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Pattern formation in *Escherichia coli*: A model for the pole-to-pole oscillations of Min proteins and the localization of the division site

Abstract: *The positioning of the division plane is one of essential processes that allow a proper cell division in all organisms. In E.coli this plane is determined by a polymeric ring of the FtsZ protein. The site of the ring assembly is controlled by the Min system that suppresses any FtsZ assembly at non-central position. The Min proteins perform a highly dynamics behavior, with a constant pole-to-pole oscillations during the cell cycle. In this project, we build a model using the equations described by Meinhardt et al. that reproduce the behavior of the system. We reproduced the main features of the system. However, the model we use had a lot of simplifications and requires some assumptions. Although, it was consistent with experimental results. Several improvements could still be done to have a better fit to the experimental data. However, even with such a simple model we were able to introduce new features such as chromosome segregation performed by MinD oscillations.*

Introduction

How bacteria find its center to localize the division machinery is a long standing question. All species of bacteria evolved diversified, more or less complex systems to regulate this crucial element of their cell cycle. The article [ref] that leads our work is trying to answer this question by modeling the Min pole-to-pole oscillations that occur in E.coli.

The Min system in E.coli is characterized by a highly dynamic behavior. A polymeric ring made out of protein FtsZ positions the division plane. The assembly site of FtsZ is controlled by the **Min system**: MinD is an ATPase that self-assembles on the membrane, and then it recruits MinC (inhibitor of FtsZ assembly). It recruits as well a MinE protein that forms a ring. Aditionaly, MinE releases MinD from the membrane. Thus, as soon as the MinD reaches its maximus, recruited MinE triggers a shift of MinD to the opposite pole. The system is resulting in **pole-to-pole oscillations** of MinD/C. The concentration of MinC is the highest at the poles, forcing FtsZ assembly to aggregate inly in the middle of the cell (Fig.1). In the

publication [ref] which results we were supposed to reproduce, the authors define a set of equations that

describe the behavior of the model (Fig. 2). With that model, they were able obtain results close to the experimental data (Fig. 3).

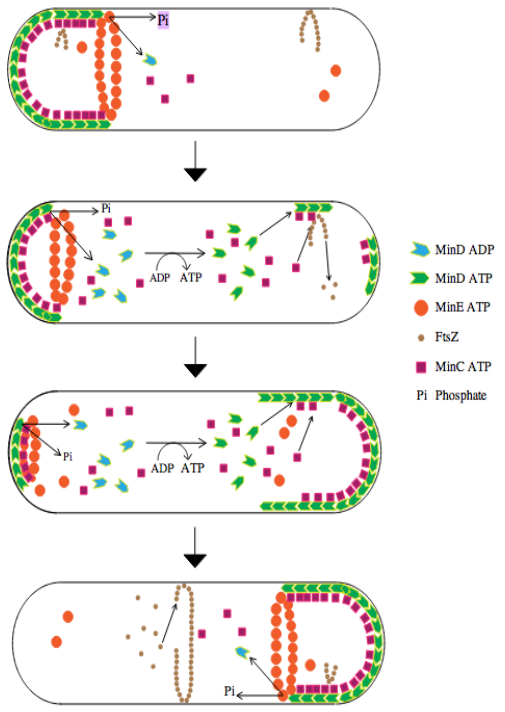


Figure 1: *Schema of the pole-to-pole oscillations of MinC, MinD, MinE and FtsZ proteins in E.Coli*

$$\frac{\partial D}{\partial t} = \rho_D d(D^2 + \sigma_D) - \mu_D D - \mu_{DE} DE + \mathcal{D}_D \frac{\partial^2 D}{\partial x^2}$$

$$\frac{\partial d}{\partial t} = \sigma_d - \rho_D d(D^2 + \sigma_D) - \mu_d d + \mathcal{D}_d \frac{\partial^2 d}{\partial x^2}$$

$$\frac{\partial E}{\partial t} = \rho_E e \frac{D}{(1 + \kappa_{DE} D^2)} \frac{(E^2 + \sigma_E)}{(1 + \kappa_E E^2)} - \mu_E E + \mathcal{D}_E \frac{\partial^2 E}{\partial x^2}$$

$$\frac{\partial e}{\partial t} = \sigma_e - \rho_E e \frac{D}{(1 + \kappa_{DE} D^2)} \frac{(E^2 + \sigma_E)}{(1 + \kappa_E E^2)} - \mu_e e + \mathcal{D}_e \frac{\partial^2 e}{\partial x^2}$$

$$\frac{\partial f}{\partial t} = \sigma_f - \rho_F f \frac{F^2 + \sigma_F}{1 + \kappa_F F^2} - \mu f + \mathcal{D}_f \frac{\partial^2 f}{\partial x^2}$$

$$\frac{\partial F}{\partial t} = \rho_F f \frac{F^2 + \sigma_F}{1 + \kappa_F F^2} - \mu_F F - \mu_{DF} DF + \mathcal{D}_F \frac{\partial^2 F}{\partial x^2}$$

Figure 2: *Equations used to model the Min system in E.coli [1f]*

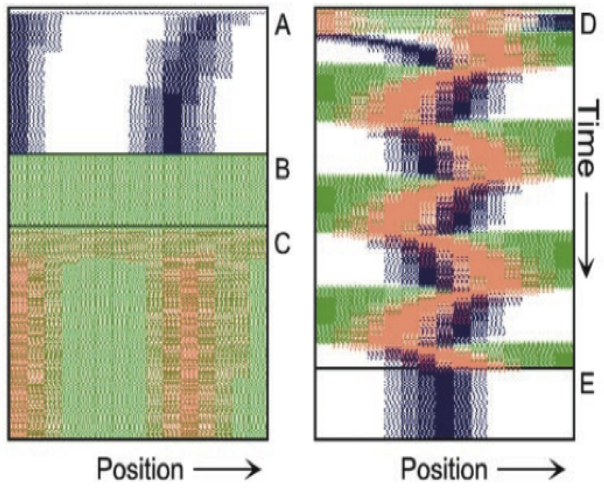


Figure 3: *(fig 1 from [1]): A: System with only F and f, B: system with only MinD/d C: MinE/e alone. D: complete model running for x=15 E: FtsZ Ring remains in place after switching off MinE/e and MinD/d.*

