Modeling partitioning of Min proteins between daughter cells after septation in *Escherichia coli*

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1. Introduction

Cell division in *Escherichia coli* is initiated by the formation of a ring of the protein FtsZ on the bacterial inner membrane. This FtsZ ring shrinks [1] as the growing septum restricts the cytoplasmic channel connecting the two daughter cells. FtsZ ring formation is targeted to the mid-cell by two independent processes. Nucleoid occlusion prevents FtsZ ring formation over the nucleoids [2–4], while polar FtsZ ring formation is prevented due to the oscillatory dynamics of the Min family of proteins. The pole-to-pole oscillation of MinD and MinE [5–7] targets MinC to the polar inner membrane where it inhibits polar FtsZ ring formation [8, 9] and prevents minicelling.

Several deterministic [10–14] and stochastic models [15–19] have been developed to explain the pole-to-pole oscillation pattern of the Min proteins. All these quantitative models have recovered oscillatory behavior, though they differ in their detailed interactions.

The FtsZ ring is the first element of the divisome to localize [20]. Induced disassembly of the FtsZ ring can occur within a minute [21], and subsequent relocalization occurs within minutes. FtsZ can localize around potential division sites of daughter cells even before septation is complete [22]. Min oscillations must persist or be quickly regenerated after septation to ensure that polar FtsZ ring formation is blocked in newly formed daughters.

The experimental phenomenology of Min dynamics during septation has not yet been well characterized. Early experiments [7, 23] indicate that Min oscillations are qualitatively unaffected by partially constricted cells. Significantly, minicelling rates in wild-type *E. coli* cells are insignificant [24], and no non-oscillating daughter cells have been reported. These observations suggest that Min oscillations persist or regenerate quickly in all daughter cells.
and, as a result, block FtsZ ring formation at the poles of newly formed daughter cells.

In a pioneering study, Tostevin and Howard [19] addressed Min oscillations after cell division with a 1D stochastic model. Their model exhibited significant asymmetry in the distribution of Min proteins between the two daughter cells after division. Approximately 20% of their daughter cells did not oscillate due to such partitioning errors. While systematic studies of partitioning errors have not been done, large asymmetries of concentrations between daughter cells have not been reported. Tostevin and Howard suggested that rapid regeneration of Min proteins could quickly recover oscillations in non-oscillating daughters. However, no such cell-cycle-dependent signal is seen in translation [25] or, for the min operon, in transcription [26]. Moreover, Min oscillations continue even when protein synthesis is stopped by chloramphenicol [5]. This indicates that proteolysis rates oscillations continue even when protein synthesis is stopped.

The model developed by Huang et al. [14] includes many of the interactions observed experimentally [35–38]:

\[
\frac{\partial \rho_{D:ADP}}{\partial t} = D_D \nabla^2 \rho_{D:ADP} - \sigma_D^D \rho_{D:ADP}^{-\sigma_D^D+\rho_{D:ADP}} + \delta_{D:ADP} \rho_{D:ADP}^{-\sigma_D^D+\rho_{D:ADP}} + \delta_{mem} \sigma_{de} \rho_{de},
\]

(1)

\[
\frac{\partial \rho_{D:ATP}}{\partial t} = D_D \nabla^2 \rho_{D:ATP} + \sigma_D^D \rho_{D:ADP}^{-\sigma_D^D+\rho_{D:ATP}} - \delta_{mem} \sigma_{D:ATP} \rho_{D:ATP}^{-\sigma_D^D+\rho_{D:ATP}}.
\]

(2)

\[
\frac{\partial \rho_{E}}{\partial t} = D_E \nabla^2 \rho_{E} + \delta_{mem} \sigma_{de} \rho_{de} - \delta_{mem} \sigma_{E:ATP} \rho_{E}.
\]

(3)

\[
\frac{\partial \rho_{de}}{\partial t} = -\sigma_{de} \rho_{de} + \sigma_{E:ATP} \rho_{E}.
\]

(4)

where \(\rho_{D:ADP}, \rho_{D:ATP}\) and \(\rho_{E}\) are the cytoplasmic densities of MinD:ADP, MinD:ATP and MinE, respectively, and \(\rho_{de}, \rho_{de}\) are the densities of membrane-bound MinD and MinDE complex, respectively.

The rates of binding of MinD:ATP to the bare membrane, the cooperative binding of MinD:ATP to membrane-bound MinD:ATP, the binding of cytoplasmic MinE to membrane-bound MinD:ATP and the hydrolysis rate of MinD:ATP from the membrane under activation by MinE are given by \(\sigma_D, \sigma_{ADP}, \sigma_D^D, \sigma_D\) and \(\sigma_{de}\), respectively.

