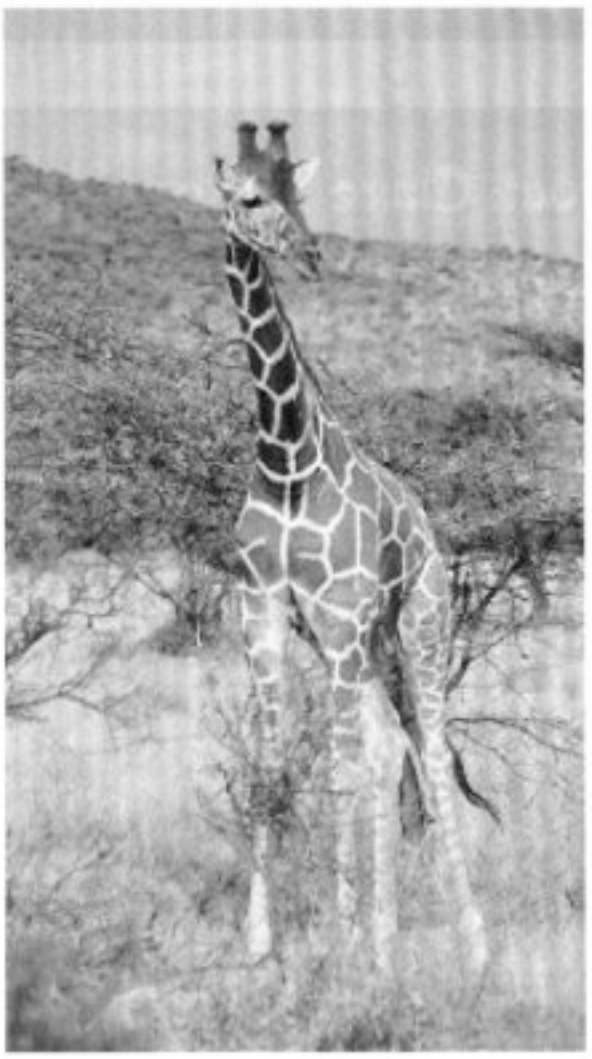


# How the leopard got its spots

## and other

# Just So stories of animal patterning

by Lewis Dartnell

***Alan Turing is considered to be one of the most brilliant mathematicians of the last century. He helped crack the German Enigma code during the Second World War and laid the foundations for the digital computer. His only foray into mathematical biology produced a paper so insightful that it is still regularly cited today, over 50 years since it was published.***

### Modelling an embryo

Turing's paper described how "reaction-diffusion equations" might be used by animals to generate patterned structure during their development as an embryo. Animals start as a single cell that divides many times to create a full-size individual. During the early stages, the small ball of cells is completely uniform, or *homogeneous*, but out of this develop the dramatic patterns of a zebra, leopard, giraffe, butterfly or angelfish. Turing was interested in how a spatially homogeneous system, such as a uniform ball of cells, can generate a spatially inhomogeneous but static pattern, such as the stripes of a zebra. He managed to formulate a series of differential equations that, when solved, show very elegantly how the diversity of wonderful patterns on animals might be created.

Imagine an embryo with two types of chemical inside it. The two chemicals, as we will see, interact to generate patterns, and so are called morphogens (morpho from the Greek for "form", and gen from the Greek for "to beget"). For the sake of this discussion, we can imagine the embryo as a one-dimensional line and look at the concentration of each of the two morphogens at each point along the line. The chemicals can diffuse left and right along the line from a point of high concentration to lower concentration, and can also be produced afresh by cells along the embryo. One morphogen is an "Inhibitor" and suppresses the production of both itself and the other chemical. The other, an "Activator", promotes the production of both morphogens.

At any time (t) and any point along the embryo (x), the concentrations of the Activator and Inhibitor are given by A(x,t) and I(x,t) respectively. But these concentrations change over time due to new production (a reaction) and diffusion. The system is therefore known as a reaction-diffusion equation. How these two concentration profiles change over time can be analysed by using the current state to calculate the state in the next time step. Doing these calculations for every point along the model embryo and for thousands of time steps would take ages without a fast computer, which is why Turing never got to see the true beauty of his equations.

