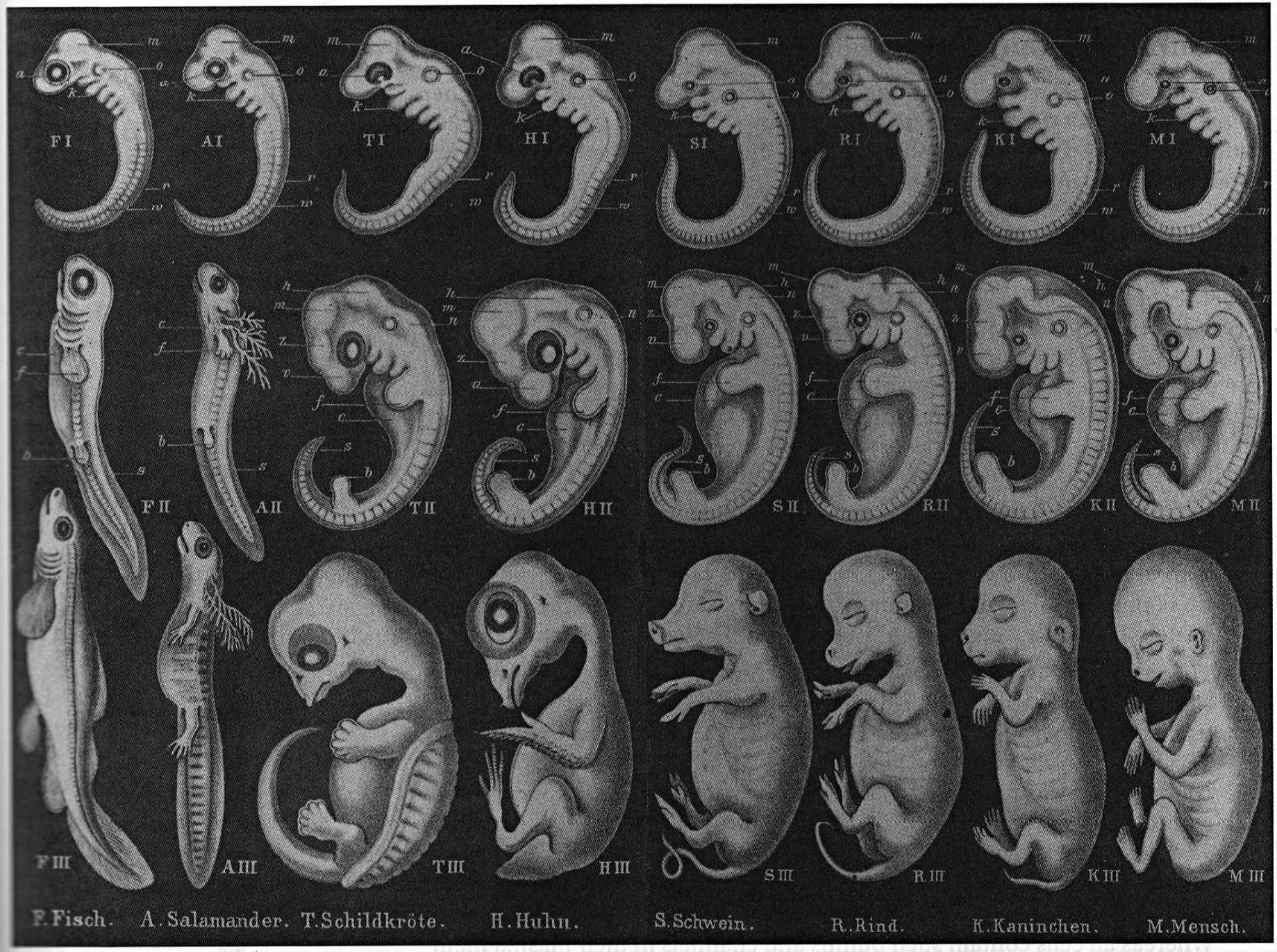
F I
A I
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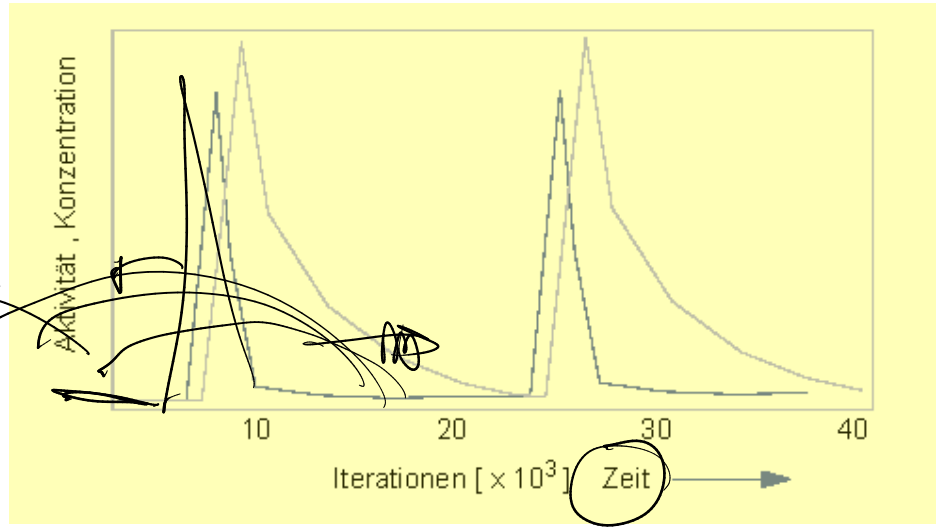
F III
A III
T III
H III
S III
R III
K III
M III
F. Fisch.
A. Salamander.
T. Schildkröte.
H. Huhn.
S. Schwein.
R. Rind.
K. Kaninchen.
M. Mensch.

