

CYTOLOGY

Organization of Chromosomes

As the genetic code is solved in more and more detail the organization of the genes on the chromosome is also being closely attended to. A model proposed by Callan¹ involves serially repeated nucleotides, or gene copies, which form a terminal master gene with a number of slave genes. This model helps to explain the behaviour of some chromosomes during the reduction division—meiosis—which involves recombination between chromosomes and gives rise to the haploid gametes of diploid organisms.

Cytological evidence shows a very wide variation in the content of DNA—together with protein, the raw material of chromosomes—in the nuclei of gametes of related diploid organisms. This would be explained if chromosomes were multistranded—that is, if they contained several parallel DNA fibres—for some could then contain more fibres than others. This, however, seems unlikely on genetical evidence; multistrandedness does not fit in with semi-conservative DNA replication or with the phenomena of mutation and recombination, all reliably demonstrated long ago. This dissimilarity of DNA content is much more acceptably explained in the light of Keyl's observations^{2,3} of the salivary gland chromosomes of *Chironomus*, a midge. He found that the ratios of DNA contents in homologous bands on the chromosomes conformed to a geometric doubling series 1 : 2, 4, 8 and 16. Keyl⁴ has shown that this is not the result of unequal DNA replication in different bands, and the explanation seems to be that there is a serial replication of genetic units along a chromosome, different amounts of duplication leading to more or less DNA in a chromosome.

Callan¹ developed this idea to propose that each chromosome may have several copies of the same gene of which the terminal one, by virtue of its position, acts as the master gene while the others are slaves. This would explain Callan's own observations of the loops on lampbrush chromosomes of amphibian oocytes. The formation and regression of these loops in different places along the chromosome can be explained if after recombination between chromatids of homologous chromosomes, restricted to the master genes, the nucleotide chains of the slave genes are matched with those of the master gene, so that the slave nucleotides come to lie adjacent to those of the master. If necessary slave nucleotides are corrected so that their nucleotide sequences conform with those of the master. Each slave sequence is matched in turn, and the uncoiling involved would produce the loops which are observed. Only slave genes would act as templates for DNA synthesis, which would occur while they are exposed in the loop. This agrees with the known function of the loops, to produce ribonucleoprotein.

Whitehouse⁵ has pointed out that the necessary separation of neighbouring master genes does not conform with data on recombination in *Aspergillus*

nidulans which imply the presence of only one copy of each master gene, each of which must be in contact with its neighbours. To reconcile this disparity Whitehouse has modified Callan's model and suggests that during meiosis, slave genes are removed from the chromatid by a crossover between the first and last members of the linear series of identical genes. While detached from their chromatid the gene copies are in the form of a closed circle. After crossing over has occurred between homologous chromatids the gene copies are replaced in their chromatid by the same mechanism by which they were removed. In a further modification of Callan's model, he suggests that only one nucleotide chain of a slave gene—the one which is a template for RNA synthesis—is matched to the master gene. Matching would always occur before the slaves function as templates.

This model now has to be tested experimentally. Hotta and Bassel⁶, for example, have electron microscope evidence that part of the DNA of the sperm of the boar, *Sus domesticus*, is circular, and some amphibian nucleoli have been shown to contain circular DNA⁷. Other such evidence should not be difficult to obtain. Chromosomes could be examined, by electron microscopy and special staining techniques, during the reduction division of meiosis, and this might reveal circular DNA molecules in all kinds of organisms. Similar investigations might also give more information about the proposed matching of master to slave in the amphibian lampbrush chromosomes. Further information about the part of these chromosomes which is responsible for the production of the nucleolus, and which is known to replicate many times and produce rings of DNA, could also be obtained. Reliable results from work such as this could be very instructive in substantiating this model for the organization of chromosomes, which is as yet very speculative.

This is an attractive model; it accounts for a variety of apparently contradictory genetical and cytological data. Fincham⁸ has used it to account for the almost continuously graded variation of derivatives of mutable genes—genes which show a much higher frequency of mutation than is usual. As a result of a mutation in the master gene the linear gene series becomes internally heterozygous, for the slaves remain normal. The instability characteristic of mutable genes would be provided by the replacement of defective nucleotides in a master by normal nucleotides from a slave, and this could be brought about by intrachromosomal crossing over and/or correction of master by slave.

¹ Callan, H., *J. Cell Sci.*, **2**, 1 (1967).

² Keyl, H.-G., *Naturwissenschaften*, **51**, 461 (1964).

³ Keyl, H.-G., *Experientia*, **21**, 191 (1965).

⁴ Keyl, H.-G., *Chromosoma*, **17**, 139 (1965).

⁵ Whitehouse, H. L. K., *J. Cell Sci.*, **2**, 9 (1967).

⁶ Hotta, Y., and Bassel, A., *Proc. US Nat. Acad. Sci.*, **53**, 356 (1965).

⁷ Miller, O. L., *J. Cell Biol.*, **23**, 60A (1964).

⁸ Fincham, J. R. S., *Nature*, **215**, 864 (1967).