A differential equation tells you how quickly one variable changes with respect to another. So the rate of change of Activator concentration between each time step is a differential equation of A with respect to t. In this case, however, A is a function of both x and t, and so differentiating with respect to only t is known as partial differentiation. It is like calculating the gradient of a hill in first the North-South, and then the East-West direction.

The rate of change of Activator concentration is given by the following partial differential equation:

$$\frac{\delta A}{\delta t} = f(A,I) + \frac{\delta^2 A}{\delta x^2}$$

It might look like really complicated, but it can be broken down into two parts; the reaction bit and the diffusion bit. The first term on the right-hand side describes how much Activator is being produced. It is a function of Activator and Inhibitor concentrations because they both affect the reaction rate. The second term is a second derivative describing how quickly the gradient of Activator is changing. It gives the rate of diffusion.

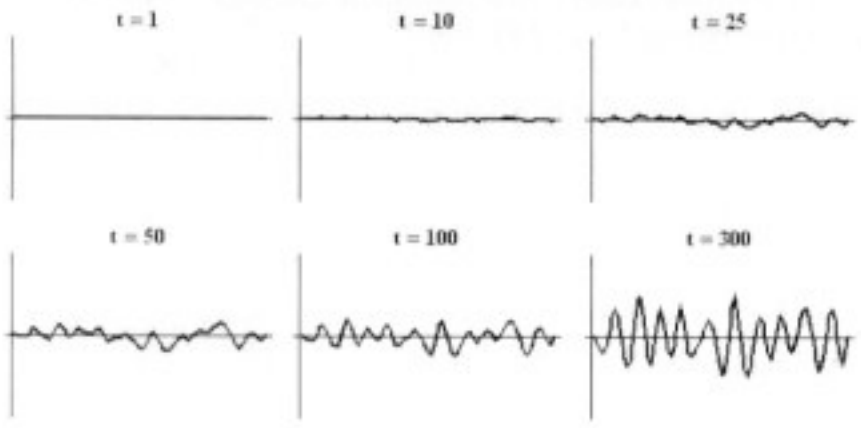
Similarly, the change of Inhibitor with respect to time is given by:

$$\frac{\delta I}{\delta t} = g(A,I) + d\frac{\delta^2 I}{\delta x^2}$$

The extra term, d, on the right-hand side is the diffusion coefficient - how much more quickly Inhibitor diffuses than Activator. The Inhibitor being a faster diffuser was shown by Turing to be pivotal in driving the process of pattern generation.

## Very perturbing

Initially (i.e. when $t$=0), the two chemicals are in equilibrium - their concentrations do not change over time. The amount of Activator and Inhibitor is just right so that the reaction and diffusion rates exactly balance. The situation is an "unstable equilibrium", however, and the first nudge, or *perturbation* in maths speak, knocks the system away from this equilibrium. It is like a pencil poised on its tip - it might be perfectly balanced but the slightest nudge pushes the pencil over and it never recovers this equilibrium point.

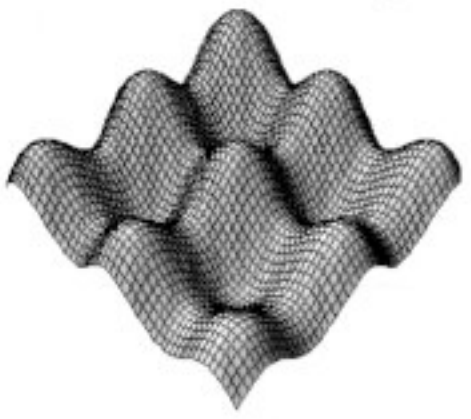



Say that, for whatever reason, the concentration of Activator increases slightly at one point. Now the local concentration of Activator is greater than Inhibitor, so more Activator is produced, and so on in a snowball effect. But Inhibitor is also being produced, and because it diffuses faster it quickly spreads to either side of the perturbation and decreases the concentration of Activator there. So you end up with a region of high Activator concentration bordered on both sides by high Inhibitor.

