

GENERAL NATURE OF THE GENETIC CODE FOR PROTEINS

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THERE is now a mass of indirect evidence which suggests that the amino-acid sequence along the polypeptide chain of a protein is determined by the sequence of the bases along some particular part of the nucleic acid of the genetic material. Since there are twenty common amino-acids found throughout Nature, but only four common bases, it has often been surmised that the sequence of the four bases is in some way a code for the sequence of the amino-acids. In this article we report genetic experiments which, together with the work of others, suggest that the genetic code is of the following general type:

(a) A group of three bases (or, less likely, a multiple of three bases) codes one amino-acid.

(b) The code is not of the overlapping type (see Fig. 1).

(c) The sequence of the bases is read from a fixed starting point. This determines how the long sequences of bases are to be correctly read off as triplets. There are no special 'commas' to show how to select the right triplets. If the starting point is displaced by one base, then the reading into triplets is displaced, and thus becomes incorrect.

(d) The code is probably 'degenerate': that is, in general, one particular amino-acid can be coded by one of several triplets of bases.

The Reading of the Code

The evidence that the genetic code is not overlapping (see Fig. 1) does not come from our work, but from that of Wittmann¹ and of Tsugita and Fraenkel-Conrat² on the mutants of tobacco mosaic virus produced by nitrous acid. In an overlapping triplet code, an alteration to one base will in general change three adjacent amino-acids in the polypeptide chain. Their work on the alterations produced in the protein of the virus show that usually only one amino-acid at a time is changed as a result of treating the ribonucleic acid (RNA) of the virus with nitrous acid. In the rarer cases where two amino-acids are altered (owing presumably to two separate deaminations by the nitrous acid on one piece of RNA), the altered amino-acids are not in adjacent positions in the polypeptide chain.

Brenner³ had previously shown that, if the code were universal (that is, the same throughout Nature), then all overlapping triplet codes were impossible. Moreover, all the abnormal human haemoglobins studied in detail⁴ show only single amino-acid changes. The newer experimental results essentially rule out all simple codes of the overlapping type.

If the code is not overlapping, then there must be some arrangement to show how to select the correct triplets (or quadruplets, or whatever it may be) along the continuous sequence of bases. One obvious suggestion is that, say, every fourth base is a 'comma'. Another idea is that certain triplets make 'sense', whereas others make 'nonsense', as in the comma-free

codes of Crick, Griffith and Orgel⁵. Alternatively, the correct choice may be made by starting at a fixed point and working along the sequence of bases three (or four, or whatever) at a time. It is this possibility which we now favour.

Experimental Results

Our genetic experiments have been carried out on the *B* cistron of the r_{II} region of the bacteriophage *T4*, which attacks strains of *Escherichia coli*. This is the system so brilliantly exploited by Benzer^{6,7}. The r_{II} region consists of two adjacent genes, or 'cistrons', called cistron *A* and cistron *B*. The wild-type phage will grow on both *E. coli B* (here called *B*) and on *E. coli K12* (λ) (here called *K*), but a phage which has lost the function of either gene will not grow on *K*. Such a phage produces an *r* plaque on *B*. Many point mutations of the genes are known which behave in this way. Deletions of part of the region are also found. Other mutations, known as 'leaky', show partial function; that is, they will grow on *K* but their plaque-type on *B* is not truly wild. We report here our work on the mutant *P 13* (now re-named *FC 0*) in the *B1* segment of the *B* cistron. This mutant was originally produced by the action of proflavin⁸.

We⁹ have previously argued that acridines such as proflavin act as mutagens because they add or delete a base or bases. The most striking evidence in favour of this is that mutants produced by acridines are seldom 'leaky'; they are almost always completely lacking in the function of the gene. Since our note was published, experimental data from two sources have been added to our previous evidence: (1) we have examined a set of 126 r_{II} mutants made with acridine yellow; of these only 6 are leaky (typically about half the mutants made with base analogues are leaky); (2) Streisinger¹⁰ has found that whereas mutants of the lysozyme of phage *T4* produced by base-analogues are usually leaky, all lysozyme mutants produced by proflavin are negative, that is, the function is completely lacking.

