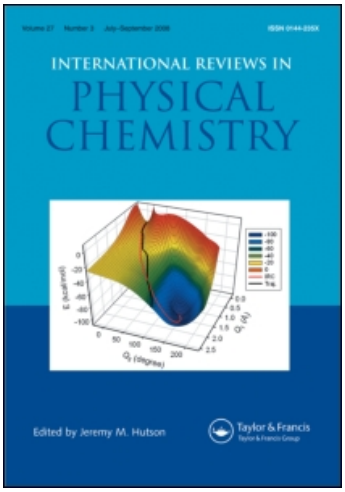

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The chemistry of materials for artificial Darwinian systems

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The chemistry of materials for artificial Darwinian systems

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The best materials for artificial systems able to evolve under natural selection are unlikely to be the same as for natural organisms. This is so particularly for genetic materials, where the overriding need for high fidelity of replication points to crystal growth processes as providing the key part of the mechanism rather than organic polymerizations. The genetic information would then have to be in the form of an aperiodic structure based on some relatively simple crystal defect capable of an immense number of permutations. Here I discuss particularly polytypism and related intergrowth phenomena, using a number of examples to illustrate suitable and unsuitable features.

1. Introduction

Natural selection as engineer

It has been a recurring idea that a living thing is a kind of machine, built from elaborately co-operating components and subcomponents. Descartes (1646) likened an animal to a clock. Coleridge (*c.* 1820), Paley (1828), Ruskin (1860), Haldane (1929), Sherrington (1940), Polanyi (1968), Monod (1972) and Dawkins (1986) have all in one way or another seen it as a distinctive feature, if not indeed the defining feature, of living things that they have the appearance of having been designed. They are 'objects endowed with a purpose or project' (Monod); 'systems whose parts co-operate' (Haldane)—and so on.

Like any complex machine an organism conforms to the laws of physics and chemistry, but it can hardly be said to be *explained* by them. As the theologian Paley (1828) put it, a watch implies a watchmaker. Dawkins (1986) agrees, sharing Paley's sense of wonder at the organized complexity of living things. But Dawkins points to a 'watchmaker' discovered by Darwin and Wallace more than a hundred years ago—evolution through natural selection.

To many physical scientists, even now, natural selection seems too simple an idea to account for so much. Certainly there *is* more to evolution. Other ideas are needed. But it seems that it is specifically the element of natural selection in the process of evolution which accounts for the machine-like properties of its products (Dawkins 1982, 1986). The new wonder is in the power of this seemingly simple process. What stops it from being more general? Why does it seem to be so narrowly confined to systems based on such a limited class of (organic) materials? Need it be so confined?

Organisms of the kind that we find on the Earth today can be seen to be special systems in two ways which I will distinguish as special-1 and special-2. They are special-1 because they are *subject* to evolution through natural selection (the definition, here, of 'Darwinian systems'). They are special-2 because they are *products* of such evolutionary processes (operating over some billions of years). Note that the 'purposeful' or 'machine-like' characteristics of organisms appear to be explicitly special-2 features. It would seem too that the narrowness of the material basis of life now is also to be seen as

special-2, as a product of evolution (Pirie 1959). And a case can be made that the first Darwinian systems in our ancestry (necessarily only special-1) would have been formed from altogether different materials from organisms now—if only because the design constraints on such initial systems would have been different from later constraints (Cairns-Smith 1975, 1982).

In any case there is nothing in the logic of natural selection to demand a particular material basis. In relation to our present concern, it is not by any means obvious that materials appropriate to natural Darwinian systems should be particularly appropriate also for Darwinian systems that we would seek to contrive in the laboratory. Certainly it is true in general that human engineering systems use different materials from their natural counterparts. Again this is because design constraints are different—there are many reasons why aeroplanes do not have feathers. There are similar reasons to think that the most easily contrived and effective artificial Darwinian systems will not be made of nucleic acids, proteins, etc. either.

2. The nature of Darwinian systems

2.1. *The significance of reproduction*

That organisms reproduce has an immediate significance: it explains the continued prevalence of special-2 objects which are bound to be more or less fragile—complex machines must break down sooner or later. But if there are many copies of a machine in existence, and if these keep on making more copies then the design may nevertheless survive in spite of some bad copies, since these eliminate themselves. Hence it is that reproduction (plus 'natural rejection') allows forms as such, rather than substances as such, to be the long term survivors. This way of surviving can be extraordinarily effective. Schrödinger (1944) commented on the persistence over many centuries of a form to be seen in family portraits of the Habsburg dynasty—the 'Habsburg lip'. But of course all the essential features of organisms are heritable and persist like this. The forms of some proteins, for example cytochrome c (Fitch and Margoliash 1967), have persisted only somewhat modified over enormous time scales—perhaps billions of years. Mountains, continents and oceans are labile in comparison.

This kind of efficient form-survival is so characteristic of life *because* it is essential for evolution through natural selection. But it is still not enough for a Darwinian evolution to take place. The most critical additional requirement is the inheritance of variations. Some arbitrary modifications to reproducing forms must be reproduced also, and there must be a rich field of such variations to explore. Natural selection then consists of the preferential survival of beneficially modified forms (that is to say forms which tend to leave more progeny in the long term). Again it does not matter that many individuals fail—and most arbitrary modifications, particularly if large, are likely to be unsuccessful. As we shall see, what matters is that there should not be too many inheritable modifications taking place, so that the original design is not degraded, and that sometimes there happen to be beneficial variants to it.

2.2. *Exploring possibility space*

Wright (1932) discussed the operation of natural selection in terms of diagrams in which differences in genetic constitution were plotted against biological fitness—that is to say the tendency to leave offspring. Since fitness is precisely what natural selection tends to optimize, one can discuss the operation of natural selection in terms of a

tendency to climb local 'adaptive peaks' ('fitness peaks'). Similar multidimensional diagrams (described as 'landscapes' because of their vastness and complexity) have often been used in discussions of evolution (for example in Waddington (1957), Cairns-Smith (1971, 1982, 1986), Dobzhansky *et al.* (1977) and Lewontin (1978)). They are the evolutionary biologist's equivalent to potential energy diagrams. (In the latter structural variables are plotted against a kind of *un*fitness to persist—potential energy.)

We can extend Wright's idea to cover arrangements of atoms rather than genes. As a more or less specific class of arrangements of atoms, a whole organism can also in principle be represented in an N-dimensional space, with an $(N+1)$th dimension used to represent its fitness. We have then a still more complex hypersurface undulating in the $(N+1)$th dimension, and a tendency for groups of reproducing organisms to climb local fitness peaks. This comes about from the following considerations.

Because of random variations appearing in offspring, a group of related organisms will be represented as a 'swarm', occupying some localized region, with the swarm always tending to diffuse over surrounding territory. Natural selection (plus the bumpiness of the landscape) oppose this diffusion: parts of the swarm that happen to lie on higher ground will become more dense through preferential survival/reproduction here, while less fit types, represented in lower regions, will be more or less rapidly thinned out and eliminated as generation succeeds generation. The overall effect, then, is for the swarm to move to higher ground arriving at and around some local adaptive (fitness) peak. This is the situation for most populations most of the time: they are more or less 'in equilibrium' with their environments.

An attractive feature of this kind of landscape model is that it gives an insight into how new species can arise. The form of the hypersurface is determined by the environment and is thus continually changing both in time and space—with changes in climate, geographical location, predators etc. The hypersurface is mobile and changeable allowing, sometimes, movements of swarms, even relatively rapid movements, to adjacent peaks (Waddington 1957).

Dobzhansky *et al.* (1977) remark that 'The question of why there should be many species [is] because there are many adaptive peaks'. Physical chemists may similarly discuss, say, the existence of different molecules in terms of potential energy wells (and catalysis in terms of changes in the forms of potential energy surfaces). Since it is the purpose of this article to see how relatively simple physico-chemical systems might be able to begin to explore a fitness landscape, I will pursue a little further the connection between physico-chemical organization, which can be said to be brought about (in part) by a tendency to fall into potential energy wells, and biological organization which results (in part) from a tendency to climb adaptive peaks.

An organism at an instant is a particular arrangement of atoms and would be represented as a single point in some suitable multi-dimensional landscape. Over time an individual organism will occupy a 'patch' of very many points. For example consider just the water in a bacterium such as *E. coli*. We can estimate the number of 'arrangements' for these molecules (more strictly microstates) from the entropy of the *ca.* 10^{-13} moles of water that such a bacterium contains—about 7×10^{-12} J K^{-1} under ordinary conditions. From Boltzmann's relationship, $S = k \ln \omega$, this corresponds to about $10^{2 \times 10^{11}}$ microstates and is still very much an underestimate of 'the number of ways of being an *E. coli*' since of course there is the other 30% or so of material—other molecules such as proteins, with numerous variable positions, conformations etc., as well as allowable variations in the concentrations, even in the types of molecules that might be present in a healthy *E. coli*.

Looked at this way *E. coli*'s 'patch' in configuration space is unimaginably big; even so such patches corresponding to viable organisms are, from another point of view, unimaginably tiny—in relation, that is, to the size of the configuration space itself. It is relatively tiny in the first place simply because *E. coli* is a condensed physico-chemical system. For example the number of microstates for 10^{-13} moles of water vapour is about $10^{4\times10^{11}}$ *times* that for the liquid. This is a measure of what would seem to be the improbability of the liquid state for this many water molecules if you did not know about intermolecular forces. In a similar vein *most* of the 'improbability' of the proteins, lipids and other components of cells can be said to be 'physico-chemical' in this sense.

Similar remarks could of course be applied to any speck of condensed matter: the point about an organism is that it occupies an *even smaller* patch in configuration space than can be accounted for in terms of physico-chemical forces: it has another 'improbability' which is the specific product of evolution through natural selection. The 'machine-like' arrangement of the molecular components in a cell requires extra specification, and this is provided largely by the specific sequencing of amino acids in the proteins which form the enzymes, membrane gates and so on. Since in the end *all* this extra specification resides in the DNA molecules whose nucleotide sequencing controls, among other things, the sequences of amino acids in the protein, we have then a rough measure of the 'biological improbability' of an organism such as *E. coli*. This is the 'improbability' of the particular DNA sequence found in a particular *E. coli*. There are four kinds of base pairs in DNA so a sequence of $4{\cdot}5\times10^{6}$ of them is one of $10^{2{\cdot}7\times10^{6}}$ possibilities. This may seem small in comparison to the 'physicochemical improbability' but it is still, of course, an immense number. Admittedly it is very much a maximum estimate: there is clearly some *set* of DNA sequences corresponding to viable versions of *E. coli*. Nevertheless it is clear that an *E. coli* is a special-2 object belonging to such a relatively minute subset of possibilities that the chances of hitting on it 'in one throw' as it were, are too small to contemplate, even given the required collection of atoms and the operation of physico-chemical laws.

Many examples have been used to illustrate the 'improbability' of organisms—sometimes to argue for the need for miracles or their equivalent. My labouring this point somewhat further here is, on the contrary, to illustrate the power of natural selection, and by implication the importance of finding artificial systems which are subject to natural selection even if only at first in a modest way.

How long would it take that monkey striking at random one key a second on a 30-key typewriter to come up with the word 'biochemistry'? It can easily be shown that the expected waiting time exceeds the age of the Earth. In this example we have supposed that there is no intermediate selection along the way. But suppose somehow the word can be built up in stages. Suppose that when 'bio' is typed this is recognized as a success so that it is selected and held on to. The monkey then proceeds with random experiments till it gets the next syllable 'chem', then 'is', and then finally 'try'. The shortening of expected waiting times is dramatic—to about 10 days in this case.

This second approach corresponds to what Dawkins (1986) calls 'cumulative selection', as opposed to 'single step selection' which would be like the first case. It is a crucial distinction. Darwinian evolution has to do exclusively with cumulative selection, with stage-by-stage modifications to past successes. But past successes have to be 'remembered' if they are to be built upon. The ability to explore an adaptive landscape, and the possibility of thus discovering complex, optimized 'machine-like' modes of survival typical of special-2 ('living') systems defines the character of the kind of special-1 (Darwinian) systems which we seek. We can write into the specification of

such systems that they have to have some kind of long term 'memory' of past successes. Let us now consider the specification for special-1 systems in greater detail.

2.3. *The genetic theory of organisms*

The required mechanisms within special-1 systems can be stated more explicitly in terms of the conventional genetic theory of organisms expressed in a diagram (modified from Maynard Smith (1975)):

$$\begin{array}{cccccccc} & \mathrm{P} & & \mathrm{P} & & \mathrm{P}' & & \mathrm{P}' \\ & \uparrow & & \uparrow & & \uparrow & & \uparrow \\ \rightarrow & \mathrm{G} & \rightarrow & \mathrm{G} & \rightarrow & \mathrm{G}' & \rightarrow & \mathrm{G}' \rightarrow \end{array}$$

An organism consists of a genotype, say G, and a phenotype, say P. G is some kind of information store (a set of genes) consisting of stable specific atomic arrangements which have the property both of being replicable and also of controlling the production of a characteristic P. In all free living organisms that we know of today G consists of DNA base sequences, while P is the rest of the organism built and maintained under the control of this information, via the control of protein synthesis and so on. According to Von Neumann (Taub 1963) *any* self-reproducing machine has to have this general form of construction, although of course particular molecular types, such as DNA and protein, are not in this general specification.

To be a Darwinian, i.e. special-1, system there is the further requirement that G must be subject to mutations, that is to say occasional random modifications, say to G′, which are inheritable and which may give rise to modified phenotypes, say P′. While the succession of genotypes provides the essential long term memory, it is on individual phenotypes that selection operates in the first place, and on which the long term survival of genetic information also depends.

Thus the genetic theory of organisms explains the way in which organisms are made in terms of the requirements for evolution through natural selection, and clarifies the distinction between heredity, which is the transmission of genetic information (through *replication* of genotypes), and development, which is the production of individual phenotypes (the *expression* of genotypes).

2.4. *Muller's minimal organism*

The idea that the simplest possible evolvable entity would consist of more or less pure genetic material (as we now call it) dates from the 'teens of this century (see Ravin (1977)). Troland (1914, 1917) had imagined the first forms of life on Earth as having consisted of 'enzymes' with the dual properties of 'autocatalysis', aiding the production of other 'enzymes' exactly like themselves (what we would call replication); and 'heterocatalysis', aiding the production of other materials unlike themselves.

