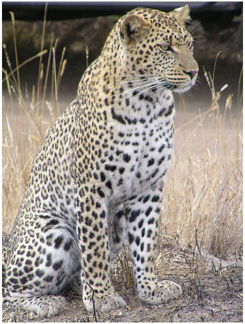
Lecture 4 – Spatially extended systems

February 18, 2020

Outline

1. Turing instability revisited.
2. Turing patterns on symmetric networks.
3. The theory of Turing patterns on directed networks.
4. Stochastic patterns for reaction-diffusion systems.

Self-organized patterns are ubiquitous in nature



The Belousov-Zhabotinsky reaction.

Highlighting the peculiarities:

- First system to display self-organization
- Regular oscillations between homogeneous states.

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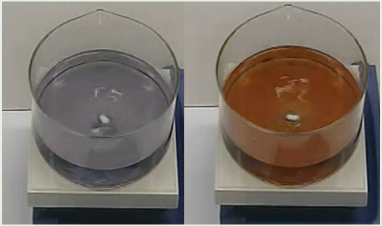

Belousov e Zhabotinsky
Med. Publ. Moscow (1959) - *Biofizika* (1964)

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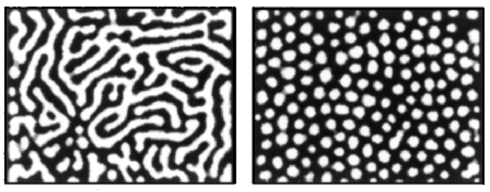

Spatially organized patterns develop (Turing instability) - Vanag e Epstein *Phys. Rev. Lett.* (2001)

1. Turing machine, a general purpose computer: concepts of algorithm and computation with the Turing machine.
2. Pivotal role in cracking intercepted coded messages during II world war.
3. Mathematical biology: chemical basis of morphogenesis.

Morphogenesis

Morphogenesis is the biological process that causes an organism to develop its shape.

Morphogenesis addresses the problem of biological form at many levels, from the structure of individual cells, through the formation of multicellular arrays and tissues, to the higher order assembly of tissues into organs and whole organisms.

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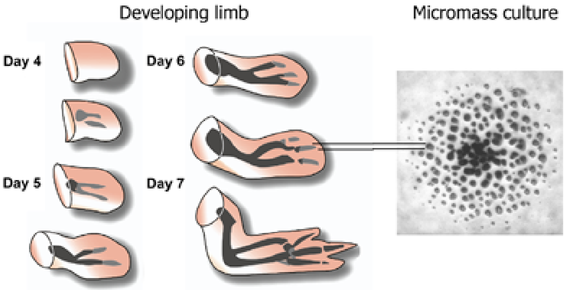
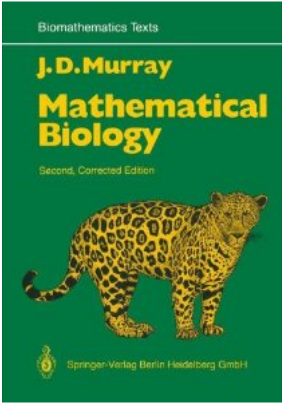


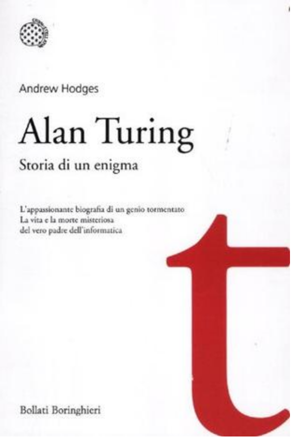
The complete and fine detailed understanding of the mechanisms involved in actual organisms required the discovery of DNA and the development of molecular biology and biochemistry.

Although the mechanism must be genetically controlled , the genes themself cannot create the patterns. They only provide a blue print or recipe, for the pattern generation.

Turing suggested that under certain conditions, chemicals can react and diffuse in such a way as to produce steady state heterogeneous spatial patterns of chemical or morphogen concentration.

Two books


Biomathematics Texts
J.D.Murray
Mathematical Biology
Second, Corrected Edition
Springer-Verlag Berlin Heidelberg GmbH


Andrew Hodges
Alan Turing
Storia di un enigma
L'appassionante biografia di un genio tormentato
La vita e la morte misteriosa
del vero padre dell'informatica
Bollati Boringhieri

Deterministic reaction-diffusion systems

Alan Turing

The Turing instability (1952)

$$\begin{aligned} \partial_t \phi &= f(\phi, \psi) + D_\phi \, \nabla^2 \phi \\ \partial_t \psi &= g(\phi, \psi) + D_\psi \, \nabla^2 \psi \end{aligned}$$

where:

1. $\phi(r, t)$ and $\psi(r, t)$ are the species concentrations.
2. D_ϕ and D_ψ denote the diffusion coefficients

An informative albeit unrealistic image (Murray) (1)

1. Consider a field of dry grass with a large number of grasshoppers which can generate moisture by sweating if they get warm.
2. Suppose the grass is set alight at some point and the front starts to propagate.
3. When the grasshoppers get warm enough they can generate enough moisture to dampen the fire: when the flames will reach the pre-moistened area the grass will not burn.
4. The fire starts to spread. When the grasshoppers ahead of the flame front feel it coming they move well ahead of it ($D_G > D_F$).
5. The burned area is hence restricted to a given domain which depends on the parameters of the game.

An informative albeit unrealistic image (Murray) (2)

1. If instead of a initial single fire there was a random scattering of them, the process would result in a final spatially inhomogeneous distribution of burnt and preserved patches.
2. Notice that the inhibitors (grasshoppers) diffuse faster than the activator (fire).

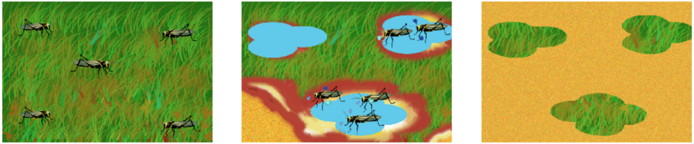


Figure 1.2: In a field with sweating grasshoppers, their combined efforts to prevent the fire from spreading would cause patches of grass in a charred area once the process has finished.

I. Stable fixed point of the aspatial model

Assume a stable homogeneous fixed point of the dynamics to exist and label it (ϕ^*, ψ^*):

$$\begin{aligned} f(\phi^*, \psi^*) &= 0 \\ g(\phi^*, \psi^*) &= 0 \end{aligned}$$

The Jacobian matrix

$$J = \begin{pmatrix} f_\phi & f_\psi \\ g_\phi & g_\psi \end{pmatrix}$$

The stability of the fixed point implies $\mathrm{Tr}\, J < 0$ and $\det J > 0$.