This process can be seen below. As the animation steps through time the concentration of Activator along the embryo organises into a series of peaks.
The reaction-diffusion equations can also be formulated for two dimensions. In this case an island of high Activator becomes surrounded by a moat of Inhibitor. Beyond this inhibitory halo, however, the levels of Inhibitor drop again and so other seeds can produce an area of high activator concentration. In this way the symmetry of the uniform concentration is broken into roughly evenly spaced regions of high Activator.

## Revealing the pattern

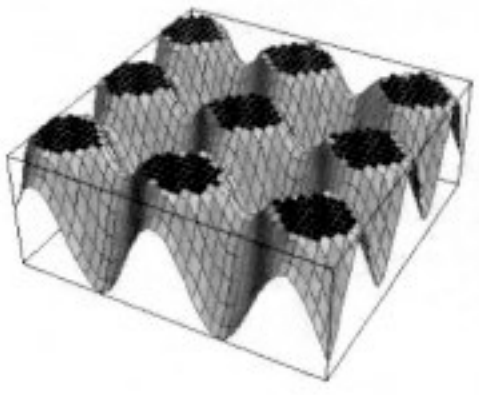
**An activator landscape**



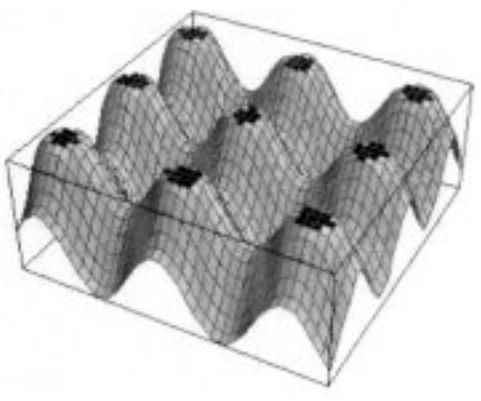
The Activator and Inhibitor are not colour pigments themselves, just the morphogens that interact to create an underlying pattern. If the Activator also promotes the generation of a pigment in the skin of the animal then this pattern can be made visible. Skin cells could produce yellow pigment unless they detect high levels of Activator instructing them to produce black. This would yield a visible pattern similar to that of a cheetah.

The size of these spots will depend on what are known as *thresholds*. The concentration of Activator can be thought of as a landscape of hills, with a certain concentration of Activator (i.e. altitude) required to turn ON the pigment. If this threshold is high, then only tiny spots at the very summit of the hills are seen, but if the threshold is lowered, then more of each hill is coloured and the spots are larger with less space between them. Such a mechanism may explain the difference in markings between two subspecies of giraffe: the Rothschild's giraffe and the Reticulated Giraffe, the first of which has smaller, more widely-spaced spots than the other.