If an acridine mutant is produced by, say, adding a base, it should revert to 'wild-type' by deleting a base. Our work on revertants of *FC 0* shows that it usually

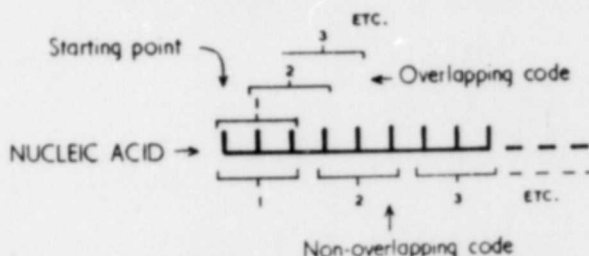


Fig. 1. To show the difference between an overlapping code and a non-overlapping code. The short vertical lines represent the bases of the nucleic acid. The case illustrated is for a triplet code

reverts not by reversing the original mutation but by producing a second mutation at a nearby point on the genetic map. That is, by a 'suppressor' in the same gene. In one case (or possibly two cases) it may have reverted back to true wild, but in at least 18 other cases the 'wild type' produced was really a double mutant with a 'wild' phenotype. Other workers¹¹ have found a similar phenomenon with r_{II} mutants, and Jinks¹² has made a detailed analysis of suppressors in the h_{III} gene.

The genetic map of these 18 suppressors of $FC 0$ is shown in Fig. 2, line *a*. It will be seen that they all fall in the $B1$ segment of the gene, though not all of them are very close to $FC 0$. They scatter over a region about, say, one-tenth the size of the B cistron. Not all are at different sites. We have found eight sites in all, but most of them fall into or near two close clusters of sites.

In all cases the suppressor was a non-leaky r . That is, it gave an r plaque on B and would not grow on K . This is the phenotype shown by a complete deletion of the gene, and shows that the function is lacking. The only possible exception was one case where the suppressor appeared to back-mutate so fast that we could not study it.

Each suppressor, as we have said, fails to grow on K . Reversion of each can therefore be studied by the same procedure used for $FC 0$. In a few cases these mutants apparently revert to the original wild-type, but usually they revert by forming a double mutant. Fig. 2, lines *b-g*, shows the mutants pro-

duced as suppressors of these suppressors. Again all these new suppressors are non-leaky r mutants, and all map within the $B1$ segment for one site in the $B2$ segment.

Once again we have repeated the process on two of the new suppressors, with the same general results, as shown in Fig. 2, lines *i* and *j*.

All these mutants, except the original $FC 0$, occurred spontaneously. We have, however, produced one set (as suppressors of $FC 7$) using acridine yellow as a mutagen. The spectrum of suppressors we get (see Fig. 2, line *h*) is crudely similar to the spontaneous spectrum, and all the mutants are non-leaky r 's. We have also tested a (small) selection of all our mutants and shown that their reversion-rates are increased by acridine yellow.

Thus in all we have about eighty independent r mutants, all suppressors of $FC 0$, or suppressors of suppressors, or suppressors of suppressors of suppressors. They all fall within a limited region of the gene and they are all non-leaky r mutants.

The double mutants (which contain a mutation plus its suppressor) which plate on K have a variety of plaque types on B . Some are indistinguishable from wild, some can be distinguished from wild with difficulty, while others are easily distinguishable and produce plaques rather like r .

We have checked in a few cases that the phenomenon is quite distinct from 'complementation', since the two mutants which separately are phenotypically r , and together are wild or pseudo-wild,

