Model of Chemotaxis Movement of *E.coli* in Narrow Channel Due to Chemo-Repellent

By

Mr. Naor Garnik

EE B.Sc, Technion Institute of Technology, 4th year

Mr. Bar Mayo

ME B.Sc, Technion Institute of Technology, 3rd year

iGEM Technion Project S.tar

The Faculty of Biotechnology and Food engineering

Technion Institute of Technology

October 2016

Acknowledgements

We would like to express our special appreciation and thanks to Professor Moran Bercovichi for helping in every part on the way in designing this model. We would also like to thank Mr. Tzvi hacnsis for his help in developing our numeric solution and Professor Roee Kishony for helping us improve it. Last special thanks to Miss. Liron Tubul and Miss. Nofar shasha for working with us on the diffusion problem.

Abstract

The goal of this model is the describe the processes inside the Flash Lab system:

- Change in the concentration of chemo-repellent.
- Change in the concentration of bacteria.

This model is based on the Keller – Segal equation of chemotaxis [1] in a one-dimensional problem (Thin channel).

It's important to notice that this model can show the overall behavior and not exact values. The final system is supposed to detect a variety of materials in many different unknown solvents, each of them has its own diffusion properties. Also, some aspects such as working conditions (temperature, humidity etc.) might change in widespread commercial use and affect the results. Taking those into account, further fitting will be necessary.

For more information on the project see: http://2016.igem.org/Team:Technion_Israel

Keywords

Chemotaxis, Chemo-repellent, Chemo-attractant.

Contents

Acknowledgements 1

Abstract 2

List of Figures 4

List of Tables 5

List of Graphs 6

List of Equations 7

Chapter 1 Introduction 8

1.1 The fluidic chip 8

1.2 Device Setup 9

1.3 Device Detection Results 9

Chapter 2 Chemo-Repellent Concentration 10

2.1 Mathematical Model 10

2.2 Model Results 11

2.2.1 Comparison to Experiment 12

Chapter 3 Bacterial Concentration 14

3.1 Mathematical Model 14

3.2 Model Results 16

3.2.1 Comparison to Experiment 18

Chapter 4 Conclusion 20

4.1 Achieved results 20

4.2 Future development 20

References 22

Appendix 23

List of Figures

Figure 1:1 Detection tool explanation.....8

Figure 1:2 The geometry of commercial fluidic chip 8

Figure 1:3 The chip setup.....9

Figure 1:4 Chemotaxis reaction in the chip 9

Figure 2:1 Diffusion of potassium permanganate in water in different times (enhanced picture) 13

Figure 3:1 Chemotaxis of *E. coli* with a S.Tar PctA receptor due to exposure to TCE (enhanced picture).....18

List of Tables

Table 2:1 Parameters for diffusion model.....11
Table 2:2 Substance for diffusion experiment.....12
Table 3:1 Parameters for chemotaxis model.....16
Table 3:2 Substance for chemotaxis experiment.....18

List of Graphs

Graph 2:1 Chemo-repellent concentration: top hat diffusion.....11
Graph 2:2 Model for chemo-repellent concentration 12
Graph 2:3 Compression diffusion model $(c = 0.00015[M])$ to experiment.13
Graph 3:1 Model for bacterial chemotaxis 17

List of Equations

Equation 2:1 Chemo-repellent diffusion problem 10
Equation 2:2 General solution for chemo-repellent diffusion problem11
Equation 2:3 Chemo-repellent concentration 11
Equation 3:2 Bacteria concentration problem 15
Equation 3:3 Bacteria concentration problem – Final Form.....15
Equation 3:4 Bacteria concentration problem starting condition.....16
Equation 3:5 Bacteria concentration problem boundary conditions 16

Chapter 1 Introduction

FlashLab, a novel detection tool based on the chemotaxis system of *E. coli*. It uses the chemotaxis system to concentrate colored bacteria, this in turn, creates a visible gradient in color – detection of target material. Using the S.tar technology, the FlashLab can detect verity of materials: hormones, amino acids, PCE etc.

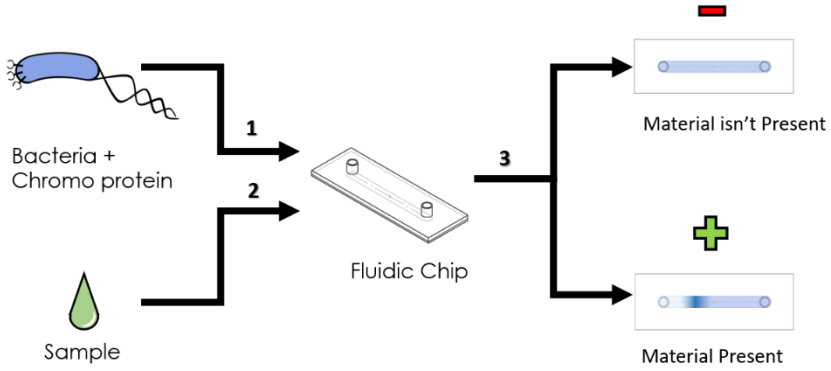


Figure 1:1 Detection tool explanation

1.1 The fluidic chip

The device is composed off a commercial fluidic chip:

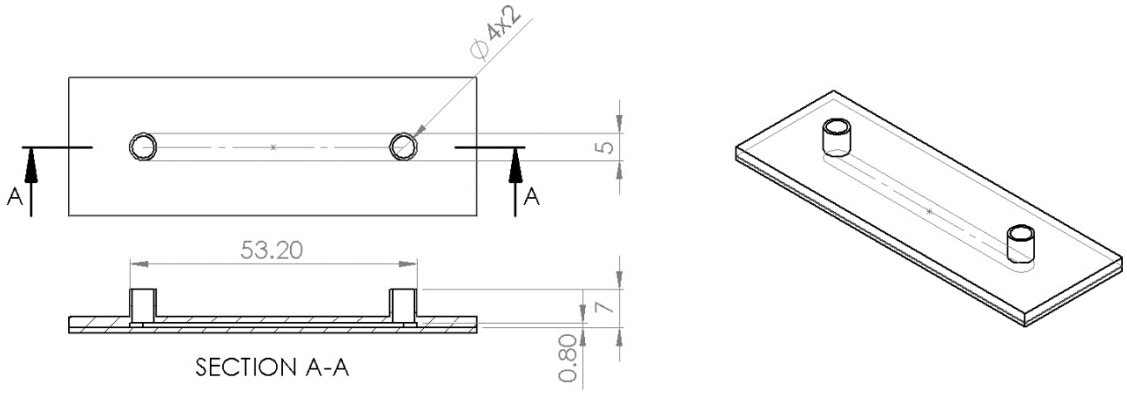


Figure 1:2 The geometry of commercial fluidic chip

The chip is open on the button part and closed with a standard microscope cover glass ($0.3[mm]$ thick). The length of the chip is much bigger than the width and height so we could assume a one dimensional channel.

1.2 Device Setup

The setup of the device is two parts process, as shown below (Figure 1:3):

a) The channel is filled with colored *E. coli* bacteria in motility buffer.
b) Sample is loaded into one of the entry slots.

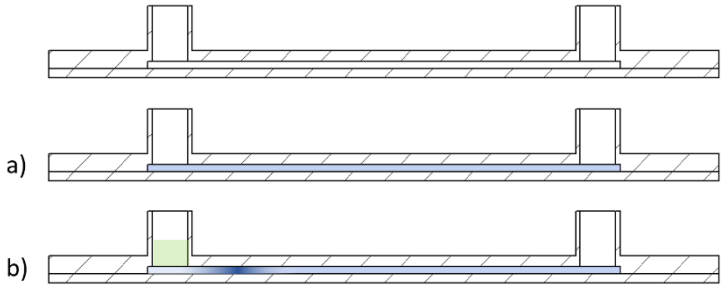


Figure 1:3 The chip setup

This model depicts the reaction for chemo-repellent. This model can be used as a bases for solving a similar problem for a chemo-attractant.

1.3 Device Detection Results

Once the sample is loaded, it diffuses into the channel. If the sample contains a repellent, the bacteria will react and move away from it as shown below:

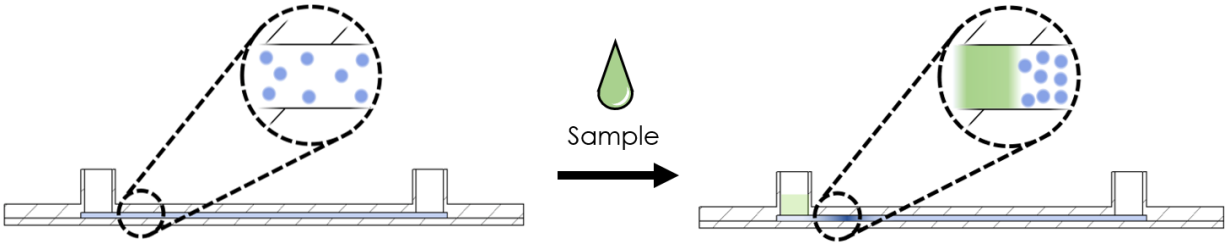


Figure 1:4 Chemotaxis reaction in the chip

This will cause changes in the bacteria concentration: very low concentration, where the repellent diffused to, next to a very high concentration, where the bacteria moved to (right picture, figure 1:4). Those changes will also be visible, as the higher concentration of colored bacteria manifests itself in a stronger color (blue gradient, figures 1:3 and 1:4).

If the sample does not contain target material, the bacteria will not react and no gradient will form.

Chapter 2 Chemo-Repellent Concentration

The basic assumptions of the model for the chemo-repellent are:

- There are no forces except diffusion:
  - Chemo-repellent concentration in the sample is relatively low and does not causes osmotic pressure.
  - The changes in pressure due to sample insertion is negligible.
  - No other significant external forces (for example, moving the chip while in use).
- The bacteria do not consume the chemo-repellent and its concentration does not change with time. This is not case with chemo-attractants.
- We expect to detect small proteins and molecules (those are the materials bacterial receptors bind to). The diffusion coefficient for such materials is about $10^{-9}\left[\frac{m^2}{s}\right]$.
- Because of the geometric properties of the channel and the expected diffusion coefficient, this is approximately a half-infinite one-dimensional problem.
- Initial condition: no chemo-repellent is present in the chip at time zero (a).
- Boundary condition: at infinite distance the concentration is zero (b) and the there is conservation of dissolved material mass (c).