The bacterium was modeled as a cylinder of length \(L\) and radius \(R\), with longitudinal interval \(dx = 0.0521\) and radial interval \(dr = 0.0416\), and with poles represented by flat, circular end-caps. Lateral growth is significantly reduced during septation [39, 40], so we accordingly keep \(L\) constant. The density of cytoplasmic MinE at the membrane surface is \(\rho_{E}(M)\), while \(\delta_{mem} \equiv \delta(r - R) + \delta(z - z_m) + \delta(z - z_m - L/2)\delta(r - r(t))\) limits reactions to the bacterial inner membrane. The last term denotes the growing septum at mid-cell, with \(r_s(t) \in [0, R]\) being the radius of the circular open portion of the cylindrical cross-section at mid-cell. Diffusion is not allowed across the septum (for \(r > r_s\)), while membrane interactions take place independently on either side of the growing septum.

Pre-septation Min oscillations were allowed to stabilize in a cell with length \(L = 5 \mu m\) before the process of septation was initiated. Septation was initiated at ten or more uniformly distributed phases of the Min oscillation period to determine the effect of this phase on the partitioning of Min proteins. Since the detailed septal closure dynamics of E. coli are not well constrained experimentally, we assume linear inward growth of the septum with the mid-cell septal radius given by

\[
r_s(t) = R(1 - (t - t_s)/t_f), \ t > t_s
\]

(6)

where \(t_s\) is the duration of septation and \(t_f\) is the time at which septation starts. The area of the growing septum is then
Figure 1. The time development of membrane-bound MinD and MinDE during and after septation, represented as spacetime plots. White and black indicate high and low linear densities, respectively. Time increases from top to bottom (total duration of 300 s is shown) while the bacterial length runs from left to right (L = 5 μm) for each of MinD and MinDE. (a) Oscillations in parent cell starting from 100 s before and ending 200 s after septation. Membrane-bound MinD and MinDE are shown in the first and second columns, respectively, as indicated. The arrowhead marks the beginning of the septation process and the emerging white bar at mid-cell corresponds to the growing septum. (b) Oscillations just before and after the end of septation. The arrowhead marks the end of the septation process and formation of two independent daughter cells. Oscillations continue in the left daughter cell through septation but are disrupted and then regenerated in the right daughter cell after septation is complete. (c) Oscillations in both daughters after completion of septation. A significant asymmetry of Min partitioning between the two daughter cells is apparent. The parameters used in this figure are ρD = 1150 μm⁻¹, ρE = 350 μm⁻¹, D0 = D1 = 2.5 μm²s⁻¹, σD0 = 0.025 μm s⁻¹, σD1 = 0.0015 μm³ s⁻¹, σE = 0.7 s⁻¹, τD = 0.093 μm³ s⁻¹, σDmax = 0.1 μm s⁻¹. The three subfigures are contiguous in time.

\[ A(t) = \pi \left( R^2 - r^2 \right) \] for \( t \in [t_s, t_i + t_s] \) (\( A = 0 \) for \( t < t_i \) while \( A = \pi R^2 \) for \( t > t_i + t_s \)). This process of septal closure mimics the process of septal growth discussed by Burdett and Murray [1]. Since MinD:ATP has a greater affinity for anionic phospholipids such as CL [31, 41], and since CL domains are found to be localized around the cell poles and septal regions [32, 33], we also considered the case in which the rate of attachment of MinD:ATP (\( \sigma_D \)) was enhanced at the polar and septal membranes (\( \sigma_{D0} + \sigma_{Dmax} \)) compared to the attachment rate elsewhere on the curved surface of the cylindrical cell (\( \sigma_{D0} \)).

Figures 1(a) and (b) show oscillations in the parent cell during the process of septation while figure 1(c) shows oscillations in both daughters after septation. A septation duration \( t_s = 512 \) s was chosen to be consistent with the proportion of septating cells observed in culture [42]. Significantly faster septation (\( t_s = 350 \) s) does not affect our results.

Figure 2. Scatter plot of linear MinD and MinE densities in the parent cell (open triangles) and non-oscillating daughter cells (•). Indicated by the solid line is the approximate stability curve for \( L = 5 \) μm, separating oscillating and non-oscillating daughter cells. The large black and gray filled circles indicate example parent cells that lead to 84% and 58% oscillating daughter cells, respectively. The smaller black and gray filled circles denote the corresponding linear densities of daughter cells produced after cell division. The open stars correspond to the black filled circle but with a septation duration of \( t_s = 350 \) s, all other points correspond to \( t_s = 512 \) s. Parameters are as specified in figure 1, but with \( \sigma_{Dmax} = 0 \).

