Turing and animal coat patterns

Ramesh Hariharan*

Department of Computer Science, Indian Institute of Science, Bangalore 560 012, India, and Strand Life Sciences, 5th Floor, Kirloskar Business Park, Bellary Road, Hebbal, Bangalore 560 024, India

The present article describes a beautiful contribution of Alan Turing to our understanding of how animal coat patterns form. The question that Turing posed was the following. A collection of identical cells (or processors for that matter), all running the exact same program, and all communicating with each other in the exact same way, should always be in the same state. Yet they produce nonhomogeneous periodic patterns, like those seen on animal coats. How does this happen? Turing gave an elegant explanation for this phenomenon, namely that differences between the cells due to small amounts of random noise can actually be amplified into structured periodic patterns. We attempt to describe his core conceptual contribution below.

Keywords: Activator and inhibitor, animal coat patterns, distributed systems, random noise.

Introduction

WE have all seen the spots of a giraffe and the stripes of a tiger (Figure 1). How do these patterns form? Presumably, there is some substance whose presence or absence at various places along the animal coat yields that pattern (there could be multiple such substances, but for simplicity let us think of just one; call this substance the *activator*). Presumably, the many cells that form the outer surface of the animal coat produce this activator. All these cells are largely identical so they should produce the same amount of the activator each. Then how does the coat pattern come about? This was the question that Turing asked and answered so elegantly in his seminal work[1].

This is a fundamental question in the study of distributed systems. How do a collection of distributed agents, all doing the exact same thing, produce a highly non-uniform, and that too periodic pattern? Symmetry would dictate that if each cell does the exact same thing and each cell has the exact same state to begin with, then the states of all the cells will remain identical at all periods of time, i.e. each cell will continue to produce the exact same amount of the activator. The appearance of patterns therefore will need some symmetry breaking.

Breaking symmetry

A number of factors destroy symmetry in practice: the gravitational field, for example. These could make the cells non-identical. However, it is not obvious how these monotone symmetry breakers could contribute to the periodic pattern of spots or stripes observed in nature.

There is an additional symmetry breaker that is ubiquitous, i.e. just random noise. The amount of the activator produced will differ from cell to cell by a small noise amount. Noise distributions found in nature are certainly not repetitive or periodic though (Figure 2); a far cry from the actual target coat pattern.

Could noise provide sufficient symmetry breaking for periodic patterns to emerge? Turing answered this as below.

Communication

Suppose there was no communication between the cells, i.e. the activator does not flow from one cell to another. Then the amount of the activator in each cell will be determined purely by its production in that cell; and the production amounts are largely the same from cell to cell, as we claimed above, modulo noise; and the distribution of noise across the cells does not form a periodic pattern. In other words, without flow of activator from cell to cell, the patterns we see in nature cannot be explained as resulting purely from symmetry breaking on account of noise.

So let us assume that the activator flows from cell to cell. It is natural for the activator to flow from a cell that has a slightly higher production (on account of noise) to a neighbouring cell that has a slightly lower production. Intuitively, this would seem to even out any cell-to-cell variations on account of noise, leading to a uniform distribution of the activator across cells, thus taking us further away from our goal of explaining how periodic animal coat patterns appear. Nevertheless, let us model the above mathematically, just so we can set the stage for making further tweaks.

Modelling communication

For simplicity, we will work in one dimension instead of the usual two dimensions associated with animal coats.

---

*e-mail: ramesh@strandls.com

Figure 1. Animal coat patterns.

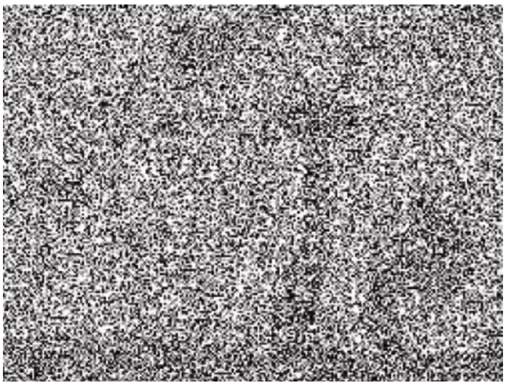

Figure 2. Noise distributions in nature.