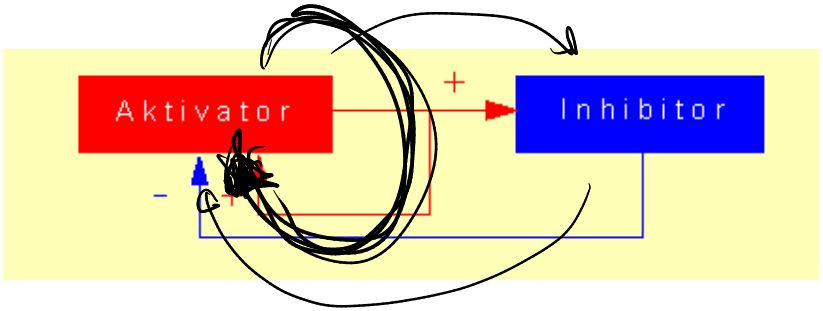
Structure formation must follow simple rulse

Approx. 150 Million years ago

Today

Gierer & Meinhardt- Model





General Scheme:
Aktivator: amplifies itself and the inhibitor
Inhibitor: inhibits the activator

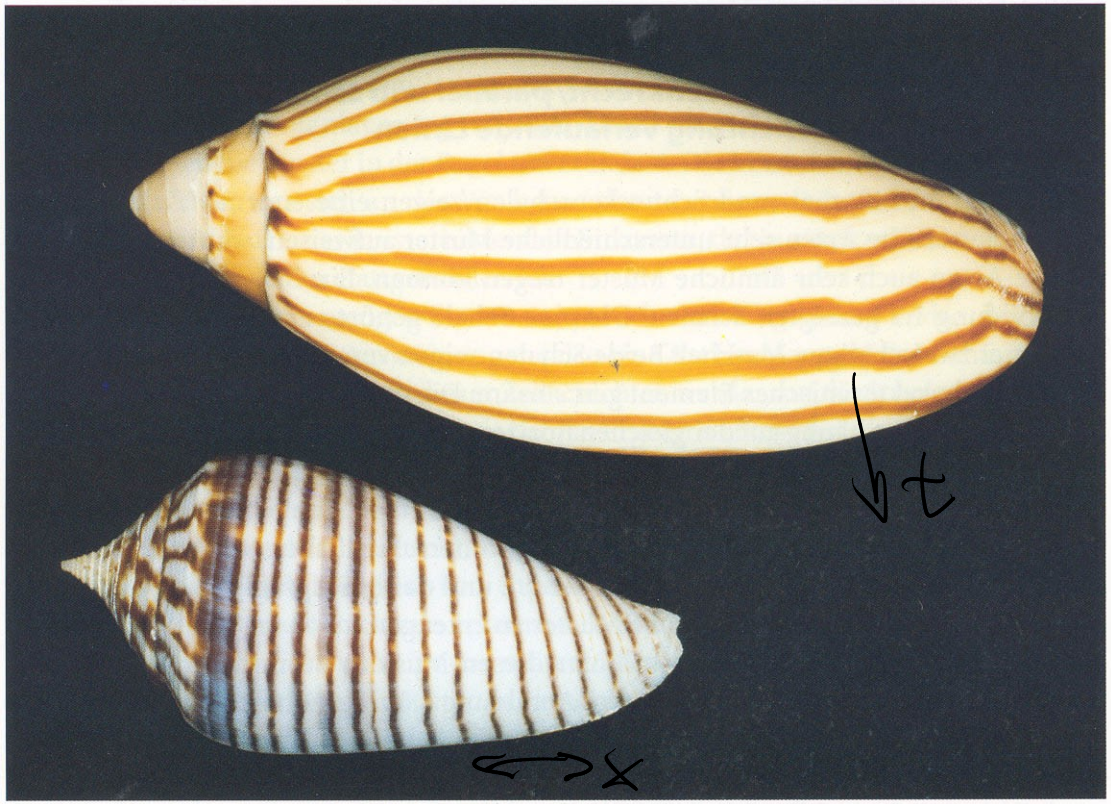
Asymmetry: Faster diffusion of Inhibitor!

Result: Oscillators
Application: Embryo development, branching of trees, fur patterns, snails and many more…

http://www.biologie.uni-hamburg.de/b-online/d28/28b.htm

Pattern formation in Biology: How snails paint their shells

How can static patterns emerge?



Direction of Growth

Two examples of elementary patterns: stripes parallel and perpendicular to the direction of growth.
- For the snail on top, the stripes are generates within periodic times at more or less the same time all over the snail shell. The result are axial patterns forming along the growth line.
- For the bottom snail, the pigmentation is generated in periodic distances at all times. So within time, the stripes are generated perpendicular to the growth direction.

from: Meinhardt, H., *Wie Schnecken sich in Schale werfen*. 1997, Berlin: Springer Verlag.

