

Modeling the Mechanics of the Division Apparatus in Bacterial Cells

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During the summer, I worked on the mechanisms of force generation during bacterial division under the direction of Dr. Eric Cytrynbaum of the UBC Mathematics Department. In the last step of cell division, the cytoplasm of the mother cell is physically divided into two parts. Both prokaryotes and eukaryotes use a contractile ring positioned at the middle of the cell to perform this step. However, prokaryotes like bacteria lack the motor proteins found in eukaryotes which are responsible for the force generation. This raises a natural question concerning the mechanism of force generation in bacterial division. Although much is known about the constituents of prokaryotic contractile ring, the physical mechanism of force generation is unclear. Knowing this mechanism will allow biologists to study the evolution of the division pathway from prokaryotes to eukaryotes. Moreover, knowledge about the mechanism helps pharmaceutical researchers design better antibiotics targeting the division process¹.

FtsZ is the major protein responsible for the assembly of the contractile ring, called the Z ring, and the recruitment of other division proteins. FtsZ is a GTPase that is able to form highly dynamic linear aggregate or protofilaments in which FtsZ subunits are constantly exchanging with FtsZ in the cytosol. Stability and curvature of these protofilaments change when

¹Lock, R. L. & Harry, E. J. Cell-division inhibitors: new insights for future antibiotics. *Nat. Rev. Drug Discovery*, **7**, 324-338 (2008).

the bound GTP is hydrolyzed to GDP. Furthermore, experimental observations suggest protofilaments may also associate laterally. Recent *in vitro* experimental studies demonstrated reconstituted FtsZ in tubular liposomes are able to form Z ring like structures and generate visible constriction in the absence of other division proteins². Thus we would like to have a model that can describe this relatively simpler *in vitro* system. Currently there are two classes of models based on these properties of FtsZ. First, there are sliding models where increasing lateral interactions drive contraction. Second, there are hydrolyze and bend models where curvature change upon GTP hydrolysis drive contraction. However, current models and simulations based on one or a combination of these ideas are rather unsatisfactory (see footnote for a recent review³).

For my USRA project, we formulated the sliding process as a first passage time problem and solved the mean first passage time through the adjoint equation approach. We then used this time as the time for one of the elementary processes in a kinetic Monte Carlo simulation. The advantage of this kind of simulation is it yields time scale information inaccessible to the simulation method employed by previous sliding models. We believe kinetic information is important in understanding how does a highly dynamic FtsZ ring generate a constriction force on a physiological time scale. Due to time constraints of the summer, we were only able to perform simulation on small test FtsZ structures. Preliminary results suggest only weak lateral interactions seem possible for the relevant processes to happen in a reasonable time frame. Toward the end of the summer, we solved the mean first passage time for sliding with a constant applied external force but have not implement this into the simulation. It will be interesting to see what happens to the test structures under an applied force. Finally, performing simulation on a ring like structure both with and without resisting force from the membrane is probably the goal for a future project.

²Osawa, M., Anderson, D. E. & Erickson, H. P. Reconstitution of contractile FtsZ rings in liposomes. *Science* **320**, 792-794 (2008).

³Erickson, H. P. Modeling the physics of FtsZ assembly and force generation. *Proc. Natl. Acad. Sci. U.S.A.* **106**, 9238-9243 (2009).