

patients with large lesions that incorporate one of these areas (the orbitofrontal cortex) treat ambiguous and risky choices differently from normal subjects.

Twenty-four different areas in the brain are more active under conditions of ambiguity than risk. Among these regions, Hsu *et al.* focused on those that previous researchers have, with some controversy, associated with the emotional side of decision-making. However, a large number of these areas (located in the temporal, parietal, and prefrontal lobes of the brain) deal with the estimation of the values of the options, which suggests that the decision process integrates emotional and computational components. The results confirm earlier findings that not only are ambiguity and risk treated differently by the brain (8), but so are related situations such as when one considers sure and risky outcomes, or

monetary gains and losses (9). Taken together, these findings support the theory of ambiguity aversion that economists have described.

What is next? Elucidating the neural processes underlying decision-making may help us understand important economic differences between ambiguity and risk. Human attitude to risk fuels the substantial profits of two large business sectors of our economy—gambling and insurance. In contrast, there is no sector served specifically by our aversion to ambiguity. This difference between risk and ambiguity is related to an experimental fact: If I ask you to choose repeatedly among risky options, your risk premium remains stable. But recent experimental evidence (10) suggests that the ambiguity premium declines as subjects repeat their choices: People slowly adjust to ambiguity; they do not adjust to

risk. Just as we learn to act optimally given the actions of others (the Nash equilibrium of game theory), by choosing repeatedly, one may be learning, slowly, to deal with ambiguity in our choices.

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## ATMOSPHERIC SCIENCE

# Land Use and Climate Change

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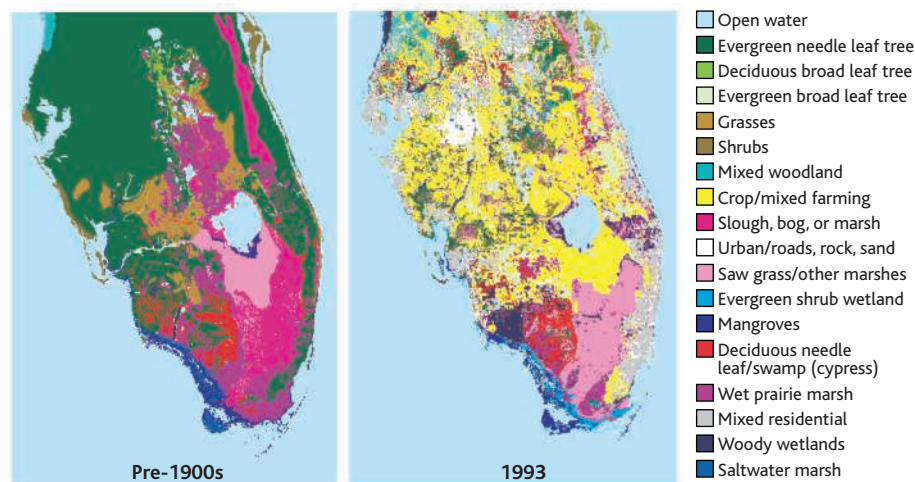
Change and variability in land use by humans and the resulting alterations in surface features are major but poorly recognized drivers of long-term global climate patterns (1, 2). Along with the diverse influences of aerosols on climate (1, 3, 4), these spatially heterogeneous land use effects may be at least as important in altering the weather as changes in climate patterns associated with greenhouse gases. On page 1674 of this issue, Feddema *et al.* report modeling results indicating that future land use and land cover will continue to be an important influence on climate for the next century (5). One implication of this work is that the Intergovernmental Panel on Climate Change (IPCC), which has yet to appreciate the significance of the full range of phenomena that drive climate change, risks rapidly falling behind the evolving science if this effect is not included. Although the impact of land use and land cover on the atmospheric concentration of carbon dioxide and methane, and on the global average surface albedo, have been included in international climate change assessments (6), the role of land use and land cover change and variability in altering regional temperatures, precipitation, vegetation, and other climate variables has been mostly ignored.

The importance of land use and land

cover change and variability should not be a surprise. On the basis of research by Avissar and co-workers at Duke University, NASA reports that “scientists estimate that between one-third and one-half of our planet’s land surfaces have been transformed by human development” (7). A large body of research has documented the major role of land use and land cover change and variability in the climate system (8–12).

