Two-dimensional spatial patterning in developmental systems

Keiko U. Torii

\[ \frac{\partial A}{\partial t} = F(A, l) + D_A \frac{\partial^2 A}{\partial x^2} \]

Change of [A] per unit time

\[ \frac{\partial I}{\partial t} = G(A, l) + D_I \frac{\partial^2 I}{\partial x^2} \]

Change of [I] per unit time

(a) Faster diffusion

(b) Slower diffusion

TRENDS in Cell Biology
Is pigment patterning in fish skin determined by the Turing mechanism?

Masakatsu Watanabe and Shigeru Kondo

Graduate School of Frontier Biosciences, Osaka University, Osaka, 565-0871, Japan
**Hox Genes Regulate Digit Patterning by Controlling the Wavelength of a Turing-Type Mechanism**

Rushikesh Sheth, Luciano Marcon, M. Félix Bastida, Marisa Junco, Laura Quintana, Randall Dahn, Marie Kmita, James Sharpe, Maria A. Ros

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**A**

- **WT (control)**
- **Hoxa13 +/+ Gli3 Xtj/Xtj**
- **Hoxa13 +/- Gli3 Xtj/Xtj**
- **Hoxa13 -/- Gli3 Xtj/Xtj**

**B**

- **AP-length**
- **Digit-period**

**C**

- **Wave-length distribution**
- **Space (P-D)**

**D**

- **(K_{hox} - Hox) \cdot Fgf**
- **Fgf**
- **g_u**
- **g_v**
- **U**
- **V**
- **f_u**
- **f_v**
Using Engineered Scaffold Interactions to Reshape MAP Kinase Pathway Signaling Dynamics

Caleb J. Bashor, Noah C. Helman, Shude Yan, Wendell A. Lim

Abiotic behavior of a pathway. The scaffold complex plays a role in shaping the quantitative response signaling between proper protein partners and folds direct information flow; they promote signalosome activation of the SP-NK1R system fol-


Along these lines, activation of the yeast mating MAPK pathway output ~1.5 times as great as wild type (blue) shows dynamics similar to wild type the wild-type, but peaks at ~35 min, and adapts to steady-state facilitated fluorescence-activated cell sorting analysis. Negative- induced cell cycle arrest. Thus, cells are uniform in size,

\[ \text{red) is MAPK phosphatase that deactivates Fus3. (1) } \]

Fig. 2. Building synthetic feedback loops by dynamically matching MAPK phosphatase to deactivates Fus3. (1)
Secreting and Sensing the Same Molecule Allows Cells to Achieve Versatile Social Behaviors

Hyun Youk¹,² and Wendell A. Lim¹,²,³*

A Addition of positive feedback link

![Diagram showing the addition of a positive feedback link in a circuit.](image)
Plants Only Need One Signal
A synthetic approach reveals extensive tunability of auxin signaling

Kyle A. Havens¹, Jessica M. Guseman¹, Seunghee S. Jang¹, Edith Pierre-Jerome¹, Nick Bolten, Eric Klavins*, Jennifer L. Nemhauser*

Department of Electrical Engineering (KAH, SSJ, NB, EK) and the Department of Biology (JMG, EPJ, JLN), University of Washington, Seattle, WA 98195

Figure 4. A) Sender-sensor multicellular auxin signaling strains. Sender cells are identical to those in Figure 3 and therefore produce auxin upon the addition of exogenous IAM and sense auxin production via an EYFP-IAA17 reporter. Sensor cells express an EYFP-IAA17 and TIR1 and are distinguished experimentally through the expression of mCherry. In coculture, IAM diffuses into sender cells where it is converted into diffusible auxin that then degrades EYFP-degron proteins in either the sender or sensor cell types. B) Auxin-induced degradation of EYFP-IAA17 in sensor cells cocultured with sender cells in 300 µM IAM. Data for sensor cells can be separated from sender cells via their mCherry signal. The line represents a LOESS fit.

