An evolutionary mechanism combining sex with elementary geometry has a lot going for it, but it still does not explain why the predominant sense of twist in nature is right-handed. It is difficult to see how this problem could be attacked except through the explicit developmental mechanism that controls hand, and here, it seems, simplicity must be discarded. Interesting but probably ultimately unhelpful observations for understanding gastropods have been made on the effect of temperature on the screw sense adopted by some other helical organisms. A considerable body of circumstantial evidence supports the idea that water temperature has determined the hand of some foraminifera tests. Left-handedness is associated with low, and right-handedness with higher temperatures, in *Globigerina truncatulinoides* and *G. pachyderma*, for example. A temperature-induced switch of hand in the highly organized multicellular structure of *Bacillus subtilis* 'macrofibres' has also been observed and studied in some detail (see, for example, ref. 12). But are either of these inversions (reflections) genetic in origin?

Better, then, to study the gastropods directly. An observation made very early on in Lymnaea may offer a starting point. A trait inherited maternally should be seen in all the offspring from the same hatching. Thus, any broods of snails should be exclusively left- or right-handed. In practice, some broods possess a few snails of the opposing hand, and in sinistral broods the mutation rate to dextrality is quite high[13]. Freeman and Lundelius have proposed[14] a genetic model for this phenomenon. The power of their model — or alternatives to it — to explain predominant right-handedness needs exploring.

What is now known from studying Lymnaea is that the dextral gene is expresed during oogenesis and its product — whatever it is — controls the symmetry of the pattern of very early cleavage. An injection of cytoplasm from dextral eggs reverses the early cleavage pattern of sinistral eggs, but one from sinistral eggs does not influence dextral ones[14]. To resolve this apparent paradox, it is suggested that the normal form of *L. peregra* is actually left-handed, switchable to right-handed by the protein product of the dextral gene. Freeman and Lundelius speculate that what they have found in Lymnaea would be found exactly reversed in a left-handed species like *P. suturalis*. It is difficult to imagine that this will not turn out to be so, and then equally difficult not to agree with the authors in concluding that the path from gene locus to cleavage pattern is likely to be far from straightforward — so far that, rather like Humpty Dumpty looking for the hippopotamus, the best instrument to be carrying on the search might be a corkscrew. □

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Oceanography

Organic matter in sea water

John I. Hedges

In contrast to the impression given by the abundant plant and animal life of coral reefs and other productive marine environments, more than 99 per cent of the organic matter in the ocean is dead, dissolved and extremely dilute. The complex mixture of organic molecules comprising this solution of degraded biochemicals, however, has a great effect on many ocean processes and plays an active role in the global carbon cycle. On page 246 of this issue[1], P.M. Williams and E. Druffel present the first detailed analysis of the radiocarbon (^{14}C) activity of dissolved organic matter in the water column of the open ocean. Their results provide new insights on the sources and dynamics of this key sea-water component.

There are three reservoirs of reactive organic matter in nature, each of which holds approximately as much carbon as occurs in atmospheric CO_2 and thus has the potential to affect the concentration of this climatically critical gas[2]. Two of these carbon reservoirs occur on land in the form of living plants and degraded organic matter in soils; the third, organic matter dissolved in sea water, is by far the least understood.

Many of the uncertainties about dissolved organic matter in sea water stem from the fact that less than 30 per cent of the component molecules have been identified[1]. This lack of detailed structural information makes it extremely difficult to identify biochemical precursors or to judge the probability of different chemical and physical transformations. Structural characterizations, however, are challenging because most analytical techniques for organic compounds are highly selective, so that many different methods are required comprehensively to characterize complex natural mixtures. In addition, few methods are sufficiently sensitive for direct quantification at the low concentrations (parts per million to parts per billion (10^9)) found in sea water, and no technique has yet been demonstrated for representatively concentrating dissolved organic matter from the mass of sea salt, which is more than a thousand times greater.

The most successful isolation method for dissolved organic matter to date, involving selective adsorption onto synthetic resins, typically recovers less than 10 per cent of the total material. This relatively nonpolar fraction of 'marine humic substances'[3,4], consists primarily of acid-rich aliphatic polymers with molecular weights of 500–1,000 that bear little resemblance to any known biochemical or humic substances in soil. Because it is largely uncharacterized, the total amount of organic matter dissolved in sea water can be quantified only by complete combustion to CO_2. This common procedure measures dissolved organic carbon (DOC), which is equivalent to about half the organic matter present.

There is growing evidence that, although only a trace sea-water component, DOC is involved in various marine processes[5,6]. Being surface-active, for example, DOC concentrates at the ocean surface where it can undergo photochemical reactions as well as affect the transfer of light, gases and wind energy. This tendency to concentrate at interfaces also causes DOC to adsorb onto particles suspended in sea water, thereby changing their charge and surface properties. Finally, some DOC components chemically combine with dissolved metals to form complexes that affect the chemical properties of sea water and phytoplankton production[6].

In the light of these many important roles and the dearth of complementary information, the dissolved-organic-radiocarbon profile reported in this issue is significant in at least two ways. First, the almost parallel exponential decreases in the radiocarbon content of both dissolved inorganic and organic carbon within the upper kilometre of the central North Pacific (Fig. 1*a* of ref. 1, on page 247) suggest that both features have a common origin in circulation processes operating in the upper ocean on a timescale shorter than the thousand-year mixing time of the global ocean. This finding provides the

most definitive evidence to date that recently formed, dissolved organic molecules are being mixed rapidly into the upper ocean. This means that labile DOC may be an important source of food deeper in the ocean than was previously thought, and that synthetic organic compounds also could penetrate rapidly and deeply into the sea.