II. The perturbation.

Introduce a small non homogeneous perturbation of the fixed point:

$$w = \begin{pmatrix} \phi - \phi^* \\ \psi - \psi^* \end{pmatrix}.$$

and linearize the reaction-diffusion equations to get:

$$\dot{w} = Jw + D\nabla^2 w,$$

where

$$D = \begin{pmatrix} D_\phi & 0 \\ 0 & D_\psi \end{pmatrix}.$$

III. Laplacian's eigenfunctions

To solve the linearized system one introduces $W_k(x)$ such that:

$$\nabla^2 W_k(x) = -k^2 W_k(x),$$

Expand the perturbation w as

$$w(x,t) = \sum_{k\in\sigma} c_k e^{\lambda(k)t} W_k(x),$$

1. c_k refer to the initial condition.
2. Equivalent to Fourier transforming the original equation.
3. $\lambda(k)$ defines the dispersion relation

Substituting the ansatz in the linear system yields:

$$\lambda W_k = JW_k - k^2 DW_k$$

or equivalently:

$$\begin{pmatrix} f_\phi - D_\phi k^2 - \lambda & f_\psi \\ g_\phi & g_\psi - D_\psi k^2 - \lambda \end{pmatrix} W_k = 0$$

We require non trivial solutions for W_k which implies that λ is determined by the roots of the characteristic polynomial:

$$det(\lambda(k)I - J - Dk^2) = 0$$

The Turing instability occurs if one can isolate a finite domain in k for which $\mathrm{Re}(\lambda(k)) > 0$.

A simple calculation (done on the blackboard) yields the following general condition for the Turing instability to sets in:

$$
\begin{aligned}
\left(D_\phi g_\psi + D_\psi f_\phi\right)^2 &> 4 D_\phi D_\psi \left(f_\phi g_\psi - f_\psi g_\phi\right) \\
\left(D_\phi g_\psi + D_\psi f_\phi\right) &> 0
\end{aligned}
$$

which sum up to the aforementioned conditions:

$$
f_\phi + g_\psi < 0 \qquad\qquad f_\phi g_\psi - f_\psi g_\phi > 0
$$

Important remarks

1. f_ϕ and g_ψ must be of opposite sign.
2. Assume $f_\phi > 0$ (activator) and $g_\psi < 0$ (inhibitor). Then, $f_\phi + g_\psi < 0$ implies:

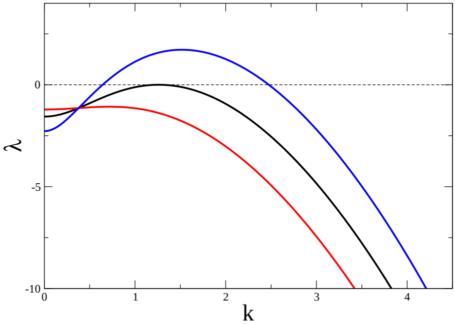
   $$f_\phi < |g_\psi|$$

   and thus:

   $$\frac{D_\psi}{D_\phi} > \frac{|g_\psi|}{f_\phi} > 1$$

   the inhibitor must diffuse faster than the activator.
3. Boundary conditions do matter.

The Brusselator model

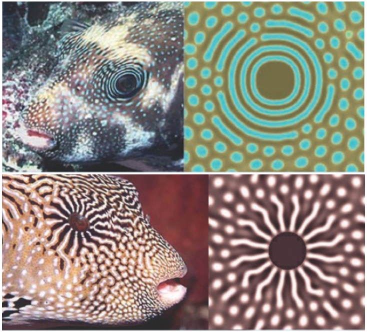


1. Species ϕ is the activator,
2. ψ play the role of the inhibitor.

$$\begin{aligned} f(\phi,\psi) &= a-(b+d)\phi+c\phi^2\psi \\ g(\phi,\psi) &= b\phi-c\phi^2\psi \end{aligned}$$

From a random perturbation of the homogeneous fixed point to a stationary pattern.

Turing patterns are widespread



Patterns on a (symmetric) network.

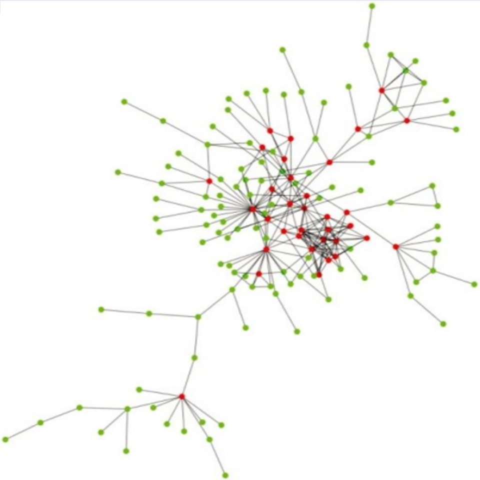
Adjacency matrix

$$\mathbf{W} = \begin{bmatrix} 1 & 0 & 0 & \cdots \\ \cdots & 0 & 1\cdots & \\ \vdots & \vdots & \cdots & \vdots \\ \cdots & 1 & 0 & 1\cdots \end{bmatrix}$$

$W_{ij} = 1$, if nodes i and j are connected $(i \neq j)$, and $W_{ij} = 0$ otherwise

$k_i = \sum_{j=1}^{\Omega} W_{ij}$ (node degree)

Scale-free network



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Reaction-diffusion equations

$$\partial_t \phi_i = f(\phi_i, \psi_i) + D_\phi \sum_{j=1}^{\Omega} \Delta_{ij} \phi_i$$

$$\partial_t \psi_i = g(\phi_i, \psi_i) + D_\psi \sum_{j=1}^{\Omega} \Delta_{ij} \psi_i$$

where $i = 1, .., \Omega$ and $\Delta_{ij} = W_{ij} - k_i \delta_{ij}$ is the discrete Laplacian operator.

Linear stability analysis on networks

Perturbation near the homogeneous fixed point

$$\phi_i = \phi^* + \delta\phi_i \quad \psi_i = \psi^* + \delta\psi_i$$

- Linearize the equations for ϕ_i and ψ_i
- Introduce the eigenvectors of the Laplacian

$$\sum_j \Delta_{ij}\Phi_j^{(\alpha)} = \Lambda^{(\alpha)}\Phi_i^{(\alpha)}$$

The eigenvalues $\Lambda^{(\alpha)}$ are real and negative.

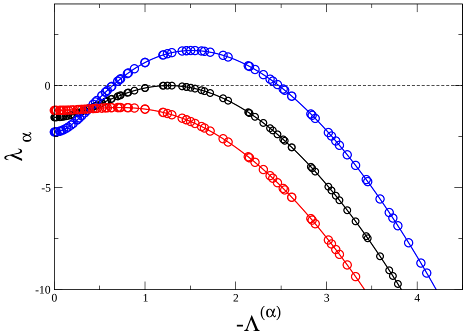
The set of eigenvectors defines a basis on which we can expand the perturbation.

$$\delta\phi_i = \sum_{\alpha=1}^{\Omega} c_\alpha e^{\lambda_\alpha \tau}\Phi_i^{(\alpha)}$$

$$\delta\psi_i = \sum_{\alpha=1}^{\Omega} c_\alpha \beta_\alpha e^{\lambda_\alpha \tau}\Phi_i^{(\alpha)}$$

Inserting in the linearized equation one gets a dispersion relation for λ_α versus $\Lambda^{(\alpha)}$, which controls the instability.

