—————————NEWS AND VIEWS—————————

not be isolated from patients' lymphocytes during treatment but that the virus reappears at the end of treatment; moreover, the control of virus spreading is not associated with an immune or clinical improvement[23,24].

A second approach involves immune stimulation or reconstruction. Immunostimulators alone, even pure interleukin-2, seem to fail to reconstitute the immune system of AIDS patients. Interferon, which has both antiviral and immunostimulant effects, seems to be of value in the treatment only of Kaposi's sarcoma, which is often associated with AIDS. In any case, since cell activation probably contributes to virus spreading and T4 depletion, the use of such drugs in patients with minor symptoms of LAV infection may be dangerous in that it could accelerate progression of the disease unless antiviral drugs were used at the same time. Immune reconstitution by bone-marrow graft or leukocyte transfusion has been found not to work because the grafted cells are rapidly reinfected by the virus[25].

The third approach would be based on the view that AIDS is an autoimmune disease. This would suggest that immunosuppressive drugs, which can limit both cell stimulation and cytotoxic mechanisms, have a role in the treatment of AIDS. In that case, treatment would be designed first to control virus replications and then to 'tolerate' non-infected cells coated with viral proteins, in the way an allograft can be tolerated. Since there is still no firm basis for such a therapeutic approach, which is potentially dangerous, caution is required before clinical trials. While immunosuppressive treatment has been used in visna-infected animals with clinical improvement of early brain lesions without any adverse results[26], there are descriptions in the literature of patients who have

died of fulminant *Pneumocyctis carinii* pneumonia after being treated with immunosuppressive drugs in ignorance that they were LAV-infected[27]. Even if cyclosporin A has some potential use in virus-induced autoimmune disease, its use in AIDS patients should await more experimental knowledge about its action on T cells, which may be highly complex[28].

Finally, because of the complexity of the pathophysiology of AIDS, only active and constant cooperation between biologists and clinicians will lead to an effective therapy, probably involving a combination of drugs and other treatments. □

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1. see *Nature* **318**, 3 (1985).
2. Montagnier, L. *et al. Human T Cell Leukamia Lymphoma Viruses* (eds Gallo, R.C., Essex, M.E. & Gross, L.) 363 (Cold Spring Harbor Laboratory, New York, 1984).
3. Sonigo, P. *et al. Cell* **42**, 369 (1985).
4. Klatzmann, D. thesis, Univ. Paris (1985).
5. Seligmann, M. *et al. N. Engl. J. Med.* **15**, 1286 (1984).
6. Gluckman, J.C. *et al. Clin. exp. Immun.* **60**, 8 (1985).
7. Fauci, A.S. *et al. Ann. intern. Med.* **102**, 800 (1985).
8. Klatzmann, D. *et al. Science* **225**, 59 (1984).
9. McDougal, J.S. *et al. J. Immun.* **135**, 3151 (1985).
10. Haase, A.T. *et al. Science* **195**, 175 (1977).
11. Narayan, O. *et al. Infect. Immunity* **41**, 67 (1983).
12. Montagnier, L. *et al. Ann. Virol. (Inst. Pasteur)* **135**E, 119 (1984).
13. Chiu, I.M. *et al. Nature* **317**, 366 (1985).
14. Klatzmann, D. *et al. Nature* **312**, 767 (1984).
15. Dagleish, A. *et al. Nature* **312**, 764 (1984).
16. Klatzmann, D. *et al. Abstr. RNA Tumour Viruses Conf.* Cold Spring Harbor Laboratory (1985).
17. Harper, M.E. *et al. Abstr. int. Conf. AIDS.* Atlanta, 27 (1985).
18. Shaw, G.M. *et al. Science* **226**, 1165 (1984).
19. Cianciolo, G.J. *et al. Science* **230**, 453 (1985).
20. Cunningham-Rundles, S. *et al. J. clin. Immun.* **3**, 156 (1983).
21. Montagnier, L. *et al. Virology* **144** 283 (1985).
22. Rossini, A.A. *et al. A. Rev. Immun.* **3**, 289 (1985).
23. Rozenbaum. W. *et al. Lancet* i, 450 (1985).
24. Lane, M.C. *et al. Cancer Res. Suppl.* **45**, 4674 (1985).
25. Lane, M.C. *et al. N. Engl. J. Med.* **311**, 1099 (1985).
26. Nathanson, N. *et al. Lab. Invest.* **35**, 444 (1976).
27. Moffat, E.H. *et al. Lancet.* i, 935 (1985).
28. Shevach, E.M. *A. Rev. Immun.* **3**, 397 (1985).

Weather forecasting

Storm hunting with fractals

from A. Hollingsworth

MRS BEETON might well have observed that to make tiger soup, first catch your tiger. Tigers for a weather forecaster are vigorous storms that put life or property at risk. They occur on scales ranging from the tornado (~1 km) to mid-latitude cyclones (~2,500 km). Locating the whereabouts of a storm and estimating its ferocity are the first steps in making a useful forecast, but the surface meteorological network is very inhomogenous, with holes of many sizes where storms can lurk undetected.