2.1 Mathematical Model

We modelled the change in concentration of chemo-repellent based on "Top Hat Function" for a diffusion problem:

$$\begin{cases} \frac{\partial v}{\partial t} - D\frac{\partial^2 v}{\partial x^2} = \frac{N}{A}\delta(x)\delta(t) & \\ v(x,0) = 0 & x > 0\ (a) \\ v(x \to \pm\infty, t) = 0 & t > 0\ (b) \\ \int_0^{\infty} v(x)\,dx = \frac{N}{A} & t > 0\ (c) \end{cases}$$

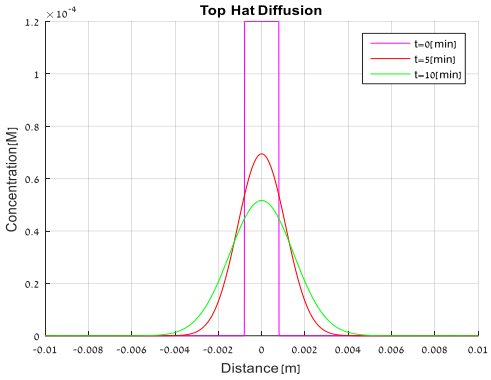
Equation 2:1 Chemo-repellent diffusion problem

$v[M]$ is chemo-repellent concentration, $D\left[\frac{m^2}{s}\right]$ is chemo-repellent diffusion coefficient, $N[mol]$ is the number of repellent atoms, $A[m^2]$ is the cut section of the channel, $h[\mathrm{m}]$ is the height if the channel, $x[m]$ is the distance on the channel and $t[s]$ is time.

The solution for this problem is:

$$v=\frac{v_o}{2}\left[erf\left(\frac{x+h}{\sqrt{4Dt}}\right)-erf\left(\frac{x-h}{\sqrt{4Dt}}\right)\right]$$

Equation 2:2 General solution for chemo-repellent diffusion problem



Graph 2:1 Chemo-repellent concentration: top hat diffusion

In our problem, we want the diffusion to start from $x=0$. Also, we take into account only the positive distance:

$$v=\frac{v_o}{2}\left[erf\left(\frac{x+2h}{\sqrt{4Dt}}\right)-erf\left(\frac{x}{\sqrt{4Dt}}\right)\right]$$

Equation 2:3 Chemo-repellent concentration

2.2 Model Results

We ran the chemo-repellent concentration equation in matlab (The code is in appendix). The parameters used:

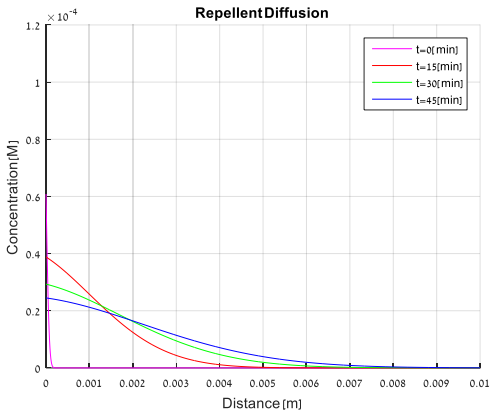
Symbol	Value
v_0	$0.00012[M]$
D*	$1.632\cdot10^{-9}\left[\frac{m^2}{s}\right]$
h**	$7.96\cdot10^{-4}[m]$

Table 2:1 Parameters for diffusion model

*This is the diffusion coefficient for potassium permanganate (see "Comparison to Experiment")

** $h=\frac{\text{Sample volume}}{\text{Reservoir cut section}}$

The output for different times:



Graph 2:2 Model for chemo-repellent concentration

The change in distance of the diffusion limit between 0 to 15 minutes, is relatively big. As the time passes the diffusion limit's speed lowers significantly and the concentration, becomes more linear.

2.2.1 Comparison to Experiment

Most diffusion experiments need a dedicated system that is based on the diffusion of an isotope or a fluorescent material that can be detected easily and very precisely. In this case, we chose a more basic system given that this is only a preliminary testing as our goal is showing that the overall system behaves as we expect.

The experiment ran as shown in the "Introduction" section: The channel was filled with bacteria in motility buffer and then the sample was inserted. We replaced the motility buffer with water and the chemo-repellent with potassium permanganate in the following amounts:

Substance	Amount
Tap water	$200[\mu l]$
Potassium permanganate solution $0.00012[M]$	$10[\mu l]$

Table 2:2 Substance for diffusion experiment

Motility buffer is mostly water (98%) and can be modelled by it. Potassium permanganate is a salt with a known diffusion limit and acts as most of the materials we want detect using our system (small molecules). Also, it has a very distinct pink color in low concentration which makes diffusion limit visible.

We ran the experiment 4 times, with a standard ruler to measure the distance of the diffusion limit.

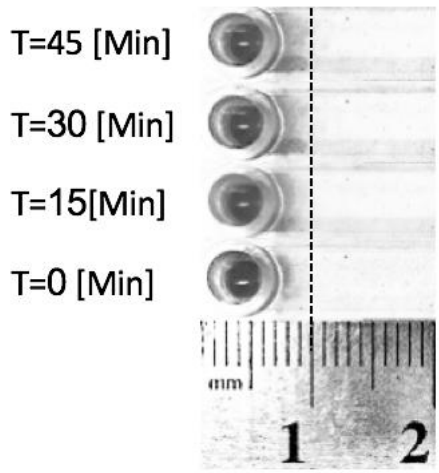
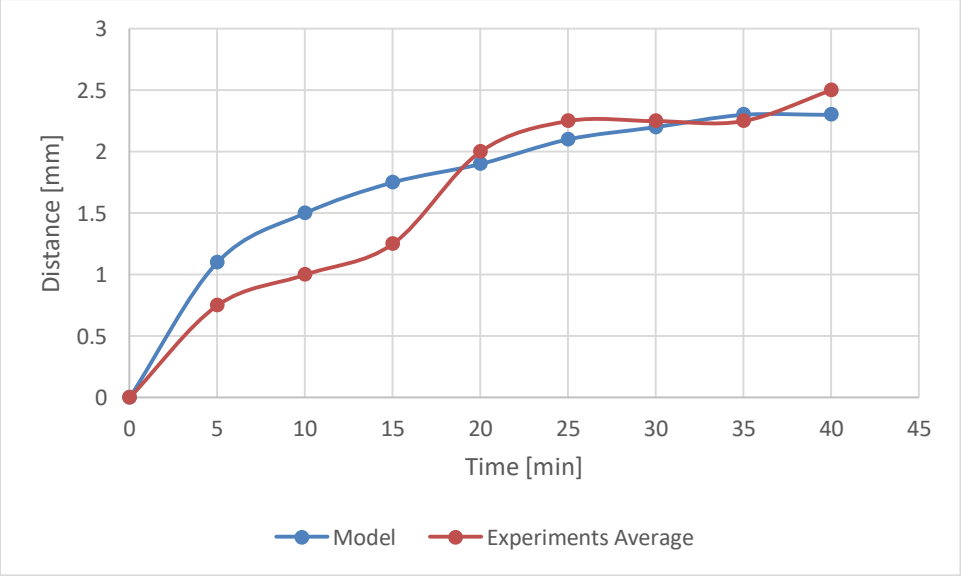


