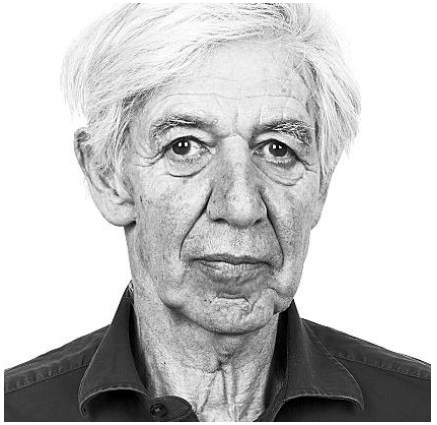
Pattern formation

Positional information: Lewis Wolpert



Lewis Wolpert
(1929-)

Positional Information and the Spatial Pattern of Cellular Differentiation†

L. WOLPERT

Department of Biology as Applied to Medicine,
The Middlesex Hospital Medical School, London, England

(*Received* 1 *July* 1969)

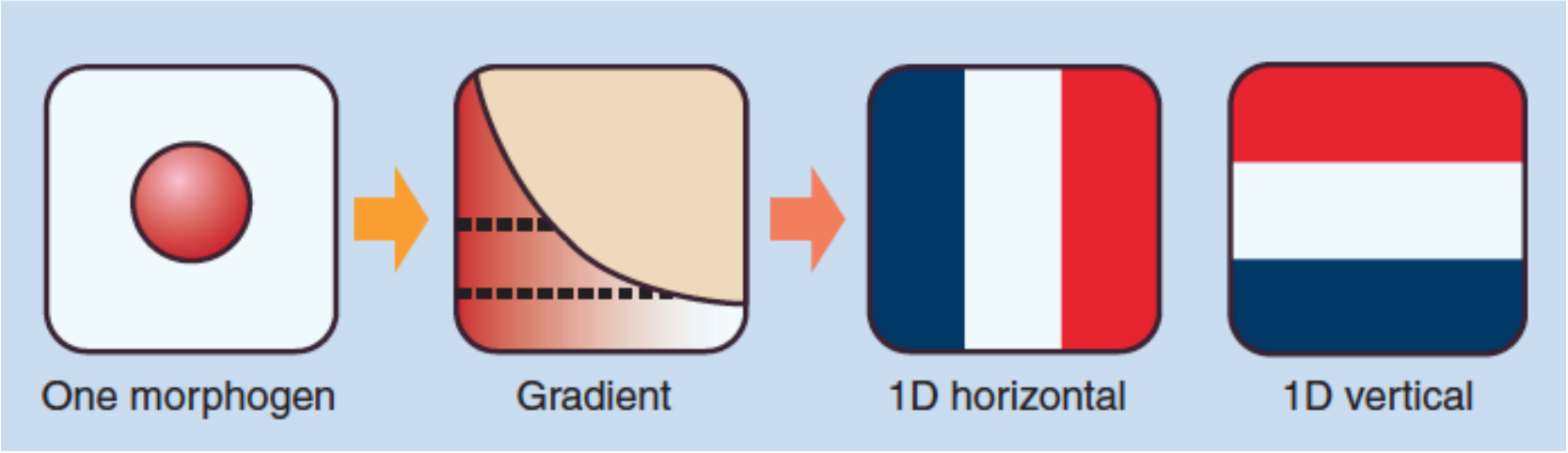
The problem of pattern is considered in terms of how genetic information can be translated in a reliable manner to give specific and different spatial patterns of cellular differentiation. Pattern formation thus differs from molecular differentiation which is mainly concerned with the control of synthesis of specific macromolecules within cells rather than the spatial arrangement of the cells. It is suggested that there may be a universal mechanism whereby the translation of genetic information into spatial patterns of differentiation is achieved. The basis of this is a mechanism whereby the cells in a developing system may have their position specified with respect to one or more points in the system. This specification of position is positional information. Cells which have their positional information specified with respect to the same set of points constitute a field. Positional information largely determines with respect to the cells'

Wolpert L(1969) *J. Theor. Biol.* **25**:1-47.