On page 43 of this issue, Lovejoy *et al.* describe this problem in the language of fractal analysis. They give a definition of the dimension of an observing network, and argue that if the dimension of the network is lower than the dimension of the field being observed, many of the most energetic entities will never be detected. Many geophysical networks including the surface weather network are patchy in coverage and therefore lack dimensional resolution. Lovejoy *et al.* argue that long-term averages of geophysical fields derived from such dimensionally incomplete networks may be substantially biased: because of the inhomogeneity of the surface network, rare but vigorous events can be missed.

This suggests a bleak view of the feasibility of useful weather forecasting, a view which is belied by the fact that economically useful forecasts are routinely made out to perhaps 3 days in the tropics, 4 or 5 days in the southern hemisphere, and 6 or 7 days in the northern hemisphere extratropics. The success of the forecasts depends heavily on data sources other than the surface network as well as on sophisticated data-assimilation systems; ultimately success depends on the fact that scale separation is a meaningful concept for many practical purposes.

Data from polar orbiting and geostationary satellites, from the balloon network and from ships and aircraft provide the main basis for routine forecasting. The geostationary satellites, of which four are currently operational, provide multi-channel measurements every half-hour

over their field of view, which is roughly within 55' of the nadir point at the equator (Fig.1). Cloud track winds can be derived from successive half-hourly scans in the visible and infrared. The satellites have a resolution of 1 km at nadir, and are invaluable for surveillance of tropical disturbances on all important scales. Two polar orbiting satellites provide radiometric soundings with good horizontal resolution four times a day, for most parts of the globe (Fig.2). Vertical structure in humidity and temperature can be derived from the soundings; in middle and high lati-
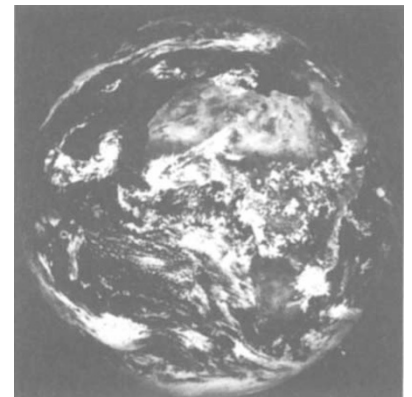

Fig. 1 Meteosat picture for 12.00 on 17 September 1985. The disturbance off the West African coast is the African wave that eventually developed into Hurricane Gloria. Cloud track winds can be estimated from successive half-hourly scans. The infrared channels enable one to estimate the height of the clouds. Pixel resolution at nadir corresponds to 1 km.
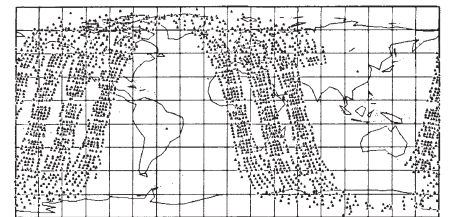

Fig. 2 Data coverage from a polar orbiter in a single six-hour period, covering about three orbits. A single orbiter can monitor every point on Earth twice a day.

tudes, the temperature soundings are valuable in inferring the winds.

The data from these diverse sources are integrated in a coherent view of atmospheric structure in space and time using four-dimensional data-assimilation methods. At the core of these techniques is a sophisticated global forecast model which provides rather accurate estimates of the expected state of the atmosphere, based on earlier observations. At any given time the observations are insufficient to determine the atmospheric structure.

Information from the forecast model is used in conjunction with the latest observations in a Bayesian estimation of the true state of the atmosphere; the forecast model is essential to resolve the underdeterminacy of the observations. There are many analogies between the methods used in this field and those used, for example, in computational vision (see Poggio, T., Torre, V. & Koch, C. *Nature*

317, 314; 1985) or the applications of the Kalman–Bucy filter in control theory (see *Data Assimilation Methods* eds Bengtsson, L., Ghil, M. & Kallen, E., 330; Springer, 1981).

Global weather forecast models solve a version of the Navier–Stokes equations for fluid flow on a grid which has a horizontal resolution of about 150 km and a vertical resolution of 1–2 km. Some important weather cannot be resolved on such a grid. The fact that one can nevertheless make useful forecasts suggests that the simplification of treating the atmosphere as smoothly varying on the smallest resolved scales is not a serious error. Statistical methods can, if necessary, be used to interpret the forecast in such a way as to recover useful local detail.   □

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Immunoglobulin genes

Inversion for gene construction

from David Baltimore

JOINING of immunoglobulin genes as an event of immunodifferentiation is not unique in the biological world. Recombination of DNA molecules is commonplace and serves many functions, including meiotic recombination, post-replicative repair, phase variation in *Salmonella* bacteria and the generation of transcribable surface antigen genes in trypanosomes. Although DNA recombination frequently occurs, somatic rearrangement of gene fragments to produce functional genes is at present known to be used only by the immune system. This specificity implies that the rearrangement process should be active only in particular cells and be targeted only to well-defined DNA segments. On page 28 of this issue Malissen *et al.*[1] have extended our understanding of the rearrangement process by their analysis of the T-cell receptor gene complex.

