Chemical basis of morphogenesis

Chem 163

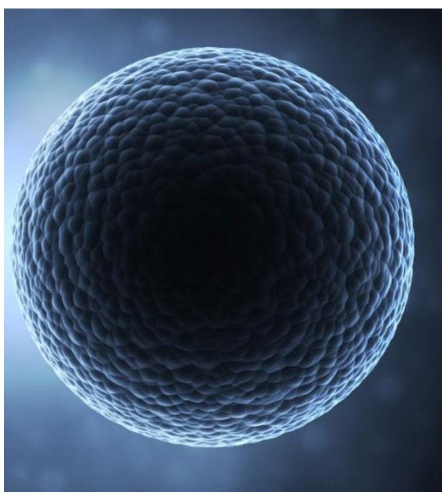
1 Nov 2022

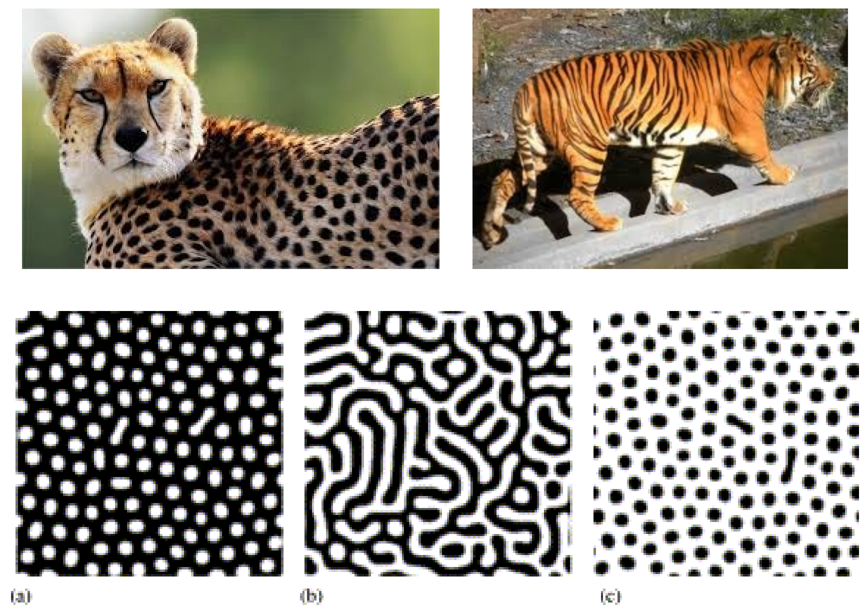
How do patterns emerge in biology?

THE CHEMICAL BASIS OF MORPHOGENESIS

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

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



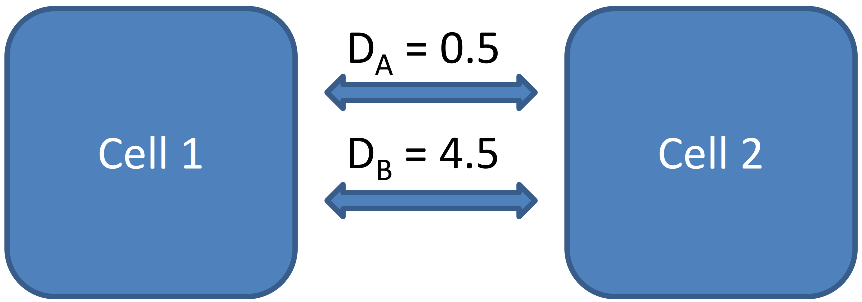


Can a chemical reaction become unstable?

Morphogens A, B

Reaction: $$\frac{dA}{dt} = 5A - 6\mathrm{B} + 1 \qquad \frac{dB}{dt} = 6A - 7B + 1$$

Diffusion: $$\frac{dA_i}{dt} = D_A(A_j - A_i) \qquad \frac{dB_i}{dt} = D_B(B_j - B_i)$$



Fixed point: A = 1, B = 1

But what if:

$$A_1 = 1 + 3\epsilon$$
$$A_2 = 1 - 3\epsilon$$
$$B_1 = 1 + \epsilon$$
$$B_2 = 1 - \epsilon$$