3. Results

3.1. Varying Min concentration

We examined the effect of varying the MinD and MinE densities in the parent cell on the partitioning of Min between daughter cells. For this purpose, we generated 420 sets of different parent cell densities (\( ρ_D, ρ_E \)). For each set, the initiation time of septation \( t_s \) was varied uniformly over the oscillation period \( T \) of the parent cell with at least ten different phases sampled for each parent cell. Min partitioning information was noted at the end of the septation, and the simulation was run for more than 15 min after the end of septation to see whether Min oscillations were regenerated in the daughter cells.

Figure 2 shows the linear density of MinD and MinE in parent cells (open triangles). Daughter cells with a variety of phases of septation start times are shown (smaller black and gray filled circles) for two representative parent cells (larger black and gray filled circles) close to and far from the stability boundary (approximately indicated by the black line), respectively. For oscillations to restart or continue in daughter cells, the ratio of MinD:MinE must be greater than \( \approx 2.7 \). Inadequate partitioning of Min results in daughter cells (×) having Min densities which fall below this threshold. The partitioning for the pole-to-pole oscillating MinD is worse than for the more mid-cell MinE, resulting in an asymmetric donut-shaped distribution of daughter cell densities for a given parent cell. Since the MinE ring closely follows the MinD cap there is a correlation between the MinD and MinE partitioning—extending the asymmetric donuts along the diagonal. For parent cell densities close to the oscillation threshold, a large
fraction of daughter cells do not oscillate. Away from the threshold a smaller fraction do not oscillate. Varying the duration of septation by moderate amounts does not change the partitioning, as illustrated by the nearly identical donuts for $t_s = 350$ s (open stars) and $t_s = 512$ s (black circles).

In figure 3(a), we show all of the partitioning donuts on one plot, where $d_f$ and $e_f$ are the fraction of MinD and MinE in the two daughter cells, respectively. The absence of any daughter cells in the central region, near $d_f = e_f = 0.5$, shows that simultaneous equipartitioning of both MinD and MinE is never observed. While there is always a septation start-time $t_s$, relative to the parent cell oscillation, that leads to perfect partitioning of MinD or MinE, there is no phase that leads to perfect partitioning of both MinD and MinE. This ‘donut hole’ is a manifestation of the phase lag between MinD and MinE oscillations, i.e. the timing of maximal MinD at mid-cell is ahead of the timing of maximal MinE. To make this clear, in figure 3(b) we have scaled all of the partitioning donuts by their RMS radius, $r_{av} = \sqrt{(d_f - 0.5)^2 + (e_f - 0.5)^2}$, and plotted the scaled densities $d_s = (d_f - 0.5)/r_{av}$ versus $e_s = (e_f - 0.5)/r_{av}$. Relative to $r_{av}$, there are no phases that approach symmetric partitioning of both MinD and MinE.

We also plotted $r_{av}$ against the oscillation period $T$ of the parent cell in figure 4 to determine if the RMS radius scales with the period of oscillation of the parent cell. We do not see perfect collapse but $r_{av}$ increases with period away from the stability boundary, indicating that the two partitioning donuts (formed by the small black or gray filled circles) shown in figure 2 are representative.

### 3.2. Enhanced MinD binding at poles and septum

To see whether a distinct phospholipid composition of the closing septum could affect the partitioning, we enhanced MinD:ATP binding ($\sigma_{D0}$) at the cell poles and the growing mid-cell septum. The degree of enhancement was constrained by the practical requirement that it did not disrupt steady oscillations in the parent cell before $t_s$. This restricted the polar enhancement $\sigma_{D_{max}}$ to less than ten times the base value of $\sigma_{D0} = 0.025 \text{ } \mu\text{m} \text{ s}^{-1}$. This is consistent with the affinity of MinD:ATP for anionic phospholipids like cardiolipin, which is nine times higher than its affinity for zwitterionic phospholipids [32]. The enhancement of MinD:ATP binding at the poles and septum slightly increased the oscillation period in the parent cell by increasing the time for dissociation of membrane-bound MinD:ATP by MinE.