**A low threshold for turning pigment ON**



**A high threshold for turning pigment ON**

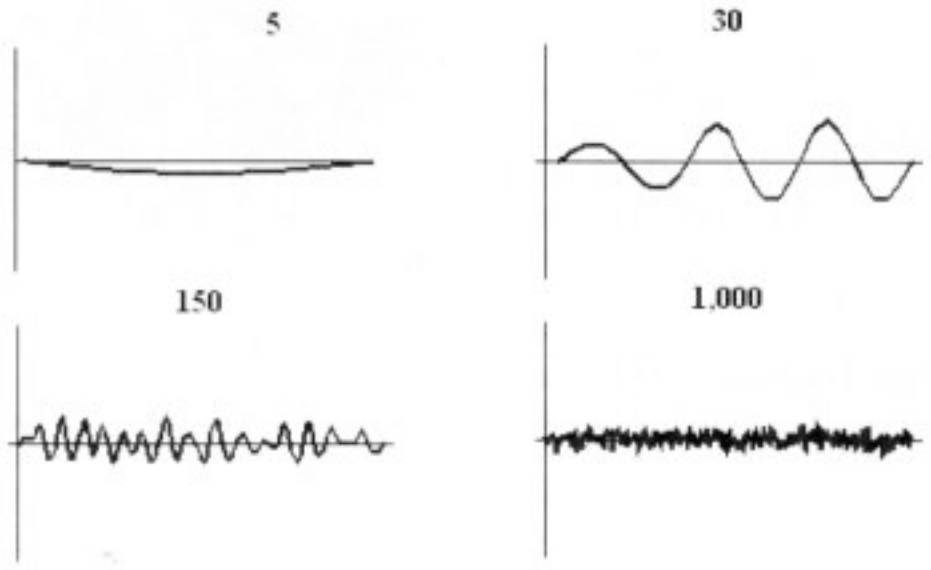


*"Imagination was given to man to compensate him for what he is not; a sense of humour to console him for what he is."*
*(Sir Francis Bacon)*

*Saturation* can also be an important factor. If the concentration of Activator can reach a maximum value (ie. it is produced as fast as it breaks down or diffuses away) then the spots may join up into stripes. This is believed to be what happens in the zebra.

### Size matters

The size of the embryo at the time of pattern generation is also very important. If the Inhibitor diffuses quickly relative to the size of the domain then few spots will be able to form. In fact, the stationary wave of Activator concentration is very similar to modes of vibration on a guitar string: only certain wavelengths can fit. The diagram below shows the reaction-diffusion simulation run on "embryos" of different sizes: 5, 30, 150 and 1000 units long. No pattern at all can form on small embryos, and on very large animals the spots are too small-scale and seem to blend together.




Some developmental biologists have argued that this explains why neither small mice nor large elephants have any patterning. Animals of intermediate size, however, can fit more and more spots along a larger embryo. If *d* (the diffusion constant) is assumed to be the same for all mammals, then this would explain why hamsters have only a few patches of colour whilst leopards have hundreds of small spots.

The size of the domain also affects the type of patterns that can form. An animal's tail can be thought of as a cylinder with a steadily decreasing radius. The top is large enough to support two-dimensional patterns like spots, but down at the bottom the domain becomes too small. The region of high Activator spreads all the way around the tail and joins up with itself, so that a spot becomes a stripe. The transition between spots and stripes is shown very well by a cheetah's tail. This aspect of the maths also explains why a spotted animal can have a striped tail, but a striped animal can never have a spotted tail.

The process of pattern generation is completed in mammals during the embryonic stage. But some animals need to keep their markings up to date as they grow to full size. The stripes along the Marine angelfish move very slowly over time as the domain size increases. The basic bands on a young fish move apart as the fish grows, with new stripes appearing or dividing off existing ones to fill in any gaps.

### Nature as Art?

The perturbations that trigger spots and stripes are usually statistical variations in the rate of morphogen production or diffusion. But physical disturbances from outside the embryo can have the same effect. The beautiful eyespots on butterfly wings are thought to rely on the principles described above, although involving more morphogens. Marta de Menezes [http://www.martademenezes.com/ ] produces art with living objects by pricking a butterfly wing with a pin while it is still developing in the chrysalis. This disrupts the concentration gradients and so alters the natural design.

### Further reading

* A. Turing (1952). The Chemical Basis of Morphogenesis. Philosophical Transactions of the Royal Society of London. Available for free download, at participating institutions, from JSTOR.http://www.jstor.org/view/

* J.D. Murray (2001). *Mathematical Biology.* Published by Springer-Verlag New York Inc.

* D.S. Jones and B.D. Sleeman (2003). *Differential Equations and Mathematical Biology.* Published by Chapman & Hall.

### Lewis Dartnell

I've always been deeply curious about things around me. When I was younger my parents gave me a remote controlled car for Christmas, which didn't survive even until the New Year before it had been taken to pieces to see how it worked. Learning a language isn't about getting full marks in a vocabulary test, it's about talking to people. In the same way, science is not about knowing lots of dry facts or the proper names for things. It is about understanding how the world around you is put together and works, and most importantly of all, enjoying the process of finding out.