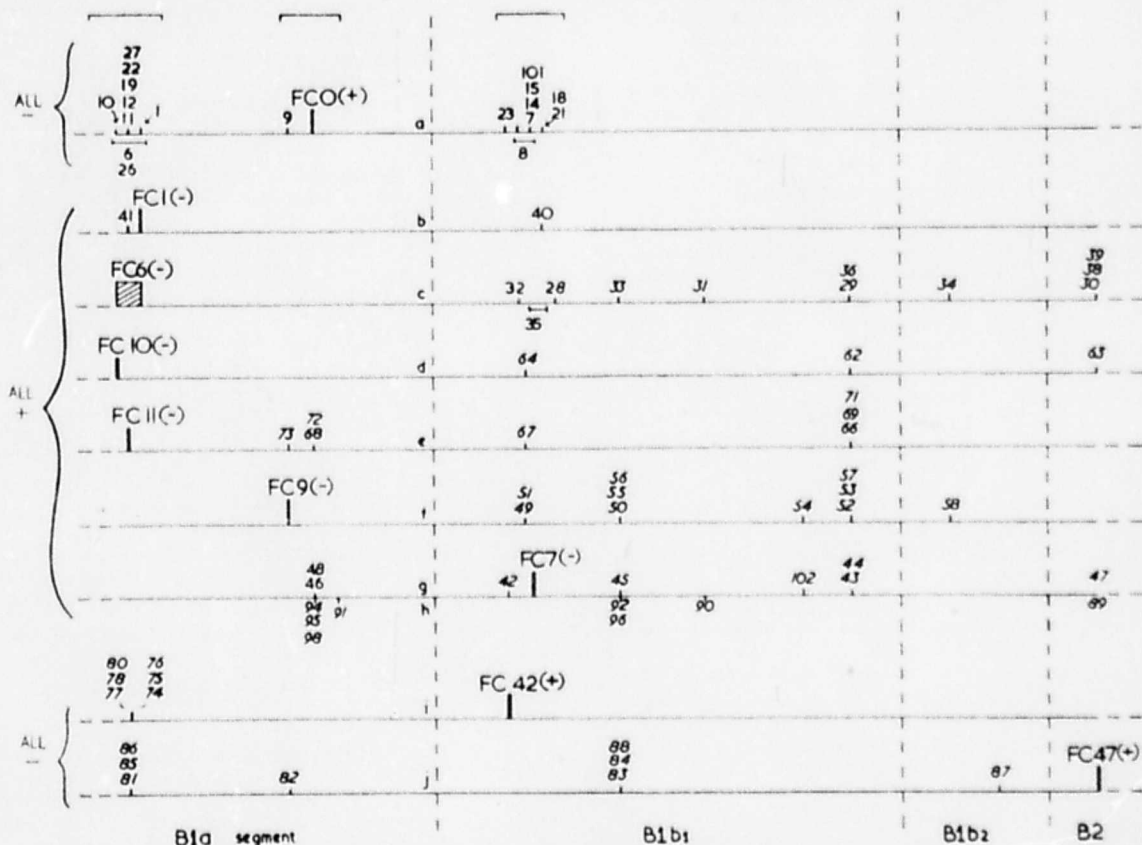


Fig. 2. A tentative map—only very roughly to scale—of the left-hand end of the B cistron, showing the position of the FC family of mutants. The order of sites within the regions covered by brackets (at the top of the figure) is not known. Mutants in italics have only been located approximately. Each line represents the suppressors picked up from one mutant, namely, that marked on the line in bold figures.

must be put together in the same piece of genetic material. A simultaneous infection of *K* by the two mutants in separate viruses will not do.

The Explanation in Outline

Our explanation of all these facts is based on the theory set out at the beginning of this article. Although we have no direct evidence that the *B* cistron produces a polypeptide chain (probably through an RNA intermediate), in what follows we shall assume this to be so. To fix ideas, we imagine that the string of nucleotide bases is read, triplet by triplet, from a starting point on the left of the *B* cistron. We now suppose that, for example, the mutant *FC 0* was produced by the insertion of an additional base at the *FC 0* site will mean that the reading of all the triplets to the right of *FC 0* will be shifted along one base, and will therefore be incorrect. Thus the amino-acid sequence of the protein which the *B* cistron is presumed to produce will be completely altered from that point onwards. This explains why the function of the gene is lacking. To simplify the explanation, we now postulate that a suppressor of *FC 0* (for example, *FC 1*) is formed by deleting a base. Thus when the *FC 1* mutation is present by itself, all triplets to the right of *FC 1* will be read incorrectly and thus the function will be absent. However, when both mutations are present in the same piece of DNA, as in the pseudo-wild double mutant *FC (0 + 1)*, then although the reading of triplets between *FC 0* and *FC 1* will be altered, the original reading will be restored to the rest of the gene. This could explain why such double mutants do not always have a true wild phenotype but are often pseudo-wild, since on our theory a small length of their amino-acid sequence is different from that of the wild-type.

For convenience we have designated our original mutant *FC 0* by the symbol + (this choice is a pure convention at this stage) which we have so far considered as the addition of a single base. The suppressors of *FC 0* have therefore been designated -. The suppressors of these suppressors have in the same way been labelled as +, and the suppressors of these last sets have again been labelled - (see Fig. 2).

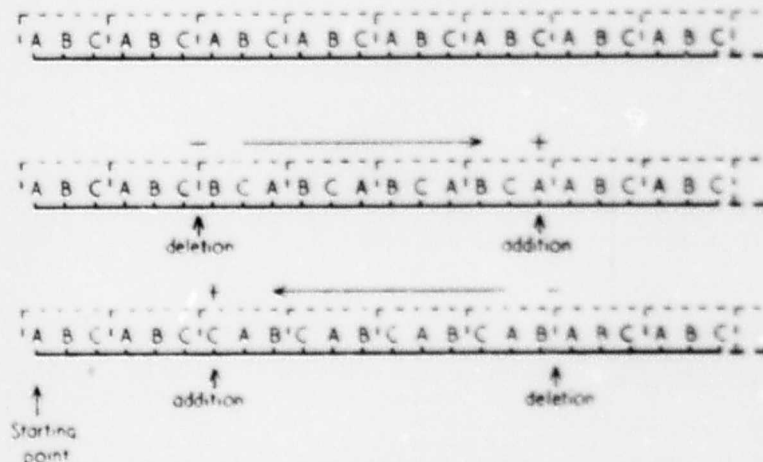


Fig. 3. To show that our convention for arrows is consistent. The letters A, B and C each represent a different base of the nucleic acid. For simplicity a repeating sequence of bases, ABC, is shown. (This would code for a polypeptide for which every amino-acid was the same.) A triplet code is assumed. The dotted lines represent the 'boundary reading frame' implying that the sequence is read in sets of three starting on the left.

