and treatment of both benign and malignant thyroid disorders. For example, radioiodide is commonly used to treat overactive thyroid glands, such as those seen in Graves' disease. Thyroid cancer cells generally retain their ability to transport iodide, although to a lesser extent than normal thyroid cells. So, for patients whose thyroids have been removed during treatment for thyroid cancer, whole-body radioiodide scanning is often used to detect cancerous cells of thyroid origin that have migrated (metastasized) to other sites in the body. Often during these clinical procedures, iodide uptake also occurs in other tissues such as salivary gland and lactating breast. This is consistent with the observation[2] that the NIS is expressed in some non-cancerous tissues near breast tumours. Administration of higher doses of radioiodide is an effective treatment for metastasized thyroid cancer.

The implications of the new findings[2] for diagnosing and treating breast cancer are uncertain, however. Unlike thyroid-cancer patients, most breast-cancer patients have functioning thyroids. Normal thyroid cells accumulate and retain iodide far more efficiently than do thyroid cancer cells, breast epithelial cells, or any other cell type[8]. The presence of a patient's normal thyroid will pose a challenge to the use of radioiodide to detect or treat breast tumours, as it will sequester nearly all the radioiodide until the thyroid itself is destroyed. Also, it is not yet known what proportion of human breast cancers express functional NIS and hence accumulate iodide. The results of Tazebay *et al.* indicate that the NIS may be incorrectly localized within the cells of some breast tumours and thus incapable of taking up iodide. So, more work is needed before we can know whether uptake of iodide in breast tumours will be of clinical use.

The results have greater implications for thyroid cancer patients. Treating such patients with radioiodide is effective when the radioiodide is retained in the cells; however, metastases can lose their ability to take up and accumulate radioiodide. In this case, thyroid cancers often develop further, and other treatments — such as external beam radiotherapy — are usually ineffective at stopping the disease. So there are intense efforts to try to stimulate such thyroid tumours to 'redifferentiate' and take up radioiodide again. Tazebay *et al.*[2] have shown that it is possible to use hormones to stimulate the expression of NIS in non-lactating mouse mammary cells. Perhaps it might be possible to stimulate thyroid metastases to express NIS in the same way, and hence to regain the ability to accumulate enough radioiodide for effective treatment. ■

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Global change

Ice sheets by volume

Peter U. Clark and Alan C. Mix

In 1840, Louis Agassiz proposed that vast ice sheets had once covered large areas of northern Europe and North America. Since then, geologists, geophysicists and geochemists have argued about the spatial extent and volume of the ice during the Last Glacial Maximum (LGM) around 21,000 years ago.

On page 713 of this issue, Yokoyama *et al.*[1] present evidence that puts a firm figure on ice volume at the LGM. Growth of continental ice lowers global sea level (referred to as glacio-eustatic sea level), so records of sea-level change can be used to reconstruct changes in ice volume. Using new records from the continental shelf off northern Australia, Yokoyama *et al.*[1] estimate that, during the LGM, the sea level was 130–135 m lower than it is now. From this value, they calculate that the LGM ice volume was $(52 \pm 2) \times 10^6$ km^3 more than the present volume of 32×10^6 km^3. In combination with other data, this information can be used to address the interplay between ice sheets, the climate system and the solid Earth.

Ice sheets have a huge impact on Earth's climate by rearranging continental drainage paths and by changing the Earth's topography and albedo (the amount of the Sun's radiation reflected from Earth). At the LGM, ice sheets were nearly 4 km high, covered some 13 times more land than they do today (excluding Antarctica, where the ice area did not change appreciably), and lowered the sea level to expose an extra 2.8×10^6 km^2 of land now under water (nearly equal to the area covered by the additional LGM ice).

