thus particularly welcome, for by seeking to account for the Icelandic condition without recourse to mantle plumes it represents one of the first serious attempts to show that data which have previously been taken to support plumes may well be explicable in more conventional terms. Thus O'Hara argues the case, rejected by Schilling, that the geochemical variations radiating from Iceland are caused not by the mixing of two primary magmas but by high and low pressure fractional crystallization dependent upon elevation. Presumably, the increasing elevation towards Iceland reflects greater magma flow but, as O'Hara admits, even his explanation begs the question of why this should be so. The point is, however, that if O'Hara's arguments are valid, the number of phenomena for which it is necessary to invoke a mantle plume is much reduced. P. J. S.

PROTEINS

Active by Association

from our Molecular Biology Correspondent

SHERLOCK HOLMES'S maxim that when you have eliminated the impossible, whatever remains, however improbable, must be the truth, has proved itself capable of wide application. It is implicit in the reasoning of Biswas and Paulus (*J. biol. Chem.*, **248**, 2894 ; 1973), whose studies on the subunit enzyme, aspartokinase, have brought to light a curious and so far unique situation. It is in all regards one of the more nightmarish allosteric systems, with control of activity by ligands operating apparently at three different sites, and, in addition, critical dependence of activity patterns on concentration and temperature.

The new work treats of the dependence of the functional properties on the subunit interaction. In the first place the stoichiometry has been established: in SDS-gel electrophoresis there are two subunits, α and β, with molecular weights of some 43,000 and 17,000, in equal molar proportions. The molecular weight of the native enzyme then corresponds to an $\alpha_2\beta_2$ structure. This Biswas and Paulus have confirmed by the invaluable cross-linking technique of Davies and Stark: treatment with a bifunctional imidoester leads to the appearance on SDS gels of four new components, in addition to the surviving monomeric α and β chains. They correspond in molecular weight to the species $\alpha\beta$, α_2, $\alpha_2\beta$ and $\alpha_2\beta_2$, thus confirming the tetrameric character of the enzyme. This distribution of cross-linked components has additional information content, however, for the absence of the β_2 or $\alpha\beta_2$ species must be taken to indicate that there are probably no β–β contacts in the native tetramer, which restricts the possible symmetrical arrangements to a form of sandwich structure, with an α–α core and one β chain attached to either α (but not to both, because then an $\alpha\beta_2$ species should be generated).

Separation of the α and β chains can be achieved without irreversible damage by dissociation to monomers in 4 M urea, and gel filtration. Removal of the urea from the α chains leads, as shown again by cross-linking, to a mixture of monomers, dimers and multiples of dimers, whereas the β chains form only some dimers.

Biswas and Paulus suggest that this pattern of self-association can follow simply from the sandwich-type structure of the tetramer, if the association sites are in some general sense adhesive, because then the α chains must be divalent, the stronger interaction occurring at the α–α interface, so that the dimeric unit is first formed, and the β chains univalent, and therefore capable only of forming closed dimers.

The interesting thing now is that not only is there activity in all the α chain species, but all the catalytic and allosteric characteristics are to be found in them. The total regain of activity, however, is no more than about 20%. No enzymatic or regulatory activity is to be discerned in the β chain. When now the renaturation experiment is done in an α–β mixture, the level of reactivation is increased by a factor of three, in a manner that depends on the square of the β chain concentration. The only role that Biswas and Paulus can envisage for the β chain therefore is as an aid to folding of the α subunits—and indeed, the very presence of β chains would of course be expected to create a trap for the native α conformation. It is, of course, conceivable that some other function may yet come to light, and also that the $\alpha\beta$ couple is the product of a single gene, and that a proteolytic scission occurs in the *Bacillus* cell after synthesis.

Immunotherapy of Cancer with Antibody in Rats

THE complexity of anti-tumour immunity, where it exists, is taxing the minds of immunologists who seek to manipulate the immune response to favour the cancer patient. Experiments on animals have shown that T lymphocytes of thymic origin can be effector cells against tumour homografts and that unaided they can apparently kill the tumour. Similarly it has been found that macrophages armed with a product of lymphocytes which have been specifically stimulated can be cytotoxic for malignant cells. More recently it has become clear that a certain class of cell can kill tumour cells if they have been coated with the appropriate anti-tumour antibody but without this sensitizing antibody (LDA) no such lethal effect is evident. The protagonists of each of these killing systems are somewhat doctrinaire and each tends to think that his notions will be of the most use in the immunotherapy of cancer. Hersey, in *Nature New Biology* next Wednesday (July 4), argues the case for LDA and demonstrates that transfer of serum antibody *in vivo* can sometimes contribute to slowing down of tumour growth.

Hersey took a transplantable rat lymphoma which is syngeneic to the PVGc hooded strain of rats and used it to immunize xenogeneic (rabbit), allogeneic (A/gus rats) or syngeneic animals. The xenogeneic and allogeneic antisera were subsequently absorbed *in vivo* in non-tumour bearing PVGc rats to produce specifically anti-tumour antisera. The tumour cells injected into syngeneic recipients were irradiated heavily to prevent their growth. All sera were titrated for LDA activity using ^{51}Cr-labelled tumour target cells and human peripheral blood mononuclear cells as effector lymphocytes. Only the rabbit anti-tumour serum had any LDA activity after absorption. All the kinds of serum were then injected into PVGc rats before or at various times after implantation of the lymphoma. The survival times were studied and it was found that there was a significant prolongation of life in those animals receiving the absorbed rabbit antiserum. The effect was most marked if the serum was administered prophylactically.

Hersey considers various explanations of his results; for example, that the antiserum in conjunction with complement exerts a direct cytotoxic effect on the tumour cells or, alternatively, that the serum removes antigen–antibody complexes from the plasma of the recipient (by reaction with free combining sites on the antigenic component of the complexes) thus unblocking an effector pathway that was previously inhibited by the complexes. Inevitably he feels that the injected antiserum acts as an LDA *in vivo* as it had *in vitro*.

Hersey goes on to indicate that passive immunotherapy with heterologous antisera might be effective in situations in which LDA activity could be measured *in vitro*. They also seem to show that in a situation in which the host makes no immune response of its own—no anti-tumour antibody was produced in the syngeneic recipients of tumour—an artificial response can be contrived by using an antibody produced in another species of animal.