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# A polymerization–depolymerization model for generation of contractile force during bacterial cell division

BIPLAB GHOSH and ANIRBAN SAIN*
Physics Department, Indian Institute of Technology Bombay, Powai, Mumbai 400 076, India
*Corresponding author. E-mail: asain@phy.iitb.ac.in

**Abstract.** During the last phase of cell division in bacteria, a polymeric ring forms at the division site. The ring, made of intracellular proteins, anchors to the cell wall and starts to contract. That initiates a dividing septum to close in, like the shutter of a camera, eventually guillotining the cell into two daughters. All through, the ring remains at the leading edge of the septum and seems to power its closure. It is not understood why does the ring contract. We propose a theoretical model to explain this. It is worth mentioning that a similar contraction phenomenon occurs for the actin ring in eukaryotes, but there it is due to motor proteins, which however, are absent in bacteria.

**Keywords.** Polymerization; intrinsic curvature; hydrolysis.

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## 1. Introduction

During binary cell division of rod-shaped bacteria the cell contracts at the vertical middle and divides into two daughter cells (figure 1). The physical origin of the contractile force is poorly understood although biochemists and molecular biologists have reported various properties of the proteins and polymers involved in this cellular phenomenon. In 1991, Bi and Lutkenhaus [1] had discovered that just before the contraction starts, a ring-shaped polymeric structure forms inside the cell and positions itself at the midcell. This ring, popularly known as the Z-ring, is somehow anchored to the cell wall of the bacteria through some anchoring proteins although the details of the anchoring mechanism is not known. As time evolves the ring contracts in radius and it is believed that through the anchors it exerts the necessary contractile force on the cell wall, which in turn invaginates radially inward to form a dividing septum. It is not known why the ring contracts or how it generates the contractile force. We propose the first quantitative model to explain this contraction phenomenon.

The ring itself is made of a certain intracellular protein called FtsZ (filament temperature sensitive Z) which shows temperature sensitive behaviour. From

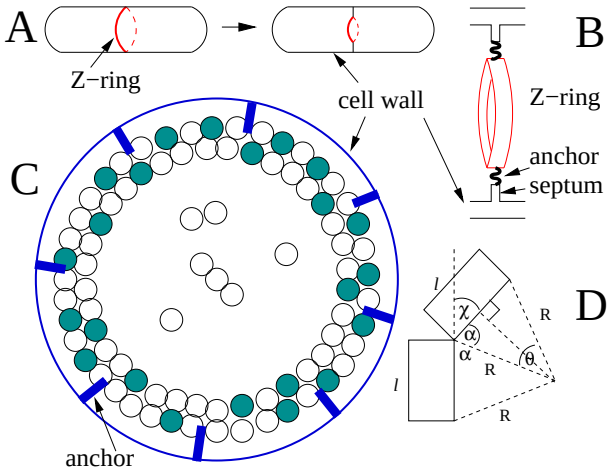


**Figure 1.** (**A**) Dividing bacteria with contracting Z-ring. (**B**) Schematic drawing of Z-ring anchored to the cell wall. (**C**) The ring is modelled by a multi-layered structure; only two layers are shown, but in our simulation we start with 7–9 layers. GTP-FtsZ and GDP-FtsZ are indicated by open (T) and filled (D) circles, respectively. Oligomers and monomers from the cytoplasm can poly/depolymerize in and out, from both the inner and the outer layers of the ring. (**D**) FtsZ monomers which are shown as circles in (C), are actually blocks of size ∼5 nm each, with intermonomer angles $\chi$. A TT pair prefers being straight, while DT or DD pairs prefer finite bending angles. From geometry intermonomer angle $\chi = \theta$ (the angle that a monomer of length $l$ subtends at the center of the ring). From geometry $l/R \simeq \chi$ for $l \ll R$ and thus description in terms $R$ or $\chi$ are equivalent.

fluorescence experiments it has been established that ring has a highly dynamic structure. It continuously exchanges its constituent FtsZ monomers, and possibly short polymers, with the cytoplasm. Attachment and detachment of FtsZ units into the ring and out of the ring, respectively, are called polymerization and depolymerization. *In vitro* experiments have found that in physiological conditions FtsZ proteins form single-stranded polymers (another example of polymerization). Higher-order structures like sheets, ribbons (which require lateral attraction between individual filaments) and even small rings also have been observed. Both polymerization and lateral bundling are enhanced when the medium has excess GTP and is suppressed when the medium has excess GDP.

