IV5. Pattern formation

In other words: "When does space matter?"

Example (cellular slime molds)

- Spores
- starvation
- amoebae
- aggregation
- advanced aggregation
- stalk
- "strep"
- mature fruiting body

The life-cycle of Dictyostelium in a prototype example of pattern formation in living organisms and is studied to understand cell differentiation and tissue and organ formation in general.

Here we focus on the process of aggregation. Aggregation in a population phenomenon. How can we understand aggregation as a consequence of processes that are described on the individual level?

The following model is due to Keller & Segel (Journal of Theoretical Biology, 1970)
i-states

A: amoeba
C: cAMP molecule

i-processes

\[ A \overset{d}{\rightarrow} A + C \]  (production of cAMP)

\[ C \overset{k}{\rightarrow} \text{(removed)} \]  (desintegration of cAMP)

C diffuses

A random movement as well as chemotaxis towards higher cAMP concentrations

Amoeba do not multiply nor die on the time-scale considered.

p-equations

\[
\begin{align*}
\frac{\partial A}{\partial t} &= -\frac{\partial}{\partial x} \left( -\mu \frac{\partial A}{\partial x} + \chi A \frac{\partial C}{\partial x} \right) \\
\frac{\partial C}{\partial t} &= +\frac{\partial}{\partial x} \left( D \frac{\partial C}{\partial x} \right) + gA - kC
\end{align*}
\]

with reflecting boundary conditions at \( x=0 \) and \( x=L \). (=zero-flux boundary)

(Interpret the various terms of \( \frac{\partial}{\partial t} \))

(and also interpret the parameters)

(explicitely)

\[ -\mu \frac{\partial A}{\partial x} + \chi A \frac{\partial C}{\partial x} = 0 \quad \Rightarrow \quad \frac{\partial A}{\partial x} = \frac{\partial C}{\partial x} = 0 \]

at \( x=0, x=L \).
Spatially homogeneous equilibrium solution.

Suppose \( A(x,t) = A^* \) and \( C(x,t) = C^* \).

Substitution into 1 gives

\[
\begin{align*}
  \varphi &= 0 \\
  \varphi &= fA^* + kC^* \\
  \Rightarrow \quad \int A^* &= fC^*
\end{align*}
\]

Stability of \((A^*, C^*)\) (\(A^*\) is also the average \(A\) denis. over \(x\)).

Spatially non-homogeneous perturbation.

\[
\begin{align*}
  \tilde{A}(x,t) &= A(x,t) - A^* \\
  \tilde{C}(x,t) &= C(x,t) - C^*
\end{align*}
\]

Substitution of 3 into 1 gives

\[
\begin{align*}
  \frac{\partial \tilde{A}}{\partial t} &= \chi \frac{\partial^2 \tilde{A}}{\partial x^2} \\
  \frac{\partial \tilde{C}}{\partial t} &= f \frac{\partial \tilde{A}}{\partial x} + \int A^* - k \tilde{C}
\end{align*}
\]

Suppose \( \tilde{A}(x,t) \) and \( \tilde{C}(x,t) \) are \( C^* \)-close to zero (i.e., spatial partial derivative up to second order are uniformly small on \([0,1]\)).

Linearization of 4 gives

\[
\begin{align*}
  \frac{\partial \tilde{A}}{\partial t} &= \chi \frac{\partial^2 \tilde{A}}{\partial x^2} \\
  \frac{\partial \tilde{C}}{\partial t} &= f \frac{\partial \tilde{A}}{\partial x} + \int A^* - k \tilde{C}
\end{align*}
\]

with reflecting bonds at \( x = 0 \) and \( x = L \).
Rewrite (6) as
\( \frac{\partial}{\partial t} \left( \tilde{A} \right) = \mathbf{L} \left( \tilde{A} \right) \)

where
\( \mathbf{L} = \begin{pmatrix} \mu \frac{\partial^2}{\partial x^2} & -\chi A^* \frac{\partial}{\partial x} \\ -\frac{\partial}{\partial x} \end{pmatrix} \)

and consider the eigenvalue problem
\( \mathbf{L} (\psi) = \lambda (\psi) \)

where \( \psi \) and \( v \) satisfy the reflecting boundary conditions
\[
\begin{cases}
-\mu \psi' + \chi A^* v = 0 \\
\psi' = 0
\end{cases}
\Rightarrow
\begin{cases}
\psi' = 0 \\
v' = 0
\end{cases}
\text{at } x = 0 \text{ and } x = L
\]

Writing out (8) explicitly we get
\[
\begin{cases}
\mu \psi'' + \chi A^* v' - 2 \psi = 0 \\
\mu \psi + \chi A^* v'' - (d + 2) v = 0
\end{cases}
\]

We try solutions of the form
\[
\psi(x) = x \cos \omega x \\
v(x) = y \cos \omega x
\]

To satisfy the boundary conditions we necessarily have
\[
\omega = \frac{n \pi}{L} \quad (n = 1, 2, \ldots)
\]

Notice that \( n = 0 \) would give \( \psi (x) = 0 \) in (8), which is not an eigenfunction.
Thus only we worked towards (6)

\[ \alpha = \frac{g}{h} \]

Note: To know solution or not the

\[ \frac{\alpha}{g} = \frac{p}{h} - \frac{h}{4} \]

Hence

\[ \frac{\alpha}{g} = \frac{p}{h} - \frac{h}{4} \]

\( P = \frac{h}{2} (p - (x + \frac{h}{2}) \cdot \frac{x}{2} + x + \frac{h}{2}) \]

\( x < \frac{h}{2} \)

\( x = 0 \)

\( x = \frac{h}{2} \)

\( y = 0 \) or \( x < \frac{h}{2} \)

To get other solutions from \( x = 0 \)

\( y = 0 \) or \( x = \frac{h}{2} \)

not an exponential function of \( x \).