Dispersion relation for the Brusselator model



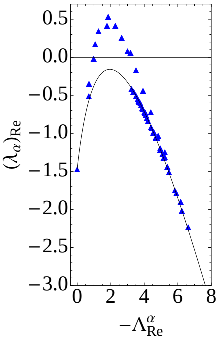
The dispersion relation is defined on the discrete support of Ω eigenvalues $\Lambda^{(\alpha)}$.

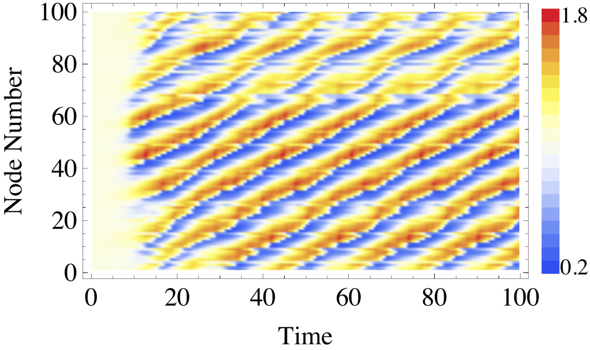
The curve relative to the continuum case is recovered by replacing $\Lambda^{(\alpha)}$ with $-k^2$.

A segregation in activator/inhibitors rich/poor nodes is found as follows the linear instability.

The active role of topology: directed networks

Self-organized waves can develop instigated by the network topology.





M. Asllani et al, Nature Communications (2014)

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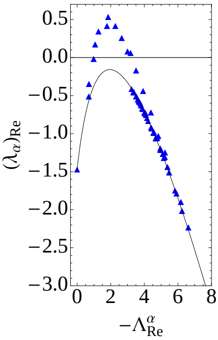

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From the linear stability analysis...

$$\Lambda^{(\alpha)} = \Lambda^{(\alpha)}_{\mathrm{Re}} + i\Lambda^{(\alpha)}_{\mathrm{Im}}$$

The modified Jacobian matrix:

$$J_\alpha = J + D\Lambda^{(\alpha)}$$

yields the dispersion relation:

$$(\lambda_\alpha)_{\mathrm{Re}} = \frac{1}{2}\left[(\mathrm{tr}J_\alpha)_{\mathrm{Re}} + \gamma\right]$$

where γ is a functions of J_α

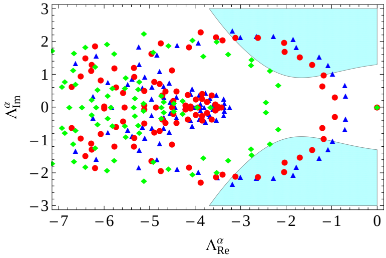
Region of instability

The instability develops when $(\lambda_\alpha)_{Re}$ is positive, namely when:

$$S_2(\Lambda^{(\alpha)}_{\mathrm{Re}})\left[\Lambda^{(\alpha)}_{\mathrm{Im}}\right]^2 \leq -S_1(\Lambda^{(\alpha)}_{\mathrm{Re}}),$$

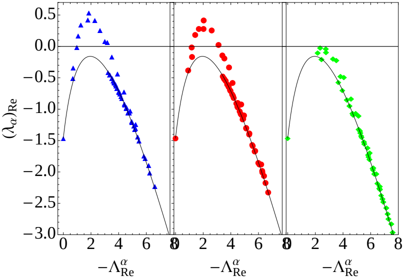
where S_1 and S_2 are polynomials of fourth and second degree in $\Lambda^{(\alpha)}_{\mathrm{Re}}$

The active role of topology



The instability region (shaded) in the $(\Lambda^{(\alpha)}_{\rm Re}, \Lambda^{(\alpha)}_{\rm Im})$ plane.

Dispersion relations for Newman-Watts networks with different p, the probability of long-range links



Example1. Spatial autocatalytic model

Autocatalytic reaction

$$X_s^j + X_{s+1}^j \xrightarrow{r_s} 2X_{s+1}^j$$

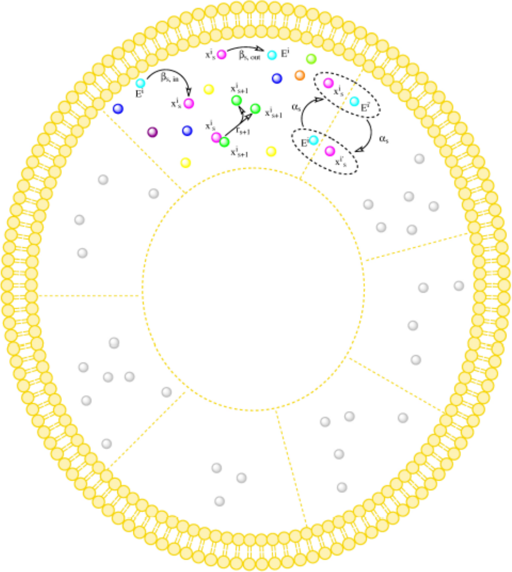
Exchange with the bulk

$$X_s^j \xrightarrow{\beta_{s,out}} E^j$$

$$E^j \xrightarrow{\beta_{s,in}} X_s^j$$

Migration between urns

$$X_s^j + E^{j'} \xrightarrow{\alpha_s} X_s^{j'} + E^j$$



Example 2. Spatial autocatalytic model

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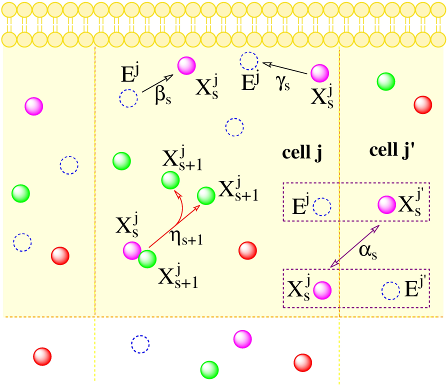


Transition associated to migration

$$
\begin{aligned}
T(n_s^j - 1, n_s^{j'} + 1 | n_s^j, n_s^{j'}) &= \frac{\alpha_s}{z\Omega} \frac{n_s^j}{N} \Big(1 - \sum_{m=1}^{k} \frac{n_m^{j'}}{N} \Big), \\
T(n_s^j + 1, n_s^{j'} - 1 | n_s^j, n_s^{j'}) &= \frac{\alpha_s}{z\Omega} \frac{n_s^{j'}}{N} \Big(1 - \sum_{m=1}^{k} \frac{n_m^{j}}{N} \Big)
\end{aligned}
$$

where z is the number of nearest neighbors that each micro-cell has. Use has been made of the condition:

$$
\sum_{s=1}^{k} \frac{n_s^j}{N} + \frac{n_E^j}{N} = 1,
$$

The master equation

Introduce $\mathbf{n} = (\mathbf{n}^1, \mathbf{n}^2, ..., \mathbf{n}^\Omega)$ where $\mathbf{n}^j = (n_1^j, n_2^j, ..., n_k^j)$. Then:

$$\begin{aligned} \frac{dP(\mathbf{n},t)}{dt} &= \sum_{j=1}^{\Omega} T^j_{loc} P(\mathbf{n},t) + \sum_{j=1}^{\Omega} \sum_{j' \in j} T^{jj'}_{mig} P(\mathbf{n},t) \\ &+ \sum_{j=1}^{\Omega} T^j_{env} P(\mathbf{n},t), \end{aligned} \tag{1}$$

where the three terms on the right-hand side refer to the local terms for the chemical reactions, the migration of chemical species between the micro-cells, and the interaction with the environment, respectively. The notation $j' \in j$ means that the cell j' is a nearest-neighbor of the cell j.

