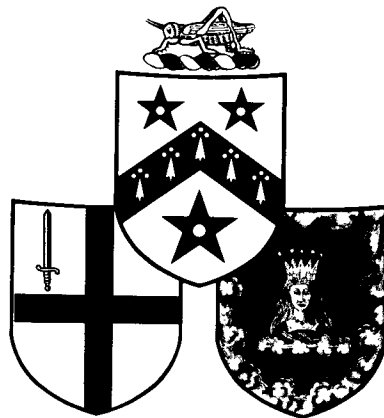


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TURING'S TIGER

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A Lecture by

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Turing's Tiger

The zebra is striped that it may graze unnoticed on the plain, the tiger that it may lurk undiscovered in the jungle; the banded Caetodont and Pomacentrid fishes are further bedizened to the hues of the coral-reefs in which they dwell. The tawny lion is yellow as the desert sand; but the leopard wears its dappled hide to blend, as it crouches on the branch, with the sun-flecks peeping through the leaves.

D'Arcy Thompson, *On Growth and Form*, Chapter XVI

Animals come in complicated shapes and patterns. They are often decorated with striking colours, too, which may form geometric arrangements such as spots (leopard), stripes (tiger, zebra), or dappling (giraffe).

How do such patterns arise?

We can try to take a hint from physics. The flow of a fluid is governed by the 'Navier-Stokes' equations, stated by Claude Navier in 1821 and reduced to simple physical principles by Sir George Stokes in 1845. The regular patterns that form in a moving fluid, such as whirlpools or ocean waves, are mathematical consequences of the Navier-Stokes equations, and in this sense the equations explain the patterns. Are there equations that similarly explain the shapes and patterns of animals? Is there a 'tiger equation' whose solutions are stripes? What might such an equation look like?

The first serious attack on this question was made by Alan Turing. Turing showed that systems of chemicals, reacting together and diffusing through tissue, can create patterns. He called these chemicals *morphogens* — shape-creators. He wrote down 'reaction-diffusion' equations to describe morphogen dynamics, and he showed that those equations lead to spontaneous pattern formation. When Turing first published his ideas, they were purely theoretical, but a good example of real-world 'Turing patterns' soon came to the attention of chemists, the so-called BZ reaction. In that particular reaction the patterns that arise are concentric rings and spirals, but reaction-diffusion equations are capable of producing a huge range of different patterns, including stripes, spots, dappling, and much else.

A bigger difficulty with the patterns that appear spontaneously in the BZ reaction is that they *move*. We don't see zebras with moving stripes, or leopards with moving spots. However, Turing showed that his equations can produce both stationary patterns and moving ones, depending on various numerical constants that arise in the chemical reactions and also on the rates at which the chemicals diffuse.

Whatever the precise mechanism of biological pattern formation might be, it is not simply that the pigments on the animal's skin or in its fur react and diffuse. It has to be some kind of multi-stage process. Moreover, it takes place in the embryo, not in the adult

animal: even if the embryo does not exhibit clear patterns, they have to be present in some cryptic form. Turing recognised this, and he saw the chemical structures in his equations as a way to produce such 'pre-patterns', which would be laid down in an embryonic organism at an early stage and would provide a kind of scaffolding for its subsequent development — in the same manner that a builder first lays out the main shape of a house, its drains and foundations, before building the walls.

To Turing, the key point was that his system produced the right *kinds* of pattern. If pigments are deposited according to the peaks and troughs of parallel waves, you get stripes; more complex systems of interfering waves produce spots; and so on. He also realised that form, rather than pattern, can be controlled in a similar way, by growing bumps and dents according to the chemical prepattern.

In particular he showed that a circular ring of cells can form wavy patterns of several kinds, which he compared to the structure of *Hydra*, a tiny creature that lives in freshwater ponds and is a bit like a miniature sea-anemone. It has a bulgy cylindrical body with tentacles at one end. The tentacles are regularly spaced, like the peaks and troughs of Turing's chemical waves. He even found that before tentacles develop, a suitable stain will reveal chemical patches where the tentacles subsequently appear. This all looked quite promising, and biologists turned to concrete examples of apparent Turing patterns in development.