One of the most fascinating features of the system is that fact that the patterns are self-organizing. We can observe it well with the model described by H. Meinhardt [1]. From a mix of proteins of equal concentrations, after a short noise period, pattern is raised by itself, just thanks to protein interactions and the way they are defined.
With this model, they were able to reproduce the pole-to-pole oscillations presented in Fig 1, (Fig **3**)

(Watchthe movie available in supplementary materials[ref]: http://www.eb.tuebingen.mpg.de/uploads/pics/min-ini.gif)

Our goal was to reproduce the model from this article, using the same set of differential equations presented in Fig 2 and then to modify/improve the model by adding or changing some features.

Report

I-Reproduce the model used in the paper

I-1 Implementation of the ODEs in Matlab: Euler method

In order to reproduce the article results, we started by implementation of the differential equations of proteins FtsZ, MinE and minD to Matlab. At the beginning, we wrote the equations only for FtsZ, bounded and unbounded using Euler method.

This method is highly useful in our case because, in contrast with Matlab ode solver, we can control the function output at each time step - iteration (that in theory should be infinitely small, but in our case we use just Δt equal to 1) through numerous iterations. At each iteration, we obtain a row of a matrix. The columns are the positions along the length. We started with the measure of the FtsZ concentrations at each of 20 positions in space along E.Coli. The visual output helps us to quickly assess the simulation result. Inspired by the figures from article [ref], we represent the position along x axis, iterations along y axis and we use the densities of pixels to express the concentration and color scale to visualize them. It is a referential scale, warm colors (red) are for the highest concentrations: cold colors (blue) are for the lower concentrations. Parameters used are the same as in the article [ref]: $\mu_F = \rho_F = 0.004$; $\kappa_F = 0$ or $= 0.2$; $\sigma_F = 0.1$; $\mu_{DF} = 0.002$; $\mathcal{D}_F = 0.002$; $\sigma_f = 0.006$; $\mu_f = 0.002$; and $\mathcal{D}_f = 0.2$. For Eqs. 3 and 4: $\rho_D = \mu_D = 0.002$; $\sigma_D = 0.05$; $\mu_{DE} = 0.0004$; $\mathcal{D}_D = 0.02$; $\sigma_d = 0.0035$; $\mu_d = 0$; and $\mathcal{D}_d = 0.2$. For Eqs. 5 and 6: $\rho_E = \mu_E = 0.0005$; $\sigma_E = 0.1$; $\kappa_{DE} = 0.5$; $\kappa_E = 0.02$; $\mathcal{D}_E = 0.0004$; $\sigma_e = 0.002$; $\mu_e = 0.0002$; and $\mathcal{D}_e = 0.2$. We are going to discuss them in the Discussion part.

At first, we neglected the effects of noise and diffusion. We obtained a graph showing increasing concentration of the FtsZ unbound over iterations homogenously (Fig. 5). The initial concentrations at each position were equal to 1. We used fixed parameter values and we replaced missing concentration of MinD by 0. Thus, we observed accumulation of FtsZ in the cytoplasm with time. There is no forces that would trigger changes in FtsZ positioning. It just remains at its position and with production rate superior to degradation rate, the concentration is grooving. This is exactly what we would expect.

```
noiseF= F(x)*(1+randi([-100 100],1,1)*0.0001);
prodF=roF *f(x)*(((F(x)*F(x))+sigF)/(1+kF*F(x)*F(x)));
degF=miuF*F(x)+miuDF*D(x)*F(x);
F(x)=noiseF+(prodF-degF+dF(x))*dt;
```

Figure 4. *Equation of FtsZ (dF/dt) from Fig. 2 in the Matlab syntax. It has been divided into functional entites: production (prodF), degradation (degF), noise (noiseF) and diffusion (dF) as a complete eqation of F(x), where x is the postion ialong E.coli. Here, starting dF=0, noiseF=0, D(x)=1, other parameters as in the article [ref].*

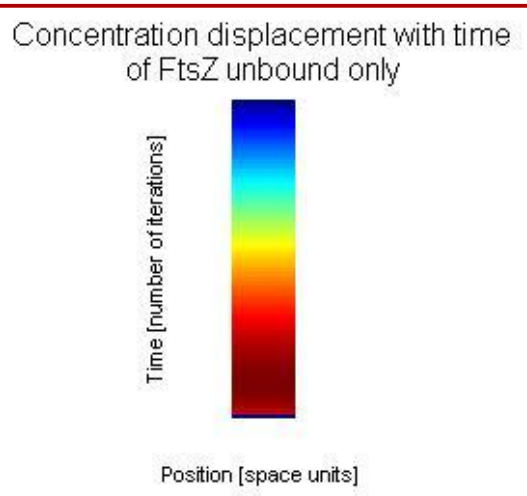


Figure 5. *The FtsZ only pattern without diffusion, for 9991 iterations and 20 space units which corresponds to 3 μm (1 space unit=1.5 μm), colors reflect concentration intensity.*

Subsequently, we added next element of the equations: diffusion effect.

It was modeled with classic equations of diffusion.

dF(x)=DifF*(F(x-1)+F(x+1)-2*F(x));

With boundary conditions:

min

dF(x)=DifF*2*(F(x+1)-F(x));

max

dF(x)=DifF*2*(F(x-1)-F(x));

and added to the 'for loop'.