Double Mutants

We can now ask: What is the character of any double mutant we like to form by putting together in the same gene any pair of mutants from our set of about eighty? Obviously, in some cases we already know the answer, since some combinations of a + with a - were formed in order to isolate the mutants. But, by definition, no pair consisting of one + with another + has been obtained in this way, and there are many combinations of + with - not so far tested.

Now our theory clearly predicts that all combinations of the type + with + (or - with -) should give an *r* phenotype and not plate on *K*. We have put together 14 such pairs of mutants in the cases listed in Table 1 and found this prediction confirmed.

Table 1. DOUBLE MUTANTS HAVING THE *r* PHENOTYPE

- With -	+ With +	
<i>FC (1 + 21)</i>	<i>FC (0 + 58)</i>	<i>FC (40 + 67)</i>
<i>FC (23 + 21)</i>	<i>FC (0 + 38)</i>	<i>FC (40 + 59)</i>
<i>FC (1 + 23)</i>	<i>FC (0 + 40)</i>	<i>FC (40 + 55)</i>
<i>FC (1 + 9)</i>	<i>FC (0 + 55)</i>	<i>FC (40 + 54)</i>
	<i>FC (0 + 54)</i>	<i>FC (40 + 38)</i>

At first sight one would expect that all combinations of the type (+ with -) would be wild or pseudo-wild, but the situation is a little more intricate than that, and must be considered more closely. This springs from the obvious fact that if the code is made of triplets, any long sequence of bases can be read correctly in one way, but incorrectly (by starting at the wrong point) in two different ways, depending whether the 'reading frame' is shifted one place to the right or one place to the left.

If we symbolize a shift, by one place, of the reading frame in one direction by \rightarrow and in the opposite direction by \leftarrow , then we can establish the convention that our + is always at the head of the arrow, and our - at the tail. This is illustrated in Fig. 3.

We must now ask: Why do our suppressors not extend over the whole of the gene? The simplest postulate to make is that the shift of the reading frame produces some triplets the reading of which is 'unacceptable'; for example, they may be 'nonsense', or stand for 'end the chain', or be unacceptable in some other way due to the complications of protein structure. This means that a suppressor of, say, *FC 0* must be within a region such that no 'unacceptable' triplet is produced by the shift in the reading frame between *FC 0* and its suppressor. But, cleverly, since for any sequence there are two possible mis-readings, we might expect that the 'unacceptable' triplets produced by a \rightarrow shift would occur in different places on the map from those produced by a \leftarrow shift.

Examination of the spectra of suppressors (in each case putting in the arrows \rightarrow or \leftarrow) suggests that while the \rightarrow shift is acceptable anywhere within our region (though not outside it) the shift \leftarrow , starting from points near *FC 0*, is acceptable over only a more limited stretch. This is shown in Fig. 4. Somewhere in the left part of our region, between *FC 0* or *FC 9* and the *FC 1* group, there must be one or more unacceptable triplets when a \leftarrow shift is made; similarly for

the region to the right of the *FC* 21 cluster. Thus we predict that a combination of a + with a - will be wild or pseudo-wild if it involves a → shift, but that such pairs involving a ← shift will be phenotypically *r* if the arrow crosses one or more of the forbidden places, since then an unacceptable triplet will be produced.

Table 2. DOUBLE MUTANTS OF THE TYPE (+ WITH -)

	<i>FC</i> 41	<i>FC</i> 0	<i>FC</i> 40	<i>FC</i> 42	<i>FC</i> 58*	<i>FC</i> 63	<i>FC</i> 38
<i>FC</i> 1	W	W	W	W	W	W	W
<i>FC</i> 86	W	W	W	W	W	W	W
<i>FC</i> 9	<i>r</i>	W	W	W	W	W	W
<i>FC</i> 82	<i>r</i>	W	W	W	W	W	W
<i>FC</i> 21	<i>r</i>	W	W	W	W	W	W
<i>FC</i> 88	<i>r</i>	<i>r</i>	W	W	W	W	W
<i>FC</i> 87	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	W	W	W

W, wild or pseudo-wild phenotype; *r*, wild or pseudo-wild combination used to isolate the suppressor; *r*, *r* phenotype.

* Double mutants formed with *FC* 58 (or with *FC* 34) give sharp plaques on *K*.

