technology that has been developed to detect trace amounts of the long-lived nickel radioisotope ^{63}Ni, which is produced from copper atoms by high-energy neutrons. Straume and colleagues have detected informative quantities of ^{63}Ni in copper samples taken as far away as 1,500 metres from the Hiroshima bomb, and their new calculations of neutron exposure agree with the DS86 estimations over these wide distances.

Closer to the centre of the explosion (around 380 metres), the DS86 estimations may indeed have been wrong. The ^{63}Ni measurements suggest that actual exposure at this distance was around 35% less than predicted, a finding that is supported by the earlier measurements in the sulphur samples[5]. But because most of the Hiroshima survivors who suffered appreciable exposure were between 900 and 1,700 metres from the explosion[5], this discrepancy is of largely academic concern.

Taken together with previous validations of the estimated γ-ray doses[5], and of the Nagasaki neutron doses[9], it is now clear that the DS86 dose estimates correctly reflect all components of radiation dose in the two cities. So where does this leave the measurements of the low-energy neutrons that initiated these investigations? Embarrassingly, recent re-analyses of these data suggest that if background radiation is taken into account (which the original analyses did not do), then the discrepancy with DS86 largely disappears[10,11].

What are the implications of the new study for risk estimates? One implication is clear: Straume *et al.*[1] have confirmed that neutrons accounted for only 1–2% of the total radiation dose received by the survivors of the atomic bomb (although after accounting for their greater biological effectiveness relative to γ-rays[2], the proportion of the total dose becomes 10–20%), so we cannot derive any useful information about the risks associated with neutron exposure from the Hiroshima bombing[12,13]. But on the positive side, we now have more confidence both in the estimates of the total radiation output from the Hiroshima bomb, and in the calculations of radiation transport through the air. We also have greater confidence in determinations of the relative proportions of γ-ray and neutron radiation to which the survivors were exposed. Will predictions of the risks associated with γ-radiation therefore become more reliable? Arguably yes, but the atomic-bomb data remain contentious as a source of risk estimates for reasons that are largely independent of the dosimetry. Stewart and Kneale[14] maintain that the survivors of the Hiroshima and Nagasaki bombings are highly 'selected', with the degree of selection depending on age as well as the dose of radiation. They argue that such selection invalidates the use of the survivor data for deriving risk estimates that are applicable to a general population.

Is this a real problem? The work of Straume *et al.*[1] and others[5,9] indicates that there are unlikely to be appreciable systematic inaccuracies in the DS86 dose estimates; however, random errors in the dose estimates for individuals still exist. For example, the bomb survivors' recall of their position in the two cities at the times of the bombings was inevitably imprecise. Interestingly, if these random individual errors are taken into account, the selection findings of Stewart and Kneale[14] largely disappear[15]. Moreover, the cancer risks derived from survivor data are statistically consistent with those observed in groups exposed occupationally[16,17] and medically[2,18]. So, despite individual errors, the collective data from the survivors of the atomic bomb are likely to remain a valuable predictor of the risks of ionizing radiation. ■

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Global change

South dials north

Thomas F. Stocker

Climate is greatly influenced by ocean circulation in the North Atlantic. But warming episodes, as glacial conditions turned into interglacials, may have been triggered by events far to the south.

The Earth's emergence from the grip of the last ice age took about 10,000 years and was a rough ride. Cycles of rapid warming and cooling preceded a final period of warming, and entry into the current interglacial, from about 10,000 years ago. The dominant player in these events is thought to have been the North Atlantic thermohaline circulation, which transports massive amounts of heat northwards from the tropics, and the effect on that circulation of perturbations in the North Atlantic itself[1]. But might the crucial dials that control this system be elsewhere? On page 532 of this issue, Knorr and Lohmann[2] present a modelling study which shows that slow climate changes in the Southern Ocean around Antarctica (Fig. 1) can influence events in the North Atlantic. Those changes, it seems, may have been ultimately responsible for the abrupt warmings recorded in the Northern Hemisphere.

The Atlantic thermohaline circulation is mainly driven by density differences in bodies of water, density being determined by temperature and salinity. Warm water flows north from the tropics, cooling and sinking as it approaches high latitudes to become a return flow at depth as North Atlantic Deep Water[3]. The traditional view, based on studies of how this 'meridional circulation' can collapse, is that bursts of fresh, less dense water from melting northern ice sheets or background noise in the North Atlantic trigger instabilities that cause it to weaken or shut down[4,5].

