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A FORMAL MODEL OF BIOLOGICAL DEVELOPMENT

The development of organisms, especially higher animals, is a mysterious process. How can a single cell, the fertilised egg (zygote) change itself into an adult containing many millions of cells all organized in a highly complex way? The awesomeness of this process is increased if one recalls that it is essentially autonomous, that all the cells in the organism are genetically identical, and that development is closely controlled. Let us say a few words about each of these aspects of development. By saying that the process is autonomous, one is drawing attention to the fact that all the information necessary to produce the adult is contained in some way in the first cell; the environment contributes no information, but simply provides energy and materials. Thus the zygote of a given species always becomes an adult of that species, whatever its environment. Growth occurs mainly through a continuing process of cell self-reproduction in the organism, but the differentiation that occurs during growth is made more difficult to understand because, as generally agreed by biologists, all the cells contain the same genetic instructions, the new cells being genotypically identical to their precursors. How, therefore, do they come to differ from each other, and to develop into elaborate spatial patterns, given this apparent limitation? Furthermore, the whole process of development is closely controlled so that different parts of the developing organism develop in relation to each other; and in many cases it is possible for the organism to overcome damage during development. Clearly, precise mechanisms for control and adaptation are involved. If one did not know better, one would be tempted to say that it would be impossible for a machine system to achieve such spectacular results. That is why the process seems to be mysterious — indeed, in the history of biology the fact of development in organisms has led some researchers (like H. Driesch [1] and W. M. Elsasser [2]) to argue that organisms cannot be machines.

From the point of view of cybernetics and general systems theory it is important that attempts should be made to understand how a machine could accomplish the feat of development. This is important because if a machine cannot develop, then the argument that there is something special about living systems still has some force. In this eventuality, the argument at the basis of cybernetics — that living and non-living systems can be understood in terms of the same principles — would be vitiated. More positively, if the principles of development could be understood, the practical implications in the long term would be enormous. If machine self-construction ever became a practical possibility, it is obvious that technology could be revolutionised.

Clearly, what is required at the outset is the formal study of a subset of what V. Aladyev [3] has referred to as homogeneous systems (at the most general level, systems in which each element behaves in the same way as every other element). The subset would be those homogeneous systems in which each element has the property of self-reproduction and in which the system starts with one element alone. We can think of the elements as automata and investigate rigorously what properties such automata would have to have to produce certain kinds of results: e. g. patterns of different kinds and different kinds of adaptive abilities. Starting with simple systems one would hope to uncover principles which could then apply to more complex systems. In biological terms one could interpret the automata as cells, the original automaton modelling the zygote, and the terminal pattern of automata representing an adult organism. The process by which the original automaton, with no information from outside, turns itself into a system with specified properties would then be taken as a model of biological development.

Biological development usually consists of both growth and differentiation. By g r o w t h is meant simply the increasing size of the organism, brought about mainly through cell self-reproduction. Differentiation is a more complicated concept, and the writer has found it useful to distinguish at least two kinds of differentiation: spatial differentiation and phenotypic differentiation (the latter being referred to as f u n c t i o n a l d i f f e r e n t i a t i o n in M. J. Apter [4]). By the former one draws attention to the changing and increasingly complex spatial pattern of cell relationships which is achieved during development. By the latter one refers to the fact that individual cells come to differ from each other, especially in terms of their functions, e. g. some cells becoming skin cells, some nerve cells, etc. So in a growing tissue of cells one can refer to the changing shape and communication pattern of cells in the tissue (spatial differentiation) and also the increasing differentiation of kinds of cells in the tissue (phenotypic differentiation). Of course phenotypic differentiation also occurs in spatial patterns, but for clarity this is not included under the heading s p a t i a l d i f f e r e n t i a t i o n. Not only does the developing organism have the power to achieve complex spatial and phenotypic differentiation, organisms also have a greater or lesser ability to regulate during development and to regenerate. By r e g u l a t e is meant that the organism will develop into a normal adult even if it is interfered with or damaged during development, for example by the removal or rearrangement of cells. By r e g e n e r a t e is meant that the organism will repair any damage done to itself when it is in its completed adult state.

Despite the importance of understanding biological development, including spatial and phenotypic differentiation and regulation and regeneration, comparatively little work has been carried out on it so far within the tradition of cybernetics and general systems theory. There are, however, many signs of an increasing interest and there is every indication that the field is beginning to develop.