The van Kampen expansion

In analogy with above we set:

$$\frac{n_s^j}{N} = \phi_s^j + \frac{1}{\sqrt{N}}\xi_s^j$$

At the leading order in $\frac{1}{\sqrt{N}}$ we get:

$$\begin{aligned}\frac{d}{d\tau}\phi_s^j &= \frac{r}{\Omega}(\phi_{s-1}^j\phi_s^j - \phi_s^j\phi_{s+1}^j) + \frac{\alpha}{\Omega}\left(\Delta\phi_s^j(1 - \sum_m \phi_m^j) + \phi_s^j\sum_m \Delta\phi_m^j\right) \\ &+ \frac{\beta_{in}}{\Omega}(1 - \sum_m \phi_m^j) - \frac{\beta_{out}}{\Omega}\phi_s^j\end{aligned}$$

where Δ is the discrete Laplacian operator $\Delta f_s^j = (2/z)\sum_{j'\in j}(f_s^{j'} - f_s^j)$.

The next–to–leading order: Fokker Planck equation

$$\frac{\partial \Pi}{\partial \tau} = -\sum_p \frac{\partial}{\partial \xi_p}\left[A_p(\boldsymbol{\xi})\Pi\right] + \frac{1}{2}\sum_{l,p} B_{lp}\frac{\partial^2 \Pi}{\partial \xi_l \partial \xi_p},$$

where the matrix A can be re-written as

$$A_p(\boldsymbol{\xi}) = \sum_l M_{pl}\xi_l.$$

To specify the Fokker-Planck equation we need to give the form of the two $(k\Omega) \times (k\Omega)$ matrices M and B.

The equivalent Langevin formulation

$$\frac{d\xi_s^j}{d\tau} = \sum_{j',r} M_{sr}^{jj'} \xi_r^{j'} + \lambda_s^j(\tau),$$

where

$$\langle \lambda_s^j(\tau) \lambda_r^{j'}(\tau') \rangle = B_{sr}^{jj'} \delta(\tau - \tau').$$

Going to Fourier space

$$\frac{d\xi_s^{\mathbf{k}}}{d\tau} = \sum_r M_{sr}^{\mathbf{k}} \xi_r^{\mathbf{k}} + \lambda_s^{\mathbf{k}}(\tau),$$

where

$$\langle \lambda_s^{\mathbf{k}}(\tau) \lambda_r^{\mathbf{k}'}(\tau') \rangle = B_{sr}^{\mathbf{k}} \Omega a^d \delta_{\mathbf{k}+\mathbf{k}',0} \delta(\tau - \tau'),$$

and where $\mathbf{k}$ is the wavevector. Both $M^{\mathbf{k}}$ and $B^{\mathbf{k}}$ are simply $k \times k$ matrices (recall that k is the number of chemical species) and the analysis from now on is as in the non-spatial case.

The matrix $M^{\mathbf{k}}$

$$M^{\mathbf{k}}_{sr} = M^{(NS)}_{sr} + M^{(SP)}_{sr}\Delta_{\mathbf{k}},$$

where the two matrices $M^{(NS)}$ and $M^{(SP)}$ are given by

$$M^{(NS)}_{ss} = -\beta - \gamma$$

$$M^{(NS)}_{sr} = \begin{cases} -\eta\phi^* - \beta, & \text{if } r = s+1 \\ \eta\phi^* - \beta, & \text{if } r = s-1 \\ -\beta, & \text{if } |s-r| > 1, \end{cases}$$

and

$$M^{(SP)}_{ss} = \alpha_s\left[1 + (1-k)\phi^*\right]$$

$$M^{(SP)}_{sr} = \alpha_s\phi^* \quad \text{if } s \neq r.$$

Fourier transform of the discrete Laplacian

$$\Delta_{\mathbf{k}} = \frac{2}{d}\sum_{\gamma=1}^{d}\left[\cos(\mathrm{k}_\gamma a) - 1\right].$$

The matrix $B^{\mathbf{k}}$

$$B^{\mathbf{k}}_{sr} = B^{(NS)}_{sr} + B^{(SP)}_{sr} \Delta_{\mathbf{k}},$$

where the two matrices $M^{(NS)}$ and $M^{(SP)}$ are given by

$$B^{(NS)}_{ss} = a^d \left[\beta(1 - k\phi^*) + \gamma\phi^* + 2\eta \left(\phi^*\right)^2 \right] \tag{2}$$

$$B^{(NS)}_{sr} = \begin{cases} -a^d \eta \left(\phi^*\right)^2, & \text{if } r = s + 1 \\ -a^d \eta \left(\phi^*\right)^2, & \text{if } r = s - 1 \\ 0 & \text{if } |s - r| > 1, \end{cases} \tag{3}$$

and

$$B^{(SP)}_{ss} = -2a^d \alpha_s \phi^* \left(1 - k\phi^*\right) \tag{4}$$

$$B^{(SP)}_{sr} = 0 \;\; \text{if } s \neq r. \tag{5}$$

Calculating the power spectrum of fluctuations

$$\sum_{r=1}^{k}\left(-i\omega\delta_{sr}-M^{\mathbf{k}}_{sr}\right)\tilde{\xi}^{\mathbf{k}}_{r}(\omega)=\tilde{\lambda}^{\mathbf{k}}_{s}(\omega),$$

Defining the matrix $\Phi^{\mathbf{k}}_{sr}(\omega)=(-i\omega\delta_{sr}-M^{\mathbf{k}}_{sr})$:

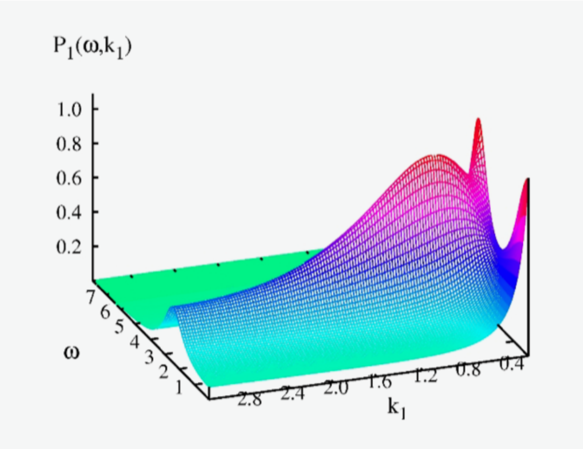
$$\tilde{\xi}^{\mathbf{k}}_{r}(\omega)=\sum_{s=1}^{k}\left[\Phi^{\mathbf{k}}(\omega)\right]^{-1}_{rs}\tilde{\lambda}^{\mathbf{k}}_{s}(\omega).$$

and:

$$P_s(\mathbf{k},\omega)\equiv\left\langle|\xi^{\mathbf{k}}_{s}(\omega)|^2\right\rangle=$$
$$\Omega a^d\sum_{r=1}^{k}\sum_{u=1}^{k}\left[\Phi^{\mathbf{k}}(\omega)\right]^{-1}_{sr}B^{\mathbf{k}}_{ru}\left[\Phi^{\mathbf{k}\dagger}(\omega)\right]^{-1}_{us}.$$

Analytical power spectrum species 1, $\alpha_i \neq 0$

- The homogeneous fixed point is stable: no deterministic patterns
- Stochastic patterns (wave like) do exist!



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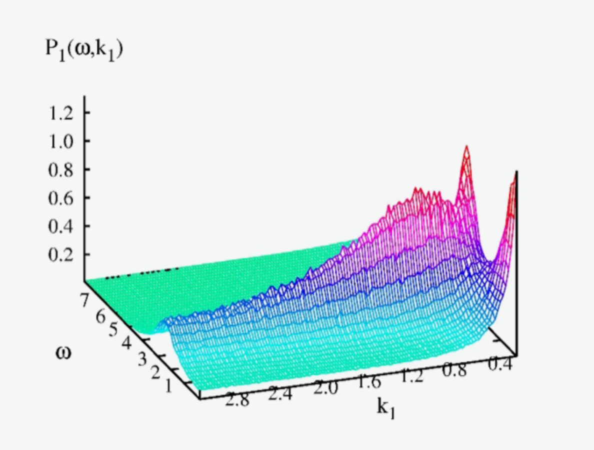

Summing up...

- Autocatalytic reactions are presumably important
- Stochastic (spatial/aspatial) model of autocatalytic cycles
- Deterministic models predict homogeneous fixed points
- Patterns (quasi cycles, waves) exist as seeded by finite size effects.

On the synchronization issue (highly speculative!)

- Imagine that the vesicle containing the chemical species grows because of the inclusion of successive membrane constituents

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On the synchronization issue (highly speculative!)

- Imagine that the vesicle containing the chemical species grows because of the inclusion of successive membrane constituents
- Suppose that the vesicle is filled by a discrete population of chemical constituents, organized in a autocatalytic cycle.
- The chemicals experience a first rapid evolution toward the stationary state, where enhanced oscillations appear due to the intrinsic finiteness.
- Such oscillations might seed an instability which could resonate with the innate ability of the container to divide, so initiating the splitting process.

In other words...

These oscillations could act as an effective switch by signaling to the membrane that the genetic evolution had been virtually taken to completion and that the fission could now occur, so ensuring that the genetic material is passed on to the daughter protocells.

Remark: discrete (network/lattice) support.

Linear Langevin equation

$$\frac{d\xi_{si}}{d\tau} = \sum_{r,j} M_{sr,ij}\xi_{r,j} + \eta_{si}(\tau)$$

where $$< \eta_{si}(\tau)\eta_{rj}(\tau') >= B_{sr,ij}\delta_{\tau\tau'}$$

Generalized transform: expand along $\Phi_i^{(\alpha)}$

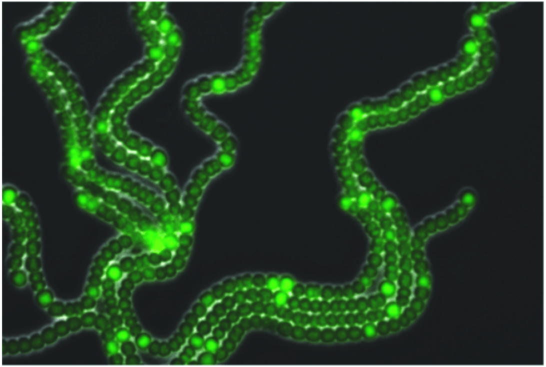
Transform

$$\tilde{f}_\alpha(\omega) = \int_0^\infty dt \sum_{i=1}^{\Omega} f_i(t)\Phi_i^{(\alpha)} e^{-j\omega t}$$

Inverse Transform

$$f_i(t) = \frac{1}{2\pi}\int_{-\infty}^\infty d\omega \sum_{\alpha=1}^{\Omega} \tilde{f}_\alpha(\omega)\Phi_i^{(\alpha)} e^{j\omega t}$$

Example 2. Pattern formation in Anabaena



- Under nitrogen deprivation, Anabaena develops patterns nitrogen-fixing cells.
- Heterocysts are separated by nearly regular intervals of photosynthetic vegetative cells.

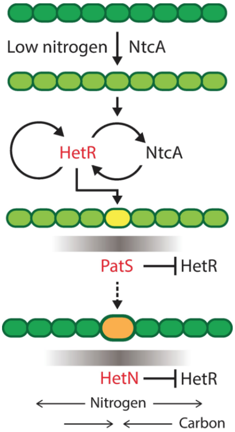


Fig 1. Basic regulatory network leading to heterocyst differentiation. In response to combined nitrogen deprivation, the NtcA protein is activated, leading to activation of expression of HetR in some cells. NtcA and HetR undergo mutual amplification, resulting in increased levels of the two regulators. In addition, HetR positively regulates its own production. During the early stages of differentiation, HetR induces expression of PatS in cells that can potentially form heterocysts (yellow). A PatS-derived peptide signal is thought to diffuse to neighbouring cells (grey gradient), where it interferes with the DNA-binding activity of HetR, causing its degradation and creating HetR gradients along filaments. At late stages (dashed arrow), HetN is produced in heterocysts (orange), and a HetN-derived signal is conveyed to neighbouring cells (grey gradient), where it inhibits HetR function and heterocyst formation. During the differentiation process, cells lose phycobilisomes and their autofluorescence declines (different shades of green). Phycobilisomes are restored when nitrogen compounds produced by the heterocysts reach the vegetative cells. For details, see Introduction. The dynamical variables of our model, the activator HetR and its inhibitors PatS and HetN, have been emphasized in red. Adapted with modifications from [6].

- Nitrogen deprivation enhances expression HetR.
- HetR positively regulates its own production.
- HetR induces expression of PatS in cells that can potentially form heterocysts (yellow).