Muller (1929) developed such ideas further, arguing that although the nature of the genetic 'autocatalysis' seemed (at that time) particularly hard to understand, nothing less would do than a 'gene' of some sort to start off the evolutionary process that led to life now on the Earth. Furthermore nothing much *more* could have been involved:

> For the more complicated we imagine any chance-supplied companion-structures... the more we run into the difficulty in trying to account for the lucky coincidence that the combined activity of the genes and of those necessary by-standing structures should have caused the reproduction, *not only* of the genes, but also of these other materials themselves. Similar considerations to those followed here also lead us to the view that probably the gene itself was not highly complicated in its essential structure, inasmuch as it had to be specifically autocatalytic in all its parts.

Muller then attempted to specify the nature of the genetic material in general terms. It had to be a material 'capable of causing the reproduction of its own specific composition, but which can nevertheless change repeatedly—"mutate"—and yet retain the property of reproducing itself in its various new forms'. He declined to take up the earlier somewhat more specific suggestion of Troland (1917) that there might be an analogy between gene replication and 'ordinary crystallization'. He gave two reasons: (i) because 'it does not go far enough'; and (ii) because 'if it did hold as pictured we should expect more evidence of gene-like action in "inorganic" material'.

Despite Muller's remarks, 'crystallization' theories of genetic replication have been another recurring theme. For example Haldane (1929), in speculating about how genes might replicate in cell nuclei, remarks that 'A crystal grows if placed in a supersaturated solution, but the precise arrangement of the molecules out of several possible arrangements depends on the arrangement found in the original crystal with which the solution is "seeded" '. Then Schrödinger (1944) likened a gene to an 'aperiodic crystal'; Hinshelwood (1951) spoke of a gene as 'capable of being copied in growth by the laying down of fresh molecules in conformity with the same design'. Even Watson and Crick (1953) originally envisaged the replication of DNA as taking place through a 'crystallization' of nucleotide units on separated DNA strands.

It has turned out that DNA replication is hardly at all like a crystallization process: the units are incorporated and joined up more or less one at a time, against an energy gradient, and with the aid of a whole team of protein molecules required at various stages of what can now be seen as an essentially complex process. In the bacterium *E. coli* there are at least 23 different kinds of polypeptide chains in all of this apparatus which has a total molecular weight in excess of 2 million daltons (Watson *et al.* 1987). It is clear that our present genetic material is part of a highly evolved *system*: DNA is hardly more a 'self replicating' entity than, say, a page of text which can be replicated in the presence of a suitably set up Xerox machine. Systems in which replication depends on machinery can no doubt be very efficient, but it is equally clear that something simpler with a more nearly 'self-replicating' genetic material would have been needed to start off the evolution of life on the Earth. Genetic materials suited to artificial systems are another matter again, but the existence of life on the Earth may perhaps be taken as an encouragement that there must exist genetic systems of an altogether simpler sort than our present DNA-based system. The first part of our task seems clear: to look for genetic materials which do not need a 'Xerox machine'.

3. Genetic materials for beginners

Using our DNA based system as an example we can see four general features that seem to be required for *any* genetic system:

(i) *aperiodicity* in the genetic material to provide it with the possibility of holding information—as in the aperiodicity of the base sequences in DNA molecules;
(ii) *stability* of the information—as is provided by the covalent bonds of DNA molecules;
(iii) *fidelity* in the copying of this information—which in DNA is partly provided by the well known base-pairing constraints, but depends also on complex replication and error correcting machinery;
(iv) *expression* of the genetic information, as in the control which DNA base sequences exert on protein synthesis etc.—again dependent on complex machinery.

Schrödinger's (1944) 'aperiodic crystal' as a description of our present genetic material aptly expresses the kind of situation required to satisfy (i): a wholly regular structure, such as a text book crystal structure or a regular homopolymer, would be no good. There would have to be irregular features, aperiodic patterns—as in a tapestry rather than a wallpaper, as Schrödinger put it. Consideration (ii) was uppermost in Schrödinger's discussions, following Timoféeff-Ressovsky *et al.* (1935). By considering the implied small size of genes, known to be located on chromosomes, it was clear that covalent bonds would be needed to maintain genetic structure against thermal destruction at ordinary temperatures.

Perutz (1987), in a distinctly critical reappraisal of Schrödinger's contribution to biology, wonders why he paid so much attention to the (static) stability of genetic information when the *real* problem was (iii) how to maintain information through repeated replication processes. Aperiodic patterns have to be accurately reproduced in each generation. (Indeed this *is* the real problem: we will return to it shortly.)

Consideration (iv) may seem to be the most difficult of all, if we are thinking about our present genetic system. This system needs exceedingly sophisticated machinery to make sense of the DNA information through protein synthesis. (A set of particularly competent enzymes are needed to prime appropriate adaptor molecules with appropriate amino acids: then ribosomes, each containing some 170 000 atoms, are the actual assembling machines which are able to read RNA 'off-prints', from different parts of the DNA, which specify different proteins...) Yet, in line with Muller's arguments about the origin of Darwinian systems on Earth, such developmental subprocesses can in principle be minimal. Genetic information has to be expressed in the sense that it must have some effect which influences its own survival/replication; but it is not in principle necessary that any other material than the genetic material itself should be involved. This point has been well made within the context of our present biochemical materials.

3.1. *The RNA option*

Like DNA, RNA is a replicable molecule—many viruses use RNA as their sole genetic material. Single stranded RNA is also capable of folding into complex forms, rather as protein molecules do, creating thereby specific pieces of machinery, such as the critical adaptor molecules required for protein synthesis. RNA can thus have both genetic and phenotypic functions. There were several early speculations on the possibility that our present genetic system started with RNA performing a double genotype/phenotype role—with especially an early catalytic role in mind (Woese 1967, Crick 1968, Orgel 1968, Sulston and Orgel 1971, Cairns-Smith 1971).

The idea that the nucleotide monomer units for RNA (or DNA) would have been present on the primitive Earth is built into many formal schemes for the origin of the first evolving systems (see, for example, Eigen (1971), Kuhn (1976), Eigen *et al.* (1981), Gilbert (1986) and Watson *et al.* (1987)). But there has been an increasing scepticism that organic molecules would have been particularly abundant in primordial oceans (Hull 1960, Hulett 1969, Rein *et al.* 1971, Dose 1975, Cairns-Smith 1975 and Nissenbaum 1976), and it is particularly hard to see how nucleotides could ever have been significant geochemical products (Cairns-Smith 1982, Shapiro 1986 and Joyce *et al.* 1987).

The question of how evolution started on the Earth has to be distinguished, it seems, from the question of how our present genetic system arose. I have suggested there was some 'low tech' genetic system which was later taken over (Cairns-Smith

1982). Our interest here in formal schemes of how RNA molecules might evolve will be mainly for the light they throw on general requirements for evolving systems.

Evolution experiments

It was shown experimentally by Spiegelman (1970) that RNA molecules can evolve *in vitro*. This was achieved using the RNA replicating enzyme of the bacterial virus Qβ. The enzyme acts on the RNA of the virus in the presence of an appropriate solution including activated nucleotide monomer units. But it can also act on other modified forms of the viral RNA. In experiments in which RNA molecules were replicated under increasingly difficult circumstances the molecules could sometimes 'learn' to overcome the difficulties. For example they could be modified through natural selection to replicate efficiently under conditions which had previously been difficult, for example in the presence of relatively high concentrations of inhibitor molecules (Staffhill *et al.* 1970). The main lesson from these experiments was to show that 'naked genes' can indeed evolve. Selection can operate on *properties* of the genetic material itself provided only that these properties depend on replicable, mutable information. In the evolution experiments with inhibitors any nucleotide sequences which bound the inhibitor molecules less strongly would tend to replicate faster and become increasingly prevalent in successive generations. The experimenter did not need to know what sequence changes would work like this. The molecules—or rather Nature's engineer natural selection—was able to discover them without intelligent intervention. These forms of molecular evolution have been widely discussed, for example by Spiegelman *et al.* (1975), Orgel (1979), Eigen (1983) and Shapiro (1986).

The need for an enzyme, extracted from a biological source, means that these systems fall short of being wholly artificial. Attempts to replicate RNA without enzymes have not so far been very successful (Orgel 1986). Although they have provided important insights into the chemistry of RNA, one has to say that the main conclusion to be drawn is that RNA itself is probably not a satisfactory candidate as a genetic material for a wholly artificial Darwinian system.

Figure 1 illustrates the general idea behind these experiments. Activated nucleotide monomers bind to a pre-existing polynucleotide strand through Watson–Crick base pairing and polymerize *in situ* to create a complementary strand which then separates so that it and the original strand can go on to make indefinite numbers of copies. It is clear that *if* such a process could be achieved it would be possible to perform evolution experiments along the lines of those just discussed. What *has* been achieved is some degree of template directed polycondensation. For example a poly(C) template acts to join together activated G units according to the formal scheme. Even here, though, not all the links in the new chain are between 5′phosphate and 3′hydroxyl—the 2′hydroxyl is more reactive so that 5′–2′ links tend to predominate. This difficulty can be largely overcome by using specially designed activated nucleotides.

But there are other difficulties. The complementary process—forming oligomers of C on poly(G)—does not work because the monomer units do not align properly. Experiments with the C-rich oligonucleotide CCGCC as template provided good evidence for template-directed polycondensation, there being a strong bias in favour of the complementary GGCGG, rather than other pentamers, in the product (Inoue *et al.* 1984), with an overall yield of 17% in relation to the added template. Nevertheless other oligomers of various lengths were also obtained, and the G-rich product was not in itself capable of being a template.

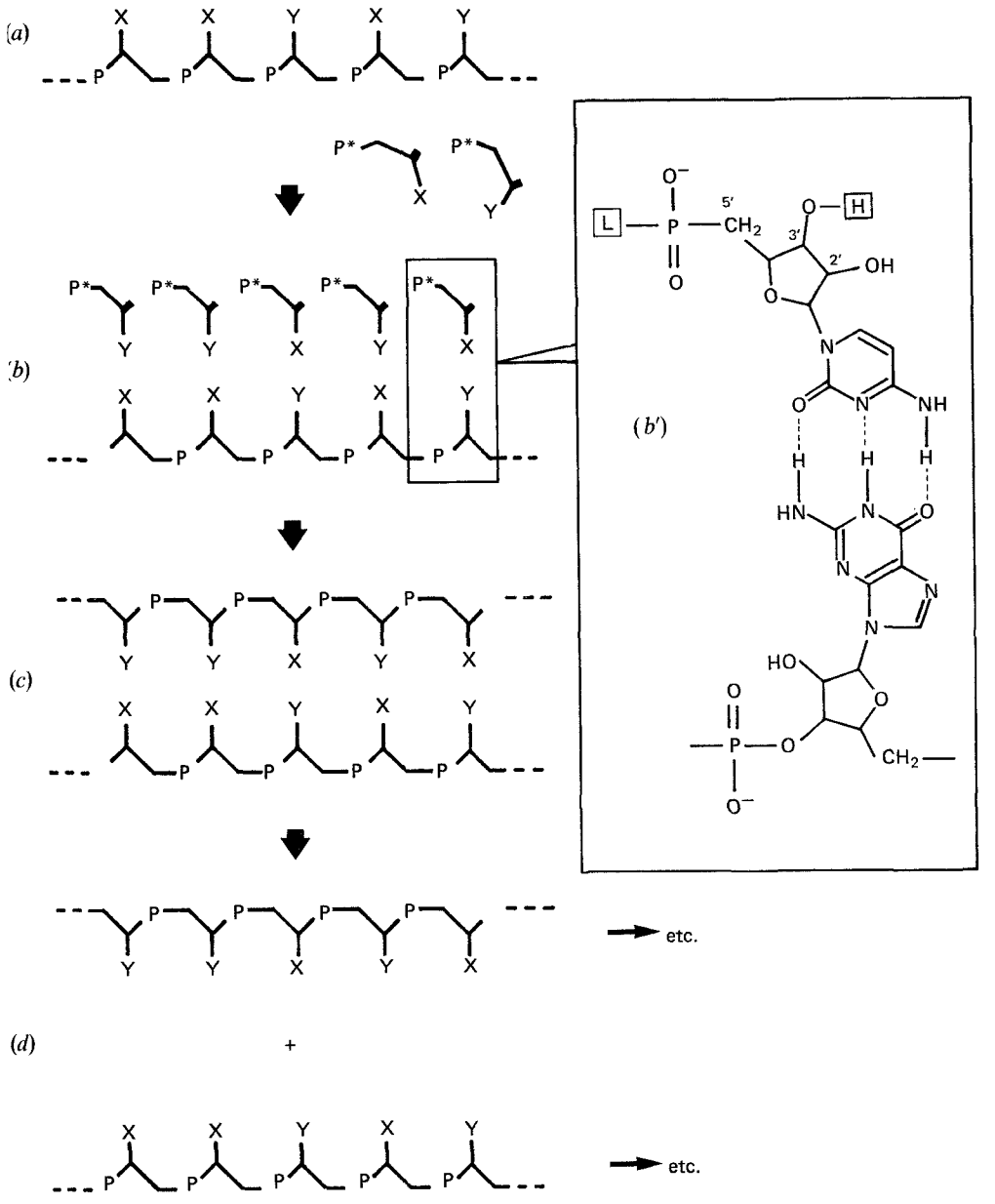

Figure 1. A plan for replicating a copolymer sequence without enzymes. (*a*) An initial (here binary) polynucleotide strand holds 'information' as an irregular sequence. (*b*) Activated nucleotide units locate on this strand in a complementary fashion. (*b′*) Close-up view for the case of an RNA molecule with X = cytosine and Y = guanine. L is a suitable leaving group activating the nucleotide (here cytidylic acid). The boxed hydrogen is also removed in the bond-forming reactions which have taken place in (*c*). (*d*) The complementary strands have now separated and are ready for another cycle of operations which will then make a copy of the original strand and its complement.