In the modelling which h a s occurred up to the present, a number of different techniques have been used. For example, M. J. Apter [4] has used the Turing machine convention in order to represent cellular instructions and shown how a number of topological patterns of interconnected cells can be obtained from such instructions. He has also demonstrated that, provided there are no limitations on the number of states or communication symbols which may be used, diverging networks (t r e e s in graph theory terms) of a n y d e g r e e of

complexity can in principle be obtained [5]. A. Lindenmayer [6,7] has also shown how different topological patterns, straight lines and trees, can be produced using the terminology of sequential machines to represent instructions. (In general this method of representing instructions is essentially the same as that for Turing machines, except that the former make no reference to tape movements.) He has derived some theorems concerning development in such systems and constructed two models to simulate the development of a particular organism (one of the red algae).

Tessellation models have been used by several workers. A tessellation is a plane divided into squares in each of which is finite state machine. In models of development all such finite state machines are identical, being governed by the same set of rules. At the start of development all the machines are in a quiescent state except for one, which represents the zygote. This machine causes the machines in one or more of its neighbouring cells to change to some non-quiescent state (this representing self-reproduction) and these in turn may influence one or more of their neighbours in a similar way. Thus a process of development is set up in which a configuration of cells increases in size until some predetermined pattern has been achieved. One researcher who has used this approach has been M. A. Arbib [8]. His original interest in using tessellation structures was in dealing with the problem of self-reproduction — a problem which many, following J. von Neumann [9] have approached by means of such structures. In M. A. Arbib's work on development the cells are given the possibility of moving in the tessellation space and of becoming attached to each other (welded) in such a way that if one cell in a set of such attached cells is moved, the others move concomitantly. Clearly these additional facilities add much to the potential of such models. V. Aladyev [3], who has also worked on problems of self-reproduction using tessellation structures, is another who has produced interesting simulations of development by means of tessellation structures. In doing this he has been concerned with problems of both spatial differentiation and phenotypic differentiation, and has produced models of regeneration as well as differentiation. One general problem of development which V. Aladyev has rightly attended to is the question of efficiency, that is, the question of how to produce given patterns using the smallest number of instructions possible. This question is important from the point of view of understanding development in living systems since the zygote must presumably be simpler in some sense than the adult to which it gives rise. Another of his concerns has been the limitations of patterns which are obtainable under different conditions. Here he has shown that tessellation models are far less limited by, say, a binary input/output alphabet than are the present writer's Turing machine models, although limitations still exist. R. Herdan [10] has also produced an essentially tessellation model of development as has M. Maruyama [11] although in the latter case development starts from more than a single cell. Finally, it should be noted that S. Ulam's work [12] is relevant to tessellation models as is the "*Life game*" of Conway (see M. Gardner's works [13, 14]).

A recent approach has been to represent genetic instructions diagrammatically in network terms [15]. One reason for doing this is that a network interpretation of gene activity is consistent with the important work of J. Monod and F. Jacob [16] on the control of gene action. Another reason is that in this way it is possible to demonstrate visually what is happening within each cell during spatial differentiation, and this makes it

possible to get across the ideas involved in a more immediate and easily understandable manner than is usually possible with automata theory models. (Indeed, the writer has made a short film entitled *"A network model of development"* which shows some systems of this kind actually developing.)

All the models noted so far have been paper-and-pencil models. It is interesting that few attempts have been made to model development in hardware terms; an exception has been the electronic model of R. J. Goldacre [17]. M. J. Apter and A. G. Wilson (unpublished) have also produced a hardware model of phenotypic regulation using a simple system of magnets. All the units in the system are identical and, irrespective of the number of them which are connected (in a straight line) or the order in which they are connected, they divide themselves by labelling into a specified number of areas in a specified order.

In the rest of this paper we shall present a further convention for the production of paper-and-pencil models of development, and look at some examples of models within it. The convention is based on a process of counting and uses the propositional calculus in the description of cellular instructions.

The convention

General

1. The developing system is a network of connected cells which at any particular moment during development assume a specifiable topological pattern. The cells in such a system will be represented diagrammatically as circles which are connected by straight lines.

2. Each such network system starts as a single cell, the behaviour of which is governed by a set of instructions. At least one of these instructions must be an instruction concerning the conditions under which self-reproduction of the cell occurs. By s e l f - r e p r o d u c t i o n is meant that in place of the original cell there are two cells with instructions which are identical to each other and to the instructions in the original cell which has now disappeared. The two new cells are connected to each other, and the topological pattern of the network at any moment is the result of the pattern of self-reproduction which has occurred up to that moment.

