

*Rb* inactivation that triggered cell-cycle re-entry. The authors went on to show that p107 and p19<sup>Arf</sup> both contributed to maintenance of the quiescent state in the germline-inactivated cells, suggesting that these proteins help to compensate for the loss of *Rb* in these circumstances.

The effects on senescent cells were even more dramatic (Fig. 1). Senescence is a condition of proliferation arrest from which cells rarely escape. Senescent cells are usually large, flat and metabolically active, yet do not divide; they express a set of characteristic 'marker' proteins; and they upregulate cell-cycle inhibitors such as p19<sup>Arf</sup> and p16<sup>Ink4a</sup> (ref. 4). Senescence can prevent mammalian cells from becoming malignant<sup>5</sup>, and may influence the efficacy of anticancer treatments<sup>6</sup>. Jacks and colleagues found that acute mutation of *Rb* in senescent MEFs forced a significant proportion of the cells back into the division cycle (as judged by the incorporation of a division-specific dye, BrdU, and by the rounding-up of large, flat cells). Moreover, many of the cells continued to divide for a number of passages.

Senescence in MEFs is probably caused by the accumulation of damaged DNA<sup>7</sup>. Usually, DNA damage is sensed by a signalling pathway involving another tumour suppressor, p53, which then halts cell division. Previous work<sup>8</sup> showed that when p53 was inhibited in senescent cells, this too caused them to round up (although most then died). An earlier study<sup>9</sup> also found that either inhibition of the p53 pathway, or a lack of at least two *Rb*-related proteins (also known as pocket proteins), can confer immortality — the ability to continue dividing — on MEFs. And the fact that *Rb*-deficient, senescent MEFs re-enter the cell cycle<sup>1</sup> is consistent with the observation that p53-mediated cell-cycle arrest requires a certain level of pocket proteins bound to the E2F protein<sup>10</sup>. All of this implies that acute, temporary loss of *Rb* might relieve a p53-imposed block in senescent MEFs, enabling them to continue proliferating with damaged DNA. That can't happen when *Rb* is inactivated in the germline, because p107 compensates.

There is increasing evidence that regulators of the p53 and *Rb* signalling pathways, such as p19<sup>Arf</sup> and p16<sup>Ink4a</sup>, respectively, have different effects on the induction of senescence in human and mouse fibroblasts. This could well relate to the propensity of MEFs to accumulate DNA damage under cell-culture conditions — putting the emphasis on the p53 pathway in these cells.

Although this might make MEFs rather atypical, Jacks and colleagues' observations<sup>1</sup> do illuminate a mechanism with broad ramifications. The instant imbalance brought about by acute loss of tumour-suppressor function can 'kick' cells into the division cycle, or overcome other mechanisms that

keep cells in check, thereby providing a window of opportunity for incipient cancer cells to progress to a more malignant state. The observation that it requires several passages before MEF cultures revived from senescence by *Rb* inactivation can re-enter senescence<sup>1</sup> supports the idea that it takes time to activate back-up systems. That this window of opportunity can present a real threat might be illustrated by the fact that 12 of the 14 senescent cultures that began dividing upon *Rb* inactivation subsequently became immortal — quite possibly as a result of acquired mutations in the p53 pathway.

One other point is worth noting. The data reported by Jacks and colleagues do not provide evidence for enduring differences in gene-expression profiles between cells that lack *Rb* from the start, and those in which *Rb* is acutely deleted. But that does not necessarily mean that there are no such

differences, fixed early in development by mechanisms such as chromatin remodeling<sup>11</sup>. Time will undoubtedly tell. ■

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## Oceanography

# Stirring times in the Atlantic

Bob Dickson

Set against certain other oceanographic phenomena in the northwest Atlantic, a class of brief and localized events that occur in the Irminger Sea may seem inconsequential. Not so, however.

On page 152 of this issue, Pickart *et al.*<sup>1</sup> describe the winter incidence and climatology of so-called 'tip-jet events' off southern Greenland, their association with storm centres tracking north-eastward into the Denmark Strait, and their effect in producing episodes of deep convective exchange in the Irminger Sea to the southeast of Greenland. That tip jets should have this effect is no surprise in itself. Although they are brief, localized, intermittent and strongly seasonal, such events are evidently associated with an intense heat flux from the ocean and a strong wind stress curl (the 'twisting' tendency in the wind stress field; Fig. 1, overleaf) that are important drivers of ocean convection. The surprise comes in the suggestion that sufficient 'Labrador Sea Water' might be produced in the winter Irminger Sea to rival that formed in the Labrador Sea itself<sup>1</sup>.

