the strains. These would therefore have become separate species as in Dobzhansky and Pavlovsky's experiments.

Sexual isolation can thus be produced by mating preferences in favour of two or more different genotypes. This is the sexual equivalent of disruptive natural selection in which different genotypes are favoured in different environments. When this occurs, the hybrids may indeed be disadvantageous, being adapted to none of the environments as well as each particular strain. This disruptive natural selection will thus allow the evolution of mating preferences in each strain, and therefore produce what may be called disruptive sexual selection.

ENZYMES

Orbital Argument

from our Molecular Biology Correspondent

SOME months ago I described what seemed at the time the obliteration by Bruice and his colleagues of Koshland's "orbital steering" theory of enzymatic catalysis. Those people who enjoy the cathartic effects of an intellectual punch-up will be delighted to see that Koshland has not taken the assault on his brainchild lying down, and has come storming back in the current issue of the *Proceedings of the US National Academy of Sciences* (Dafforn and Koshland, *Proc. US Nat. Acad. Sci.*, **68**, 2463 ; 1971).

The argument really hinges on how close must be the angular restriction on the line of attack of one reactant by another in order to bring about a rate enhancement of a good many orders of magnitude. Bruice *et al.* concluded from some very straightforward calculations of orientation factors that large enhancements demand an angular precision of the order of 0.1°, which would fall within the range of normal vibrations. Dafforn and Koshland criticize the logic which leads to this conclusion, first of all on the grounds that the orientation of only one of the reactants was considered, and secondly that the calculation pertains to a substantially higher rate increase than it is necessary to find, given that there is some choice in distributing rate-enhancement factors between different possible causes. Adjustments for these considerations, say Dafforn and Koshland, bring the angular restriction up to the altogether more reasonable level of 10°—though this is still not very different from room-temperature vibrations. They go on to show that if one computes the entropic effect of rotational immobilization of the reactants, that is to say one locks them in a favourable orientation for attack, one can come by an adequate enhancement factor. They also then calculate the change in the energy of the transition state, corresponding to a given change in the angle of approach, using a simple harmonic oscillator model with a reasonable value for the bending force constant. Depending on the force constant chosen, the rate factor falls off fairly rapidly with angular distortion.

What then are we to believe? It is clearly possible for theoreticians to hurl formulae at each other, which prove their opposing cases with comparable conviction, and presumably to their entire satisfaction. It is perhaps not unfair to take the view that the onus of persuasion is on Koshland, because his notion does represent a departure from implicit chemical thinking. His classical calculations inevitably make several considerable numerical assumptions about the nature of the transition state. Moreover, there are the quantum mechanical calculations of Port and Richards to be considered (*Nature*, **231**, 312 ; 1971).

Storm and Koshland, in their original formulation of the "orbital steering" concept, gave as evidence in its favour the relative rates of intramolecular esterification in a set of compounds in which the reacting carboxyl and hydroxyl groups were positioned with different degrees of rigidity, and also the relative rate of thioester formation when sulphur was present in place of oxygen. Port and Richards have simply calculated the overlap integrals for the orbitals involved in the reaction, on the grounds that these must be expected to reflect the relative reaction rates, if the orientation factor is indeed dominant. As one might intuitively expect for the set of components, on the grounds of the diffuseness of molecular orbitals, the variation in overlap integrals is slight. Port and Richards concede that more refined calculations would be both possible and desirable, but their results as far as they go certainly argue against the importance of the critical angular orientation factor.

At the very least then one may say that Koshland's case is not proven, though of course the strategy of destruction is always much the easier in such a situation. In Koshland's favour it might be argued that orbital steering should not be discarded until a good alternative can be found, and Koshland rejects the proximity effect (that is the translational, as opposed to rotational immobilization of the reactants, in juxtaposition at the active site) as a

Defective Mouse Sarcoma Virus

AS RNA tumour virologists learn progressively more about the biology of the mammalian and in particular mouse sarcoma and leukaemia viruses, it is becoming increasingly apparent that these viruses are capable of essentially the same range of interactions with their host cells as their avian counterparts, the Rous sarcoma viruses and avian leukosis viruses. In *Nature New Biology* next Wednesday, for example, Gazdar, Phillips, Sarma, Peebles and Chopra describe the isolation and properties of a noninfectious mouse sarcoma virus which is reminiscent of the noninfectious Rous sarcoma viruses produced by certain chick cells transformed by Bryan high titre Rous sarcoma virus in the absence of an avian leukosis helper virus.

Gazdar *et al.* noticed that two lines of hamster cells derived from sarcomas induced in hamsters by mouse sarcoma virus liberated typical C-type virus particles with all the biophysical parameters of the sarcoma leukaemia viruses. These virus particles, in spite of the fact that they are liberated from hamster cells, proved to cross react with antisera against the mouse sarcoma and leukaemia viruses but failed to cross react with antisera directed against hamster leukaemia viruses. In short, the virus liberated by the hamster cells is antigenically related to mouse, not hamster, C-type viruses.

Is the virus from the hamster cells infectious? All the attempts which Gazdar and his colleagues have made to transform mouse rate and hamster cells growing in a variety of culture conditions have failed and neither does the virus induce sarcomas or leukaemias when injected into newborn rats, mice or hamsters. Gazdar *et al.* were, however, able to prove that these apparently noninfectious mouse C-type virus particles do indeed contain that part of the mouse sarcoma virus genome which is responsible for transformation and sarcomagenesis by sedimenting this virus with mouse leukaemia virus. During such co-sedimentation the two viruses are presumably physically fused together, for the pelleted virus particles will transform cells and at low efficiences induce sarcomas. After sedimentation alone neither the noninfectious sarcoma virus nor the leukaemia virus has these properties.

Gazdar and his colleagues conclude that the virus which they have isolated from these hamster cells contains the mouse sarcoma virus genome but lacks helper leukaemia virus of either mouse or hamster origin. The parallels and differences between this virus, another defective mouse sarcoma virus isolated recently by the same group (*Proc. US Nat. Acad. Sci.*, **68**, 1520 ; 1971), and the defective Rous sarcoma viruses discovered and studied by Weiss and the Hanafusas deserve and are no doubt receiving further attention.