Positional information: the French flag model

Considering one fixed source of a diffusible molecule - the morphogen

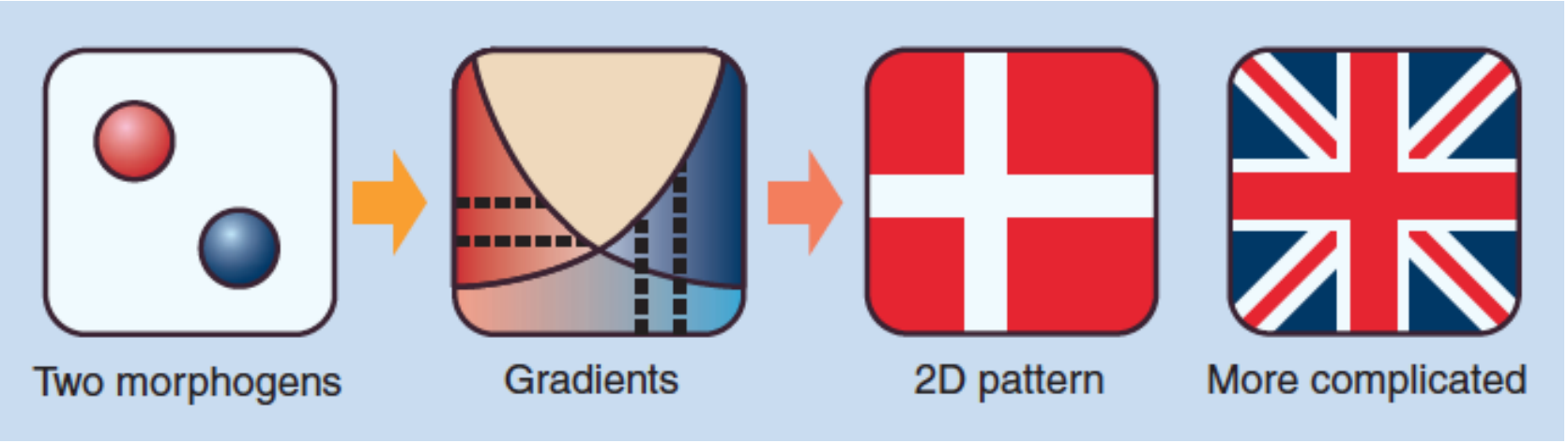
- This morphogen produced at a specific position forms a gradient by diffusion.
- The gradient is totally dependent on the pre-pattern of the morphogen source (boundary condition).
- Positional information: cells “know” their position from the concentration of the morphogen
- Cell differentiation is totally dependent on the localization and shape of the morphogen gradient



Positional information: the French flag model

Two or more morphogens

- If the system includes a second morphogen, more complex patterns can be produced
- The pattern of cell differentiation is still totally dependent on the initial pre-pattern of the morphogen sources
- No interactions between the morphogens are considered - the system is not self-regulating.



Reaction-Diffusion systems: Alan Turing

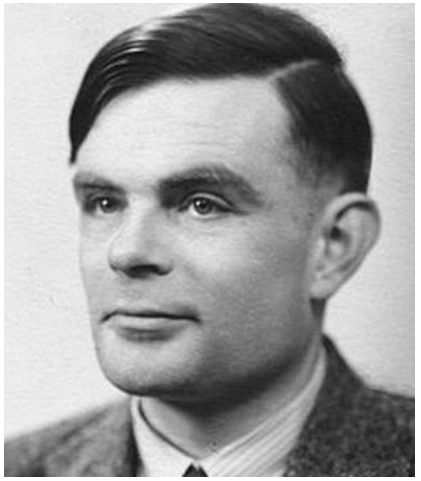
THE CHEMICAL BASIS OF MORPHOGENESIS

By A. M. TURING, F.R.S. *University of Manchester*

(*Received* 9 *November* 1951—*Revised* 15 *March* 1952)

It is suggested that a system of chemical substances, called morphogens, reacting together and diffusing through a tissue, is adequate to account for the main phenomena of morphogenesis. Such a system, although it may originally be quite homogeneous, may later develop a pattern or structure due to an instability of the homogeneous equilibrium, which is triggered off by random disturbances. Such reaction-diffusion systems are considered in some detail in the case of an isolated ring of cells, a mathematically convenient, though biologically unusual system. The investigation is chiefly concerned with the onset of instability. It is found that there are six essentially different forms which this may take. In the most interesting form stationary waves appear on the ring. It is suggested that this might account, for instance, for the tentacle patterns on *Hydra* and for whorled leaves. A system of reactions and diffusion on a sphere is also considered. Such a system appears to account for gastrulation. Another reaction system in two dimensions gives rise to patterns reminiscent of dappling. It is also suggested that stationary waves in two dimensions could account for the phenomena of phyllotaxis.

The purpose of this paper is to discuss a possible mechanism by which the genes of a zygote may determine the anatomical structure of the resulting organism. The theory does not make any new hypotheses; it merely suggests that certain well-known physical laws are sufficient to account for many of the facts. The full understanding of the paper requires a good knowledge of mathematics, some biology, and some elementary chemistry. Since readers cannot be expected to be experts in all of these subjects, a number of elementary facts are explained, which can be found in text-books, but whose omission would make the paper difficult reading.