We have tested this prediction in the 28 cases shown in Table 2. We expected 19 of these to be wild, or pseudo-wild, and 9 of them to have the *r* phenotype. In all cases our prediction was correct. We regard this as a striking confirmation of our theory. It may be of interest that the theory was constructed before these particular experimental results were obtained.

Rigorous Statement of the Theory

So far we have spoken as if the evidence supported a triplet code, but this was simply for illustration. Exactly the same results would be obtained if the code operated with groups of, say, 5 bases. Moreover, our symbols + and - must not be taken to mean literally the addition or subtraction of a single base.

It is easy to see that our symbolism is more exactly as follows:

$$+ \text{ represents } +m, \text{ modulo } n$$

$$- \text{ represents } -m, \text{ modulo } n$$

where *n* (a positive integer) is the coding ratio (that is, the number of bases which code one amino-acid) and *m* is any integral number of bases, positive or negative.

It can also be seen that our choice of reading direction is arbitrary, and that the same results (to a first approximation) would be obtained in whichever direction the genetic material was read, that is, whether the starting point is on the right or the left of the gene, as conventionally drawn.

Triple Mutants and the Coding Ratio

The somewhat abstract description given above is necessary for generality, but fortunately we have convincing evidence that the coding ratio is in fact 3 or a multiple of 3.

This we have obtained by constructing triple mutants of the form (+ with + with +) or (- with - with -). One must be careful not to make shifts

Table 3. TRIPLE MUTANTS HAVING A WILD OR PSEUDO-WILD PHENOTYPE

<i>FC</i> (0 + 40 + 38)
<i>FC</i> (0 + 40 + 58)
<i>FC</i> (0 + 40 + 57)
<i>FC</i> (0 + 40 + 54)
<i>FC</i> (0 + 40 + 55)
<i>FC</i> (1 + 21 + 23)

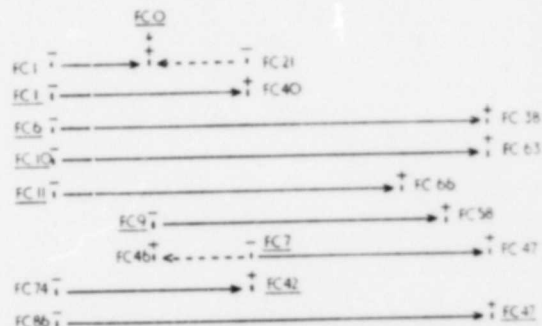


Fig. 4. A simplified version of the genetic map of Fig. 2. Each line corresponds to the suppressor from one mutant, here underlined. The arrows show the range over which suppressors have so far been found, the extreme mutants being named on the map. Arrows to the right are shown solid, arrows to the left dotted.

across the 'unacceptable' regions for the ← shifts, but these we can avoid by a proper choice of mutants.

We have so far examined the six cases listed in Table 3 and in all cases the triples are wild or pseudo-wild.

The rather striking nature of this result can be seen by considering one of them, for example, the triple (*FC* 0 with *FC* 40 with *FC* 38). These three mutants are, by themselves, all of like type (+). We can say this not merely from the way in which they were obtained, but because each of them, when combined with our mutant *FC* 9 (—), gives the wild, or pseudo-wild phenotype. However, either singly or together in pairs they have an *r* phenotype, and will not grow on *K*. That is, the function of the gene is absent. Nevertheless, the combination of all three in the same gene partly restores the function and produces a pseudo-wild phage which grows on *K*.

This is exactly what one would expect, in favourable cases, if the coding ratio were 3 or a multiple of 3.

Our ability to find the coding ratio thus depends on the fact that, in at least one of our composite mutants which are 'wild', at least one amino-acid must have been added to or deleted from the polypeptide chain without disturbing the function of the gene-product too greatly.

This is a very fortunate situation. The fact that we can make these changes and can study so large a region probably comes about because this part of the protein is not essential for its function. That this is so has already been suggested by Champe and Benzer¹³ in their work on complementation in the *r*_{II} region. By a special test (combined infection on *K*, followed by plating on *B*) it is possible to examine the function of the *A* cistron and the *B* cistron separately. A particular deletion, 1589 (see Fig. 5) covers the right-hand end of the *A* cistron and part of the left-hand end of the *B* cistron. Although 1589 abolishes the *A* function, they showed that it allows the *B* function to be expressed to a considerable extent. The region of the *B* cistron deleted by 1589 is that into which all our *FC* mutants fall.