3. When a cell is connected with another, it can communicate directly with it. It cannot communicate directly with any other cell.

4. The network may differentiate not only spatially but phenotypically, i. e. the cells may come to label themselves differently. To do this, instructions are required which specify the different conditions under which each label is to be adopted.

5. The developing network is assumed to act synchronously.

6. The instructions must be complete and consistent. That is to say, they must be adequate to achieve a given specified terminal topological pattern (and possibly also phenotypic, or labelling, pattern) and there must be no contradiction between instructions such as would occur if the same conditions specified incompatible outcomes in different instructions.

Counting

1. A cell which finds itself not communicating with another cell to its left or right (i. e. which is at the end of a line in the network) counts 1 and passes this message to the cell (or cells) with which it does immediately communicate on its other side.

2. Any cell which receives a number as an input message automatically adds 1 to this number. It then passes the resulting number to the cell (or cells) with which it communicates on its other side. The effect of this is that counting occurs from left to right and right to left across lines of cells in the network.

3. The count number of a cell is the input number plus 1, i. e. it is the same as the number which it outputs. Such a count represents the condition or part of the condition of the cell (as referred to above) which determines the behaviour of the cell. It is not to be confused with the labelling process which might be part of such behaviour (see item 4 under the heading *"General"*).

4. For the sake of convenience and conceptual simplicity it is assumed that after the instructions have been obeyed in each cell at each moment t, recounting takes place throughout the network before $t+1$. So at $t+1$ the instructions which take effect do so on the basis of the new count numbers within each cell since the previous moment t. In other words, there are alternate cycles of counting and instruction-obeying, the counting cycle taking place between moments.

5. A number of different counting operations can take place concurrently in a network and each is depicted by a different letter. These can be thought of most simply as representing different substances whose amounts are increased by a constant amount in each cell in turn. A given cell therefore may have possession at any given moment of a number of counts of different substances. In such a case the condition of the cell is the logical conjunction of these counts. Such a condition can be thought of in automata theory terms as specifying the internal state of the cell/automaton.

6. It is assumed that each network counts in terms of substance a from the beginning. It does not matter in which direction the network counts in terms of a, and this could be determined randomly on each occasion. However, let us assume for consistency that a is always counted in the right hand direction, i. e. the process starts in the cell which is initially the furthest to the left once there is more than one cell in the network.

7. The counting process is assumed to occur in the way specified above and is not spelled out in the instructions for each developing network. The instructions therefore specify simply what the cell does as a result of such counting. This simplifies the representation of instructions in the different networks.

The instructions

1. "R" represents self-reproduction.

2. Some of the notation of the propositional calculus is used in the representation of instructions: namely "." which stands for "and", "∨" which stands for "or" and "≡" which stands for "is equivalent to". Conventional mathematical notation is used inside the brackets in these instructions. Each cell then contains an instruction list using this notation. An example of an instruction would be:

$$(a=3) \,.\, (b=15) \equiv R,$$

which can be read as "an a count of 3 and a b count of 15 in a cell, means that it will reproduce".

3. In instructions governing phenotypic differentiation, Greek letters will be used as labels (in order to avoid confusion with the substances used in counting). Thus the instruction

$$(a=1).(b>5)\equiv\alpha$$

would mean that "an a count of 1 and a b count greater than 5 in a cell, means that the cell will become an α-type cell". Such a label is not permanent, but depends on the situation which gave rise to it continuing.

4. We shall assume that, using the predicate calculus, the following formula is appended to each instruction to the left of the "$\equiv$" symbol: $\cdot\sim(\exists x)\ (\exists x)$.

Here, "$\exists$" stands for "an expression other than the expression already contained in that part of the formula to the left of the "$\equiv$" symbol". The effect of this is that if there is any further input other than that specified, the instruction is vitiated and the outcome is not achieved.

Self-Reproduction

1. When self-reproduction occurs, the two daughter cells are, unless otherwise specified, aligned along the axis in which the counting takes place.

2. Reproduction can also take place in such a way as to set up a new axis. In this case, one daughter cell remains in the row while the other daughter cell finds itself free on one side. Whichever cell is the latter can then start a new counting process in the opposite direction to the counting of a (see item 1 under "*Counting*" above) using a new letter. The letter used is specified in the relevant instruction; for example, the symbol R^c would mean that the daughter cell bounded only on one side counts 1 of substance c and hence sets up a new counting process. To keep things reasonably simple, it is assumed that this counting proceeds as far as the end of the new axis which has been set up, but no further.

