

always generated by an arithmetic procedure, so that there is nothing random about them, and they are called instead pseudorandom numbers. They may still be treated as random numbers and the acceptability of a particular procedure depends on whether statistical tests detect serious departure from the basic requirement that the numbers should appear to be independent and identically distributed.

Apart from these tests, the distributional properties of the  $\{u_i\}$  are not easy to obtain because of the number-theoretic difficulties involved. Until these are overcome there can be no certainty that there is not hidden in some particular procedure a highly undesirable property, so that when all the work is done some doubts may linger about the validity of the results.

One such undesirable property has been discovered by George Marsaglia (*Proc. US Nat. Acad. Sci.*, **61**, 1; 1968) in the most commonly used procedure, the multiplicative congruential generator. According to this procedure,  $u_i = r_i/m$ , where

$$r_{i+1} = kr_i \text{ modulo } m \quad (i=1,2,\dots)$$

For a binary computer with 32-bit words,  $m=2^{32}$  would be chosen and then  $k$ , so that the necessarily periodic sequence  $\{u_i\}$  has maximum period  $m/4$ , and so that the correlation between the  $u_i$  is kept as small as possible. A possible value for  $k$  might be  $3^{17}$ . In this case the  $u_i$  will be, to a very close approximation, uniformly distributed on the interval (0,1), but will still be quite highly correlated with each other. Marsaglia proves a geometrical result which is particularly illuminating of the non-independence between the  $u_i$ . He shows that all the  $n$ -tuples  $\pi_i = (u_i, u_{i+1}, \dots, u_{i+n-1})$ , ( $i=1,2,\dots$ ), for a particular sequence  $\{u_i\}$  lie on as few as  $(n!m)_n^1$  hyperplanes through the unit cube in  $n$  dimensions. In the case  $m=2^{32}$ ,  $n=10$ ,  $(n!m)_n^1$  lies between 40 and 41, so that in this case the  $\{\pi_i\}$ , far from being dense in the unit 10-cube as we should like them to be, are constrained to lie on as few as 41 hyperplanes. In the case  $m=2^{32}$ ,  $n=3$ ,  $(n!m)_n^1$  lies between 2,952 and 2,953. The procedure will produce 357,913,941 independent points in the unit 3-cube, and then we should expect to need at least  $10^8$  planes to pass through all these points, in contrast to the bound 2,953.

It is difficult to discover such results, even more difficult to work out their effect, and no doubt more difficult still to correct them.

## ENZYMES

### Migrating Hydrogen

from our Enzymology Correspondent

$B_{12}$  enzymes catalyse some very ambitious and ill-understood carbon rearrangements, such as the conversion of methylmalonyl-CoA to succinyl-CoA, and glutamate to  $\beta$ -methylaspartate. Somewhat more modest in their demands on mechanism are the  $B_{12}$ -catalysed hydrogen shifts, of which until recently the only example was the diol dehydrase reaction—the conversion of vicinal diol to aldehyde. In 1965 the category expanded from one to two with the discovery in a clostridial species of ethanolamine deaminase. The clostridium involved can survive on either choline or ethanolamine as its sole source of carbon and energy: the enzyme can convert ethanolamine to acetaldehyde.

A way of purifying the enzyme was published a few months ago (*J. Biol. Chem.*, **243**, 1787; 1968), and a sophisticated mechanistic analysis of the purified enzyme has already appeared (*J. Biol. Chem.*, **244**, 449; 1969). Bernard Babior has investigated the behaviour of ethanolamine dehydrogenase with various deuterated and tritiated substrates, and has also used mass spectroscopy and nuclear magnetic resonance to characterize the isotopic constitution of the products.

The enzyme revealed a large deuterium isotope effect: its rate with 2-aminoethanol-1,1- $D_2$  was 6.8 times lower than with unlabelled aminoethanol. All the deuterium of the labelled substrate turned out to be retained in the product acetaldehyde: when the reaction was carried out with undeuterated substrate in  $D_2O$ , no label appeared in the product acetaldehyde.

If the acetaldehyde produced was promptly reduced to alcohol, trapped as an ester, and then subjected to nuclear magnetic resonance spectroscopy, it was possible to show that the deamination of ethanolamine was accompanied by the migration of one hydrogen from the carbinol carbon of the substrate to the methyl carbon of the product. A subtle piece of kinetics established that the removal of a hydrogen atom from the carbinol carbon is stereospecific: the use of  $^{18}O$  established that the oxygen atom of the substrate becomes the oxygen atom of the product.

So far, so good—the enzyme was behaving as straightforwardly as anyone could wish. But in two respects its performance was less clear-cut. The tritium isotope effect turned out to be about 6—less than the deuterium effect. Furthermore, experiments with mixtures of undeuterated and doubly deuterated substrate gave a definite indication of some intermolecular transfer of hydrogen. In each experiment a small amount of monodeuterated product appeared.

Dr Babior attributes the high deuterium isotope effect to some secondary phenomenon arising from the dideteration of the substrate, and he points out that intermolecular hydrogen transfer has already been observed with the sister enzyme diol dehydrase, where the migrating hydrogen is intermediately bound to enzyme-bound  $B_{12}$  coenzyme. So the overall atomic working of ethanolamine deaminase seems established. But there is clearly some way to go in terms of curly arrows: an attractive mechanism would hinge on the transfer of a hydride ion from the substrate to  $B_{12}$ , followed by its use as a nucleophilic attacking group at the amino carbon of the substrate. But this is as yet pure conjecture.

## MAMMALS

### Name that Mammal

NATURALISTS who like to have the latest guides to the flora and fauna will have to spend four shillings as quickly as possible, for the British Museum (Natural History) has published the second edition of its booklet *The Identification of British Mammals* by C. B. Corbet. Ninety-five species are listed, including eight that have become extinct during the past 2,000 years, and there are keys for identification by external appearance, or using skulls.

The wolf, *Canis lupus*, has been extinct in Britain since the mid-eighteenth century, and the brown bear, *Ursos arctos*, since about the tenth century, whereas