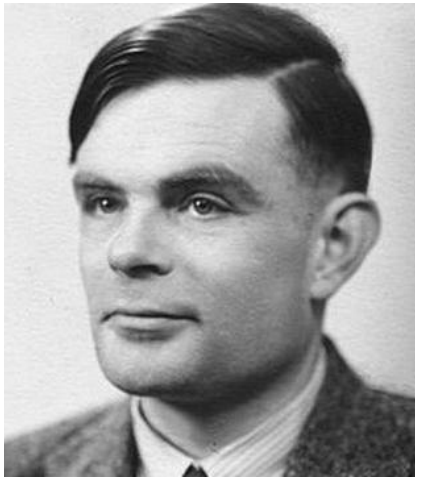


Alan Turing
(1912-1954)

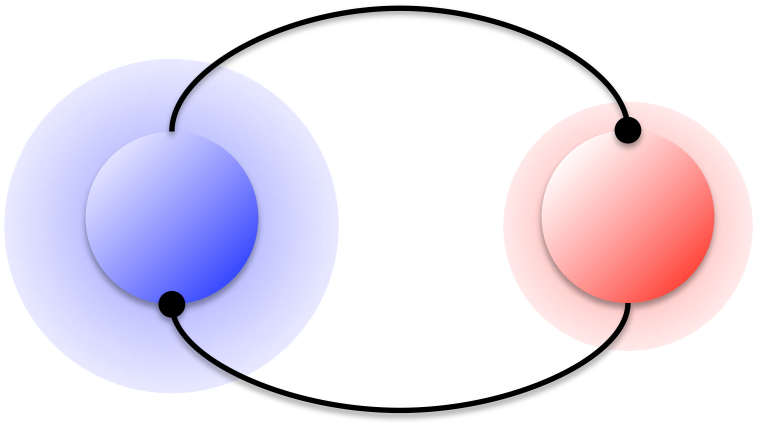
Turing, AM (1952). *Phil Trans R. Soc. B* **237**(641): 37–72.

Reaction-Diffusion systems: Alan Turing

"A system of chemical substances, called morphogens, reacting together and diffusing through a tissue, is adequate to account for the main phenomena of morphogenesis. Such a system, although it may originally be quite homogeneous, may later develop a pattern or structure due to an instability of the homogeneous equilibrium, which is triggered off by random disturbances."



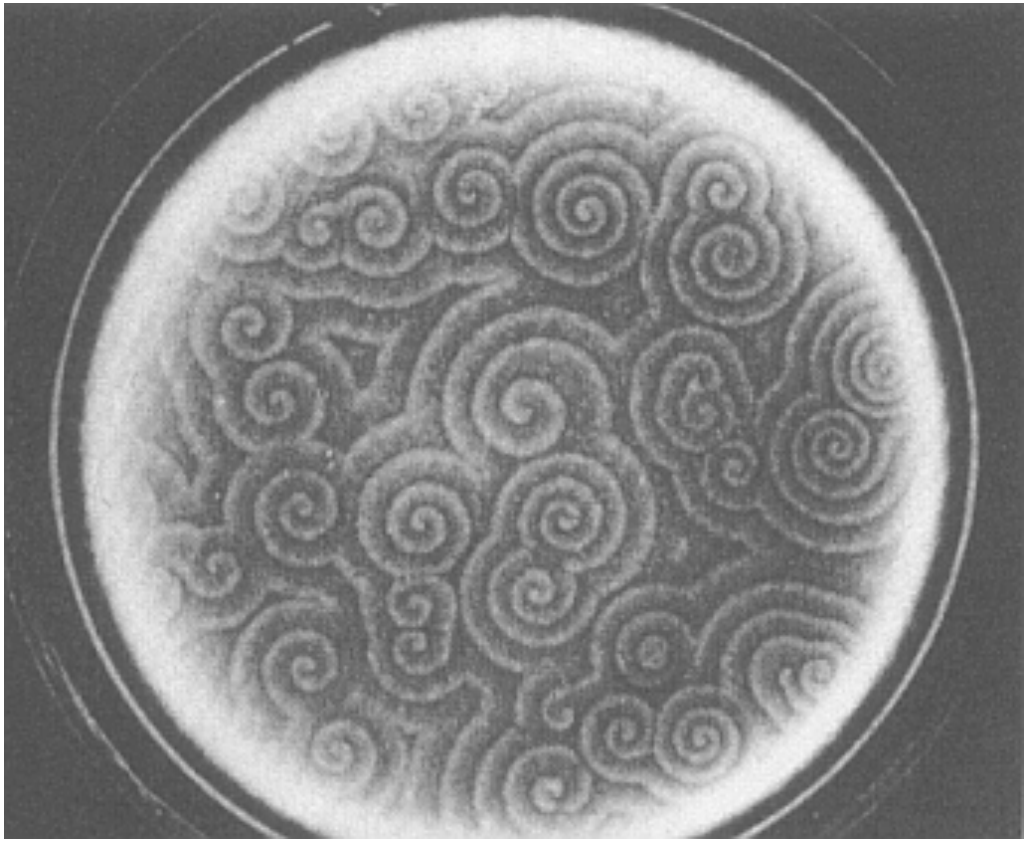
Alan Turing
(1912-1954)



