ent during glacial times. Perhaps coccolithophorids, which make small plates of $CaCO_3$, were relatively more abundant then. Without a stable initial condition, size frequency loses its reliability as an indicator of dissolution.

The consideration of shell thickness was initiated by Lohmann (*7*), who heroically measured all three exterior dimensions of thousands of individual microscopic shells and weighed each of them to compute the thickness of the walls between the chambers. He found that the shell walls get systematically thinner with increasing water depth above the sediments. This is consistent with the effect of pressure on solubility, but the novelty was that the wall thinning began at depths where the overlying water is highly supersaturated with respect to $CaCO_3$. This is presumably the result of respiratory CO_2 driving down the pH of sediment pore waters. Here at last was a reliable indicator of the initial stages of $CaCO_3$ dissolution, which would be useful in regions in the middle water column where the column was supersaturated with respect to $CaCO_3$ (1 to 4 km)

Broecker and Clark streamlined the method by mechanically sieving a narrow shell size range and then weighing an ensemble rather than individual shells. They found a good correlation between shell thickness at the top of the sediment core and CO_3^{2-} concentration in the overlying water (*8*). Broecker and Clark now extend this work to the last glacial (*1*). The thickness results indicate that during this time, the intermediate Atlantic CO_3^{2-} concentration was considerably higher than it is today whereas that in the deep Atlantic was lower, leading to a dramatic gradient in CO_3^{2-}.

These results are apparently inconsistent with the distributions of geochemical proxies of dissolved nutrients, the $\delta^{13}C$ and the trace Cd concentrations of foraminifera, which uniformly show nutrient-rich waters at these sites. However, pH and nutrients may deviate from each other to some extent because CO_2 is transported through the atmosphere and nutrients are not. More startling is the inference that the gradient in deep ocean CO_3^{2-}, which is indicative of the flow path of ventilated water, was reversed during glacial time. If proven correct, this difference would have profound implications for the circulation of the deep ocean and the climate of the atmosphere above that drove it.

One of the longest sections in Broecker and Clark's report (*1*) is the discussion of caveats. One is the possibility that shells from different regions, climates, or CO_2 concentrations (*9*) may differ systematically in their shell weights before any dissolution has taken place. Broecker and Clark (*8*) have already documented an offset between the Atlantic and the Pacific and Indian present-day oceans. Even this possibility cannot explain all of the discordant results from different foraminiferal species in cores from the same region (*10*).

More measurements from around the world may or may not end up telling a coherent story. But however it turns out, Broecker and Clark are to be commended for making every effort to test and validate this novel technique. Thus does paleoceanography proceed by proxy.

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PERSPECTIVES: CLIMATE

Climate Variability and the Influence of the Sun

Joanna D. Haigh

The search for the signs of solar variability in climate records has historically been dogged by overstated claims and dubious statistics. In addition, ground-based measurements were insufficiently sensitive to detect variations in the Sun's radiative output. As a result, the subject has tended to be marginalized by the meteorological establishment. However, recent evidence from satellite data has shown that the term "solar constant" is a misnomer. Furthermore, climate change attribution requires the ability to separate natural climate-forcing mechanisms from human-induced factors. It is thus more important than ever that the influence of solar variability on climate is assessed and understood.

To detect a solar influence on climate, two key challenges must be met. First, reliable and consistent long-term indices of meteorological and solar parameters must be constructed. Second, any solar influence must be separated from other influences in what is an inherently highly variable and noisy nonlinear system. Even when a statistically robust solar signal emerges from the data, the mechanisms by which the solar influence acts remain to be explained, particularly because the irradiance variations are small and their direct effect must be amplified in the climate system. Hence, dynamical and physical feedbacks need to be considered. Among these effects may be the coupling of processes in the lower atmosphere to ocean circulation or to the middle atmosphere.

On page 2130 of this issue, Bond *et al.* (*1*) meet the first challenge mentioned above. They investigate the influence of the Sun on the climate of the North Atlantic region during the Holocene (from about 11,000 years ago to the present) using data extracted from deep-sea sediment cores. The level of solar activity is estimated from the concentrations of ^{14}C and ^{10}Be isotopes, which are produced by the action of galactic cosmic rays. Cosmic rays are more intense at Earth's surface when the Sun is less active. The climate is indicated by the concentrations of mineral tracers, which were deposited from drift ice circulating in the subpolar North Atlantic. Increases in the tracers indicate a southward expansion of cooler, ice-bearing water.

