Activator-Inhibitor Systems

Sabine Pilari

Activator-Inhibitor System

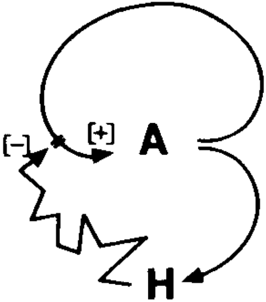


Figure: activator-inhibitor system (Meinhardt, Models of Biological Pattern Formation, 1982)

- activator a: autocatalysis, induction of inhibitor production
- inhibitor h: antagonist
- h diffuses more rapidly than a

Activator-Inhibitor System

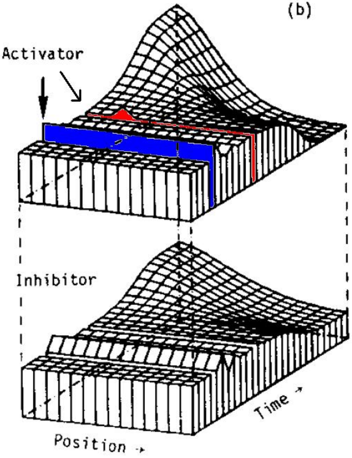


Figure: activator and inhibitor profile after some perturbation (Meinhardt, Models of Biological Pattern Formation, 1982, modified)

Activator-Inhibitor System: Example

Possible activator-inhibitor system:

$$\frac{da}{dt} = \frac{pa^2}{h} - \mu a + D_a \frac{d^2 a}{dx^2}$$
$$\frac{dh}{dt} = p' a^2 - \nu h + D_h \frac{d^2 h}{dx^2}$$

Discretization of diffusion term ($D_a \frac{d^2 a}{dx^2}$) in 1-dimensional system:
$\frac{da_i}{dt} = D_a(a_{i-1} - 2a_i + a_{i+1})$

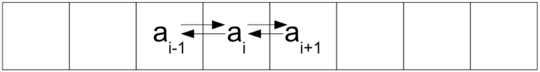


Figure: Diffusion in a 1D array of cells

Multiple Activator Maxima

Range of a substance:
Mean distance between production and decay of the substance

New maximum could arise if

- field size is much larger than inhibitor range
- activator increases or inhibitor decreases

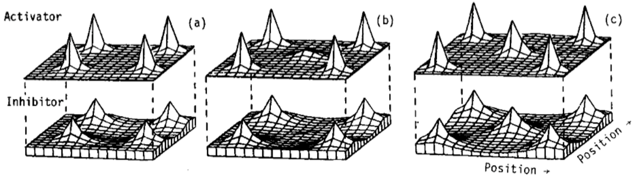


Figure: Development of a new activator maxima (Meinhardt, Models of Biological Pattern Formation, 1982)

Example: Marine Hydroids

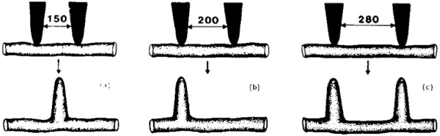
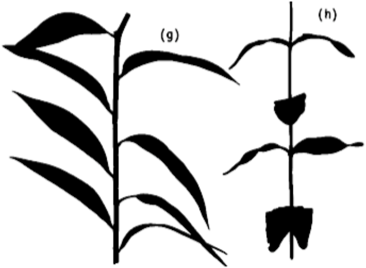


Figure: Formation of activator maxima in Marine Hydroids (Meinhardt, Models of Biological Pattern Formation, 1982)

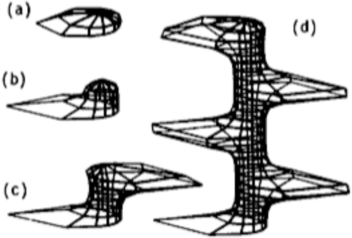
- Marine Hydroids form colonies by a branching network of stolons
- growing stolon $\hat{=}$ activator maximum
- minimum distance between stolons because of inibitor range

