Orchestrating Chromosome Segregation using the Par system

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***Short Abstract* — In E.Coli, the Par system is responsible for specific chromosome and plasmid segregation. In Caulobacter Crescentus several events lead to the segregation of newly replicated chromosome into the future daughter cell. Several events, from the tethering of the origin, to replication, followed by active transport of the replicated origin to the opposite pole must be orchestrated. Here we extend a recently published model for Par function to include the other cellular processes that are involved in segregating the origins to the poles, and show how the observed dynamics emerges from the coordinated activity of simple stochastic processes.**

I. Introduction

In prokaryotes the ParA/B system is responsible for actively segregating replicated chromosomal and plasmid DNA during division. The system functions as a molecular motor that rectifies motion in one direction, leading to directed transport. ParB binds to ParS sequences on DNA which in turn interacts with ParA:ATP filaments that are bound to the surface of the nucleoid. The interaction of ParB-ParS with ParA:ATP stimulates hydrolysis that in turn leads to the depolymerization of ParA filaments [1,2]. It is believed that the ParB:ParS complex is then translocated along with the depolymerizing ParA filaments leading to active transport of the attached DNA[2,3,4]. The partitioning of plasmids by the Par system leads to the replicated plasmids being positioned uniformly along the cell's length. Recent computational modeling has been able to reproduce the observed partitioning results [4]. The Par system is also used to segregate replicating chromosomal DNA, and in Caulobacter Crescentus, several other processes are involved. In particular, the origin of replication is tethered to one of the poles and upon replication only one of the ParB bound origins is seen to get transported by the ParA gradient that exists in the cell [6]. How does tethering affect the action of the ParA/B system and how does the ParA gradient get formed from the localization of ParB? In this work we extend previous modeling efforts to address these questions.

II. Model

The prior computational model for ParA/B function[5] for the partitioning of plasmids consisted of a 1D ParA filament model coupled with ParB stimulated ParA depolymerization leading to ParB translocation. Here, we extend that model to consider the situation of chromosome segregation in C. Crescentus. We used Gillespie algorithm to study the system as sets of reactions. In Addition, We include tethering of the origin to the pole via an attractive interaction between ParB and a polar localized protein called PopZ. PopZ is modeled via a spatially symmetric bipolar concentration. Its effect on ParA/B is included by making the ParB off-rate from ParA dependent on PopZ, where having greater PopZ leads to a higher off-rate. This reflects the competition between ParB interacting with either ParA or PopZ.

III. Results

In the absence of interaction between ParB and PopZ, the model leads to localized single ParB:ParS at the midcell. We determine the necessary ParB:PopZ kinetics so as to localize/tether the ParB bound origin to one of the poles. We then show how such a localization of ParB can lead to the formation of the observed ParA filament gradient seen in the cell. Upon replication, the effective repulsion between ParB:ParS complexes that arises because of competition between depolymerizing ParA filaments. Our model can capture the observed temporal pattern of the replicated origin translocating along the cell's length. We find that too strong an interaction between PopZ and ParB localizes both ParB focus to the old pole while too weak an interaction results in uniform positioning of origins along the cell axis.

IV. Conclusion

Using simulation methods we extend previous ParA/B proteins Models for Caulobacter Crescentus via using extra interacting element PopZ to the existing model. Our Results indicates that relative proteins interaction strength (especially ParA-PopZ interaction) and PopZ spatial/temporal pattern are tuned such that the replicated origin can overcome the PopZ interaction and move toward the new pole during the cell replication period. Interestingly, at the same time the other origin is anchored in the old pole via a PopZ localized cluster.

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