Jim Murray studied the formation of dappling on giraffes and stripes in zebras and big cats, enunciating the memorable theorem that 'an animal can have a spotted body and a striped tail, but not a striped body and a spotted tail'. This is based on the general principle that spots arise when stripes lose stability, and this normally happens only when the surrounding space gets *bigger*. Maynard Smith showed that hairs on the fruit fly *Drosophila* occur in a variety of Turing-like patterns whose genetic variants are *also* Turing patterns. It is hard to explain this if patterns are arbitrary consequences of DNA codes — why should natural selection prefer Turing patterns?

However, these initial successes turned to failure as other systems, such as feather development, fell apart under scrutiny. When feathers are grown at different temperatures, the observed quantitative changes in their patterns do not fit Turing's equations. The discovery of DNA and advances in genetics posed further problems for Turing's theories. The fruit fly *Drosophila* is one of the geneticist's favourite experimental animals, because it breeds rapidly, can be kept easily in the laboratory, and exhibits a huge range of different forms. An enormous amount is now known about fruit fly genetics, and it looks as if *Drosophila* builds striped patterns in a manner that is quite different from Turing's model. Indeed, the evidence is that it implements genetic instruction to build the stripes *one at a time* — quite unlike the reaction-diffusion pre-pattern mechanism, which lays down the entire pre-pattern in one go.

Yet another problem with Turing's theory of morphogens is that many apparent Turing patterns in adults are laid down early in development, when the organisms's shape was quite different. The 'eyes' on a peacock's tail *look* like BZ rings; but if they have a chemical precursor it must be laid down when the feathers are tiny cylinders. The pre-pattern required inside the cylinders doesn't look at all like a nice BZ ring. And to make matters worse, experimental chemists were having trouble creating the static chemical patterns required by Turing's theories. The best they could achieve was the mobile patterns of reactions such as BZ. Now the essence of Turing's approach is that the mathematics drives the chemistry, which in turn drives the biology. Unfortunately, even the chemistry wasn't working. By the 1970s most biologists had got bored with finding Turing patterns that weren't, and had moved on. Instead, they concentrated on the DNA code, and its

implementation.

Mathematicians were less worried about the failures of Turing's equations, because they saw those equations as just one example chosen from an almost infinite range of possible equations with similar properties. They realised that all systems *like* Turing's — including more elaborate 'mechano-chemical' equations describing the interaction of chemical changes and tissue growth — would produce the same general range of patterns. The specifics of particular equations were unimportant: what mattered was the common features of the whole class of equations, which were the key to the general problem of pattern-formation.

As the twentieth century draws to a close, Turing's ideas are once more coming back into vogue, but in a more subtle guise. Mathematicians are introducing models that are closer to real biology, but that exhibit the same general mechanism of pattern formation. Brian Goodwin has studied models of development in which, as a creature develops, its older parts become relatively fixed in form. If the creature begins with circular symmetry, then the initial stages of growth also have circular symmetry; and that symmetry may become 'frozen in' as the creature ages. Eventually the symmetry breaks, say via one of Turing's waves; and then the creature develops a number of equally spaced bulges that grow into branches or tentacles or petals. So the symmetry of the creature changes as you cast your eyes along the tissue from old to new — just like *Hydra*. Goodwin's equations successfully describe one key step in the morphogenesis of *Acetabularia*, a single-celled marine alga, which follows a similar pattern. The creature begins as a spherical egg, which puts out a root-like structure and a stalk. The stalk grows, and produces a ring of small hairs, called a *whorl*. The tip continues growing from the centre of the whorl, producing more whorls; then it develops a capped structure which gives it its common name, mermaid's cap. Goodwin's equations relate the formation of the whorl to a broken symmetry in the distribution of calcium within the organism, which in turn affects its local growth rate and hence its shape.