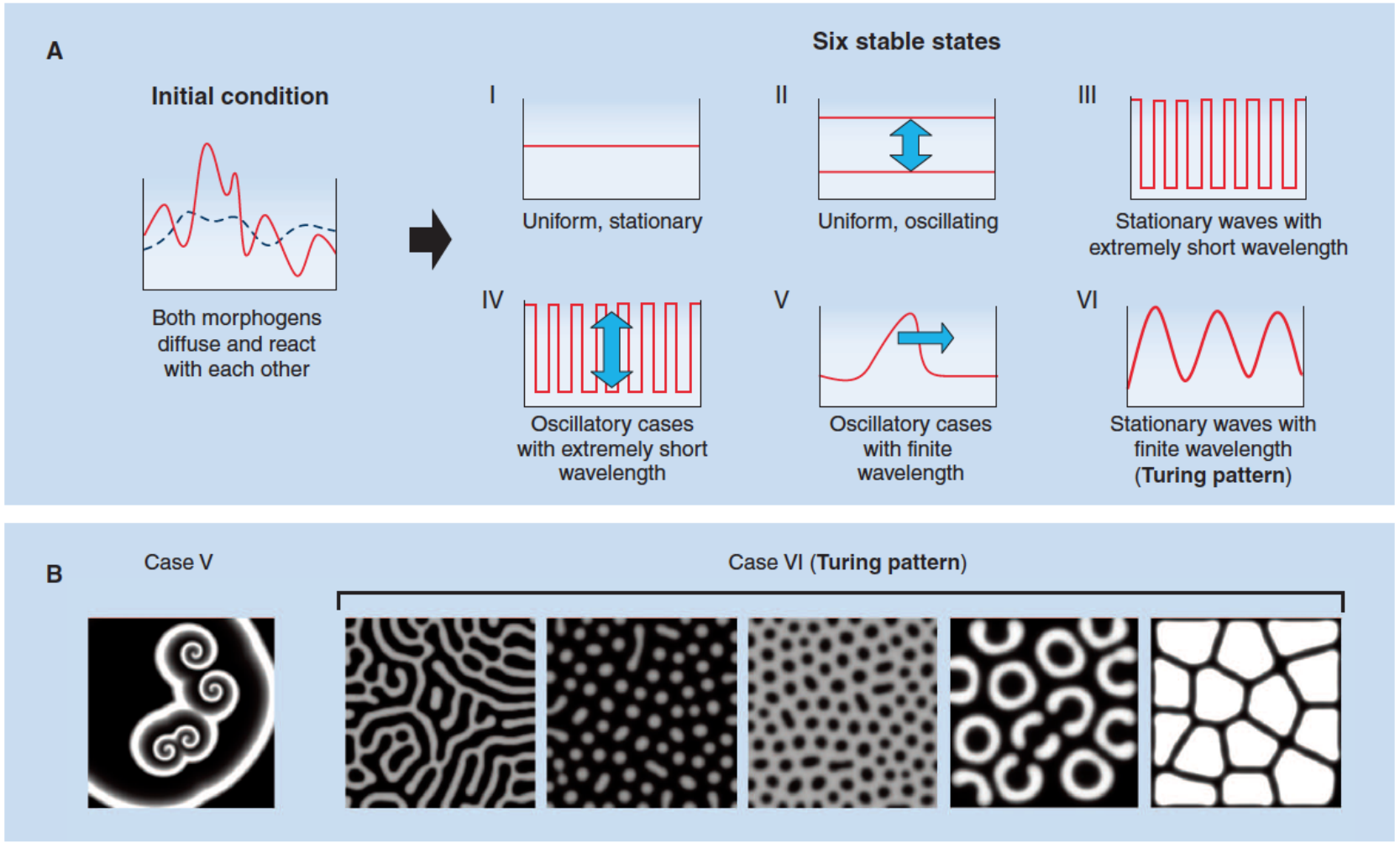
$$\frac{dx}{dt} = 5x - 6y + 1$$

$$\frac{dy}{dt} = 6x - 7y + 1 \quad (+ \text{diffusion})$$

Reaction-Diffusion systems: Belousov-Zhabotinksky reaction



Reaction-Diffusion systems: Turing instabilities



Reaction-Diffusion systems: Alan Turing model

If there are interactions between two diffusible molecules, and their diffusion coefficients are different

- The system can become self-regulated
- More complex patterns of cell differentiation can be generated
- Spontaneous patterns can be generated, independently of any initial pre-pattern. The existence of fixed sources of morphogens is not a necessary condition. Small random fluctuations are sufficient to trigger pattern formation, even from homogeneous initial conditions
- The patterns are independent of the size and shape of the tissue

Reaction-Diffusion systems: Hans Meinhardt & Alfred Gierer

Hans Meinhardt (1938-)

Alfred Gierer (1929-)

Reaction-Diffusion systems: Hans Meinhardt & Alfred Gierer

A Theory of Biological Pattern Formation

A. Gierer and H. Meinhardt
Max-Planck-Institut für Virusforschung, Tübingen, Germany

Received: September 8, 1972

Abstract

One of the elementary processes in morphogenesis is the formation of a spatial pattern of tissue structures, starting from almost homogeneous tissue. It will be shown that relatively simple molecular mechanisms based on auto- and cross catalysis can account for a primary pattern of morphogens to determine pattern formation of the tissue. The theory is based on short range activation, long range inhibition, and a distinction between activator and inhibitor concentrations on one hand, and the densities of their sources on the other. While source density is expected to change slowly, e.g. as an effect of cell differentiation, the concentration of activators and inhibitors can change rapidly to establish the primary pattern; this results from auto- and cross catalytic effects on the sources, spreading by diffusion or other mechanisms, and degradation.