Thus \( \frac{x}{h} \) is linear equation.

\[ 0 = \left( \frac{x}{h} \cdot \frac{h}{2} \right) \cdot \left( \frac{x}{h} \cdot \frac{h}{2} + \frac{h}{2} \right) \]

Subject to function of \( \frac{x}{h} \) and \( \frac{h}{2} \).
Since \( p > 0 \) (see (15)), it follows that (6) has a solution \( z \) with \( \text{Re}(z) > 0 \) if and only if \( L < 0 \), i.e.,
\[
\mu (\theta \omega^2 + k) < \chi A^* f
\]
Substitution of (12) into (15) gives
\[
\mu \left( \frac{\omega^2}{L} + k \right) < \chi A^* f \tag{16}
\]

If there exists an \( n > 1 \) such that (16) is satisfied, then the operator \( \mathcal{L} \) (see (9)) has a positive eigenvalue \( \lambda \) (largest solution of (16)), and hence the spatially homogeneous equilibrium \((A^*, C^*)\) of (1) is unstable, and we have the beginning of aggregation of amoeba.

If (16) with "\( \geq \)" (instead of "\( < \)") is satisfied for all \( n > 1 \), then \((A^*, C^*)\) is stable (no aggregation).

Further interpretation of (16):

It can be seen that the following factors promote aggregation:

- Low random motility \( (\mu) \) of amoeba
- Low diffusion rate \( (D) \) and low rate of degradation \( (k) \) of CAMP
- Low chemotactic sensitivity \( (\chi) \), high amoeba concentration \( (A^*) \) and high CAMP-production rate \( (f) \)
- Large domain \( (L) \).
What patterns will emerge in case of instability?

The emerging pattern is given by the eigenfunction (u,v) corresponding to the maximum eigenvalue of the operator L.

$n=1$ minimizes the LHS of (15) as a function of $n$, and therefore the first pattern to be seen (as we change parameters from the stable region to the unstable region) is given by $u = \cos(\pi x / L)$.

So, we get bifurcation of the domain $[0,1]$ into a half with high cell concentration and a half with low cell concentration.

As instability increases further, patterns of smaller wavenumber appear (i.e., with $n=2,3,...$).

How do you calculate which value of $n$ gives the largest eigenvalue and therefore determines the wavelength of the emerging pattern?

From (15) and (16)

\[ \lambda(w^3) = \frac{1}{2} \left(-p(w^3) + \sqrt{p(w^3)^2 - 4q(w^3)} \right) \]

\[ p(w^3) = \omega^2 (\mu + D) + k \]

\[ q(w^3) = \omega^2 \left( \mu \left( D\omega^2 + k \right) - XA^* \right) \]
Calculate the value of \( w^* \) that maximizes \( \lambda(w^*) \) in (i), and call this value \( \nu_{opt}^* \).

Then \( \nu_{opt} = \left[ \frac{1}{2} \sqrt{\nu_{opt}^*} \right] + 1 \) or \(\nu_{opt} = \left[ \frac{1}{2} \sqrt{\nu_{opt}^*} \right] + 1 \)
in the value of \( \nu \) that maximizes \( \lambda(w^*) \).

Notice that \( \nu_{opt}^* \) is independent of \( L \).

If \( \nu_{opt}^* \) is known, then \( \nu_{opt} \) roughly increases linearly as a function of \( L \).

Dependence of \( \nu_{opt} \) on the other parameters is best illustrated numerically.
Note as a function of the other model parameters
Local stability analysis of the spatially homogeneous equilibrium solution \((A^*, C^*)\) shows how an initial perturbation will grow, and hence what pattern will initially emerge (number and position of aggregations of cells).

But what will be the final pattern after a long time?

From \(0\) we get the equil. equ.

\[
\begin{align*}
0 &= (\mu A' + XAC')' \\
0 &= \partial C'' + fA - hC \\
& \text{with bound. co}nds.
\end{align*}
\]

\(0 = \mu A' + XAC' \quad \text{at } x = 0, L\)

\(0 = C' \quad \text{at } x = 0, L\).

From \(\otimes\), first equation, we get

\(\mu A' + XAC' = \text{constant}\).
From the boundary conditions, it follows that this constant is zero:

\[ 0 = \mu A' + XAC \quad \forall x \in [0, L] \]

Solve for \( A' \):

\[ A = ae^{-\frac{x}{Mc}} \quad \text{for some constant} \ a > 0. \]

Substitute this into the 2nd equation of \( \times \):

\[ 0 = DC'' + be^{-\frac{x}{Mc}} - kC \]

for some constant \( b > 0 \).

Phase plane analysis:

\[
\begin{align*}
C' &= H \\
DH' &= kC - be^{-\frac{x}{Mc}}
\end{align*}
\]

Thus, \( H = 0 \) has a unique solution \( C^* \) for \( C \).

\[ y = be^{-\frac{x}{Mc}} \quad \text{and} \quad y = kC \]
Phase portrait:

\[ C^* \text{ is the only equilibrium}
\] (i.e., there is no other equilibrium than the spatially homogeneous equilibrium).

So, what happens eventually after a perturbation of the (unstable) spatially homogeneous equilibrium solution? If there is no alternative equilibrium density (Exercise).