3. Normally it will be necessary on the first reproduction in a developing network to initiate a counting process in the direction opposite to the direction in which the a substance is counted. This is achieved by means of the instruction "$(a=1)\equiv R^b$" which in effect acts to polarise the system.

4. Reproduction is complete before the next counting cycle takes place (see item 4 under the heading "*Counting*").

Some developing networks

To achieve unlimited growth in a straight line from one end only, the following instruction is all that is needed: "$(a=1)\equiv R$". What happens here is that the leftmost cell at each moment, which counts $a=1$, reproduces; in this way the line of cells extends leftwards at the rate of one cell per moment. To achieve unlimited growth from both ends of the line simultaneously, two instructions are needed:

$$\begin{cases}(a=1)\equiv R^b,\\ [b=1]\vee[(a=1).(b>1)]\equiv R.\end{cases}$$

The first instruction brings about the first reproduction and sets up an axis along the line of cells in which the substance b is counted in the opposite direction from substance a. The second instruction specifies that the rightmost cell, which counts $b=1$, reproduces; also, the leftmost cell, which counts $a=1$, reproduces if its b count is greater than 1 (i. e. this relates to the second and all subsequent reproductions by the leftmost cell in the system, such reproductions occurring without the setting up of a new axis). In this case, the line of cells extends, after the first reproduction, at the rate of two cells per moment — one at each end of the line.

If the instruction "$(a=1) \equiv R^b$" is used on its own, the result is unlimited growth from one cell. What happens here is that the same cell continually reproduces and sets up new axes. Thus after three reproductions the net will appear as in Fig. 1.

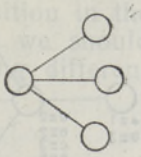

Fig. 1.

For spatial differentiation into more complicated patterns of finite size, longer instruction lists are needed. For example, suppose we want a straight line of cells with a side-branch at a particular point. The instructions necessary to produce a straight line of any length with a side-branch of any length at any point in the line are as follows:

$$\begin{cases} (a=1) \equiv R^b, \\ (a=x).(b=2) \equiv R^c, \\ [(b=1).(1 \leqslant a < y)] \vee [(c=1).(a<z)] \equiv R, \end{cases}$$

where x is the number of cells to the right in the line where the branch is to occur; y is the number of cells in the line, and z is the number of cells in the side-branch plus x. For example, if we set $x=3$, $y=6$, and $z=5$, we produce the network shown in Fig. 2. The count numbers in each cell when the pattern has been completed in this net have been entered on the figure.

Further branches can be added at any point in the line by adding further instructions of the form "$(a=x).(b=2) \equiv \equiv R$", adding an appropriate superscript letter to "R" in each case, and adding further disjunctive expressions, to specify the length of each such line, to the third instruction.

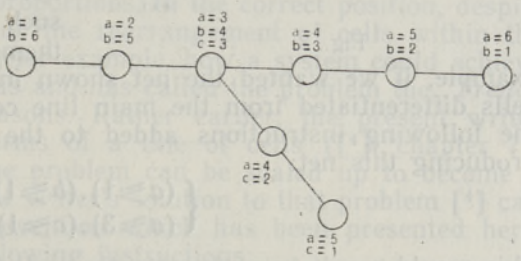

Fig. 2.

If the reader works step-by-step through the instructions which relate to Fig. 2, he will realise why, for example, the second instruction contains the expression "$(b=2)$" and not "$(b=1)$". If it had been the latter the instructions would have been inconsistent, the second instruction conflicting with the first expression of the final instruction: "$(b=1).(1 \leqslant a < y)$". Using "$(b=2)$" in the second instruction means that the first reproduction is along the *a/b* axis, and the second one sets up a new *a/c* axis. (Both cannot be done at the same moment.) Again the reader will notice that the main-line cell which is connected with the branch (the third from the left in our example) does not continue to reproduce and set up new branches, because after the first reproduction which set up the branch it has a c count. Following item 4 under the heading "*Instructions*" in the convention, this makes the second item no longer applicable. So the presence of the branch in this case inhibits further branches being produced at this point.