Second, DOC in the deep ocean has a mean age of roughly 6,000 years (approximately twice the previously suggested value[7]), which shows how unreactive this material is and refines significantly the global carbon cycle. This more precise radiocarbon measurement indicates that organic molecules dissolved in the deep sea on average survive approximately six exposures to concentrated light and life at the ocean surface during global circulation and are even more refractory than previously indicated. In addition, it is now clear that the amount of carbon that must enter or leave the ocean DOC pool per year (10^{14} grams of carbon; ref. 1) is much less than 1 per cent of the organic matter synthesized annually by marine plankton and only half the mass of DOC discharged into the ocean annually by rivers.

This result, together with the estimate that the amount of organic matter deposited in marine sediments does not exceed a quarter of the DOC input from rivers, indicates that most of the DOC entering the ocean from land, and most of it cycling within the ocean itself, must be destroyed by oxidation to CO_2. This implication, supported by the observation that the organic materials in all three reservoirs are compositionally dissimilar[4,7-10], is surprising because both riverine and deep-ocean DOC are relatively resistant to biodegraduation[10]. Ironically, Williams and Druffel's measurements[1] not only indicate that deep-ocean DOC is more refractory than previously thought, but also point towards an as-yet undiscovered process by which the sea eventually recycles this huge reservoir of recalcitrant organic molecules back to inorganic carbon. □

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Virology

Vector-directed interleukin expression and infection

Brigitte A. Askonas

THERE is a continued need to develop vaccines against serous infections that do not permit the use of attenuated infective particles. Purified components of pathogens are often poorly immunogenic and in most cases do not induce relevant responses of cytotoxic T cells. One approach to vaccine development is to insert genes encoding single viral antigens into vaccinia virus[1,2], and an interesting novel variant of this method has now been developed by Ramshaw and colleagues, who reported their results in *Nature* last month[3], and by Flexner *et al.*, who report their results on page 259 of this issue[4].

In the standard approach[1,2], the inserted gene as well as vaccinia virus (VV) proteins are expressed by the infected cells *in vivo* or *in vitro* to mimic antigen presentation in a normal virus infection. The recombinant VV proteins are good inducers of antibodies and different T-cell responses, and are excellent tools to study the T-cell repertoire for viral components (for example, influenza or respiratory syncytial virus components; refs 5, 6). But vaccination using such constructs can lead to disseminated vaccinia infections in immunosuppressed hosts. In their new work, Ramshaw *et al.* and Flexner *et al.* insert the gene encoding human or murine interleukin-2 (IL-2) into vaccinia virus that can contain additional viral genes such as influenza haemagglutinin (HA) or nucleoprotein (NP). IL-2 amplifies T-cell responses and also acts on B cells of the immune system. Ramshaw *et al.*[3], using athymic nude mice as a model of an immunodeficient host, demonstrate that infection (local or intravenous) of IL-2/HA/VV causes clearance of vaccinia virus by day 11, whereas HA/VV leads to persistent vaccinia infection. In normal mice, inclusion of the IL-2 gene in recombinant VV does not influence the rate of virus clearance.

Flexner *et al.* in this issue[4] present more extensive data in a model of disseminated VV infection. Inbred athymic nude mice die within a few days following intraperitoneal infection with recombinant vaccinia virus constructs. Inclusion of the IL-2 gene in the vaccinia virus vector results in survival for more than 60 days. It is of particular interest that evidence for IL-2 production in host mice could be obtained even 6 days after infection. This raises the question as to which cell types are able to produce IL-2 following vaccination, because athymic mice have no functional T cells. It is possible that T-precursor cells are activated to differentiate into lymphokine-activated killer cells, with dramatic results: although vaccinia infection is not totally prevented, VV titres in affected tissues are strikingly low.

In normal host mice of the BALB/c strain, infection by recombinant vaccinia virus with inserted influenza HA or NP genes results in complete or partial protection, respectively, against lethal challenge with the homologous influenza virus. Co-expression of IL-2 in these vectors does not enhance partial protection nor does it overcome lack of protection by NP/VV in mice of the B10.A(5R) strain. The latter strain shows no NP-specific cytotoxic T cells as it expresses only NP non-responder class I alleles of the major histocompatibility complex[7].

The preliminary data of Flexner *et al.*[4] show variable effects on antiviral antibody formation by the IL-2/HA/VV vector, depending on the mouse strain and route of infection. The immunological effects of including the IL-2 gene in the recombinant vaccinia virus need to be studied, and particularly the long-term priming of B- and T-memory cells, the main aim of vaccination to protect against exposure to natural infection.

The concept of using recombinant vaccinia virus for clinical applications remains questionable, but it should be possible to develop additional vectors for the expression of desired growth or differentiation factors for possible clinical use. The observations by Flexner *et al.*, that IL-2 is produced for several days *in vivo*, is encouraging, because IL-2 and many interleukins or interferon-γ have very short half-lives when administered directly *in vivo*. Thus, continued production of a growth factor *in vivo* may modulate responses in severe immune disorders. The next step is to analyse the immunological effects induced by co-expression of IL-2 in recombinant vaccinia in athymic or other immunodeficient or immunosuppressed hosts. □

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