Figure 2:1 Diffusion of potassium permanganate in water in different times (enhanced picture)

As expected by the mathematical model, the diffusion limit starts moving relatively fast and its speed decreases rapidly. The difference in distance between the models to the experiment can be explained by:

- The actual diffusion limit is in too low of concentration of potassium permanganate to be seen in the naked eye. If the visible concentration is about $0.000015[M]$ the experiments results lines up with the model.
- The roller is a crude measuring tool. Its mistake is $\pm 0.5[mm]$.
- Difficulties loading the sample in a uniform way, especially in low volumes. Mistakes in loading the sample inside the bacterial fluid and not on, or sticking the drop of sample to one of the entry slot walls will cause uneven diffusion.



Graph 2:3 Compression diffusion model $(c = 0.00015[M])$ to experiment

Chapter 3 Bacterial Concentration

The basic mathematical model for bacteria chemotaxis is the Keller-Segal equations of chemotaxis:

$$\frac{\partial u}{\partial t} = \nabla\left(k_1(u,v)\nabla u - k_2(u,v)u\nabla v\right) + k_3(u,v)$$

Equation 3:1 Keller-Segal equation

$u[M]$ is bacteria concentration, $v[M]$ is chemo-repellent concentration, $k_1\left[\frac{m^2}{s}\right]$ is bacteria diffusion coefficient, $k_2\left[\frac{m^2}{M\cdot s}\right]$ is bacteria chemotactic coefficient, $k_3\left[\frac{M}{s}\right]$ is bacteria life and death, $x[m]$ is the distance on the channel and $t[s]$ is time.

The base assumptions for model for the chemo-repellent are:

- k_2 describes how sensitive is the bacteria to changes in chemo-repellent concentration. In other words, as its negative value decreases the bacteria will react more violently to same repellent exposure.
- Because of the geometric properties of the channel, this is approximately a one dimensional problem.
- We ran our tests in a short time scale $\left(t < 30[\min]\right)$ so we presume that the change in concentration of bacteria due to life and death is negligible, $k_3 = 0$.
- The chemo-repellent concentration is known for every x and t.
- There are no changes in bacteria concentration at the start (a) and at end of the channel (b).

3.1 Mathematical Model

Under these assumptions the equation takes the form:

$$\begin{cases} \dfrac{\partial u}{\partial t} = k_1 \dfrac{\partial^2 u}{\partial x^2} - k_2 v_x^{'} \dfrac{\partial u}{\partial x} - k_2 v_{xx}^{''} u \\ \dfrac{\delta u}{\delta x}(0,t) = 0 \qquad\qquad t > 0 \ (a) \\ \dfrac{\delta u}{\delta x}(x_{end},t) = 0 \qquad\qquad t > 0 \ (b) \end{cases}$$

Equation 3:2 Bacteria concentration problem

The above partial differential equation cannot be solved analytically, so we must turn to numerical analysis tools. The implicit Euler method is one of the most basic numerical methods for the solution of ordinary and partial differential equations. This method is guaranteed to be stable and gives us the solution for the entire space in a single point in time.

Using the following discretization:

$$\begin{cases} \dfrac{\partial u}{\partial t} = \dfrac{u_i^{r+1} - u_i^r}{\Delta t} \\ \dfrac{\partial u}{\partial x} = \dfrac{u_{i+1}^{r+1} - u_{i-1}^{r+1}}{2\Delta x} \\ \dfrac{\partial^2 u}{\partial x^2} = \dfrac{u_{i+1}^{r+1} - 2u_i^{r+1} + u_{i-1}^{r+1}}{(\Delta x)^2} \end{cases}$$

The equation takes the following discrete form:

$$\frac{u_i^{r+1} - u_i^r}{\Delta t} = k_1 \frac{u_{i+1}^{r+1} - 2u_i^{r+1} + u_{i-1}^{r+1}}{(\Delta x)^2} - k_2 v_x^{'} \frac{u_{i+1}^{r+1} - u_{i-1}^{r+1}}{2\Delta x} - k_2 v_{xx}^{''} u_i^{r+1}$$

$$\left(\frac{1}{\Delta t} + \frac{2k_1}{(\Delta x)^2} + k_2 v_{xx}^{''} \right) u_i^{r+1} + \left(-\frac{k_1}{(\Delta x)^2} + \frac{k_2 v_x^{'}}{2\Delta x} \right) u_{i+1}^{r+1} + \left(-\frac{k_1}{(\Delta x)^2} + \frac{k_2 v_x^{'}}{2\Delta x} \right) u_{i-1}^{r+1} = \frac{1}{\Delta t} u_i^r$$