Then $\frac{d\epsilon}{dt} = 2\epsilon$

Together: $$\frac{dA_i}{dt} = D_A\left(A_j - A_i\right) + 5A_i - 6B_i + 1$$

$$\frac{dB_i}{dt} = D_B\left(B_j - B_i\right) + 6A_i - 7B_i + 1$$

Chemical reactions in continuous space

$$\frac{\partial A}{\partial t} = D_A \nabla^2 A + F(A, B)$$

$$\frac{\partial B}{\partial t} = D_B \nabla^2 B + G(A, B)$$

Assume an equilibrium exists, i.e.:

$$F(A_0, B_0) = 0$$
$$\mathrm{G}(A_0, B_0) = 0$$

Expand around equilibrium:

$$\mathrm{A} = \mathrm{A}_0 + U$$
$$\mathrm{B} = \mathrm{B}_0 + W$$

$$F(A_0 + U, B_0 + W) \approx aU + b\,W$$
$$G(A_0 + U, B_0 + W) \approx cU + dW$$

where

$$\left.\frac{\partial F}{\partial A}\right|_{A=A_0, B=B_0} = a$$

$$\left.\frac{\partial F}{\partial B}\right|_{A=A_0, B=B_0} = b$$

…

Linearize the equations around equilibrium

$$\frac{\partial U}{\partial t} = D_A \nabla^2 U + aU + bW$$

$$\frac{\partial W}{\partial t} = D_B \nabla^2 W + cU + dW$$

Ansatz: $U(\mathbf{r},t) = u(t)e^{i\mathbf{k}\cdot\mathbf{r}}$
$W(\mathbf{r},t) = w(t)e^{i\mathbf{k}\cdot\mathbf{r}}$

$$\frac{\partial u}{\partial t} = -k^2 D_A u + au + bw$$

$$\frac{\partial w}{\partial t} = -k^2 D_B w + cu + dw$$

Or equivalently

$$\frac{d}{dt}\begin{pmatrix} u \\ w \end{pmatrix} = \begin{pmatrix} a - k^2 D_A & b \\ c & d - k^2 D_B \end{pmatrix} \begin{pmatrix} u \\ w \end{pmatrix}$$

Which is of the form

$$\frac{d\mathbf{v}}{dt} = \mathbf{L}\mathbf{v}$$

Solving the equations:

$$\frac{d\mathbf{v}}{dt} = \mathbf{L}\mathbf{v} \qquad \mathbf{v}(t) = e^{\mathbf{L}t}\mathbf{v}(0)$$

$$\begin{pmatrix} \dot{u} \\ \dot{w} \end{pmatrix} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \begin{pmatrix} u \\ w \end{pmatrix}$$

$$\det \begin{pmatrix} a-\lambda & b \\ c & d-\lambda \end{pmatrix} = 0$$

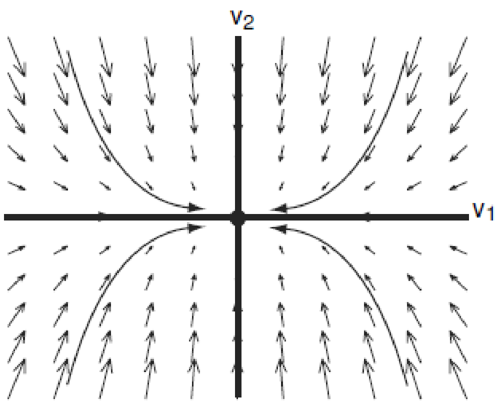
$$\lambda^2 - \tau\lambda + \Delta = 0 \qquad \tau = \mathrm{tr}\, L = a + d \qquad \Delta = \det L = ad - bc$$

$$\lambda_1 = \frac{\tau + \sqrt{\tau^2 - 4\Delta}}{2} \quad \text{and} \quad \lambda_2 = \frac{\tau - \sqrt{\tau^2 - 4\Delta}}{2}$$

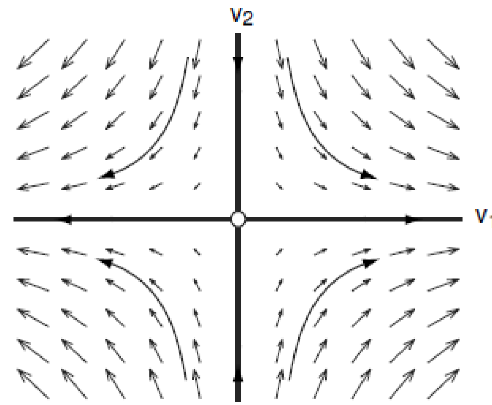
$$\begin{pmatrix} u(t) \\ w(t) \end{pmatrix} = c_1 e^{\lambda_1 t} v_1 + c_2 e^{\lambda_2 t} v_2$$

λ_1 and λ_2 could be complex!