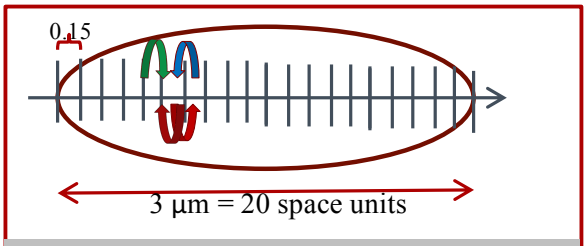


Figure 6 *Graphical illustration of division of E.coli and diffusion model used*

Due to the diffusion the molecules diffuse with the speed indicated by diffusion coefficient on the right and on the left of current position (-2*F(x)). There are also molecules diffusing from neighbor positions (+F(x-1)+F(x+1)). Following the assumption of the article [ref] authors, we considered that the cell membrane is impermeable and molecules cannot diffuse outside the cell. Therefore, at the extreme positions (1 and 20), we consider only the diffusion into cell center direction, however, at a double rate.

In order to observe if the implementation of the diffusion effect worked well, we impose high concentrations at medium position (10) and zeroes at all other positions. We can notice then how the concentration spread along the cell over iterations. This exactly what we expected from diffusion effect added to the equation.

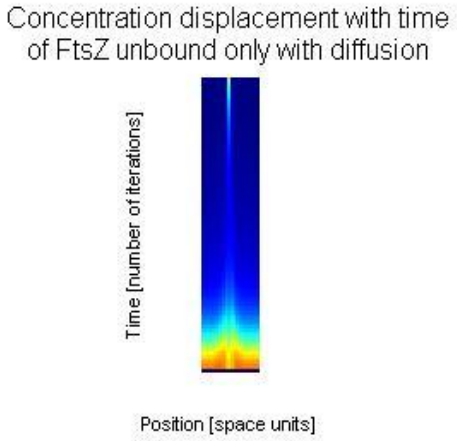


Figure 7*. The FtsZ only pattern with diffusion, for 9991 iterations and 20 space units which corresponds to 3 µm (1 space unit=1.5 µm), colors reflect concentration intensity.*

Then we could add the last element, noise. By generating little random numbers and adding it into concentration at each position, we reproduce biological stochasticity in protein production and degradation. We used guidelines from the article [ref], that the noise should be a random fluctuation of less than 1% of protein concentration. However, it is not précised how it is implemented. We just multiply random number from the interval (-0.01 0.01) by the computed protein concentration. We successfully reproduced Fig 1 from the article (Fig. 8).

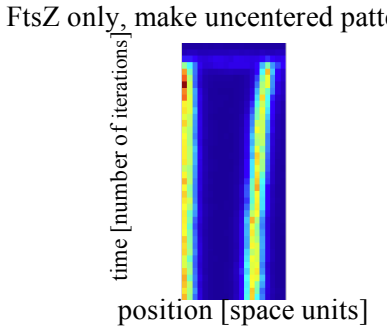


Figure 8. *The FtsZ only pattern with diffusion and noise, for 20000 iterations and 20 space units which corresponds to 3 µm (1 space unit=1.5 µm), colors reflect concentration intensity. (Fig. 1A from the article [1])*

By simulating MinD (Fig. 9) only we observed that it does not make oscillations by itself. Its distribution in the cytoplasm and in the membrane is quite homogeneous.

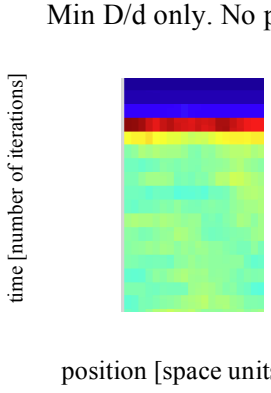


Figure 9. *MinD only does not form any pattern, for 20000 iterations and 20 space units which corresponds to 3 µm (1 space unit=1.5 µm), colors reflect concentration intensity. (Fig. 1B [1])*

When the MinE precursor production switched on (σe =0.002). MinE on its own would make a stable pattern. However, from the plot (Fig. 10) we can observe that this pattern is not really well defined.

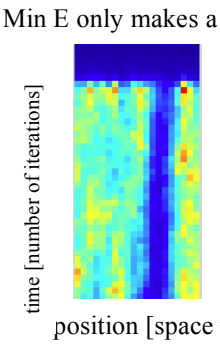
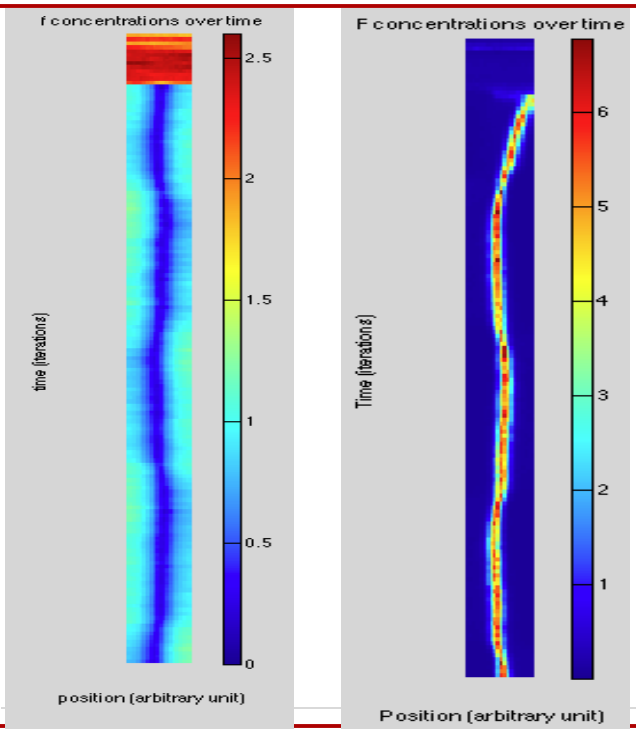