**Auxin Meets CRISPR**

**RECV**

**SEND**

*A. tumefaciens* attached to a carrot cell (Wikipedia)
Cooperativity To Increase Turing Pattern Space for Synthetic Biology
Luis Diambra,*†§ Vivek Raj Senthivel,‡§ Diego Barcena Menendez,‡§ and Mark Isalan,*†§

• What do we need to get activator inhibitor patterning?
• Faster diffusion of the inhibitor than the activator
• High cooperativity/non-linearity
• Faster degradation of the activator
• ...

*Cooperativity To Increase Turing Pattern Space for Synthetic Biology
Using Engineered Scaffold Interactions to Reshape MAP Kinase Pathway Signaling Dynamics

Caleb J. Bashor,1,2 Noah C. Helman,1 Shude Yan,1 Wendell A. Lim1*

**A**

Synthetic negative feedback

IN

OUT

Synthetic positive feedback

IN

OUT

**B**

Time course

Transcriptional activity (Fluorescence/min)

Positive feedback

WT

Negative feedback

Dose-response (t = 90 min.)

Fluorescence/cell

Positive feedback

$\text{n}_H = 2.42 \pm 0.19$

WT

$\text{n}_H = 1.12 \pm 0.08$

Negative feedback

$\text{n}_H = 1.15 \pm 0.12$
Using Engineered Scaffold Interactions to Reshape MAP Kinase Pathway Signaling Dynamics

Caleb J. Bashor,¹,² Noah C. Helman,¹ Shude Yan,¹ Wendell A. Lim¹*

D

Constitutive expression of negative modulator

Inducible expression of positive modulator

Ultrasensitive Switch

WT
nH = 1.21 ± 0.06

Circuit
nH = 2.84 ± 0.19

Fluorescence / cell

α-factor (µM)
Secreting and Sensing the Same Molecule Allows Cells to Achieve Versatile Social Behaviors

Hyun Youk$^{1,2}$ and Wendell A. Lim$^{1,2,3*}$

A Addition of positive feedback link & signal degradation (Bar1)

![Diagram of secretion and sensing interactions](image)

- **Signal from others**
  - Bar1
  - Other cells

- **Signal from self**
  - Bar1

- **Ste2**
  - rtTA

- **MFα1**
  - GFP
  - TET

- **P_FUS1**
  - P_varied

- **P_TET**
  - P

- **Doxycycline**

- **α**

The diagram illustrates the interaction between secreted and sensed signals, emphasizing the role of positive feedback in regulating expression and behavior.
### WHAT ARE THE TIME SCALES FOR DIFFUSION IN CELLS?

One of the most pervasive processes that serves as the reference time scale for all other processes in cells is that of diffusion. Molecules are engaged in an incessant, chaotic dance, as characterized in detail by the botanist Robert Brown in his paper with the impressive title "A Brief Account of Microscopical Observations Made in the Months of June, July, and August, 1827, On the Particles Contained in the Pollen of Plants, and on the General Existence of Active Molecules in Organic and Inorganic Bodies". The subject of this work has been canonized as Brownian motion in honor of Brown's seminal and careful measurements of the movements bearing his name. As he observed, diffusion refers to the random motions undergone by small scale objects as a result of their collisions with the molecules making up the surrounding medium.

The study of diffusion is one of the great meeting places for nearly all disciplines of modern science. In both chemistry and biology, diffusion is often the dynamical basis for a broad spectrum of different reactions. The mathematical description of such processes has been one of the centerpieces of mathematical physics for nearly two centuries and permits the construction of simple rules of thumb for evaluating the characteristic time scales of diffusive processes. In particular, the concentration of some diffusing species as a function of both position and time is captured mathematically using the so-called diffusion equation. The key parameter in this equation is the diffusion constant, $D$, with larger diffusion constants indicating a higher rate of jiggling around. The value of $D$ is microscopically governed by the velocity of the molecule and the mean time between collisions. One of the key results that emerges from the mathematical analysis of diffusion problems is that the time scale $\tau$ for a particle to travel a distance $x$ is given on the average by

$$\tau \approx \frac{x}{D},$$

indicating that the dimensions of the diffusion constant are length/time. This rule of thumb shows that the diffusion time increases quadratically with the distance, with major implications for processes in cell biology as we now discuss.

