I. INTRODUCTION

[I need a lot of references here!!! (And the writing is just terrible)] It is vital that the process of bacterial cell division result in a single nucleiod in each daughter cell. The cell must avoid minicelling, or splitting into daughter cells with lopsided volumes. One of the mechanisms the cell employs in order to avoid this is to allow a long FtsZ polymer chain to develop on the cell wall in the center of the cell. This chain acts as a guide for the cell splitting . Huang et all have shown in simulation that a system of Min protein interaction within the cell will lead to a natural oscillation of the MinC protein, which exhibits an aversion to the FtsZ polymer, from one cell end to the other that will leave the center free of any build up of MinC. This will allow for the PtsZ chain to develop in the center and not at the ends, where the two nucleiods are housed. The interaction takes place between MinE,MinD, and MinC, which naturally associates with MinD.

Mannik et all have shown that the formation of irregular cell shapes adversly effects the Min system's ability to maintain their regular oscillatory behavior (cramming into spaces).

A. What is the MinD system and why is it important?

B. How proteins move in cell

II. METHODS AND INITIAL CONDITIONS

The model for the behavior of the MinD and MinE proteins inside the cell implemented the same set of 5 reaction-diffusion equations described in the paper by Huang et al (equations 1, 2, 3, 4, and 5). A 3d grid was constructed in cartesian coordinates with a grid spacing of .05 μm. From there, we were able to define a cell shape on the grid, and solve the reaction-diffusion equations numerically to observe the time evolution of the MinD and MinE concentrations inside the cell.

Our simulation used the same diffusion constants and reaction rates as Huang et al, which are

$$\mathcal{D}_D = \mathcal{D}_E = 2.5\mu\text{m}^2 \ / \ \text{sec},$$
$$\sigma_D^{\text{ADP} \rightarrow \text{ATP}} = 1/\text{sec}, \sigma_D = 0.025\mu\text{m/sec},$$
$$\sigma_{dD} = 0.0015\mu\text{m}^3/\text{sec},$$
$$\sigma_{de} = 0.7/\text{sec}, \sigma_E = 0.093\mu\text{m}^3/\text{sec}.$$

To test our computational model, we implemented a pill shaped cell, and tested using the same cell parameters as Huang et al, which were a radius of 0.5 μm in the middle and at the spherical endcaps, and two different cell lengths of 4 μm and 10 μm. We found the same type of oscillations as in their paper using these initial conditions, verifying that our model works as intended. Below are snapshots of MinD and MinE concentrations at 5 second timestamps in the 4 μm cell:

[insert 5 second time stamps of 4 μm sim]

We then began to define other, non-traditional cell shapes for the purpose of modeling squished and perturbed E. coli cells, which were created experimentally in Mannick et al. To achieve this, we went with a cartesian lattice rather than the cylindrical lattice used in Huang et al's simulations, as it allows for more flexibility in defining the cell shape. Some of the cell shape models included a flattened pill (stadium shape), an ellipsoid, a spherical cell, and various randomly generated smooth shapes, such as those in the figures below.

[insert memf print of 2-3 cell shapes]

To interpret the results, we generated several different plot views of the printed simulation data. These plots included a time averaged view of the protein densities in the cell; a plot tracking the location of protein concentrations that were global maxima in space and local maxima in time; and an animated view that showed the actual dispersion of protein concentrations in the cell over time.

A. Mathematical Model

III. SPECIFIC RESULTS

A. Pill Shape

[Be more exact about what exactly Nd is versus nATP, in terms of the unit and dimensions. The plotting may need to be changed] Figure fluctuations at a point in space adjecent to a polar wall. At each collection of peaks the proteins reach their zenith in an order that agrees with the qualitative picture described by Huang[**?**], except for nADP peak. The peaks start with a maxima of ATP-MinD accumulating at the walls **[Need a better way to refer to compounds]**. This peak is followed by a peak in Nde, or ATP-MinD-MinE, as the cell is converted on the wall from the former to the latter compound. As this compound splits apart and leaves the wall we see a peak in nE, or MinE in the cytoplasm. This is then followed by a broader peak in nATP, or the MinD-ATP compound, as minD-ADP is (changed but I forgot the name for it) into minD-ATP in the cytoplasm. The minD-ATP naturally diffuses away from the pole, which is shown by the broad nature of this peak. All of these peaks fit the qualitative picture except for the sharp MinD-ADP peak. One could except that it is a sharp peak, meaning that the MinD-ADP proteins do not last in the cytoplasm for very long before they are converted (once again forgot the name) into MinD-ATP.

The location of the peak in the time dimension is troubling, however, since that we would expect it to occur just after the peak in Nde, since the wall-bound MinD-ATP-MinE proteins are the ones that split up and leave the wall, creating both the MinE and the MinD-ADP. One would expect to see the minD-ADP peak to coincide in time with the minE peak, but it instead coincides with the wall-bound MinD-ATP-MinE peak. (Although you can maybe sort of convince yourself otherwiase, really looking at it).