Regular Patterns

Phyllotaxis - regular spacing of leaves



(a) Spacing of leaves



(b) Formation of new leaves

Figure: taken from Meinhardt, Models of Biological Pattern Formation, 1982

Irregular Patterns

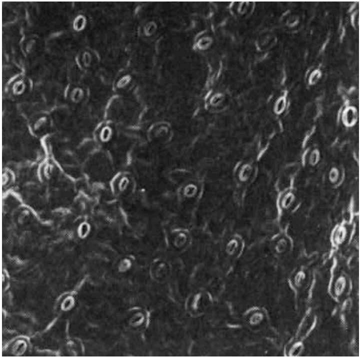


Figure: Stomata on a leaf (Meinhardt, Models of Biological Pattern Formation, 1982)

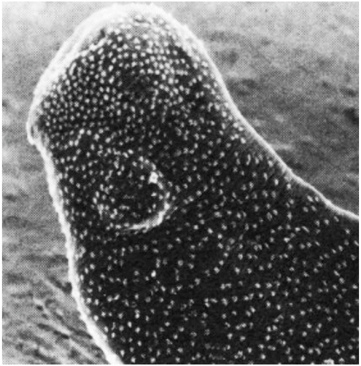


Figure: Cilia on *Xenopus* embryo (Meinhardt, Models of Biological Pattern Formation, 1982)

Alternatives: Gray-Scott Model

Reaction-diffusion model proposed by Gray and Scott (Gray and Scott, *Chem. Eng. Sci.*, **38**, 29, 1983)

Chemical equations:

$$\begin{aligned} U + 2V &\rightarrow 3V \\ V &\xrightarrow{k} P \end{aligned}$$

+ constant feed term F for U
+ feed process consumes U and V

Differential equations:

$$\begin{aligned} \frac{dU}{dt} &= -UV^2 + F(1-U) + D_U \frac{d^2U}{dx^2} \\ \frac{dV}{dt} &= +UV^2 - (F+k)V + D_V \frac{d^2V}{dx^2} \end{aligned}$$

Gray-Scott Model

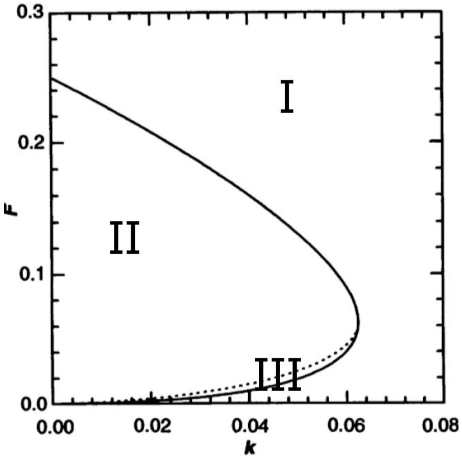


Figure: Phase diagram of the reaction kinetics (Pearson, Complex Patterns in a Simple System, 1993)

Gray-Scott Model

Example simulations

Gradients in Pattern Formation

Marvin Schulz

Initial disturbance

- Activator-inhibitor system requires initial stochastic disturbance
- Where does this disturbance come from?

What is so Nice About a Gradient

- Gradient of substance x can determine region of activator maximum for further processes
- Stable gradient gives cell / cell population a polarity
- Reusable in different developmental processes

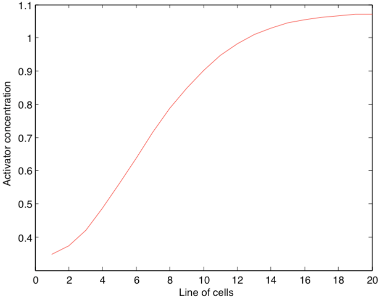


Figure: Gradient across a line of cells

How a Gradient is Build up

Characterization:

- Impermeable boundaries
- Maximum is build up at one side
- Only one maximum in field

How a Gradient is Build up

First solution

- Cell contains a source producing substance x on one side and a sink consuming x on the other side
- Details of gradient heavily depend on parameters (field size, ...)
- Shifts the polarity determination to a different level

How a Gradient is Build up

Second solution

- Activator-inhibitor system
- Large inhibitor range prevents further maxima
- Activator range ≈ field size
  → maximum shifts to one side

