Noise propagation in the detailed model of glnALG operon in *E. coli*

Frank J. Bruggeman[1,2] and Maciej Dobrzyński[1,3]

***Short Abstract* — We analyze stochastic effects in a detailed kinetic model of the glnALG operon in *E. coli* under the control of the two-component signaling network consisting of the sensor NRI and the response regulator NRII. We investigate a set of simple core models to address the question whether noise (variance/mean^2) in the number of transcripts produced from this operon depends on signaling, transcription initiation, or elongation.**

***Keywords* — noise, detailed kinetic model, transcription, signaling.**

I. Introduction

PROCESSES within molecular networks invariably generate noise in copy numbers of molecules. The coupling of these processes may act as mechanisms attenuating and amplifying noise (Hooshangi et al. 2005). One mechanism by which biochemical networks can protect themselves against noise is large copy numbers of their reactants. Surprisingly, key phenomena for cellular adaptation, i.e. signaling and gene expression, rely on mechanisms with low copy numbers (10 to 100 molecules). Is this so because noise does not matter so much? or because it is beneficial to the fitness of population? or because noise amplification is actually a very unlikely phenomenon?

II. Results

The conditions for the steady-state noise in molecular number, say for molecule y, to depend on the noise in the molecule number of molecule x, can be derived using linear noise approximation. Consider the following macroscopic rate equations: $d\langle n_y\rangle/dt=f(\langle n_x\rangle,\langle n_y\rangle)$, $d\langle n_x\rangle/dt=g(\langle n_x\rangle)$. Whether the noise in y will depend on the noise in x is determined by (Paulsson 2005): (i) the extent of noise in x, (ii) the sensitivity of the steady state of y for x, and (iii) the extent of time scale separation between processes in which x and y are involved. But what does this now imply for the induction of transcription by a signaling network in a real case? We address this issue by analyzing the stochasticity in a detailed kinetic model of the glnALG operon in *E. coli* under the control of the two-component signaling network consisting of the sensor NRI and the response regulator NRII (Ninfa et al. 2000).

To answer the question whether the noise in the number of transcripts produced from this operon depends on signaling, transcription initiation, and elongation we investigate a set of simple core models and compare them with the detailed model. We consider the consequence of mRNA length, the motion of RNA polymerase along DNA, statistics of open complex formation/degradation, and the level of signaling molecules for the noise in open complex formation and the steady-state level of transcripts.

References

[1] Hooshangi S, Thiberge S, Weiss R (2005) Ultrasensitivity and noise propagation in a synthetic transcriptional cascade. *PNAS* **102**, 3581-3586.

[2] Paulsson J (2005) Models of stochastic gene expression. *Physics of Life Reviews* **2**, 157-175.

[3] Ninfa AJ, et al. (2000) Integration of antagonistic signals in the regulation of nitrogen assimilation in Escherichia coli. *Curr Topics Cell Regul* **36**, 31-75.

[1]CWI (Center for Mathematics and Computer Science), Kruislaan 413, 1098 SJ Amsterdam, The Netherlands.

[2]Molecular Cell Physiology, Faculty of Earth and Life Sciences, Vrije Universiteit, De Boelelaan 1085, 1081 HV Amsterdam, The Netherlands.

[3]E-mail: m.dobrzynski@cwi.nl