The Chemical Basis of Morphogenesis

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Contents

1 Introduction

Turing proposed a molecular mechanism that results in the formation of biological or developmental patterns in nature.
An initially homogeneous system under equilibrium may drift off from homogeneity due to instability due to random disturbances.
This theory can explain how to determine the anatomical structure of an organism. The reaction and diffusion of chemical substances called morphogens account for the main pheonomena of morphogenesis.Turing hand calculated a dappled pattern of morphogens which is shown in 2 (will be discussed in detail in later sections) . It can explain the phenomena of gastrulation by the analysis of chemical waves on a sphere and how breakdown of symmetry occurs so that we obtain a complex structure like that of a horse starting from initially symmetrical structure like that of a blastula.
Different biological patterns can be explained by this mechanism. For example, zebra stripes, spots on cheetahs, hydra tentacles, angelfish stripes, palatal rugae, etc. [1]. The code for all the simulations is available in : Code

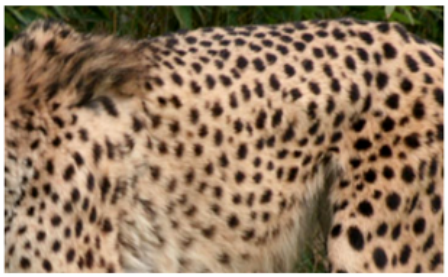

Figure 1: Animal markings (observed in cheetah)[2,fig.2(b)]

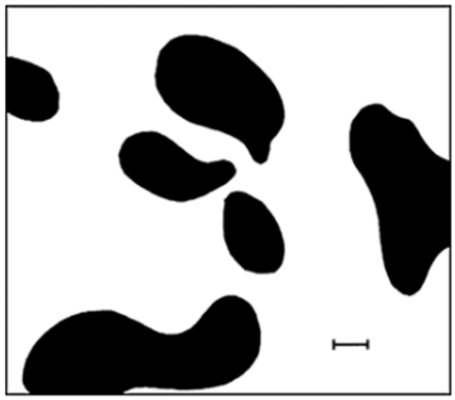

Figure 2: Turing's hand-calculated 'dappled pattern' created by a morphogen scheme in two dimensions .[1,fig.2]

The formation of spatial patterns is an elementary process in the development of an organism. To explain the development of complex anatomical structures , this work will first discuss instability and how it leads to pattern formation in the ring of cells, and then the results will be extended to continuous tissue and then to spherical systems.

2 Model of the embryo

Before we move on to discuss instability and change in the state of a system, we need some mathematical description for the embryo. Model can take 2 forms :

- Geometrical points : The cells can be idealized to occur in discrete geometrical points
- Continuous distribution : The matter of the embryo will be assumed to have a continuous distribution.

The state of the system is influenced by chemical and mechanical factors.

- Mechanical factors include positions, masses, velocities, and elastic properties of cells and the forces between them.
- Chemical factors include the diffusibilities of substances and the rates at which chemical reactions take place.

Other factors, such as electrical properties, affect the internal structure of the cell. But in this study, we will ignore them. Mechanical and chemical aspects are sometimes correlated, but we will deal with a system where we can deal with them separately and also where we can safely ignore the mechanical aspect [1] . Thus , this study will focus on the chemical properties of the system.

3 Morphogens and morphogenesis

The biological process that causes a cell, tissue or organism to develop its shape is called morphogenesis.
Chemical substances called morphogens account for the main phenomena of morphogenesis [1]. They react and diffuse leading to biological and developmental patterns in organisms . They trace the heterogeneity in organisms.
Consider the example in 3 taken from [4] , it consists of a homogeneous system with compartmentalized reaction space consisting of chemical substances (morphogens) . Suppose some random disturbance occurs and there occurs diffusion and chemical reactions of these morphogens . This results in the separation of system into 2 zones - one where there are increased reactions and other with decreased reactions . This leads to distortion of homogeneity . An activator - inhibitor system can form various biological patterns in nature .

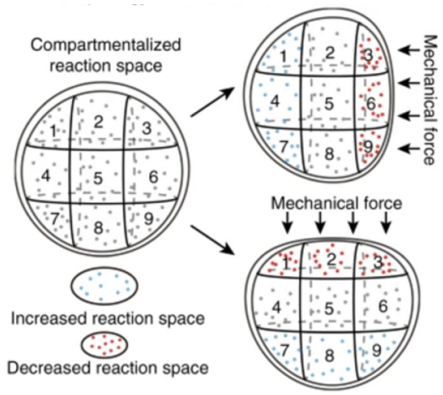

Figure 3: Morphology induced biochemical alteration[4,fig 2(e)]

Examples of morphogens : evocators of waddington (1940) , hormones , skin pigments , signalling molecules(e.g. Shh , FGF) , genes . Shh acts as an inhibitor and FGF as activator and they form an activator-inhibitor pair which leads to development of periodic rugal patterns in mammalian palates . Genes form a special class of morphogens . They catalyse the production of other morphogens .