The nature of the enzymes involved in the immunoglobulin gene rearrangement process, their control and their targeting specificity remain mysterious — we are still trying to understand the ground rules. One of the more obscure aspects is the relative placement and orientation of the gene fragments to be recombined to produce the immunoglobulin molecule. Although textbooks and the diagramatic slides shown by many immunologists blithely display strings of variable (*V*), diversity (*D*) and joining (*J*) segments, the only situation where a complete physical linkage has been achieved for all the elements of an immunoglobulin gene-segment joining system is with chicken lambda genes[2]. For all mammalian sys-

tems, the relative positions and orientations of the elements to be joined are incompletely established. Various arguments give a strong indication of the organization and orientation of the immunoglobulin heavy-chain gene segments[3,4], but the situation for the kappa light-chain genes is uncertain. The joining of kappa-chain gene segments involves a recombination between one of many hundreds of *V* segments with one of four *J* segments.

Although the *V* and *J* segments have not been physically linked in recombinant DNA clones, Lewis *et al.* in 1982 proposed that at least some of the kappa *V* regions occur in the DNA chain in the opposite transcriptional orientation to the *J* segments[5]. This proposal was based on the observation that in certain cells that have productively rearranged their DNA, segments of DNA remain that should have been deleted if both *V* and *J* were found in the same orientation[5-7]. If a *V* segment were in the opposite orientation to a *J* segment, joining the two elements would have to invert the intervening DNA rather than deleting it. Such an inversion would not remove any large segments of DNA from the cell but would simply reconfigure the existing DNA. This proposal met with much disbelief largely, I believe, because the DNA gymnastics involved seemed formidable although, in fact, they are quite ordinary (see the figure).

A decision about whether inversional joining is a mechanism of rearrangement was approached in two further papers by Lewis *et al.*, who used an artificial DNA construct with inverted *V* and *J* segments

that would rearrange after integration into certain cells[8,9]. This work showed that inversional joining is a feasible mechanism, but left open the question of whether it actually occurs in normal B-cell maturation. Two indirect pieces of data argued for inversional joining[10,11], but both involved abnormal events. The direct demonstration of inversional joining in the kappa gene of a plasmacytoma was made by Feddersen and Van Ness[12], who found that they could recover both products of a natural joint and showed that the two had to arise by inversional joining. This directly implied that some *V* regions are in opposite orientation to the *J* regions.

Malissen *et al.* have now extended the analysis to the *V* regions of the T-cell receptor gene complex. Here they have uncovered a most surprising situation (one that could as easily have been true of kappa light-chain genes and may yet turn out to be). They have shown that at least one *V* segment is downstream of the constant (*C*) regions. In all previously characterized systems of immunoglobulin-related genes, the *V* segments have been thought to be upstream of the other segments. For immunoglobulin heavy-chain genes, joining is accompanied by deletion of the intervening DNA[3] and this requires that the
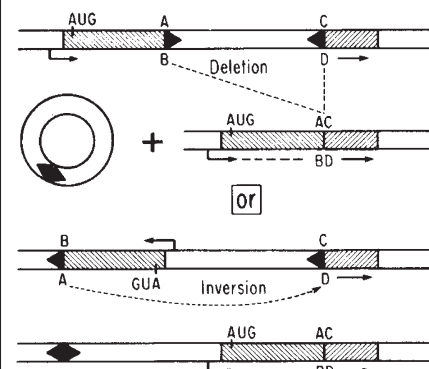
The difference between deletional and inversional joining. The difference is solely in topological orientation of the two participating pieces of DNA. The units to be joined (the *V* and *J* units shown here) are identical but in one case they are located in the DNA in the same transcriptional orientation and in the other in opposite orientation. The biochemistry of joining is identical in both: the same sequences are joined to one another. This can be seen by following the locations of the hypothetical sequences A, B, C and D. In both cases of joining, A is joined to C and B is joined to D. The consequences of deletional and inversional joining are quite different. In the first, a segment of DNA containing the joining signals is released as a circle and discarded from the cell. In the second, no segment of DNA is lost from the cell but the inversion causes the back-to-back apposition of the joining signals. ⌐→, Site of initiation of transcription with direction indicated; AUG, codon in *V* region that initiates translation; ▶, signal encoded in the DNA that specifies a site for joining (a conserved heptamer and nonamer).