Modelling Collaboration

The 2016 iGEM team of the Technion institute of technology came up with the idea to compare their molecule sensing system based on chemotaxis to aerotaxis, to gain a deeper understanding of bacterial taxis. This is where we, the iGEM team 2016 Freiburg, stepped in and offered our help with the modelling part.

“Aerotaxis is a particular form of ‘‘energy taxis’’. It is based on a largely elusive signal transduction machinery. In aerotaxis, oxygen dissolved in water plays the role of both attractant and repellent.” [1]

To be more specific, we tried to reproduce a mathematical model of the spatial gradient assay for aerotaxis.

Aerotaxis is mainly dependent on four equations.

The first equation describes the oxygen concentration dependent on time and place. With L=function of oxygen concentration, D=diffusion constant of oxygen, kappa=rate of oxygen consumption per cell and b=bacterial density.

$$\frac{dL}{dt} = D * \frac{d^2L}{dx^2} - kappa * stepfunction[L] * b \qquad (1)$$

The step function ensures, that there is no oxygen consumption when the oxygen concentration drops below zero. The oxygen concentration is the main factor that has an influx on the bacterial metabolism. The bacterial cell can sense its internal energy by signalling pathways, which control the movement of the bacteria.

The movement of the bacteria can be predicted by assuming, that the bacteria can only move from left to right. The function frl describes the change from left to right and logically flr describes the change from right to left. With v=speed of the bacteria and E=maximal internal energy minus minimal internal energy.

$$frl = f(E, [\frac{dE}{dL} * (\frac{dL}{dt} + v * \frac{dL}{dx})]) \qquad (2.1)$$

$$flr = f(E, [\frac{dE}{dL} * (\frac{dL}{dt} - v * \frac{dL}{dx})]) \qquad (2.2)$$

With these two equations we can calculate the total amount of bacteria moving either left or right. r[t,x] describes the bacteria moving to the right and l[t,x] and describes the bacteria moving to the left.

$$\frac{dr}{dt} = -v * \frac{dr}{dx} - frl + flr \qquad (3.1)$$

$$\frac{dl}{dt} = -v * \frac{dl}{dx} + frl - flr \qquad (3.2)$$

Now, we can calculate the density b[x,t] of the bacteria with this simple equation.

$$b[x,t] = r[x,t] + l[x,t] \qquad (4)$$

Modelling in Mathematica

Calculation of the oxygen concentration

L'[t, x], t =d*L''[t, x], x - Kappa*Stepwise function[{0, L[t, x] <= 0}, {1, L[t, x] > 0}]*b

L[t, x]=function of oxygen concentration

d=diffusion constant

Kappa=rate of oxygen consumption

b=bacterial density

L[t,x] is found by numerical solving of the equation (1), followed by the integration of interpolation function, resulting in this oxygen distribution over time.

