BE STILL, MY CHEMICAL HEART CELLULAR AUTOMATA IN CHEMISTRY AND IMMUNOLOGY

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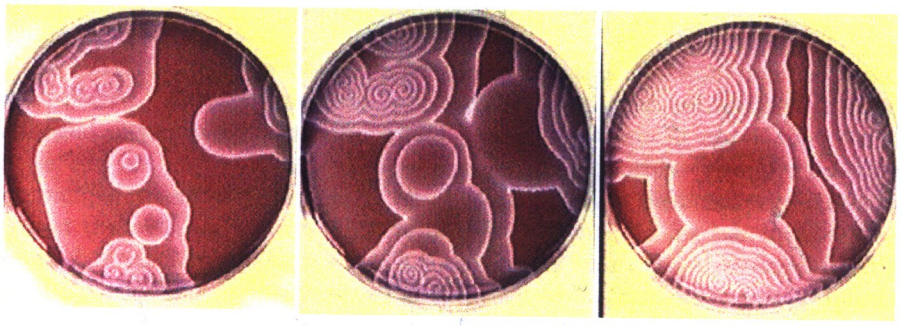
Introduction

This project uses a model related to a cellular automaton to explore waves propagating through a chemical system. The model exhibits similar behaviour to the Belousov-Zhabotinsky chemical reaction. In this reaction the colour changes which accompany the reaction are seen to oscillate in time, and to form swirls in the reaction vessel as the reaction proceeds. What makes this kind of reaction particularly interesting is that similar spiral patterns of reactions have been found in living tissue, in particular heart tissue, so that it is possible that our body depends at a very basic level on such oscillating chemical reactions.



A simplified model

Gerhardt and Schuster[1] at the University of Bielefeld in Germany invented a simpler model, which can be described in terms of the spread of an infection[2]. Space is divided into square cells, and each cell is described by a state number between 0 and some maximum value n: a cell in state 0 is 'healthy' and one in state n is 'ill'. Cells in intermediate states are called 'infected'. The 'infection' spreads at a rate determined by two parameters k1 and k2 in addition to a constant rate g. Time is imagined to advance in clock-like ticks.

This relatively simple system shows three different kinds of behaviour: type I, with mostly healthy cells (waves of infection that soon die out); type II, with intervals in which there were many infected cells (waves travelling in circular bands with varying width); type III with very regular alternations of healthy and unhealthy cells (more regular spatial waves); type IV with rapid oscillation about some intermediate level of infection (spiral patterns).

After each tick, any healthy cell will have a new state which depends on the number of infected neighbours, A, and the number of

[1] M Gerhardt and H Schuster. A cellular automaton describing the formation of spatially ordered structures in chemical systems. *Physica D: Nonlinear Phenomena*, 36(3):209 – 221, August 1989

[2] Their model was based on a chemical reaction taking place at the surface of tiny catalyst particles of platinum. Carbon monoxide CO and oxygen combine to form carbon dioxide CO_2 on the surface of the catalyst. The heat given off by the reaction changes the state of the catalyst so that any CO remaining on the catalyst is released, the catalyst cools, and the process starts again.

ill neighbours, B. There are two ways of specifying the neighbours: either they share sides with the cell being considered (so that in two dimensions each cell has four neighbours) or they share a side or a corner (eight neighbours in two dimensions). Cells at the edges and corners of the whole region will have fewer neighbours[3]. The new state of a cell that starts out healthy is $\lfloor B/k1 \rfloor + \lfloor A/k2 \rfloor$, where the notation $\lfloor\ \rfloor$ denotes rounding down to the next lowest integer. If the result is greater than n, set it to n.

[3] Or you can wrap cells around, so that the cell at the bottom of the mesh is imagined to be above that at the top, and so on.

A cell that is already infected gets worse at a steady rate g, and is also influenced by the state of its neighbours: if the sum of the state numbers of its *infected* neighbours is S, after the tick of the clock its state will be $\lfloor S/A \rfloor + g$. If the result is greater than n, set it to n.

Finally, any cell that is in state n (i.e. 'ill') at time t undergoes a miraculous cure to state 0 ('healthy') at time $t + 1$.

The project

Overall, there are several parameters to explore, and you should write a computer program for the model. Mathematica will be suitable, but use any language you like. The size of the grid, N cells on each side, should be taken as about 20 to start with. You might want to try larger systems later. For the number of states, n, 100 is a suitable choice. Suitable values of $k1$ and $k2$ are between 1 and 5 (a useful starting point is $k1 = 2$, $k2 = 3$). You should explore different values of the infection constant, g, between 1 and 20. Aim to show the four different types of behaviour. You should experiment with different initial patterns. You should also investigate how the results depend on the choice of the number of neighbours (four or eight, as described above).

Consider how best to display your results. It may be useful to map the state of the cell onto a range of colours, to display the spatial patterns. It will also be useful to display the fraction of infected cells as a function of time to illustrate the different regimes.

Extensions

The cellular automaton approach may be applied to immunology[4]. Consider a system in which each cell can contain any or all of antibodies A, lymphocytes B, helper cells H, suppressors S and viruses V. Each of these may be present in high (1) or low (0) concentra-

[4] Avidan U. Neumann. Control of the immune response by a threshold automata model on a lattice. *Physica A: Statistical and Theoretical Physics*, 162(1):1 – 19, 1989

tion, and interact as follows:

$$A \leftarrow BHV \tag{1}$$
$$B \leftarrow (B + V)H \tag{2}$$
$$H \leftarrow H + (1 + S)V \tag{3}$$
$$S \leftarrow H + S \tag{4}$$
$$V \leftarrow V(1 - A). \tag{5}$$
$$\tag{6}$$

These mean that antibodies will only be present when B cells, helpers and viruses are all present; B cells will grow if viruses and/or B cells are present together with helpers; helper cells arise if other helper cells are present or if viruses are present suppressors are not; suppressors form either suppressors or helpers; antibodies destroy viruses. In a binary model, one takes any value greater than 1 to equal 1. Generally the stable states are $ABHSV = 00000$, 01100, 01110, 01000 or 01001. Introduce neighbour rules which allow viruses or antibodies to arise in a cell if the majority of surrounding cells contain V or A respectively.

Alternatively, note that similar models have been used to model the spiral waves observed in *Xenopus laevis* oocytes[5].

[5] J Lechleiter, S Girard, E Peralta, and D Clapham. Spiral calcium wave propagation and annihilation in Xenopus laevis oocytes. *Science*, 252(5002):123–126, 5 April 1991; S Girard, A Lückhoff, J Lechleiter, J Sneyd, and D Clapham. Two-dimensional model of calcium waves reproduces the patterns observed in Xenopus oocytes. *Biophys J.*, 61(2):509–517, February 1992; and I. Bezprozvanny. Theoretical analysis of calcium wave propagation based on inositol (1,4,5)-trisphosphate (InsP3) receptor functional properties. *Cell Calcium*, 16(3):151–166, September 1994

References

[1] I. Bezprozvanny. Theoretical analysis of calcium wave propagation based on inositol (1,4,5)-trisphosphate (InsP3) receptor functional properties. *Cell Calcium*, 16(3):151–166, September 1994.

[2] M Gerhardt and H Schuster. A cellular automaton describing the formation of spatially ordered structures in chemical systems. *Physica D: Nonlinear Phenomena*, 36(3):209 – 221, August 1989.

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[5] Avidan U. Neumann. Control of the immune response by a threshold automata model on a lattice. *Physica A: Statistical and Theoretical Physics*, 162(1):1 – 19, 1989.

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