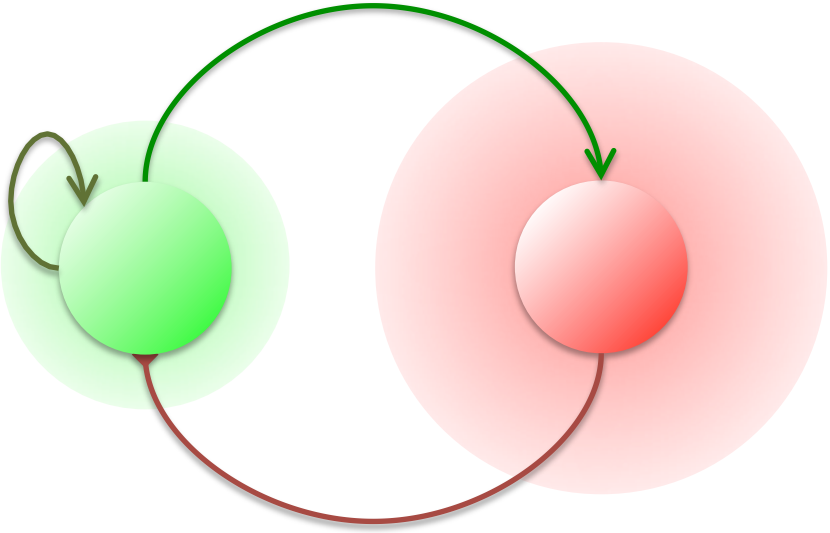
in embryology and regeneration is the formation of a spatial pattern of tissue structures. Starting from almost homogeneous tissue, different areas develop strikingly different structures. In some cases, their proportions are regulated to be independent of total size. The pattern may be aperiodic or periodic.

The formation of a morphological pattern is generally assumed to result from a primary pattern (Child, 1941; Waddington, 1962) of morphogen concentrations, or other physical parameters varying in space, often called gradients or fields. Several types of theories have been proposed for this primary pattern: A patterned morphogen distribution can result from auto- and cross

Gierer, A. and Meinhardt, H. (1972). *Kybernetik* **12**: 30-39

Reaction-Diffusion systems: Hans Meinhardt & Alfred Gierer

Local self-enhancement and long range inhibition (lateral inhibition)



$$\frac{\partial a}{\partial t} = \frac{\rho\, a^2}{h} - \mu_a a + D_a \frac{\partial^2 a}{\partial x^2} + \rho_o$$

$$\frac{\partial h}{\partial t} = \rho\, a^2 - \mu_h h + D_h \frac{\partial^2 h}{\partial x^2}$$