Figure 10. *MinE only forms a pattern, for 20000 iterations and 20 space units which corresponds to 3 μm (1 space unit=1.5 μm), colors reflect concentration intensity. (Fig1C[1])*

I-2 Complete model

It took us a lot of time to make all equations work because they all interconnected. We had to rewrite the code many times, changing just the text formatting. We did not identify the initial problem; we did not modify any of equations. Finally, we managed to obtain the output without errors with nice protein concentration oscillations (Fig.11)



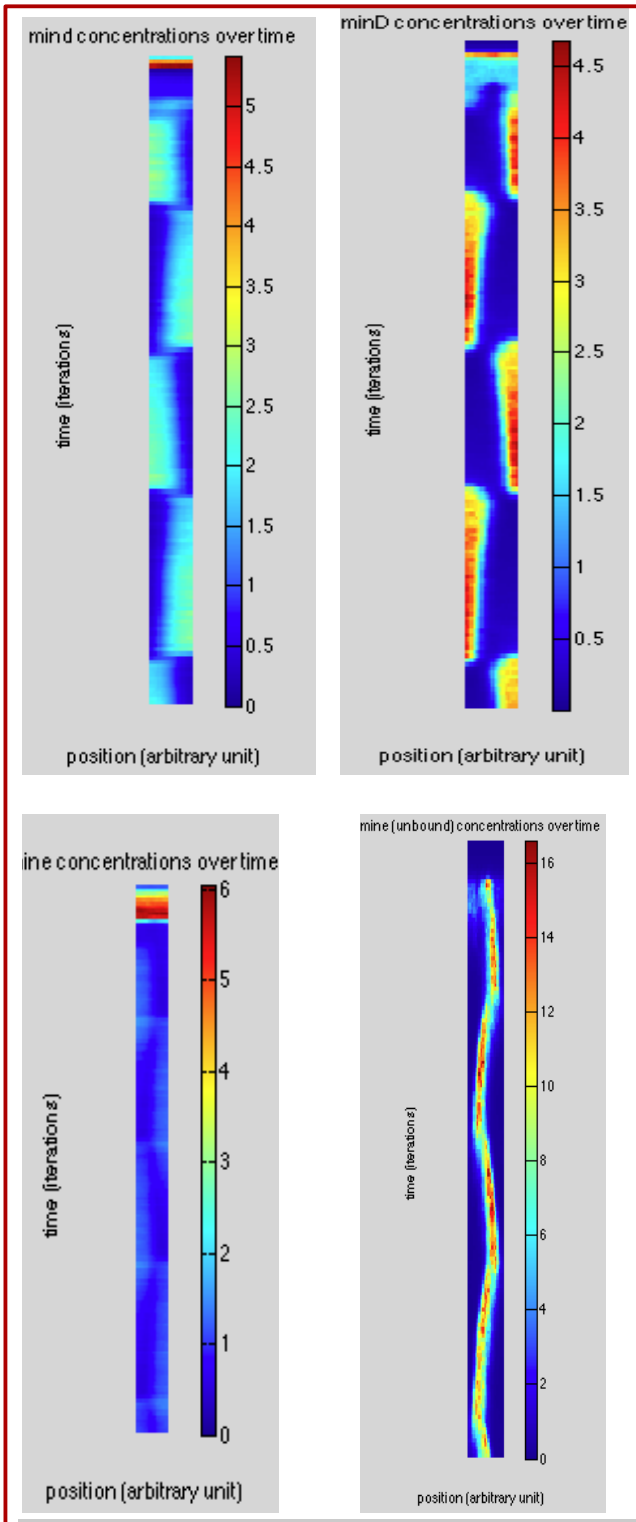


Figure 11*: Evolution of the concentrations of the different compounds of the system over time. All compounds of the system, represented one by one: f, F, d, D, e and E.*

We plotted all the protein profiles separately. Here, the graphs show how each compounds of the system evolve over time. We can see that we have nice MinD pole-to-pole oscillation that leads to the center positioning of FstZ. As expected, where the concentration of MinD (actually MinC) is the lowest (center), concentration of FtsZ is the highest. FtsZ by the antagonism with MinC is forced to stay only in the center. Then, FtsZ ring is the factor that initiates E.coli membrane division by contracting. Furthermore, MinD oscillations would not be possible without MinE which recruited by MinD causes its dissociation from the membrane and causes its shift to the opposite pole. All those events can be read from the plots (Fig. 11). It illustrates well the biological system described in the literature [1].

Interestingly we can see that the system needs some time to setup the oscillation pattern. The first

Then we proceeded to reproduce the next figure from the article [1], 1D. We plotted all the proteins, and then superposed them to see better proteins behavior regards each other with longer iteration time. In the article [ref], cycle', it is not précised though how this term is defined. The authors [1] refer as the full MinD oscillation time 50s what corresponds in their case to 80000 iterations.

If we consider the full MinD oscillation cycle as the time that takes MinD when it is at one pole to shift to the other pole and then go back, in our case it took around 20 000 iterations, so one iteration corresponds to $2.5*10^{-3}$s. We do not know where this dissonancy between the computed times comes from, probably the given numbers are from the E.coli divided in 15 space units. Therefore, we consider it is not very important difference as the general pattern of protein concentration is well reproduced.

