Book Reviews

PERSPECTIVE ON THE CODE

The Biological Code

By M. Ycas. (North-Holland Research Monographs—Frontiers of Biology, Vol. 12.) Pp. xiii+360. (North-Holland: Amsterdam and London, 1969.) 89*s*.

I AM sure that most people will agree that the most important advance in our understanding of biology in the first half of the sixties was the solution of the genetic code. How this was achieved is the subject of Dr M. Ycas's monograph. But it was in the early days of coding, the 1950s, that the incubation of many ideas, often unpublished, occurred; this was necessary for the emergence of a theoretical framework on which the more spectacular discoveries of this decade could be placed. It is difficult to know where the ideas of coding started, but in 1945 Beadle had arrived at the conclusion that the function of one protein depended on the integrity of one gene. The intervening period up to 1953, when the structure of DNA was proposed by Watson and Crick, saw a significant advance in ideas when Dounce, in 1952, indicated that the relationship between a protein and nucleic acid might simply be a linear one: that nucleotide sequence might govern amino-acid sequence.

Precise thoughts about the coding problem really only started in 1954, when Gamow, to whose memory Ycas's book is appropriately dedicated, published his "diamond" code. The ideas here were that each amino-acid could fit into a cavity in a double-helical DNA molecule, with a specificity determined by the bases around that cavity. The precise interactions were unknown, but this proposed code was fully overlapping: that is, for each successive amino-acid, the DNA template had to be moved one base-pair along. This code could cope with only twenty amino-acids—fewer than were then generally supposed to be coded by DNA. It seems that as early as 1953, Watson and Crick had privately selected a list—and what we now know is the correct list—of just twenty coded amino-acids. But it was not until the early 1960s, with the code almost solved, that the standard twenty were generally agreed upon. At a meeting, for example, in 1959, when asked, "What about an insane protein like poly-D-glutamic acid?", Crick replied, "Sir, poly-D-glutamic acid is not a protein!". The importance of Gamow's initiative in guessing at the code was his hope that one might be able to deduce the nature, and perhaps the details, of the genetic code without knowing the biochemical pathway relating the two. Fortuitously, this did not turn out to be the case.

The coding game at this time was principally one for numerologists, finding ways in which four bases could be used to code for about twenty amino-acids. In 1957, Brenner proved that a fully overlapping code was too restrictive to accommodate the protein sequences then existing. Two other codes, the "combination code" of Gamow and Ycas (1955) and the "comma-less code" of Crick, Griffiths and Orgel (1957), eventually fell by the wayside. Much ingenuity went into their construction. The latter code overcame the difficulty of selecting the correct reading frame in a non-overlapping code. This was achieved by arranging that circular permutations of a codon were nonsense (that is, if CAT.CAT codes for a homo-dipeptide, ATC and TCA cannot code for any amino-acids). This reduced the sixty-four triplets to just twenty—at that time thought to be too good a coincidence not to be true. But a major dilemma with this code is that it did not permit any large variations in DNA base composition without a corresponding change in amino-acid composition—it was later found that different strains of bacteria violate this requirement. And so, by 1959, Crick felt, and stated, that the coding problem was at a very low ebb.

In the meantime, our knowledge of the biosynthesis of proteins on ribosomes was advancing, primarily through the work of Zamecnik and his colleagues. Of particular importance was the discovery of transfer RNA by Hoagland in 1958, a molecule whose existence had been predicted as early as 1955 by Crick (in a note to the RNA Tie Club—a group of Gamow's friends). The actual template for protein synthesis was presumed to be the RNA molecules in ribosomes. But the really major discovery, which opened the biochemical attack on the genetic code, was the finding by Brenner and Gros and their colleagues in 1960 of messenger RNA. Because some 5 per cent of the cellular RNA only is messenger RNA, this meant that around 95 per cent of the RNA had to be discarded (as an information carrier)—at that time a revolutionary concept. Then followed the discovery by Nirenberg and Matthaei that poly U codes for polyphenylalanine, and thence the solution of the code.

In *The Biological Code*, Ycas starts by tracing these early developments in ideas of how genes could code for proteins. There then follows a detailed account of how the code was solved and upon what evidence this solution was based. This evidence often came from rather unrelated approaches, and it is therefore particularly helpful that this wide range of information has been brought together into a well integrated pattern. This includes the evidence from the various point mutations, the elegant story of frame-shift mutations and detailed analyses, arranged in a historical manner, of the important results derived from *in vitro* studies where synthetic messengers were used to code for specific copolypeptides. And, finally, the Nirenberg and Leder binding assay and Khorana's work. A clear understanding of the code necessitates a proper understanding of how proteins are synthesized, how the messenger is punctuated, and the role of the adaptor transfer RNA in this process. After concentrating on these topics, Ycas ends with a discussion of the universal nature of the code, and how it may have evolved. This monograph has a well compiled index and, most usefully, a full list of about nine hundred key papers on which the whole story is based. There are few people who have contributed and watched the code grow up from its infancy. Dr Ycas is one of them. It is indeed fortunate that somebody, so well placed to review the solution of the code, has done the job. There are a few errors which the biochemist may notice, but these should not deter anybody interested in understanding how the code was solved from enjoying this modestly priced book.

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AMERINDIAN SOCIETIES

Man's Rise to Civilization

As Shown by the Indians of North America from Primeval Times to the Coming of the Industrial State. By Peter Farb. Pp. xx+332. (Secker and Warburg: London, May 1969.) 55*s*.

FROM the time of discovery to the present day, American Indians have exercised a strong influence over our minds and imaginations. The appeal of the Wild West begins with playing cowboys and Indians, but goes on to Westerns and thrillers on television. The many facets of their