4 Breakdown of symmetry

A spherically symmetrical structure only under the influence of chemical reactions and diffusions will be expected to remain in the spherically symmetrical state . But , if this was true it would have not been possible to get a complex structure like that of a horse starting from a spherically symmetrical structure of a blastula . This is because we cannot ignore any minor deviations from

the spherically symmetric structure . Also , there are Irregularities / statistical fluctuations in the number of molecules involved in chemical reactions or diffusion which leads to instability . Thus , we obtain a final new stable equilibrium where this symmetry is lost . [1]

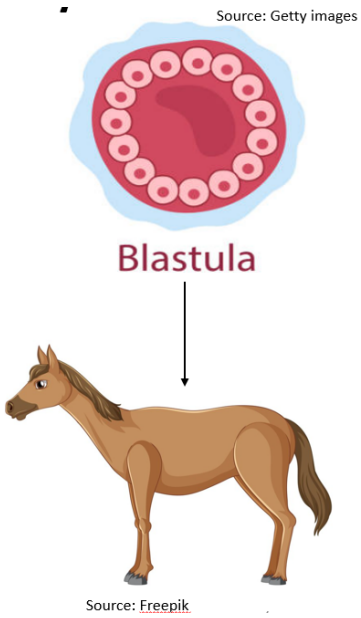

Figure 4: From blastula to horse

5 Example (2 cell system)

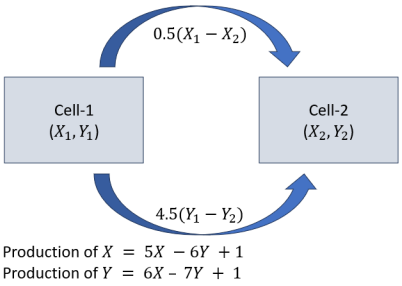

Figure 5: 2 cell system

Consider a 2 cell system with 2 cells - cell-1 and cell-2 . There are 2 morphogens in each cell - X and Y . Cell-1 has concentrations as X_1 ,Y_1 and cell - 2 as X_2

,Y_2 . The diffusion constant for X,Y are 0.5 and 4.5 respectively . Production rate of X is $5X - 6Y + 1$ and that of Y is $6X - 7Y + 1$. The system is under equilibrium for $X = Y = 1$. Both the cells will have a concentration of 1 for both morphogens in this equilibrium and there is 0 rate of production and no passage of morphogens by diffusion for either of the morphogens .
But suppose a random disturbance causes a small change from this equilibrium and the concentrations become $X_1 = 1.06, Y_1 = 1.02, X_2 = 0.94, Y_2 = 0.98$. We find an exponential drift from equilibrium occurs . The logarithm of concentration of the morphogen against time step is shown in figures 6 and 7 . This leads to instability in the system .

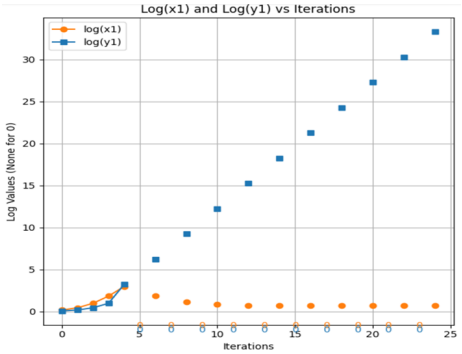

Figure 6: Log(concentration) vs time for 1st cell

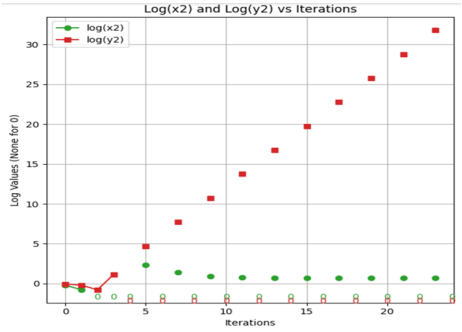

Figure 7: Log(concentration) vs time for 2nd cell

Now , before we conclude that instability arises in the system we need to first identify whether the reaction rates are actually feasible and thus we define some set of imaginary reactions which can provide these rates . Figure 8 shows the possible reactions . They all obey the law of chemical kinetics and thus we get the desirable rates of production for the morphogens . [1]

