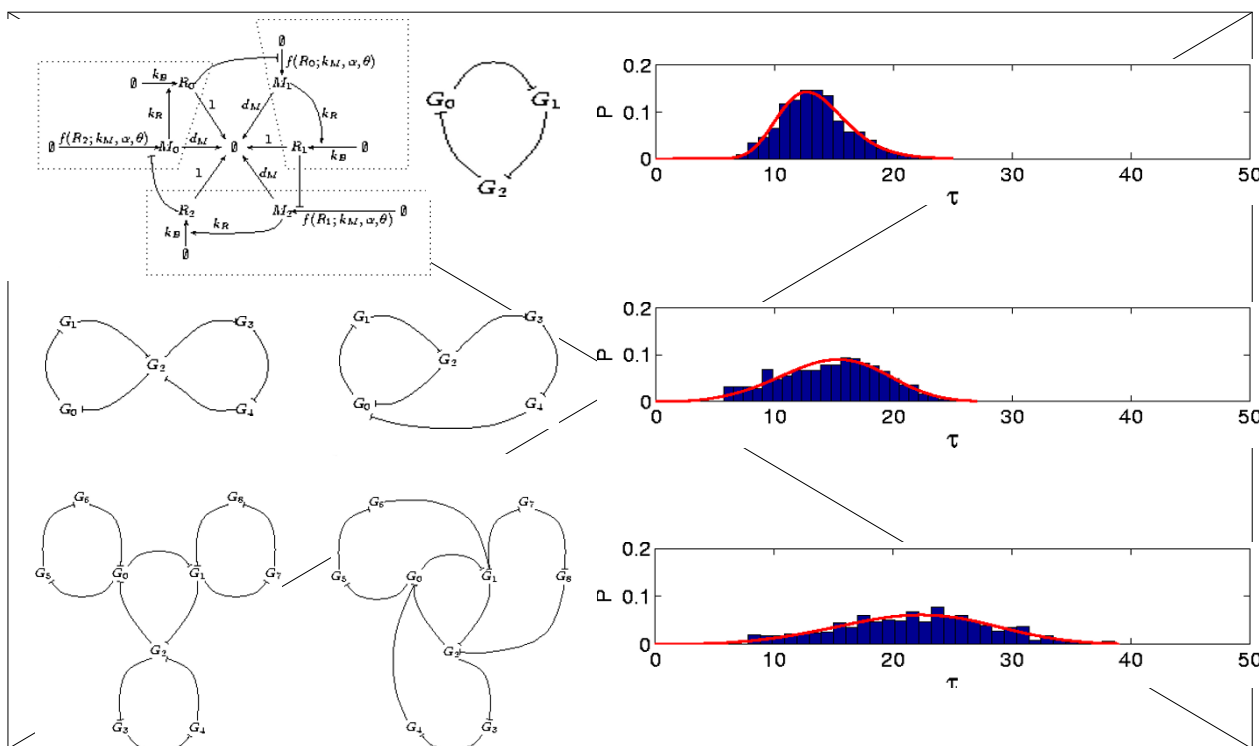


Figure 1

Top left: Original repressilator with three genes consisting of an mRNA and a protein for each gene. Top center: Reduced notation of the repressilator with only the genes and the inhibitory connections shown. Top right: Histogram of the period with a fitted generalized Gamma distribution. Second row: Two different ways of interlocking two repressilators. The histogram of periods corresponds to the circuit in the middle column and has a higher mean but approximately the same coefficient of variation as above. Bottom row: Two symmetric circuits derived from the interlocking of four repressilators. The histogram of the periods for the circuit in the middle has a mean which is almost double that of the top histogram but the same coefficient of variation.

References

1. Elowitz MB, Leibler S: **A synthetic oscillatory network of transcriptional regulators.** *Nature* 2000, **403**:335-339.
2. Hemberg M, Barahona M: **Perfect sampling of the chemical master equation for gene regulatory networks.** *arXiv.org:q-bio/0610050*.

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