Pattern formation in Biology: How snails paint their shells

Aktivator-Inhibitor Model:

The Activator activates and triggers the prigmentation
Nonlinear reactions of only two diffusing molecules

Importent ingrediences:
- Autocatalysis (Activator catalyses its own production)
- Nonlinear backaction between Activator and Inhibitor
- Fluctuations (breaks Symmetry)
- Different Diffusion coefficients between Activator and Inhibitor
  (Typically, the inhibitor diffuses faster: local selfamplification, long range inhibition)

For comparison: the Belousov-Zhabotinski Reaction was described with Activator-Substrate model.
The back action is due to missing substrate where as a result no activation can be performed any more.

In the following we will describe an activator which also stimulates the inhibitor,
but which suppresses further activation.

from: Meinhardt, H., *Wie Schnecken sich in Schale werfen*. 1997, Berlin: Springer Verlag.

Pattern formation in Biology: How snails paint their shells

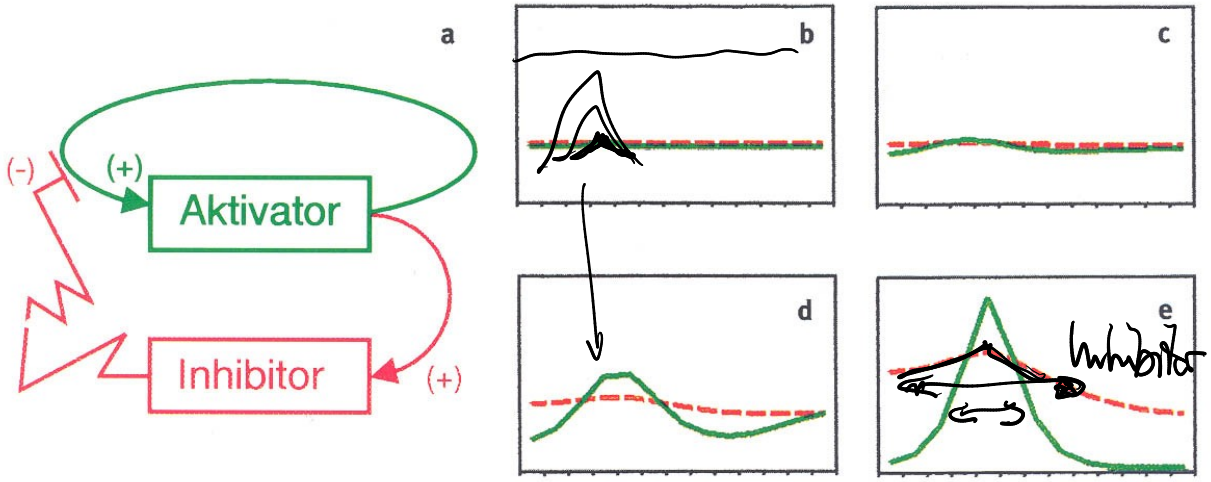
Spontaneous Pattern formation (example):

Aktivator / Inhibitor everywhere in steady state
Local fluctuations in the activator concentration
→ Activator concentration raises strongly due to autocatalysis
→ The local enhancement of activator increase a local concentrion of inhibitors

Different Diffusion coefficients of Activator / Inhibitor $(D_{Inhibitor} >> D_{Activator})$

→ Inhibitor spreads faster than activator
→ in distant regions the inhibitor prevails
→ in local regions the activator dominates
→ Creation of a peak
→ Creation of periodic peaks due to cross inhibition

→ **Pattern formation by local selfamplification and long range inhibition**



Pattern formation by local self-activation and long range inhibition. (a) Reaction scheme. An Activator catalyses his own production and those of a faster spreading antagonist, the inhibitor. (b-e) Steps of pattern formation after a local disturbance. Computer simulation of a linear chain of cells. The homogeneous distribution of both molecules are unstable. A minimal local increase of activator is self-amplifying until a stable steady state is reached at which the self activation and the surrounding inhibiation balance each other.

from: Meinhardt, H., *Wie Schnecken sich in Schale werfen*. 1997, Berlin: Springer Verlag.

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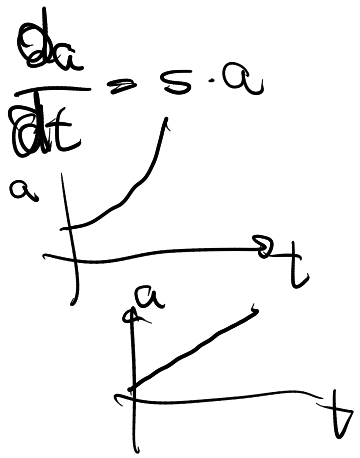
Mathematical Description



$$\partial a/\partial t = s\,(a^2/b + b_a) - r_a a + D_a\,\partial^2 a/\partial x^2$$

$$\partial b/\partial t = s\,a^2 + b_b - r_b b + D_b\,\partial^2 b/\partial x^2$$