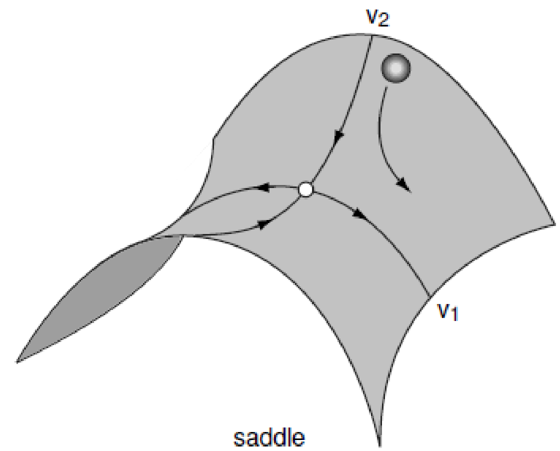
Types of fixed points in 2D



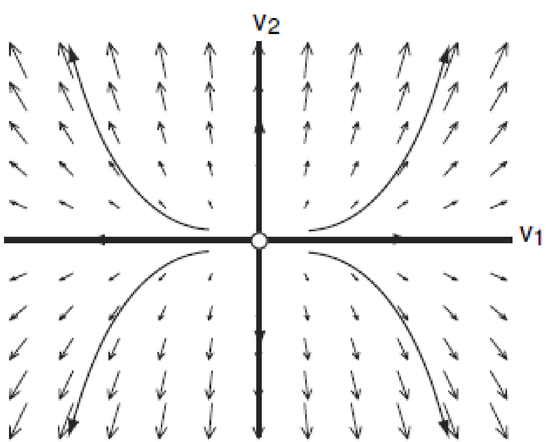
stable node



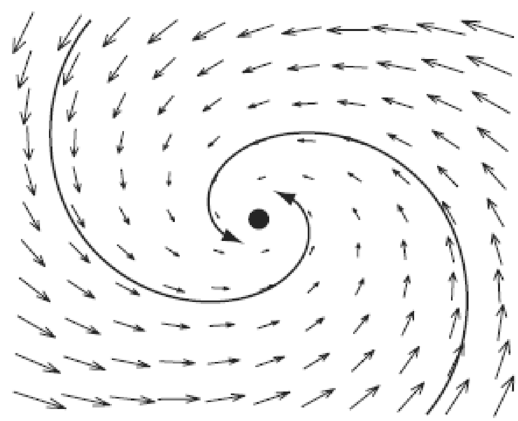
saddle

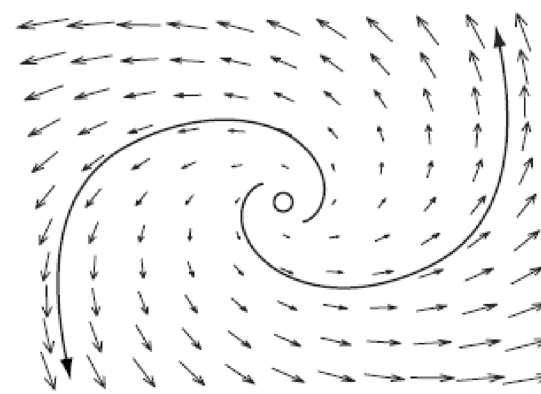


saddle

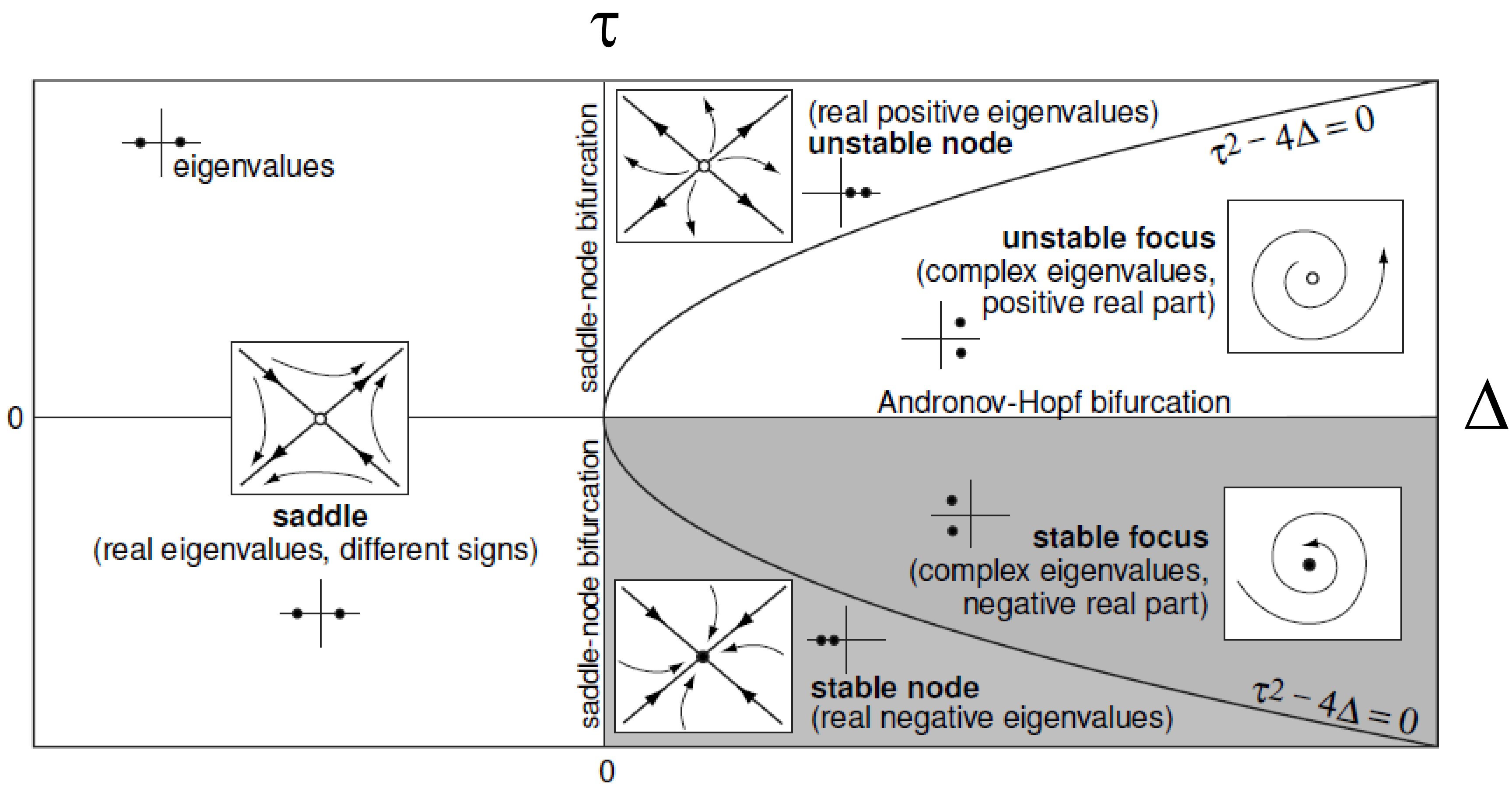


unstable node


stable focus


unstable focus

Classifying the fixed points



Back to Turing

Instability if either eigenvalue of

$$\mathbf{L} = \begin{pmatrix} a - k^2 D_X & b \\ c & d - k^2 D_Y \end{pmatrix}$$

$$\lambda = \frac{\tau \pm \sqrt{\tau^2 - 4\Delta}}{2}$$

Has positive real part.
Value of k which maximizes *Real*(λ) dominates.

$$= \frac{a+d}{2} - \frac{\mu'+\nu'}{2} U \pm \sqrt{\left\{\left(\frac{\mu'-\nu'}{2} U + \frac{d-a}{2}\right)^2 + bc\right\}}$$