Although I was fairly good at all of my GCSE subjects, deciding what to continue at A-levels was the easiest decision of my life. I just chose the subjects I enjoyed most: the three sciences and mathematics. A-level studies are the first opportunity you get to really think for yourself and do your own thing in research. For my physics project, I had a

great time studying impact craters. I used a video camera to watch in slow-motion the effects of firing marbles from a homemade catapult into a tray of sand.

I understood most of the A-level maths syllabus, but I've never had an intuitive feel for maths, and so decided to continue with a degree in Biological Sciences. There never really was the question of not going to university - I loved learning new things and wanted to continue. I chose what I thought to be one of the best Biology courses, at the University of Oxford.

The first year of a degree is always very broad, and I did not enjoy some of the material in the lectures. But the weekly essays are a really good chance to explore around what you find interesting about a subject, and discussing things in tutorials, although hard work, really gets things straight in your mind. Following your own ideas is absolutely encouraged at university, and I did my research project on analysing the songs of humpback whales for evidence of language.

After graduating I took a well-needed break from study, and spent a year working on a BBC educational website and travelling through South America with friends. But I was never really settled working in an office, and started looking around for an interesting PhD. I found a four-year course that a new Department of University College London was running. Interdisciplinary work, i.e. collaboration between scientists from completely different backgrounds, is becoming very important in science now, especially in biology. The PhD programme in Bioinformatics which I was accepted on to includes training in lots of different skills. And so I have spent the last year learning lots of useful maths tricks, computer programming, lecturing skills, and so on. My research at the moment is into how animals might use optical illusions to camouflage themselves from predators.

For me though, simply finding out fascinating new things is not enough, I'm always telling friends about them as well. Science Communication was the next obvious step for me, and I have spent the last two years entering every single popular science writing competition I heard about. Last year I came second in the THES/OUP science writing competition with an article about the surprising similarities between language and the structure of proteins, and things are starting to take off from there. I hope you enjoyed the article about leopard spots, and if you're interested the rest of my writing is up on my website: www.ucl.ac.uk/~ucbplrd

*This article first appreared in +Plus Magazine, May 2004. http://pass.maths,org.uk/issue30*

# An A- Z of Inspirational Lives

**We make no apologies for the eclectic roll call here! Some are the usual candidates, some are personal favourites but the contributions of all have enriched our world in some way.**

**A**

**André-Marie Ampère (1775 – 1836)**

By the age of twelve, this child prodigy was a proficient mathematician. During his career as a physicist, he explored the connection between electricity and magnetism and formulated Ampère's law. The development of the galvanometer was inspired by his use of a freely moving needle to measure the flow of electric current. The 'amp' as a unit of electric current was named after him.

**B**

**Louis Braille (1809 – 1952)**

Braille's method of representing letters by groups of dots embossed in cardboard was devised as he taught at the National Institute for Blind Youth in Paris. This remarkable man blinded himself with a knife at the age of three, was a proficient musician and created such a successful tool for blind readers that his system has also been applied to music, mathematics and non-Roman scripts.

**C**

**Sir Noel Coward (1899 –1973)**

Coward appeared in his first play at the age of twelve and went on to become a popular actor, playwright and composer, appreciated most for his witty and satirical depiction of the interwar years. His plays, *The Vortex* (1924), *Hay Fever* (1925) and a musical, *Bitter Sweet* (1929) have been successful in London and New York. Coward wrote and produced the classic film, *Brief Encounter* in 1945 and was knighted in 1970.

**D**

**René Descartes (1596-1650)**

Descartes is most widely known as a philosopher but he also excelled in mathematics where he is credited with the invention of co-ordinate geometry. His philosophy is based on the only certainties Descartes perceived, that of his own existence (I think, therefore I am) and the existence of God. Descartes died in 1650 having contracted pneumonia whilst tutoring Queen Christina of Sweden in mathematics.