Joining two Genes Together

We have used this deletion to re-inforce our idea that the sequence is read in groups from a fixed starting point. Normally, an alteration confined to the *A* cistron (be it a deletion, an acridine mutant, or any other mutant) does not prevent the expression of the *B* cistron. Conversely, no alteration within the *B* cistron prevents the function of the *A* cistron. This implies that there may be a region between the

two cistrons which separates them and allows their functions to be expressed individually.

We argued that the deletion 1589 will have lost this separating region and that therefore the two (partly damaged) cistrons should have been joined together. Experiments show this to be the case, for now an alteration to the left-hand end of the *A* cistron, if combined with deletion 1589, can prevent the *B* function from appearing. This is shown in Fig. 5. Either the mutant *P43* or *X142* (both of which revert strongly with acridines) will prevent the *B* function when the two cistrons are joined, although both of these mutants are in the *A* cistron. This is also true of *X142 S1*, a suppressor of *X142* (Fig. 5, case *b*). However, the double mutant (*X142* with *X142 S1*), of the type (+ with -), which by itself is pseudo-wild, still has the *B* function when combined with 1589 (Fig. 5, case *c*). We have also tested in this way the 10 deletions listed by Benzer⁷, which fall wholly to the left of 1589. Of these, three (386, 168 and 221) prevent the *B* function (Fig. 5, case *f*), whereas the other seven show it (Fig. 5, case *e*). We surmise that each of these seven has lost a number of bases which is a multiple of 3. There are theoretical reasons for expecting that deletions may not be random in length, but will more often have lost a number of bases equal to an integral multiple of the coding ratio.

It would not surprise us if it were eventually shown that deletion 1589 produces a protein which consists of part of the protein from the *A* cistron and part of that from the *B* cistron, joined together in the same polypeptide chain, and having to some extent the function of the undamaged *B* protein.

Is the Coding Ratio 3 or 6?

It remains to show that the coding ratio is probably 3, rather than a multiple of 3. Previous rather rough estimates^{10,11} of the coding ratio (which are admittedly very unreliable) might suggest that the coding ratio is not far from 6. This would imply, on our theory, that the alteration in *FC 0* was not to one base, but to two bases (or, more correctly, to an even number of bases).

We have some additional evidence which suggests that this is unlikely. First, in our set of 126 mutants produced by acridine yellow (referred to earlier) we have four independent mutants which fall at or

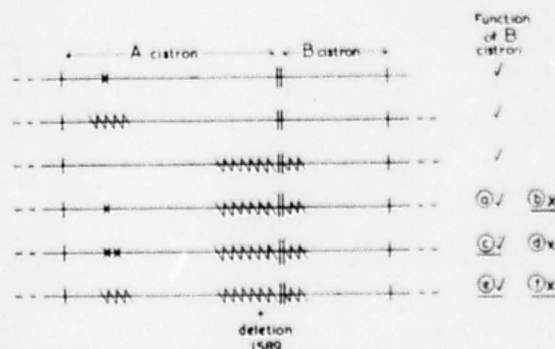


Fig. 5. Summary of the results with deletion 1589. The first two lines show that without 1589 a mutation or a deletion in the *A* cistron does not prevent the *B* cistron from functioning. Deletion 1589 (line 3) also allows the *B* cistron to function. The other cases, in some of which an alteration in the *A* cistron prevents the function of the *B* cistron (when 1589 is also present), are discussed in the text. They have been labelled (a), (b), etc., for convenience of reference, although cases (a) and (d) are not discussed in this paper. ✓ implies function; × implies no function.

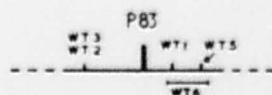


Fig. 6. Genetic map of *P83* and its suppressors, *WT1*, etc. The region falls within segment *B9a* near the right-hand end of the *B* cistron. It is not yet known which way round the map is in relation to the other figures.

close to the *FC 9* site. By a suitable choice of partners, we have been able to show that two are + and two are -. Secondly, we have two mutants (*X146* and *X225*), produced by hydrazine¹², which fall on or near the site *FC 30*. These we have been able to show are both of type -.

Thus unless both acridines and hydrazine usually delete (or add) an even number of bases, this evidence supports a coding ratio of 3. However, as the action of these mutagens is not understood in detail, we cannot be certain that the coding ratio is not 6, although 3 seems more likely.

We have preliminary results which show that other acridine mutants often revert by means of close suppressors, but it is too sketchy to report here. A tentative map of some suppressors of *P 83*, a mutant at the other end of the *B* cistron, in segment *B 9a*, is shown in Fig. 6. They occur within a shorter region than the suppressors of *FC 0*, covering a distance of about one-twentieth of the *B* cistron. The double mutant *WT (2 + 5)* has the *r* phenotype, as expected.

Is the Code Degenerate?