Each FtsZ monomer is in fact attached either to GTP or GDP. FtsZ-GTP can convert to FtsZ-GDP under hydrolysis reaction which keeps occurring frequently. When a constituent FtsZ-GTP gets hydrolysed the filament can also break at that point. Henceforth, we will denote an FtsZ-GTP by T and an FtsZ-GDP by D.

The puzzle remains as to how does the Z-ring contracts while undergoing continuous poly/depolymerization. The precise arrangement of the monomers/polymers in the Z-ring is not known. This is because neither single FtsZ monomers nor polymers can be detected under fluorescence microscope as they are ∼5 nm wide (while the diffraction limit of visible light is ∼200 nm). Other than the lateral bundling

and polymerization tendencies, FtsZ polymers have another interesting mechano-chemical property. They prefer to be straight when its units are bound to GTP, but hydrolysis of GTP to GDP induces local bending in the polymer (along with the possibility of breakage). It emerges that FtsZ-GDP filaments have intrinsic curvature [2] although the preferred radius of curvature ($R_0$) varies (12.5–100 nm) [3,4], depending on the environment. But in a given experiment all the minirings are of the same characteristic size ($R_0$) which we assume to be its intrinsic curvature. Incorporating all these mechano-chemical properties of FtsZ we build a model and demonstrate via simulation that hydrolysis-induced curvature of the polymers bias the poly/depolymerization kinetics and result in the net contraction of the ring. The model is schematically described in figure 1.

## 2. Model

We model FtsZ filaments as semiflexible polymers with intrinsic curvature [5]. The filament is described by position vector $\vec{r}(s), s \in [0, L]$ with curvature energy,

$$H = \frac{\eta}{2} \int_0^L \left( \frac{1}{R(s)} - \frac{1}{R_0} \right)^2 \mathrm{d}s. \tag{1}$$

Here $L$ is the length of the filament, $\eta$ is the bending rigidity, $1/R(s) = |\mathrm{d}^2\vec{r}(s)/\mathrm{d}s^2|$ is the local curvature and $1/R_0$ is the intrinsic curvature. The Z-ring may have the shape of an annular disc with a lateral thickness 20–40 nm [6], but to focus on its radial contraction, here we model it as a bundle of concentric filaments forming a flat annular disc (see figure 1), perpendicular to the long axis of the rod-shaped bacteria. The filaments fit on the ring as circular arcs, stabilized by its lateral attraction with the neighbouring layers of the ring. Each circular layer in the ring is approximated by a regular polygon with large number of sides of size $l$ each (equal to the size of the monomer) with intermonomer bond angle $\chi$, as shown in figure 1D.

The discretized semiflexible polymer consists of monomers attached to each other. The monomer of adjacent rings also touch each other. Curvature is a nonlocal feature of a polymer, which arises from molecular interactions that extend over few consecutive monomers on a chain. Here we approximate this interaction in terms of the angle that two neighbouring monomers make. But the intermonomer angle can be approximated as $\chi \sim l/R$ (see figure 1D). Depending on the neighbours (DD, TD or TT) the preferred angles are different, larger for TD and DD compared to TT. Hence the discretized form of eq. (1) can be written as the sum over curvature energies of all the intermonomer bonds indexed by $i$.

$$H = \frac{\eta}{2} \sum_i \left( \frac{1}{R_i} - \frac{1}{R_0^i} \right)^2. \tag{2}$$

Here, $1/R_i$ is the local curvature at $i$ (which is determined by the circular layer on which the filament sits) and $1/R_0^i$ is the intrinsic curvature of a dimer centered at $i$. $R_0^i$ can take three values, namely $R_0^{\mathrm{DD}}$, $R_0^{\mathrm{DT}}$ and $R_0^{\mathrm{TT}}$ corresponding to the dimers DD, DT and TT, respectively.

