which was on the same spacecraft, was in an unfavourable mode. During the crossing reported by Mozer *et al.* the same particle detectors show no sign of the acceleration (Heikkila *op. cit.*).

Although the latest result of Paschmann *et al.* provides strong support for magnetic connection it also reinforces the criticisms of Heikkila (*op. cit.*). If the effect is so easily detected in this crossing why has it never been reported before? If magnetic connection occurs it can hardly be such a rare event as the present observational statistics imply. Is it confined to a small region of the magnetopause or are there special conditions yet to be identified? Other examples, which Paschmann *et al.* say have already been found in the ISEE data, may provide the answers and help us find out what controls the rate of energy input from the solar wind into the magnetosphere. □

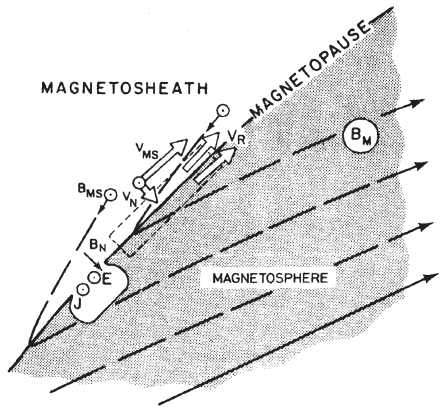

Fig. 2 The configuration of magnetic (*B*) and electric (*E*) fields and plasma flow (*V*) (broad arrows) when magnetic connection occurs at the magnetopause. The enhanced flow caused by acceleration in the layer, V_R, exceeds the normal flow of solar wind plasma past the magnetosphere V_{MS}.

Immunoglobulins and histocompatibility antigens

from Arnold Feinstein

THE family of antibody molecules, or immunoglobulins, for all its magnificent variety and versatility of structure, function and specificity, has evolved by the multiplication of a gene coding for a single ancestral polypeptide sequence, corresponding to a size of about 12,000 molecular weight. As a result of tandem duplication, followed by limited divergence, four or five homologous sequences can be seen repeated along the heavy polypeptide chains of antibody molecules. The κ or λ light chain found in association with each heavy chain is formed from two such homologous regions. In both heavy and light chains hypervariable stretches conferring antigen-binding specificity are confined to the most N-terminal homology region, the so-called variable region. Crystallographic studies of a few immunoglobulins have revealed that variable and constant homology regions are independently folded similarly, but distinguishably, into individual domains.

What makes it quite certain that the chains of all known antibodies are strings of such similarly folded domains is that all the characteristic conserved features of the folded domain, seen by crystallographers, are easily detected in each of the homologous sequences recurring along all the known immunoglobulin polypeptide chains (see Beale & Feinstein *Q. Rev. Biophys.* **9**, 135; 1976). These features include the β strands which form two β sheets, the bends between the strands, and the disulphide bridge lying between the two sheets and linking them. In this way we have the rare good fortune to be able to come close to the tertiary structure of an immunoglobulin domain from a knowledge of only its primary sequence. Now that the sequences of more proteins are becoming available, the basic immunoglobulin domain structure seems to be cropping up in several unrelated membrane proteins.

It has been evident for some time that another remarkable family of molecules, the classical transplantation antigens (the histocompatibility antigens), are in part coded for by genes which have evolved from the same ancestral immunoglobulin gene although the two loci are completely unlinked. These highly polymorphic antigens are present on most cells, and are extremely important, not only as the critical targets in graft rejection, but also for their involvement in the recognition by cytotoxic T lymphocytes of viral and other cell surface antigens (see *News & Views* **274**, 12, 840; 1978). The histocompatibility antigens consist of two non-covalently associated polypeptide chains, the heavier one, which carries the alloantigenic specificities, being a 44,000 molecular weight glycopeptide; the other subunit, β2 microglobulin, has a molecular weight of 12,000, and its invariant amino acid sequence was found, surprisingly, to be homologous to that of a constant immunoglobulin domain, including the characteristic disulphide-bridged loop. Moreover, all the three-dimensional structural features of this domain referred to earlier can be recognised.

In antibody molecules constant domains regularly associate in pairs, so that when two disulphide-bridged loops of appropriate size were seen in the heavy chain of the transplantation antigen, it seemed very likely that at least one of these looped regions would be folded like an immunoglobulin domain, and would be associated with β2 microglobulin. Indeed, the familiar features of a constant immunoglobulin domain could already be seen in a tentative sequence of one of these regions, in a human histocompatibility antigen, which was published last year by Strominger and his colleagues.

In this issue of *Nature* (page 266) Orr *et al.* present the complete sequence of this region, referred to as ac2, and confirm in detail its immunoglobulin-like structure. But what of the other more N-terminal disulphide-looped region? (see Fig. 1 of Orr *et al.* for the relative arrangement of the regions). The sequence of this region too has now been published (*Proc. natn. Acad. Sci. U.S.A.* **76**, 4395; 1979) and it is disappointingly apparent that, apart from the sequence around the most N-terminal cysteine, the overall pattern of conserved features typical of an immunoglobulin domain are not clearly seen. Thus, even if this region were derived originally from an ancestral immunoglobulin gene, it has adaptively lost a number of its features. For this reason, ac2 is a more likely candidate for the region with which β2 microglobulin is associated.

There is however, certain to be a concerted effort to predict a plausible structure for the region N-terminal to ac2, following the realisation that this part of the molecule is important in T cell recognition. This awareness has been highlighted by studies of mutant mice, where dramatic functional changes have been correlated with single amino-acid substitutions in this region (see Kohn *et al. Immunogenetics* **7**, 279; 1978). Not only can such mutations lead to graft rejection, but the specificity for T cell recognition of viral antigens seen in association with the original and with the mutant molecule can be quite different.

It appears that each of the different types of polypeptide chain known to contain immunoglobulin or related sequences is controlled by one of five genetic regions, which are not detectably linked in the species studied. It seems that we can now add a sixth. Thy-1 is a glycoprotein which has been isolated by an Oxford group from rat brain, but it is also abundant on rodent thymus cells. Its sequence indicates that Thy-1 resembles a single immunoglobulin domain (see Campbell *et al.* this issue of *Nature*, page 341). Although the function of this molecule is unknown, we should in general resist the expectation that invariant proteins structurally related to immunoglobulins will have specific recognition properties analogous to those of the specialised variable domains of antibodies. We do not know what function the ancestral polypeptide served, but we have every indication that it owes its extensive proliferation, unique in mammals, to its striking adaptability to a variety of functions.

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