Knorr and Lohmann[2] have looked instead at how this circulation can resume after being stalled. They find that, once a threshold is reached, slowly increasing sea surface temperatures around Antarctica and receding sea-ice cover lead to the North Atlantic thermohaline circulation being rapidly switched on. The abrupt increase of meridional heat transport by the ocean causes a sea surface warming of up to 6 °C in the northern North Atlantic within a few decades. These results constitute significant progress in climate studies. They show that slow changes in the south can have abrupt and far-distant consequences, and they link processes operating on scales of thousands of years (such as alterations in Earth's orbital parameters) with the faster changes occurring in, for example, the thermohaline circulation or ice-sheet discharges.

Knorr and Lohmann's climate model is a comparatively simplified one which is efficient for investigating processes associated with deep-ocean circulation and its long

adjustment time. But it largely omits ocean interactions with atmospheric dynamics, particularly with the hydrological cycle. As in many models, the Atlantic thermohaline circulation exhibits hysteresis behaviour when affected by freshwater fluxes — that is, the route taken to an end point is not the same as the return route to the starting point, and this property is at the heart of the mechanism described by Knorr and Lohmann. Here, hysteresis implies that, within a certain range of heat and freshwater exchange between the atmosphere and ocean, the thermohaline circulation can be either weak or strong.

In the authors' experiments, ocean surface parameters south of 30° S are modified slowly from those of glacial conditions to those characteristic of the present interglacial (sea surface temperatures increase and sea ice retreats). Both effects decrease the density of surface waters and, because of Earth's rotation, the Antarctic Circumpolar Current accelerates. This increases the return flow of near-surface waters into the South Atlantic via paths that affect the salt balance of the Atlantic basin[6]. Northward motion of water masses also increases in the North Atlantic, bringing denser, salty waters from the tropics into the 'sinking' regions at high latitudes, where they eventually kick-start thermohaline circulation and meridional transport of heat.

Another mechanism of distant triggering of thermohaline circulation in the Atlantic has been proposed[7,8], invoking injection of fresh water from the Antarctic ice sheet. In consequence, the density of deep and intermediate waters from Antarctica, which compete with North Atlantic Deep Water, is reduced, ultimately accelerating the thermohaline circulation[9]. This mechanism may also be active in Knorr and Lohmann's simulations: in their model, at 30° S, most of the Atlantic Ocean below a depth of 500 m becomes fresher, and hence less dense, when the surface conditions around Antarctica are forced to change.

PLANETARY VISIONS LTD/SPL

Figure 1 **Southern perspective: a satellite view of Antarctica and the Southern Ocean. Knorr and Lohmann's study[2] suggests that events in this region could have triggered warming in the north.**

The North Atlantic thermohaline circulation is known to be vulnerable to pulses of melt water into, or close to, the areas where deep water forms at high latitudes, and this can shut down deep-water formation[4], with possible global implications through the operation of the 'bipolar seesaw'[10]. In this mechanism, an abrupt cooling in the north, caused by the shut-down of the thermohaline circulation, would initiate a slow warming in the south. Given these overall results[2,7,8], however, it seems that reactivation of that circulation is likely to stem from events in the far south: by southern warming and increased northward advection of salt at the surface; or by a reduction in the density of deep waters of southern origin entering the Atlantic Ocean at depth, so giving way to enhanced formation of North Atlantic Deep Water. An overall, speculative view of events between 20,000 and 10,000 years ago is shown in Box 1.

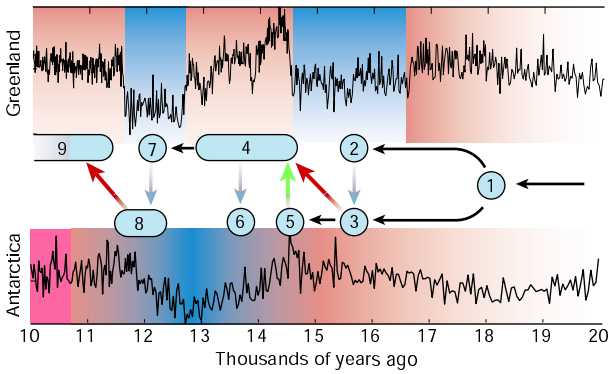
Other distant effects have been proposed as triggering abrupt change in the North Atlantic. For example, shifts in the frequency and amplitude of the El Niño–Southern Oscillation (ENSO) in the tropical Pacific could alter the freshwater budget of the

Box 1 The rough ride through deglaciation

The upper and lower panels here show high-pass filtered 'proxy' temperature records from ice cores in Greenland[12] and Antarctica[13], respectively, indicating the abrupt coolings and warmings between 20,000 and 10,000 years ago, superimposed on the general warming trend that characterized the transition from glacial to interglacial conditions. The centre panel shows the inferred courses of events in the north and south.