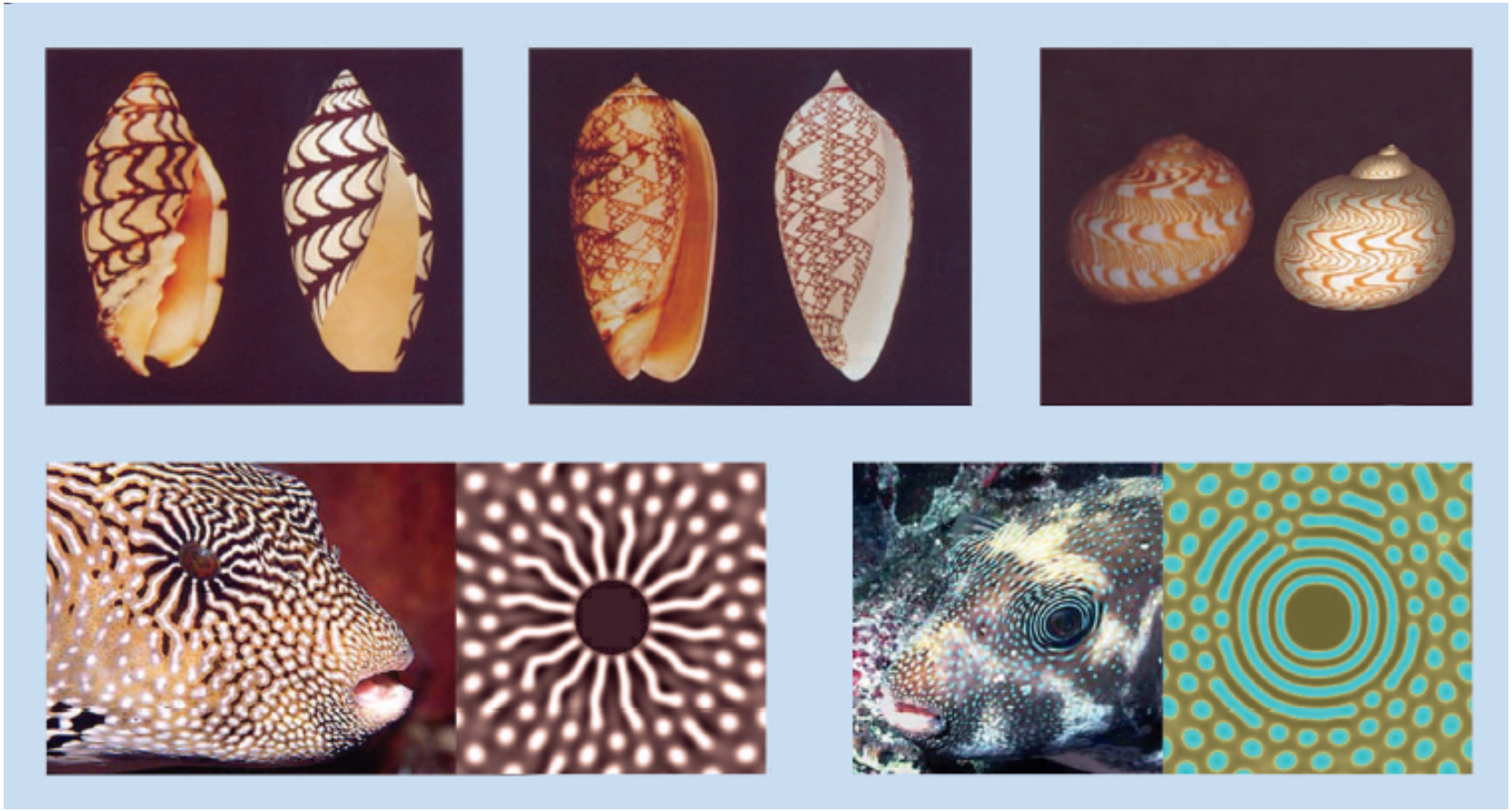
Reaction-Diffusion systems: Hans Meinhardt & Alfred Gierer

Local self-enhancement and long range inhibition

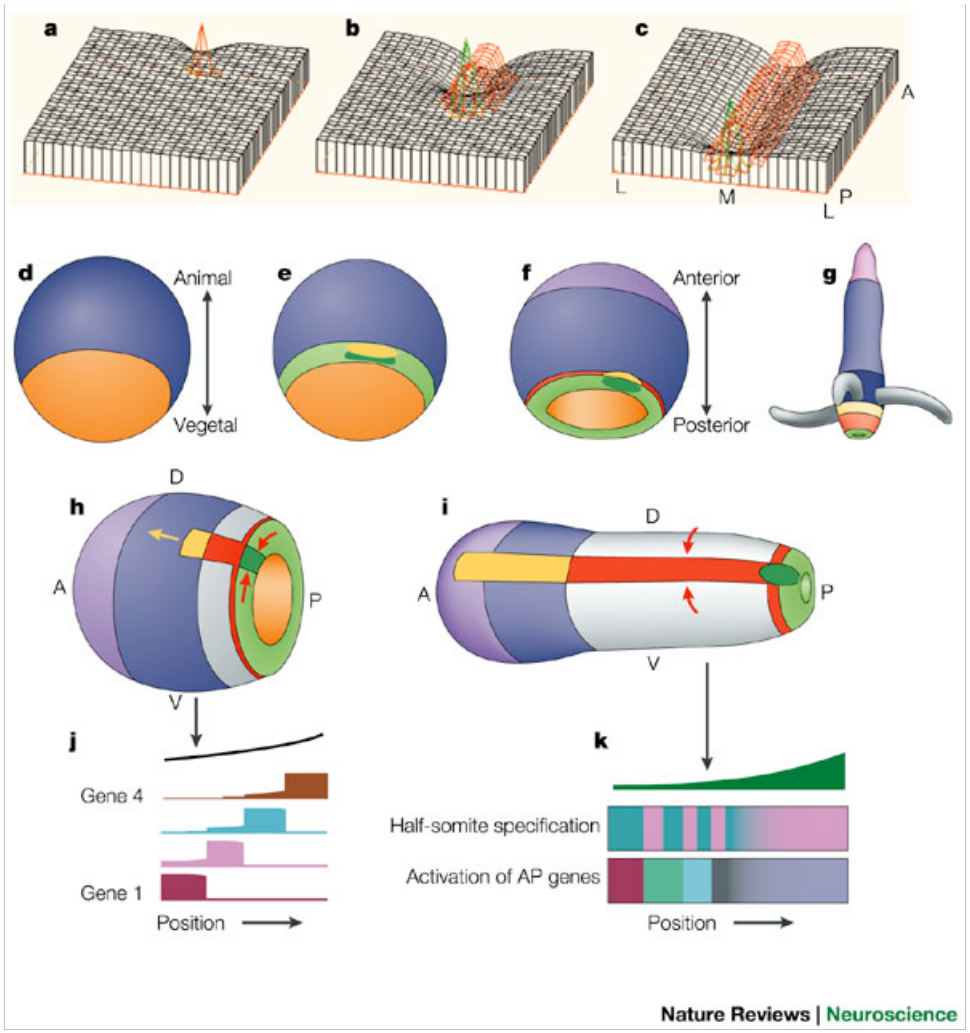
"Alan Turing — most famous for his work on the theoretical basis of computing — was clearly the first to show that patterns can arise if two substances with different diffusion rates interact. In our work, we showed that pattern formation is possible if, and only if, a local self-enhancing process is coupled with an antagonistic reaction with a long range. These conditions are not inherent in Turing's paper, but one can show that Turing's equations satisfy our conditions. The self-enhancement is required to amplify minute deviations from a homogeneous steady state, while the long-range inhibition makes sure that self-enhancement remains spatially confined and does not lead to an overall explosion. Our activator–inhibitor mechanism is a special example of this and, for instance, the Nodal–lefty2 interaction involved in mesoderm and left–right patterning follows this scheme."