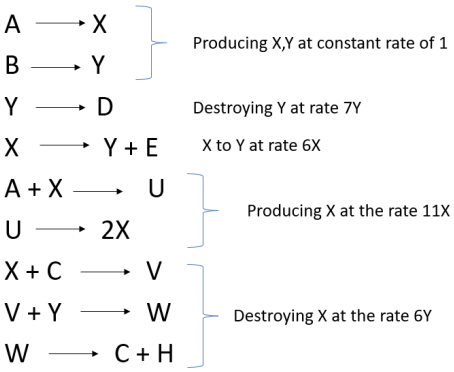

Figure 8: Possilble reactions

6 Reaction and diffusion in ring of cells

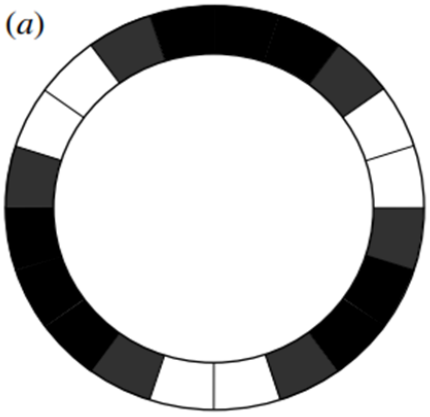

Figure 9: The morphogen pattern in a ring of cells as deduced by Turing [2,fig.2(a)]

Consider N cells and in cell r concentrations are X_r and Y_r and diffusion of cell r occurs with cell r+1 and r-1 . The cell-to-cell diffusion constant for X will be called u, and that for Y will be called v. Concentrations X and Y increasing at at the rate f(X, Y) and rate g (X , Y) respectively .

$$\frac{dX_r}{dt} = f(X_r, Y_r) + u(X_{r+1} + X_{r-1} - 2X_r)$$

$$\frac{dY_r}{dt} = g(X_r, Y_r) + v(Y_{r+1} + Y_{r-1} - Y_r)$$

Suppose the system is under equilibrium for $X = h, Y = k$. Let x_r, y_r be small disturbances around this equilibrium . So , if we ignore the higher order terms , one can write ax+by for f(h+x, y+k) and cx+dy for g(h+x, y+k). The four quantities a, b, c, d may be called the 'marginal reaction rates'. Collectively they may be described as the 'marginal reaction rate matrix'. When there are M morphogens this matrix consistsof M^2 numbers.[1]

Then the reactions can be written as :

$$\frac{dx_r}{dt} = ax_r + by_r + u(x_{r+1} + x_{r-1} - 2x_r)$$

$$\frac{dy_r}{dt} = cx_r + dy_r + v(y_{r+1} + y_{r-1} - y_r)$$

In order to solve these equations we introduce new set of co-ordinates $\xi_0, \ldots, \xi_{N-1}$ and $\eta_0, \ldots, \eta_{N-1}$

ξ_s and η_s are DFTs of X and Y respectively thus :

$$\xi_r = \frac{1}{N}\sum_{s=1}^{N} \exp\left[-\frac{2\pi irs}{N}\right] x_s,\ \eta_r = \frac{1}{N}\sum_{s=1}^{N} \exp\left[-\frac{2\pi irs}{N}\right] y_s,$$

Now after making these substitutions we obtain :

$$\frac{d\xi_s}{dt} = \left(a - 4\mu \sin^2 \frac{\pi s}{N}\right) \xi_s + b\eta_s.$$

$$\frac{d\eta_s}{dt} = c\xi_s + \left(d - 4\nu \sin^2 \frac{\pi s}{N}\right) \eta_s.$$

They form a standard pair of separable differential equations in 2 variables and they can be solved to obtain the general solution .

Let p_s and p'_s be the roots of the equation

$$\left(p - a + 4\mu \sin^2 \frac{\pi s}{N}\right)\left(p - d + 4\nu \sin^2 \frac{\pi s}{N}\right) = bc$$

then the solution of the equations is of the form

$$\xi_s = A_s e^{p_s t} + B_s e^{p'_s t},\ \eta_s = C_s e^{p_s t} + D_s e^{p'_s t},$$

where, however, the coefficients A_s, B_s, C_s, D_s are not independent but are restricted to satisfy

$$A_s\left(p_s - a + 4\mu \sin^2 \frac{\pi s}{N}\right) = bC_s,\ B_s\left(p'_s - a + 4\mu \sin^2 \frac{\pi s}{N}\right) = bD_s,$$

X_r, Y_r (the actual concentrations) the solution can be written

$$X_r = h + \sum_{s=1}^{N} (A_s e^{p_s t} + B_s e^{p'_s t}) \exp\left[\frac{2\pi i r s}{N}\right],\ Y_r = k + \sum_{s=1}^{N} (C_s e^{p_s t} + D_s e^{p'_s t}) \exp\left[\frac{2\pi i r s}{N}\right].$$