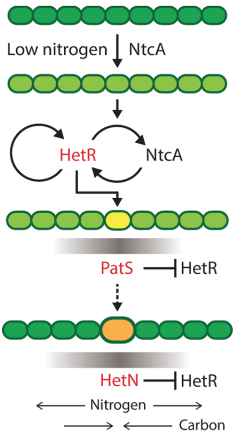


Fig 1. Basic regulatory network leading to heterocyst differentiation. In response to combined nitrogen deprivation, the NtcA protein is activated, leading to activation of expression of HetR in some cells. NtcA and HetR undergo mutual amplification, resulting in increased levels of the two regulators. In addition, HetR positively regulates its own production. During the early stages of differentiation, HetR induces expression of PatS in cells that can potentially form heterocysts (yellow). A PatS-derived peptide signal is thought to diffuse to neighbouring cells (grey gradient), where it interferes with the DNA-binding activity of HetR, causing its degradation and creating HetR gradients along filaments. At late stages (dashed arrow), HetN is produced in heterocysts (orange), and a HetN-derived signal is conveyed to neighbouring cells (grey gradient), where it inhibits HetR function and heterocyst formation. During the differentiation process, cells lose phycobilisomes and their autofluorescence declines (different shades of green). Phycobilisomes are restored when nitrogen compounds produced by the heterocysts reach the vegetative cells. For details, see Introduction. The dynamical variables of our model, the activator HetR and its inhibitors PatS and HetN, have been emphasized in red. Adapted with modifications from [6].

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Deterministic Turing patterns

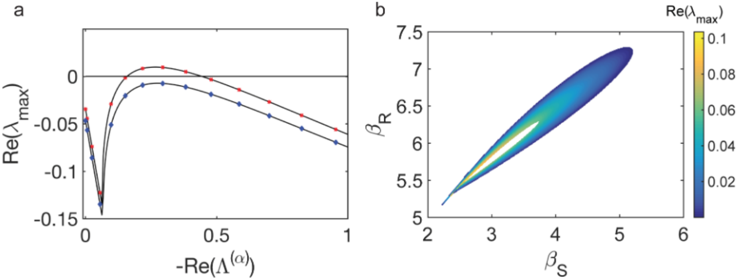
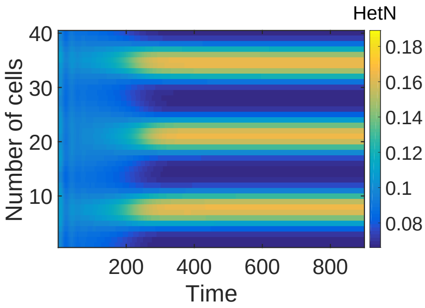


Fig 3. Conditions for a deterministic Turing instability. (**a**) Dispersion relations for $\beta_R = 6.5$ and $\beta_S = 3.65$ (blue diamonds) and $\beta_R = 6.5$ and $\beta_S = 3.7$ (red stars). The data used in this figure are included in S1 Data. (**b**) Region in the plane (β_S, β_R) where the maximum of $\lambda_{Re}(\Lambda^{(\alpha)})$ is positive and the equilibrium point is stable, for a ratio of diffusion coefficients $\frac{D_S}{D_N} = 3$. Parameters are set as $k_R = 0.2$, $\alpha_R = 0.2$, $K = 2$, $k_S = 0.1$, $\alpha_S = 0.1$, $\mu_S = 0.1$, $k_N = 0.7$, $\alpha_N = 0.3$, $\mu_N = 3$, $D_S = 3$, $D_N = 1$, and $\Omega = 40$.

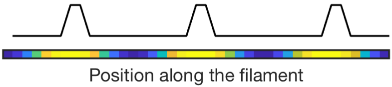
https://doi.org/10.1371/journal.pbio.2004877.g003

Deterministic Turing patterns

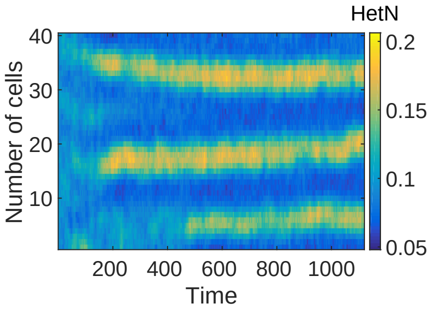


Pattern of HetN.

Project on the 1D chain.

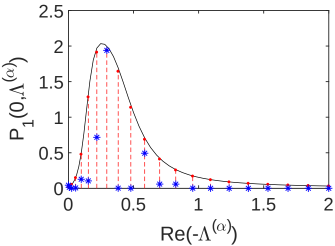


Stochastic Turing patterns

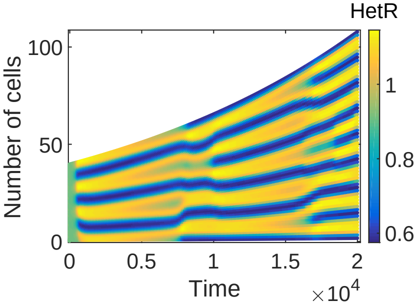


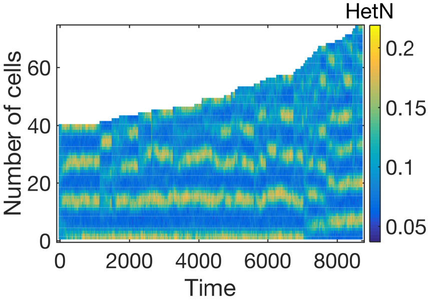
Pattern of HetN.

Power spectrum.



Accounting for cell duplication.

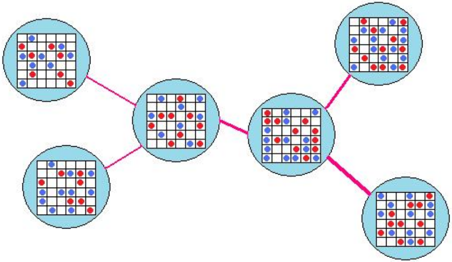




Example 3. Patterns seeded by stochastic finite size effects

Adjacency matrix

- X_i and Y_i identify individual elements of the two species.
- The index i stands for the node to which the elements belong.
- Reactions are local.
- Migration between adjacent nodes is allowed.



M. Asllani, Phys Rev E (2012)
M. Asllani, Europ. Phys. J. B.(2013)

Stochastic moves: the Brusselator

Reaction rules

$$
\begin{aligned}
E_i &\xrightarrow{a} X_i \\
X_i &\xrightarrow{b} Y_i \\
2X_i + Y_i &\xrightarrow{c} 3X_i \\
X_i &\xrightarrow{d} E_i
\end{aligned}
$$

Diffusion between adjacent nodes

$$
\begin{aligned}
X_i + E_j &\xrightarrow{\mu} E_i + X_j, \\
Y_i + E_j &\xrightarrow{\delta} E_i + Y_j.
\end{aligned}
$$

- $n_i \rightarrow$ number of molecule X in node i
- $m_i \rightarrow$ number of molecule Y in node i
- $N \rightarrow$ number of molecules which can be hosted in any node.