To analyze the effect of enhanced MinD binding at the poles and growing septum on the number of oscillating daughters, we compared the results from 50 parameter sets with and without septal and polar enhancement. In this comparison, the concentrations of MinD and MinE were varied while all other parameters were kept fixed and

**Figure 3.** (a) Fractions $d_f$ versus $e_f$ of MinD and MinE, respectively, in oscillating as well as non-oscillating daughters for all parent cells. Black $\times$ indicates non-oscillating daughter cells, while gray filled squares indicate oscillating daughter cells in cases where both daughters oscillate. Filled upper triangles correspond to fractions in the oscillating daughter for cases where only one daughter oscillates. The two daughter cells of a given parent are symmetrically placed around $d_f = e_f = 0.5$. (b) A plot of the scaled relative fractions of MinD versus MinE in the two daughter cells.

**Figure 4.** The RMS magnitude of partitioning error $r_{av}$ versus the oscillation period of the mother cell $T$. The period increases as the mother cell Min concentrations are moved away from the stability boundary shown in figure 2. While there is no precise scaling collapse, the trend is for less accurate partitioning as distance from the stability boundary (and hence $T$) increases—maintaining the non-oscillating daughters shown in figure 2. We do not find a significant dependence of $r_{av}$ on the septation duration $t_s$. |
enhancement of the MinD binding rate) was obtained. The best 85% figure (obtained with or without polar and septal peaks, and hence weak and non-central lateral peaks. Parameters are as specified in figure 1, except for $\sigma_{{Dmax}} = 0.1 \mu m s^{-1}$ or $\sigma_{{Dmax}} = 0$. The overall percentage of oscillating daughter cells increased by a small amount (2%) when enhanced polar and septal MinD:ATP attachment rates were used. More specifically, for parent cell density close to the stability threshold (large gray filled circle in figure 2), the enhancement of MinD:ATP binding at the poles and septum led to a modest increase (at most 2%) in the number of daughters which restart oscillations after septation. However, for parent cell densities far from the stability threshold (large black filled circle in figure 2) no significant increase in the number of oscillating daughters was obtained with enhanced MinD:ATP binding at the poles and growing septum.

3.3. Varying interaction parameters

In another attempt to increase the fraction of oscillating daughter cells after septation, we explored the parameter space of interactions in the Huang et al model [14]. Since most of the parameters are experimentally underdetermined, some flexibility is possible in the choice of parameters while insisting upon stable oscillations. In this context, the Min concentration, diffusivities, reaction rates and $\sigma_{{Dmax}}$ were all independently varied over plausible ranges for a fixed cell length. The parameter space was explored to move toward symmetric partitioning of MinD and MinE in non-oscillating daughter cells. Each parameter was varied over a range spanning almost an order of magnitude relative to the benchmark values which were chosen to be the parameters specified in Huang et al. However, no improvement upon the best 85% figure (obtained with or without polar and septal enhancement of the MinD binding rate) was obtained.

3.4. Phase dependence of partitioning

Why do we never see 100% of the daughter cells oscillating? The pattern of end-to-end oscillation of MinD continues largely unchanged throughout septation (see, e.g., figure 1), even as the period lengthens somewhat, so that when the closure of the septum coincides with MinD being localized predominately at one pole then the MinD will be badly partitioned between the two daughter cells. In figure 5, we plot the longitudinal position of the radially integrated MinD and MinE peaks away from the cell poles at the end of septation when $t = t_s + t_r$. Figure 5(a) shows parent cells that lead to two oscillating daughters, while figure 5(b) shows parent cells that lead to only one oscillating daughter. We see that two oscillating daughters typically result from septation events where both MinD and MinE have a substantial peak at the mid-cell. When two oscillating daughters result despite polar maxima of MinD and MinE, a substantial mid-cell accumulation of MinD is also present. A non-oscillating daughter cell is typically produced when MinD has a large peak near one pole.

Figure 6 illustrates the spatial profile of radially integrated MinD and MinE for three different phases at the end of septation. Figure 6(a) corresponds to a phase where oscillation restarts in both daughters after septation. Adequate partitioning is reflected in large peaks of radially integrated MinD (solid line) and MinE (dashed line) near the midpoint of the cell. Figure 6(b) corresponds to a phase where inadequate partitioning is manifest in the large peaks of radially integrated MinD (solid line) and MinE (dashed line) near one pole of the cell. Only one oscillating daughter results. Figure 6(c) shows a peak in the radially integrated MinD and MinE near