[1]

7 Continuous ring of tissue

Now lets extend the analysis to a continuous ring of tissue . The position of a point of the ring can then be described by the angle θ which a radius to the point makes with a fixed reference radius ρ. Let the diffusibilities be μ' and ν' . Initially diffusibilites were measured with reference to unit in which diameter of cell is measured now they are measured with respect to the reference radius ρ . [1]

Then $\mu = \mu' \left(\frac{N}{2\pi\rho}\right)^2$, $\nu = \nu' \left(\frac{N}{2\pi\rho}\right)^2$. The equations are $\frac{\partial X}{\partial t} = a(X-h) + b(Y-k) + \frac{\mu'}{\rho^2}\frac{\partial^2 X}{\partial \theta^2}$,

$$\frac{\partial Y}{\partial t} = c(X-h) + d(Y-k) + \frac{\nu'}{\rho^2}\frac{\partial^2 Y}{\partial \theta^2},$$

The general solution of these equations is :

$$X_t(\theta) = h + \sum_{s=-\infty}^{\infty} \left(A_s e^{p_s t} + B_s e^{p'_s t}\right) e^{is\theta},$$

$$Y_t(\theta) = k + \sum_{s=-\infty}^{\infty} \left(C_s e^{p_s t} + D_s e^{p'_s t}\right) e^{is\theta},$$

where p_s, p'_s are now roots of

$$\left(p - a + \frac{\mu' s^2}{\rho^2}\right)\left(p - d + \frac{\nu' s^2}{\rho^2}\right) = bc,$$

and

$$A_s\left(p_s - a + \frac{\mu' s^2}{\rho^2}\right) = bC_s,$$

$$B_s\left(p'_s - a + \frac{\mu' s^2}{\rho^2}\right) = bD_s.$$

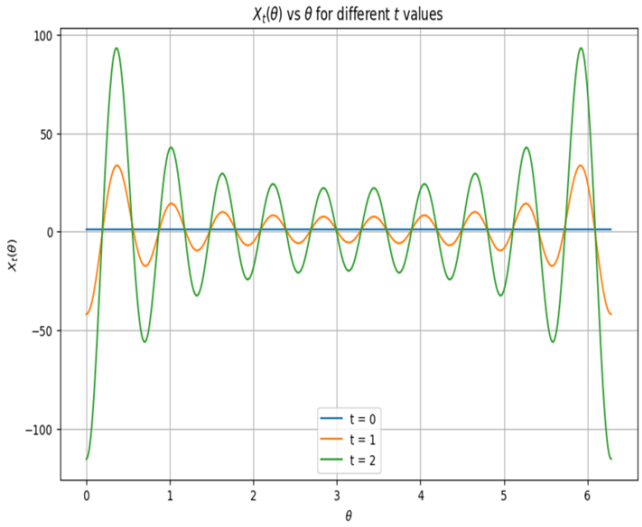

Figure 10: $X_t(\theta)$ vs θ for different t values

X and Y are functions of angle θ and can be expanded as a Fourier series provided, for instance, that its first derivative is continuous.

$$X(\theta) = \sum_{s=-\infty}^{\infty} G_s e^{is\theta} \quad (X(\theta) \text{ being values of } X \text{ at } t = 0)\,,$$

$$Y(\theta) = \sum_{s=-\infty}^{\infty} H_s e^{is\theta} \quad (Y(\theta) \text{ being values of } Y \text{ at } t = 0)\,,$$

then the required initial conditions are satisfied provided $A_s + B_s = G_s$, and $C_s + D_s = H_s$. The values A_s, B_s, C_s and D_s can be found unless $p_s = p'_s$. Its solution may be found as the limit of the normal case . [1]

8 Numerical example

In this section , we will discuss a numerical example to explain how pattern formation occurs . It is very difficult to specify the actual reactions taking place in the system so we will assume some imaginary reactions which can provide the desirable reaction rates .
We need to specify some details of the system before solving the problem .

- **Number and dimensions of cells of ring :** We will consider a ring of 20 cells with 0.1mm diameter each . The number of cells are reasonably small to avoid the continous approximation of tissue .

- Diffusibilities of the morphogens . We will consider 2 morphogens - X and Y with diffusibilities $\mu = 5 \times 10^{-8}\,\mathrm{cm}^2\,\mathrm{s}^{-1}, \nu = 2.5 \times 10^{-8}\,\mathrm{cm}^2\,\mathrm{s}^{-1}$ respectively .