If the code is a triplet code, there are 64 ($4 \times 4 \times 4$) possible triplets. Our results suggest that it is unlikely that only 20 of these represent the 20 amino-acids and that the remaining 44 are nonsense. If this were the case, the region over which suppressors of the *FC 0* family occur (perhaps a quarter of the *B* cistron) should be very much smaller than we observe, since a shift of frame should then, by chance, produce a nonsense reading at a much closer distance. This argument depends on the size of the protein which we have assumed the *B* cistron to produce. We do not know this, but the length of the cistron suggests that the protein may contain about 290 amino-acids. Thus the code is probably 'degenerate', that is, in general more than one triplet codes for each amino-acid. It is well known that if this were so, one could also account for the major dilemma of the coding problem, namely, that while the base composition of the DNA can be very different in different micro-organisms, the amino-acid composition of their proteins only changes by a moderate amount¹³. However, exactly how many triplets code amino-acids and how many have other functions we are unable to say.

Future Developments

Our theory leads to one very clear prediction. Suppose one could examine the amino-acid sequence of the 'pseudo-wild' protein produced by one of our double mutants of the (+ with -) type. Conventional theory suggests that since the gene is only altered in two places, only two amino-acids would be changed. Our theory, on the other hand, predicts that a string of amino-acids would be altered, covering the region of the polypeptide chain corresponding to the region on the gene between the two mutants. A good protein on which to test this hypothesis is

the lysozyme of the phage, at present being studied chemically by Dreyer¹⁷ and genetically by Streisinger¹⁸.

At the recent Biochemical Congress at Moscow, the audience of Symposium I was startled by the announcement of Nirenberg that he and Matthaei¹⁹ had produced polyphenylalanine (that is, a polypeptide all the residues of which are phenylalanine) by adding polyuridylic acid (that is, an RNA the bases of which are all uracil) to a cell-free system which can synthesize protein. This implies that a sequence of uracils codes for phenylalanine, and our work suggests that it is probably a triplet of uracils.

It is possible by various devices, either chemical or enzymatic, to synthesize polyribonucleotides with defined or partly defined sequences. If these, too, will produce specific polypeptides, the coding problem is wide open for experimental attack, and in fact many laboratories, including our own, are already working on the problem. If the coding ratio is indeed 3, as our results suggest, and if the code is the same throughout Nature, then the genetic code may well be solved within a year.

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SCIENCE AND WORLD AFFAIRS

THE Seventh Pugwash Conference on Science and World Affairs was held at Stowe, Vermont, during September 5-9. Forty-one scientists from twelve countries attended the Conference*.

This Conference had as its theme "International Co-operation in Pure and Applied Science". The previous conferences have been chiefly concerned with ways of preventing the misuse of science in the wholesale destruction of mankind. In this Conference at Stowe, constructive international co-operation in science was discussed, because it is a way to create trust between nations, a trust which develops from common interests and from experience in working together.

Science misused by nations to foster their competitive interests as world powers makes possible the destruction of mankind. Science used co-operatively by all nations for the increase of human knowledge and the improvement of man's productive capacity can give all men on Earth a satisfactory and worthwhile life. Scientists bear a responsibility both to foster the constructive use of science and to help in preventing its destructive use.

The deliberations of the Conference were carried out in plenary sessions and in meetings of working groups. Similar suggestions for co-operative research

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activities arose independently from different working groups, and this is reflected in several places in the statement. This is a welcome indication of the essential unity in science. The discussions were carried on in a spirit of friendly co-operation, and full agreement was reached by the entire Conference on the suggestions enumerated here.

(I) Co-operation in the Earth Sciences

The planet Earth is the common abode of all humans. They have a common interest, both intellectual and practical, in increasing the knowledge of the structure and dynamics of the Earth.

The following proposals were made by the Conference.

- (A) *A survey of the entire ocean in three dimensions.*
 (1) *The ocean floor.* An international programme was proposed to develop a detailed map of the floor of the world ocean, including sub-bottom reflecting layers.
 (2) *Waters of the ocean.* An international programme should be devised to survey and map the three-dimensional distribution of temperatures, salinity, density, dissolved oxygen, and nutrient salts, under average conditions, of the ocean and synoptic surveys to develop the broad picture of seasonal and shorter-period changes in more limited areas, as well as the study of the interactions among the major bodies of water in the ocean.

(3) *Ocean life.* An international survey and mapping showing the major biological provinces of the ocean and determination of the fertility of the waters at all levels in the food chain and the standing crop of food materials available for human use should be undertaken.

(B) *Earth's crust and mantle. Deep drilling programme.* The objective of drilling through the

Earth's crust to the mantle at selected points around the globe presents many unsolved technical problems which call for international collaboration. It was agreed, therefore, that the calling of an international conference on these problems is an urgent first step.