Experiments with random CU copolymers as templates (Joyce *et al.* 1984) showed that sequences were not being accurately copied (possibly in part because of slippage along the template, or loops being formed in the daughter strands), while similar experiments with polyCG templates (Joyce and Orgel 1986) ran into difficulties with 'self-structures'—the tendency for stretches of the single stranded template RNA molecules to pair up with other parts of the same or other molecules....

The overall impression of schemes along the lines of figure 1 is that they are formally sound but impracticable—rather as Watson and Crick's similar original scheme for DNA replication in cells was formally sound, but turned out not to be the way that cells do it: they *need* a 'Xerox machine'. One suspects from these careful and detailed experimental investigations carried out over the last two decades that a 'Xerox machine' of *some* sort is also an essential part of the package for a genetic system based on RNA replication.

The idea of using RNA-like molecules with modified backbones offers a new range of possible systems (Joyce *et al.* 1987). Perhaps among such modified RNAs a more nearly 'self-replicating' molecule will be discovered, to shed light on the origins of our molecular biology—and perhaps also to provide new materials for artificial Darwinian systems.

Another possibility for some future RNA based system comes from the startling discovery that not only might RNA molecules have acted as catalysts in the past, but some RNA molecules *actually do so* in contemporary organisms. They can act as enzymes for breaking and re-joining other RNA molecules (Kruger *et al.* 1982, Guerrier-Takeda *et al.* 1983, Bass and Cech 1984). This has suggested the idea that an RNA replicating enzyme might be possible, and hence a replicating system made only of RNA molecules (Cech 1986, Gilbert 1986, Darnell and Doolittle 1986, Westheimer 1986). But as I will try to indicate now, when it comes to the design of 'low tech' artificial systems altogether different materials—crystalline materials—are more promising.

3.2. *Crystal genes*

Crystals have far more interesting structures than Muller could have imagined in 1929. Apart from the newer 'non-classical' crystallography (Mackay 1986 a, b), there are many kinds of small scale 'defects', both physical and chemical, being revealed by high resolution electron microscopy (HREM) (see, for example, Hutchinson *et al.* (1977) and Rao and Thomas (1985)). Far from being a strange conjecture the aperiodic crystal is commonplace: many crystals can in principle hold enormous amounts of information in the form of some more or less aperiodic defect structure. Furthermore it is clear that at least in some cases defect structures are propagated through the processes of crystal growth.

Figure 2 shows how information in the form of one-dimensional or two-dimensional defect structures might be replicated. There is nothing very difficult about the individual processes required. Crystals can have defects arrayed in one or two dimensions, they may grow preferentially on certain faces, and be liable to cleave along certain planes. But all this has to be appropriately combined. Above all inappropriate processes have to be kept at bay. Most large crystals, for example, are full of gross three-dimensional defects of the sort to be avoided. Big, more or less rapidly grown crystals such as copper sulphate will have formed in a somewhat haphazard way with, for example, branching dendrites criss-crossing and overlapping, with bits of crystal breaking off, with other bits joining together, annealing, reforming... The final nice solid-looking crystal is likely to consist of many somewhat misaligned regions with,

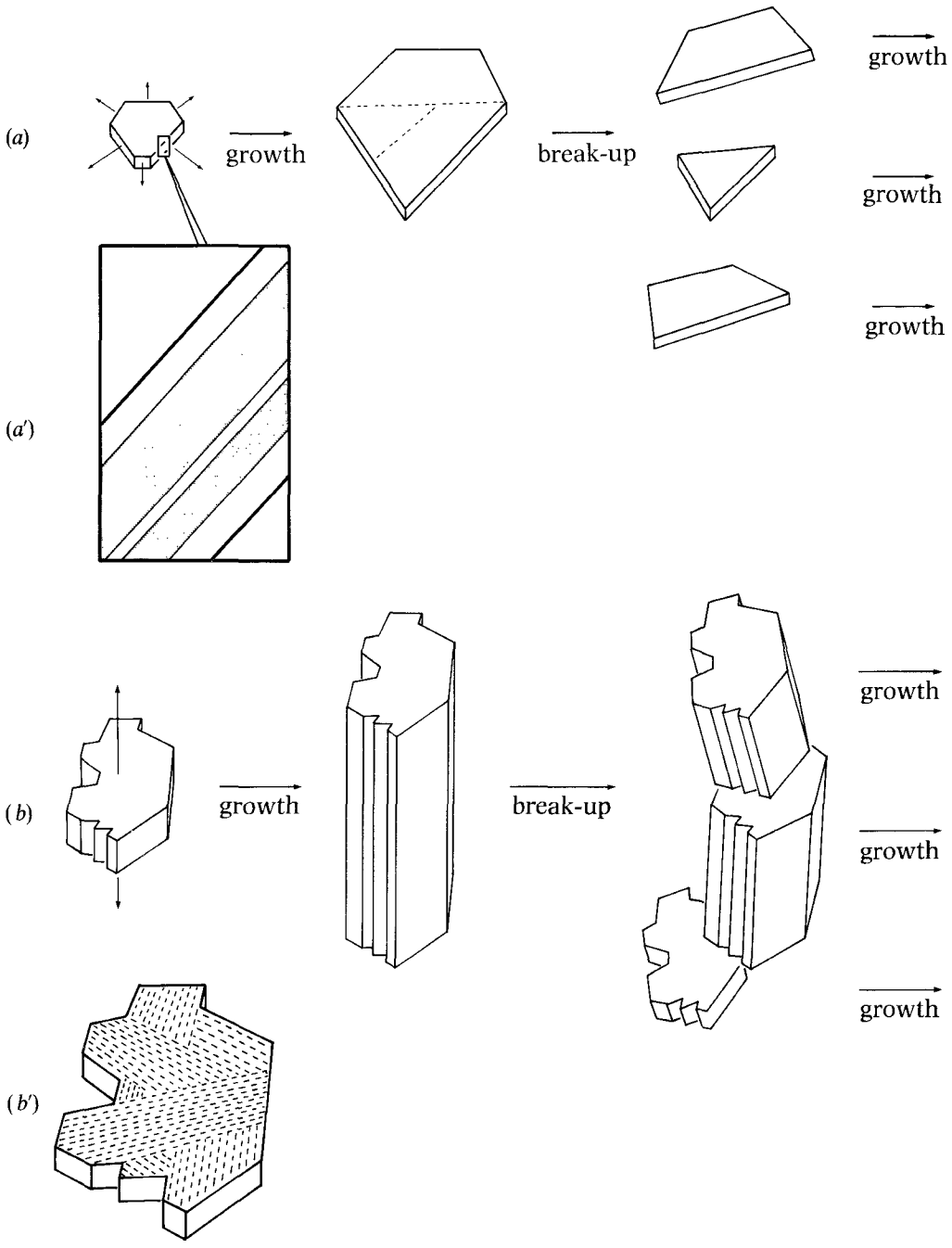

Figure 2. Alternative plans for replicating defect structures in crystals. (*a*) In a one-dimensional 'crystal gene' an aperiodic stacking sequence (*a'*) constitutes the 'information' which is amplified through exclusive sideways growth of the stack. The replication cycle is completed through cleavage in planes which cross the stacking direction. (*b*) In a two dimensional 'crystal gene' a planar aperiodicity, such as a domain pattern, (*b'*) is repeated through growth which takes place exclusively in the third dimension. The replication cycle is completed through cleavage within the plane in which the 'information' is held.

often, inclusions of solvent and so on. It is generally a story of careless beginnings followed by patch-up. Crystal gene growth processes will have to be much better disciplined in the first place and although, as we shall be discussing, error correction mechanisms through local dissolving and reforming will be an essential part of this, large scale patch-up must be avoided. Indeed the kinds of materials and growth conditions which lead to big and beautiful crystals should perhaps be viewed with some suspicion. Not that crystal genes would have to be very big—for example a one-dimensional type (figure 2 (*a*)) only 5 μm thick could still hold the equivalent to a 200-long AB sequence as a 'bar code' pattern of broad and narrow stripes in a crystal of the sort shown in figure 3.

As with figure 1, figure 2 is a formalism which falls short of practical realization to the point at which evolution experiments would become feasible. I will be arguing that the formalism of figure 2 is nevertheless closer to the realities of chemistry. For all the larger scale vagaries of crystal growth processes, electron microscope studies in particular make it clear that on intermediate and smaller scales highly organized processes--and of the right sort—often take place during the growth of crystals.

Thinking again about those four general features required of a genetic system, it is already clear that *aperiodicity* is no particular problem for crystals. *Expression* of information we can leave until later, only noting at this stage that properties of crystalline materials are often more or less dependent on defect structures, and recalling that properties of a genetic material can themselves be forms of expression of genetic information in suitable circumstances.

3.2.1. *Stability of information*

A major point in favour of an organic-molecular genetic material like DNA or RNA is in the kinetic stability of the covalent bonds that hold organic molecules together. It is not so clear that information written in the form of defect structures can ever be so stable. Dislocations in metals, for example, are notoriously mobile even at ordinary

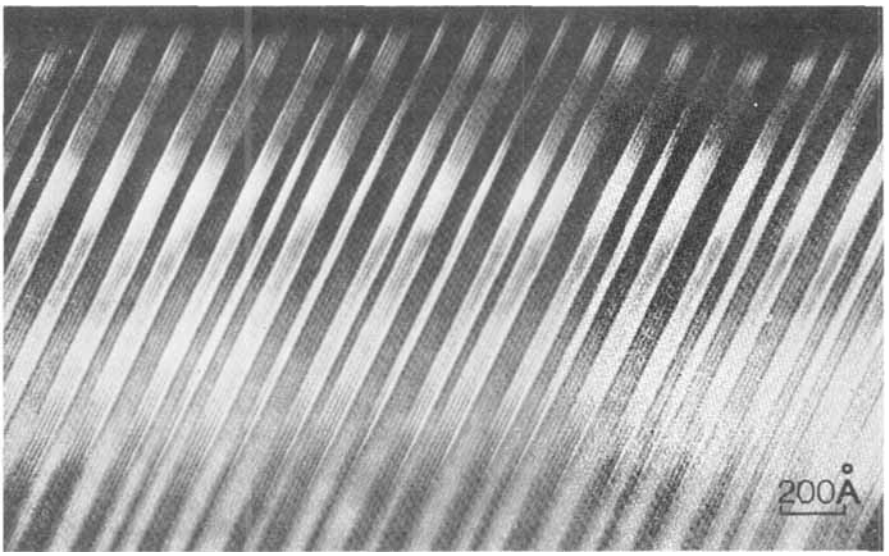

Figure 3. High resolution electron micrograph of an irregular complex stacking sequence in a barium ferrite (van Landuyt *et al.* 1974).

temperatures, and new dislocations, twinnings, and so on, are easily introduced through mechanical stresses. Malleable and 'soft' crystals generally, including all purely organic crystals, seem unpromising on this count. But there are many kinds of crystals which are largely or entirely held together through strong covalent (or partly covalent) bonds. The most prominent class here are *ceramics*: their crystals are typically hard, because of the strength of the bonding and brittle, indicating an absence of mobile defects.

3.2.2. *Fidelity of replication*

It is difficult to exaggerate the importance of fidelity of replication for any evolutionary process that is to proceed beyond a trivial level (Eigen 1971, Eigen and Schuster 1977, Eigen 1983 and Kirkwood *et al.* 1986). Inheritable, effectively random changes in the genetic information—mutations—have an analogous role to kinetic motion in chemical reactions. Mutations allow the evolutionary landscape to be explored, as kinetic motion allows the exploration of potential energy surfaces. But, like kinetic motion, mutations actually militate against high levels of organization being achieved. High mutation rates, like high temperatures, are destructive.

What might we mean by a 'high' mutation rate? Imagine a genetic copolymer with 100 units in it. This would need a fidelity of emplacement of new units during template reproduction of better than 99·9% if mistakes were not to accumulate disastrously over a few hundred copies of copies of copies... Indeed after 10 such 'generations' you would already expect one mistake if the accuracy was merely 99·9%. The situation gets worse with larger amounts of information: thus a 1000-long copolymer would be lucky to get through one replication unscathed. Yet a 99·9% yield would usually be regarded as very good indeed for an organic–synthetic reaction. Organisms cope with this, and indeed hold onto genetic information for billions of years, through two strategies. The first is to keep replication errors down. For bacteria the error rate is of the order of 10^{-10}, and for higher organisms is more like 10^{-12} per nucleotide unit inserted (Drake 1969). The tactics here are in the use of that highly evolved many-enzyme 'Xerox machine'. One part of that machine, the enzyme that adds nucleotide units during DNA replication, can at least hold and constrain the template to improve kinetic control. But this is not enough. With simple kinetic control of this sort—as for example with RNA viruses which have a much simpler 'Xerox machine'—the error rate is too high for genotypes with more than about 10^4 nucleotide units: no RNA viruses have more than this (Eigen and Shuster 1977, Eigen 1983). For bigger genotypes, elaborate error correction mechanisms have to be built in which are expensive both in energy and time (Kirkwood *et al.* 1986).

The second strategy is selection: in effect to overproduce copies and throw away the poor ones. This is what I referred to as 'natural rejection'. It is a means, often, of maintaining the status quo: genotypes which produce inferior phenotypes are less likely to survive as copies in subsequent generations.

These two strategies are not, however, simply alternative means to the same ends, as we can see by thinking about extreme cases. Think of the following copolymer sequence: AABAAA. One way of getting a whole beakerful of this sequence would be by perfect replication of an initial 'seed' sequence. Another way we might think of would be through a totally incompetent 'replication' followed by selection, with new sequences being produced in fact at random and those which happen to read AABAAA being selected. Clearly this second procedure is wasteful, but worse than that, such 'simple selection' (selection without replication) rapidly becomes impossible as the sequence

information increases. Even when the amount of information is not more than that in the word 'biochemistry', wrong sequences so outnumber correct ones that simple selection fails—at least for monkey typists. That molecules might work faster than that makes little difference to the general conclusion: there are far more different 200-long AB-sequences, for example, than there are atoms in the Earth. What simple selection can do in such circumstances would be to find very broad classes of sequences—for example A-rich sequences, or sequences of a certain general length, and so on—but there would be no scope for progress beyond that.