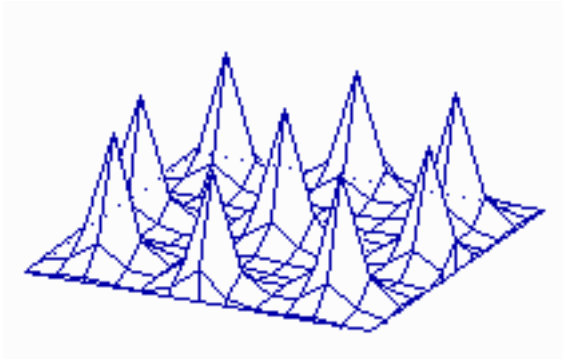
Current Biology (2008) 18, R401-R402

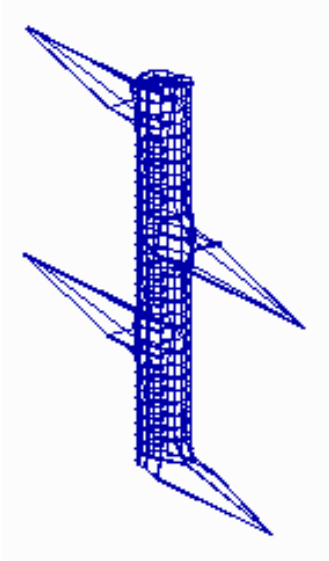
Reaction-Diffusion systems: Hans Meinhardt & Alfred Gierer