Non-linear coupled partial differential equations

a^2/b -> Production rate of activator; autocatalytic and nonlinear (a^2)
the more activator is around, the more it is created.
Inhibitor b suppresses the growth of activator.

a^2 -> Productions rate of inhibitor, stimulated by activator

s -> Density of production source. Describes ability for autocatalysis

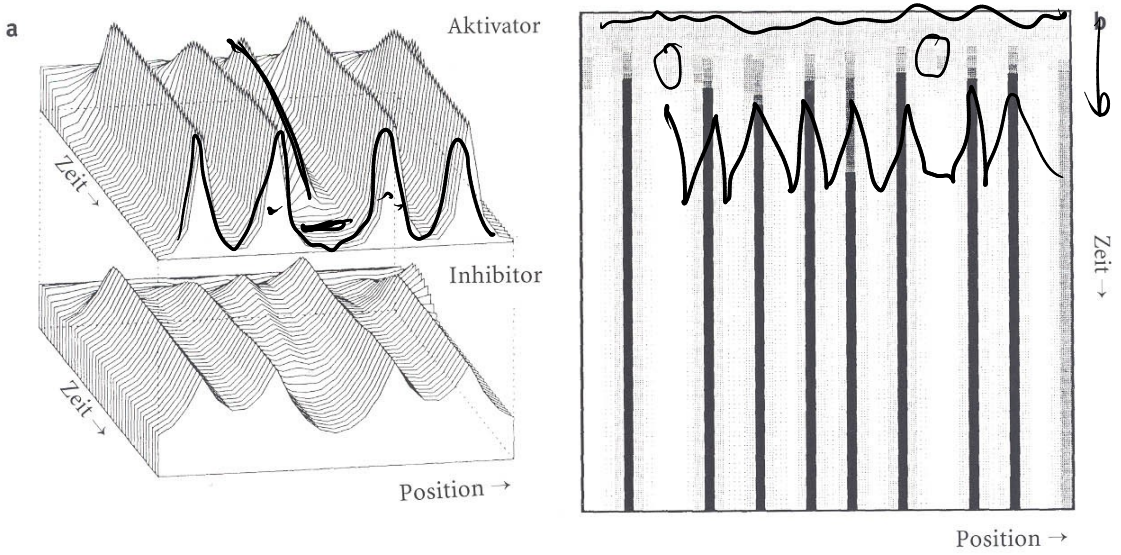
b_a, b_b -> spontaneous background production of activator/inhibitor („leakages“)

$r_a a$, $r_b b$ -> Decay rate. Molecules have s finite lifetime. Without production, an expontial decay prevails.

$D_a\,\partial^2 a/\partial x^2$, $D_b\,\partial^2 b/\partial x^2$ -> Diffusion ($D_b >> D_a$)

from: Meinhardt, H., *Wie Schnecken sich in Schale werfen*. 1997, Berlin: Springer Verlag.

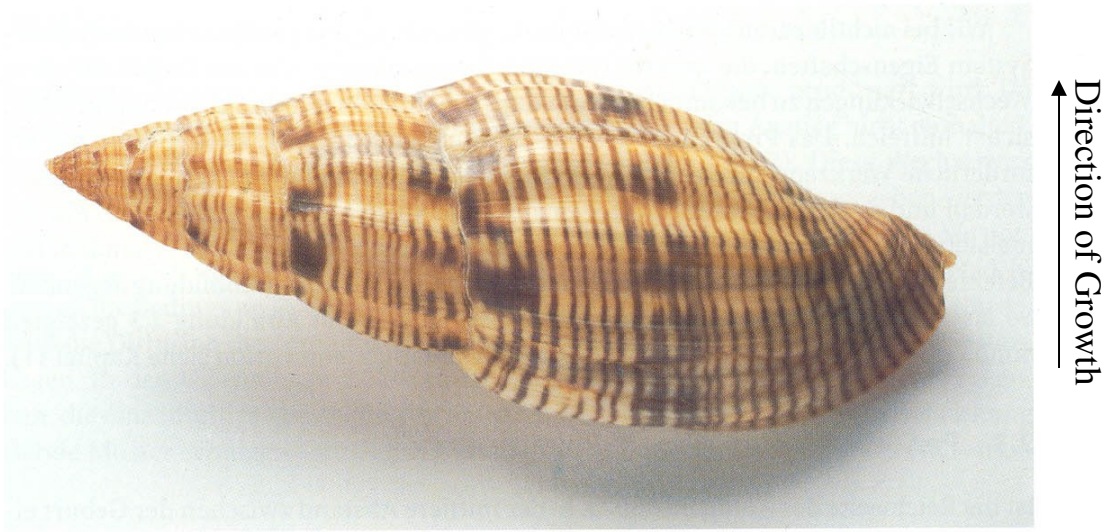
Pattern formation in Biology: How snails paint their shells



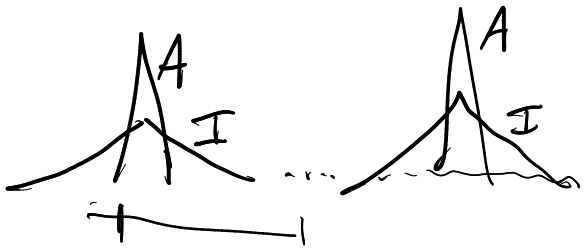
Solution of the Differential equation

→ Possibility to create stripe patterns spontaneously

→ Minimal distange is given by the reach of the inhibitor.