Figure 5. Non-polar ‘lateral’ peak location of radially integrated MinD and MinE at the end of septation for phases which lead to (a) two oscillating daughters and (b) one oscillating daughter. Oscillations are observed in both daughters for 12 out of the 20 septating phases. Only half the cell length is plotted since the peak locations for different septating phases are symmetric about the mid-cell. In general, two oscillating daughters result from a strong central peak of MinD at the completion of septation while one oscillating daughter results from polar peaks, and hence weak and non-central lateral peaks. Parameters are as specified in figure 1, except for $\sigma_{{Dmax}} = 0.1 \mu m s^{-1}$, $t_r = 512 s$ and $\sigma_{{Dmax}} = 0$. The overall percentage of oscillating daughter cells increased by a small amount (2%) when enhanced polar and septal MinD:ATP attachment rates were used. More specifically, for parent cell density close to the stability threshold (large gray filled circle in figure 2), the enhancement of MinD:ATP binding at the poles and septum led to a modest increase (at most 2%) in the number of daughters which restart oscillations after septation. However, for parent cell densities far from the stability threshold (large black filled circle in figure 2) no significant increase in the number of oscillating daughters was obtained with enhanced MinD:ATP binding at the poles and growing septum.
Figure 6. Profile along the cell length $x$ of radially integrated (linear) densities of MinD (solid line) and MinE (dashed line) for three different phases of septation, at the time of septal closure: (a) leads to two oscillating daughter cells and exhibits strong central MinD and MinE peaks, (b) leads to only one oscillating daughter cell and exhibits a strong polar peak of both MinD and MinE and (c) leads to only one oscillating daughter cell and exhibits a strong polar peak of MinE. The parameters used are the same as in the previous figure.

the mid-cell and pole, respectively. The resulting inadequate partitioning of MinE between the two daughters ensures that the ratio of MinD:MinE falls below the threshold required to regenerate oscillations in one of the daughters. This leads to a non-oscillating daughter and corresponds to the points with a large mid-cell MinD peak in figure 5(b).

4. Discussion and conclusions

We have explored the impact of MinD and MinE concentration, interaction parameters, end-cap and septal cardiolipin patches on the partitioning of Min proteins between daughter cells after septation in the model of Huang et al [14]. While concentration close to the stability threshold for oscillations led to less than 50% of daughter cells oscillating after septation, no combination of concentration, interaction parameters and/or cardiolipin patches led to more than $\approx 85\%$ of daughter cells oscillating after septation. These results are comparable to those of Tostevin and Howard [19], despite significant differences in the Min models that were used. They studied a stochastic one-dimensional model with explicit MinD polymerization, while we used a deterministic three-dimensional model without filamentous MinD structures. We do not expect that the inclusion of stochastic effects would significantly change our results, following [16].

We found that plotting the MinD versus MinE densities in the daughter cells leads to a donut structure around the parent cell densities, and that varying the phase of the septal closure with respect to the end-to-end Min oscillation of the parent cell leads to daughter Min densities varying around the donut. The ‘missing hole’ of the donut, i.e. the absence of daughter cells with the same Min densities as the parent cell, arises from the phase difference between the leading MinD cap-forming and lagging MinE ring-forming oscillations. Furthermore, we find that there is always a phase of septation timing that leads to non-oscillating daughters. We believe that this is a fundamental aspect of end-to-end Min oscillation: when the MinD cap is at one pole, the distal pole is stable. This should be a generic feature of all Min oscillation models. The robustness of the best percentage of oscillating daughters under changes in concentration, parameter variation, heterogeneous perturbations, model variation, dimensionality and stochastic effects supports this conclusion.

How might $E. coli$ achieve its (observed) negligible level of mini-celling? We see four basic possibilities. As suggested by Tostevin and Howard [19], the non-oscillating daughters could be rescued by rapid regeneration of Min concentration. This would require Min synthesis to be regulated in a cell-cycle-dependent manner. Because the average concentration of the two daughter cells equals their parent cell, rapid synthesis leading to recovery in one daughter cell would lead to a spike in overall Min concentration right after septation. However, there is no evidence of such fine-tuned regulatory control, or cell-cycle dependence, of Min concentration [25, 26]. Moreover, lack of adequate partitioning would give rise to substantial asymmetry of Min proteins in the two daughter cells that should be apparent in experimental studies—especially with the simple inducible promoters (not actively regulated) typically used in Min-GFP fusion studies [5–7, 23, 29, 30, 34, 35]. In our simulations we found that the fraction of the parent MinD and MinE in daughter cells can be as low as 15% and 25%, respectively. The lack of any reports of such large visible asymmetries argues against rapid Min regeneration.