And we can write it as follow:

$$\begin{cases} A_{\text{sub}} = -\dfrac{k_1}{(\Delta x)^2} - \dfrac{k_2 v_x^{'}}{2\Delta x} \\ A_{\text{diag}} = \dfrac{1}{\Delta t} + \dfrac{2k_1}{(\Delta x)^2} + k_2 v_{xx}^{''} \\ A_{\text{super}} = -\dfrac{k_1}{(\Delta x)^2} + \dfrac{k_2 v_x^{'}}{2\Delta x} \end{cases}$$

$$\begin{pmatrix} A_{\text{sub}} & A_{\text{diag}} & A_{\text{super}} \end{pmatrix} \begin{pmatrix} u_{i+1}^{r+1} \\ u_i^{r+1} \\ u_{i-1}^{r+1} \end{pmatrix} = \frac{1}{\Delta t} u_i^r$$

Equation 3:3 Bacteria concentration problem – Final Form

With the starting condition:

$$u(x,0)=1\forall x$$

Equation 3:4 Bacteria concentration problem starting condition

And the boundary conditions which translate to the following discrete conditions:

$$\begin{cases} u_{I+1}^{r+1}=u_{I-1}^{r+1} \\ u_{0}^{r+1}=u_{2}^{r+1} \end{cases}$$

Equation 3:5 Bacteria concentration problem boundary conditions

With I being the final value of i – index of location.

The above conditions keep the flux of bacteria zero on both sides of the chip as is the case in the actual chip, no bacteria enter or exit the chip during the run.

The above equation was entered into the Thomas-Three-Diagonal algorithm for solving matrix equations, giving us the solution for the entire space of the problem in a specific point in time. By advancing in time as we solve the equation at each time point we get the solution for the bacterial concentration for every x,t.

3.2 Model results

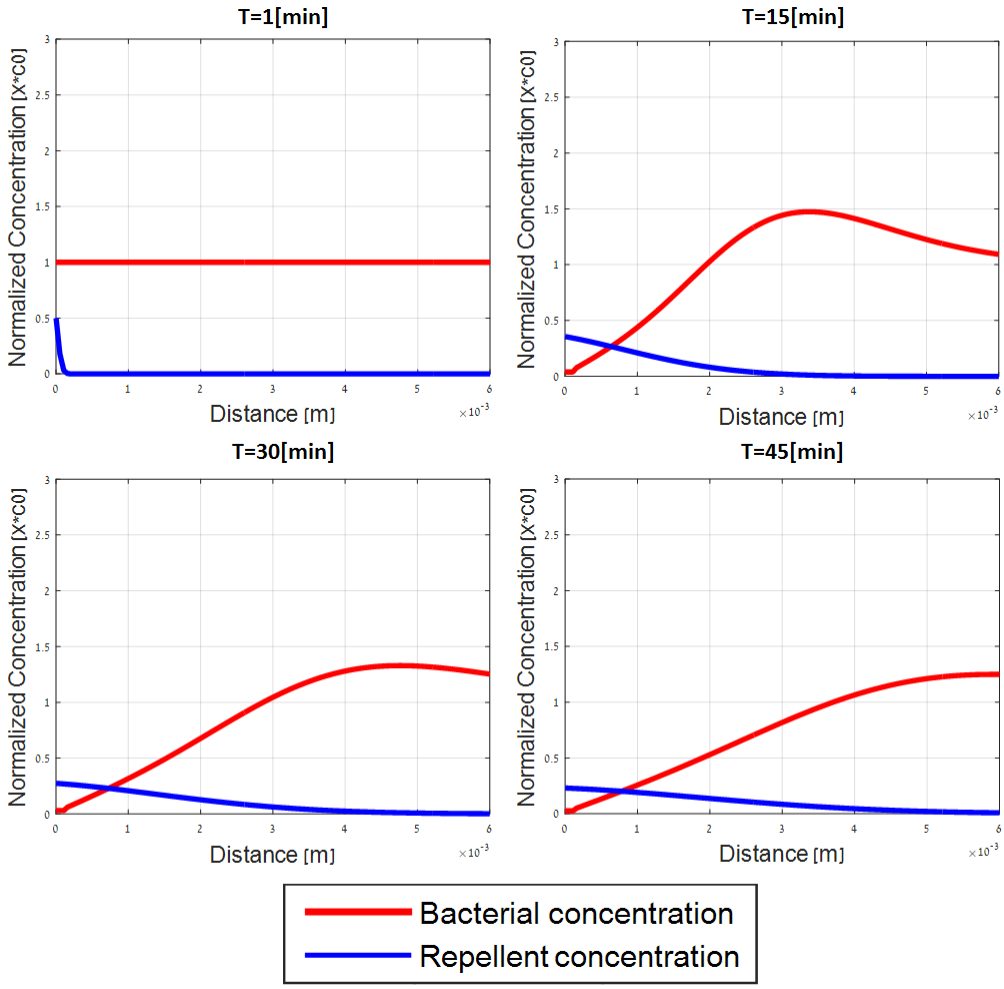
We ran the chemo-repellent concentration equation in matlab (The code is in appendix). The parameters used:

Symbol	Value
v_0	1 (normalized)
k_1	$10^{-8.4}\left[\frac{m^2}{sec}\right]$
k_2	$-10^{-8}\left[\frac{m^2}{sec}\right]$

Table 3:1 Parameters for chemotaxis model

Notice, the results are normalized to enables us to show them on the same scale.