So imagine a one-dimensional chain of cells $0 \ldots n-1$ (actually, a cycle to avoid special handling at the boundaries, so cell $n-1$ has cells 0 and $n-2$ as neighbours).

Let $f_i(t)$ denote the amount of the activator in cell i at time t. Assume that there is initial production of the activator given by $f_i(0) = 1 + \varepsilon_i$, where ε_i denotes a small noise term. Subsequently, at each time unit, the activator flows from a cell with higher amount to a neighbouring cell with lower amount, at a rate proportional to the difference in amounts. The proportionality constant $\alpha > 0$ reflects the viscosity properties of the activator. We can now write down the time evolution of $f_i(t)$ as follows.

Activator dynamics

$$\begin{cases} f_i(t+1) \leftarrow f_i(t) + \alpha[f_{i-1}(t) - f_i(t)] + \alpha[f_{i+1}(t) - f_i(t)], & (1) \\ \qquad\qquad \leftarrow (1-2\alpha)f_i(t) + \alpha f_{i-1}(t) + \alpha f_{i+1}(t). & (2) \end{cases}$$

How do we solve the above for $f_i(t)$ as t grows larger and larger? We need the following tool for this.

A mathematical tool

It would have been relatively easy to solve for $f_i(t)$ if it depended solely on $f_i(t-1)$, and not on $f_{i-1}(t-1)$ and $f_{i+1}(t-1)$ as well. A common trick (the Fourier transform[2]) is often used to remove the dependency of $f_i(t)$ on $f_{(i-1)}(t-1)$ and $f_{(i+1)}(t-1)$. This requires writing the $f_i(t)$s in terms of a new set of variables $a_i(t)$s, via multiplication by an invertible matrix, as below.

$$\begin{bmatrix} f_0(t) \\ f_1(t) \\ f_2(t) \\ \vdots \\ f_{n-1}(t) \end{bmatrix} = \begin{bmatrix} \omega^{0.0} & \omega^{0.1} & \omega^{0.2} & \cdots & \omega^{0.(n-1)} \\ \omega^{1.0} & \omega^{1.1} & \omega^{1.2} & \cdots & \omega^{1.(n-1)} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ \omega^{(n-1).0} & \omega^{(n-1).1} & \omega^{(n-1).2} & \cdots & \omega^{(n-1).(n-1)} \end{bmatrix} \times \begin{bmatrix} a_0(t) \\ a_1(t) \\ a_2(t) \\ \vdots \\ a_{n-1}(t) \end{bmatrix}.$$

where $\omega = e^{\sqrt{-1}\frac{2\pi}{n}} = \cos\frac{2\pi}{n} + \sqrt{-1}\sin\frac{2\pi}{n}$,

$$f_i(t) = \sum_{k=0}^{n-1} a_k(t)\omega^{i.k}, \quad a_k(t) = \frac{1}{n}\sum_{i=0}^{n-1} f_i(t)\omega^{-i.k}. \tag{3}$$

So instead of working with $f_i(t)$s directly, we can work with the $a_k(t)$s instead and transform these back to $f_i(t)$s whenever desired. We will see how this is done next, but first a few interesting observations. Note ε_i below is a small random noise amount.

$$[\forall i : f_i(t) = 1] \Leftrightarrow [a_0(t) = 1 \text{ and } a_1(t) \cdots a_{n-1}(t) = 0], \tag{4}$$

$$[\forall i : f_i(t) = 1 + \varepsilon_i] \Rightarrow [a_0(t) \cdots a_{n-1}(t) \neq 0]$$
with high probability, (5)

$$\left[a_k(t) = \overline{a_{n-k}(t)} \neq 0 \text{ and } a_i(t) = 0, \forall i \neq k, n-k\right]$$

$$\Rightarrow \left[f_i(t) \propto \cos\frac{2\pi i.k}{n}, \forall i\right], \tag{6}$$

$f_i(t)$ is then periodic in i with period n/k.

In particular, note the last property above; if all but $a_k(t)$, $a_{n-k}(t)$ (which in turn are complex conjugates of each other) vanish over time, then the resulting $f_i(t)$ will be periodic in i with period n/k (note that k should divide n for true periodicity; if k does not divide n, then $f_i(t)$ will still be roughly periodic).