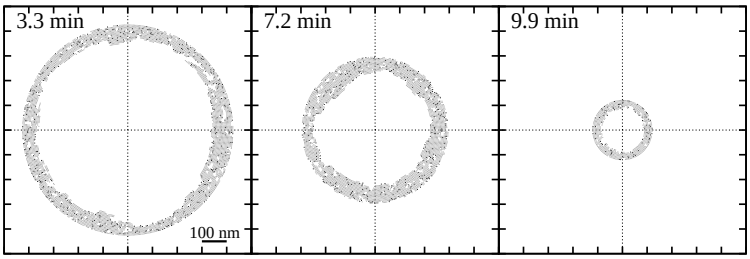


**Figure 2.** Configurations of the contracting Z-ring at specified times. Grey and black dots denote FtsZ-GTP and FtsZ-GDP, respectively. The simulation was started at $t = 0$, with an initial ring of outer radius 500 nm, consisting of nine layers and with 10% of the FtsZ units at its inner and outermost layers as FtsZ-GDP. A Monte-Carlo simulation is used to study the ring dynamics, on a circular, spatial grid. Three types of Monte-Carlo (MC) moves: polymerization, depolymerization and intralayer diffusion of FtsZ units were attempted. MC trials for polymerization and depolymerization were kept equal in the simulation. A constant hydrolysis rate was maintained at the two peripheries only. In poly/depolymerization trials we allowed both monomers and oligomers (up to tetramers, in decreasing proportion) to attach to or detach from both the inner and outer peripheries of the ring. Polymerization trials are allowed with T, TT, TTT and TTTT strands only while depolymerization of all possible types were allowed.

Other than the curvature energy we have considered two more contributions to the total energy: (1) attractive interaction between the adjacent monomers of a polymer and (2) the lateral attraction between the polymers. The 1st one is often referred to as the polymerization energy and the 2nd one makes bundling among polymers possible. Both these energies are assumed to be independent of the curvature of the polymer but depend on the GTP/GDP content of the monomers. The ring provides a template onto which the monomers and oligomers polymerize; depolymerization also occurs out of the ring. The kinetics of the processes are controlled by the free energy change, consisting of all the three types of energy described above. The simulation procedure is briefly described in the caption of figure 2.

## 3. Results and discussion

We have shown that despite having an equal rate of poly/depolymerization trials on both the peripheries of the multi-layered ring, it manages to contract (see figure 2) exploiting the difference in the curvature-induced strain between its outer and inner peripheries. It turns out that net depolymerization takes place at the outer periphery and net polymerization takes place at the inner periphery. We have also estimated the mean turn-over time of FtsZ filaments to be 14 s, of the same order as found in experiments [7,8]. It also turns out that the ring can generate radial contractile force of the order of 0.5 pN/nm along its perimeter. This force is

somewhat weak compared to what is required to pull a strip of membrane area of 30 nm width against an internal pressure of 3 atm (bacteria's internal presure). Recent work [9] which gives detailed consideration to the elastic deformation of the cell wall during the contraction, concludes that the ring might be a minor contributor of the contractile force. But their work is based on the assumption that contraction at the midcell proceeds simultaneously with the bacteria's growth in length. Also cryo-elecron microscopy is beginning to have a closer look at the *in vivo* structure of the Z-ring. Initial reports [10] claim that in *Basilus Subtilis* bacteria, instead of a ring, single-stranded filaments criss-cross the perimeter of the midcell. A new type of force generation mechanism will be required if really that is the case.

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