- **Reactions concerned :** We will consider 4 isomeric substances (i.e they are rearrangement of same atoms - A,X,Y,B and some other substances - C , C' , W . A will be considered to have highest free energy while B with the least free energy . The energy for the entire process is derived by degradation of A into B . C is catalyst for conversion of Y into X . The system is unstable for sufficient concentration of C .Figure 11 shows the reactions concerned . The net effect of these reactions is to convert X to Y and also produce X and Y at some production rates .

$$
\begin{aligned}
Y + X &\longrightarrow W \\
W + A &\longrightarrow 2Y + B \quad \text{instantly ,} \\
2X &\longrightarrow W \\
A &\longrightarrow X \\
Y &\longrightarrow B \\
Y + C &\longrightarrow C' \quad \text{instantly,} \\
C' &\longrightarrow X + C
\end{aligned}
$$

Figure 11: Reactions concerned

- **Reaction rates :** Figure 12 shows the rates of the concerned chemical reactions . They all follow the laws of chemical kinetics and their net effect is conversion of X to Y at the rate $\frac{50XY+7X^2-55(1+\gamma)}{32}$ and producing X at a constant rate of 1/16 and destroying Y at Y/16 .

$$
\begin{aligned}
Y + X &\longrightarrow W \quad \frac{25}{16}XY \\
2X &\longrightarrow W \quad \frac{7}{64}X^2 \\
A &\longrightarrow X \quad \frac{1}{16} \times 10^{-3}A \\
C' &\longrightarrow X + C \quad \frac{55}{32} \times 10^{3}C' \\
Y &\longrightarrow B \quad \frac{1}{16}Y
\end{aligned}
$$

Figure 12: Reaction rates

Special units (s.u) are introduced where a unit of time refers to 1000s and unit of concentration is $10^{-11} molecm^{-3}$. Thus in s.u diffusibilites are 0.5 and 0.25 for X and Y respectively .

- **Information about random disturbances :** There will be some statistical fluctuations or randomness in the number of molecules involved in chemical reactions or diffusions . The errors will be assumed to follow gaussian distribution . For reaction rate F , root mean square irregularity in quantity reacting in τ s.u. is $0.004\sqrt{F\tau}$ and root mean square irregularity in quantity passing through wall is $0.004\sqrt{(M_1 + M_2)\mu\tau}$ (here M_1 and M_2 are the concentrations of morphogen with diffusibility μ in the 2 cells where diffusion occurs) . Other disturbances from neighbouring anatomical structures are also possible but we will ignore them and focus only on these 2 irregularities .

- **Information about distribution , in space and time of the morphogens and identifying which are of nature of evocators :** The substance C is of the nature of evocator . Concentration of A(fuel substance) is assumed to be constant . Combined concentration of C , C' changes with passage of time and is assumed to be same in all cells .

	first specimen				second specimen: incipient	'slow cooking': incipient	four-lobed equilibrium	
	incipient pattern		final pattern					
cell number	X	Y	X	Y	Y	Y	X	Y
0	1·130	0·929	0·741	1·463	0·834	1·057	1·747	0·000
1	1·123	0·940	0·761	1·469	0·833	0·903	1·685	0·000
2	1·154	0·885	0·954	1·255	0·766	0·813	1·445	2·500
3	1·215	0·810	1·711	0·000	0·836	0·882	0·445	2·500
4	1·249	0·753	1·707	0·000	0·930	1·088	1·685	0·000
5	1·158	0·873	0·875	1·385	0·898	1·222	1·747	0·000
6	1·074	1·003	0·700	1·622	0·770	1·173	1·685	0·000
7	1·078	1·000	0·699	1·615	0·740	0·956	0·445	2·500
8	1·148	0·896	0·885	1·382	0·846	0·775	0·445	2·500
9	1·231	0·775	1·704	0·000	0·937	0·775	1·685	0·000
10	1·204	0·820	1·708	0·000	0·986	0·969	1·747	0·000
11	1·149	0·907	0·944	1·273	1·019	1·170	1·685	0·000
12	1·156	0·886	0·766	1·451	0·899	1·203	0·445	2·500
13	1·170	0·854	0·744	1·442	0·431	1·048	0·445	2·500
14	1·131	0·904	0·756	1·478	0·485	0·868	1·685	0·000
15	1·090	0·976	0·935	1·308	0·919	0·813	1·747	0·000
16	1·109	0·957	1·711	0·000	1·035	0·910	1·685	0·000
17	1·201	0·820	1·706	0·000	1·003	1·050	0·445	2·500
18	1·306	0·675	0·927	1·309	0·899	1·175	0·445	2·500
19	1·217	0·811	0·746	1·487	0·820	1·181	1·685	0·000

Figure 13: Concentration table [[1] , table 1]

2 cases are considered :

- **Quick cooking :** γ is increased from -1/4 to +1/16 with an increment of 1/128 at each time step . This experiment was conducted on the 2 specimens , the experimental results obtained by Turing for morphogen(Y) pattern for first specimen is figure 14 . The simulation carried out in figure 15 didn't exactly match the results of Turing but gave a pattern for Y concentrations . Here , the instability changes quickly .