The partitioning problem can be avoided if the Min oscillations ‘double-up’ before septation, leading to two
symmetric oscillations in the two halves of the parent cell. A closing septum would then maintain symmetric Min distributions in the daughter cells. Indeed, we were hoping to promote this effect with the introduction of cardiolipin patches at poles and septum—without success. While there has been one experimental report of a doubling of oscillation for deeply constricted cells [7], this must be approached with caution due to the difficulty of distinguishing partial from full septation. We never found any evidence for doubling up of oscillations in our simulations. In all cases, we found that oscillations continue until just before the end of septation. Indeed, the Min oscillation wavelength of ≈8 μm seen in filamentous cells [5] would suggest that it is difficult to spontaneously generate $L = 2 \mu m$ oscillations while significant connection between the two ends of the parent cell remains.

Distortion and/or disruption of the Min oscillation by the growing septum before septal closure might also lead to symmetric partitioning of Min between the daughter cells. We do find that MinD binding to the sides of the growing septum improves partitioning. This was evident by comparing the partitioning for a finite septation time ($t_r = 512 s$) with instantaneous septation ($t_r = 0$). In the latter case, no MinD can accumulate on the septum before the daughter cells are separated. This resulted in highly skewed Min distributions between the two daughter cells (results not shown). However, significant partitioning errors still occur with gradual septal growth. Moreover, no significant improvement in partitioning was observed when the MinD binding was enhanced at the mid-cell. We also found that Min oscillation was often temporarily disrupted in one daughter cell despite acceptable partitioning for oscillation in both daughters. The time required for recovery of steady oscillations was sometimes as large as 15 min. This is much larger than the dynamical time scale of FtsZ rings [22], though, as shown by Tostevin and Howard [19], stochastic effects may eliminate or significantly decrease the regeneration time of oscillations. Disruption of the Min oscillation in both daughter cells by the late stages of septation may therefore be a viable partitioning mechanism in vivo especially if the resulting uniform distribution of Min is sufficient to block septation [43] in the face of fast FtsZ dynamics [22] while the Min oscillation is being regenerated. However, in our model we did not observe disruption in both daughter cells even with enhanced MinD binding at the growing septum.

Finally, the cell may coordinate the septate closure with the Min oscillation. As seen in figure 1, there are a number of phases where both daughter cells oscillate after septation. As shown in figure 5(a), and illustrated in figure 6(a), most of those phases correspond to mid-cell MinD and MinE peaks. Triggered septal closure occurs at intervals. At these phases would always recover Min oscillation in both daughters. Such triggered septal closure could result from the participation of the C-terminal domain of MinC in FtsZ ring disassembly toward the end of septation [44]. Since septation occurs in δmin mutants [43], any such effect would have to accelerate septation rather than cause it. Narrow constrictions have been observed in cryoelectron tomography studies of Caulobacter crescentus [45], though too infrequently to indicate a significant septation pause. In E. coli, mutations of the N-terminal domain of FtsK lead to the stalling of septation at a very late stage with deep constrictions [46], leading to speculation about pores between the daughter cells before septal closure [47]. The triggered septal closure discussed here would only require a pause (or speed-up) of at most one-half period of the Min oscillation that could be lifted (or imposed) by the MinC at mid-cell.

The challenge lies in understanding how Min oscillations can persist or be regenerated in both daughter cells after septation, in the face of partitioning errors due to the end-to-end oscillation of the Min proteins. Without one or more of the additional mechanisms discussed above, we expect significant partitioning errors, leading to non-oscillating daughters, in all Min models. Experimental characterization of the Min oscillations during and after septation, and quantitative assessment of Min partitioning between the daughter cells will be invaluable in sorting out which of these four partitioning mechanisms, or what combination of these four mechanisms, plays a role in E. coli. We believe that the last mechanism, of triggered septal closure, is most likely the dominant mechanism in vivo. Reproducing figure 3 from experimental images of newly septated cells should be straightforward if both MinD and MinE have distinct fluorescent tags (see, e.g., [29]). The average of each fluorescent signal of the two daughter cells can be used to independently scale the corresponding MinD or MinE signal, without the need for calibration even in the face of photo-bleaching. Non-regenerating mechanisms of partitioning, such as septal triggering, would lead to a ‘double-bar’ pattern of MinD versus MinE densities in the daughter cells (looking like _) rather than the connected donuts seen in figure 3.

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Glossary

1d. one dimensional
3d. three dimensional
RMS. root mean square
CL. cardiolipin

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