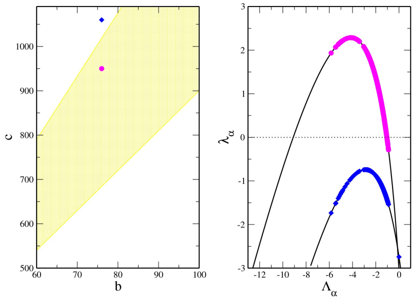
On the technical details

- Define the discrete concentrations $\mathbf{n} = (n_1, \cdots n_i, \cdots n_\Omega)$ and $\mathbf{m} = (m_1, \cdots m_i, \cdots m_\Omega)$
- Write down the Master Equation that governs the dynamics of the probability $P(\mathbf{n}, \mathbf{m}, t)$
- Working under the linear noise approximation:

$$\frac{n_i}{N} = \phi_i(t) + \frac{\xi_i}{\sqrt{N}}, \qquad \frac{m_i}{N} = \psi_i(t) + \frac{\eta_i}{\sqrt{N}},$$

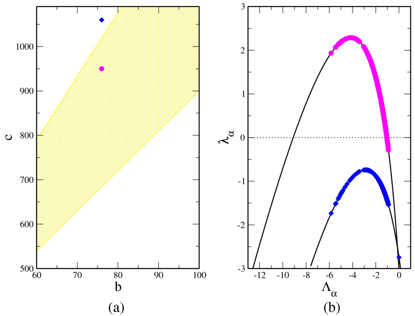
  where $\phi_i(t)$ and $\psi_i(t)$ represent the continuous concentration.
- Perform a perturbative (system size) expansion in the small parameter $1/\sqrt{N}$.

Leading order ($N^{-1/2}$) : mean-field equations

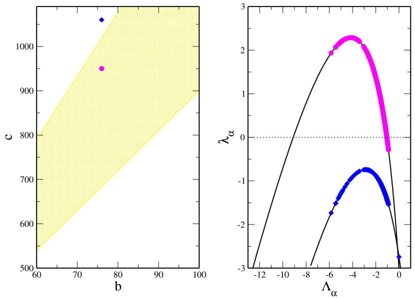


(a) (b)

Leading order ($N^{-1/2}$) : mean-field equations

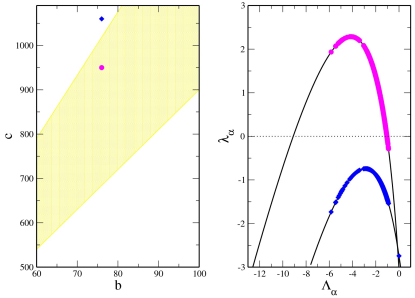


Leading order ($N^{-1/2}$) : mean-field equations



(a) (b)

Stochastic patterns



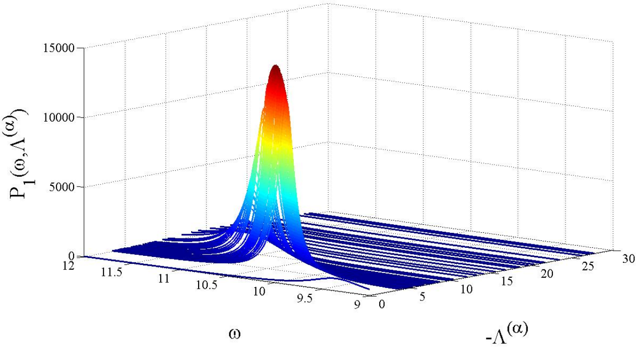
(a) (b)

The next–to–leading order (N^{-1})

Linear Langevin equation

$$\frac{d\xi_{si}}{d\tau} = \sum_{r,j} M_{sr,ij}\xi_{r,j} + \eta_{si}(\tau)$$

where $\quad < \eta_{si}(\tau)\eta_{rj}(\tau') >= B_{sr,ij}\delta_{\tau\tau'}$



Example 4. Excitatory-inhibitory neurons.

Label X and Y individual excitatory and inhibitory elements.

Birth-death scheme

$$\varnothing \xrightarrow{f[s_x]} X \qquad \varnothing \xrightarrow{f[s_y]} Y$$

$$X \xrightarrow{1} \varnothing \qquad Y \xrightarrow{1} \varnothing$$

where:

- $s_x = -r\left(\frac{n_Y}{V} - \frac{1}{2}\right)$.
- $s_y = r\left(\frac{n_X}{V} - \frac{1}{2}\right)$.
- $r > 0$ is the only free parameter.
- n_X and n_Y identify the number of elements of type X and Y.

Logic flow

a. Introduce $P_{\mathbf{n}}(t)$ to label the probability for the system to be in state $\mathbf{n} = (n_X, n_Y)$ at time t.

b. The dynamics of the system is governed by a master equation.

c. Perform a Kramers-Moyal expansion, $1/\sqrt{V}$ acting as small parameter.

Fluctuating hydrodynamic approximation

$$
\begin{aligned}
\dot{x} &= -x + f\left[-r(y-\frac{1}{2})\right] + \frac{1}{\sqrt{V}}\left[x + f\left(-r(y-\frac{1}{2})\right)\right]^{1/2}\eta_x \\
\dot{y} &= -y + f\left[r(x-\frac{1}{2})\right] + \frac{1}{\sqrt{V}}\left[y + f\left(r(x-\frac{1}{2})\right)\right]^{1/2}\eta_y
\end{aligned}
$$

- stochastic non linear equations.
- multiplicative noise.
- η_x and η_y are delta correlated Gaussian variables.

Deterministic limit, $V \to \infty$

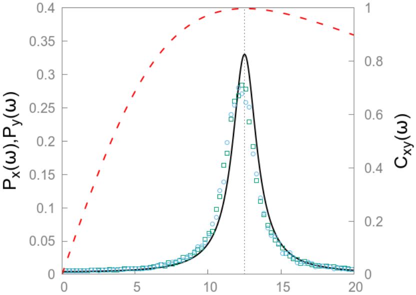
The deterministic model admits a fixed point $x^* = y^* = 1/2$. The linear stability analysis returns $\lambda = -1 \pm i\frac{r}{4}$

Fluctuations and quasi-cycles

Linear noise approximation

- $x(t) = x^* + V^{-1/2}\xi_1$
  $y(t) = y^* + V^{-1/2}\xi_2$
- $\dot{\xi}_i = \sum_j J_{ij}\xi_j + \eta_i$ with $i = 1, 2$

where $\eta_i(t)$ is a Gaussian noise with $< \eta_i(t)\eta_j(t') >= \delta_{ij}\delta(t - t')$.