So it is only when the error rate is very modest, when not too many alternatives are being put up, that selection from these alternatives can contribute to the preservation of detailed genetic information over the long term. It can add a final touch, as it were, but accuracy of replication is the principal limiting factor on the long term potential for evolution through natural selection. This point is confirmed by the very low spontaneous mutation rates discovered in all organisms—particularly higher organisms which have more to lose. It is no exaggeration to say that the evolution of our DNA-based life-form beyond trivial levels has depended on the astonishing level of accuracy achieved in the replication of DNA molecules—astonishing, that is, because the process typically depends on a series of some billions of organic chemical reactions.

Now the whole point of designing artifical Darwinian systems would be to allow evolutionary processes to go beyond the sorts of information levels that can be arrived at 'in a single throw' by simple selection of chance events. Whichever way we look at it, high replicative accuracy is imperative—and it is here that ordinary organic chemical reactions appear to be so hopeless, and ordinary crystal growth processes so interesting.

3.2.3. *The error correction mechanisms of crystal growth*

It is worth noting an important difference between a crystal—even a covalent crystal—and an organic macromolecule. A typical organic macromolecule is held together by bonds which are not only strong but are (effectively) *irreversible under the conditions of formation.* Indeed, as in all the main biopolymers, the bonding in DNA might be said to be doubly irreversible: neither the formation of DNA by condensation of its nucleotide units, nor the reverse hydrolytic reaction, takes place spontaneously at a significant rate under normal conditions. The nucleotide units have to be activated—energy has to be expended to make the bonds in the first place—while the hydrolytic reactions, although thermodynamically favoured, are inhibited by high activation energy barriers.

By contrast the characteristic mode of formation of a crystal is a 'self assembly' of units. This requires that the units are held together by bonds which are *reversible under the conditions of formation.* In such a 'self assembly' the units can come and go repeatedly until they find an energetically favourable arrangement. This bonding reversibility is a major factor in allowing billions upon billions of units to be neatly located and arranged.

Another factor is closeness of the packing of units in crystals. The strongest of all the intermolecular forces are thus brought into play, namely the repulsive forces. A well formed crystal can have a strong selective preference for the units out of which it is made: there may be comparatively little room to accommodate mistakes without local or even quite extensive destabilization of the crystal. Mistakes thus tend to be self-correcting. For example for crystals growing slowly from a solution at low supersaturation the *net* rate of addition of units to the crystal will be far lower than the

total rate: building and dissolution go on together and are in near balance, so there is little chance of even slightly less stable packing arrangements persisting since, with them, the balance will tend to tip in favour of dissolution. Hence crystal growth processes have a built-in error correction mechanism, the accuracy of which can be tuned by adjusting a level of supersaturation (which must be kept fairly low in any case).

Steric effects are seldom as powerful in organic chemical reactions as they are in crystal growth processes. This would be particularly the case for the sort that we have to imagine as contributing to template replication of an organic copolymer (figure 1). In the growth of an organic polymer chain on another chain as template, there would tend to be fewer constraints than in the packing of units in a crystal to fill all three dimensions. However the even more serious problem is that mistakes cannot easily be put right if the bonding is irreversible. The polymerization of molecules which are held together by bonds strong enough to preserve information will then lack the 'error correction' mechanisms of crystal growth.

The main problem for a crystal gene is the converse one: improved accuracy of recognition of incoming units seems to go hand in hand with a much poorer stability of the information itself. How can information be reliably preserved in a structure which is held together by reversible bonds? Most of the answer here is to make the structure big enough. In the first place information can be written on a larger scale than in, say, DNA, with domains rather than individual atoms or molecules as the effective informational units. Such would be co-operatively more stable. We can imagine crystal genes as being several orders of magnitude bigger than molecular genes with a similar information content. The schemes in figure 2 incorporate this idea. Neither in the one-dimensional nor in the two-dimensional types is there any requirement that the aperiodicity should be on a very small scale.

Another well-known device to increase the security of information generally is redundancy—having the information repeated many times. This too is incorporated into the schemes in figure 2: in both the one-dimensional and two-dimensional types the information is repeated indefinitely (in two and one dimension(s) respectively).

The next question is about how the error correction mechanisms are to 'know' which defects are errors to be corrected, and which represent the genetic information to be preserved at all costs. Given fairly large domains it is not difficult to see how, once a pattern of domains is established, it will tend to be copied in growth. This will minimize local mismatches. Imagine a striped (one-dimensional) or mosaic (two-dimensional) pattern of domains on a growing crystal surface. There are some sideways mismatches—at the domain boundaries. If the next layer growing on top copies the domain pattern exactly then there will be another set of similar sideways mismatches produced in the new layer, but there will be no vertical mismatches. Any other pattern of domains in the new layer will produce new vertical mismatches leading to local instability and a greater tendency to re-dissolve. Hence the domain pattern will tend to be copied not eliminated, while deviations from that copying will tend to be 'corrected'. A defect structure may thus be kinetically stabilized (but by a kind of local thermodynamic control—local lowest points on some complex energy hypersurface are discovered).

Yet we must admit that (global) thermodynamic control is a continual threat—and in theory must win eventually. Internal annealing and Ostwald ripening are particular forms of that threat in providing possible routes to 'blank perfection'. On the other hand we know from the mineral world that annealing processes can be very slow indeed. Silicates, for example micas or feldspars, are typically crammed with twinnings

and other metastable features; even very small scale features such as fission tracks, which may have shown little sign of healing over millions of years (Fleischer *et al.* 1975). Again the covalency of so much of the bonding in silicates is no doubt part of the secret here.

Another part appears to be in the difference between the reversibility of bonding at (some) surfaces of such crystals and deeper inside. Clay minerals, zeolites and feldspars can grow from dilute aqueous solutions even at ordinary temperatures (Siffert 1978, 1986, Sheppard and Gude 1973, Odin 1986, Harder 1986), showing that the bonding must be reversible in the presence of water at the growing surfaces. On the other hand wholesale internal reorganization of such structures through annealing generally requires very much higher temperatures (Dowty 1980)—around 1000°C for potassium feldspar (Sipling and Yund 1974). This is not particularly surprising since the two kinds of processes are likely to have very different mechanisms. In adding or subtracting units from the growing surface of a silicate crystal water is actively involved. Water is eliminated when the silicic acid and hydrated metal ion units join together; and water must be added for these units to free themselves again. Even where, as with zeolites, there is water within the crystal structure, the more constrained conditions within the crystal may prevent suitable orientations of the species taking part in these covalent reactions.

Such crystals will still be subject to Ostwald ripening—through defect-containing crystals redissolving and recrystallizing to give slightly more stable crystals. Yet there may be little thermodynamic drive for this in many cases. The energy penalty of, for example, twinning or different polytype stackings may be quite small, as indicated by their ubiquity in the mineral world.

4. Model materials for crystal genes

4.1. *Vermiform kaolinite*

The kaolinite group of clay minerals have a relatively simple crystal structure based on the kaolinite unit layer (figures 4 and 5). Kaolinite is nevertheless remarkable for the variety of its morphologies (Keller 1978). One of these is the 'worm-like' or vermiform type (figure 6). These crystals look rather like the idealized two-dimensional crystal genes in figure 2(*b*), and they tend to cleave appropriately too. Furthermore the deep grooves running along the length of the columnar stacks suggest some form of twinning—quite possibly the 'pseudotwinning' found in large kaolinite vermiforms by Mansfield and Bailey (1972), where different patches of the kaolinite layers have one of three orientations of octahedral vacancies (figure 7). Since in the ideal kaolinite structure the octahedral vacancy orientations are preserved between the layers stacked on top of each other (Bailey 1963), it seems at least possible that specific, complex 'crazy paving' patterns of domains are replicated during the growth of these crystals—as in figure 2(*b*) (Cairns-Smith 1982, Bailey 1986).

Although conceivable as a primary genetic material for the early evolution of life on the Earth, vermiform kaolinite is of less direct interest for us here, since it has not so far proved possible to grow similar kaolinite vermiforms artificially. This form of kaolinite appears to require low temperatures to form in Nature (Keller and Hanson 1975) and presumably it grows only very slowly. The main point for us here is that overall morphology—here columnar crystals with constant (complex) cross-sections—can be a useful guide in the search for appropriate combinations of defect structure, growth modes and cleavage characteristics. One-dimensional crystal genes are perhaps the

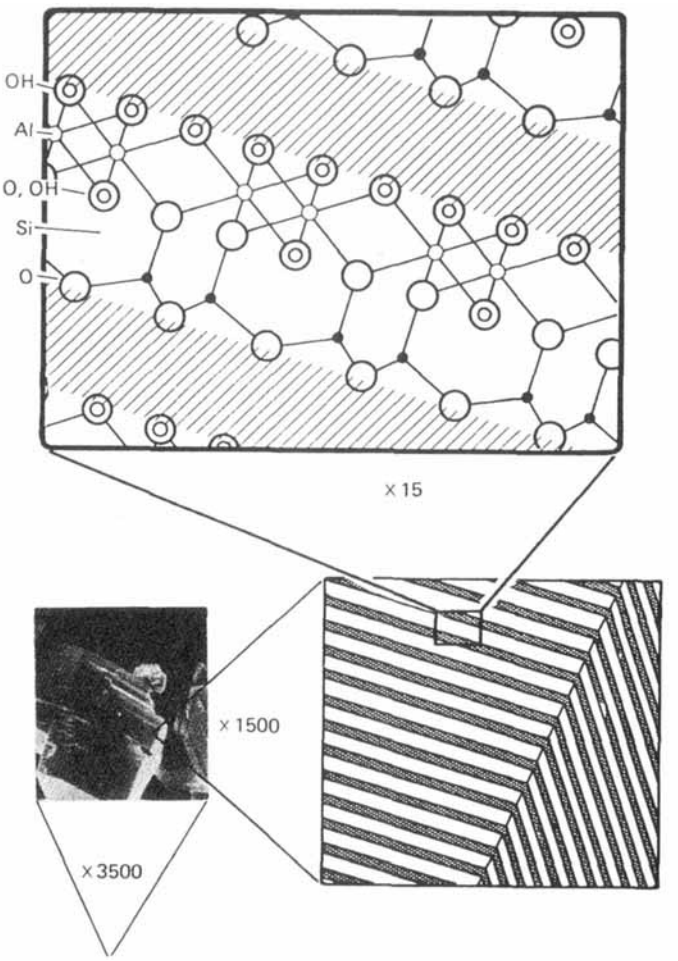

Figure 4. The side view of kaolinite layer structure (Cairns-Smith and Hartman 1986).

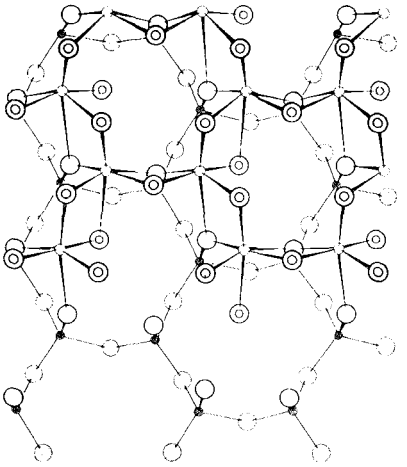

Figure 5. Part of a kaolinite layer is here viewed from above (tilted about 20° from the normal on a horizontal axis) partly cut away to show the lower siloxane sheet more clearly. Larger circles are oxygen atoms (the double ones hydroxides) at different levels: those at the lowest level are shaded. The smaller circles are silicon atoms (shaded) and aluminium atoms (open) (Cairns-Smith and Hartman 1986).

Figure 6. Kaolinite vermiforms (Keller and Hanson 1975)

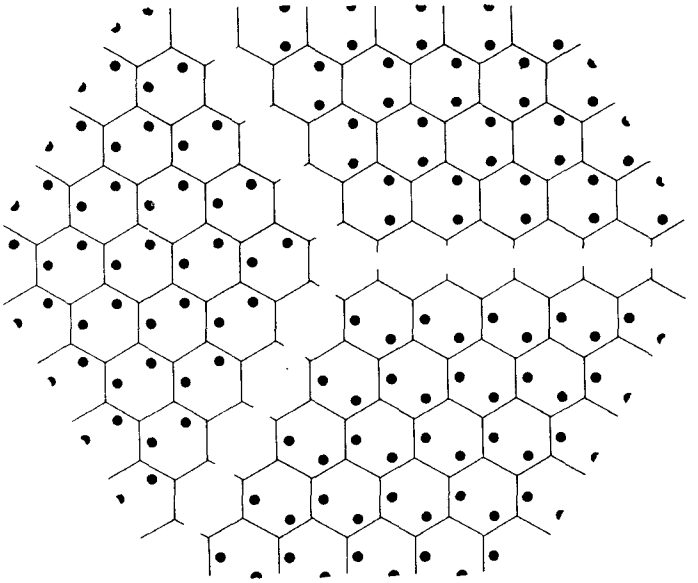

Figure 7. Simplified view of domains in a kaolinite vermiform layer (Cairns-Smith (1982), after Mansfield and Bailey (1972)).

most promising class for artificial Darwinian systems, mainly on account of the widespread occurrence of a class of phenomena of which polytypism is the purest example.

4.2. *Polytypism and related phenomena*

The textbook polymorphic material exists in two or several crystal structures, stable within different regimes of temperature and pressure, with also perhaps a number of phases metastable under all conditions. Haldane's analogy between crystal growth and gene replication, referred to earlier, depended on the idea that metastable phases can sometimes be induced to crystallize when a melt or supersaturated solution is suitably 'seeded'. The most critical limitation of this idea (if it is to go beyond an analogy and be taken seriously as the basis for a Darwinian process) is that any evolution based on such a mode of replication is restricted by the number of reasonably stable polymorphic forms possible. At first sight it might seem that there could never be *very* large numbers of ways of packing units so as to make reasonably stable crystals. Yet this intuition would be wrong. Polytypism is a kind of polymorphism which depends on permutations of layer stacking sequences—somewhat like an abacus (Mackay 1986c): the possibilities can be, to all intents and purposes, infinite.