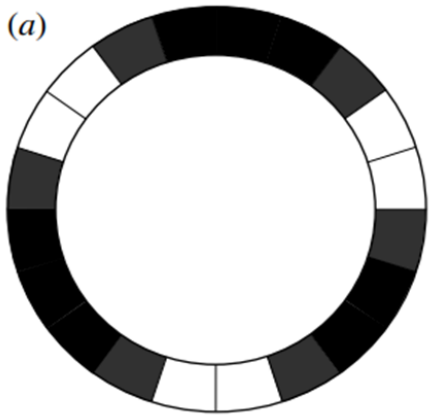

Figure 14: The morphogen pattern in a ring of cells as deduced by Turing[[2],fig 2(a)]

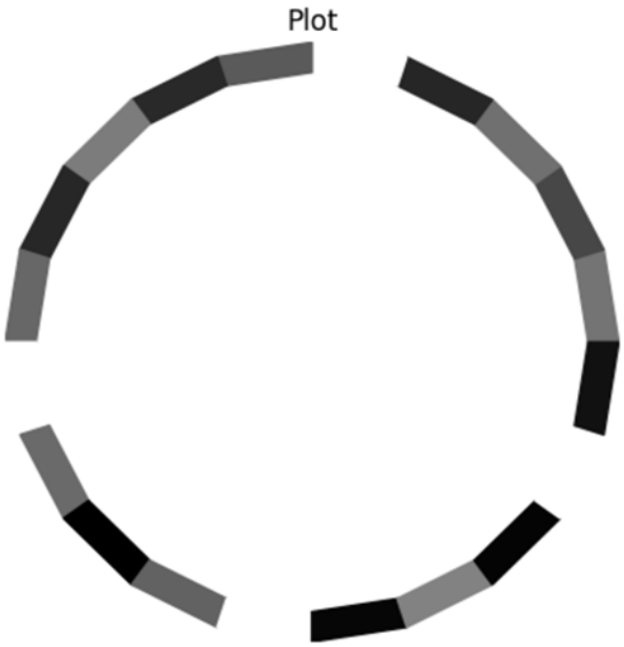

Figure 15: Experimental result for Y concentration

Only Y values are shown in table because the X and Y values are correlated and the final pattern obtained is also similar to the first pattern (obtained by renumbering of the cells) .

- **Slow cooking :** The instability is allowed to change slowly in this case . γ is increased slowly at rate 0.00001 from a value of -0.01 to 0.003 .[1]

9 Chemical waves

The pattern obtained in the previous section is an example of stationary wave pattern with some finite number of peaks observed in the ring . Reactions and diffusion thus give rise to chemical waves in system where the changes in concentrations could be visualised in the form of stationary or travelling waves. Blastula can be considered a spherical shell and thus :

$$\frac{\partial X}{\partial t} = a(X-h) + b(Y-k) + \mu' \nabla^2 X,$$
$$\frac{\partial Y}{\partial t} = c(X-h) + d(Y-k) + \nu' \nabla^2 Y.$$

Here , ∇^2 is laplacian in spherical co-ordinates . A point on sphere can be expressed as : $\sum_{n=0}^{\infty} \left[\sum_{m=-n}^{n} A_n^m P_n^m(\cos\theta) e^{im\phi}\right]$. Thus , the following equations are obtained for X and Y :

$$X = h + \sum_{n=0}^{\infty} \sum_{m=-n}^{n} \left(A_n^m e^{iq_n t} + B_n^m e^{iq_n' t}\right) P_n^m(\cos\theta) e^{im\phi},$$

$$Y = k + \sum_{n=0}^{\infty} \sum_{m=-n}^{n} \left(C_n^m e^{iq_n t} + D_n^m e^{iq_n' t}\right) P_n^m(\cos\theta) e^{im\phi},$$

Here summation has multiple terms which refer to different components with different wavelengths in the pattern .
Spherical harmonics pattern theory can be applied to gastrulation . Consider $\mu' = 2$, $\nu' = 1$, $a = -4$, $b = -8$, $c = 4$, $d = 7$. . For these values , we obtain degree 1 harmonics pattern ($n_0 = 1$) .