Solving for $f_i(t)$

Substituting eq. (3) in eq. (2), we get:

$$\sum_{k=0}^{n-1} a_k(t+1)\omega^{i.k} \leftarrow (1-2\alpha)\sum_{k=0}^{n-1} a_k(t)\omega^{i.k}$$

$$+\alpha\sum_{k=0}^{n-1} a_k(t)\omega^{(i-1).k} + \alpha\sum_{k=0}^{n-1} a_k(t)\omega^{(i+1).k}. \tag{7}$$

Next, for each k, we get an expression for $a_k(t+1)$ purely in terms of $a_k(t)$ and k below.

Identifying coefficient of $\omega^{i.k}$ on both sides

$$\begin{aligned}
a_k(t+1) &\leftarrow a_k(t)(\alpha\omega^{-k} + \alpha\omega^{k} + (1-2\alpha)) \\
&\leftarrow a_k(t)\left(2\alpha\cos\frac{2\pi k}{n} + (1-2\alpha)\right) \\
&\leftarrow a_k(t)\left(2\alpha\left(\cos\frac{2\pi k}{n} - 1\right) + 1\right) \\
&\leftarrow a_k(t)\left(-4\alpha\sin^2\frac{\pi k}{n} + 1\right).
\end{aligned}$$

As a consequence (recall $\alpha > 0$, and $a_0(0) \neq 0$ by eq. (5))

$$\lim_{t\to\infty} a_k(t) = \begin{cases} a_0(0) \neq 0 & \text{if } k = 0 \\ 0 & \text{if } k > 0 \text{ and } |-4\alpha\sin^2\frac{\pi k}{n} + 1| < 1 \\ \text{undefined} & \text{if } k > 0 \text{ and } |-4\alpha\sin^2\frac{\pi k}{n} + 1| \geq 1. \end{cases}$$

So if $|-4\alpha\sin^2(\pi k/n) + 1| < 1$ holds for all k from 1 to $n-1$, then $a_1(t) \cdots a_{n-1}(t)$s die out with time, leaving only $a_0(t)$; then due to eq. (4), all $f_i(t)$s become identical with time, as expected. Setting $\alpha < 1/2$ suffices for the above. For $\alpha \geq 1/2$, there is no convergence.

Introducing an inhibitor

Taking stock now, just flow of the activator from cell to cell is not sufficient to yield interesting periodic patterns; all one gets is a flat profile. Something more is needed. Let us now introduce another substance called the *inhibitor*; the inhibitor is produced in response to increasing amounts of the activator and destroys the activator. In order for the activator to not disappear completely, some amount of it must be produced at an on-going basis as well; just the initial values do not suffice. Let $g_i(t)$ be the amount of the inhibitor in cell i at time t. We can now write the time-evolution rules for $f_i(t)$ and $g_i(t)$ as below. Note that we use simple linear dependency of $f_i(t+1)$, $g_i(t+1)$ on $f_i(t)$ and $g_i(t)$ here. The parameters of this linear dependency are β, γ, β', γ'; we will study how these can be constrained to yield the desired periodic behaviour later. Note also that the communication between cells reflected by flow of the activator and inhibitor is modelled as earlier, with parameters α, α'.

Activator dynamics:

$$\begin{cases}\begin{aligned} f_i(t+1) \leftarrow\, & f_i(t) + \alpha[f_{i-1}(t) - f_i(t)] \\ & + \alpha[f_{i+1}(t) - f_i(t)] + \beta f_i(t) - \gamma g_i(t) \\ \leftarrow\, & \alpha f_{i-1}(t) + \alpha f_{i+1}(t) + (1 + \beta - 2\alpha) f_i(t) \\ & - \gamma g_i(t). \end{aligned}\end{cases}$$

Inhibitor dynamics:

$$\begin{cases}\begin{aligned} g_i(t+1) \leftarrow\, & g_i(t) + \alpha'[g_{i-1}(t) - g_i(t)] \\ & + \alpha'[g_{i+1}(t) - g_i(t)] + \beta' f_i(t) - \gamma' g_i(t) \\ \leftarrow\, & \alpha' g_{i-1}(t) + \alpha' g_{i+1}(t) + (1 - \gamma' - 2\alpha') g_i(t) \\ & + \beta' f_i(t). \end{aligned}\end{cases}$$