The authors show that each of the expansions of cooler water that occur roughly every 1500 years was associated with a strong minimum in solar activity. This remarkable result provides strong evidence that solar activity does indeed modulate climate on centennial to millennial time scales. The authors suggest that changes in ocean thermohaline circulation, associated with the supply of fresh, low-density water from the drift ice and coupled to atmospheric circulations, may amplify the direct effects of small variations in solar irradiance.

To learn more about potential mechanisms by which the solar signal may be amplified, we need to consider the natural modes of climatic variability in the climate system. The El Niño–Southern Oscillation phenomenon is the leading mode of natural variability in the tropics, although its influence is felt globally. At higher latitudes in the Atlantic, the leading winter mode is the North Atlantic Oscillation. These modes may be influenced by external forcing factors, which include natural components (such as solar variability or

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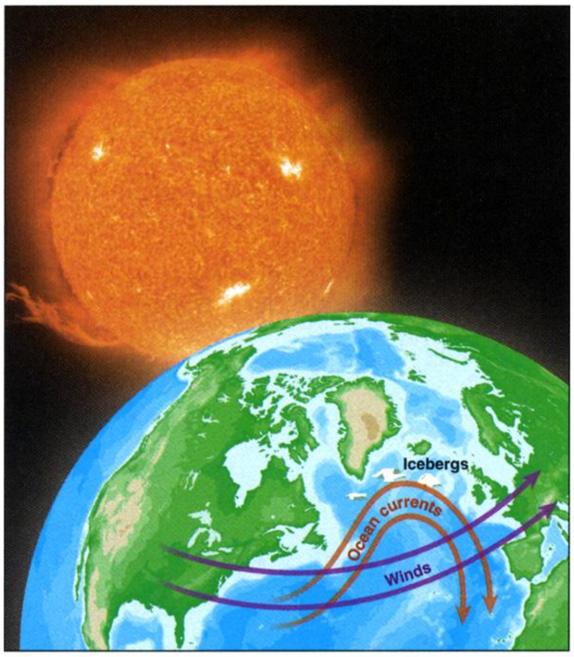
volcanic eruptions) as well as anthropogenic ones (such as increasing concentrations of "greenhouse" gases). Much effort is required to separate the signatures of these different forcings in climate records.

Over the Atlantic in winter, the average sea level pressure near 25° to 45°N is higher than that around 50° to 70°N. This pressure gradient is associated with the storm tracks that cross the ocean and determine, to a large extent, the weather and climate of Western Europe. Since the 1930s, it has been known that variations in the pressure difference are indicative of a large-scale pattern of surface pressure and temperature anomalies from eastern North America to Europe. If the pressure difference is enhanced, then stronger than average westerly winds occur across the Atlantic, cold winters are experienced over the northwest Atlantic, winters are warm over Europe, Siberia, and East Asia, and conditions are wetter than average in Scandinavia and drier in the Mediterranean. The fluctuation of this pattern is referred to as the North Atlantic Oscillation (NAO); the pressure difference between, say, Portugal and Iceland can be used as an index of the strength of the NAO.



Effects of solar variability. Ocean circulation, the transport of drift ice, and the position of the jet stream in the North Atlantic may all respond to changes in the Sun's radiative output.

SOURCE: NASA

Some authors regard the NAO as part of an even larger mode of variability, a barometric "seesaw" between the north polar region and the mid-latitudes in both the Atlantic and Pacific. This mode is called the Arctic Oscillation (AO). A similar effect in the Southern Hemisphere high latitudes is referred to as the Antarctic Oscillation (AAO).

Using observational records of pressure, temperature, and precipitation from individual stations, values for the NAO index have been reconstructed back to 1658 (*2*). The index shows large interannual variability, but over the past two decades the NAO has been strongly biased toward its positive, westerly, phase; it has been suggested that this might be a response to global warming. Computer models of the general circulation of the atmosphere (GCMs) simulate NAO-type variability quite successfully (*3*), and some GCM studies do show increasing values of the NAO index with increased greenhouse gases. However, this is not true of all models, and some studies suggest that the NAO pattern itself may be modified in a changing climate so that the use of simple indices may not be appropriate.