To illustrate this potential consider the simplest possible case of polytypism to be seen in structures arising from the closest packing of spheres. Here a hexagonal structure is produced if the third layer of spheres is placed immediately above the initial layer—to give an ABABAB... stacking sequence—while a cubic structure results from the ABCABCABC... sequence produced when the spheres in any given layer are consistently offset from those in the layer two below. This might seem to exhaust the possibilities, but of course that is not so. For every layer after the second one there is a choice between two arrangements—so that after, say, 200 layers have been stacked the number of possible arrangements, 2^{198}, comfortably exceeds the number of atoms in the Earth.

Now it is true that generally speaking simple regular arrangements, such as hexagonal or cubic, are energetically favoured, so that under conditions of (global) thermodynamic control simple layer sequences tend to be produced. On the other hand the common occurrence of mis-stackings, even in essentially regular structures, as well as the common occurrence of highly disordered stacking sequences, shows that the energy differences between different stacking modes are often quite small. This is not surprising since, as with simple sphere packing, the structural differences may appear only in relationships between next-but-one (and often more remote) neighbours.

It is clear that having a very large number of different arrangements all of which have closely similar energies is one of the requirements for a good information store. Another is that any one of these arrangements once set should persist indefinitely. We will now consider examples of a number of materials which show stacking permutations, and where these conditions appear to be met.

4.2.1. *Silicon carbide*

Among polytypic materials my first example is the most notorious. It can have enormously long and complicated stacking sequences (with period well over 1000 Å) (Dubey *et al.* 1977), and yet its basic structure is very simple—a diamond-like structure with every alternate atom a silicon. One can think of such a structure as a stack of puckered nets of fused cyclohexane-like units. In one of the simplest stacking modes the holes in the nets are directly superimposed (but with each 'cyclohexane' ring having the opposite conformation to those above and below it). This gives a hexagonal structure. In the cubic structure the holes in adjacent nets are consistently offset so that the centre of any hole has an atom, not a hole, directly above and below (and in this case all the cyclohexane-like rings have the same conformation). Now, as with the closest packing of spheres, these two simple alternative stacking modes can be permuted to give a virtually infinite number of possible structures—polytypes.

This potential for complex polytypism is far more fully realized in silicon carbide than in, say, metals with structures based on closest packing of spheres. Part of the reason for this is, no doubt, because of the difference in the bonding. Although the bonding in metals is strong it is not directional. The atoms can fairly easily slip past each other, and during crystal growth they will be subject to global as well as local thermodynamic control: the growing crystals will relatively easily anneal and reform so that the most stable arrangement can be arrived at, even if the energy differences between different arrangements are quite small. A covalently bonded crystal on the other hand may not be able to anneal so easily: only bonds at the surface are readily formed and broken (because of the 'elbowroom' needed for covalent reactions). So metastable arrangements inside the crystal are more likely to persist.

4.2.2. *Micas*

Mica polytypism is based on more complex kinds of layers in which the sequences are purely of interlayer rotations rather than off-sets, and thus less likely to be disturbed mechanically. Figure 8 is a simplified side view of the mica structure and shows that there is indeed no off-set between the unit layers. There is however an off-set *within* the layers—see also in the formalized top view of a mica layer given in figure 9. The mica layer structure can thus be said to have an arrow in it—a directionality determined by the direction of the *intra*layer off-set. Thus one (ideal) mica unit layer can stack on top of another in any of six different orientations, in each of which the interlayer potassium ions should be similarly twelve co-ordinated with hexagons of oxygen atoms above and

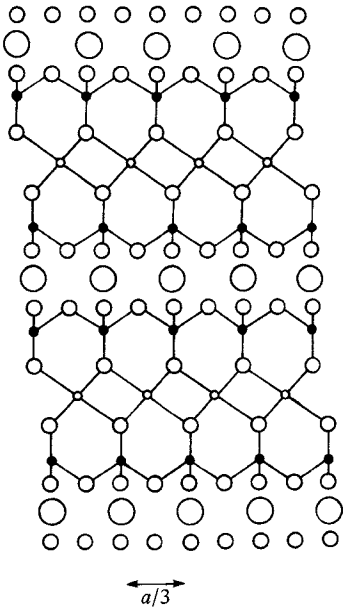

Figure 8. The side view of mica along the *y*-axis. Large, middle and small open circles are, respectively, potassium ions, oxygens, and octahedral cations. Black circles are silicon *or* aluminium atoms in tetrahedral positions.

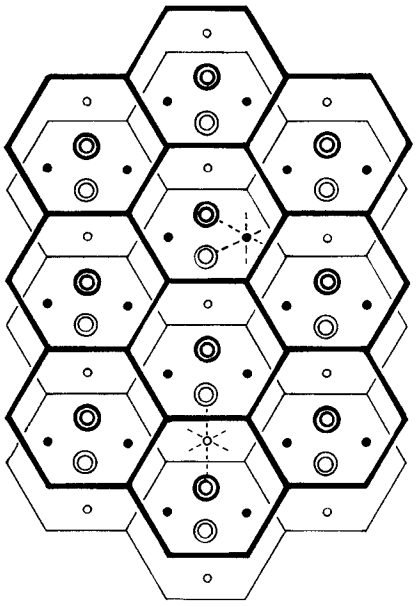

Figure 9. Simplified top view of a mica unit layer showing displacement, by $a/3$, of the upper and lower alumino-siloxane nets. Double circles are hydroxyls. The central plane of octahedral sites are of two kinds, M(1) (open circles) and M(2) (black circles) (Cairns-Smith (1982), after Smith and Yoder (1956)).

below. In fact there are distortions to the ideal structure leading to six-coordination of the potassium ions (Bailey 1966, 1980, Güven 1971).

In muscovite mica the distortions are strengthened by there being a pattern of octahedral vacancies—in the M(1) sites (figure 9)—and stacking tends to be consistently either with a 0° rotation (the 1M polytype) or 120° (the 2M, or 3T polytypes), although there are also disordered muscovite polytypes (Ross *et al.* 1966) which would in principle be able to hold information. In phlogopite mica all three octahedral sites tend to be occupied, there is less distortion of the unit layers and a richer polytypism—in particular in irregular sequences and long range repeats to be discussed in the next section.

It remains a weakness of the micas that they are not covalently bonded in three dimensions. On the other hand the layers are fairly highly charged and the interlayer potassium ions are nested into depressions in the silicate layers above and below: the layers hold together well. But during processes of crystal growth, one can imagine a stacking sequence being disturbed by layer stacks sometimes coming apart. Another more remote possibility is shear along the central octahedral plane of the unit layer: this could in principle alter the direction of the 'arrow' within a layer deep inside a crystal.

4.2.3. *Chlorite*

Chlorite has a magnesium hydroxide-like layer in place of the planes of potassium in normal micas. Also the silicate unit layers are less highly negatively charged—more talc-like than in phlogopite. The polytypism is much more complex than in the micas due to the additional stacking permutations introduced by the hydroxide layers (Brown and Bailey 1962, Lister and Bailey 1967). Some of these complications come from interlayer off-sets, where there is much disorder—probably due to the ease with which such off-sets can be disturbed mechanically.

For chlorites, however, there is the possibility of an altogether different form of one-dimensional information storage, one which would not easily be disturbed by mechanical slippage since the information would be held as a sequence of layer types rather than only of interlayer relationships. High resolution electron microscope studies have revealed that hydroxide layers are quite often either missing or present in excess (Thomas 1984).

4.2.4. *Zeolites*

As was clear from the example of silicon carbide, polytypism does not depend on the crystal structure having (like mica) an overtly layered structure. Indeed among silicates the three-dimensional framework types, feldspars and zeolites, constitute a large group of structures rich with possibilities for one-dimensional information storage in the form of stacking sequences of two-dimensional units—all the more secure, perhaps, for being covalently bonded in all three dimensions.

The basic building blocks of the framework silicates are SiO_4 and AlO_4 tetrahedra. These 'tetrahedral elements' can be joined together through shared oxygen atoms at their corners to make a more or less complex scaffolding which will have a negative charge depending on the extent to which the AlO_4 elements are incorporated in the frame rather than SiO_4. Counterions, such as K^+, Na^+, Ca^{2+}..., lie within the frame to neutralize such charges. In the various zeolites there are particularly large and varied

cavities and channels which can hold, also, water. An idealized general formula for framework silicates can thus be written as

$$(\text{Cations})^{km+}[\text{Al}_k, \text{Si}]_m\text{O}_{2m}.n\text{H}_2\text{O}$$

where $n=0$ for feldspars: in zeolites smallish organic molecules may substitute for water—and indeed the cations too may be organic—and such guests are usually relatively easily exchanged.

Sodalite (idealized formula $(\text{Na}_6)[\text{Al}_6\text{Si}_6\text{O}_{24}].n\text{H}_2\text{O}$), chabazite $((\text{Ca}, \text{Na}_2)[\text{Al}_2\text{Si}_4\text{O}_{12}].n\text{H}_2\text{O})$ and erionite $((\text{Na}_2, \text{K}_2, \text{Ca}, \text{Mg})_{4\cdot5}[\text{Al}_9\text{Si}_{27}\text{O}_{72}].n\text{H}_2\text{O})$ are examples of natural zeolites with distinctive properties—morphologies, absorption characteristics and so on; yet these zeolites, belonging to the so-called ABC-6 or chabazite group, can be seen to be structurally related in a way that is quite like the relationship between the various polytypes arising from close packing of spheres (Smith and Bennet 1981, Millward *et al.* 1985).

We can build up an idea of the structure of sodalite, for example, by imagining first a set of alumino-siloxane hexagons (figure 10 (*a*)) arrayed in a plane—in the 'A' positions shown in figure 10 (*b*). Another set of hexagons is now placed in a plane above these but in the 'B' positions and connected up to those in the first plane through sloping four-membered rings (figure 10 (*c*)). A third plane is now added with the hexagons in the C-positions similarly connected up to the hexagons in the plane beneath them. After that the A-plane is repeated, and so on: i.e. the stacking sequence in sodalite is ABC...

Other structures in this group of zeolites are built in the same way except that they have different sequences: for example chabazite itself reads AABBAACC..., erionite AABAAC..., and so on. The analogy with close packing of spheres is obvious and there is a similarly infinite richness of possibilities. Unlike the closest packing of spheres which we were thinking about earlier, pairs of planes in these zeolites often have the hexagons directly superimposed (as in chabazite and erionite). In that case the joining four-membered rings are not sloping but vertical (figure 10 (*d*)).

Figure 11 (*a*) and (*b*) show the structure of erionite with its characteristic pattern of voids and channels. Figure 11 (*c*) illustrates how different stacking sequences can easily be incorporated into the same piece of crystal. Notice that 'information' in the form such stacking sequences is far from a formal abstraction. This 'information' expresses itself directly as a distinctive pattern of voids and channels with, potentially, specific physical and chemical properties. There is now every prospect of being able to read off complex information of this sort through high resolution electron microscopy (Millward *et al.* 1985).

A somewhat similar case arises with the industrially important high silica synthetic zeolites ZSM-11 and ZSM-5 (Kokotailo and Meier 1980). The first of these consists of a stacking and joining of unit layers in such a way that neighbouring units are related by a mirror plane. This gives a structure with straight intersecting channels in two dimensions. In ZSM-5 one of the sets of channels is zig-zag. This results from a different arrangement of the same unit layers—this time they are related to their neighbours by an inversion.

That, however, is not the end of it. A potentially infinite number of crystal structures can be made through permutations of these two stacking relationships. Intergrowths of this sort have been observed by HREM (Millward *et al.* 1983).

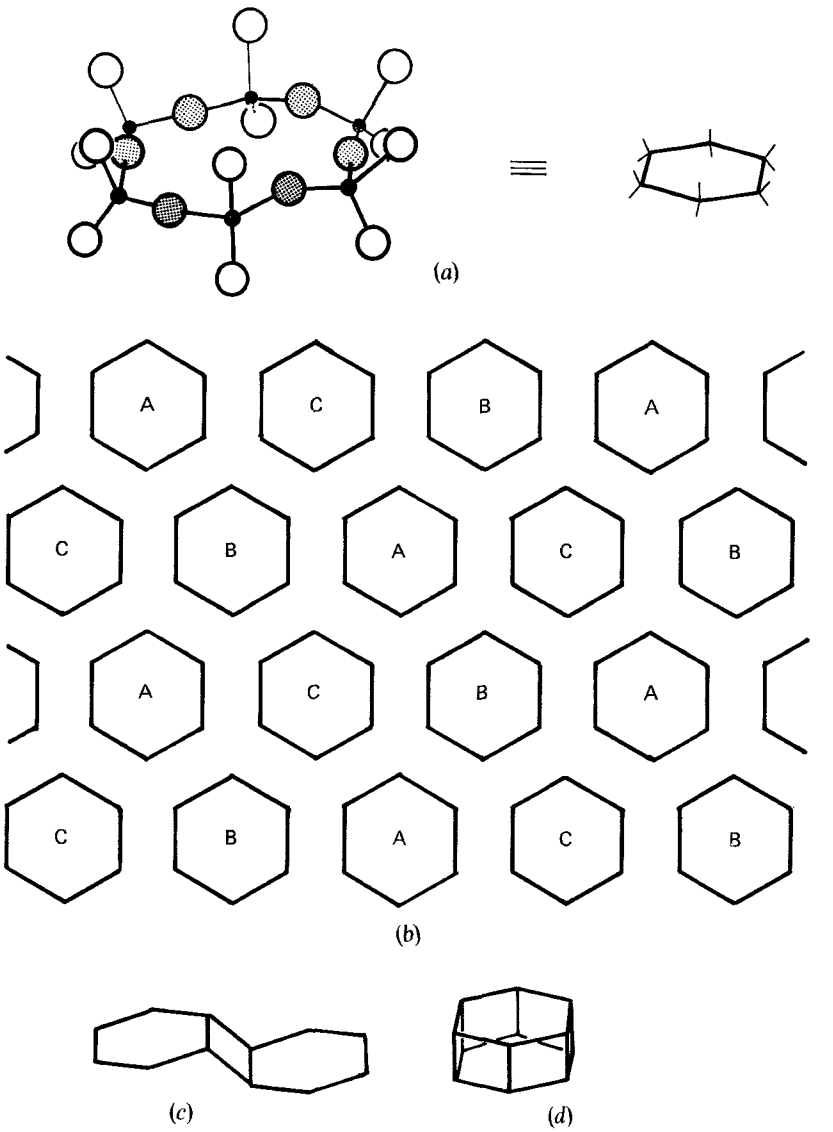

Figure 10. The ABC-6 group of zeolites can be thought of as being made from planes of 'six-membered' alumino-siloxane rings, as in (*a*) where the small circles are silicon *or* aluminium atoms and the larger circles are oxygens. The open circles are oxygen atoms which make the connections with other similar rings in planes above and below. The rings in any plane are in one of three sets of positions (*b*), and are joined to those above and below them by means of 'four-membered' rings which are either sloping (*c*), or vertical (*d*), according to whether the rings in two successive layers occupy the same or a different set of sites. Different members of the group have different ABC sequences (see also figure 11).