The Labrador Sea, which lies to the south and west of Greenland, is of particular climatic importance. It is at the headwaters of the Atlantic Ocean's thermohaline 'conveyor', and is the basin where a wide range of water masses, including the output from Arctic and subarctic seas, are received, stored, transformed and discharged to form the deep western boundary current — the abyssal limb of the Atlantic conveyor. The loss of heat and buoyancy under the chill northwesterly airflow from Arctic Canada in winter has also made the Labrador Sea one of

the main global centres of deep convective exchange. It is thus a site where one of the principal vertically homogeneous 'mode waters' of the ocean — Labrador Sea Water (LSW) — is formed, and where the signal of climate change can be transferred to great ocean depths.

Over the past three or four decades, a broad range of upstream influences have come together to drive ocean variability in the Labrador Sea on multi-decadal timescales and at all ocean depths. The most dramatic instance has been the observed transfer of 'freshening' from subarctic seas to the entire water column of the northwest Atlantic.

In the upper ocean, this occurred through the relatively fresh, relatively shallow, mix of Pacific water, Arctic ice-melt and Arctic river discharge that passes south to the Atlantic on either side of Greenland. There is clear, if indirect (proxy), evidence of a 40-year increasing trend in the amount of fresh near-surface waters passing south from the subarctic around the western margins of the Labrador Sea<sup>2</sup>. In the Labrador Sea itself, these cool, fresh surface conditions were picked up and mixed to intermediate depths of more than 2,000 m by convective exchanges of intensifying — and ultimately of record — vigour, stimulated by the chill northwesterly airflow sweeping out of Arctic Canada at that time. By 1994, the layer of convectively formed LSW was fresher, colder, deeper and denser than at any other time in

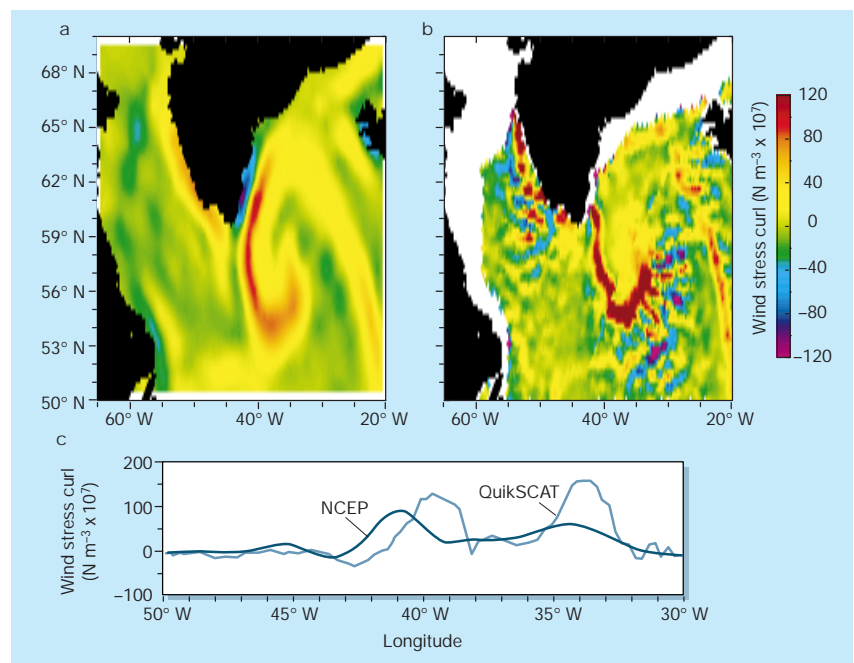
the history of measurements there. Finally, in the lower layers, a long-term and broad-scale freshening of the seas north of Iceland<sup>13–5</sup> was communicated south to the deep ocean by the two dense overflows that descend from their spillways across the Greenland–Scotland Ridge to ventilate the deep and abyssal Atlantic; this entire system of overflow and entrainment has freshened steadily over the past four decades<sup>6</sup>.

