Exploring Reaction-Diffusion and Pattern Formation

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Abstract. This article reviews the development of the concept of reaction-diffusion leading to pattern formation in living organisms. The article commences with an historical background and then describes biological development, and ideas of the formation of patterns using dynamic activator inhibitor systems. In addition to this, different models to represent such systems and their computer simulations are discussed.

1 Introduction

The first steps toward the sciences arose out of the recognition of patterns and structures. Patterns are all around us in the living and the non-living world. Formation of galaxies, mountains, rivers, crystals, zebra stripes, flower petals and butterfly wings are all examples of ordered structures and regular patterns. While it seems likely that evolution plays the major role in creating, selecting and exploiting features in living organisms, there can be no denying the role of physics in nature. Physical structures can emerge naturally without the selection pressure of natural evolution: sand dunes, snow flakes, clouds and cracks in the ground can all self-organise into ordered and repetitive forms with clearly defined patterns.

The existence of such natural pattern has led many researchers to hypothesise that in some of the features of life, natural evolution has exploited the automatic pattern-formation machinery provided by physics instead of creating her own from scratch. In this article we focus on this class of patterns, namely pattern formation of living organisms. We explore an understanding of reaction-diffusion systems and see how they may enable the emergence of pattern formation in living organisms.

2 Review of Reaction Diffusion

2.1 Biological Development

We each begin life as a single cell, and eventually become adults made up of approximately 10^{15} cells of about 200 different types (in humans) organized in a very complicated arrangement. Once this single cell (zygote) has been formed by fertiliza-

tion, it begins a period of rapid division. This divides the embryo into a number of cells each containing an identical copy of the genome.

But a fundamental question still has not been fully answered. How does a highly organized body plan emerge from a homogeneous fertilized egg? The breakdown of symmetry and formation of pattern in the embryo is one of the most important questions of development of biological form.

2.2 Historical Perspectives of Reaction-Diffusion and Pattern Formation

In his book "On Growth and Form" (1917), D'Arcy Thompson (Biologist, zoologist and mathematician) attempted to reduce biological phenomena to mathematics.

Alan Turing was also interested in biology and was heavily influenced by D'Arcy Thompson. His interest in the brain structure and development led him to the broader question of biological development. He saw the origins of biological forms as one of the fundamental problems in science and believed that the main problem for biology was to account for pattern and form. He looked for answers in chemistry.

In his paper "Chemical basis of morphogenesis" (1952), Turing proposed a hypothetical chemical reaction that could spontaneously break the symmetry in an initially uniform mixture of chemical compounds, leading to stable spatial patterns. He was hoping that this would provide a model for how patterning takes place in an initially homogeneous fertilized egg. Turing discovered that patterns could be formed if two substances with different diffusion rates reacted with each other. He proposed that the driving force of symmetry breaking (triggered by random disturbances) could occur through the reaction of certain chemical "species", and their diffusion through masses of non-growing tissues in which they were dispersed. He called these chemicals *morphogens* –conveying the idea of form producers.

Diffusion is the action of spreading of morphogens through the tissue. *Reaction* (chemical) is the process that creates and destroys morphogens, based on their concentration in each cell. In Turing's chemical system, diffusion is competing with an autocatalytic chemical reaction. He proposed a process by which a chemical A (activator) generates more of itself by autocatalysis at the rate dependant on the amount of A already present. The chemical A also activates the formation of a chemical I (inhibitor) that inhibits the generation of A. He showed that if in a chemical system, two chemicals react with each other and diffuse at different rates, they can form stable patterns. This chemical system is called a reaction-diffusion system and is able to produce stable stationary patterns, as occur in biological pattern formation. However, at the present we have no proof as to whether Turing's system has anything to do with morphogenesis since the evidence of the presence of reacting morphogens has not been found yet.

2.3 Creating Turing Patterns with Real Chemicals

Creating Turing patterns in a real reaction have proved to be extremely difficult. In 1990 Patrick De Kepper and colleagues carried out an oscillatory chemical reaction involving chlorite and iodide ions and malonic acid (CIMA) in a thin layer of gel that was continuously fed from opposite directions with fresh reagents. Similar to the Tur-

ing's scheme, the CIMA reaction has an explicit activator and inhibitor. Different rates of diffusion have been introduced in the CIMA reaction by conducting it in a polymer gel. Qi Ouyang and Harry Swinney showed that the pattern disappeared if the gel was warmed above 18^{o}C, and that it reappeared when the gel was cooled. This abrupt and spontaneous patterning in response to a gradual change in conditions is what is expected of a Turing structure. They were also able to demonstrate another of the enticing predictions of the Turing instability: the possibility of forming new stable patterns by changing the reaction conditions. By increasing the iodide concentration or lowering the malonic acid concentration, they broke the symmetry in a new way, forming stripes instead of spots.