Creation of stable patterns (a) Computersimulation of a linear in einer linearen chain of cells. The creation of activator (top) and inhibitor (bottom) is plotted as a function of time. We simulate a length much largetr than the reach of the inhibitor. Several peaks are created, initiated by random fluctuations. A maximal and minimal distance is forming. The pattern formation is more regular when it is already created under cell division (b) Simulation with different parameters, more similar to the shell pattern. (c) Shell of Lyra planicostata taiwanica.



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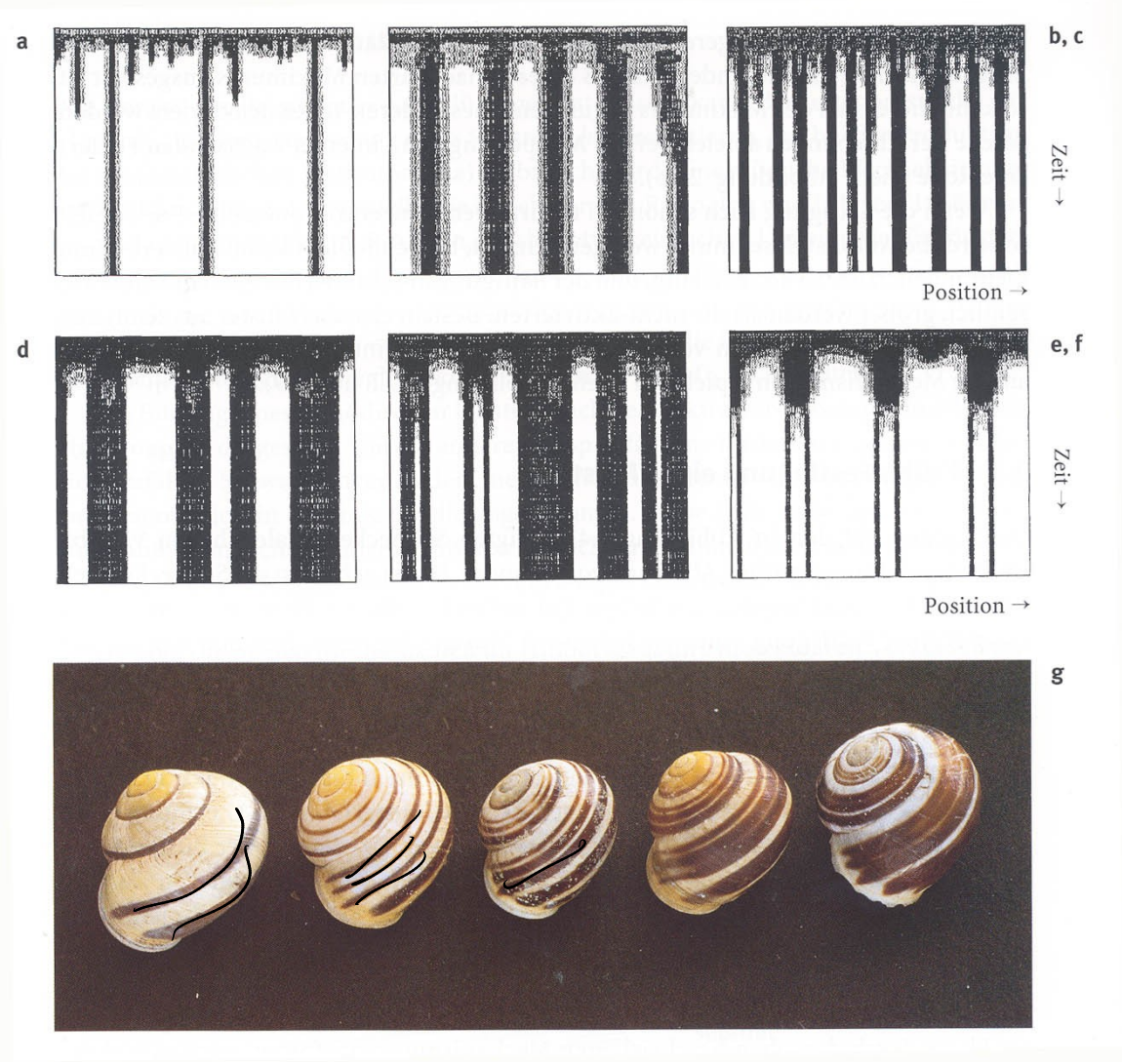
Increasing der Activator-Diffusion-coefficient →

With saturation of Autocatalysis



Refinement of Model:

prevously: Activator concentration can activate itself without limits: $\partial a/\partial t = s (a^2 / b)$

now: Saturation of autocatalysis: (starting with a destinct level of a the creation of activator a will not be further stimulated)

$\partial a/\partial t = s (a^2 / (b(1+s_a a^2)))$

-> $s (a^2 / b)$ for small a

Width of stripes and regularity of distances. (a) An activator with large reach create thin stripes with large intermediate distances. Without saturation, the distances between peaks can vary due to the small interaction between peaks. (b) A larger activator diffusion results in more regular distances between stripes. (c) Under saturation of autocatalysis, stripes with unregular widths and unreagular distances are created. (d-f) If the communication between cells is disturbed in early stages, these irregularities are more prominent. (g) Stripes of different characteristics are found for the garden snail Cepaea nemoralis.