Branches can, of course, also be added to branches. Here is an example of a pattern in which this occurs. The instructions are:

$$\begin{cases} (a=1) \equiv R^b, \\ (a=2).(b=2) \equiv R^c, \\ (a=3).(c=2) \equiv R^d, \\ (a=2).(b=2).(c=3) \equiv R^e, \\ (a=4).(e=2) \equiv R^f, \\ [(b=1).(1 \leqslant a < 3)] \vee [(c=1).(1<4)] \\ \vee [(d=1).(a<4)] \vee [(e=1).(a<7)] \vee [(f=1).(a<6)] \equiv R. \end{cases}$$

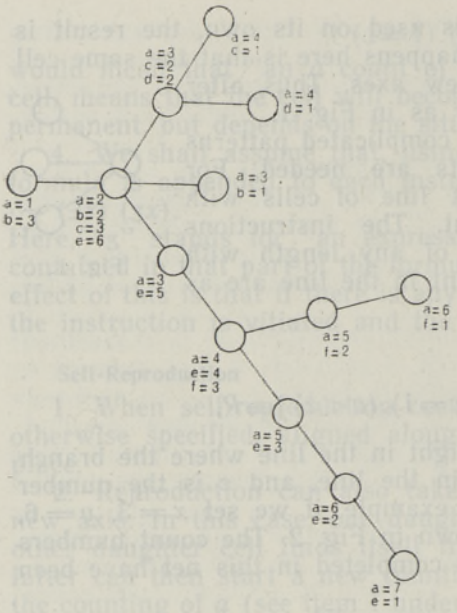

Fig. 3.

The first instruction polarises the system in terms of counting. The next four instructions specify where, and when during development, the branches occur. The final instruction specifies the length of each branch. The resulting pattern is shown in Fig. 3. It should be noted that various other sets of instructions could also be found to produce this topological pattern.

It can be seen then that any diverging pattern can be produced in this way, irrespective of the number of branches there are, where they occur, and how long they are.

What about phenotypic differentiation? Instructions may be added to the instructions needed to produce networks of different spatial patterns, such that cells in these nets label themselves in different ways. For example, if we wanted the net shown in Fig. 2 to have its side-branch cells differentiated from the main line cells, we could achieve this with the following instructions added to the instructions already given for producing this net:

$$\begin{cases} (a \geqslant 1).(b \geqslant 1) \equiv \alpha, \\ (a \geqslant 3).(c \geqslant 1) \equiv \beta. \end{cases}$$

This would result in each main line cell being labelled α, and each side-branch cell being labelled β. And if, say, we wanted the main line in the finished net to consist of two cells to the left of one kind and four to the right of another kind, we could replace the first instruction above by:

$$\begin{cases} (a \geqslant 1).(b \geqslant 5) \equiv \alpha, \\ (a \geqslant 3).(b \geqslant 1) \equiv \gamma. \end{cases}$$

Following these particular instructions, the cells would only label themselves after development had proceeded a certain distance.

All this may seem unnecessary. It could be argued that cells are already phenotypically differentiated by being in different internal states — in the present models by having different count numbers of different substances. Indeed, some of the writer's Turing machine models [5] have been considered by him in this light, and V. Aladyev [3] has also equated phenotypes with internal states in some of his models. However, although different internal states may have a functional significance in the development of an organism, the phenotypes of the adult may have a significance for it quite apart from its development; we should surely wish to distinguish the ends and means of development in our models in the same way. In any case, if we do not, then difficulties may arise where the attempt is made to design a system which will produce a specified pattern of spatial and phenotypic differentiation. This is because the internal states required to produce the pattern of spatial differentiation may be quite different from the pattern of phenotypic differentiation which is required in these cells. Another difficulty arises

specifically for the counting models presented here if we equate the internal states with phenotypes. This is that each cell in such models has a unique internal state (since each cell is in unique position in the network). But in most models of phenotypic differentiation we should want subsets of cells to be identical with each other, forming different phenotypic areas.

Networks which regulate

As noted earlier, in biological systems it is often the case that if cells are removed or re-arranged during development, the system can adapt so that it still finishes up with parts of the right proportion in the right position, and this is known as regulation. It is clearly related to the control exercised by biological systems during development which has the effect of maintaining the parts roughly in proportion to each other whatever the absolute size of the system. We must now see if we can deal with this kind of phenomenon in terms of the modelling convention used here.