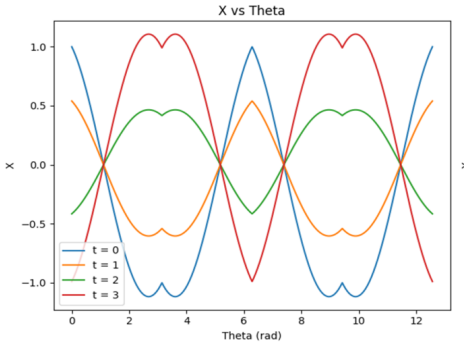

Figure 16: X vs θ at different t (degree 1 harmonic)

The $n_0 = 1$ term will dominate in the summation and we obtain the following equations :

$$X - h = e^{iq_{n_0}t} \sum_{m=-n_0}^{n_0} A_{n_0}^m P_{n_0}^m(\cos\theta) e^{im\phi}$$

$$b(Y - k) = \left(q_{n_0} - a + \frac{\mu'}{\rho^2} n(n+1) \right) (X - h).$$

We will obtain X of this form :

$$X - h = A\cos\theta + B\sin\theta\cos\phi + C\sin\theta\sin\phi \tag{1}$$

$$X - h = A' cos\theta'$$

$$A' = \sqrt{A^2 + B^2 + C}$$

The breakdown of homogeneity is symmetrical but around new axis and angle θ' is measured around the new axis . Suppose first morphogen promotes growth hormone , thus there will be greater growth at one end of the axis leading to the distortion of spherical symmetry similar to that of blastula to form gastrula (called gastrulation) .[1]

10 Types of behaviour in ring

Different behaviours are observed in the ring for different values of marginal rates and diffusibilities .[1]

- **(a) Stationary case with extreme long wavelength :** In this case contents of all the cells are same .
- **(b) Oscillatory waves with extreme long wavelength :** There is an oscillatory departure from equilibrium .
- **(c) Stationary waves of extreme short wavelength :** If number of cells are odd - the difference in concentration varies from 0 at one point to maximum at diametrically opposite point . For even number of cells- same content exists in alternate cells .
- **(d) Stationary waves of finite wavelength :** This case has a lot of biological significance and most of the results obtained by Turing were based on this . Here , stationary waves are obtained with finite number of lobes .
- **(e) Oscillatory case with finite wavelength :** This results in travelling waves . This behaviour occurs only when the number of morphogens are greater than or equal to 3 .
- **(f) Oscillatory case with extreme short wavelength :** In this case , metabolic oscillations occur with neighbouring cells that are 180 degrees out of phase . This behaviour occurs only when the number of morphogens are greater than or equal to 3 . [1]

11 Biological interpretations of results

Now , lets discuss the interpretations of these behaviours .

- Consider a behaviour(case (a)) where drift from equilibrium in one cell causes drift in same direction in adjacent cells . Since morphogens can travel a limited distance this results in a dappled pattern of morphogens (fig.17)

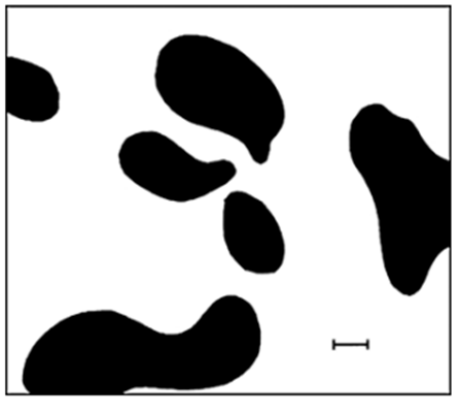

Figure 17: Turing's hand-calculated 'dappled pattern' created by a morphogen scheme in two dimensions .[1,fig.2]

- In case (b) a drift from equilibrium in one cell leads to oscillatory drift from equilibrium in adjacent cells .
- In case (c) a drift from equilibrium in one cell leads to drift from equilibrium in adjacent cells but in opposite direction . No biological examples of this case are observed in nature .
- Case (d) has a lot of biological significance . A wave pattern with no variation in time is observed . The number of peaks(n) are given by :

  n = circumference / chemical wavelength

  Examples of such stationary wave patterns are observed in woodruff leaves where the leaves occur in whorls of stem . The number of leaves vary from 5-9 and their number can be obtained by the formula of number of peaks (circumference / chemical wavelength) . Similar pattern is found in *hydra* where the tentacles occur in whorls .