4.2.5. *Barium ferrites*

This group of materials combines several of the structural features that we have been discussing. They consist of close packed planes of, mainly, oxygen atoms with, mainly, iron (III) atoms nested in sites lying between the oxygens. The additional components are barium atoms which substitute for one in four of the oxygens in some of the planes; and some divalent metal ions such as zinc, magnesium, nickel, and/or iron (II) which occupy a limited number of the small cation sites. As with the silicon carbide

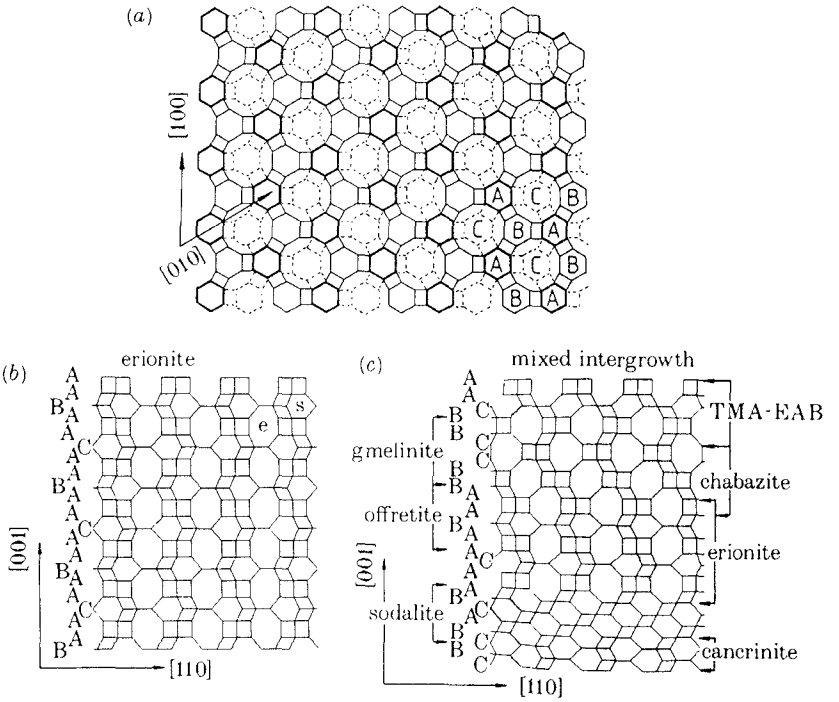

Figure 11. Idealized schematic drawings of framework structures related to the ABC-6 family of zeolites; (*a*) [001] projection showing interconnections between successive layers—AABAAC—in erionite; (*b*) [100] projection for erionite. The positions of A, B and C layers along [001] are indicated; channels bounded by eight-membered rings 'e' and six-membered rings, 's', are also shown; (*c*) [100] projection of a hypothetical arrangement of intergrown segments of several ABC-6 zeolites. It can be seen that the zeolites can be specified by the appropriate pattern of 'e' and 's' channels (Millward *et al.* 1985).

and zeolite examples these structures have strong bonds in all three-dimensions but, as with micas, the layers are complex—and, as with chlorites, they are of different kinds.

The two main kinds of layers are shown in figure 12. The so-called M-layers [$BaFe_{12}O_{19}$] have one central plane of oxygens in which one in four of the oxygen atoms are substituted by barium. In the Y-layers [$Ba_2Me_2Fe_{12}O_{22}$] there are two such barium substituted planes as well as some additional small divalent cations. These layers are readily permuted having the same a-dimensions and indeed essentially the same slice of structure where they join with each other. A common theme is for single M-layers to interrupt stacks of Y-structure. Making use of the difference in thickness between the M- and Y-layers, and of the fact that M-layers are more resistant to etching by acid, Kohn *et al.* (1967) were able to deduce long repeating sequences from an electron microscope study of etch-pits (figure 13). Subsequently, direct lattice imaging by HREM (Van Landuyt *et al.* 1974, Anderson and Hutchinson 1975) has allowed both disordered sequences (figure 3) and long period ordered sequences (figure 14) to be read off.

4.3. *Questions of crystal growth*

It is clear that in some cases polytypes are thermodynamic equilibrium phases. Lead iodide, for example, undergoes a reversible phase transition from one stacking mode (2H) to another (12R) at 367 K (Salje *et al.* 1987). On the other hand it is equally

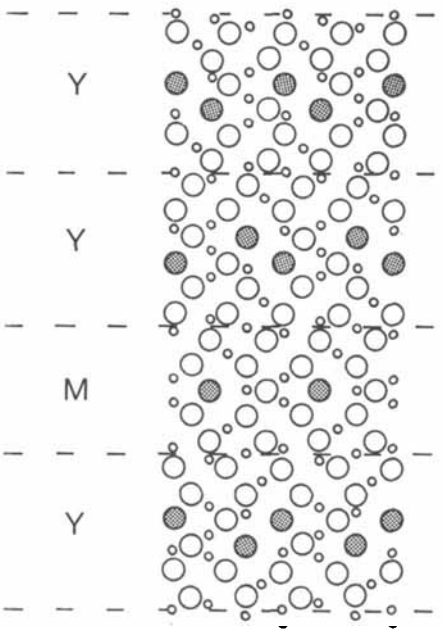

Figure 12. A mixed stack of Y- and M-layers in a barium ferrite—see text. Large open circles are oxygen atoms and shaded ones barium. The small circles are Fe^{3+} and M^{2+}. (From data in Smit and Wijn (1959).)

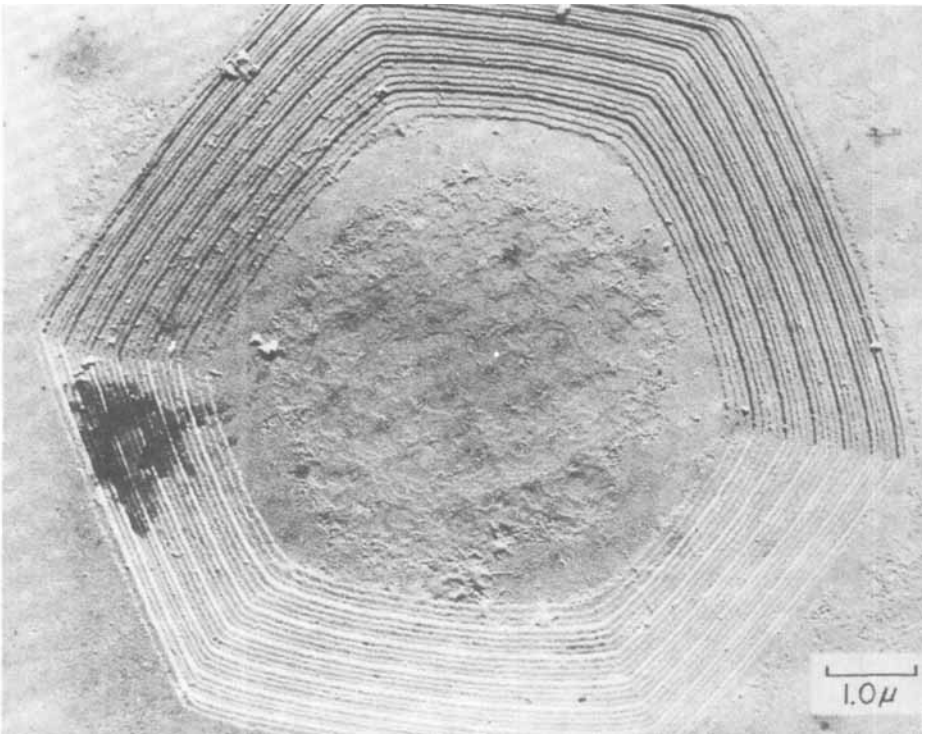

Figure 13. An etch pit on a crystal of a barium ferrite showing that the crystal contains a long repeating sequence of layers. This was shown to be MYYYYYYYYYMYMYYMYYY (see figure 12), the depths of the steps corresponding to the blocks of Y-units (Kohn *et al.* 1967).

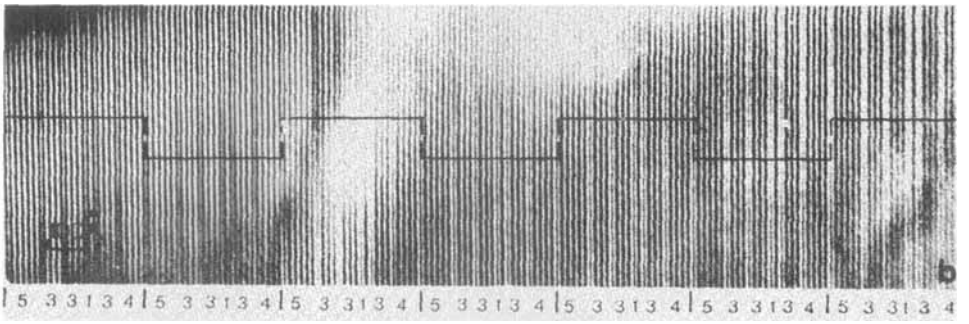

Figure 14. High resolution electron micrograph showing a complex regular stacking sequence in a barium ferrite--viz. $MY_5MY_3MY_3MYMY_3MY_4$ (van Landuyt *et al.* 1974).

clear that many polytypes are metastable (Krishna 1983). Thus although the simpler silicon carbide polytypes can be assigned stability ranges, metastable polytypes can be successfully grown even above 2000°C (Tairov and Tsvetkov 1984). Among regularly repeating sequences the main distinction appears to be between short period structures, where thermodynamic considerations may predominate, and the more complicated long period structures, where details of crystal growth mechanisms may play a crucial part (Pandey and Krishna 1983).

Even where a polytype sequence is metastable arguments may remain as to whether, when the layers were being formed, the layer sequencing in some complex polytype was dominated by thermodynamic or kinetic considerations. There will generally be different and changing gradients of concentration and temperature among growing crystals. It is a reasonable conjecture that irregular banding, such as that shown in figure 3, might be a kind of tree-ring pattern--that is to say an historical record of successions of conditions experienced by an individual crystal, with the 'decisions' of when to change from one domain to the next depending on local thermodynamic conditions from instant to instant.

Then again, long range modulations may result from periodic release of strains inherent in a basic structure. This may be responsible for the somewhat irregular two-dimensional domaining of kaolinite layers (Mansfield and Bailey 1972) and is very likely to be so for the periodic inversion of the layers in antigorite (Kunze 1956, Thomas *et al.* 1978 9). Regular long range repeats of units of different chemical composition may be explained similarly in terms of the operation of elastic forces (Rao and Thomas 1985) for example in $BaBi_8Ti_7O_{27}$ which consists of recurrent intergrowths of lamellae of composition $Bi_4Ti_3O_{12}$ and $BaBi_4Ti_4O_{15}$ (Jefferson *et al.* 1984).

It is clear, then, that neither irregularities nor long range repetitions by themselves necessarily imply replication: the first may result from a fluctuating environment during crystal growth, or may have been introduced mechanically during or after the growth process, while the second may be a thermodynamic feature of the crystal structure itself. It is where these two features come together that we have the strongest evidence for a copying process of some sort having been involved: where there are long range *repetitions* of highly *irregular* sequences (as, for example, in figure 14).

There is evidence in any case against the idea that continually fluctuating local growth conditions account for the irregularities in the barium ferrites. Savage and Tauber (1967) made a study of more than 50 samples prepared under a variety of growth conditions, with variations in composition, the nature of the divalent metal, the (flux) solvent, the temperature range, and so on. There was little or no indication of

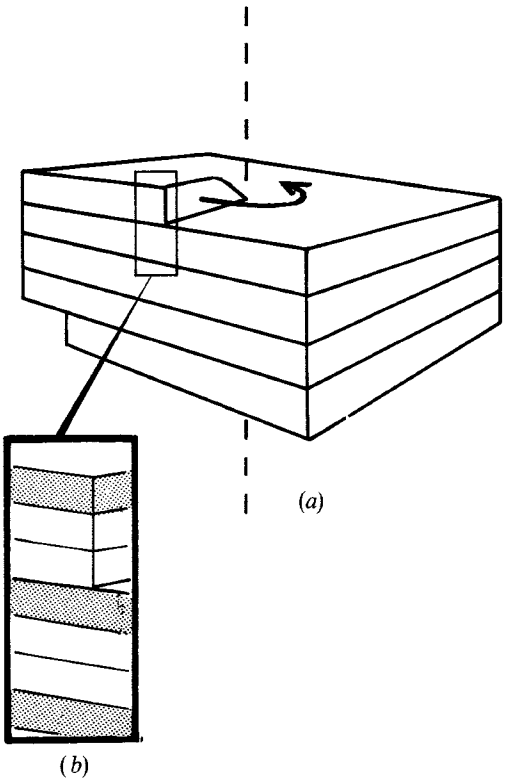

Figure 15. (*a*) A screw dislocation avoids the need for surface nucleation of new layers during crystal growth. In this idealized case the crystal consists, in effect, of just one (helicoidal) layer. (*b*) A screw dislocation may be many unit layers deep (see also figure 17) and thus provide a critical part of the mechanism for replicating some stacking sequence (of types or orientations) of such layers.

dependence of the polytypes produced on such conditions. The results were consistent with statistical expectations: the simpler kinds, such as MYMYM, were common, while more complex types were individually less common and became unique for crystallographic repeats of beyond 80 anion layers or so (repeats of up to 654 anion layers were found). These results suggest a role for chance events in the initial stages: in setting up a particular sequence *which was then copied with great fidelity* with little sensitivity, from then, to local fluctuations in conditions.