One example of how land use and land cover affects global climate is the changing spatial and temporal pattern of thunderstorms. Land use and land cover change and

variability modify the surface fluxes of heat and water vapor. This alteration in the fluxes affects the atmospheric boundary layer, and hence the energy available for thunderstorms. As shown in the pioneering work of Riehl and Malkus (13) and Riehl and Simpson (14), at any time there are 1500 to 5000 thunderstorms globally (referred to as “hot towers”) that transport heat, moisture, and wind energy to higher latitudes. Because thunderstorms occur over a relatively small percentage of Earth’s surface, a change in their spatial patterns would be expected to have global climate consequences. The changes in the spatial patterning of thunderstorms result in regional alterations in tropospheric heating that directly change atmospheric and ocean circulation patterns, including the movement and intensity of large-scale high- and



**Changing surface patterns.** Vegetation classification of the Florida peninsula before 1900 (left) and in the 1990s (right), which shows the dramatic conversion of the region’s landscape during the 20th century. [Reprinted from (21) with permission]

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low-pressure weather systems (15). Most thunderstorms (by a ratio of about 10 to 1) occur over land (16), and so land use and land cover have a greater impact on the climate system than is represented by the fraction of area that the land covers.

To understand how these changes are important, consider the analogy of the global effects of the El Niño–Southern Oscillation (ENSO), a regional phenomenon of the Pacific Ocean. ENSO events have global effects because they are of large magnitude, have long persistence, and are spatially coherent (17). Land use and land cover change and variability have spatial scales similar to those associated with the sea surface temperature anomalies of an ENSO (18, 19). This climate phenomenon also is of large magnitude, has long persistence, and is spatially coherent. Thus, land use and land cover have a first-order role as a climate-forcing effect, as Feddema *et al.* further demonstrate (1). Feddema *et al.* used the U.S. Department of Energy Parallel Climate Model (DOE-PCM) to perform climate change simulations with different scenarios of landscape change during the current century. Their study shows that future land use decisions can alter IPCC climate change simulations from those based solely on atmospheric composition change.

To keep up with evolving science, the IPCC assessment currently under way should include land use and land cover

change and variability as a first-order climate forcing, along with the other spatially heterogeneous climate forcings as identified in a recent report of the National Research Council on radiative forcing (1). To fully consider the effects of land use and land cover on climate, the IPCC also should move beyond globally and zonally averaged temperatures as the primary climate metric. Although the globally averaged surface temperature change over time may in fact be close to zero in response to land use and land cover change and variability, the regional changes in surface temperature, precipitation, and other climate metrics can be as large as or larger than those that result from the anthropogenic increase of well-mixed greenhouse gases. Moreover, people and ecosystems experience the effects of environmental change regionally, and not as global averaged values.

The issue of a “discernable human influence on global climate” (20) misses the obvious, in that we have been altering climate by land use and land cover change since humans began large-scale alterations of the land surface. The Feddema *et al.* study shows that we will continue to alter the regional and global climate system in the 21st century, and these changes will act as a climate-forcing effect. Such changes are bound to complicate any efforts to stabilize the climate system that focus only on a subset of first-order climate forcings.

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## NEUROSCIENCE

# Synaptic Membranes Bend to the Will of a Neurotoxin

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Discovery in neurobiology is replete with examples of scientists using toxins that bind, neutralize, or cleave physiologically important cellular proteins. The inhibitory binding of saxitoxin and tetrodotoxin to the sodium channel, conotoxin and spider toxins to the calcium channel,  $\alpha$ -bungarotoxin to the acetylcholine receptor, and clostridial toxins to SNARE proteins that facilitate high-fidelity membrane fusion—these toxins were not only

instrumental in their respective isolation and investigation but enabled the dissection of basic cellular and physiological mechanisms. On page 1678 in this issue, Rigoni *et al.* (1) report how the action of phospholipase A2, a neurotoxic component of snake venom that paralyzes the neuromuscular junction, reveals a new regulatory mechanism for neurotransmitter release at the synapse. Lysophospholipids and free fatty acids, the hydrolytic products of this lipase, alter the energetics of the presynaptic membrane, thus affecting its disposition to bend and fuse with synaptic vesicles. This finding may not only explain the long-standing mystery of the molecular mechanism of action of presynaptic neurotoxins that have phospholipase A2 activity, but it also demonstrates the critical importance of membrane lipid composition for synaptic activity.

Phospholipase A2 hydrolyzes stable membrane lipids into lipids that cannot form bilayers. Rather, the lipid products form micelles (lysophospholipids) and inverted micelle-like structures (fatty acids) that reveal a positive and negative spontaneous monolayer curvature, respectively (2, 3) (see the figure). Our current understanding of the molecular pathway of biological membrane fusion began with experiments in which these curvature-promoting lipids revealed curvature-sensitive intermediates during calcium-dependent exocytosis, intracellular vesicle trafficking, and virus–host cell membrane fusion (4, 5). In a “hemifusion intermediate” (6–9), the contacting leaflets of two apposing membrane bilayers merge. Negative-curvature lipids such as unsaturated fatty acids promote hemifusion, but positive-curvature lysophospholipids inhibit this process (6). In contrast, the opening of a fusion pore within the hemifusion structure (the pore connects the two aqueous environments delineated by the two apposing membranes) depends on the lipid composition of the distal monolayers of the membrane bilayers. Opening of a fusion pore is inhibited by unsaturated fatty acids but promoted

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