$$\frac{\partial \lambda}{\partial k} = 0$$

$$\mu' = D_A \quad \nu' = D_B$$

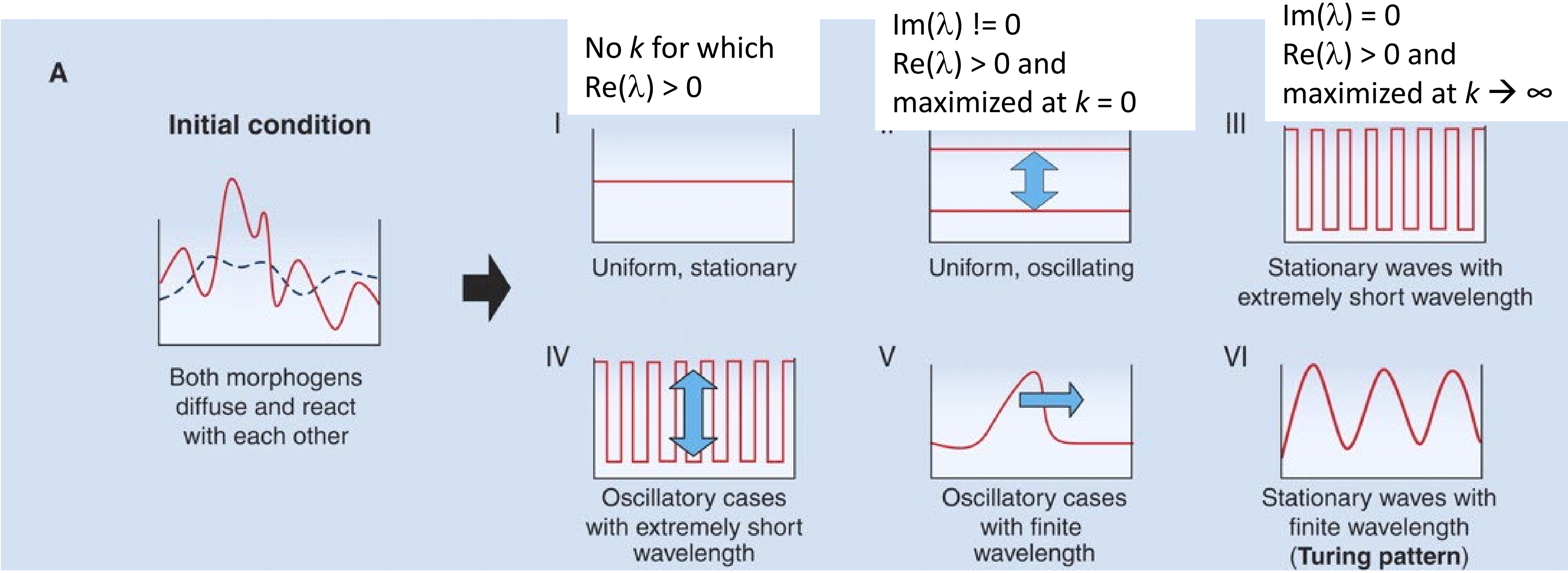
$U = k^2$

Turing Equation can lead to diverse types of dynamics

No k for which $\mathrm{Re}(\lambda) > 0$

$\mathrm{Im}(\lambda) \; != 0$
$\mathrm{Re}(\lambda) > 0$ and maximized at $k = 0$

$\mathrm{Im}(\lambda) = 0$
$\mathrm{Re}(\lambda) > 0$ and maximized at $k \rightarrow \infty$