2.4 Living Reaction-Diffusion Systems

Kondo and Asai discovered that the stripes in a marine angelfish of the species pomacanthus semicirculatus do not seem to be fixed into the skin at an early stage of development - they continue to evolve as the fish grows. As they grow, the stripes get wider, but when the body reaches 4 cm there is an abrupt change: a new stripe emerges in the middle of the original ones. This process repeats again when the body grows to about 8 or 9 cm. Kondo and Asai pointed out that since a reaction-diffusion process is apparently still going on in the adult fish rather than during the embryonic pre-pattern stage in patterned mammals, it might be easier to identify the chemical species responsible in this case.

In vertebrates, the most plausible suspect for a morphogen is a molecule known as retinoic acid. Retinoic acid has an important role in local signaling in vertebrate development. A variety of experiments have shown that retinoic acid can alter cells' positional values in limb development.

2.5 Cellular Automata and their Application to Reaction-Diffusion Systems

One method of modeling Turing systems is by the use of non-linear partial differential equations. Another method is to use cellular automata, models in which the fate of a cell is determined be the states of its neighbours through a set of local rules. Cellular automata can act as good models for physical and biological phenomena since each cell updates itself independently, basing its new state on the appearance of its immediate surroundings (locality) and on some generally shared laws of change.

2.6 Different Systems of Equations and their Computer Simulation

Different systems of equations have been used for pattern formation using reaction-diffusion. Three principal systems and their computer simulations will be introduced in this section. However the mathematical equations will be skipped for the purposes of this article.

Turing.

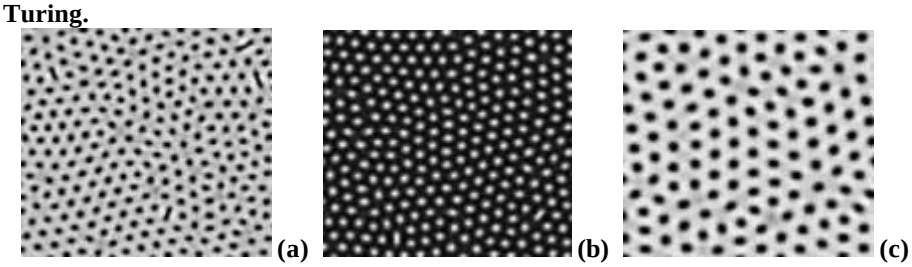

Fig. 1. (a) and **(c)** show the activator concentration **(b)** shows the inhibitor concentration

Meinhardt.

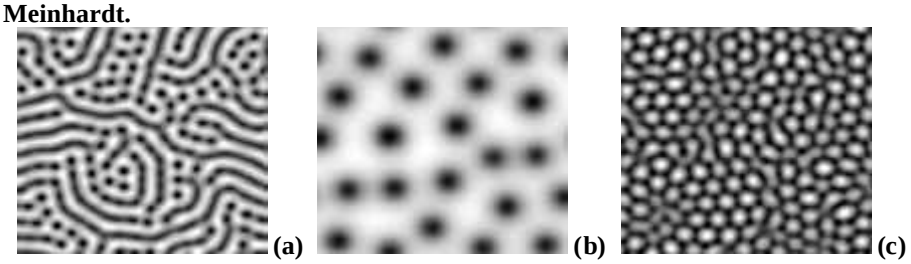

Fig. 2. Lighter areas represent higher concentrations of the activator chemical.

Gray-Scott Equations.

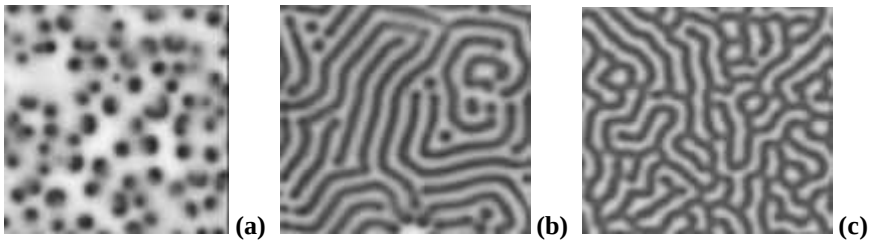

Fig. 3. The pattern in **(a)** is continuously in motion. The pattern in **(b)** seems stationary for a short while and then the motion starts again indefinitely. The pattern in **(c)** is stationary

3 Conclusions

Pattern formation has long fascinated mankind, but nature is not ready to give up all her secrets. While the reaction-diffusion systems suggested by Turing may provide some answers, it is difficult to apply these ideas to biology. Although the application of reaction-diffusion systems is often used to explain animal skin pattern generation, from our explorations of the equations, we can conclude that the patterns emerging from these systems resemble more the patterns of microscopic organisms, for example, bacteria and mold. But the final pattern is often not the most interesting of behaviours. Sometimes the *movement* of the patterns is incredibly organic and lifelike.