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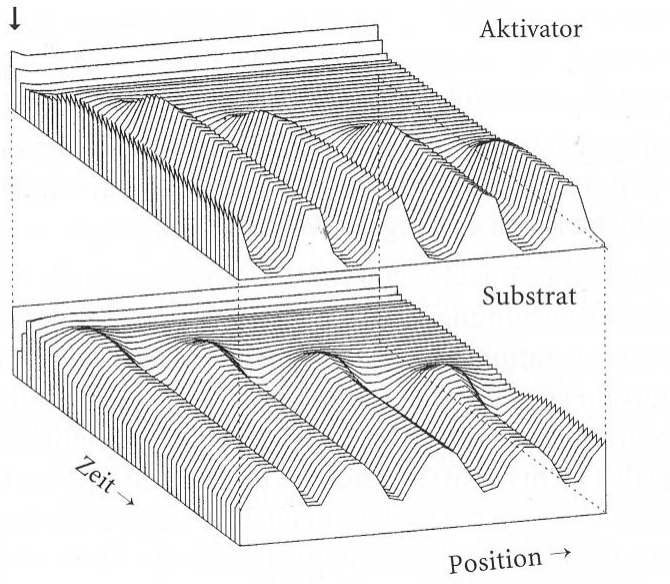
Alternative to Activator-Inhibitor-Model: Activator-Substrate-Model:

→ Autocatalysis of Activator
→ Activator can only be formed if enough subsrate is availlable
→ Diffusions coefficient for substrate is much larger than the activator ('fast feeding molecules').

Generation of pattern:
Fluctuation → the activator concentration raises locally
Autocatalysis → more activator is created locally
Due to the creation of activator the substrate is depleted locally. Since the substrate diffuses faster than the activator → the surrounding supplies more substrate by diffusion → locally stable maxima of activator concentration → "peak".



Pattern formation due to Activator-Substrate machanism. Activation is triggered by a locally enhanced activator concentration (arrow). This increase feeds from surrounding substrate and creates a stable peak. Another peak can only form in a distance from the first one.

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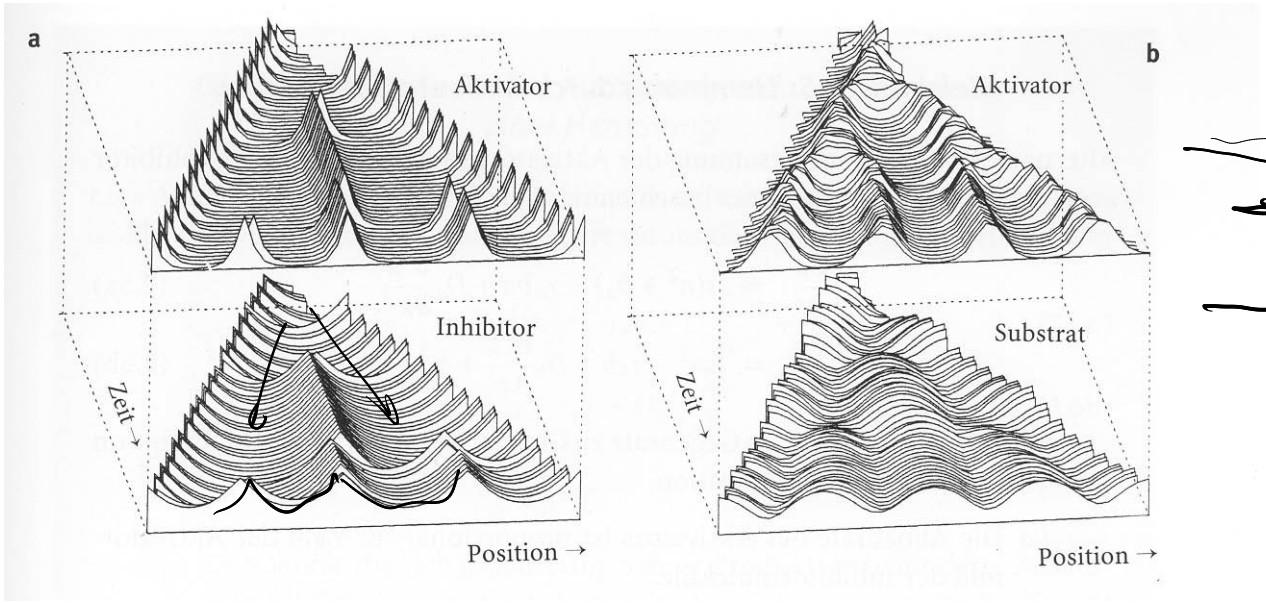
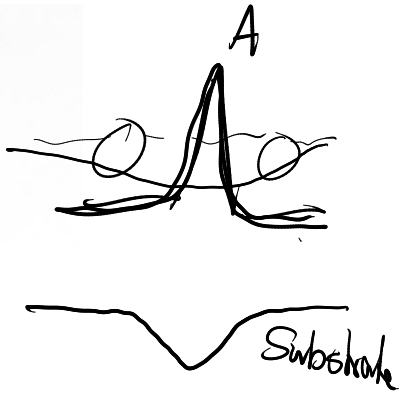
Activator-InhibitorModel versus Activator-Substrate Model:

→ In the Activator-Substrate Model the peaks are broader and more dense
→ In both cases there exist a minimal distance between peaks





Different behaviour under growth of cells. (a) Under Activator-Inhibitor, new areas are activated to create a new peak due to depletion of inhibitor in the space between peaks which then cannot suppress random creation of new peaks by fluctuations. (b) Under the Activator-Substrate model, the maxima are moving towards larger substrate concentratoin, creating splittings of peaks. However with including saturation, both models behave very similar.