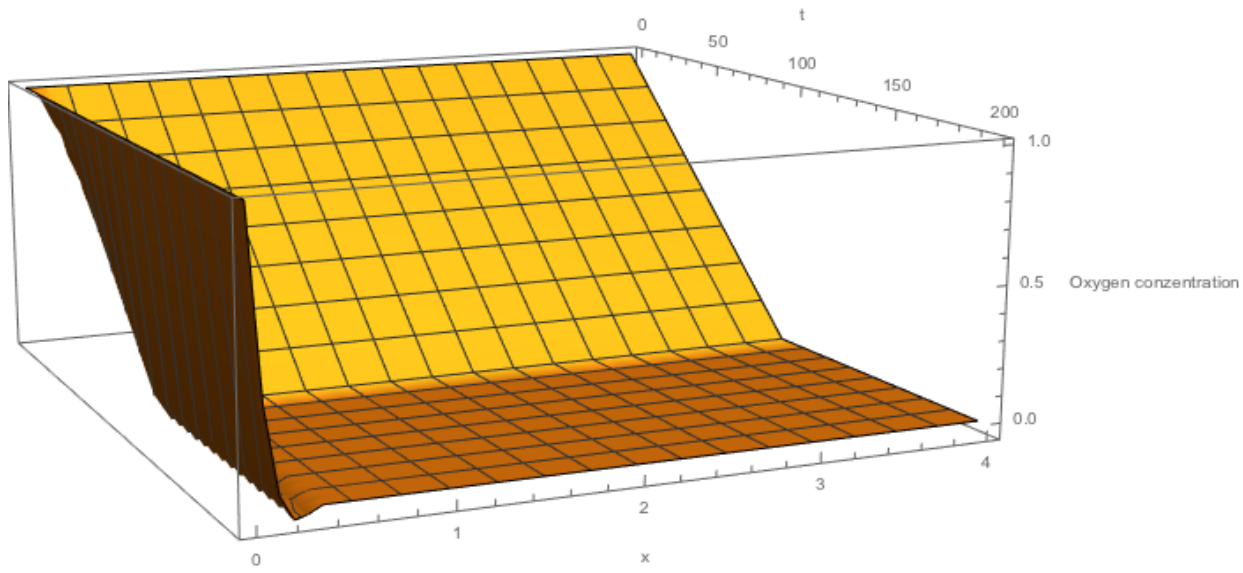

Fig. 1: oxygen concentration over time and place

{D=2*10^-9, kappa=10^-6, b=10^4}

As you can see the bacteria are consuming the oxygen over time. We assume that the oxygen only comes form the left side, because we are simulation a spatial gradient assay for aerotaxis. This is approximated by choosing special initial conditions.

Calculation of the internal energy E

Out of the oxygen concentration we can calculate the internal energy. The internal energy is defined by the following conditions.

$x<0,0,$

$0<=x<llmax,0,$

$llmax<=x<lmax,(Emax/(lmax-llmax))*x-llmax,$

$$lmin<=x<llmin,((Emax/(llmin-lmin))*(-x+lmin))+Emax,$$

$$lmax<=x<lmin,Emax,$$

$$llmin<=x,0$$

x=oxygen concentration

llmax=Upper detectable oxygen concentration

lmax=Upper favorable oxygen concentration

Emax=favorable oxygen concentration

lmin=Lower favorable oxygen concentration

llmin=Lower detectable oxygen concentration

These conditions where concluded from the figure 2(a). [1]

Resulting in this change of the internal energy over time.