Reaction-Diffusion systems: Hans Meinhardt & Alfred Gierer

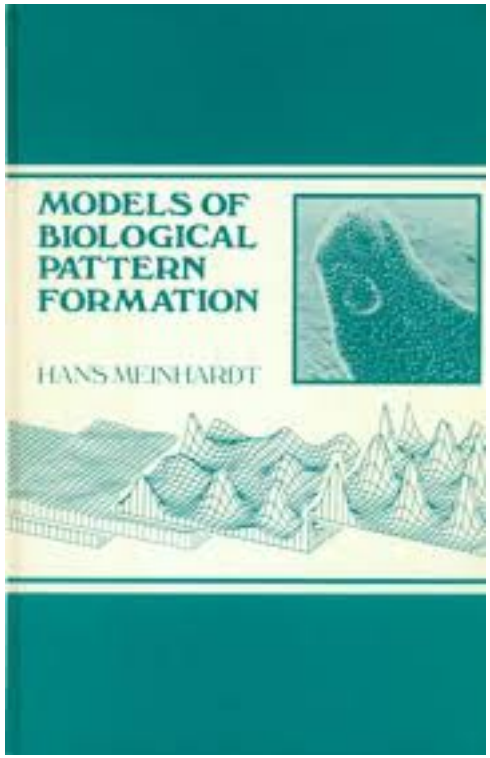


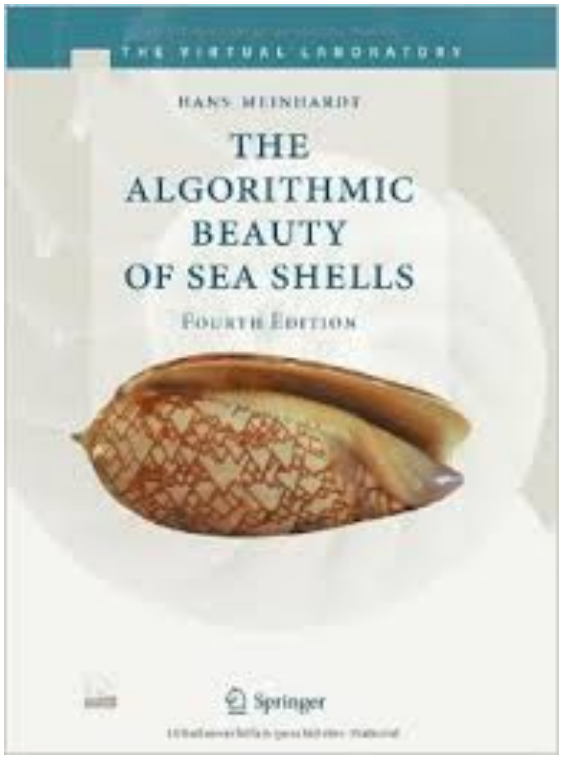




Nature Reviews Neuroscience (2004) 5, 502-510

Reaction-Diffusion systems: Hans Meinhardt & Alfred Gierer

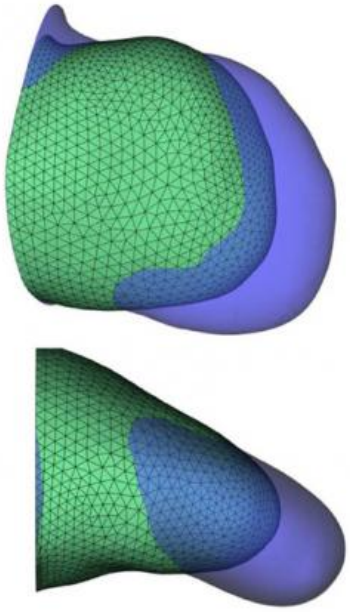




http://www.eb.tuebingen.mpg.de/research/emeriti/hans-meinhardt/home.html

A recent example: digit formation in vertebrates

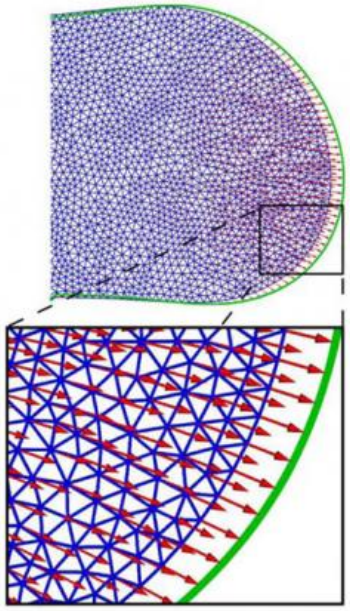
James Sharpe (CRG, Barcelona, Spain)



3D FINITE ELEMENT MODEL

Boehm et al (2010)
PLoS Biology 8(7):e1000420

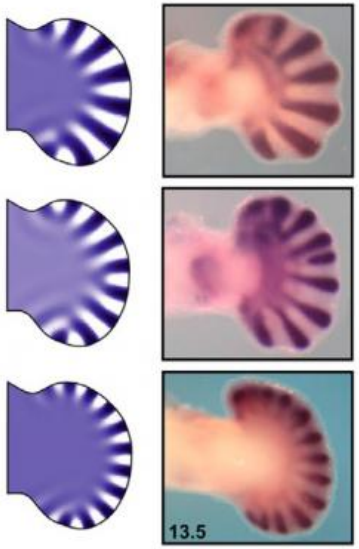
Commentry:
- PLoS Biology 8(7):e1000421
- New Scientist 2880:38



2D FINITE VOLUME MODEL

Marcon et al (2011)
PLoS Computational Biology 7(2):e1001071

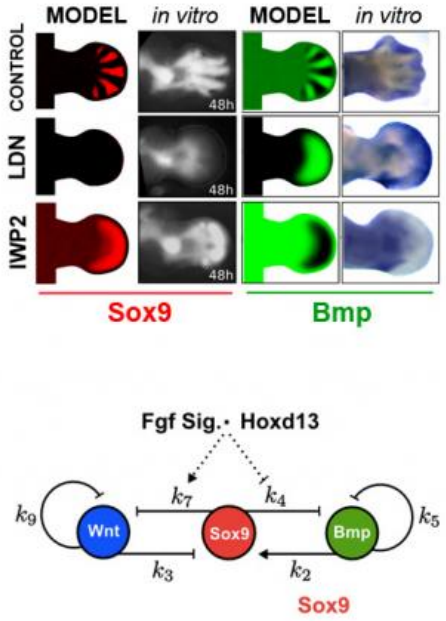
Commentry:
Nature Reviews Genetics 12:230



REACTION-DIFFUSION MODEL

Sheth et al. (2012)
Science 338:1476

Commentry:
- Science 338:1406
- Science Signalling 6:pe14



TURING MODEL

Raspopovic et al. (2014)
Science 345:566

Commentry:
- Science 345:516