The classical explanation for complex polytypism is indeed along these lines—Frank's screw dislocation mechanism (Frank 1951) (see figure 15). In support of this idea screw dislocations were found in silicon carbide (Verma 1957, Golightly 1969), in micas (Amelinckx 1952), in barium ferrites (Cook and Nye 1967, Tolksdorf 1973), and in other polytypic materials. On the other hand screw dislocations are not always found where they might be expected: for example they are not in evidence in the barium ferrites studies by Kohn *et al.* (1967). While a screw dislocation mechanism is the most widely favoured, especially to explain long range repeats, the only point of general agreement is that no one mechanism can account for all cases (Trigunayat and Verma 1976, Krishna 1983, Jepps and Page 1983).

4.3.1. *The importance of sideways growth*

In thinking about polytypes and other layer intergrowths one naturally concentrates attention on the stacking direction—on how the layers are related to each other. One may be perplexed, then, as to how the next layer in a long repeating sequence could ever 'know' which way to be: how a layer growing on the surface of a crystal could copy the nature or orientation of some other layer a thousand ångströms below it. But that is not what has to happen. The sides of the crystals have the full sequence displayed on their surfaces, as does the side of the step (or set of steps) produced by a sufficiently deep screw dislocation. *Exclusive sideways growth* could indeed provide part of the explanation for complex long range repeating stacking sequences: any strong tendency for simple layer-on-layer growth would tend rapidly to disturb long range repeat sequences by adding new 'information'.

A screw dislocation mechanism has the best of two worlds. In one sense it is a layer-on-layer mechanism, in that the crystal grows in the layer stacking direction. But in another sense it is a form of sideways growth. The overall effect may be to grow the crystal up the c-axis, but the blow-by-blow process, the addition of individual ions from solution, is happening all the time by a sideways extension of the 'step'. It is like tacking into the wind: a way of making progress in a direction which is 'disallowed'.

Side faces of a complex polytypic stack might be expected to grow more easily than the top and bottom faces since the side faces are likely to have a more complex grooved structure (Vand and Hanoka 1967), making it easier for new units to find attachment sites.

Sideways growth is likely to be particularly strongly favoured when the materials have complex layers. The mica unit layer, for example, is indeed a unit: it owes its stability to being complete—with interlayer potassium ions in place too. It would make little sense to imagine the growth of a new layer on a mica crystal by, first, the emplacement of an array of potassium ions on the surface, followed by a layer of alumino-siloxane hexagons to which aluminiums, magnesiums etc., then attach themselves... All such intermediate stages would be hopelessly unstable. Even the first stage would not happen since the selectivity of the mica structure for potassium depends on the potassium ions being caged by the silicate layers above and below so that water can be excluded (Eberl 1980, 1986). An open surface will, I suspect, prefer hydrated sodium or calcium ions—especially in marine pore-water where nevertheless (mica-like) illites often form against the potassium/sodium ratio of seawater.

By growing sideways on the other hand, so that only the edges of unit layers (or stacks of unit layers) are ever added to, silicic acid and hydrated metal ions can join on, one at a time, in a balanced way. In particular local charge balance can be maintained all the time. For example, the Al-for-Si substitutions in the tetrahedral sheets of the mica structure can be matched to the level required to balance the K^+ ions which are at the same time fitting in between the layers.

The same is presumably true of the complex barium ferrites where the M and Y unit layers can be seen to be made up of sub-layers (Smit and Wijn 1959) which, on their own, would be highly charged (Kohn and Eckart 1964, Anderson and Hutchison 1975). Even without the evidence of the long range repeats we might thus have suspected from these structural considerations that barium ferrites would have a strong tendency to grow sideways.

To judge from the diaphanous, membranous character of so many natural smectites (Wilson and Pittman 1977, Grim and Güven 1978) and also of synthetic ones (Baird *et al.* 1973) smectite clay minerals seem to form by a kind of two-dimensional

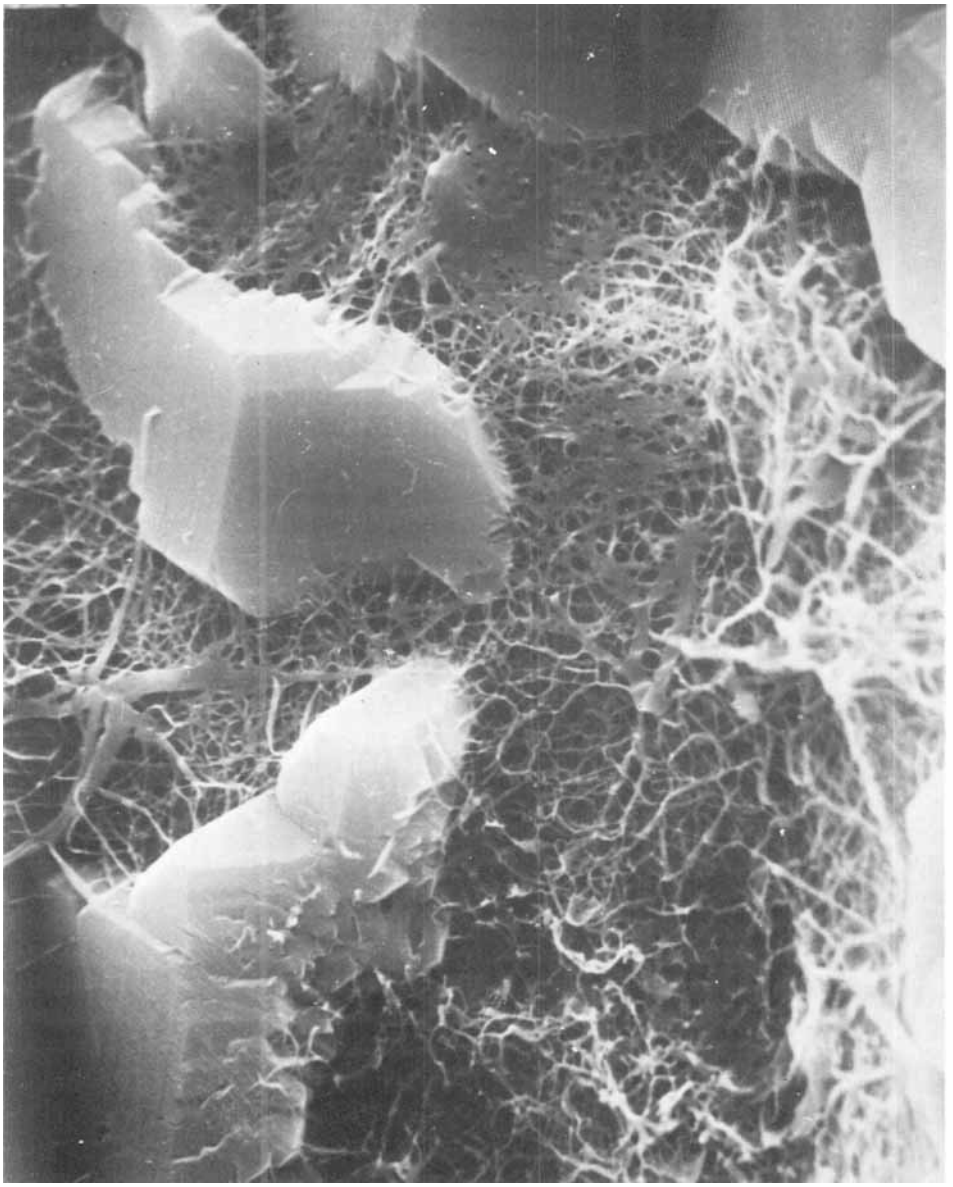

Figure 16. A scanning electron micrograph of freshly fractured sandstone from the Magnus field, North Sea, after critical point drying. The filamentous material is illite (McHardy *et al.* 1982).

polymerization. The marine illites studied by McHardy *et al.* (1982) are an even more striking example. A sample of these crystals would consist typically of, say, four mica-like unit layers with potassium ions held between the layers by the relatively high Al-for-Si substitutions. The outer surfaces of these very thin lath-like crystals (shown in figure 16) appear to have a lower more smectite-like charge—as in the two-layer mineral rectorite (Lagaly 1979).

Now according to McHardy *et al.*, when a sample of such an illite is prepared for X-ray diffraction analysis the crystals pile on top of each other creating smectite-like

interlayer regions between every N unit layers where N is the number of layers in the crystal. The result may then be read as a regularly interstratified illite/smectite. It had long been a mystery how every (say) fourth layer 'knew' that it was time to be smectite. This work provides a neat explanation—which depends on the illite crystals having a very strong tendency indeed to maintain a constant thickness (or rather thinness)—possibly in part because of inhibition of layer-on-layer growth processes: these crystals appear to have grown exclusively sideways.

Baronnet (1980) has reviewed ideas connecting polytypism with crystal growth processes in micas. Modifying and elaborating on earlier theories, particularly those of Amelinckx and Dekeyser (1953) and Smith and Yoder (1956), Baronnet invokes screw dislocation mechanisms to account in some detail for the forms of polytypism observed, particularly in phlogopite where complex polytypism is common. A typical rather simple case would be where a basic, say 1M, polytype structure is interrupted—but regularly—by a 'fault' in the stacking, say a pair of contrary rotations by 120°. From electron microscope studies (Baronnet 1972, 1973, 1975) the phlogopite crystals appear to grow in two stages. The first stage, according to Baronnet, takes place at high supersaturation and is a dislocation-free layer-on-layer stage. This makes platelets with a basic polytype structure. In the second stage a screw dislocation mechanism takes over which may then give rise to more complex repeating features.

A simple layer-on-layer, ion-by-ion, mechanism of the kind objected to above can be avoided with a minor modification to Baronnet's picture—still in keeping with his electron microscopic evidence. This would be to suppose that the very first events were in the growth of single (I would guess smectite-like) layers by two-dimensional polymerization, and that these pile on top of each other to create the initial seeds for a multilayer phlogopite platelet to begin to form. As the flexible platelets continue to grow sideways they are subject to a number of kinds of accident. Bits may break off and some of these bits may adhere to other platelet surfaces creating somewhat better organized surface seeds one or more unit layer deep. Then again the plates may shear to create screw dislocations according to the classical picture (Frank 1951).

Barronnet has another mechanism for generating screw dislocations which can almost be seen in action in his vivid electron micrographs. Screw dislocations can be produced with indefinitely large Burgers vectors, through the (flexible) layers growing round on top of themselves without necessarily shearing at all (figure 17). Given moderately flexible layer stacks (and a large enough hole in the middle) there would appear to be no limit to the depth of stack which could be replicated through a screw dislocation of this sort.

4.3.2. *A cautionary tale—post-growth effects*

Although a screw dislocation is involved in generating quite complex repeating sequences in vapour-grown zinc sulphide crystals, this appears *not* to be the result of a copying process during growth, but instead a post-growth effect which can take place at ordinary temperatures. It appears that as the crystals cool the layers within a multiple screw dislocation ramp may slip past each other, and since every nth layer is connected by the (n-deep) screw dislocation the slippages can take place in a regular way (Steinberger 1983, Mardix *et al.* 1968).

Zinc sulphide is a less covalent (and much softer) material than the structurally similar silicon carbide, which no doubt accounts in part for this effect (Trigunayat and Verma 1976), although silicon carbide itself undergoes solid state transformations between polytypes at high temperatures, typically in the region of 2000°C (Jepps and

Figure 17. A deep screw dislocation with a hollow core in a synthetic phlogopite (Baronnet 1972).

Page 1983). Another apparently similar example to zinc sulphide is the unusually soft and plastic material silver iodide, where polytypic transformation can take place at room temperature over periods of months or years (Prager 1983).

These examples emphasize the virtues of hardness in potential crystal genetic materials. In any case the growth conditions should be well below the melting point—i.e. from solution or from the vapour—to discourage annealing processes (Tairov and Tsvetkov 1984). This is especially the case if the information is to be held as a pure polytype stacking sequence without the extra security of chemical differences between layers.

4.4. *Completing a replication cycle*

A high fidelity of emplacement of new units on a template is the first and most critical step in making a copy. If, as appears to be the case, a copying mechanism is responsible for some long range repeating polytype sequences then in such cases, and in terms of the number of units being accurately emplaced, such crystal systems can be said to be many orders of magnitude more efficient than the non-enzymic RNA systems discussed earlier. But in neither case is there a complete replication cycle—essential if evolution experiments are to be performed. What more will be needed for crystal genetic systems to be realized?

4.4.1. *Cleavage planes and growth directions*

The crystals must cleave in such a way as to expose the information—i.e. across the exclusive directions of growth (figure 2). For crystal genes based on materials with layered (crystal) structures, such as kaolinite or mica, the preferred cleavage is in the layer stacking planes. This is ideal for two-dimensional crystal genes (figure 2 (*b*) and 6), but not for one-dimensional types which have been our main concern here. For these, in-layer cleavage would have to be inhibited, and cleavage across the stacking planes encouraged instead. Even materials such as silicon carbide, feldspars, zeolites or ferrites, which have similarly strong bonding in three dimensions, often cleave in the polytype (or quasipolytype) stacking planes. Anderson and Hutchison (1975) found that stacking plane cleavage was favoured for barium ferrites, but the crystals nevertheless often broke at right angles to this—indeed the technique of electron microscopic examination being used depended on this happening. How can such appropriate cleavage modes be encouraged?

Although a tendency to grow through screw dislocations is an indication of a preference for sideways growth of polytype stacks, it is the sideways growth which is important rather than the screw dislocations as such. Indeed an ideal situation might be one in which there is exclusive sideways growth, but in which screw dislocations do not form. A crystal which is growing like this will have a thin platey morphology and thus become more and more liable to cleave in the appropriate way. A growth mode of this sort has been noted in the early stages of the development of lead iodide crystals (Frank 1951), where sideways growing plates were produced which were shown (from interference colours) to be of rigorously constant thickness. The illites discussed above provide another example. It would seem that these very thin crystals stay like that because they are bounded top and bottom by solvophilic (smectitic) surfaces which not only do not grow upwards, but do not even adhere to each other very well. The branching-lath habit of these crystals is another feature which might help to encourage appropriate cleavage. One might seek to build similar features into the design of a one-dimensional crystal genetic material.