Subsequently, we carried on with representation of other figures from the article [1 (Fig. 12)]. After 70 000 iterations of the complete system including FtsZ, MinD and MinE we observed FtsZ positioned in the center and oscillations of Min proteins, then we removed MinD (σd = 0) and MinE(σe = 0), during next 20 000. FtsZ still remains in place. MinD disappearance has no impact on the established FtsZ pattern. It may signify that once the center found, FtsZ does not need Min proteins any more to effectuate cell division.

FtsZ (red), MinD (green), MinE (blue)

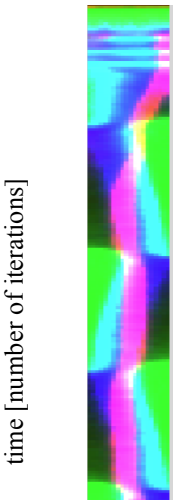


Figure 12. *FtsZ, MinD and MinE plotted together in red, green and blue respectively, for 80 000 iterations and 20 space units which corresponds to 3 μm (1 space unit=1.5 μm) (Fig1D [1])*

FtsZ (red), MinD (green), MinE

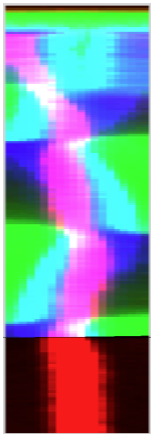


Figure 13 *. FtsZ, MinD and MinE plotted together in red, green and blue respectively, for 70 000 iterations and 20 space units which corresponds to 3 microm (1 space unit=1.5 microm), then for subsequent 20 000 iterations MinD and MinE was switched off, in these conditions FtsZ remains in place (1E[1])*

I-3 Growing and division

Next question that we tried to answer was: what is protein 'behavior' after the division in our model. Does FtsZ can find the center in the growing cell? Thus, we modified the code to observe protein concentration in a growing E.Coli after division. We set the initial length after division to 10 space units (half of the one we used before). We replaced inexistent part with concentration equal to 0 (black). After 1600 iteration time step E.Coli grows in length by 2 space units unilaterally till it reaches 20 space units (Fig. 14). Then the bacteria can divide again. As in the article [ref], we could observe that after separation into two parts, MinE waves and the oscillations form side to side of MinD are reestablished fast.

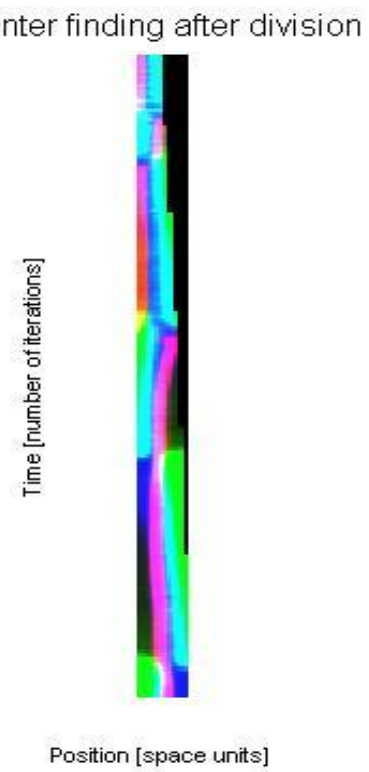


Figure 14. *After division the central position of the FtsZ signal is restored in a growing cell; number of iterations=106000, elongation of 2 units after 16000 iterations, length after division=10 space units, maximal bacterial length = 20 space units. (Fig. 2 [1])*

Inspired by the article [1], we also made E.Coli grow bigger than 'normal', up to 32 space units. With long enough iteration's number, since the cell reaches 30 space units, we notice the separation of FtsZ ring that is following MinD and MinE movement (Fig. 15). We can suppose that it is a plausible division moments. It means also that in our model cell has its maximal length. When it is exceeded bacteria cannot divide anymore in the center because two or more FtsZ rings are formed. This result has been confirmed in a wet lab [1].

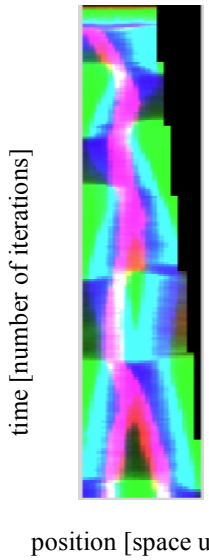


Figure 15*. Center finding and division. T=106000, step=16000, x=32 (Fig. 3 [1])*

I-4 Testing different parameters

Inverse relationship of the MinD and MinE concentrations on oscillation frequency: playing with parameters values.

The model we used strongly suggests that the MinD oscillation frequency is inversely related to the MinD/MinE ratio in the cell, and this by a direct consequence of the assumed interaction.