It also remains uncertain how important coupling with either sea surface temperatures and/or the state of the middle atmosphere might be in producing a realistic NAO/AO pattern. Planetary-scale waves, produced in the lower atmosphere by longitudinal variations in topography, propagate upward in winter high latitudes through the stratosphere and deposit momentum and heat, which feed into the general atmospheric circulation. Where this wave absorption takes place depends on the ambient temperature and wind structure. Thus, any changes induced in the mean temperature structure of the stratosphere may result in a feedback effect on lower atmosphere climate. An analysis (*4*) of zonal wind observations does suggest a downward propagation of AO patterns in many winters. This offers a plausible mechanism for the production of NAO/AO-type signals in tropospheric climate by factors that affect the heat balance of the stratosphere (*5*), specifically solar variability. Data and modeling studies have shown such a response to heating in the lower stratosphere by volcanic eruptions (*6*).

On page 2149 of this issue, Shindell *et al.* (*7*) use a computer model of the atmosphere, coupled to a simple representation of the oceans, to study the influence of solar activity on climate on a centennial scale. They compare the climate response to a reduction in total solar irradiance estimated for the late 17th century "Maunder Minimum" in solar activity to the situation 100 years later. The authors find a pattern of winter temperature change mainly represented by a reduced AO index and show that this is similar to a climatology of the period derived from proxy indicators of temperature change.

Some previous model studies (*8–11*) of the effects of short-term (11-year cycle) solar variability on climate have demonstrated the importance of the accurate representation of the middle atmosphere. Because variations in solar irradiance at ultraviolet (UV) wavelengths are one to two orders of magnitude larger than in the visible, the direct thermal signal of solar variability is much larger in the middle atmosphere. By keeping sea surface temperatures fixed, these modeling studies were largely able to separate the stratospheric from any surface-induced effects. All found an enhanced tropospheric response when stratospheric ozone was allowed to increase in response to the greater UV. This suggests that the stratosphere may play an important role in determining tropospheric climate.

The conclusions concerning the mechanisms involved were, however, somewhat different in the different studies. Shindell *et al.* (*11*) invoked wave-mean flow interaction, as described above, to explain the winter hemisphere effects. Larkin *et al.* (*10*) focused on changes in the zonal mean circulations in the troposphere, specifically the weakening and poleward shift of the subtropical jet streams at higher solar activity. Both these processes may be important, but the summer hemisphere response is more easily explained by the latter and observations show a more robust solar signal in summer (*12*), at least on the 11-year time scale. In their new report, Shindell *et al.* (*7*) find that the stratospheric effects become even more important with larger changes in solar irradiance because of nonlinear effects in the temperature dependence of ozone. This result needs to be confirmed with more complete models of stratospheric chemistry.

Bond *et al.*'s drift ice data (*1*) are consistent with a general cooling during the Maunder Minimum. However, the chronologies of the drift ice records from different sites show broadly similar trends. This is not consistent with a weakening of the NAO/AO, which would predict the site off East Greenland to be relatively warmer during solar minimum than those off Ireland and Newfoundland. The drift ice data thus do not show the same pattern of response to solar activity as the temperature reconstruction (*13*) used by Shindell *et al.* (*7*), and their model results, for the Maunder Minimum. If this disparity is real, it suggests that different factors are important over varying time scales, with, for example, changes in deep ocean circulation becoming more substantial over periods greater than centuries.

The two studies contribute new evidence of the effects of solar variability on climate (see the figure) and indicate avenues for further research into the mechanisms involved. It is clear that the complex links between the middle and lower atmospheres and between the atmosphere and oceans are key to a better understanding of these mechanisms.

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PERSPECTIVES: SIGNAL TRANSDUCTION