Using eq. (3), we write $f_i(t) = \sum_{k=0}^{n-1} a_k(t)\omega^{i.k}$ and $g_i(t) = \sum_{k=0}^{n-1} b_k(t)\omega^{i.k}$. Substituting as in eq. (7)

$$a_k(t+1) \leftarrow a_k(t)\left(-4\alpha\sin^2\frac{\pi k}{n} + 1 + \beta\right) - \gamma b_k(t),$$

$$b_k(t+1) \leftarrow b_k(t)\left(-4\alpha'\sin^2\frac{\pi k}{n} + 1 - \gamma'\right) - \beta' a_k(t).$$

Rewriting in matrix form:

$$\begin{bmatrix} a_k(t+1) \\ b_k(t+1) \end{bmatrix} = \left(\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} - \begin{bmatrix} 4\alpha\sin^2\dfrac{\pi k}{n} - \beta & \gamma \\ -\beta' & 4\alpha'\sin^2\dfrac{\pi k}{n} + \gamma' \end{bmatrix}\right)\begin{bmatrix} a_k(t) \\ b_k(t) \end{bmatrix}. \tag{8}$$

Solving for $a_k(t)$, $b_k(t)$

To solve for $a_k(t)$, $b_k(t)$, as t grows, we need to consider what happens when we repeatedly multiply a matrix

$(I-A)$ with an initial vector, where A is as given below.

$$A=\begin{bmatrix} 4\alpha\sin^2\dfrac{\pi k}{n}-\beta & \gamma \\ -\beta' & 4\alpha'\sin^2\dfrac{\pi k}{n}+\gamma' \end{bmatrix},$$

$$\begin{bmatrix} a_k(t+1) \\ b_k(t+1) \end{bmatrix}=(I-A)^{t+1}\begin{bmatrix} a_k(0) \\ b_k(0) \end{bmatrix}.$$

Let e_1, e_2 be the eigenvalues of A (assume $e_1 \neq e_2$ via slight perturbation of the parameters if necessary; this ensures that the corresponding eigenvectors are linearly independent). The eigenvalues of $I-A$ are $1-e_1$, $1-e_2$. Recall from the definition of eigenvalues that repeated application of $(I-A)$ to a non-zero vector (non-zero because of initial noise according to eq. (5)) converges to the 0 vector if $|1-e_1|$, $|1-e_2| < 1$, and diverges to increasingly larger values if either $|1-e_1| > 1$ or $|1-e_2| > 1$. We capture sufficient (but not necessary) conditions for each consequence below. Note here that e_1, e_2 may be complex, in which case they are complex conjugates of each other, i.e. $a \pm \sqrt{-1}b$.

$$\lim_{t\to\infty}|a_k(k)| = \begin{cases} 0 & \text{if } e_1, e_2 \text{ are not real, } e_1e_2 < e_1+e_2, \\ 0 & \text{if } e_1, e_2 \text{ are real, } 0 < e_1+e_2 < 1, e_1e_2 > 0, \\ \infty & \text{if } e_1, e_2 \text{ are real, } 0 < e_1+e_2 < 1, e_1e_2 < 0. \end{cases}$$

The sufficiency of the first condition above can be seen as follows: if e_1, e_2 are not real, then $e_1e_2 = a^2 + b^2 < e_1 + e_2 = 2a$ implies that $|1-e_2|^2 = |1-e_1|^2 = (1-a)^2 + b^2 = 1 + a^2 + b^2 - 2a < 1$. For the second condition above, note that this implies $0 < e_1$, $e_2 < 1$ and therefore $|1-e_2|$, $|1-e_1| < 1$. For the last condition above, note that this implies $\min\{e_1, e_2\} < 0$ and therefore $\max\{|1-e_2|, |1-e_1|\} > 1$.