The theory states that the aversion of the FtsZ polymer to the MinC protein is responsible for the FtsZ polymer setting up in the center of the cell as opposed to at the cellular poles. The MinC protein in turn natrually associates with the minD protein that is modelled in Huang's differential equations. **[look this up and write this again]** The theory is dependent on there being a significant difference in protein density between the center and polar regions. It is worthwhile examining this difference in detail. Figure fluctuation over time at a point adjacent to the polar cell wall and at a point adjacent to the cell wall in the center region of the cell. The different proteins show different relationships between their maxima and minima. The MinD-ADP show sharp spikes at the poles and much smaller oscillations at in the middle. The values at the poles are always greater than those in the middle, and the polar peaks exhibit densities that are roughly 2.5 times greater than the maxima in the center (**[this factor and the following factors will be put into a table of comparisons for each protein and for the different cell sizes]**). The MinD-ATP densities show a very different trend. For these it is the center density that is almost always greater than the polar density. The difference in density at the pole versus the middle is a factor of roughly .85 (once again we'll do this more officially in a table). The MinE is similar to the MinD-ADP comparison. It shows a difference in maxima by a factor of roughly 2. The MinC protein is associated with the minD protein, so perhaps the most important camparison is between the nfl-MinD (MinD protein in all its forms) at the ends and in the center of the pill. This shows sharp spikes at the pills and a maxima difference factor of roughly 1.25. **[I'd like to analyze further what this means for the FtZ polymer. Would a difference like this really have a big effect? What sort of effect should it have, looking at experimental data? One thing is that Mannik (is it Mannik?) genetically deletes the MinC protein and they get 73 percent proper cell division. It really would be good to do a more extensive analysis here, referencing what other papers say about this.]**

It would be good here to add the time map plots and discuss the idea about the proteins spending most of their time in the center of the cell.

Figure **??** also shows that the middle density oscillates at a frequency that is twice that of the polar regions, which is to be expected considering the symmetry of the center compared to the that of the polar regions. Also, the difference between density maxima and minima each oscillation is smaller for the middle points than for the polar points. This is evident from simply watching the simulation movies - the fluctulations are more extreme in the polar regions.

Add a table here that shows the period of oscillations versus the cell dimensions. Do the mathematical solution of the differential equations for an infinite long cylinder with different widths to see how fast the mxima move and compare (Dr. Roundy says that making the radial speed infinite would help.

B. Randst shape

1. *Randst-96-Star*

2. *Randst-97-*

3. *Randst-98-Actually Random*

4. *Randst-99*

IV. INTERPRETATION OF DATA

V. CONCLUSION

APPENDIX

VI. BELOW ARE NOTES FOR THE WRITING

VII. INTRODUCTION

[I need a lot of references here!!!] It is vital that the process of bacterial cell division result in a single nucleiod in each daughter cell. The cell must avoid minicelling, or splitting into daughter cells with lopsided volumes. One of the mechanisms the cell employs in order to avoid this is to allow a long FtsZ polymer chain to develop on the cell wall in the center of the cell. This chain acts as a guide for the cell splitting process. Huang et all have shown in simulation that a system of Min protein interaction within the cell will lead to a natural oscillation of the MinC protein, which exhibits an aversion to the FtsZ polymer, from one cell end to the other that will leave the center free of any build up of MinC. This will allow for the PtsZ chain to develop in the center and not at the ends, where the two nucleiods are housed. The interaction takes place between MinE,MinD, and MinC, which naturally associates with MinD.

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A. What is the MinD system and why is it important?

-Systm of proteins in E.Coli and other cells. -Theorized to be instrumental in cell citokenisis. Reference experiments

B. How proteins move in cell

-Reference experimental showing proteins oscillating -Reference theory showing difEQ model shows oscillations -Reference Mannik shoving into crevices. -Worthwhile studying effect of walls shape on the movement of cells (Sign post of what to expect from this paper)

VIII. METHODS AND INITIAL CONDITIONS

A. Mathematical Model

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To interpret the results, we generated several different plot views of the printed simulation data. These plots included a time averaged view of the protein densities in the cell; a plot tracking the location of protein concentrations that were global maxima in space and local maxima in time; and an animated view that showed the actual dispersion of protein concentrations in the cell over time.

IX. SPECIFIC RESULTS

X. PILL SHAPE

Pill Normal section - Our goal with this project was to test whether or not the computational model developed by Huang et al was consistent with the newer experimental results (squishing E Coli) produced by Mannick et al. We generally see that:

- Protein concentrations bounce around to areas with high curvature. - - example: nflD randst 1 6 6 99 tri-polar zones with tri-polar concentrations - - nflE the same - There is some time delay between where different protein types appear.

The pills with larger cylindrical widths, 4.00 3.00 (the wider pill shapes) exhibit oscillations with maxima reached on either side (half period times) 30s, 70s, 110s, so first half oscillation occured in 30s, the next two in 40s

The 4.00 2.00 pills exhibit a similar pattern, but max out at times 25s,55s,85s,115s, so thirty seconds each half period. Seemed once again that the first oscillation had a higher max density, then settled down. I wonder if extremely increasing the starting condition density lopsidedness will still yield a settle down pattern with the same max densities? Is this dependent on shape/size?