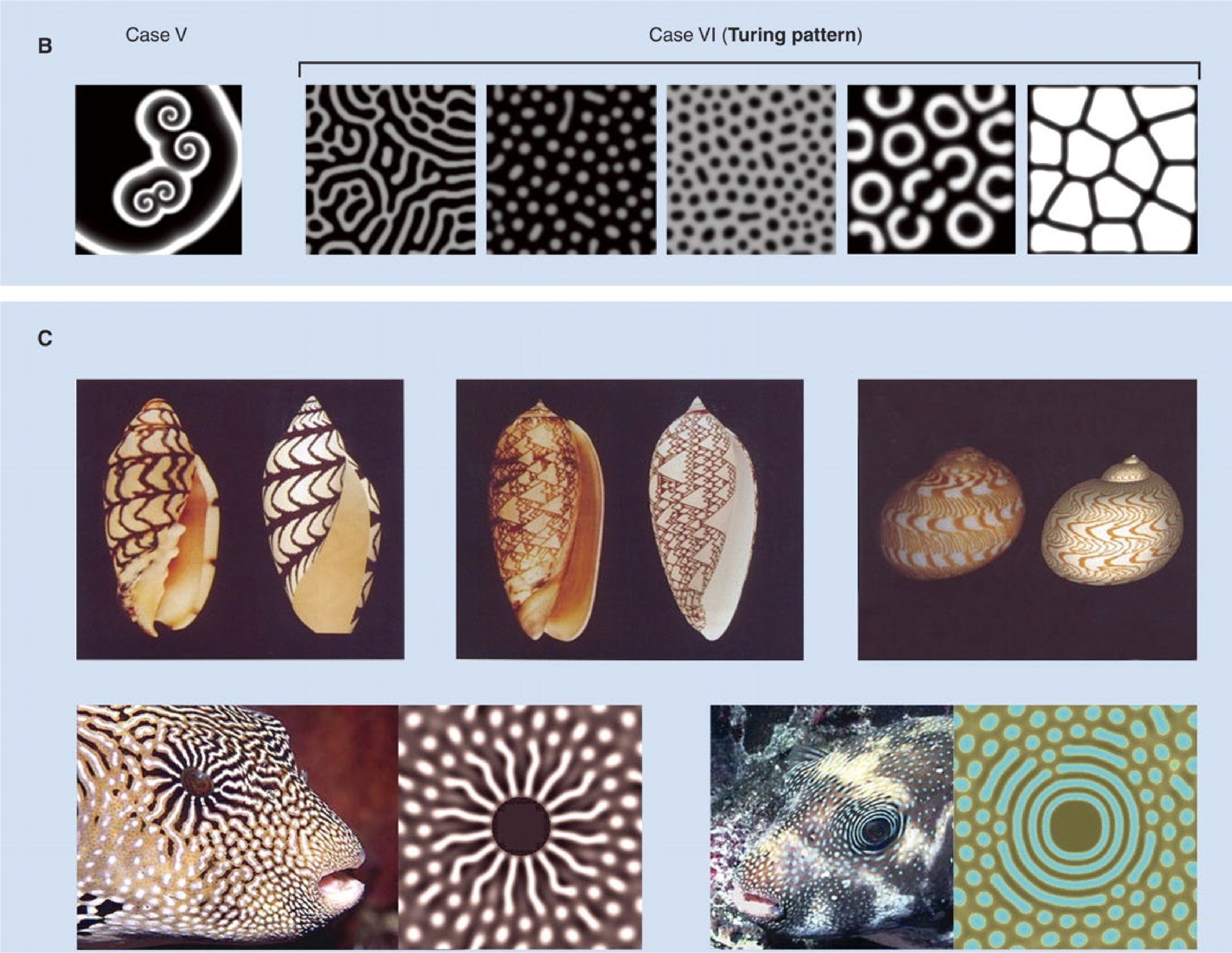


$\mathrm{Im}(\lambda) \; != 0$
$\mathrm{Re}(\lambda) > 0$ and maximized at $k \rightarrow \infty$

$\mathrm{Im}(\lambda) \; != 0$
$\mathrm{Re}(\lambda) > 0$ and maximized at finite k

$\mathrm{Im}(\lambda) = 0$
$\mathrm{Re}(\lambda) > 0$ and maximized at finite k

Kondo, Shigeru, and Takashi Miura. "Reaction-diffusion model as a framework for understanding biological pattern formation." *science* 329.5999 (2010): 1616-1620.


B
Case V
Case VI (Turing pattern)
C

Voltage as a morphogen?

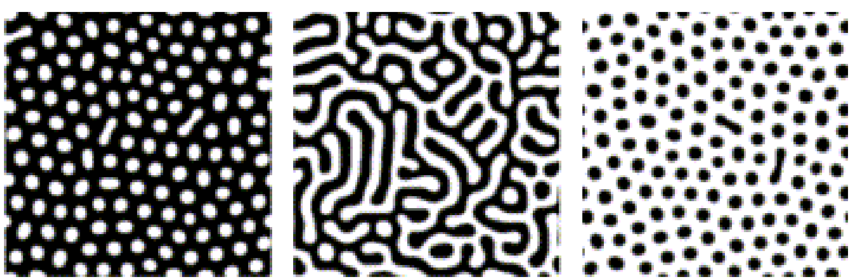
THE CHEMICAL BASIS OF MORPHOGENESIS

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

(Received 9 November 1951—Revised 15 March 1952)

$$\partial_t \mathbf{q} = \underline{\underline{\mathbf{D}}}\, \nabla^2 \mathbf{q} + \mathbf{R}(\mathbf{q})$$

Requires ≥ 2 morphogens for pattern formation



(a) (b) (c)

A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

By A. L. HODGKIN and A. F. HUXLEY

From the Physiological Laboratory, University of Cambridge

(Received 10 March 1952)

$$\partial_t V = \frac{G_{cxn}}{C_m} \nabla^2 V + \frac{1}{C_m} i(V, Ca^{2+})$$

$$\partial_t \mathrm{Ca}^{2+} = D\, \nabla^2 \mathrm{Ca}^{2+} + g_{Ca}(V_{Ca} - V)$$

?

The Hodgkin Huxley equations (with Ca^{2+}) are mathematically equivalent to the Turing reaction diffusion equation