Many of these individual changes are beyond the range of our past experience. Most have their origins in the long-period amplification of the leading mode of wintertime atmospheric forcing in these waters, the North Atlantic Oscillation (NAO). By the early 1990s, the NAO had evolved to its most extreme positive state in the 175 years of instrumental recording and possibly much longer<sup>7</sup> (the positive state of the NAO is one in which an intensified winter pressure gradient between Iceland and the Azores drives strong mid-latitude westerlies). As a result, between 1966 and 1994, in what we believe to be the largest change in the modern instrumental oceanographic record, a sustained climatic change imposed on Arctic and sub-arctic seas was transferred to all layers — shallow, intermediate, deep and abyssal — of the northwest Atlantic.

Set against events of such monumental scale, the new mode of ‘LSW’ production reported by Pickart *et al.*<sup>1</sup> may seem small beer. But not so. The mechanism they describe is certainly strongly intermittent, occurring only in winter, and with a ten-day period and three-day average duration. Nonetheless, when Pickart *et al.* add up the numbers, they conclude that the heat flux and strong wind stress curl associated with these tip-jet events drive localized convection of sufficient depth (up to 2,000 m) and persistence to produce significant quantities of ‘LSW’ outside the Labrador basin.

Pickart *et al.* appeal more to ocean modeling than to ocean observations to support their suggestion. And in fact, as long as our knowledge of change in these remote waters is so heavily based on occasional (usually non-winter) surveys, and while the signal of decadal change in classic LSW is still passing through these waters, it may prove difficult to assess the importance of convection in the Irminger Sea more directly. However, there are good reasons for persisting in the attempt.

The first is the central role of these waters in the Earth’s climate system. Through the northwest Atlantic ‘junction box’ pass all of the deep and bottom waters that collectively form and drive the abyssal limb of the Atlantic meridional overturning circulation. And around it pass the freshwater flows from the Arctic that, in model experiments, are implicated in slowing that circulation down. Furthermore, a sizeable body of theory<sup>8–11</sup> now suggests that the vertical circulation too may help determine the rate of the



**Figure 1** The finer scales of satellite sensing. A conclusion to be drawn from the study by Pickart *et al.*<sup>1</sup> is that fine-scale ocean forcings may influence climate. As shown in these images, satellite-borne instruments now provide a remarkable ability to provide synoptic coverage of winds at the 25-km scale over water. This new capability is demonstrated for 12 January 2001, as a wind jet develops at the southern tip of Greenland (the central black image), in association with a rapidly moving cyclonic centre over the Irminger Sea to the southeast. a, Conventional analysis of wind stress curl distributions from the National Centers for Environmental Prediction (NCEP). b, The higher resolution available from the radar scatterometer on the QuikSCAT satellite<sup>15</sup>. This image reveals intense, small-scale features and fronts, crucial to the field of wind stress curl that — as the twisting tendency of the wind stress field — drives ocean upwelling and convection. c, Graphical depiction of the large differences in the recorded amplitude of wind stress curl between the two techniques, for latitude 56.5° N. (Analysis kindly provided by Dudley Chelton, Oregon State Univ.)

overturning circulation by setting the density of the water column. Predictions of the ocean’s role in climate therefore depend on portraying the convective processes of this area with appropriate realism.

It is possible, too, that the relative importance of the phenomenon described by Pickart *et al.* may be growing. In recent winters, a slow eastward displacement of the NAO pattern has reduced the incidence of chill northwesterly winds over the Labrador Sea while increasing the northwesterly airflow from south Greenland across the Irminger Sea. Although the effects of greenhouse gases have produced this kind of shift in models<sup>12</sup>, Hurrell *et al.*<sup>13</sup> conclude that it is more likely to be the intrinsic result of a more NAO-positive climate. Its significance is not only that the warmth of recent winters over the Labrador Sea has, since 1996, brought a dwindling to extinction of deep, dense LSW production<sup>14</sup>, but also that the northwesterly winds over southeast Greenland seem a necessary stimulus for tip-jet forcing of convective events in the Irminger Sea, as described by Pickart and colleagues.

The climatic influence of those events will be felt through the conversion of such intermittent and small-scale events in the

atmosphere into a sustained ocean response. The challenge now is to observe that response directly, and the necessary new ocean-profiling sensor systems have already been deployed for that purpose off southeast Greenland. ■

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