The results are as follows:



Graph 3:1 Model for bacterial chemotaxis

Model conclusions:

- The peak of bacterial concentration is caused by the bacterial chemotactic response, moving away from the chemo-repellent, and concentrating.
- The "wave" of bacterial concentration starts moving relatively fast, and slows down quickly. This is due to the change in repellent concentration. The "wave" converges to $\sim 7[mm]$
- The bacteria react significantly less to a normalized repellent concentration of less than ~ 0.3. This is approximately where the two graphs intersect.
- As the concentration of repellent goes down, the bacteria are less reactive. This continues as the bacteria's diffusion speed surpasses the chemotaxis rate. In other words, more bacteria move away from the concentration peak than into it for $T > 15[\min]$

- Projecting this on the chip color experiment, we can predict there will be three shades of color: weak where the bacteria moved from (low concentration), strong where the bacteria moved to (high concentration) and on the far end, unchanged as the bacteria were not exposed to the repellent.

3.2.1 Comparison to Experiments

The experiment ran as shown in the "Introduction" section: The channel was filled with bacteria in motility buffer and then the sample was inserted. We used engineered *E. coli* with a S.Tar PctA receptor taken from a plate and suspended in motility buffer. The chemo-repellent used is TCE.

Substance	Amount
***E. coli* with a S.Tar PctA receptor in motility buffer**	$180[\mu l]$
TCE	$30[\mu l]$

Table 3:2 Substance for chemotaxis experiment

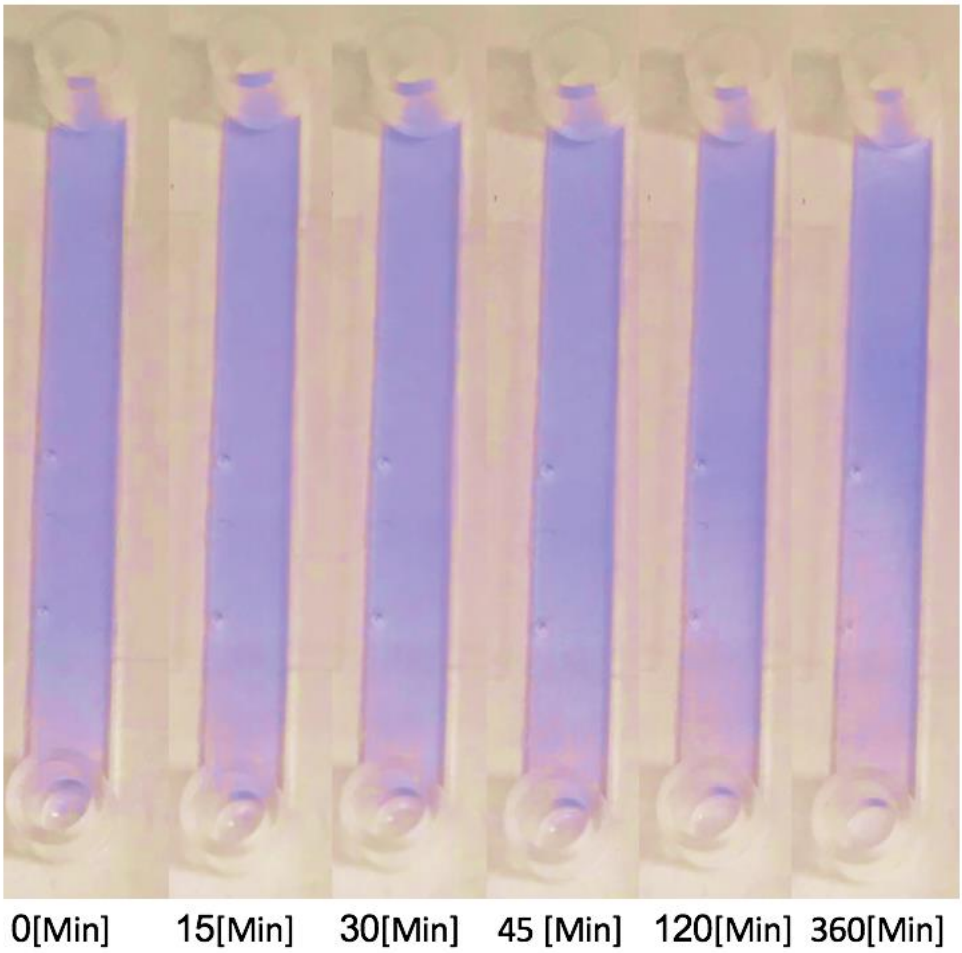


Figure 3:1 Chemotaxis of *E. coli* with a S.Tar PctA receptor due to exposure to TCE (enhanced picture)

As expected, a visible cluster of strong dark blue has formed next to a lighter shade due to chemotactic activity. Furthermore, the distance the bacteria passed is only a few millimeter as the model predicted.

The time scale does not line up: The color darkens as the experiment continues. This will probably be corrected by using more accurate diffusion and chemotactic coefficients.

Some of the inconsistencies between the model and the experiment (like the uneven cluster of colored bacteria) can be explained by problems loading the chemo-repellent as shown in the chemo-repellent concentration experiment.