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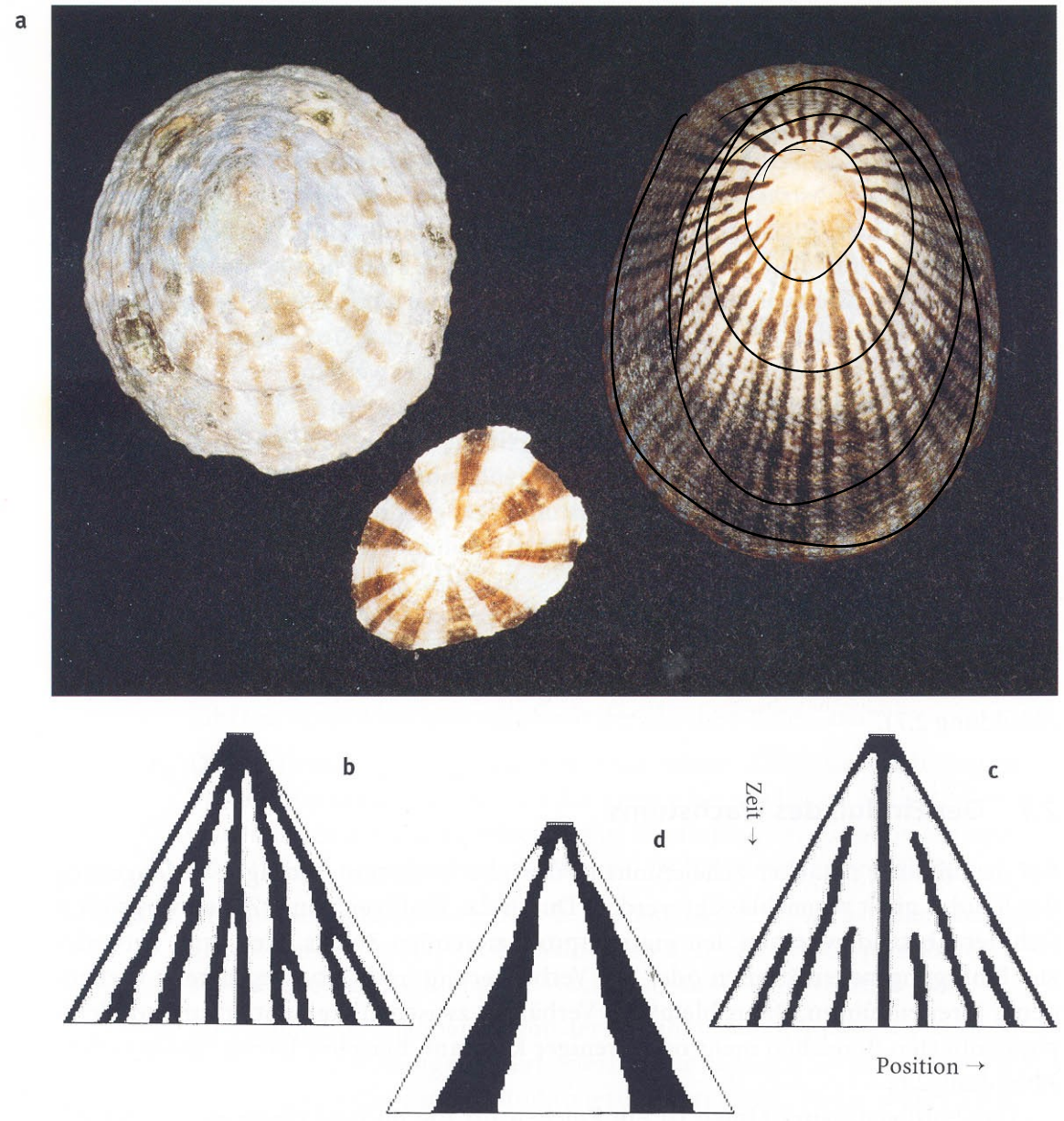

Pattern formation under growth conditions (cell division). (a) Natural patterns. There exist division of peaks, insertion of new lines or the linear broadening of lines. (b-d) Computer simualtions with an activator-inhibitor model. Growth is simulated by inserting new cells at given times. (b) Under saturation of activator, the maxima become more broad until they divide into two. (c) Without saturation, new maxima are inserted when the distance between peaks is too large. (d) Successive broadening of peaks exist if the pigment production is inherited to the daughter cell without modification, assuming a local bistability of the activator-inhibitor model: after initial peak generator, all cells above or below a thresgold remain activated or unactivated.

