Intra-and intercellular fluctuations in Min protein dynamics decrease with cell age

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***Short Abstract* — Self-organization of proteins in space and time is of crucial importance for the functioning of cellular processes. Often, this organization takes place in the presence of strong random fluctuations due to the small number of molecules involved. We report on stochastic switching of the Min-protein distributions between the two cell-halves in short Escherichia coli cells. A simple computational model provides strong evidence that the macroscopic switching is rooted in microscopic noise on the molecular scale. In longer bacteria, the switching turns into regular oscillation required for positioning of the division plane. As the pattern becomes more regular, cell-to-cell variability also lessens.**

***Keyword* — Cell-to-Cell variation, Min proteins, stochastic model, proteins fluctuation, noise**

I PURPOSE

Subcellular structures are often formed by a small number of proteins. Examples in prokaryotes are: the Soj proteins in Bacillus subtilis, the Min proteins in Escherichia coli [1], as well as the rings and helices formed by FtsZ and MreB in many bacteria. Typically these structures consist of few hundred molecules. Such small numbers can imply large random fluctuations in space and time. In the context of gene expression, random fluctuations contribute essentially to the dynamics. In particular, they directly lead to intercellular fluctuations, and can play an important role in cell fate decisions [2]. In this context, cell size can act as a control parameter to regulate either the amplitude of fluctuations [3] or the distribution of phenotypes they generate [3]. Here we have studied intra- and intercellular fluctuations in E. coli and in particular the spatiotemporal patterns formed by the Min proteins that select the division site [1]. The proteins MinC, MinD and MinE make up the Min system that helps to select the cell middle as the division site [1]. The spatial distribution of the Min proteins has been reported to change periodically with time, such that most of the proteins reside for about 40s in one cell half and subsequently for the same time in the opposite cell half. Computational analysis of the Min-protein dynamics indicate that the observed pattern is self-organized [4,5] This idea is supported by experiments in vitro in which planar and spiral waves of MinD and MinE emerged spontaneously in the presence of ATP on a supported lipid bilayer [6].

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II RESULTS

We observed the distribution of MinD for 40 minutes in each of 209 cells, during which individual bacteria grew roughly 0.5µm. In cells shorter than 2.5µm, instead of oscillating regularly, MinD typically shifted stochastically from one cell half to the other. The residence times of MinD in one cell half varied largely in these cells, whereas complete switching from one cell half to the other occurred in an interval of less than 15s. The distribution of residence times has an algebraic tail, with a decay exponent of 2.1 ± 0.2. For cell lengths between 2.5µm and 3µm, the Min pattern typically changed from stochastic switching to regular oscillations with a period of about 80s. Cells longer than 3.5µm invariably displayed regular oscillations. A particle-based model of the Min-protein dynamics suggests that the random switching in short cells is due to microscopic fluctuations in the molecular processes involved rather than external noise. Moreover, our experimental and theoretical analysis analysis suggest that the transition from stochastic switching to regular oscillations in not merely an effect of changing the cell size. Instead, in our simulations a change in the activity of the Min proteins as the cell age, or an increasing in protein concentration and/or a decreasing in the density of the membrane binding sites can account for the transition. Additional experimental work is necessary to understand what the precise mechanism is for the transition from stochastic switching to regular oscillations and why this transition exist.

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