(1) About 18,000 years ago, changes in Earth's orbital parameters initiate the end of the ice age through increased solar radiation. (2) Fresh water from melting northern ice sheets shuts down thermohaline circulation in the North Atlantic. (3) A 'seesaw' mechanism (grey arrow), which connects the polar regions north and south[10], enhances warming in the south. This warming turns on the thermohaline circulation in the Atlantic rapidly, by both (4) a surface advection of saline waters[2] and (5) a large-scale discharge of melt water in the south[14], which reduces the density of deep water masses formed around Antarctica[7,8].

The north is now in a warm phase, and the seesaw produces (6) the cooling seen in Antarctica from around 14,000 years ago[15], and also accelerates melting of northern ice sheets, which reduces the Atlantic thermohaline circulation and triggers an abrupt cooling in the north (7). This stimulates, again by the seesaw, southern warming (8). Finally, the southern warming turns on the thermohaline circulation in the North Atlantic, leading to the final warming in the north (9) that marks the beginning of the current interglacial.



The grey vertical arrows indicate the operation of the seesaw. The red and green arrows indicate the two different mechanisms[2,7,8] that emerge from modelled simulations of climate, and that are proposed to be the southern cause of switching on the thermohaline circulation in the North Atlantic. **T.F.S.**

tropical Atlantic, and so influence thermohaline circulation in the north of the ocean[11]. But these mechanisms will remain speculative as long as we lack adequate temperature reconstructions or other estimates of ENSO strength during deglaciation. All in all, the tropics are probably the biggest wild card left in the game of understanding abrupt climate change.

This point takes us back to a limitation of Knorr and Lohmann's study[2]. Because atmospheric dynamics are neglected, changes of ocean circulation patterns and their effect on atmosphere–ocean heat exchange and the freshwater balance through the hydrological cycle cannot be accounted for. So the next steps will be to perform experiments using more comprehensive models to test the importance of the processes that these authors have identified. ■

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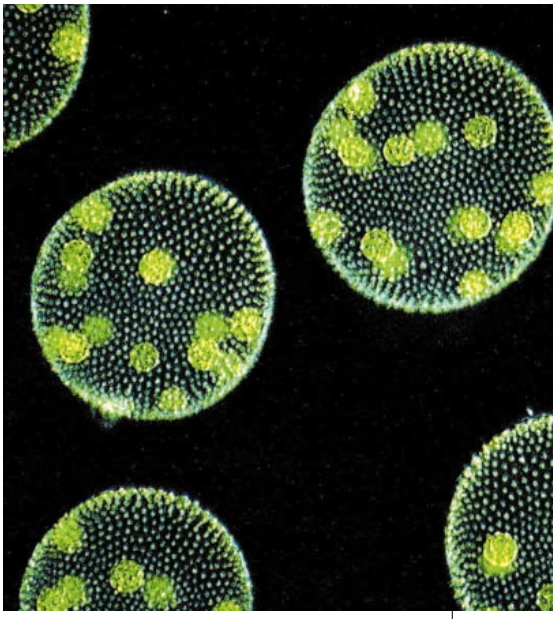

Figure 1 ***Volvox carteri*. The adult organism consists of some 2,000 small somatic cells located on the surface of a hollow sphere, and around 16 large reproductive cells just below, within a transparent extracellular matrix. By a series of predetermined cell divisions each reproductive cell will become an embryo that finally turns inside out by a process called inversion, to produce a juvenile with all its cells in the adult orientation.**

Developmental biology

How to turn inside out

Rüdiger Schmitt and Manfred Sumper

The discovery that a molecular motor of the kinesin family is involved in turning a multicellular green alga inside out might have implications for similar events in animal development.

Something quite remarkable happens to embryos of the multicellular green alga *Volvox carteri*: they turn completely inside out to establish the adult body plan. This inversion process closely resembles the initial stages of the more complex gastrulation that occurs in animal embryos — so *Volvox* could arguably be considered a simple model for analysing the principles that direct such changes in shape. As they describe in *Cell*, this idea led Nishii and colleagues[1] to re-examine and dissect the process of inversion in *Volvox*. Their concept helps to explain the biomechanics and the driving forces behind the curling of a cellular sheet.