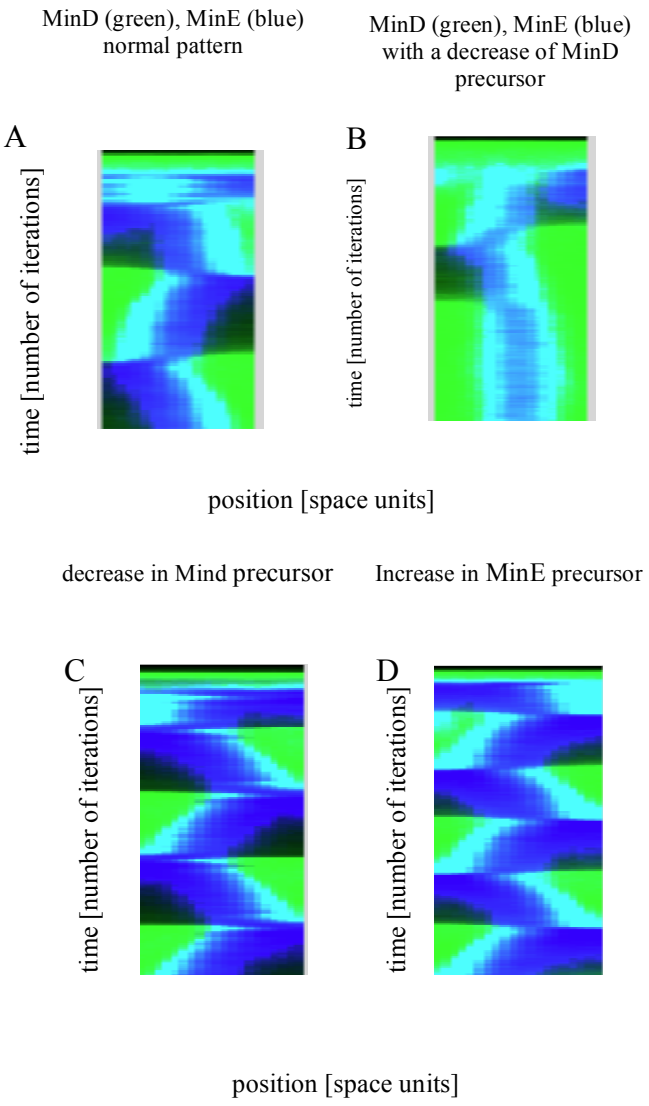


Figure 16. *MinD and MinE with changed parameters. A.normal pattern B. sigmae from 0.002 to 0.004 C. sigmae=0.001 D. sigmad from 0.0035 to 0.002 (Fig. 4l [1])*

In order to see that effect we changed the parameters values of the system (as the authors did in the Fig 4 [1]). Increases of the MinE precursor production (Mine) lead to a higher oscillation frequency (Fig. 16B) an inversely a decrease leads to lower oscillation frequency (Fig. 16C).Finally we decrease the MinD precursor's synthesis, leading to more rapid oscillation (Fig. 16 D).

All of these observations are consistent: if we increase the MinE concentration, it will result in an accelerated removal of MinD, leading to faster oscillations. Inversely if we had more MinD, more molecules accumulated in the tip and it takes longer to remove them. We managed to reproduce all figures from the article. The figures we obtained with matlab correspond perfectly to those in the article, what means that the proposed model is easily reproducible.

II-Research project

II-1 Considered project extensions

After reproducing the results of the paper, we thought about several ways to improve our model:

Chromosome segregation by the E.coli Min system [2]

It is a very recent publication (13/09/10). It is a very Interesting article showing experimentally and by modeling that the Min system play a role in the segregation of the chromosomes during the mitosis. It could be a good occasion to implement our model with a phenomenon of biased diffusion.

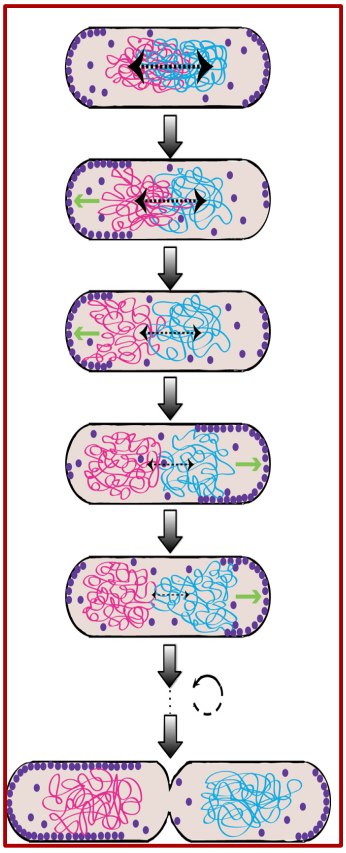


Figure 17: *Proposed model of chromosome segregation by the Min system. The cartoon shows a slowly dividing* E. coli *cell with only two duplicated chromosomes over time (from top to bottom). For simplicity, only MinD (violet dots) and only one DNA strand are shown. Entropic repulsive forces that move chromosomes apart are shown as black arrows pointing toward the poles, while the action of the Min system that creates an oscillating gradient of chromosome tethering sites is shown as green arrows pointing toward one pole during one cycle of the oscillation.*

Temperature Dependence of MinD Oscillation in *Escherichia coli:* Running Hot and Fast[3]

In this option we will look at environmental factors, mainly the temperature and the response of the system in the time.
We could also see how the production rates change according to the composition of the media and how it affects the oscillation, and therefore the division process. We could implement this by using Arhenius laws, for temperature dependence of the reaction rate.

Noise-induced Min phenotypes in *E. coli* [4]

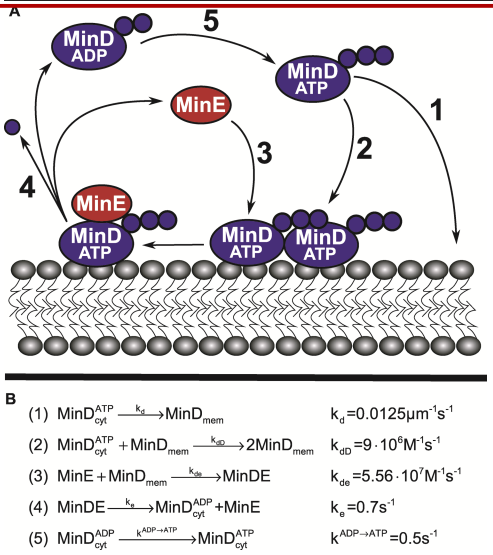


Figure 18: *precised intermediate reactions that we would like to implement*

Here we would like to implement detailed step of the reaction by using the equations proposed in the models for the intermediary step.
The final goal would be to make the model more precise in the time according to the E.Coli division cycle.

Implementation 2D and 3D diffusion
Our Model is using only one dimension diffusion, obviously an important features that could be implemented is a 2D (and later 3D) diffusion, allowing us to be closer to the reality (we can see E.coli as a cylinder).