By eq. (6), periodic behaviour can be obtained by driving all but a handful of $a_k(t)$s to 0. To this end, we set $0 < e_1 + e_2 < 1$ and $e_1e_2 < e_1 + e_2$, for all k; in addition, we set $e_1e_2 > 0$ for most k; for the exceptions, we set $e_1e_2 < 0$. Since $e_1 + e_2$ is the trace (sum of diagonal entries) of the matrix A, and e_1e_2 is the determinant, we can rewrite the above conditions as below.

$$0<\left[4(\alpha+\alpha')\sin^2\frac{\pi k}{n}-\beta+\gamma'\right]<1,\ \forall k, \tag{9}$$

$$\left[16\alpha\alpha'\sin^4\frac{\pi k}{n}+4(\gamma'\alpha-\beta\alpha')\sin^2\frac{\pi k}{n}+(\gamma\beta'-\gamma'\beta)\right] < \left[4(\alpha+\alpha')\sin^2\frac{\pi k}{n}-\beta+\gamma'\right],\ \forall k, \tag{10}$$

$$0<\left[16\alpha\alpha'\sin^4\frac{\pi k}{n}+4(\gamma'\alpha-\beta\alpha')\sin^2\frac{\pi k}{n}+(\gamma\beta'-\gamma'\beta)\right], \text{ for most } k, \tag{11}$$

$$\left[16\alpha\alpha'\sin^4\frac{\pi k}{n}+4(\gamma'\alpha-\beta\alpha')\sin^2\frac{\pi k}{n}+(\gamma\beta'-\gamma'\beta)\right]<0, \text{ for very few } k. \tag{12}$$

Choosing α, α', β, β', γ, γ'

We can now write sufficiency constraints on the various parameters to satisfy eqs (9)–(12).

Equation 9. Since this holds for all k, the extremes $k = 0$ and $k = n - 1$ require us to choose parameters so

For $k = 0$, $k = n - 1$ respectively:

$$\begin{cases} \gamma' > \beta, & (13) \\ [4(\alpha+\alpha')-\beta+\gamma'<1] \Rightarrow [4(\alpha+\alpha')<1]. & (14) \end{cases}$$

Equations 11 and 12. The roots (treating $\sin^2(\pi k/n)$ as a variable) are as below and the only values of k violating eq. (11) are those for which $\sin^2(\pi k/n)$ is between these two roots; call this the *exception range*.

$$\frac{4(\beta\alpha'-\gamma'\alpha)\pm\sqrt{16(\beta\alpha'-\gamma'\alpha)^2-64\alpha'\alpha(\gamma\beta'-\gamma'\beta)}}{32\alpha'\alpha}. \tag{15}$$

We want the exception range to be completely between 0 and 1, and we want this range to be small; we can capture these constraints as below.

$$\left[0<\frac{4(\beta\alpha'-\gamma'\alpha)}{32\alpha'\alpha}\right] \Leftrightarrow [0<(\beta\alpha'-\gamma'\alpha)] \Rightarrow [\alpha'>\alpha] \text{ (use eq. (13))}. \tag{16}$$

$$\left[\frac{4(\beta\alpha'-\gamma'\alpha)}{32\alpha'\alpha}\right]<1, \tag{17}$$

$$[16(\beta\alpha'-\gamma'\alpha)^2-64\alpha'\alpha(\gamma\beta'-\gamma'\beta)>0] \Leftrightarrow \left[\gamma\beta'<\gamma'\beta+\frac{(\beta\alpha'-\gamma'\alpha)^2}{4\alpha'\alpha}\right], \tag{18}$$

$$\left[\sqrt{16(\beta\alpha'-\gamma'\alpha)^2-64\alpha'\alpha(\gamma\beta'-\gamma'\beta)}/32\alpha\alpha'\right] \text{ is small.} \tag{19}$$