A way of formalising this problem is to ask how an area of cells can phenotypically differentiate into a number of vertical segments of specified proportion and maintain these proportions, in the correct position, despite increases or decreases in size or the rearrangement of cells within the area. L. Wolpert [18] has asked, for example, how a system could achieve this in terms of three equal areas and has called the problem the *"French Flag Problem"* for obvious reasons. Rather earlier, the present writer posed the same problem in terms of a line of cells ([4], chapter 7). Clearly, any solution to the line problem can be scaled up to become a solution to the area problem. The writer's solution to that problem [4] can be restated in terms of the convention which has been presented here. The solution is given in the following instructions:

$$\begin{cases} \frac{a}{b} < \frac{1}{2} \equiv \alpha, \\ \frac{1}{2} < \frac{a}{b} < 2 \equiv \beta, \\ 2 < \frac{a}{b} \equiv \gamma. \end{cases}$$

This kind of solution can be generalised to any number of equal lengths of cells in a line of cells. For example, for a line of six equal parts the instructions would be:

$$\begin{cases} \frac{a}{b} < \frac{1}{5} \equiv \alpha, \\ \frac{1}{5} < \frac{a}{b} < \frac{1}{2} \equiv \beta, \\ \frac{1}{2} < \frac{a}{b} < 1 \equiv \gamma, \\ 1 < \frac{a}{b} < 2 \equiv \delta, \\ 2 < \frac{a}{b} < 5 \equiv \varepsilon, \\ 5 < \frac{a}{b} \equiv \zeta. \end{cases}$$

It can also be generalised to unequal lengths — as would occur in the example just given if fractions and whole numbers different from those given were substituted at appropriate points in the instructions.

It is clear that this will work if the line of cells is interfered with when it is complete as well as during development (if we assume that counting continues to take place in the complete system). It is therefore a model of regeneration as well as regulation.

Using the present convention it is possible to model the regulation and regeneration not only of phenotypic differentiation, but also of spatial differentiation. For example, in the net shown in Fig. 2, if any number of main line cells are removed, taking with them the side-branch or not, the system will regenerate and produce the same net again. If the removal occurs during development, the same result is achieved, but now one would refer to it as regulation. (This helps to bring out the rather arbitrary distinction between regulation and regeneration.) An exception to this is if the one or two leftmost cells are removed; in this case the branch will not dissolve and reappear in the new correct position, and hence the final pattern will to this extent be incorrect. Also, if the side-branch itself is removed, it will not be regenerated; however, if the second instruction to produce the net in Fig. 2 had been "$(a = 3).(b = 4)$" (which also works) instead of "$(a = 3).(b = 1)$", the side-branch would be regenerated. It is clear that the regulation of spatial differentiation is more difficult than phenotypic differentiation and, interestingly, this is quite consistent with what is known of the capabilities of biological systems.

A further point which the reader may have noticed: if any single cell is removed from any of these nets it will turn itself into a complete network again. If there was an instruction that specified that under certain conditions a cell in a developing net would detach itself, then the net would not only be self-constructing but also self-reproducing. Instructions for other nets using this general convention have been described by M. J. Apter [5].

Discussion

The approach described in the previous sections is in at least two ways an advance over the writer's models described elsewhere using the Turing machine convention, and his network models. Firstly, communication between cells can here have both qualitative and quantitative features, and both features may be involved in determining the behaviour of a cell. This would appear to be more realistic from the point of view of biological simulation. Secondly, self-reproduction involves here the production of two identical cells in place of one. In the Turing machine and network conventions, when a cell reproduced, one new cell was reproduced and the original cell remained in existence. Although the new cell was identical with the original in terms of its instructions, the original cell had the possibility of being in a different state from the new cell. In the present convention, in contrast, both the new cells on reproduction are in an identical state as well as having identical instructions. This, too, would appear to be more realistic from the point of view of the simulation of biological systems.

Does the idea of counting on which these models are based have any validity in biological terms? There are several points to note here. One is that it has been demonstrated that such behaviour could be displayed by cells containing genetic units of the kind postulated by J. Monod and

F. Jacob [16] (see [4], chapter 7). Another is that it is manifestly the case that many organisms must count if they are to develop correctly. For example, most men develop five fingers on each hand. J. M. Smith [19] has discussed this phenomenon interestingly from the point of view of theoretical biology. It is therefore not impossible that counting is used in the course of other developmental processes the end-products of which do not at first sight require counting. It should also be added that even if the cell does not count digitally, the development of spatial patterns may depend on processes which could have the same effect, such as the continuous amplification or diminution of substances across the organism.