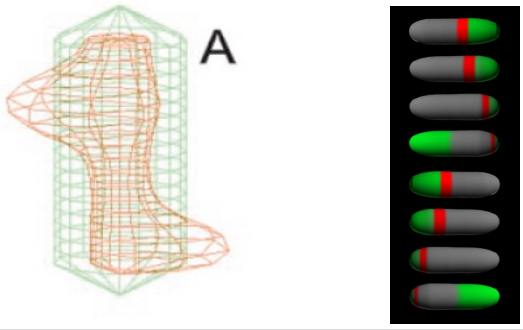


Figure 19: *graphical representation of one of proposed 3D models of MinD oscillations.*

II-2 Implementation of the project: Chromosome segregation by the E.coli Min system [2]

Along the different projects we had, we choose this one. We thought that it could be really interesting to model this additional functionality of the Min system.

II- 3 Introduction of the concept

A little bit of background is necessary to fully understand the approach of this paper. First, the existence and nature of active chromosome segregation in bacteria has been a long standing debate. As we know, the bacteria do not have any cytoskeleton. The main idea was that the chromosomes segregation was performed by entropic forces. Although, numerical simulations have shown that entropy alone is not sufficient to complete segregation of bacterial chromosomes.

In this article [2], the authors have proceeded in two steps: first they made a model to show that the chromosome segregation by the Min system is possible. Afterwards, the model has been proved experimentally.

Our goal was to integrate the DNA segregation by the MinD system into our model (from scratch, because the authors did not give their model mathematical form)

II-3 Implementation of the chromosome segregation in our model

Unfortunately, as they did not give any equations of their model, we decided to try to reproduce the main idea of the system (represented in Fig 17.) from scratch. In that purpose we tried to implement a bias diffusion model. We had a hard time to implement it. Due to the lack of time, we decided first to implement a very simplified version of the biased diffusion:

```
U=-Gauss([1:20]',x0,b).*D.^n*alpha;
Force=-diff(U);
FT=sum(Force);
x0=x0+FT*gama;
```

In our system we define two Gaussian distributions of concentrations; each of them corresponds to a chromosome. The two Gaussian have the same spread, at the beginning they just differ by the positions (x0) of their mean.

We implement next a force **that is proportional to the MinD concentrations at each position** (representing the pulling force exerted by MinD over the DNA).

Then **we make the sum of the difference of the forces** (it gives the direction and the intensity of the pulling). Then **we move the mean of the Gaussian** to the direction indicated by the sum of all the forces. **The move is proportional to a factor** (that allow us to tune the strength of the pulling).

The process is also explained in the following figure:

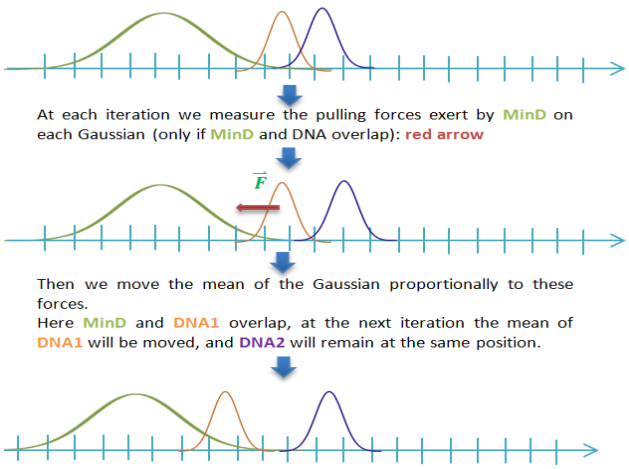


Figure 20: *Explanation of our chromosome segregation model.*

It is important to note that we choose all the parameter completely arbitrary. If we had more time, we would have look at experimental results to try to find good/realistic parameters value.

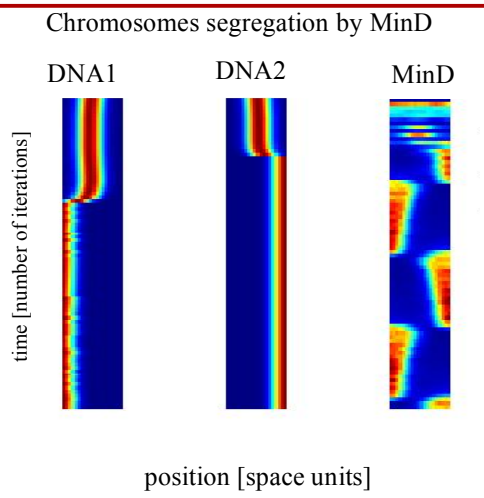


Figure 21: DNA1, DNA2 and MinD patterns. Shifting of position of DNA2 the right, then DNA1 to the left following MinD pole-to-pole first oscillation.

In that plot we use an coefficient equal to two. We choose this value to add some non-linearity to the pulling.

We can observe that we effectively have a segregation of the two chromosomes, it seems that is effectively due to the MinD oscillations, but we had to be sure of it.

The first most obvious control was to remove MinD of the system:

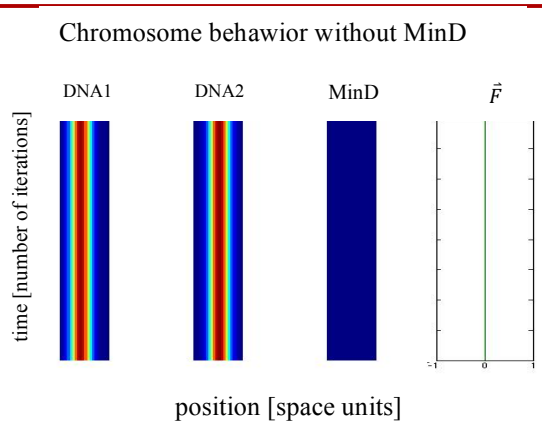


Figure 22: *Control; patterns of DNA1 and DNA2 in the absence of MinD and pulling forces ($\vec{F}$).*

As expected the segregation does not work anymore.