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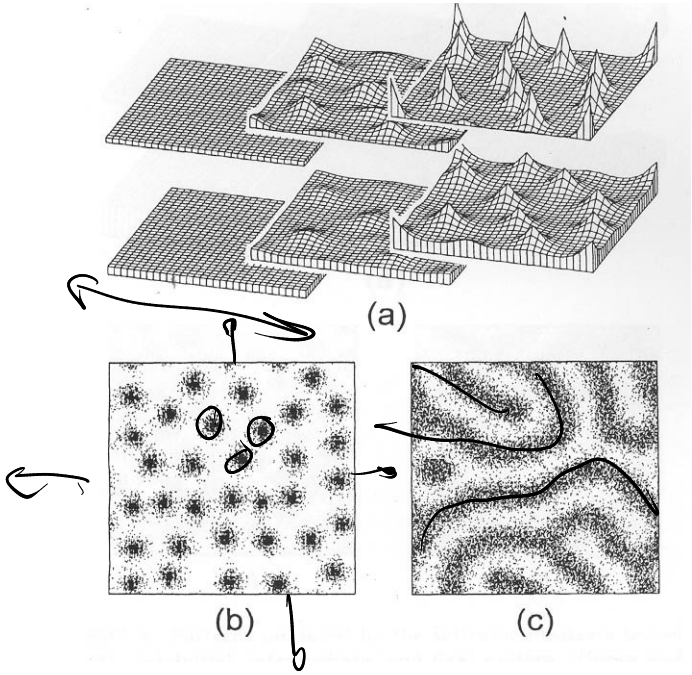
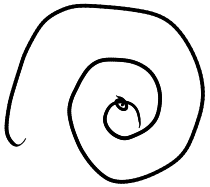
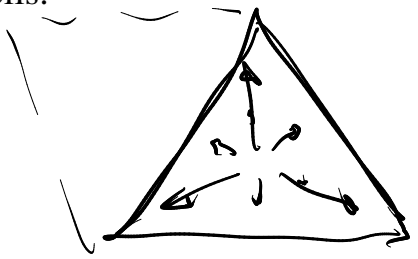


Patterns created in 2D by the activator-inhibitor model. (a) Initial, intermediate and final activator concentration (top) and inhibitor concentration (bottom). (b) Result of a simulation for a larger area. The concentration of activator is visualized by the density of pixels. (c) Same, but now with saturation of the autocatalysis, allowing the formation of stripe patterns of activated cells.





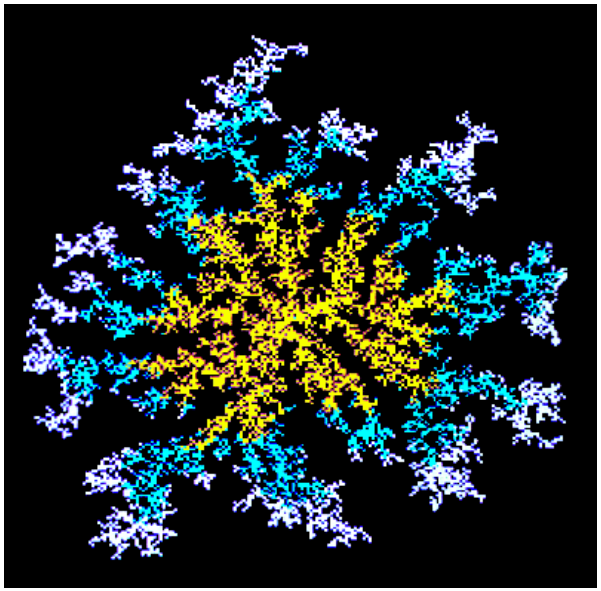
Until now we only discussed the one-dimensional diffusion elong a growth line. The state of cells are fixed in the solid shell. Diffusion can only happen in the one dimensionwhere the shell is created.

However in two dimensions more komplex stripes are possible – depending on the level of saturation of the autocatalysis. More komplex patterns are possible due to the hierarchical coupling of several activator-inhibitor systems.

The patterns of snails can be described by the shown principles.

From: Koch, A.J. and H. Meinhardt, *Biological pattern formation: from basic mechanisms to complex structures.* Reviews of Modern Physics, 1994. **66**(4): p. 1481-1507.

Biological Pattern formation:
Primitive model of diffusion limited aggregation



sprawling and radial growth of lichen
on the surface of a stone

Fractal patterns in nature: Many irregular patterns are not simply random. They often display an underlying structure, a kind of regular irregularity that can be mathematically described. Such objects have been called fractals, a term coined by Benoit B. Mandelbrot of IBM's Watson research center meaning broken or fragmented. Fractals are intricate structures that continue to show rich detail no matter how closely one zooms in for a look. Two scientists, Thomas A. Witten III and Leonard M. Sander have proposed a very simple mechanism for certain fractal forms. They call the process diffusion-limited aggregation. Imagine sticky particles coming into contact with each other and aggregating to form a cluster. Start with one particle in the center and release another sticky particle which randomly diffuses inward. When the particle finds the one in the center it sticks and stays put. Now repeat the process over and over, thousands of times. A meandering, tenuous cluster will grow.

taken from: http://www.scottcamazine.com/personal/DesignNature/