Experiments with numerical climate models often target the LGM climate to evaluate climate sensitivity to radiative 'forcing' from such factors as ice albedo, the amount of CO_2 in the atmosphere and variations in the Earth's orbital parameters. The models show that ice sheets contributed as much as 50% of the total forcing[2]. But uncertainties remain. Although the outlines of most of the major ice sheets are now reasonably well known, in some regions the geological record of ice-sheet extent is difficult to interpret — particularly in northern Eurasia[3,4]. Because

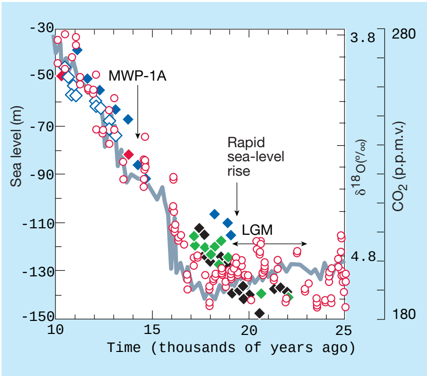

Figure 1 **Sea-level estimates for 25,000–10,000 years ago compared to marine oxygen isotope and atmospheric CO_2 records. The rise over this period is taken to be due to glacio-eustatic effects (that is, the retreat of ice sheets). The new data of Yokoyama *et al.*[1] are shown as black diamonds; green diamonds represent data from Barbados corals corrected by Yokoyama *et al.* Other estimates[12] are based on previous eustatic corrections to coral-reef data in Barbados (blue diamonds), Tahiti (red diamonds) and New Guinea (open blue diamonds). Generally, these estimates match the values implied by the oxygen-isotope ($\delta^{18}O$) record (grey line)[16]. But a rapid rise in sea level about 19,000 years ago, identified by Yokoyama *et al.*, precedes the rapid changes in both $\delta^{18}O$ and atmospheric CO_2 (open red circles)[17]. MWP-1A (meltwater pulse 1A) is an interval of rapid sea-level rise first dated in the Barbados record[18]. LGM, Last Glacial Maximum[17]; p.p.m.v., parts per million by volume.**

the ice sheets left little direct evidence of their height, estimates of LGM ice volume have come largely from indirect evidence or from glaciological modelling. The resulting figures, put in terms of equivalent sea-level lowering, have ranged from 80 m to as much as 165 m.

Among the indirect indicators are oceanic oxygen isotopes, expressed as $\delta^{18}O$ in parts per thousand, preserved in fossil shells. Ice-sheet growth caused a measurable change in the $\delta^{18}O$ composition of the global ocean[5], but the relative contributions of other factors (such as temperature and local salinity) to this signal remain poorly understood, and floating ice shelves would change $\delta^{18}O$ but not sea level. In another approach, records of local isostatic responses (that is, the rise and fall of the Earth's crust) to changes in ice thickness or water depth can be inverted to estimate ice thickness[6]. However, uncertainties in model parameters, and the brevity of critical time series, mean that several solutions are possible[7]. Finally, modelling of ice volume based on the area occupied by former ice sheets initially assumed that the conditions at the base of ice sheets, which control ice profile, were the same in the past as they largely are now. Yet they may have been very different[8].

The most direct evidence of LGM ice volume comes from records of lower sea level. But there are two difficulties: finding a well-preserved and dateable record of LGM sea level, and then distinguishing the isostatic from the glacio-eustatic component of the signal. Yokoyama *et al.*[1] addressed these difficulties by dating geological records on the tectonically stable northern Australian continental shelf, and deriving the glacio-eustatic component by accounting for the isostatic effect on the shelf caused by the sea-level rise that accompanied deglaciation.

Their results resolve a long-standing controversy. Furthermore, they suggest that the LGM ice volume was relatively stable for at least 3,000 years, implying that the ice sheets approached isostatic and, perhaps, dynamical equilibrium. Their analysis also indicates that the LGM was terminated by a rapid rise in sea level 19,000 years ago (Fig. 1). Such an abrupt event may record a climatic or other instability that triggered the demise of the ice sheets[1,8], and may help to explain the conflicts with ice-volume reconstructions based on inversion of past sea levels[7].

Useful though they are, the new data do not show how the ice was distributed among individual ice sheets. Once the spatial extent of the former ice sheets in northern Eurasia is resolved[3,4], models should converge on some reasonable distribution of ice that sums to 130–135 m of lowered sea level. This is important, as climate models are sensitive to regional details of ice extent and height.