In the embryos of most multicellular animals, sheets of cells invaginate during gastrulation, neurulation and organ formation. Gastrulation is the central process in early animal development, and occurs during the blastula stage — when the embryo consists simply of a hollow ball of cells. It involves complex movements that carry those cells whose descendants will form the future internal organs from their superficial position on the blastula to their definitive positions inside the embryo. Similarly, neurulation in vertebrates involves a complicated curling of a cellular sheet to form the neural tube, which in turn develops into the central nervous system.

Gastrulation has fascinated developmental biologists ever since it was recognized in 1874 (for a historical review, see ref. 2). Nearly 100 years ago, the Italian embryologist Angelo Ruffini first described the appearance of elongated cells — known as bottle or flask cells — at the onset of the process in amphibians. Then, in his classic papers on amphibian gastrulation, Johannes Holtfreter[3,4] claimed that the ability to invaginate is an innate property of flask cells. Modern investigations confirm that the number and arrangement of the flask cells are critical factors for proper initiation of invagination. But, as pointed out by Keller[5], what flask cells do — and how, in a biomechanical sense, they do it — remains to be elucidated. *Volvox carteri*, a much simpler organism, might be the Rosetta Stone that enables researchers to unlock the problem.

Volvox is a multicellular green alga (Fig. 1) that exhibits the simplest kind of differentiation — the division of labour between just two types of cell. The adult organism consists of about 2,000 mortal somatic cells, which make up the surface of a hollow sphere, and 16 larger, potentially immortal reproductive cells just below the surface. The development of *Volvox* starts with a single reproductive cell, which undergoes a patterned sequence of 11 cell divisions. The first five divisions are symmetrical, resulting in an embryo consisting of 32 cells of similar sizes. But the sixth division of the 16 most anterior cells is asymmetric, and results in the production of 16 cell pairs of unequal size. The larger cells will become the new reproductive cells.

As a result of geometrical constraints, at the end of the 11 cell divisions the embryo is inside out with respect to the adult configuration: the large reproductive cells protrude from the surface, and the bases of the developing flagella of all the somatic cells point to the interior of the hollow sphere. So cell division is followed by inversion, in which the curvature of the embryo is reversed to establish the adult configuration. Development of *Volvox* therefore resembles that of classic models of animal development, such as sea urchins and nematode worms, in that an important differentiating cell division is visibly asymmetric, and the adult configuration is attained by a gastrulation-like event.

How does inversion come about? First, the phialopore (a slit at the anterior end of the embryo) widens, and four lips of cells bend outwards and backwards over the adjacent cells — in other words, they curl outwards. The region of maximum curvature moves progressively towards the posterior pole, until the inverted region almost surrounds the posterior (non-inverted) hemisphere. At that point the posterior hemisphere 'snaps' through the opening at the equator, and the phialopore lips move to seal the gap at what is now the posterior pole.

Flask-shaped cells that are linked by a network of cytoplasmic bridges are the key

players in this dramatic shape change. Cells become flask-shaped — with a long stalk at their outer end — near the bend region, and they then move inwards relative to the network of cytoplasmic bridges, which runs through each cell and connects it to its neighbours. This is the key point in Kirk's model of inversion[6,7]: as flask cells proceed from being linked at their widest point to being linked at their thin outermost ends, the cell sheet is forced to curl sharply outwards (Fig. 2).

Nishii *et al.*[1] now propose that this displacement of flask cells relative to the cytoplasmic bridges is driven by a motor protein — a newly discovered kinesin denoted InvA.