One of the most striking investigations into the mathematical basis of natural pattern is current work on seashells. D.M.Raup, C.Illert, and others have written down mathematical equations for shell growth which successfully reproduce the forms found in nature. Over many years Hans Meinhardt has made a study of the *markings* on shells, showing that despite their great variety and intricacy they can nearly all be produced by Turing models. Shells grow along their edge, which is overlapped by the animal's 'mantle', which secretes new material for the shell and also pigment. The 'olive shell' *Oliva porphyria* has a rounded, elongated shape, decorated with apparently random brown triangles on a pale background. Astonishingly, not only *can* such irregular patterns be produced by Turing models, but in fact it is rather easy to create them. The effect is an instance of mathematical 'chaos' in spatial patterning.

Old theories never die... For years it had been assumed that the big problem with Turing's theory was its tendency to produce moving patterns much more readily than stationary ones. Obviously the patterns on living organisms *don't* move... Big problem.

But...

Sometimes the patterns on organisms *do* move. They move rather slowly, which is why we don't generally notice, but they move. In fact, Turing's model predicts that they should move slowly. The organism that caused this latest change in thinking is a small tropical marine fish, the angelfish *Pomacanthus*. Juveniles are about 2 cm long, adults three to four times that length. There are many different *Pomacanthus* species, and they exhibit a variety of patterns. *P. semicirculatus*, for example, has curved stripes that

run 'vertically' down the body, whereas *P. imperator* has 'horizontal' stripes that run the length of its body. Over time, the stripes change their pattern. This is especially clear for *P. semicirculatus*, because the young fish have only three stripes, but the adults have twelve or more, so somehow the number of stripes has to increase as the fish develops. In fact, the changes occur in a rather curious manner. Start with a juvenile fish having three stripes, and watch it grow. At first, the stripes expand with the fish, becoming more widely spaced: this is what you would expect if the pattern were laid down once and for all. But at that stage, relatively suddenly, new stripes begin to appear between the original ones, restoring the original size of spacing. At first they are thinner than the old stripes, but they gradually thicken. When the body length reaches about 8 cm, the process is repeated a second time.

This sequence of changes has been modelled using reaction-diffusion equations by Shigeru Kondo and Rihito Asai. Their model involves just two chemicals, and assumes that the underlying tissue consists of a row of cells, some of which duplicate every so often. Their results reveal a natural pattern of stripes, which widen, without changing their number, until the tissue becomes sufficiently large, at which point the number of waves doubles, with new stripes appearing between the old ones.

An even more dramatic scenario arises in the horizontal striping of *P. imperator*. It also develops additional stripes as it grows, but various of the stripes 'unzip' and split into two. This type of wave rearrangement is known to physicists by the term 'dislocation', and it is widely observed in a variety of systems. In particular, it occurs in reaction-diffusion systems. To say that the stripe 'unzips' is a slight simplification, because it suggests that a single stripe turns into two by developing a Y-shaped branch-point. It *can* happen this way, but there are also more complicated dislocations in which stripes rearrange themselves by disconnecting and reconnecting, and Kondo and Asai saw these too. They use the observed spacings of stripes in the fish to estimate the diffusion rates for their hypothetical morphogens, and the results are within the range you'd expect if each morphogen were some kind of protein molecule.

Changes occurring in stripe patterns in angelfish are thus consistent with mathematical equations of Turing's general type, and — crucially — they are *not* what you would expect in patterns are simply laid down, cell by cell, by genetic switches. So it looks as if something mathematical, accessing the laws of physics and chemistry, must be going on in addition to genes switching each other on and off.

Early mathematical equations for development were too far removed from real biology to provide accurate models. The current emphasis on DNA goes too far the other way: it explains the productions of proteins, but it does not adequately explain how the proteins are assembled to form an organism, or — crucially — why nature so often prefers mathematical patterns. To see the difference between the two approaches, and how both fall short of reality, imagine a vehicle (corresponding to a developing organism) driving through a landscape (representing all the possible forms that the organism might take, with valleys corresponding to common forms and peaks to highly unlikely ones). In models like Turing's, once you have set the vehicle rolling, it has to follow the contours of the landscape. It can't suddenly decide to change direction and head uphill if the 'natural' dynamic is to continue straight ahead into the nearest valley. In contrast, the current view of the role of DNA sees development as an arbitrary series of instructions: 'turn left, then straight ahead of a hundred metres, then turn right; stop for ten seconds; reverse five metres; turn left...' Any destination is possible given the right instructions, and no particular destination is preferred.