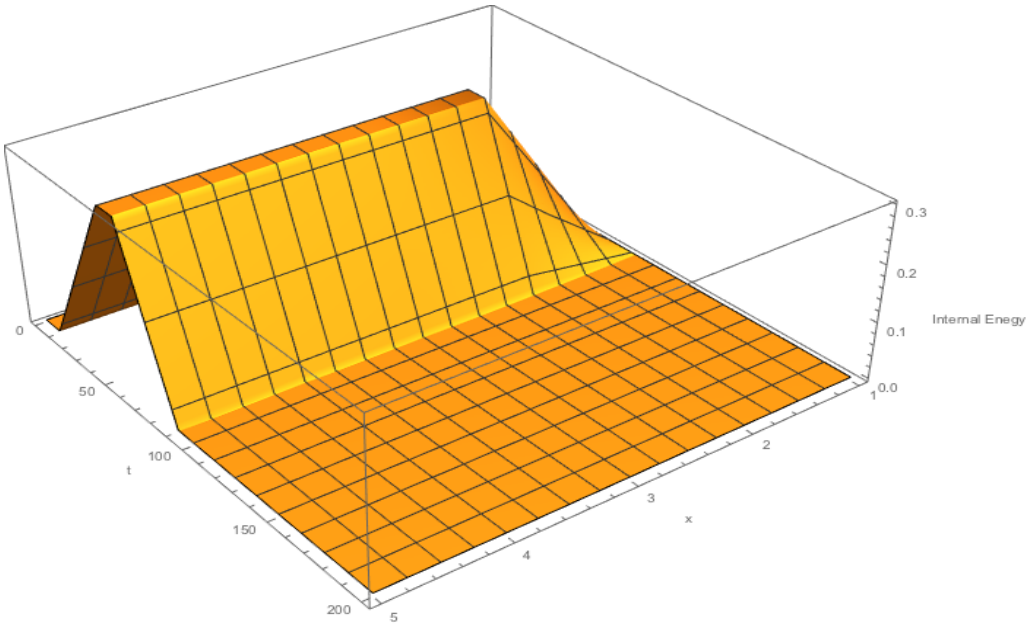

Fig 2. Internal energy over time and place with the previously calculated values

{llmax=0.1, lmax=0.4, lmin=0.5, llmin=0.9, Emax=lmax - llmax}

Here you can see that Emax is reached approximately at t=50. At this point the bacteria would not search further for an optimal oxygen concentration because their metabolism is already at their best. Above t=50 the oxygen concentration is to low so that oxygen is working like an attractant. Below t=50 the oxygen concentration is to high so that oxygen is working like a repellent. As opposed to aerotaxis, chemotaxis only works as repellent or attractant.

Summery

Through our project, we gave the iGEM team of the Technion institute of technology an opportunity to view their project from a different perspective and also giving them an even deeper insight into the world of bacterial taxis.

By making a few small changes to the equations, the system of equations is transposable to chemotaxis. The best and most impacting example would be: excluding the conditions {lmax <= x < lmin, Emax}, {lmin <= x < llmin, ((Emax/(llmin - lmin))*(-x + lmin)) + Emax} and {llmin <= x, 0}, so that the bacteria are not searching for the optimal concentration of a substance but instead for the highest concentration of a substance.

[1]=Mazzag, B. C., I. B. Zhulin, and Alexander Mogilner. "Model of bacterial band formation in aerotaxis." *Biophysical journal* 85.6 (2003): 3558-3574.

Code:

```
Condi = {
  d -> 2*10^-9,
  \[Kappa] -> 10^-6,
  b -> 10^4
  };

tmax = 200;
xmax = 4;

llmax = 0.1;
lmax = 0.4;
lmin = 0.5;
llmin = 0.9;
Emax = lmax - llmax;

equ = {

  D[L[t, x], t] ==
   d*D[D[L[t, x], x]] - \[Kappa]*
    Piecewise[{{0, L[t, x] <= 0}, {1, L[t, x] > 0}}]*b
  };
Init = {
  L[0, x] == 1,
  L[t, 0] == 1
  };
last = Join[equ, Init] /. Condi;
solo = NDSolve[last, {L[t, x]}, {t, 0, tmax}, {x, 0, xmax}];
Plot3D[{L[t, x] /. solo},
 {t, 0, tmax}, {x, 0, xmax},
 AxesLabel -> {"t", "x", "Oxygen conzentration"}, PlotRange -> All,
 ImageSize -> 700]
Table[{L[t, x] /. solo}, {t, 0, tmax}, {x, 0, xmax}] // MatrixForm;
k = Flatten[Table[{L[t, x] /. solo}, {t, 0, tmax}, {x, 0, xmax}]];
```

```
sign[x_] := Which[
   x < 0, 0,
   0 <= x < llmax, 0,
   llmax <= x < lmax, (Emax/(lmax - llmax))*x - llmax,
   lmax <= x < lmin, Emax,
   lmin <= x < llmin, ((Emax/(llmin - lmin))*(-x + lmin)) + Emax,
   llmin <= x, 0
   ];
j = sign /@ k;
ArrayReshape[j, {tmax, xmax + 1}] // MatrixForm;
ListPlot3D[ArrayReshape[j, {tmax, xmax + 1}],
 AxesLabel -> {"x", "t", "Internal Enegy"}, ImageSize -> 700]
```