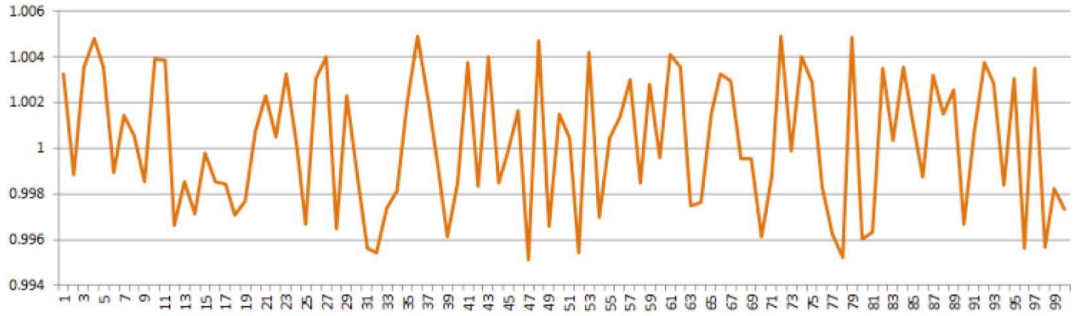

Figure 3. Initial values $f_i(0)$; noise perturbations around 1.

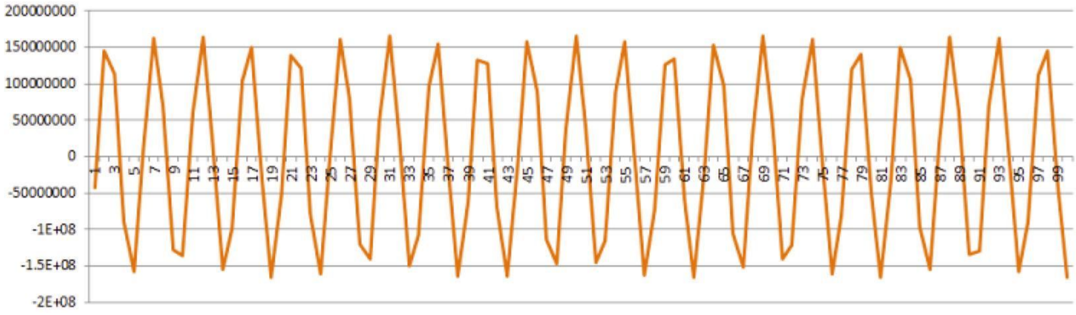

Figure 4. $f_i(100{,}000)$, periodic with period ~ 5 = 100/20.

Equation 10. Since this holds for all k, we need to choose parameters so

For $k = 0$ and $k > 0$ respectively

$$\begin{cases} \gamma\beta' < \gamma'\beta - \beta + \gamma', & (20) \\ 4\alpha\alpha' < \alpha + \alpha' \text{ (use eq. (16))}. & (21) \end{cases}$$

To satisfy all the above constraints, we start with choosing α', α satisfying eqs (14) and (16); note eq. (21) is automatically satisfied. Next choose β, γ' to satisfy eqs (13), (14), (16) and (17); note that all these are simultaneously satisfiable by choosing small enough and mutually close β, γ'; note also that the location of the exception range can be modulated to be anywhere in the $0 \cdots 1$ range by an appropriate choice of β, γ'. Finally, we choose $\gamma\beta'$ very close to its upper limit indicated by eqs (18) and (20) to satisfy eqs (18)–(20) simultaneously; note that the width of the exception range can be modulated by the closeness of $\gamma\beta'$ to its upper limit above.

With the above choice of parameters, only $a_k(t)$s for which $\sin^2(\pi k/n)$ in the narrow exception range above survive with time; all other $a_k(t)$s vanish. If the number of such ks is small, then by eq. (6), $f_i(t)$ shows roughly periodic behaviour as time progresses. And this is how Turing showed small random noise can be amplified to rough periodic behaviour. Equation (16) states that the *inhibitor needs to flow faster than the activator* for this to happen.

Table 1. Example parameters

Parameter	Value
n	100
α	1/32
α'	1/8
β	1/8
γ	1/10
γ'	1/7.5
β'	2.5/10

An example

A concrete example can help illustrate this phenomenon more clearly. Consider the choice of parameters shown in Table 1. With this choice, the centre of the exception range is at 0.366666666667 and the width of the range on either side of the centre is 0.033333333. Then $\sin^2(\pi k/n)$ is in this exception range for $k = 20$, 21 and $k = 79$, 80. By eq. (6), we would then expect $f_i(t)$ to be periodic with period close to 5 = 100/20 for sufficiently large t. This matches well with simulation results shown in Figures 3 and 4.