Chapter 4 Conclusion

4.1 Achieved results

This model predicts the overall behavior of our system. In our experiments we were able to show that the concentration of the repellent acts as we expected in terms of changes in the diffusion limit's velocity. When compared to the bacterial concentration, again, the experiments showed a similar behavior as the numeric solution of Keller-Segal equation.

As explained before, this model requires further fitting to get more accurate results. Not only by using more accurate coefficients, but with improving the system itself.

4.2 Future development

We would like to improve the model and design new ones based on it. First, develop models for the different coefficients in the Keller-Segal equation: bacteria diffusion coefficient, chemotactic coefficient and bacteria life and death. Ideally, finding ways to control these coefficients by changing such things as the number of flagella or receptors a cell has, or even manipulating the biological tracks of the bacteria. This will enable us to get even more accurate results. Second, to build a library of different receptors and target materials the bacteria react to. Third, expanding our model so it could predict movement of bacteria in different geometric constructs such as funnels or U-bends. This research can be the basis of a prototype commercial device.

As for the first part, we worked with iGEM Freiburg in developing a function for the chemotactic coefficient. Also, we designed a new assay for experimentally measuring it.

This assay, named Trap & Track is a novel way to detect chemotaxis on the nanometric level. By using it we can measure the exact repellent concentration that induces chemotaxis and calculate the chemotactic coefficient accurately for every material. A detailed explanation about the assay can be found here (link to best measurement page on the wiki).

As for the second part, The S.Tar system enables us to change the receptors a bacterium has and by that, change the materials it repels from. In the future, this system can be expanded to control the efficiency of these receptors and even control other aspects of the chemotaxis pathway such as the flagella.

The third and final part is to improve the device itself. We designed a new fluidic chip and fabricated it in different methods (Link to design page). This new design will give us a more controlled diffusion by cancelling out most of the flow and fixing the diffusion source. Also, by changing the geometry of the channel, the bacteria concentration will increase and

cause a more noticeable signal. This will improve the accuracy of the experiments we run, and in turn, our overall model.

References

[1] KELLER, Evelyn F.; SEGEL, Lee A. Model for chemotaxis. *Journal of theoretical biology*, 1971, 30.2: 225-234.

[2] MAZZAG, B. C.; ZHULIN, I. B.; MOGILNER, Alexander. Model of bacterial band formation in aerotaxis. *Biophysical journal*, 2003, 85.6: 3558-3574.

Appendix

Chemo-repellent Matlab code:

```
clear all;
close all;
clc;

% This model was designed and created by iGEM Technion 2016

% The model simulates the change in repellent concentration in a confined space.

% For a detailed explanation about this model and more information
% about our project please visit: http://2016.igem.org/Team:Technion_Israel

x = -0.01:0.00001:0.01;%Distance - m
t = 0.001:60:3600;%Time - sec
v0 = 0.00012;%Startin Concentration - C
D = 1.632*10^(-9);%Diffusion Constant - m^2/sec
h = 7.96*10^(-4);%Height of the sample in the entry slot - m

figure;
% The plot is animated to present the reaction over time


for i = 1:length(t);
  v(i,:) = (v0/2)*(erf((x+2*h)/sqrt(4*D*t(i)))-(erf((x)/sqrt(4*D*t(i)))));
  if i >= 2
    set(p1(i-1),'Visible','off');
  end
  grid on
```

```
    p1(i,:) = plot(x,v(i,:),'Color','black');
    xlabel('Distance [m]','fontsize',26);
    ylabel('Concentration [M]','fontsize',26);
    title('Repellent Concentration','fontsize',26);
    ylim([0.000015,0.00004]);
    xlim([0,0.003]);
    getframe;

end
```

Chemotaxis Matlab code:

model:

```
close all;
clear all;
clc;

% This model was designed and created by iGEM Technion 2016

% The model simulates the chemotactic reaction of a bacterial
% population to a repellent in a confined space.

% For a detailed explanation about this model and more information
% about our project please visit: http://2016.igem.org/Team:Technion_Israel

S = 0.0532; % length of the channel

% The function bacterial_conc calculates the repellent and bacteria
% concentration for all points in time and space

[x,t,v,U] = bacterial_conc(1,2702, S, 100, 1000, 10^-8.4, -10^-8);
%t_start,t_final,x_final,t_points,x_points,k1,k2
```

```
figure;

% The plot is presented as normalized concentration vs location in the
% channel. The plot is animated to present the reaction over time


for i = 2:(length(t)-2)
   % The following if statement removes plot lines from previous time
   % points.
   if i >= 3
      set(p1(i-1),'Visible','off');
      set(p2(i-1),'Visible','off');
   end
   p1(i) = plot(x,U(i,:),'Color','red','Linewidth',2);
   grid on
   xlabel('Distance [m]','fontsize',26);
   ylabel('Normalized Concentration [x*c0]','fontsize',26);
   title('Repellent & Bacterial Concentration','fontsize',26);
   xlim([0,0.004]);
   ylim([0,3]);
   hold on;
   p2(i) = plot(x,v(i,:),'Color','blue','Linewidth',1.2);
   hold off;
   Lgnd = legend('Bacterial concentration','Repellent concentration','Location','northeast');
   set(Lgnd,'FontSize',16);
   getframe;

end
```