How a Gradient is Build up

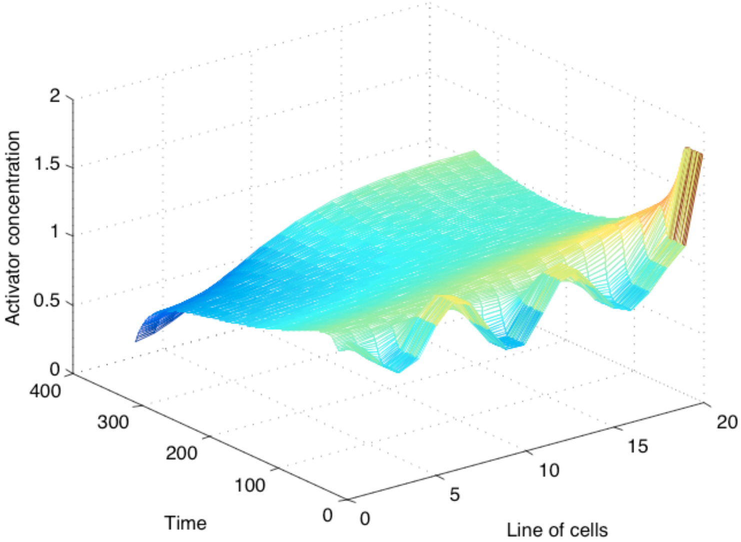
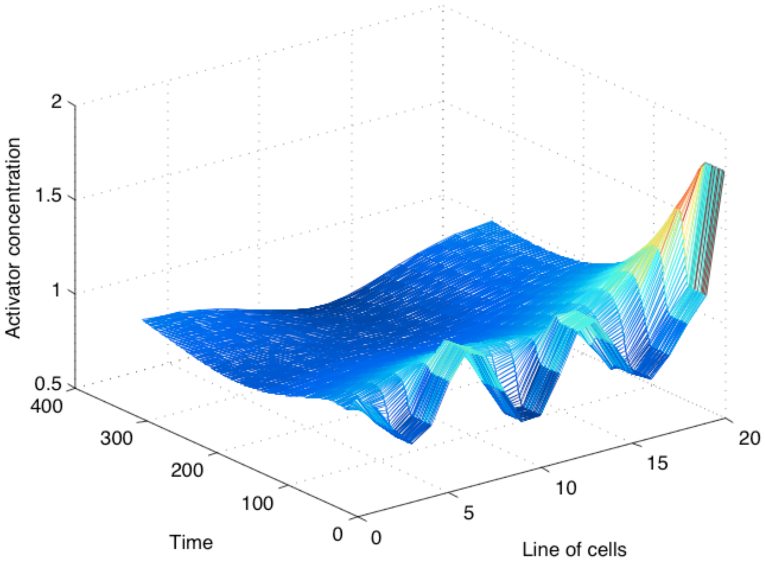


Figure: Simulation of the gradient building process

How a Gradient is Build up



Gradient recovery

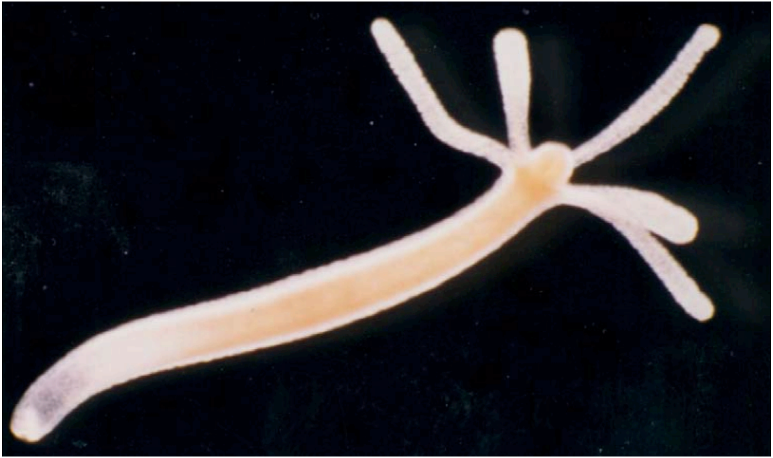


Figure: Hydra, taken from Meinhardt: Elementary networks ...

Gradient recovery

- Head of hydra gets lost
- Loss of activator maximum and location of inhibitor production
- Inhibitor is degraded
- Basal activator production rises activator concentration above threshold
- New activator maximum is formed

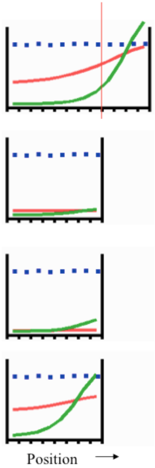


Figure: Gradient recovery, taken from Meinhardt: Elementary networks ...