### Table 1: A compilation of empirical diffusion constants showing the dependence on size and cellular context

<table>
<thead>
<tr>
<th>molecule</th>
<th>measured context</th>
<th>diffusion coefficient (µm²/s)</th>
<th>BNID</th>
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<tbody>
<tr>
<td>H₂O</td>
<td>water</td>
<td>2000</td>
<td>104087, 106703</td>
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<tr>
<td>H₂O</td>
<td>nucleus of chicken erythrocyte</td>
<td>200</td>
<td>104645</td>
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<tr>
<td>H⁺ (from H₃O⁺ to H₂O)</td>
<td>water</td>
<td>7000</td>
<td>106702</td>
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<td>O₂</td>
<td>water</td>
<td>2000</td>
<td>104440</td>
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<td>CO₂</td>
<td>water</td>
<td>2000</td>
<td>102625</td>
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<td>tRNA (≈20 kDa)</td>
<td>water</td>
<td>100</td>
<td>107933, 107935</td>
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<td>protein (≈30 kDa GFP)</td>
<td>water</td>
<td>100</td>
<td>100301</td>
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<td>protein (≈30 kDa GFP)</td>
<td>eukaryotic cell (CHO) cytoplasm</td>
<td>30</td>
<td>101997</td>
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<tr>
<td>protein (≈30 kDa GFP)</td>
<td>rat liver mitochondria</td>
<td>30</td>
<td>100300</td>
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<td>protein (NLS-EGFP)</td>
<td>cytoplasm of D. melanogaster embryo</td>
<td>20</td>
<td>109209</td>
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<td>protein (≈30 kDa)</td>
<td>E. coli cytoplasm</td>
<td>7-8</td>
<td>100193, 107985</td>
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<tr>
<td>protein (≈40 kDa)</td>
<td>E. coli cytoplasm</td>
<td>2-4</td>
<td>107985</td>
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<tr>
<td>protein (≈70-250 kDa)</td>
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<td>protein (≈140 kDa Tar-YFP)</td>
<td>E. coli membrane</td>
<td>0.2</td>
<td>107985</td>
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<tr>
<td>protein (≈70 kDa LacY-YFP)</td>
<td>E. coli membrane</td>
<td>0.03</td>
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<td>fluorescent dye (carboxy-fluorescein)</td>
<td>A. thaliana cell wall</td>
<td>30</td>
<td>105033</td>
</tr>
<tr>
<td>fluorescent dye (carboxy-fluorescein)</td>
<td>A. thaliana mature root epidermis</td>
<td>3</td>
<td>105034</td>
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<tr>
<td>transcription factor (Lacl)</td>
<td>movement along DNA (1D, in vitro)</td>
<td>0.04 (4×10⁵ bp²s⁻¹)</td>
<td>102036</td>
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<tr>
<td>morphogen (bicoid-GFP)</td>
<td>cytoplasm of D. melanogaster embryo</td>
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<td>morphogen (wingless)</td>
<td>wing imaginal disk of D. melanogaster</td>
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<tr>
<td>mRNA</td>
<td>various localizations and sizes</td>
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<td>110667</td>
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<tr>
<td>ribosome</td>
<td>E. coli</td>
<td>0.04</td>
<td>108596</td>
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</tbody>
</table>
A chemical approach to designing Turing patterns in reaction-diffusion systems

(pattern formation/nonlinear dynamics)

István Lengyel* † and Irving R. Epstein* ‡

\[ X + S \rightleftharpoons SX, \quad K = \frac{s_x}{s_x} = \frac{k_+}{k_-}, \quad K' = Ks_0. \quad [2] \]

If the spatial distribution of \( S \) is uniform, the new reaction-diffusion system is described by

\[ \frac{\partial x}{\partial t} = f(x, y, p) - k_+s_0x + k_-s_x + D_x \frac{\partial^2 x}{\partial z^2} \quad [3a] \]

\[ \frac{\partial y}{\partial t} = g(x, y, p) + D_y \frac{\partial^2 y}{\partial z^2} \quad [3b] \]

\[ \frac{\partial s_x}{\partial t} = k_+s_0x - k_-s_x. \quad [3c] \]