Figure 19: *Hydra* (Source: Freepik)

Figure 18: Woodruff leaves (Source: Freepik)

- Case (e) results in 2 sets of travelling waves – one travelling clockwise and another travelling anticlockwise .
- In case (f) metabolic oscillations occur with adjacent cells of opposite phase . However, no examples of this behaviour are observed in nature . [1]

12 Theory of biological pattern formation (Gierer and Meinhardt)

One of the elementary process of development in organisms is the –formation of spatial patterns in tissue . Since , non linear kinetics are too general to obtain meaningful interpretations , 3 restrictions are imposed [3] :

- short range activation
- long range inhibition
- distinction between activator , inhibitor concentrations and their sources

  $a(x,t)$ = activator concentration

  $h(x,t)$ = inhibitor concentration

  source density of activator = $Q(x)$

  source density of inhibitor = $Q'(x)$

13 A Method for Generating Simple Theories of Pattern Formation

An approximation equation was proposed in [3] for generating morphogen concentrations .

$$\frac{\partial a}{\partial t} \approx \gamma \varrho \frac{a^k}{\bar{a}^k} \left(1 - \frac{\beta}{\varrho} \frac{\bar{a}^n}{a^m}\right)$$

This equation is said to generate patterns if : $n > m > 0$.

The release of inhibitor depends on activator and inhibitor is assumed to spread fast within a wider area .

Assuming even distribution : $\begin{aligned} \varrho &\approx \bar{\varrho}, \\ a &\approx \bar{a} \end{aligned}$

Here $\bar{a}$ and $\bar{\varrho}$ are mean concentrations of activator and its source respectively averaged over entire area .

If, in a particular region, ϱ and/or a is slightly above average, a will increase. If

$$\begin{aligned} \varrho &= \bar{\varrho} + \Delta\varrho, \\ a &= \bar{a} + \Delta a \end{aligned}$$

then

$$\frac{\partial a}{\partial t} \approx \gamma \varrho \bar{\varrho} \bar{a}^{k-1} \left(\frac{\Delta\varrho}{\varrho} + m\frac{\Delta a}{a}\right).$$

From this equation it is clear that a region of high source density increases production of a and fires gradient and this results in the entire activation getting concentrated in a small area . [3]

14 Specific models

Some models were proposed in [3] based on which different equations are obtained for the morphogens .

- **Depletion model :** sources of distribution are activated by activator a(x, t) and also by substance s(x, t) which is in turn depleted by activation .

$$\frac{\partial a}{\partial t} = \varrho_0 \varrho + c\varrho a^2 s - \mu a + D_a \frac{\partial^2 a}{\partial x^2}$$
$$\frac{\partial s}{\partial t} = c_0 - c' \varrho a^2 s - vs + D_s \frac{\partial^2 s}{\partial x^2}$$

- **Activator-inhibitor model :** activator (a) and inhibitor (h) act on sources $Q(x)$ and $Q'(x)$ .Activation and inhibition of sources are some powers of a and h . There can be 2 further cases :
  - **Common sources :** Activator and inhibitor have common sources .

$$\frac{\partial a}{\partial t} = Q_0 Q + cQ\frac{a^2}{h^4} - \mu a + D_a \frac{\partial^2 a}{\partial x^2}, .$$

$$\frac{\partial h}{\partial t} = c'Q\frac{a^2}{h^4} - \nu h - D_h \frac{\partial^2 h}{\partial x^2}$$

  - **Different sources :** Activator and inhibitor have different sources .

$$\frac{\partial a}{\partial t} = \varrho_0 \varrho + c\varrho \frac{a^2}{h} - \mu a + D_a \frac{\partial^2 a}{\partial x^2},$$
$$\frac{\partial h}{\partial t} = c' \varrho' a^2 - vh + D_h \frac{\partial^2 h}{\partial x^2}.$$

15 Conclusions

- Turing's theory of morphogenesis explains various biological patterns and development in organisms .
- Chemical substances called morphogens which react and diffuse cause morphogenesis
- This theory can be applied to fields like developmental biology , chemistry or even astrophysics (reaction-diffusion can explain the formation of spiral galaxies) .

References

[1] Turing A. 1952 The chemical basis of morphogenesis. Phil. Trans. R. Soc. Lond. B 237, 37–72. (doi:10.1098/rstb.1952.0012)

[2] Ball P. 2015 Forging patterns and making waves from biology to geology: a commentary on Turing (1952) 'The chemical basis of morphogenesis'. Phil. Trans. R. Soc. B 370: 20140218. http://dx.doi.org/10.1098/rstb.2014.0218

[3] Gierer, Alfred and Hans Meinhardt. “A theory of biological pattern formation.” Kybernetik 12 (1972): 30-39.

[4] Chen, Q., Shi, J., Tao, Y. et al. Tracing the origin of heterogeneity and symmetry breaking in the early mammalian embryo.Nat Commun 9, 1819 (2018). https://doi.org/10.1038/s41467-018-04155-2