Power spectral density matrix

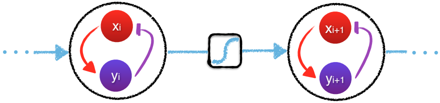
$$P_{ij}(\omega) =< \tilde{\xi}_i(\omega)\tilde{\xi}_j^*(\omega) >= \sum_{l=1}^{2}\sum_{m=1}^{2} \Phi_{il}^{-1}(\omega)\delta_{lm}\left(\Phi^{\dagger}\right)_{mj}^{-1}(\omega)$$

where $\Phi_{ij} = -J_{ij} - i\omega\delta_{ij}$

Visualizing quasi-regular oscillations

Finite size corrections do matter: macroscopic order can emerge as mediated by the microscopic disorder (inherent granularity and stochasticity)

Directed chain of neuromorphic units



Birth-death scheme

$$\varnothing \xrightarrow{f[s_{x_i}]} X_i \qquad \varnothing \xrightarrow{f[s_{y_i}]} Y_i$$
$$X_i \xrightarrow{1} \varnothing \qquad Y_i \xrightarrow{1} \varnothing$$

- $s_{x_i} = -r\left(\frac{n_{Y_i}}{V} - \frac{1}{2}\right) + D\left(\frac{n_{X_{i-1}}}{V} - \frac{n_{X_i}}{V}\right) - D\left(\frac{n_{Y_{i-1}}}{V} - \frac{n_{Y_i}}{V}\right)$.
- $s_{y_i} = r\left(\frac{n_{X_i}}{V} - \frac{1}{2}\right) + D\left(\frac{n_{X_{i-1}}}{V} - \frac{n_{X_i}}{V}\right) - D\left(\frac{n_{Y_{i-1}}}{V} - \frac{n_{Y_i}}{V}\right)$.

- $r > 0$ and $D > 0$ are free parameters.
- n_{X_k} and n_{Y_k} identify the number of elements of type X and Y in cell k.

Deterministic limit

$$
\begin{aligned}
\dot{x}_i &= -x_i + f\left[-r\left(\frac{n_{Y_i}}{V}-\frac{1}{2}\right) + D\left(\frac{n_{X_{i-1}}}{V}-\frac{n_{X_i}}{V}\right) - D\left(\frac{n_{Y_{i-1}}}{V}-\frac{n_{Y_i}}{V}\right)\right] \\
\dot{y}_i &= -y_i + f\left[r\left(\frac{n_{X_i}}{V}-\frac{1}{2}\right) + D\left(\frac{n_{X_{i-1}}}{V}-\frac{n_{X_i}}{V}\right) - D\left(\frac{n_{Y_{i-1}}}{V}-\frac{n_{Y_i}}{V}\right)\right]
\end{aligned}
$$

Homogeneous fixed point:
$x^* = y^* = 1/2\ \forall i$.

Jacobian and stability.

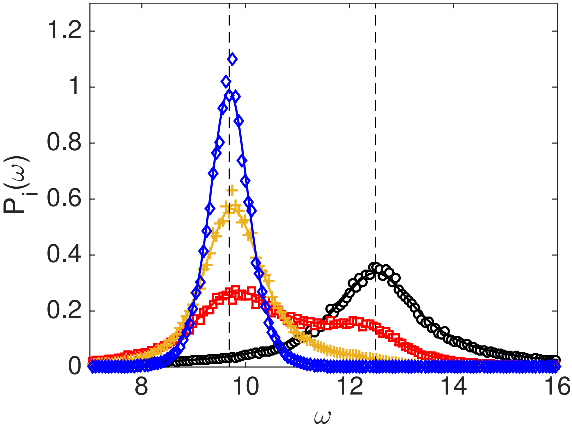
$$
J = \begin{pmatrix}
E_1 & 0 & 0 & 0 & 0 \\
S_2 & E_2 & 0 & 0 & 0 \\
0 & S_3 & E_3 & 0 & 0 \\
0 & 0 & \ddots & \ddots & 0 \\
0 & 0 & 0 & S_\Omega & E_\Omega
\end{pmatrix}
$$

E_i are identical for $i \geq 2$

- $\lambda_{1,2} = -1 \pm i\frac{r}{4}$
- $(\lambda_i)_{3,4} = -1 \pm \sqrt{-\frac{r}{8}(\frac{r}{2} - D)}$
  $i = 2, ..., \Omega$

Stable for $D < r/2$.
$\omega_0 = r/4$, $\omega_1 = \sqrt{\frac{r}{8}(\frac{r}{2} - D)}$.

Linear noise approximation: theory vs. simulations.

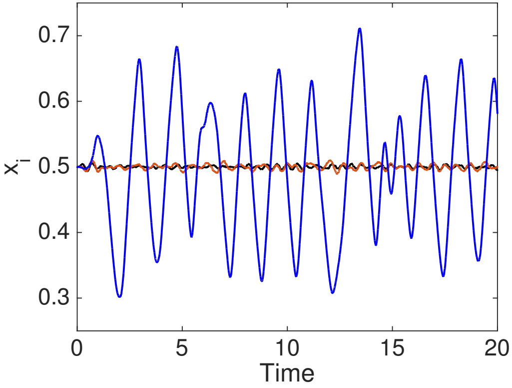


Act on D to select a frequency and amplify the signal along the chain.

On the amplification process

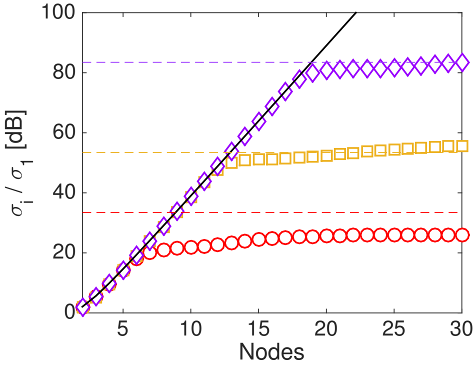
Stochastic trajectories as seen on different nodes of the chain.

Superposing the outcome



The amplification proceeds steadily along the chain. Saturation is attained when the fluctuations hit the boundaries.

The amplification is exponential.

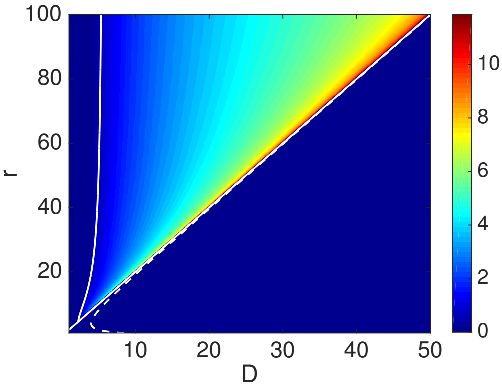


- Π is the distribution of fluctuations
- σ_i is the associated standard deviation on node i

Fokker-Planck equation

$$\frac{\partial}{\partial \tau}\Pi = -\sum_{i=1}^{2\Omega} \frac{\partial}{\partial \zeta_i}\left[(J\zeta)_i \Pi\right] + \frac{1}{2}\sum_{i=1}^{2\Omega} \frac{\partial^2}{\partial \zeta_i^2}\Pi$$

The rate of exponential amplification in the (D,r) plane.



The region of parameters that yields the sought amplification is delimited by the white solid curves (exact [right] and approximate [left]).

I. Tuning the frequency

II. Detecting a small amplitude noisy signal

Deterministic + noisy external input on node 1.