Plasmid behaviour under Par system control

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The underlying mechanism of the ParA-ParB protein interaction that causes plasmid translocation and equidistant spacing between multiple plasmid foci has been widely discussed but a comprehensive study that describes how system parameters lead to either oscillatory behaviour or stable plasmid arrangements requires further explanation. In this study we provide a deterministic model that includes finite substrate size effects on protein concentrations that can reproduce a wide range of the observed plasmid behaviour.

Keywords **— ParA-ParB system, Plasmid translocation, spatial oscillations, deterministic model**

I. Review

The spatial organization of low-copy plasmids in bacteria is mediated by the Par protein system consisting of two proteins, ParA and ParB, and a *cis*-acting centromere-like site on the plasmid, *parS.* ParB specifically binds to *parS* and by interacting with ParA bound to the nucleoid, is able to orchestrate the movement and positioning of plasmids inside the cell [1]. Various theoretical models have been proposed that explain how plasmid translocation arises from ParA-ParB interactions [2,3] and recently simulations based on one such model have successfully achieved the required positioning of multiple plasmids at equi-distant locations along the length of the cell [3].

However, live imaging has revealed complex plasmid behaviours ranging from pole to pole oscillations in cells with single plasmids, to states with stably positioned plasmids within cells with inhibited division [4]. Given these observations, it is unexplained whether the plasmids are undergoing sustained oscillations or settling towards fixed point positions within the cell. Additionally, super-resolution microscopy has revealed differences in the stable positions of F plasmids in *E. Coli* and chromosomal foci in *B. Subtilis* both of which are controlled by the same Par system [5].

It also remains to be understood how system parameters like cell length and plasmid number affect the organization and dynamics of plasmid foci. Since these parameters change during the cell-cycle, simulations that include cell-cycle durations and plasmid replication events are required to provide a complete explanation of the observed plasmid behaviour in-vivo.

II. Results

Previously we developed model that was able to describe the locomotion of an in-vitro system that was actively driven by the Par system [6]. Here we combine it with finite substrate length to obtain equi-distant plasmid positioning and further extend it to provide a comprehensive description of all factors that affect plasmid dynamics within the cell. These key parameters are the number of plasmids within the same cell, the length of the nucleoid to which ParA is bound, the rate at which ParA hydrolyzation is mediated by ParB, the rate at which ParA rebinds (closely related to total ParA within the cell), and the ratio of the length scale over which the plasmid hydrolyzes ParA to the length scale over which it is tugged by ParA dimers.

From the deterministic model we are able to analytically calculate the boundary in parameter space that separates oscillatory plasmid behaviour from stable, equi-distantly spaced fixed points. We find important differences in the location of this boundary depending on whether ParA resources are unlimited (in-vitro) or limited (in-vivo). We also find that increasing the number of plasmids pushes a system with oscillatory behaviour towards stable fixed points while increasing nucleoid length has the opposite effect on the system. Furthermore, we outline the in-vivo conditions required to observe plasmid oscillations and find that realistically it is impossible to observe three plasmid oscillation in a bacterial cell of regular size. Interestingly, finite size effects are observed as the distance separating two oscillatory plasmid trajectories is reduced as system size is increased. We show through simulations how plasmid segregation is robust to replication events during a single cell-cycle. Finally, we discuss the parameter ranges within which the plasmid positions in the super-resolved images provided by [5] can be obtained.

III. Conclusion

Our results show that plasmid number and the length of the nucleoid can drive the system to switch from oscillatory dynamics to stable equi-distantly placed fixed points along the cell. Bacterial systems might be poised near this boundary to achieve the faithful segregation of genetic material. We suggest further experiments that could probe the changeover from oscillatory to stable plasmid dynamics.

References

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