However, note two problems. First, the $f_i(t)$ profile across the cells i is centred around 0, alternating between negative and positive values. But activator amounts cannot be negative in reality. Second, the amplitude of the profile grows with time, because the surviving $a_k(t)$s keep growing in magnitude with time; this is also not possible in reality. While shifting the centre-line is possible by adding a fixed offset to the activator and inhibitor

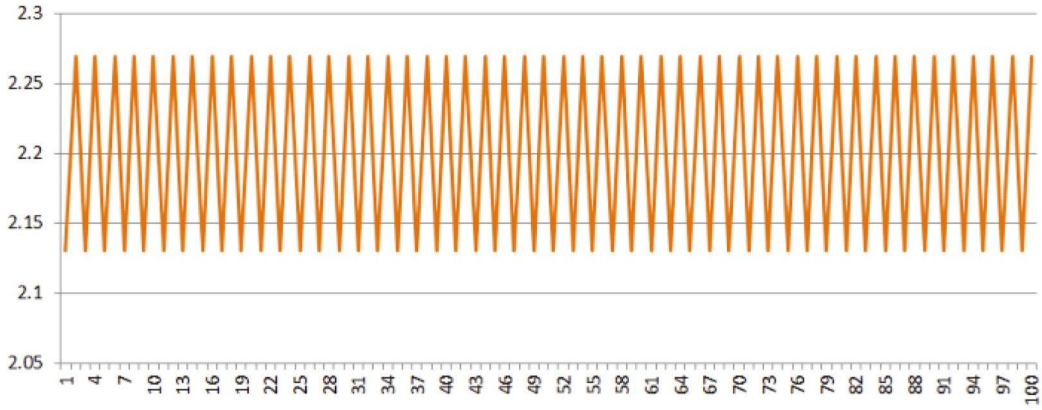

Figure 5. $f_i(100, 000)$, periodic with period ~ 2.

Table 2. Example parameters

Parameter	Value
n	100
α	0.01
α'	0.3
γ	0.2
Δ	0.2
Δ'	2.0

dynamics, dampening the amplitudes requires introduction of nonlinear terms, as we see below.

Dampening the amplitude

A number of elegant, nonlinear models have been found to dampen the amplitude above, resulting in all positive values for the activator and the inhibitor. One such model was proposed by Schnakenberg[3], and is described below. Note the $f_i^2(t)g_i(t)$ nonlinear term below.

Activator dynamics:

$$f_i(t+1) \leftarrow \alpha f_{i-1}(t) + \alpha f_{i+1}(t) + (1-\gamma-2\alpha) f_i(t) + \gamma f_i^2(t) g_i(t) + \gamma^* \Delta.$$

Inhibitor dynamics:

$$g_i(t+1) \leftarrow \alpha' g_{i-1}(t) + \alpha' g_{i+1}(t) + (1-2\alpha') g_i(t) - \gamma f_i^2(t) g_i(t) + \gamma^* \Delta'.$$

An example choice of parameters is shown in Table 2, and simulation results are shown in Figure 5. As can be seen below, the $f_i(t)$ profile is now in the 2.1–2.3 range.

Conclusion

A phenomenon that is all around us, a question waiting to be asked, a simple but striking problem formulation, and an elegant mathematical solution: all these ingredients make Turing's contribution one of immense conceptual beauty. We have presented only the one-dimensional picture above. In two dimensions, an analogous argument and appropriate parameter settings can be used to derive a roughly periodic signal in just one of the dimensions (i.e. stripes) or on both dimensions (i.e. spots). Of course, the stripes need not be axis-parallel. For more information on this topic and a description of the state-of-the-art, see http://www.resnet.wm.edu/~jxshix/math490/lecture-chap5.pdf and https://ctbp.ucsd.edu/summer_school07/UCSD-Keshet2.pdf.

---

1. Turing, A., The chemical basis of morphogenesis. *Philos. Trans. R. Soc. London, Ser. B*, 1952, **237**; http://www.turingarchive.org/browse.php/B/22.
2. Joseph Fourier, J. B., (Freeman, A., translator), *The Analytical Theory of Heat*, The University Press, 1878.
3. Schnakenberg, J., Simple chemical reaction systems with limit Cycle behaviour. *J. Theor. Biol.*, 1979, **81**(3); doi:10.1016/0022-5193(79)90042-0.