Metastable Genetic Systems

from a Correspondent

THE EMBO Workshop on metastable genetic systems, which was organised by J. R. S. Fincham (University of Leeds) and R. Ecochard (Ecole Nationale Superiéure Agronomique, Toulouse) in Leeds from September 17 to 21, aimed to review and compare mutable systems in higher plants, and to draw on contributions from others fields so that a synthesis of ideas might be attempted.

The meeting began with a survey of the extensive work on mutable systems in maize, where 'controlling elements' (transposable fragments of DNA detectable only by their effect on loci governing visible characters) suppress the action of the gene with which they are currently associated, giving wild type clonal patches when they detach and become associated with another locus. G. R. K. Sastry (University of Leeds) described the work of Brink on paramutation, and McClintock's experiments with controlling elements were summarised by P. Peterson (Iowa State University of Science and Technology). O. E. Nelson (University of Wisconsin) spoke about his use of a controlling element to detect functionless chromosome segments and thus elucidate chromosome structure. G. Gavazzi (University of Milan) has found that the mutable and paramutagenic functions of the R^{st} (*R*-'stippled') allele can be independently affected by mutagens.

Mutable systems were reported in *Antirrhinum* by B. J. Harrison (John Innes Institute, Norwich) and in *Impatiens* by Sastry. Both systems seem best interpreted as being analogous to those in maize despite the absence so far of apparent transposition. F. Saccardo (CNEN, Centro Studi Nucleari Casaccia, Rome) described a type of mosaicism in pea caused by chromosome imbalance in the presence of dicentrics. A. Deshayes (Laboratoire de Mutagènese, INRA, Dijon) presented a system of variegation in tobacco, where dark and pale green sectors are generally twinned, indicating unequal segregation, possibly of a controlling element, or of a chromosome fragment.

Paramutation is a phenomenon observed principally in maize and also in other plants, whereby one allele is heritably altered by the influence of another. Harrison's *Antirrhinum* system included a new example, and data of A. Durrant (University College of Wales, Aberystwyth) on 'hairy septa' in flax, another. Further cases were described, in tomato, by Ecochard and R. Hagemann (Martin-Luther University, Halle, GDR). Hagemann also reviewed paramutation and suggested that the term be restricted to cases where the effect is specific, more or less permanent, occurring in the majority of vulnerable cells, and is exerted by one false allele on another at the same locus. This definition covered the examples presented at the meeting as well as two established systems in maize, and one in *Oenothera* dating from 1937.

Papers were then presented by workers using animal systems more amenable to molecular analysis than those in higher plants. A particularly attractive model was presented by E. Boncinelli (Istituto Internazionale di Genetica e Biofisica, Naples), who with F. Ritossa is working on the 'bobbed' locus in *Drosophila.* The deleterious 'bobbed' phenotype, which gives a subnormal number of copies of the rRNA cistron, results from deletion in this region. But when heterozygous with a total deletion of the region the 'bobbed' allele increases its rRNA output sufficiently to give a normal phenotype, and exhibits a 'magnified' number of cistron copies. Boncinelli envisages a magnification complement of non-integrated copies of the cistron, superfluous when a wild type allele is present, but brought into operation by integration during meiosis when necessary for survival. The system conforms to a formal definition of paramutation, and provoked speculation as to whether the integration and consequent activation of previously superfluous copies of cistrons might illustrate a form of regulation. At the 'bobbed' locus, and perhaps the 'hairy septa' locus of flax for which Durrant described an apparently similar magnification response to heterozygosity with the null allele, a regulation mechanism may be seen operating normally. Most paramutation systems in plants, where the change is away from wild type, possibly illustrate the same function in aberrant form.

Position effect variegation was described in *Drosophila* by H. J. Becker (University of Munich) and in mouse by B. M. Cattanach (MRC Radiobiology Unit, Harwell), both cases being caused by the spreading effect of neighbouring heterochromatin. Becker showed that determination of presumptive eye cells to become red or pale is clonal, and reversible during the first few cell generations after determination. In the mouse, partial reversion of heterochromatin-mediated inactivation can occur with advancing age. These heterochromatic effects, it seems, may well involve some secondary structure of the DNA, which would need to be heritable.

Work on overall karyotype structure was represented by H. C. Macgregor and S. Mizuno (University of Leicester), who compared salamander species with widely differing DNA contents and found more homology between the slow-renaturing (unique) sequences than between the reiterated sequences. They considered reiterated DNA areas to be control regions. A novel proposal by F. Quetier (University of Paris, Orsay) provided a possible mechanism for narrow bands of highly reiterated DNA, such as spacer DNA in the nucleolus, to act as quantitative regulators for their adjacent single-copy regions. According to the model, each of the repeated sequences is a 'ticket' somehow nullified by a round of transcription and, when no 'tickets' remain, transcription ceases.

The concept of progressive nullification of a series of different alleles emerged from the work of D. de Nettancourt (Centre Commun de Recherches, Brussels), who has found that in a self-incompatibility system governed by the *S* gene in *Lycopersicon peruvianum,* forced selfing is followed by the appearance of a new *S* allele and loss of an existing one. The specificity of the new allele could always be predicted from knowledge of alleles initially present. This work suggests a number of slightly differing sequences all simultaneously present but only one active, with the order of succession preordained. As with the comparable situation in vertebrate immunoglobulin systems the switching mechanism is unknown.

Finally, there were reviews of microbial systems which show parallels with some of the plant systems. P. van de Putte (Medical Biological Laboratory, Rijswijk) described the mutagenic bacteriophage Mu, which integrates anywhere in the *Escherichia coli* chromosome, inactivating the host gene. P. Starlinger (University of Cologne) dealt with the transposable insertion sequences IS1 and IS2 found in the *E. coli* genome, which cause polar mutations by integration into operons. H. Saedler (also from Cologne) described complete reversion of the bacterial gene by accurate excision of IS1, and permanent inactivation by deletion following inaccurate excision. He compared these features with observed behaviour of plant genes associated with controlling elements. Following a short review of plant viruses by M. W. Johnson (John Innes Institute, Norwich) the question was raised of a possible viral origin for controlling elements. But it was evident that they could only be regarded as very degenerate viruses, having lost the ability to replicate autonomously and to produce an infective particle.

A large proportion of the meeting's time was devoted to informal discussion. The plant geneticists were challenged from the standpoints of the other fields, and even faced with scepticism due to the paucity of physical evidence, although the genetic evidence is overwhelming. The impression was that outlooks were widened on both sides.