

# Modelling Polar Retention of Complexes in *Escherichia Coli*

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Even single-celled organisms, such as *Escherichia coli*, possess a far from random internal organization, as the cytoplasm is a crowded, heterogeneous environment. Some proteins preferentially locate at the cell poles (e.g. those involved in chemo-taxis), while others, e.g. involved in gene expression, locate at mid-cell, within a structure known as nucleoid.

Recent live cell microscopy measurements have studied the spatiotemporal distributions of a large complex, composed of a synthetic RNA tagged with multiple MS2-GFP proteins. In these studies it was observed that, at short time scales, the motion of the complexes is sub-diffusive with an exponent that is robust to physiological changes and, at long time scales, the complexes tend to localize at the cell poles [1]. Further, it has been shown that these MS2-GFP-RNA complexes are retained at the poles, as shown in Figure 1A, most likely due to the presence of the nucleoid at mid-cell [2]. This hypothesis arises from the observation of a strong anisotropy in the displacement distribution where the border of the nucleoid is expected to be (Figure 1B). However, the observed long-term spatial distribution of complexes could also, theoretically, arise from heterogeneities in the speed of the complexes along the major axis of the cell.

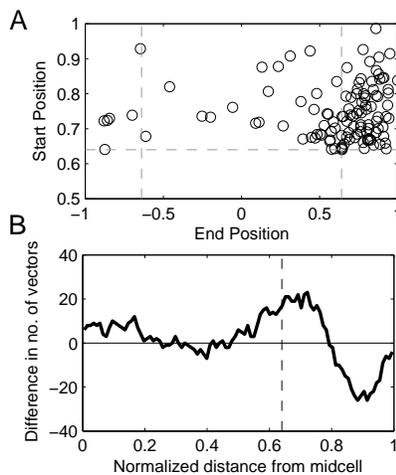


Fig. 1: (A) Relationship between the position along the major axis where each complex was last observed and the absolute position where it was first observed at a pole. Here, an end position of +1 indicates that the complex remained at the same pole as it was first observed in, while -1 indicates that it traveled to the other pole. All 160 cells were born during the measurement period and contained only one complex during their lifetime. (B) Difference between the numbers of displacement vectors that are directed towards the poles and towards the mid-cell along the major cell axis. The differences in numbers were calculated from the displacement vectors originating within windows extending 0.05 normalized cell lengths around that point. All 49 cells were born during the measurement period and contained one complex in their lifetime. In both figures, the horizontal and vertical dashed lines represent the detected separation between the mid-cell and poles.

Here, we use stochastic modelling to determine, from the observations, which of the two possible retention mechanisms is taking place. We model the cell as a compartmentalized 1-dimensional space and the motion of the complexes along the major cell axis with unimolecular reactions following the Reaction-Diffusion Master Equation [3]. The cell geometry and retention mechanisms are accounted for by tuning the propensities of the forward and reverse reactions. These propensity functions account for the combined effects on the motion of the complexes of the rod shape of the cell, the pole caps and, the nucleoid.

Using this model, with parameters tuned to match the measurements reported in [2], we show that both an anisotropy in the displacement vectors and a reduced velocity at the poles produce good fits with the measurements. However, the model with varying speed along the major cell axis, at the time scale of the measurements, was unable to reproduce the observed anisotropic displacement distribution at the border between the mid-cell and poles. We conclude that the polar retention most likely relies on these anisotropies in the displacement distribution rather than differences in speeds, consistent with the hypothesis that the observed long-term behavior is the result of macromolecular crowding, likely due to the nucleoid. Overall, the spatiotemporal kinetics of the complexes suggests that nucleoid occlusion is a source of dynamic heterogeneities of macromolecules in *E. coli* that ultimately generate phenotypic differences between sister cells.

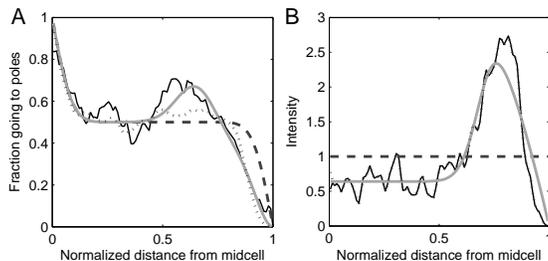


Fig. 2: (A) Measured fraction of displacement vectors originating within a window extending 0.05 normalized cell lengths around that point which are directed towards the pole (black line), model prediction with homogenous speed (without nucleoid (dashed line) and with nucleoid (gray line)), and with differing speed without nucleoid (dotted line). Note that the dashed line is superimposed by the gray line in the left side of the graph. (B) Measured spatial distribution of fluorescence intensities of complexes (black line) model prediction with homogenous speed (without nucleoid (dashed line) and with nucleoid (gray line)), and with differing speed without nucleoid (dotted line). Note that the dotted line is superimposed on the black line of the graph.

## References

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3. Gardiner, C.W., McNeil, K.J., Walls, D.F., Matheson, I.S.: Correlations in Stochastic Theories of Chemical Reactions. *J. Statistical Phys.* 14, 307 (1976)