The true picture, however, must combine genetic 'switching' instructions and free-

running mechano-chemical dynamics. If a car driving through a fixed landscape follows an arbitrary series of instructions, it is very likely to drive into a lake or off the edge of a cliff and it has little chance of reaching the top of a mountain. On the other hand, a car with a driver has more freedom in selecting destinations than a free-running vehicle without any controls. In the same manner, an organism cannot take up any form at all: its morphology is constrained by its dynamics the laws of physics and chemistry as well as by its DNA instructions. But the DNA instructions can make arbitrary choices between several different lines of development that are consistent with the dynamical laws. The new mathematical models are finally beginning to put these two aspects of development together. It is not DNA alone, or dynamics alone, that controls development. It is both, interacting with each other, like a landscape that changes shape according to the traffic that passes through it.

Further Reading

- R. Tucker Abbott, *Seashells of the World*, Golden Press, New York 1985. [I bought this little paperback in the Houston Science Museum: it's delightful. Colour illustrations of hundreds of seashells.]
- Brian Goodwin, *How the Leopard Changed its Spots*, Weidenfeld and Nicolson, London 1994. [Why development and evolution are dynamic phenomena, not just rampant genes. Required reading from one of the world's most original biologists.]
- Stuart A. Kauffman, *At Home in the Universe*, Viking, New York 1995. [A more personal view of self-organization and the search for laws of complexity. Required reading from another of the world's most original biologists.]
- Hans Meinhardt, *The Algorithmic Beauty of Sea Shells*, Springer-Verlag, Berlin 1995. [Profusely illustrated collection, in colour, of sea shell patterns and corresponding mathematical models produced by reaction-diffusion. Go and buy it, *now*. Buy ten, and give them to your friends — especially the ones who take pride in their ignorance of mathematics.]
- J.D.Murray, *Mathematical Biology*, Springer-Verlag, New York 1989. [A genuine textbook, this one, with all the formulas — but highly readable if you skip the technical bits, with lots of pictures.]
- Przemyslaw Prusinkiewicz and Aristid Lindenmayer, *The Algorithmic Beauty of Plants*, Springer-Verlag, New York 1990. [The mathematics of the plant world. Lots of marvellous illustrations, many in colour.]
- Ian Stewart and Martin Golubitsky, *Fearful Symmetry*, Blackwell, Oxford 1992; Penguin, Harmondsworth 1993. [A whole new way of looking at pattern, complexity, and the generation of order in nature.]
- D'Arcy Wentworth Thompson, *On Growth and Form* (2 volumes), Cambridge University Press, Cambridge 1942. [The great classic, full of thoughtful insights and thought-provoking examples.]
- Art Wolfe and Barbara Sleeper, *Wild Cats of the World*, Crown, New York 1995. [A glorious reminder that nature still has the edge on mathematics when it comes to beautiful patterns and dynamic movement.]
- Lewis Wolpert, *The Triumph of the Embryo*, Oxford University Press, Oxford 1991. [A leading biologist discusses the development of organisms.]

Gresham College was established in 1597 under the Will of the Elizabethan financier Sir Thomas Gresham, who nominated the Corporation of the City of London and the Worshipful Company of Mercers to be his Trustees. They manage the Estate through the Joint Grand Gresham Committee. The College has been maintained in various forms since the foundation. The one continuing activity (excepting the period 1939-45) has been the annual appointment of seven distinguished academics "sufficiently learned to reade the lectures of divyntyte, astronomy, musicke, and geometry" (appointed by the Corporation), "meete to reade the lectures of lawe, phissicke, and rethoricke", (appointed by the Mercers' Company). From the 16th century the Gresham Professors have given free public lectures in the City. A Mercers' School Memorial Chair of Commerce has been added to the seven 'ancient' Chairs.

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