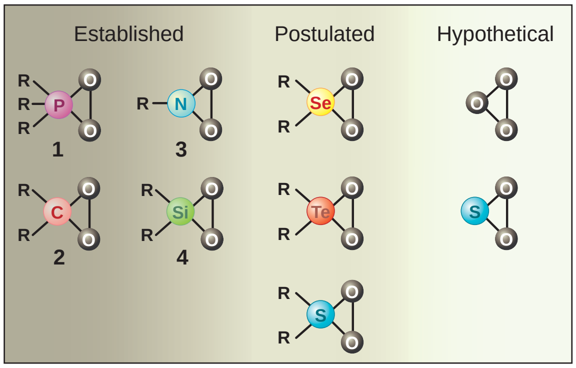

Shades of confidence in the assignment of peroxide structure.

R_2SeO_2, R_2TeO_2, and R_2SO_2, for which only kinetic and computational data exist, is more tenuous. Computational studies predict that cyclic O_3 (ozone) and cyclic SO_2 can exist, but experimental evidence remains elusive. Many other cyclic peroxides have been proposed, but their structures and reactivities are yet to be characterized (*5*).

Chemists have invested much synthetic effort into devising new peroxides, in the hope that these compounds will enable the selective introduction of oxygen into alkanes and related organic species. To synthesize new peroxides, chemists can introduce architectural changes in the compound. Such changes may result in changed reactivity. Modification of the R group in heteroatom-containing dioxiranes provides an unlimited number of potential analogs.

For example, bulky side groups may be used to protect unstable compounds and help deduce structure. In 1973, Collman *et al.* showed that a transient intermediate in the reaction of iron(II) porphyrin with $^3O_2$ can be stabilized if the adduct is not permitted contact with another porphyrin (*6*). A similar "steric" strategy has been used by Sander *et al*. (*7*) on mesityldioxirane and by Ho *et al*. (*1*) on phosphadioxirane. They use bulky R groups that prohibit or slow contact with another substrate molecule once the dioxirane is formed. Electronic factors also play a role in dioxirane stability and reactivity.

Theoretical calculations have helped to predict the reactivity and other properties of dioxiranes (*8*). By allowing transition states on the potential energy surface to be probed in detail, such calculations can provide information that is inaccessible by experiment. Calculated transition state geometries have, for example, shed light on the epoxidations of ethylenes by dioxiranes. Combined computational and experimental studies are particularly important for studying the reaction mechanism of new peroxides and their potential to serve as oxygen atom donors to other molecules.

A major goal of oxygen chemistry is the functionalization of molecules with controllable selectivity (*9*). Several groups have shown that dioxiranes of the R_2CO_2 type may be used to transfer an oxygen atom regio- and stereoselectively. Chiral dioxiranes have been remarkably successful in enhancing the selectivity in alkene and alkane oxidations. Singlet oxygen, hydroxyl radical, hydrogen peroxide, and molecular oxygen are themselves oxidizing agents. However, their chemistry can be unselective, because it is often governed by zwitterionic, (di)radical, or electron-transfer reactions. This lack of stereochemical control has limited the use of these oxygen sources in synthetic and industrial applications. Dioxiranes of the R_2CO_2 type appear to be less prone to interact with substrates by electron transfer. Dioxiranes may not suffer the same problems as the other oxidants and may therefore be useful in applications.

The method used by Ho *et al.* for obtaining direct evidence for dioxirane intermediates (*1*) may also be used to study more complicated biological or inanimate systems. For example, recent evidence suggests that a dioxirane intermediate arises in a DNA base reaction with $^1O_2$ (*10*). It is as yet unclear to what extent three-membered ring peroxides occur in living material. Spectroscopic characterization is the best tool for identifying reactive intermediates such as dioxiranes. Indirect methods can probe in vivo activity more easily, but they often cannot discriminate between different oxidizing agents.

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ATMOSPHERIC SCIENCE

Ozone and Climate Change

David J. Karoly

Many studies into the possible causes of recent climate change have tried to separate natural climate variability from human influences, such as increasing greenhouse gases. In 2001, the Intergovernmental Panel on Climate Change concluded that "most of the observed (global) warming over the last 50 years is likely to have been due to the increase in greenhouse gas concentrations" (*1*). Less attention has been paid to the possible impact of human-induced ozone depletion in the stratosphere on climate in the lower atmosphere.

Over the past 40 years, climate has warmed over much of the Southern Hemisphere. The circumpolar westerly winds have also increased in strength, as a result of increasing atmospheric pressure at mid-latitudes and decreasing pressure and temperatures at high latitudes. These observed changes in Southern Hemisphere climate at high latitudes have a distinct seasonal structure, with largest amplitude in late spring and summer. Thompson and Solomon (*2*) have argued that they may be caused by stratospheric ozone depletion over Antarctica in spring.

On page 273 of this issue, Gillett and Thompson (*3*) report a modeling study of the seasonality, spatial structure, and amplitude of high-latitude climate change in the Southern Hemisphere. They show that the observed spring and summertime changes can indeed be explained as a response to Antarctic ozone depletion. It is the first modeling study to show quantitative agreement between observed climate change in the lower atmosphere and the climate response to ozone depletion in the stratosphere. Together with other research presented at a recent workshop (*4*), it helps to quantify the possible influence of the stratosphere on weather and climate.

