direction of the connecting strands until they fuse in the mid-line around the periphery of the spokes, at a diameter of 1,000 Å. This interpretation of the structure implies that there are no transmembrane proteins in the usual sense; the proteins of the pore complex merely provide a grommet which stabilizes the hole formed by local fusion of the paired membranes. The eight 'ribosomal' particles were attached only to the cytoplasmic face of the grommet. These particles were readily removable by high salt or EDTA, leaving a structure which at this resolution had eight twofold symmetry axes at right angles to the main eightfold axis.

These findings provoke many further questions about both the structure and function of the pore complex. It has long been known that the nuclear membrane is freely permeable to ions and small metabolites and that even molecules as large as about 90 Å in diameter can pass across with little hindrance. This is consistent with the structure proposed by Unwin and Milligan, but it is less easy to see how ribosomal particles (200 Å in diameter), assembled in the nucleus, manage to pass through the pore. It is possible that this process may be energy dependent and that some movement of plug or spokes is involved. Further structural questions concern the proteins which form the pore structure. Earlier work by Krohne, Franke and Scheer (*Expl Cell Res.* **116**, 85; 1978) has shown only two major components (MW 73,000 to 150,000) in purified pore complexes, together with several minor components. It should be possible to determine the location of at least the major constituents by immunological methods. Beyond this there is the problem of how the assembly of such large structures is controlled. From the dimensions it can be calculated that each of the major constituents (plugs, rings and spoke assembly) must contain several hundred molecules of their constituent protein subunits, giving them 'molecular weights' of 20–40 million. There is no way in which so many identical building blocks will assemble spontaneously into a precise limited structure without some guiding activity by the minor protein constituents or other cellular components.

These provocative developments provide an interesting example of the information which can be extracted from electron micrographs by modern image processing methods, even in the absence of extensive repeating structures. □

A novel gene splice in phage Mu

from Neville Symonds

GENE expression is usually thought of as being controlled through the action of proteins, such as repressors and effectors. Recently, a different mode of control has been reported whereby inactive genes are relocated by some type of recombination process to new sites where transcription takes place. Examples of recombinational control are mating type in yeast (Leupold *Nature* **283**, 811; 1980), phase variation in *Salmonella* (Zieg & Simon *Proc. natn. Acad. Sci. U.S.A.* **77**, 4196; 1980) and host range in phage Mu (Van de Putte *et al. Nature* **286**, 218; 1980). The last example refers to the unexpected finding that two types of Mu phage can be detected which differ with regard to the bacteria they can infect. The difference in host specificity is correlated with the two possible orientations observed in the G region of Mu, an invertible segment of about 3,000 base pairs. With G in one orientation, designated (+), Mu phage can adsorb to one set of hosts, which includes *Escherichia coli* K12; in the other orientation, (−), the phage adsorb to a different set, including certain *Citrobacter* and *Shigella* strains. How does the oscillation in G orientation bring about alterations in host specificity?

In general terms the answer to this question has been known for some time. With G in the (+) orientation, two Mu genes, S and U, which code for tail fibres and enable the phage to adsorb to certain hosts, are expressed; in the (−) orientation two alternative genes, S′ and U′, are expressed, so the host range is altered. The actual genetic mechanism by which this switch is accomplished has, however, only now been elucidated and is described by Giphart-Gassler and co-workers in this issue of *Nature* (p.339).

The intriguing point to the story is that, in a manner somewhat reminiscent of that used to create diversity among immunoglobulins, the variation between the S and S′ genes is brought about by joining a constant DNA sequence, S_c, adjacent to G with either of two different sequences S_v or S_v' located within G. In the (+) orientation, transcription starts at a promoter site outside G, proceeds through S_c and S_v, and then through the adjacent U gene which lies wholly within G. Tail fibres corresponding to S and U are therefore produced. In the (−) orientation the situation is reversed, the reading being in the order $S_c + S_v'$, U′, so that S′ and U′ tail fibres are made but not those corresponding to S and U.

The recombinational control which underlies the three examples mentioned above and is exemplified by the variation in host range of Mu is fundamentally different from control of protein synthesis by positive and negative feedback circuits. Such circuits are able to modulate the activity of genes and, in the extreme case, turn them off completely. Recombinational control, on the other hand, introduces a two-way switch into these circuits, allowing alternative pathways to be introduced into the system. This added flexibility is useful when only one of two possible phenotypes can be tolerated at a particular time. It is well known from experiments involving mixed infection of cells with wild-type phage and host-range phage mutants that progeny particles which receive a mixed complement of tail fibres acquired from different parents have the worst of all worlds, not being able to adsorb properly to any of the usual hosts. If the host range of a phage, such as Mu, is to be extended by providing two distinct sets of tail fibres, then it is clearly advantageous that only one set or the other should be synthesized at any stage — a two-way switch is therefore appropriate.

The precise recombinational mechanism by which the switch between mating types is instituted in yeast, where some type of gene conversion seems to occur, is different from the inversion systems used to bring about phase variation in *Salmonella* or the alternation in host range shown by Mu (and also by phage P where a closely related system operates). All these inversion switches use site-specific recombination systems which act on the short inverted repeats at either end of the relevant inverted region, and which are catalysed by genes immediately adjacent to it. Surprisingly, although the invertible regions in *Salmonella* and Mu are quite distinct, there is some sequence homology between their inverted repeats. The *gin* gene which mediates G inversion and the *hin* gene mediating inversion in *Salmonella* can complement each other (Szekely & Simon *J. Bact.* **148**, 829; 1981). The known recombinational switches of the inversion type therefore all seem to stem from some common origin. Another evolutionary oddity of the G system is that the emergence of two kinds of Mu phage with different host ranges would be expected to lead to an increase in the number of bacterial strains which harbour Mu prophage. However only the original Mu isolate detected in *E. coli* K12 has ever been reported. Whatever the reason for this, the whole of the G region has been preserved in the Mu phage we have, even though within K12 strains part of the region (and the *gin* gene) could easily be deleted and the phage locked in the (+) orientation. Perhaps there is still another twist to come in the G story by which G and *gin* are implicated in some other aspect of the Mu life cycle. □

Neville Symonds is Professor of Microbial Genetics in the School of Biological Sciences, University of Sussex, Brighton BN1 9QG.

0028-0836/82/210288-01$01.00