The 4.00 0.50 pill seemed to show oscillations of 20 second half periods very consistently. Density maximum did not seem to lose intensity. Seemed to be the same each oscillation.

Also with this, when look at the periods and max denisty/min density ratio, consider the size dimensions of the pill shape and see if can see a mathematical relation.

The nflE 4.00 0.50 shows a very large difference in center highest density versus pole highest density (during a maxima). Is this perhaps the protein that's more important.

Looking at the extrema plots - one very interesting thing is the 4.00 2.00 ATP extrema, which shows the extrema only in the center of the cell. The other proteins for this shape show the extrema to be at the ends. Also, it

seems the 4.00 3.00 cell shapes for these plots are missing. Very interesting to see if there is a certain protein that has its maxima in the center of the cell, while the others have maxima elsewhere. Tells a story that could maybe relate to the other shapes.

Also, try starting the cells with density only in the corner. Now the extrema go down the center of the cell, see if there would remain a lopsided nature of the oscillations if you started it like this instead.

The very long cells have very long periods

The time map plots seem inconsistent in that some show the highest densities on the poles, some in the centers, some on just one pole. For these want to run starting from a time when the proteins are evenly spread out (so between two maxima) and stop at a similar pointe at the end.

The time map plots that I believe though sometimes show that the max density time-wise is actually in the middle of the cell! Make sure we have a good, longer view of this being true.

Important

Pill Short - -Know how short is too short

Randst 99 -

XI. RANDST SHAPE

whats the difference between the extremes in density at different places (like the density max at the poles and at the rims in the center). Still need to do this.

There are sudden bursts in the nflE protein plots, at the poles. Their density maxima build very quickly then diffuse more slowly.

A. randst-96

The star shape (randst-96) Shows oscillations in nflD horizontally, two poles to two poles. There is sometimes a small amount of lag between the upper maxima moving horizontally and the lower. Half periods take roughly 25s. Dimensions are roughly 5.00 by 5.00? Check this. The nflE short bursts do develop lag between when the top and the bottom go off. Should coordinate this with the nflD lag.

Tried to see if there is a time correlation between nflE and nflD but the maxima seem to appear in the poles at roughly the same time.

Watched Nd and nE simulations next to each other at same time. Both have maxima that build up right at the walls (in the corners) and then subside. It's clear that the nE density bursts appear directly after the Nd bursts. The Nd bursts are subsiding as the nE bursts are rising up. The Nd reaches a time maxima just before the nE. This is true in each corner, so that when the maxima are lopsided top to bottom - when the top right corner maximizes first, say, the interplay between nE and Nd remains very clear in those corners where and when maxima occur.

Watched nATP and nADP together. nATP maxima seem to follow slightly after nADP maxima. This is not surprising since in rotation nATP follows after nADP. nATP maxima is more spread out - inbetween pole maxima there is more spread out maxima in the center. This should show itself in the time map plotting. About this - the percentage difference seem to be the same between the non-max places and max places, roughly, its just that the nATP seems to have a max region that covers a wider area throughout the oscillation (or at least in between the maxima points in the oscillation).

Also watched the Nd next to the nATP. The Nd maximize more extreme in the corners up against the walls. The nATP density follows the Nd maxima, it looks like the nATP maxima follows the Nd. So if the Nd appears somewhere (in a corner) then the nATP will travel there to follow.

B. randst-97

Randst 97 nflE starts with small maxima, not much difference at all, then actually builds to high maxima at the poles.

C. randst-99

Randst 99 (sort of triangle) is roughly dimensions of 3.5 by 3.5? nflD oscillations appear to be half periods of 25s as well. Maxima appear at the poles and in the interim there are weak maxima in center pole.

D. randst-98

Funny randst shape 98 shows nflD oscillations of about 30s or so.

nADP and nATP side by side. nADP maximizes in the corners right before the nATP maxima follows. Makes sense looking at equations. Once again the nATP maxima is more spread out, where maxima in nADP appear more just at walls.

Nd and nATP side by side. Nd maximizes at walls and the nATP moves in to follow it

Nd and nE side by side. Nd maximizes in corners and then the nE also maximizes in the corners. The nE maxima appear in these sort of quick bursts in the corners, along with a slower broader movements away from that corner after the burst and into the next, where another sharp burst occurs. The Nd bursts occurs after the Nd as subsided in that corner, and really by the time the burst maximizes, the Nd is already on its way over and starting to build on the otehr side.

Randst nflD doesn't show much oscillation at all, but we start it so that the density is not max at the pole.

Randst 98 -
Randst 97 -
Randst 96 -
Triangle -

XII. INTERPRETATION OF DATA

-Discussion of conceptual reasons of why we see what we see -Plots that are more interpretive (area-rating) - Some sort of predictive claim?

XIII. ANIMATE?

XIV. CONCLUSION