Patterns in Nature

rule
Coordinated Expression
Coordinated Movement
Real life pattern formation by coordinated cell movement
The Key Elements

- Proliferation
- Position
- Movement
Our Aim

Engineer cells to build a novel pattern by controlling cell movement
Motility of *E. coli*

- **Swimming**: CCW rotation
- **Tumbling**: CW rotation

Modified from *Nature Reviews Microbiology* 3, 611-620
Motility Mechanism in *E. coli*

- MCP
- CheA
- CheY
- CheZ
- B
- P
- W
- M

CCW rotation

Modified from ‘www.rowland.harvard.edu/.../images/fret1.jpg’
Generation of \textit{cheZ} Knockout Strain

Recombineering

PCR confirmation

\begin{tabular}{|c|c|}
\hline
WT & \textit{\Delta}cheZ \\
\hline
\includegraphics[width=0.4\textwidth]{WT.png} & \includegraphics[width=0.4\textwidth]{Delta.png} \\
\hline
\end{tabular}
Programmed Motility in *E. coli*

AHL (Cell density)

CCW rotation

CW rotation
Low-density Mover

\[ \rho \]
Single-cell-level Movement

<table>
<thead>
<tr>
<th>Wild Type Cell</th>
<th>Low Cell Density (OD₆₀₀~0.5)</th>
<th>High Cell Density (OD₆₀₀~2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low density mover</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
<tr>
<td></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
</tbody>
</table>
Overall Pattern?
Cell Random Walk as Diffusion

Cell swims with the average speed $v_0 \sim 20\mu m/s$

and mean tumbling frequency $f \sim 0.5$Hz to 2Hz

$$D = \frac{v_0^2}{f} = 100 - 800 um^2 / s$$
Front Propagation for Growing Population of *E. coli*

Fisher’s Equation For Cell Density $\rho$:

$$\frac{\partial \rho}{\partial t} = D_\rho \nabla^2 \rho + \gamma_0 \rho \left(1 - \frac{\rho}{\rho_s}\right)$$

Migration Speed:

$$= 2\sqrt{D_\rho \gamma_0}$$
Novel Devices: Movie-taker
Experimental video of WT strain
Low-density Mover Strain
Density-Dependent Motility

\[ \frac{\partial \rho}{\partial t} = \nabla^2 (D_\rho (\nabla^2 \rho)) + \gamma_0 \rho (1 - \rho / \rho_s) \]

Regions with low cell density near the peak emerges!
Full model

\[
\frac{\partial \rho}{\partial t} = \nabla^2 (D_{\rho}(h) \rho) + \gamma(n)(\rho - \rho / \rho_s)
\]

\[
\frac{\partial h}{\partial t} = D_h \nabla^2 h + \lambda \rho - \beta h
\]

\[
\frac{\partial n}{\partial t} = D_n \nabla^2 n - \gamma(n) \rho
\]

\[\rho: \text{Cell Density}\]

\[h: \text{Density of AHL}\]

\[\beta: \text{AHL Degradation Rate}\]

\[\lambda: \text{AHL Synthesis Rate}\]

\[n: \text{Density of Nutrient}\]

\[\gamma: \text{Cell Growth Rate}\]
Experimental Modeling

Experimental
Multiple Initial Spots

Modeling

Experimental
Measurements to maturate the modeling
Multiple Rings

\[ \frac{\partial \rho}{\partial t} = \nabla^2 (D_\rho(h)\rho) + \gamma(n)\rho \]

\[ \frac{\partial h}{\partial t} = D_h \nabla^2 h + \lambda \rho - \beta h \]

\[ \frac{\partial n}{\partial t} = D_n \nabla^2 n - \gamma(n)\rho \]