The toggle switch in dividing cells

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***Short Abstract* — We analyze the stochastic toggle switch model in dividing bacterial cells. We show that the cell cycle length has a huge impact on the stability of epigenetic states. Lack of nutrients and suppression of the cell growth can decrease spontaneous switching rates even by two orders of magnitude.**

***Keywords* — stochastic simulations, non-equilibrium processes, dividing cells, bistability**

I. Motivation

Gene expression in bacterial cells is considered noisy. Randomness in molecules levels, which follows from small numbers of mRNA and protein molecules enables transitions between distinct epigenetic states. Additionally in bacteria the average protein life-time is typically longer than the cell cycle, which causes that the system is far from equilibrium. Therefore the analysis of the toggle switching rates should take into account cell divisions, and the cycle length.

II. Model

We analyzed a stochastic model of the bacterial genetic toggle switch in dividing cells. Processes of mRNA transcription, protein translation, dimerization and gene repression by protein dimer of the competing gene product are explicitly included in the model (Fig. 1). The cell growth and division times are determined by a house-keeping protein level (included in the model). The cell divides when this level doubles. Thus, the cell growth rate is governed by the house-keeping protein translation rate, which we assume to be a monotonous function of the nutrients level. We consider different cases of the cell division from the fully symmetric with molecules distributed equally between daughter cells to asymmetrically dividing cells with binomial distribution of molecules.

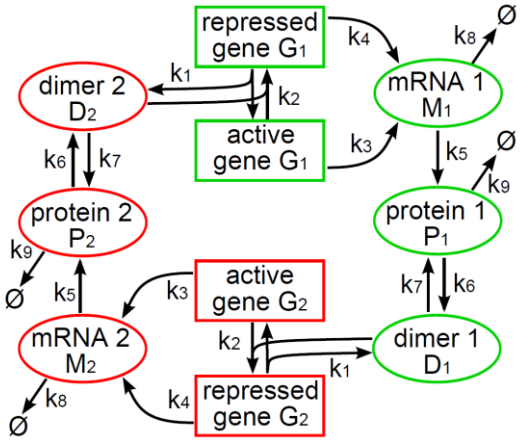

Figure 1. Schematic of the toggle switch model.

III. Results

We found that elongation of cell cycle decreases toggling rates in bacteria. Fast dividing cells, even when cell divisions are fully symmetric, switch about 40 times more often than the non-dividing and non-growing cells of constant volume equal of the volume of dividing cell just after division. Asymmetry (binomial distribution of molecules) of division further increases switching rates, but only less than two times. The switching rates dependence on the cell cycle length (1h to 10h) is shown in the Figure 2.

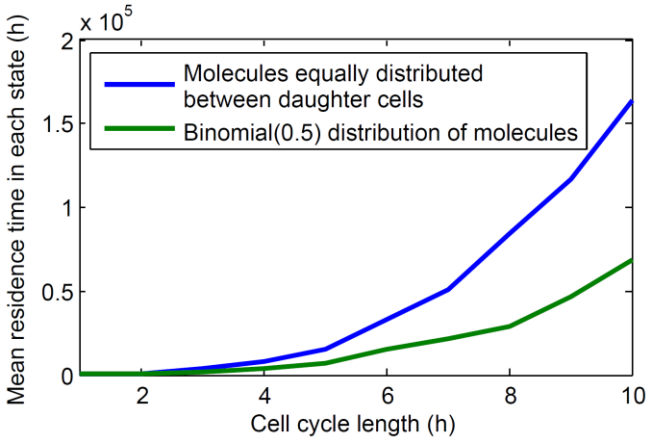

Figure 2. Mean waiting time for a switch as a function of the cell cycle length.

These results show that the cell cycle length and cell divisions have a huge effect on the stability of the epigenetic states of bacteria.

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