repellent_conc:

```
function [ v,x,t,dv1,dv2 ] = repellent_conc( t_start, t_final, x_final, t_points,x_points )
```

```
% The purpose of this function is to calculate the repellent concentration
% and its first and second derivatives for all x and t.
% Repellent is assumed to diffuse into the channel, resulting in a top hat
% function.

%Diffusion
   t = linspace(t_start,t_final,t_points); %Time - sec
   x = linspace(0,x_final,x_points); %Distance - m
   D = 1.632e-9; %Diffusion Constant - m^2/sec
   h = 7.96*10^-4; %Height of the sample in the entry slot - m
   v = zeros(length(t),length(x));
   dv1 = zeros(length(t),length(x));
   dv2 = zeros(length(t),length(x));
   for i = 1:length(t);
      for r = 1:length(x)
         v(i,:) = (0.5)*(erf((x+2*h)/sqrt(4*D*t(i)))-(erf((x)/sqrt(4*D*t(i)))));
         dv1(i,r) = (0.5)*(-exp(-(-h+x(r))^2/(4*D*t(i))./(sqrt(pi*D*t(i)))+exp(-
(h+x(r))^2/(4*D*t(i))./(sqrt(pi*D*t(i))));
         dv2(i,r) = (0.5)*((x(r)-h)*(exp(-(-h+x(r))^2/(4*D*t(i))))/(2*D*t(i)*sqrt(pi*D*t(i)))-
((x(r)+h)*exp(-(h+x(r)).^2/(4*D*t(i))))/((2*D*t(i)*sqrt(pi*D*t(i)))));
      end
   end
```

bacterial_conc:

```
function [x,t,v,U] = bacterial_conc( t_start, t_final, x_final, t_points, x_points, k1, k2 )

% The purpose of this function is to calculate the bacterial concentration
% in the channel for all x and t. To do this, the function calls the
% function repellent_conc which return the repellent concentration.

% This function uses a The backwards Euler method - an implicit numerical method
% to solve the partial differential equation which describes chemotaxis.
```

```
% In Backwards Euler, a matrix A is built to march the finite difference
% solution forward in time. In each time step the matrix contains the
% bacterial concentration for the entire space. The solution then becomes a
% simple matrix equation: U_tk_1 = inverse(A)*(U_tk + b):
% U_tk_1 being the bacterial concentration for the entire space in the
% next time point.
% U_tk is the bacterial concentration in the current time point
% b represents a vector with boundary conditions

% To perform the matrix inversion we use the Thomas-Three-Diagonal
% algorithm.
% We thank Mr. Zvi Hantzis from the faculty of mechanical engineering
% in the Technion for sharing with us the implementation of this
% algorithm.



% using an implicit numerical method
S = x_final; % length x-direction

n = x_points; % number of points in x
m = t_points;  % number of points in t

dx = S/n;
dt = t_final/m;

[v,x,t,diff_v,diff2_v] = repellent_conc(t_start,t_final,x_final,m,n+1);
%t_final,x_final,t_points,x_points
% v = repellent concentration
% diff_v = first derivative of v
% diff2_v = second derivative of v
```

```
% Dirichlet boundary conditions through vector b
b= zeros(1,n+1);

%start condition
U_tk = ones(1,n+1);
U=zeros(m,n+1);
U(1,:) = U_tk;

% U_tk_1 = inverse(A)*(U_tk + b):
for i = 2:m-2
  for r = 1:n+1
    if r == 1 || r == 2
      Asubs(i,r) = -k1/(dx^2)-(k2/(2*dx))*diff_v(i,r);
      Adiag(i,r) = 1/dt+2*k1/(dx^2)+(k2)*diff2_v(i,r);
      Asuper(i,r) = Asubs(i,r);
    elseif r == n+1
      Adiag(i,r) = 1/dt+2*k1/(dx^2)+(k2)*diff2_v(i,r);
    else
      Asubs(i,r) = -k1/(dx^2)-(k2/(2*dx))*diff_v(i,r);
      Adiag(i,r) = 1/dt+2*k1/(dx^2)+(k2)*diff2_v(i,r);
      Asuper(i,r) = -k1/(dx^2)+(k2/(2*dx))*diff_v(i,r);
    end
  end

  %b(n+1) = -Asuper(i,end);
  U_tk_1 = ThomasTriDiag(Asubs(i,:),Adiag(i,:),Asuper(i,:),b+(U_tk)./dt);
  U(i,:) = U_tk_1;
  U(i,1) = U(i,2);
  U(i,3) = U(i,2);
  U(i,end) = U(i,end-1);
```

```
    % for next time step - march solution forward in time
    U_tk = U_tk_1;
End
```

ThomasTriDiag:

```
function x=ThomasTriDiag(a,b,c,d)

% Function to solve A*x=B by Thomas algorithm where the matrix a is
% a tridiagonal matrix, N by N:
% A(1,:)=[b(1),c(1),     0,0,...             ,0   ]
% A(2,:)=[0,   b(1),c(1),0,0,...             ,0   ]
% :
% :
% A(i,:)=[0,0,..,0,a(i),b(i),c(i),0,0,...    0,0   ]
% :
% :
% A(n,:)=[0,0,...                0,0,0,a(N),b(N)]
% B(i)=d(i)

% Input:
% a: Vector of length N - 1 containing the subdiagonal.
% b: Vector of length N containing the diagonal.
% c: Vector of length N - 1 containing the superdiagonal.
% d: Vector of length N containing the right hand side.

% Output:
% x Solution of A*x=B, Vector of length N.

%% Forward elimination:
N=length(d);

for i=2:N
```

```
    temp=a(i-1)/b(i-1);
    b(i)=b(i)-temp*c(i-1);
    d(i)=d(i)-temp*d(i-1);
end

%% Backward substitution:
x(N)=d(N)/b(N);
for i=N-1:-1:1
    x(i)=(d(i)-c(i)*x(i+1))/b(i);
end
return;
```