Of course, trends in Southern Hemisphere climate at mid- and high latitudes are also observed in winter. It is difficult to argue that ozone depletion in spring could be their cause. Climate models forced with increasing atmospheric greenhouse gas concentrations also show an increase in the circumpolar westerly winds in the Southern Hemisphere and an increase in the southern annular mode (SAM), with increased pres-

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The author is in the School of Meteorology, University of Oklahoma, Norman, OK 73019, USA. E-mail: dkaroly@ou.edu

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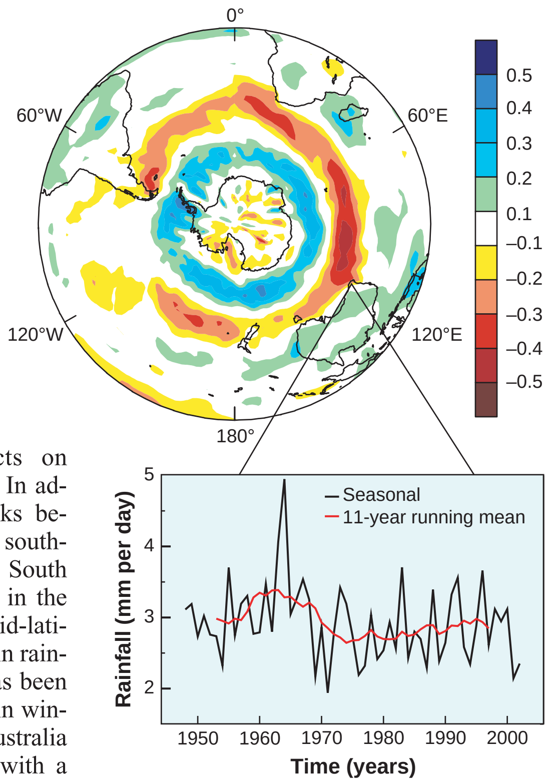
sure at mid-latitudes and decreased pressure at high latitudes (*1*). Increasing greenhouse gases have probably contributed to the observed Southern Hemisphere warming at mid- and lower latitudes and to the observed circulation changes (strengthening of the SAM) in winter. However, the magnitude of the circulation response in these climate models is not nearly as strong as that found in the observations or in the ozone-forced model response in summer (*3*).



Climate connections. (Top) Relation between variations of the southern annular mode (SAM) and rainfall in the Southern Hemisphere, based on data from a long control climate model simulation (*7*). Similar results are obtained with the climate model of Gillett and Thompson (*3*). **(Bottom)** Time series of winter rainfall in southwest Western Australia. The decrease in rainfall is consistent with the observed increasing trend in the SAM.

The recent changes in the Southern Hemisphere circulation at high latitudes have clear impacts on Antarctica and the Southern Ocean. In addition, there may be important links between SAM variations and rainfall in southern Australia, New Zealand, and South America (see the figure). Increases in the SAM, with increasing pressure at mid-latitudes, are associated with decreases in rainfall between 35° and 50°S. There has been a substantial reduction (15 to 20%) in winter rainfall in southwest Western Australia over the past 50 years, associated with a southward shift in the winter rain-bearing weather systems (*5*). Fyfe has noted this southward shift in Southern Hemisphere extratropical cyclones in both observational data and model responses to increasing greenhouse gases (*6*).

The observed rainfall trends in southwest Western Australia are much greater than expected from most climate model simulations with increasing greenhouse gases. Furthermore, they occur in a season when there is likely to be little influence from stratospheric ozone depletion. Hence, natural decadal climate variations are likely to be an important factor in these rainfall decreases.

Recent climate changes in the Southern Hemisphere are likely to result from a complex combination of natural climate processes (associated with interactions between the atmosphere, oceans, and sea ice) and human influences (including decreases in stratospheric ozone and increases in atmospheric greenhouse gases and aerosols). Untangling the separate contributions is crucial for understanding recent regional climate variations, such as the rainfall trends in Western Australia, and for predicting how climate is likely to change in the future. Gillett and Thompson (*3*) have taken an important step in this direction in showing that the recent summer circulation changes in the Southern Hemisphere high latitudes are likely to be caused by stratospheric ozone depletion.

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NEUROSCIENCE

Feeling the Pain of Social Loss

Jaak Panksepp

The Greek philosopher Zeno of Citium (356 to 264 B.C.), the founder of Stoicism, considered pain to be one of nine forms of grief. We often speak about the loss of a loved one in terms of painful feelings, but it is still not clear to what extent such metaphors reflect what is actually happening in the human brain? Enter Eisenberger and colleagues (*1*) on page 290 of this issue with a bold neuroimaging experiment that seeks to discover whether the metaphor for the psychological pain of social loss is reflected in the neural circuitry of the human brain. Using functional magnetic resonance imaging (fMRI), they show that certain human brain areas that "light up" during physical pain are also activated during emotional pain induced by social exclusion.

You might wonder how one measures the feeling of social exclusion while the subject is lying in an MRI machine. Eisenberger *et al.* circumvented this obvious problem in a clever way. In their study, the 13 participants observed a virtual ball-tossing video game while brain blood flow was monitored by MRI. During a baseline period, subjects were led to believe that they were only observing the game. During the experimental phase, however, they became active participants in the game. Within a few throws of the ball, the two other "players" (actually computerized stooges) stopped throwing the ball to the subjects, leading them to feel excluded (*2*). The subjects experienced emotional distress as indicated by substantial blood-flow changes in two key brain areas. One of these areas, the anterior cingulate cortex, has been implicated in generating the aversive experience of physical pain. Eisenberger and colleagues demonstrate that the greater the feeling of social distress, the more this brain area becomes activated. The other brain region, in the prefrontal cortex, showed an opposite pattern of activity, becoming more active when the distress was least. In other words, the two brain areas involved in the distressing feelings of social exclusion responded in op-

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The author is at the J. P. Scott Center for Neuroscience, Mind and Behavior, Department of Psychology, Bowling Green State University, Bowling Green, OH 43403, USA, and at the Falk Center for Molecular Therapeutics, Department of Biomedical Engineering, Northwestern University, Evanston, IL 60201, USA. E-mail: jpankse@bgnet.bgsu.edu