But some significant puzzles remain in reconciling the various data sets. For example, the new sea-level estimates support a change of some 1.4‰ in the $\delta^{18}O$ budget of the whole ocean. This is consistent with some estimates of deep-sea cooling[9], but it conflicts with those based on pore-water data[10]. Similarly, the isotope-budget data suggest that temperatures in the oceanic warm pools, such as the western tropical oceans, were relatively stable — this runs counter to temperature indices based on strontium:calcium ratios in fossil corals[11].

One next step will be to confirm the Australian record using other sea-level archives, such as submerged coral reefs. Corals that grow on the ocean margins can be accurately dated, and coral records from Barbados, New Guinea and Tahiti provide valuable information on past ice volume. But existing coral records[12] miss both the LGM low sea level and the early jump in level of around 19,000 years ago seen in the Australian record. Combining coral records with the new data, however, suggests that deglaciation was punctuated by two, or perhaps three, brief intervals when rates of sea-level rise exceeded 5 m per century (Fig. 1).

The inferred sea-level jump of 19,000 years ago precedes the first prominent decrease in marine $\delta^{18}O$ by about 3,000 years (Fig. 1), and if this is correct it indicates a decoupling of the timing or amplitude (or both) of the sea-level and isotope records during this early phase of deglaciation. Such a misfit is too large to be accounted for by ocean mixing[13]. Together with a similar lag in increasing atmospheric CO_2, these relations seem to require ocean cooling associated with the jump in sea level, or dynamic changes involving the collapse of ice on land compensated by growth of floating ice shelves. Such a shift might displace water in the ocean without modifying the oxygen isotope budget, while helping to keep CO_2 in the deep sea.

What really happened early in deglaciation remains a matter of debate[14]. So too does the timing of events as reflected in ice cores and marine sediments. But all of these factors are crucial to understanding the cause of deglaciation, as well as the potential for ice-sheet instability in the future. These issues, among others, will be addressed at a meeting in October this year held under the auspices of the "Environmental Processes of the Ice Age: Land, Oceans, Glaciers" (EPILOG) programme[15]. ■

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Daedalus

Shuffling around

Storage is costly for manufacturers and distributors alike. Indeed, 'just in time delivery' transformed the economics of many companies simply by reducing their burden of storage. Yet in any warehouse, over half the space is always empty — the bays and aisles needed for access to the goods.

In this connection Daedalus recalls the '15 puzzle', the mathematical amusement in which a tray of four units square contains 15 numbered tiles and one space. By repeatedly moving an adjacent tile into the space, you can shuffle the tiles into almost any chosen pattern. (In fact, just half the imaginable arrangements are accessible.) So DREADCO engineers are now inventing a '15-puzzle warehouse'. Instead of a fixed floor, it has a number of mobile platforms running on a grid of rails set out in a square pattern. Each platform carries a tower of pallets bearing the goods to be stored. They completely fill the warehouse, except for one space. Yet that single space allows the platforms to be shuffled indefinitely. Any desired platform can be rapidly brought to the loading bay for the delivery or replenishment of its contents.

The mathematics of the 15-puzzle warehouse (or rather its generalization, the '*NM-A* warehouse', where *N* and *M* are the unit numbers of its sides, and *A* is the number of empty spaces needed for fast enough access to the least accessible platform) will be subtle indeed. While DREADCO's hardware team consider the wheels, rails and motors needed to drive the platforms around under computer control, their software colleagues are writing the algorithms to access any platform or succession of platforms in the fewest moves. The final fully automated installation will need no fork-lift trucks to ferry goods around. A simple computer command will rapidly bring any desired sequence of goods or empty platforms to the one portal that handles all transactions. Storage costs will plummet.

The *NM-A* principle should also usefully apply in other fields. The *NM-A* car-park, its vehicles packed in a solid rectangular array, will save vast amounts of urban space. A naive owner may be dismayed to see his vehicle zig-zag away into the crowded mass. But once in the matrix it will be impossible to steal or steal from, and only the owner's ticket in the car-park computer will shuffle it back to the exit. But an *NM-A* library, or even an *NM-A* supermarket, would probably be intolerably inconvenient. Customers for these amenities need to browse around. **David Jones**