(C) *Total environmental forecasting.* An international conference should be called to consider and to organize the establishment of a world-wide network of radio-telemetering observational buoys. This system of buoys would render continuous reports on atmospheric conditions and so contribute to the completion of the world weather map. It would also continuously monitor the energy and water vapour energy exchange between the ocean and the atmosphere, and would observe the changes in the flow of ocean currents in three dimensions. Over a sufficiently long time-period, such a network of buoys would help to assign reliable values to the rate of overturn of the ocean as a whole, a key problem in both climatological forecasts and in the safe disposal of radioactive wastes at sea. The hydrographic offices of the major maritime nations, as well as the World Meteorological Organization, should be encouraged to stimulate such a programme.

(D) *Resources.* (1) *Fresh water.* The rising world population and the increasing concentration of that population in metropolitan centres is already pressing on the water resources easily available for direct human consumption, for industrial purposes, and for agriculture. It was agreed that an international conference should be called to consider the organization of an international hydrological decade for the study of the many unknowns that surround this ominous development.

(2) *Living resources of the ocean.* Acre per acre the oceans to-day sustain at least as large a plant crop on the average as does the land, yet man now gets only about 1 per cent of his food requirements from the sea. The oceans, therefore, offer a means for the rapid solution of the protein deficiency afflicting two-thirds of the world population. It is apparent that these resources can best be exploited to this end through international co-operation. The ultimate aim should be to elevate the fishing industry from a hunting industry to an agricultural technology.

(3) *Mineral resources of the ocean floor.* Recent investigations of the ocean floor show a vast reserve of minerals, especially nickel, cobalt, copper and manganese. By means of bottom-photography organized on a world-wide basis, the potentiality of this reserve may be more fully assessed. The necessary observational programme could be organized by the Scientific Commission for Oceanographic Research.

(4) *Natural catastrophes.* Earthquakes, tsunamis, volcanic eruptions, hurricanes and tornadoes constitute the principal hazards of this kind.

With respect to the first three, a better international seismological network, including better instrumentation and distribution of stations, is required. More detailed studies of hurricanes and tornadoes would reveal whether or not man can exert some control over these phenomena.

To implement these programmes, it is recommended that in so far as possible existing international organizations be the means of furthering these programmes.

(II) Co-operation in Space Research

Though the Conference felt that there should be close co-operation in space research it should be real-

ized that complete co-operation in this field, as in some others, will become possible only when the arms race is ended, international tensions are reduced, complete and general disarmament becomes a reality, and the need for secrecy disappears. But certain advances in the presently established co-operation in space are possible now, and certain others could be studied now with the hope of realization in the not too distant future.

(A) First, an increase in the exchange of scientific information in areas such as the physics of space and the effects of the space environment on life is recommended. It is further recommended that periodic international symposia be devoted to such subjects.

(B) The exchange of methods, and of information on instruments, for scientific space studies which have no military importance is also recommended.

(C) The orderly assignment and use of radio frequencies in space should be encouraged. Strong support should be given to the initiative in this direction taken by the International Telecommunications Union, and it is to be hoped that a final solution can be reached within two years.

(D) The expansion of existing systems of satellite tracking stations is recommended. Bilateral agreements between different nations, including (within the limits of military security) an agreement between the United States and the U.S.S.R., on the common use of tracking stations; such a bilateral agreement could serve as the first step in this direction.

(E) International agreement should be reached on a co-ordinated programme for the use of rocket and satellite during the Quiet Sun Year (planned for the second half of 1962).

(F) Similar agreement should be reached on co-operation in the use of rockets and satellites in the projected world magnetic survey. This agreement should include arrangements for simultaneous observation from satellites launched into different orbits by different nations. This co-operation could be organized in the framework of the Committee on Space Research.

(G) The desirability of international world-wide systems of communications satellites and of meteorological satellites is endorsed by the Conference, since these would clearly be in the interests of all mankind. It is realized that certain difficulties now stand in the way, but it is to be hoped that the Governments of the United States and the U.S.S.R., as well as of other nations embarking on rocket and satellite programmes, will undertake a common study of the ways to overcome them.

(H) It is recommended that co-operation should be established in the instrumental study of the Moon, and also that the basic principles of the International Antarctic Treaty be applied to the Moon and other cosmic bodies.

(I) The calling of an international conference or symposium to consider how to avoid the biological and radioactive contamination of extra-terrestrial bodies is strongly urged.

(III) Co-operation in the Life Sciences

Among the many fields of biology in which international co-operation is possible, some are particularly well suited by their nature and importance for combined efforts. These, which relate especially to the promotion of human welfare, have been given primary concern by the Conference.