Spacial Gene Activation Patterns

Hox genes in *Drosophila m.*

- Different genes active in different parts of the body
- Responsible for segmentation

Spacial Gene Activation Patterns

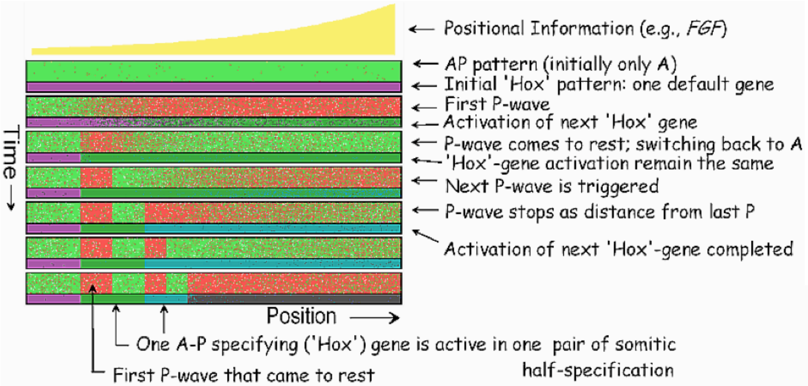


Figure: Hox gene activation, taken from Meinhardt: Elementary networks ...

Spacial Gene Activation Patterns

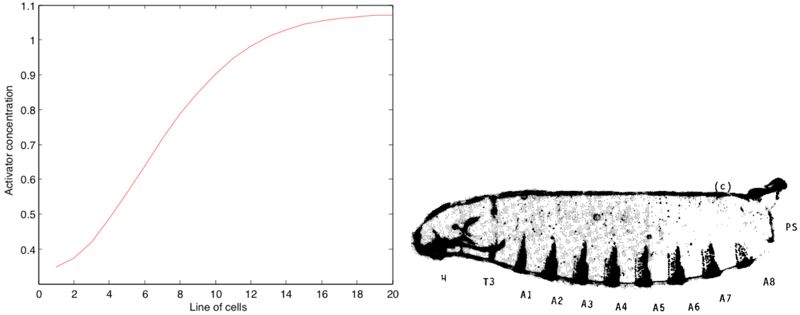


Figure: Normal development of *Drosophila m.*, right side taken from Menhardt: Models of ...

Spacial Gene Activation Patterns

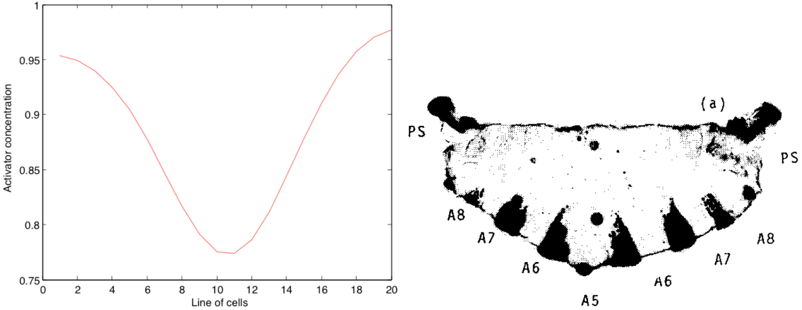


Figure: Double abdomen development of *Drosophila m.*, right side taken from Menhardt: Models of ...

Advantages of a Gradient

- Polarity ensures location of further activator maximas and their uniqueness
- Even shallow gradients are sufficient
- Easy to recover
- Explains segmentation

Pattern formation

- Pattern formation occurs during different stages of the development of all organisms
- Mathematical models describing pattern formation depend on
  - Activator - inhibitor models with different ranges
  - Local instability / global stability
- Different patterns are determined by the models parameters rather than by the models structure

Thank you for your attention

References

- Turing, A.: The chemical basis of morphogenesis, Phil. Trans. Royal Soc. London, **237** (1952), 37-72.
- Meinhardt, H.: Elementary networks for pattern formation in early development (Presentation at FEBS meeting, Gosau 2007)
- Meinhardt, H.: Models of biological pattern formation (1982)
- Pearson, J.: Complex patterns in a simple system, Science **261**, 189-192 (1993)
- Gray, P. and Scott, S.K., Chem. Eng. Sci. **38**, 29 (1983)