A further advantage of the present approach is that it combines the modelling of spatial and phenotypic differentiation in the one model, using the same convention, and that it is possible to simulate regeneration and regulation in terms of it as well as growth and differentiation. Clearly, however, it needs to be developed further. In particular, methods need to be developed for producing nets with convergence — that is, in graph theory terms, to produce nets which contain cycles — and methods need to be developed to deal with areas of cells as well as lines of cells. Tessellation models may have an advantage as far as the production of areas of cells is concerned — and the convention used in this paper could be modified without too much trouble to refer to tessellation structures. A disadvantage of tessellation models, however, is that they are limited in terms of pattern; for example, it is impossible for any one cell to be directly connected with more than eight other cells in tessellation space, and these cells have to be its immediate neighbours within this space. With converging nets such limitations could prove to be highly restrictive.

At the beginning of the paper it was pointed out that development involved a single cell turning itself into a highly complex adult. Such a process must, it seems, require an increase in complexity during development. The most fundamental problem of development is to understand how a system can make itself more complex, and how it can do it to the degree that one supposes is involved in higher organisms. One difficulty in dealing with this problem is that we need a satisfactory measure for complexity. V. Aladyev [3] has suggested one measure for the complexity of tree structures, but ideally what is required is a method which will allow us to measure the complexity of instructions, as well as the patterns which result from them, in the same way, so that it will be possible to compare the two and decide whether the resulting pattern is more or less complex than the instructions. However, even using the concept of complexity in an intuitive way, it could be argued that quite complex instructions have been required in the writer's models described in this paper to produce rather modest results, and that therefore these models are unsatisfactory in this respect. Such an argument would be a little unfair in that large networks of a given pattern can be produced with the same instructions as small networks, by simply substituting larger numbers than has been done in the examples here at the appropriate points in the formulae. In this respect these models are similar to Aladyev's, and an improvement over some of the writer's earlier models. However, increasing complexity presumably involves more than increasing size. It is clear, therefore, that the present models constitute only a first step in attempting to solve the problem of designing self-complexing systems — and this is a problem which is as challenging as any problem of a cybernetic nature could possibly be.

One difficulty in dealing with this problem of self-complexing faces all paper-and-pencil models. It is related to a problem dicussed by R. Rosen [20]. In the living system, many developmental events may not need explicit representation in genetic terms because advantage is taken of the fact that some changes will necessarily have certain physical and chemical effects. To give a simple example: if one cell in a ring of cells changes in size, this would result in other cells in the ring having to change their shapes or orientations in order to adjust to it. Only the original change would have to be represented genetically, all the subsequent changes being governed by the mechanics of the situation. In contrast, in paper-and-pencil models all effects may have to be specified explicitly in the instructions, and so the instructions in such models may become more complex than they would otherwise have to be. Tessellation models, like those of V. Aladyev [3], are possibly at an advantage here in that geometric effects may be produced by certain instructions without being specified as such. However, it may well be the case that sooner or later we shall have to turn back to hardware modelling if we are to continue to make progress in understanding and simulating development.

V. Aladyev has said *"... at the present stage of preliminary and general research on the problem of development, it is desirable to have as rich a variety of ideas and models as possible, rather than one, however good it may be"* ([3] p. 240). The present writer is in agreement with this, and it is in this spirit that he wishes to add the models described in this paper to the now growing repertoire of models of biological development.

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FORMAALNE BIOLOOGILISE ARENGU MUDEL

Artiklis esitatakse uus lähenemisviis bioloogilise arengu teoreetiliste mudelite ülesehitusele ja sellest lähtudes vaadeldakse mõningaid mudelite näiteid. Uus lähenemisviis baseerub sellel, et rakkude instruktsioonide kirjeldamiseks kasutatakse arvutusprotsessi ja propositsionaalset arvutust. Artikli lõpus arutletakse mõningaid bioloogilise arenguga seotud perspektiivseid probleeme.

М. АПТЕР

ФОРМАЛЬНАЯ МОДЕЛЬ БИОЛОГИЧЕСКОГО РАЗВИТИЯ

В настоящей статье предлагается новый подход к построению теоретических моделей развития и с этой точки зрения рассматриваются некоторые примеры моделей. Этот подход базируется на использовании процесса счета и пропозиционального исчисления в описании клеточных инструкций. Статья заканчивается обсуждением некоторых перспективных проблем, связанных с процессом биологического развития.