RIPping Tyrosine Kinase Receptors Apart

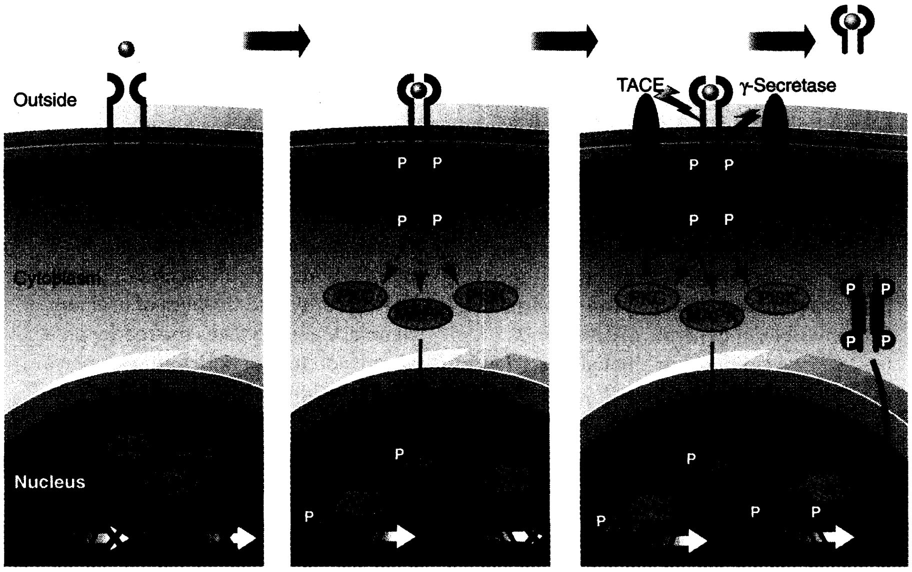
Carl-Henrik Heldin and Johan Ericsson

Tyrosine kinase receptors are transmembrane proteins that transduce signals controlling cell growth, survival, motility, and differentiation. These signals are activated by binding of a ligand (usually a growth factor) to the receptor, which then forms a dimer. This dimer adds phosphate groups to itself (autophosphorylation), resulting in the creation of docking sites that bind to downstream signal transduction molecules containing Src homology 2 (SH2) domains. Upon ligand binding, a number of signaling pathways can be activated, each one consisting of a chain of signaling molecules that indirectly alter the expression of target genes in the nucleus (see the figure). On page 2179 of this issue, Ni *et al.* (*1*) show that ErbB-4, a member of the epidermal growth factor (EGF) tyrosine kinase receptor family, also activates gene expression in a more direct manner. The ErbB-4 receptor undergoes proteolysis within its plasma membrane domain—a process called RIP for regulated intramembrane proteolysis—and its intracellular portion moves to the nucleus, where it may affect the transcription of target genes (see the figure).

There are two steps to the proteolysis of ErbB-4. First, most of this receptor's ectodomain is cleaved off by a membrane-associated metalloprotease called TACE. Next, the remaining part of the receptor is cleaved within its transmembrane domain by a second protease. This scenario is remarkably similar to the cleaving of certain other proteins that undergo RIP. These include Notch, a receptor involved in fate decisions during embryonic development; amyloid precursor protein (APP), a transmembrane protein of unknown function from which the extracellular β-amyloid peptide implicated in Alzheimer's disease is derived; and sterol regulatory element binding proteins (SREBPs), transmembrane proteins of the endoplasmic reticulum that regulate lipid metabolism (*2*). In all of these cases, most of the protein ectodomain is removed during the first cleavage. This triggers a second cleavage in the transmembrane domain, leading to the release of the cytoplasmic portion of the protein, which moves to the nucleus. Interestingly, the enzyme that catalyzes the secondary cleavage of ErbB-4, Notch, and APP is γ-secretase, also called presenilin (*3*). This γ-secretase is an aspartyl protease with the unusual ability to cleave proteins within their transmembrane domains. It spans the membrane several times and may form a channel-like pore in which proteolysis can occur.

There is firm evidence that the intracellular portions of Notch and SREBP modulate gene transcription (*2*). Notch interacts with the coactivator p300 (*4*), and SREBPs contain well-characterized DNA binding and transactivating domains that interact with a number of other transcription factors and coactivators (*5*). Furthermore, the intracellular portion of APP forms a complex with the nuclear adapter protein Fe65 and with Tip60 (which has histone acetyltransferase activity like p300), and stimulates transcription when fused to the DNA binding domains of the heterologous transcription factors Gal4 or LexA (*6, 7*). The important question provoked by the Ni *et al.* findings (*1*) is whether the intracellular region of cleaved ErbB-4 is able to affect gene expression in the nucleus.

Ni and colleagues found that blocking γ-secretase activity overcame the ligand-induced growth inhibition of fibroblasts overexpressing ErbB-4. This suggests that release of the intracellular portion of the



Regulated intramembrane proteolysis of a tyrosine kinase receptor. Binding of a ligand to its tyrosine kinase receptor induces activation and autophosphorylation of the receptor and the creation of docking sites for signaling proteins containing SH2 domains. In this way, different signaling pathways, such as that containing mitogen-activated protein (MAP) kinase, are activated. In a separate signaling pathway, PLC-γ activates PKC, which then activates the metalloprotease TACE. This enzyme cleaves off the ectodomain of the receptor and allows intramembrane cleavage of the remaining part by γ-secretase. The cleaved cytoplasmic region of the receptor then moves to the nucleus, where it may affect the transcription of target genes.

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