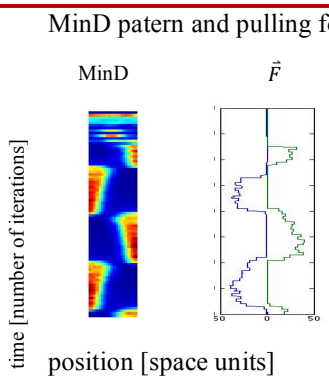


Figure 23: *Force and MinD oscillations plotted over time. Forces depend strongly on the MinD concentration and Force direction depends on the position of MinD. Blue: force exerted on the DNA1, green force exerted on DNA2.*

Here we plotted 'FT' over the time. It allows us to directly have a look at the force exerted by MinD on the DNA.
In blue it is the force exerted by mind on the first chromosome and in green on the second one.
It is important to notice that our system does not work if the two Gaussian start at the same position, suggesting that this mechanism is not sufficient alone. It needs an initiation by other mechanisms (probably the entropic forces).

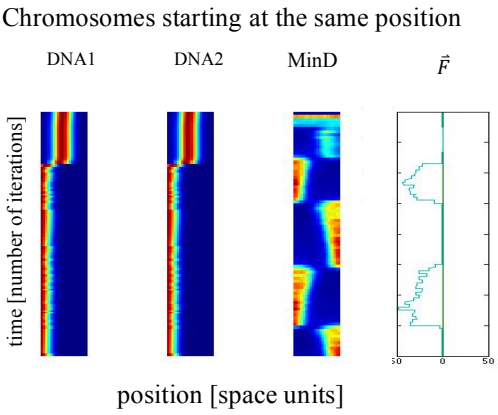


Figure 24*: DNA1 and DNA2 at the same starting position in the cell, forces blue for DNA1 and green for DNA2 are superposed; all DNA goes to one side.*

II- 4 Conclusions

Taken together these two controls strongly suggest that our system works. However, several things could still be improved.

As it stands before, we should use more biologically relevant parameters, we should also implement a natural diffusion for the two chromosome, we can think about others forces apply on the DNA, such as attraction/repulsion between the two DNA, and we should also link all our results into one model of bacteria that grows, segregate it is DNA after replicate it and then divide.

Part III - Discussion

In this project we have built a model that reproduces the pattern formation in *E. coli*: a pole-to-pole oscillation of Min proteins. To construct this model we used the set of equations used in our reference article [1].

Our model works and reproduces the Min proteins' pole-to-pole oscillations. It is very interesting to see that this model can self-assemble (with just a little bit of noise implemented).

This is a very robust system which allows a bacteria to make a good positioning of it is center for the division.
What it is interesting, it is also that with this system the question: "where is my center" is changed into "where are my poles" with the need to have proteins that localized the poles (here MinD). Another question that could be raised is: why *E.coli* uses such complex system instead of just a system that relies on a self-activation/substrate-depletion system (for instance *S. pombe*)? The answer could be that a dynamic system like that is probably more robust in a way that it is really precise and can self-assemble regardless of the initial conditions, a self-activation/substrate-depletion system is more likely to generate pattern formation in poles instead of center, which is avoid in our system.
"Our data show the remarkable ability of wild-type E. coli to carry out cell division in very large and irregular morphologies. The majority of observed divisions occurred around the volumetric center of the mother

cell. Although the frequency of central divisions decreased with the increasing cell size, the accuracy of this type of division remained essentially unaffected by the shape and size of the cell." [6]

However several improvements of this model could be made.

First, some parameters used in the equations are chosen completely arbitrary by the authors, additionally this model contain several simplifications (for example, here MinD and MinC are consider to be one unit). One could ask the biological relevance of those parameters. Second, lot of simplifications were done in this model (a lot of reactions are grouped), we should add the detailed steps of proteins interactions, allowing a better fit to experimental data. Third, we consider in our model a very simple diffusion/spatial organization, our model need to be improved into a 3D spatial organization in order to have relevant results.

After building this model, we wanted to introduce new features, among all our ideas of project we choose to implement a mechanism of chromosomes segregations performed by the Min oscillation system. We were inspired by a very recent publication [2]. We introduced this new feature from scratch. After several trials we managed to introduce the chromosome segregation to our model. Here again, several improvements could be done, for instance, diffusion could have been implemented, more realistic or biologically relevant parameters should have been found and etc.

But it is interesting to see that with such a basic and quite old model [1], we were able to reproduce the results from a model that have just been published [2].

To finish this project we had a look at the literature to find the current state of the art about these systems, here we discuss some results we have found (on the top of all the articles presented in the extension of the projects [2,3,?]). We found an impressive amount of studies, showing that this system continues to be intensively studied under each aspect and it is approached from many angels. Here we present a selection of some interesting aspects that have been developed.

There are several studies about the robustness of the system which have shown that the min system is a very robust system (Varma et al. [7] and Männik et al. [6]). Moreover, several studies about the biochemical properties of the system have been carried out (Szeto et al [8]. And the dynamics of the system have been also studied (Shih et al. [9]). Although, some aspects of the protein dynamics are still not completely understood.

To conclude, we have seen that *E.coli* Min proteins dynamics form a very robust system that allows the bacteria to find its center, even for mutant with extreme modification in their shape. The main feature of this system can be well reproduced with a simple model using just a few equations. Many extensions of this model can be proposed and Min system remains in the center of interest of many research teams all over the world.

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