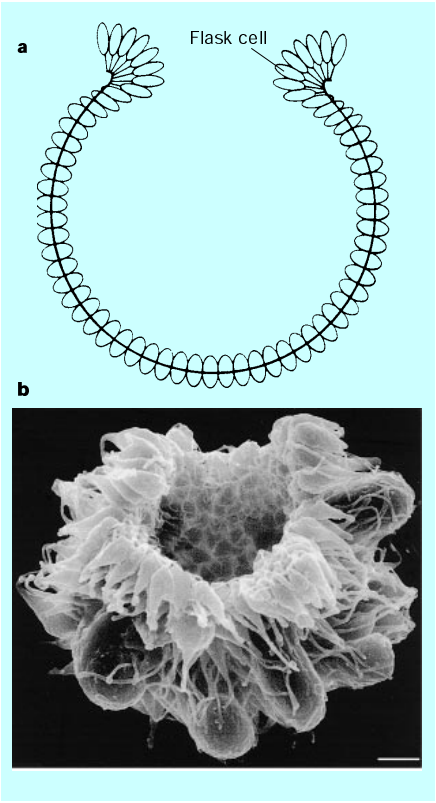

Figure 2 **Inverting *Volvox*.** a, **Cross-section through an inverting embryo. The continuous black line represents the system of cytoplasmic bridges that connects the cells and holds them together. The force necessary for inversion is generated by a change in cell shape, together with cell movement. First the cells become flask-shaped by forming long, narrow 'stalks' at their bottom (outward) ends; then they move inwards relative to the cytoplasmic bridges to a point where they are only linked at their narrow tips. These actions produce a bend region, where the cell sheet is folded back on itself. The results of Nishii *et al.*[1] suggest that a newly discovered kinesin, InvA, is located in the cytoplasmic bridges, and that, by moving along the microtubule filaments lining the flask cells, InvA produces the force that drives the cell body past the bridges to form the bend.** b, **An embryo with a mutation in InvA; it is unable to invert fully.** a **and** b **are reproduced from refs 9 and 1, respectively. Scale bar, 5 μm.**

The authors started by generating mutant *Volvox* embryos with defects in inversion. They then analysed one such mutant in depth, and found that although its cells became appropriately flask-shaped, they failed to move relative to the cytoplasmic bridges. Nishii *et al.* went on to show that the gene affected in this mutant encodes a kinesin, and that this molecular motor is located in the cytoplasmic bridges.

Each flask cell has cytoskeletal filaments of microtubules that run along its length, just inside the plasma membrane, and Nishii *et al.* propose that InvA molecules attempt to move downwards on these filaments. But, because the InvA molecules are anchored to the bridges, and the bridges themselves are fixed in place, InvA cannot move significantly. Instead the force produced by this motor causes the microtubules — and consequently the whole cell — to move past the cytoplasmic bridges. This perpendicular movement eventually connects the cells at their thin outermost ends and so creates a sharp bend.

The discovery of a special kinesin as part of the machinery that causes the curling of a cellular sheet in *Volvox* will stimulate a search for a related motor protein with the same function in animals. Might such a motor exist? It seems plausible: molecules such as cytoskeletal proteins are found in most organisms, from unicellular yeasts to humans, and were probably present in the unicellular common ancestor of plants and animals. Their existence there would predetermine similar solutions to given morphogenetic problems. Moreover, if the displacement of asymmetrically shaped cells with respect to a fixed framework of cell–cell connections is the key concept underlying curling, then the cytoskeleton and cell–cell adhesion systems would have to play a key part. This would mean that similar mechanisms operate even in evolutionarily very distant[8] organisms, from multicellular algae to animals. ■

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Materials science

The road to diamond wafers

S. T. Lee and Y. Lifshitz

Diamond could rival silicon as the material of choice for the electronics industry, but has been held back by the difficulty of growing large enough wafers. This problem may now be solved.

Diamond is the king of gemstones. Less well known is that it could also be an outstanding semiconductor material, superior in many ways to silicon, which is currently the most widely used electronic material. Diamond devices could operate at higher temperatures (more than 400 °C) and higher power than those of silicon, as well as being faster, denser and more resistant to radiation. But practical diamond electronics will need large-area, single-crystal diamond wafers to be fabricated, analogous to the 6–12-inch silicon wafers commonly used in the semiconductor industry. Two papers from Golding and colleagues, in *Applied Physics Letters*[1] and *Diamond and Related Materials*[2], now show that this may be possible if sapphire wafers are used as substrates on which to grow the diamond.

Diamond can be grown on diamond ('homoepitaxy') by chemical vapour deposition: a diamond substrate, at a temperature of 600–800 °C, is exposed to an ionized mixture of roughly 1% hydrocarbon and 99% hydrogen. Electronics-grade diamond has been made in this way[3]. The newly grown diamond wafer can be cut from the diamond substrate, and the process can be repeated many times, reusing the substrate. But single-crystal diamond substrates are small and expensive, so this is not a viable way to fabricate large-diameter diamond wafers.

The alternative is to grow diamond on a foreign (non-diamond) single-crystal wafer — this is 'heteroepitaxy', the oriented growth of one crystal on another. Heteroepitaxy is readily achieved if the atomic spacings in the foreign substrate match those in diamond crystals. Of the various substrates tested — such as silicon, silicon carbide, nickel, cubic boron nitride and platinum — iridium is the best found so far[4]. The quality of epitaxial growth is measured by the average angular spread of the diamond-crystal orientation along a certain direction (also called mosaicity). The minimum angle achieved is 3.9° for silicon, less than 2° for platinum, 1.5° for