Inorganic or organic growth inhibitors are the classical method of controlling the morphologies of inorganic crystals by inhibiting growth on certain faces (Buckley 1949). There is room for design work here, as has been shown more recently in relation to the growth of organic crystals (Berkovitch-Yellin *et al.* 1982, Addadi *et al.* 1982, 1985). Crystal habits may be dramatically altered by small amounts of molecules that have been 'tailor-made' to attach to particular crystal faces. One might imagine large organic molecules being designed to fit with certain surface hole patterns on a zeolite and so inhibit growth on certain faces.

Suitable cleavage planes might also be engineered—for example through slightly mis-sized ions being delivered during the growth process in pulses, so as to create planes of weakness across the directions of growth. Andersson and Hyde (1974) have discussed 'chemical twinning', where impurities fit into the slightly mis-sized sites that are inevitably arrayed along twin planes. It might thus be possible to induce suitable twin planes though the presence of appropriate impurities.

4.4.2. *Protective media*

Crystal growth in gels, where this is feasible, has several advantages (Henisch 1979) It mitigates the effects of spontaneous seeding, by keeping unwanted seeds localized; it provides protection against mechanical accidents, which may cause crystals to break inappropriately; and it may allow one to see more clearly a sequence of growth events.

Crystallites can be kept separate by being enveloped in solvophilic macromolecules—the classical technique of protecting a 'hydrophobic' with a 'hydrophilic' colloid as in the protection of gold sols by gelatin; or by adsorbing highly charged molecules—as in the 'peptization' of clays with organic or inorganic polyanions (van Olphen 1977). More generally crystallites might be kept apart through a suitable choice of the solvent conditions so that the crystallites form a protective double charge layer.

Another more general protective technique would be to keep the population density of the crystals low, and not to let the crystals grow very large, to minimize mechanical accidents and stresses.

4.4.3. *Seeding*

Even if we have crystals which grow appropriately and cleave appropriately; and even if we can control conditions of supersaturation to prevent spontaneous nucleations, there is still the problem of getting the newly cleaved faces actually to grow again. Crystal surfaces are easily poisoned, or damaged, or subject to spontaneous reorganization so that growth may be inhibited or otherwise deranged. It might be necessary to undersaturate the solutions from time to time so as to get rid of debris and create new growing surfaces.

Tairov and Tsvetkov (1984) describe experiments in which silicon carbide was grown on a seed crystal consisting of two different polytypes. The new crystal grew on an oblique face of the seed (on which the characteristic stacking patterns were exposed) and in the process inherited the local polytype structures. There are, however, few similar reports in the literature of specific seeding of polytypes.

5. Natural selection of crystals

5.1.1. *Selection for speed of replication*

Frank (1949) in the very paper in which he first proposed the screw dislocation mechanism for crystal growth remarked that 'The effect which dislocations have upon

crystal growth produces a rather odd natural selection...'. Natural selection is exactly what it is: like rabbits, dislocations may owe their prevalence to the efficiency of their reproduction. But why, then, if natural selection is actually going on, do ordinary crystallization processes not eventually generate crystals with 'life-like', manifestly special-2, properties?

The reasons are not hard to see. In the first place screw dislocations are rather simple things in themselves, and although they may occur in quite complex combinations the more complex ones are less good at promoting crystal growth than the simpler types (Frank 1949). There is a parallel here with one of the experiments on evolving enzyme-replicated RNA molecules (Mills *et al.* 1967): when the only selection pressure applied was to favour fast replication the RNA molecules obliged by becoming shorter and shorter—reminding us that subtle and complex selection pressures are needed to produce subtle and complex organisms even if a reasonably accurate genetic system is there. Then of course the other reason why ordinary crystallization processes would not be expected to get very far is that one does indeed need accurate replication—and complex patterns of screw dislocations are not bound to replicate very accurately, and generally speaking will not do so.

We should note the distinction between replication of a screw dislocation or pattern of screw dislocations, and the replication of a polytype sequence by a screw dislocation mechanism—which is what we have been largely discussing here. On this topic too, though, Frank (1951) was thinking in 'selectionist' terms, pointing out that the hexagonal as opposed to the cubic form of lead iodide has a platey habit which encourages the development of screw dislocations through shearing at some stage—so that we might say that the hexagonal form has selective advantage because it brings about its own preferential reproduction.

Projecting into the future (and supposing now that conditions have been found for the efficient breeding of particular polytype sequences) we can imagine several ways in which more complex replicating stacking sequences might be preferred. (For a similar discussion by a biologist see Bloch (1986).) This could be so even where all that is being selected for is speed of replication. For example the groove structure of the edges of a polytype stack are likely to be affected by the sequence as can be seen by implication from the etch pits in figure 13. As remarked earlier, such grooving is likely to affect the rate of sideways growth.

Then again some stacking sequences might cleave more easily than others and hence be selected. For example suppose that small differences between the a-dimensions for different stacking modes led to lamellar crystals developing a slight curl if the stacking sequences within them were asymmetric. This would induce a strain if the crystals were to pile on top of each other. Such might then cleave more easily....

5.1.2. *Selection for fidelity of replication*

As an aside it is perhaps worth pointing out here that once we had achieved sufficiently faithful replication of a genetic material to set in train Darwinian evolutionary processes, there would from then on be a tendency, at least, for further improvements in replicative efficiency. Braterman (1986) describes this as 'the pedigree principle'—a tendency (as with racehorses) to favour not only a particular characteristic, but that that characteristic should breed true. Consider any replicable feature which gives crystals that possess it a selective advantage (in any way whatever): any *other* replicating feature which assists fidelity of replication in general will now *also* have a selective advantage.

5.1.3. *Overlapping subsets*

I insert here another aside. The above formal consideration is an example of a still more general feature of Darwinian systems: that they may come simultaneously to belong to many different subsets of some immense number of possible structures. To put it another way, they can be tailor-made. Each feature (like each measurement of a suit) may be nothing very extraordinary: but the appropriate combination of many features, the appropriate overlap of subsets, may be very extraordinary indeed. (It is the difference between chance and engineering: between typing 'bio' and typing 'biochemistry'.

5.2. *Properties as phenotypes*

Here we return to an idea discussed in relation to RNA evolution: that almost any *property* of a genetic material might have a selective advantage in suitably contrived circumstances—and would become subject to evolution through natural selection if, also, such a property was information-dependent. For example, suppose that some kinds of stacking sequences affected, say, crystal habit, or magnetic properties, or electrostatic polarization of the crystals, or ability to adsorb some particular molecule and hence alter surface characteristics... It might be possible then to devise a separator to select continuously those crystallites which had such properties to a pre-determined degree, while removing others from the zone of crystallization.

In relation to the problem of the origin of life on the Earth, I have suggested a rather simple situation—clays growing in a sandstone—where shape, size and stickiness might constitute especially simple phenotypes of this 'direct-acting' sort (Cairns-Smith 1966, 1982, 1985). Then again the growing crystals could be challenged with difficult conditions. Recall that enzyme-replicated RNA molecules were challenged with dyes and overcame the challenge through selection of mutants which did not bind the dyes so strongly. With one-dimensional crystal genetic systems the corresponding experiments might be with added materials which slow down growth on some but not other kinds of grooving....

5.2.1. *Separating selection from replication*

Let us consider first a typical evolution experiment as it might be carried out on microorganisms. The first step is to grow up a batch of the organisms. Then a small sample of this is used to seed a new batch which is in turn grown up—and so on. In such circumstances those types which reproduce fastest will be most likely to be carried on between the batches and will eventually become the only types present. In this sort of experiment selection is for reproductive efficiency and the general conditions for selection are the same as those for reproduction. However, there would be no need in principle for conditions for selection and reproduction to be at all similar. It would simply be a matter of putting in suitable 'hoops' between the removal of the sample from batch N and its use to seed batch $N+1$. For example it might be possible to grow the crystals at a temperature of about 1000°C but then select them on the basis of, say, catalytic or superconducting properties at very much lower temperatures.

Such examples give some hint of future prospects, but of course they are well in the future, and no doubt it is the wrong way round to think first of some desirable defect-dependent property and then wonder how it might be evolved through replication of the causative defect structure. The right way round will be to do it the way Nature (presumably) did for life on the Earth. First we must find a competent genetic system,

and then see what properties appear with the exploration of the relevant evolutionary landscape. You might say that the whole of life now on the Earth is the result of an exploration of the possibilities inherent in replicating DNA molecules.

5.2.2. *Indirect action*

This richness of possibilities inherent in a structurally somewhat limited molecule comes mainly from the indirect way in which DNA operates. A particular DNA message survives not for what it is, exactly, but because it can specify other things—RNA and protein molecules—which then, as catalysts etc, have further more remote effects. Who is to say that silicon carbide or barium ferrites do not have some similar potential? There is as yet no known limit to the complexity of stacking sequences which are (apparently) replicated during the growth of these crystals, and it would take no more than a few hundred permutable layer units to create an immense set of possibilities to be explored.

So far the kinds of possibilities which we have contemplated have been restricted to direct properties and combinations of such properties, but there is no hard line between this and more remote ways of being successful through bringing about a development process by the specification of other materials than the genetic material itself. The simplest way might be for the crystal genes to stimulate other inorganic precipitation around them through heteronucleation. A particularly fascinating form of inorganic precipitation can occur when barium or calcium carbonate precipitates in silica gel (Garcia-Ruiz 1985). Silicate membranes form at the same time as the carbonate crystals, giving rise to complex morphologies—the nature of the membrane being influenced by the carbonate crystals and vice versa. Perhaps the nature of such processes could be influenced by the presence, also, of crystal genes.

Another thought might be to consider the specification of protein-like polymers. One can at least imagine a zeolite, for example, with a propensity to adsorb, say, two kinds of monomer units in two kinds of holes arrayed on its 'informational' surfaces—figure 11 (*c*) shows complex patterns of such holes. These monomers might be induced to polymerize *in situ* so as to make a copolymer with a specified sequence capable, perhaps, of folding into a complex two-dimensional object. There would be no need for as many as twenty units, as in proteins: RNA with only four units can fold in wonderfully elaborate ways capable of specific binding and catalysis. Although protein-like, in so far as they could fold in information-dependent ways, I am not imagining that molecules designed to work with, say, zeolites would be structurally much like either proteins or polynucleotides. Now crystallites with such polymer-forming talents and which were growing, say, in a porous medium, might then be more or less successful according to the kinds of polymers with which they were surrounding themselves—because these polymers could act as protective materials, or could catalyse the breakdown of other organic molecules which were growth inhibitors...

The above fantasies are of Darwinian systems somewhat along the lines of natural organisms in so far as the processes of genotype replication, expression and selection are taking place under more or less the same general conditions of temperature solvent and so on. An advantage of Darwinian systems with no pretensions to being so life-like would be that *each* of these general conditions could be distinct.

Let us suppose now that we have found a batch of some genetic crystal which can produce a promising type of polymer. We would take seeds from this to grow up, say, 100 tubes, each a more or less separate clone from one or a few of the initial crystallites. In this part of the procedure we would be using *replication conditions.* We would now

take samples from each of the tubes and apply, now, *expression conditions*—e.g. organic polymerizing conditions—to make samples of polymers to be tested for (say) catalytic properties, under *selection conditions.*

By using *samples* in this way the critical replicating conditions need never be disturbed: for example the whole replication cycle might take place at temperatures needed for flux-growing barium ferrites (around 1200°C) with supersaturation levels being carefully maintained from generation to generation, even though the testing procedures were performed at room temperature. It would not matter if, say on cooling, the test samples permanently lost their ability to replicate, so long as their informational defect (e.g. polytype) structures were not so seriously deranged as to no longer have any specific effects.

Returning to our thought experiment: tube no. 67, let us say, is found to have contained the most effective genetic crystallites. The residue of this tube is then used to seed a further 100 tubes as before... Supposing that the mutation rate (controlled through supersaturation levels) was such that at each stage there would be about 10 slightly different modifications to choose from, then after 100 such cycles we could have chosen one from 10^{100} possibilities. (This is admittedly a rather formal calculation, but it illustrates again the speed with which cumulative selection can arrive at 'the impossible'.)

Of course, as discussed earlier, it is not so much the *amount* of ordering that selection can bring about which is remarkable (the condensation of a vapour is far more impressive in this respect), it is the *kind.* Reproducing/mutating systems can ride an evolutionary landscape, a landscape of machines, of 'systems whose parts co-operate'.

5.3. *An intermediate goal*

To be able to take a single crystallite with a given arbitrary defect structure—and breed from it vast numbers of crystallites with more or less exactly the same structure is the starting skill for any serious evolution experiments of the kind we have been imagining. It would also be a test of the idea that, for example, some particular complex polytype had arisen from a copying process (and not, say, from a post-growth transformation).

The copying test, however, need not be as rigorous as this. Even a badly mutated polytype structure, might still be discernible, by examination of the seed and the products, as having been derived by inheritance from that seed. More to the point, perhaps, even just to be able to prejudice the character of the polytype structures in a product by seeding might be important for the manufacture of materials with useful polytype-dependent properties.

Some progress has been made in the direction of specific seeding (Tairov and Tsvetkov 1984), but not much. No doubt it is difficult to get seeds to re-grow, as discussed at the end of the previous section; and other ways of controlling the kinds and general proportions of different intergrowths have been preferred. No doubt it is easier to alter temperatures, proportions of reactants, amounts of impurities, and so on, than to have to deal with notoriously fickle and fragile seedlings. But the amount of control which can be exerted on the microstructure of a crystal by altering general conditions is necessarily limited by the number of variables which can be adjusted. Burdett (1987) has commented that in solid state chemistry 'Synthetic techniques are at the Neanderthal stage compared to those used in organic synthesis'. Specific seeding of defect structures will surely be a major part of the emerging post-Neanderthal phase, along with improved control of crystal growth directions and cleavage characteristics.

The prize will be, first, a much better control of crystal microstructure with then the possibility of making artificial Darwinian systems ('artificial life' as Langton (1987) would call it). That should be motivation enough.

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