a virulence mechanism that benefits the bacteria early in granuloma formation. This may permit an early, synergistic phase of unimpeded bacterial proliferation, whereas later in the infection, the pathogen must face the host's acquired cell-mediated immune response, which is bacteriostatic.

Further work will need to confirm that ESAT-6–mediated induction of MMP-9 secretion can be reproduced in other systems, including cultured epithelial cells in vitro. It is also unclear how ESAT-6 reaches the epithelial cells. If ESAT-6 migrates extracellularly, this would provide a point of vulnerability because neutralizing antibodies might interrupt the pathogenic signal. However, ESAT-6–based tuberculosis vaccines have not shown dramatic effectiveness in animal models (*8*). Clearly, the findings from the *M. marinum*–zebrafish system must be translated to *M. tuberculosis* and mammalian models.

With case rates of multidrug-resistant and extensively drug resistant tuberculosis at 5 and 0.5%, respectively, there is an urgent need for new drugs (*9*). Importantly, the results of Volkman *et al*. reveal at least two new therapeutic opportunities. Whereas traditional antimicrobial compounds kill bacteria, a new antivirulence approach would inhibit or neutralize critical microbial virulence factors. Examples of antivirulence strategies include antitoxin therapies for diphtheria, botulism, and tetanus, and a small molecule that blocks cholera pilus and toxin expression (*10*). ESAT-6 may be just such an antivirulence target; though clearly dispensable for bacterial viability, the granuloma program of the pathogen is crippled without it.

A second therapeutic avenue may be host-directed therapy. Although routinely used for managing infectious diseases such as pediatric meningitis (with corticosteroids and antibiotics) and hepatitis C (with the cytokine interferon-α-2b and antivirals), the concept of correcting host responses that are subverted by pathogen virulence strategies has not been fully exploited. The findings of Volkman *et al*. point to MMP-9 as a host target to inhibit in tuberculosis. Inhibitors of these proteases are already being developed as therapeutics for common noninfectious diseases such as osteoarthritis, chronic obstructive pulmonary disease, cirrhosis, metastatic cancer, and myocardial infarction. Indeed, there is evidence that MMP-9–deficient mice may be naturally resistant to *M. tuberculosis* (*11*). Moreover, host-directed therapies would not be plagued by the emergence of rapid resistance due to overuse, as is the case with drug-resistant staphylococci, enterococci, and mycobacteria.

Sixteen years ago, "Remodeling schemes of intracellular pathogens" (*12*) highlighted the finding that once engulfed by a macrophage (and internalized into the cell's phagosome compartment), *M. tuberculosis* modifies its intracellular environment to facilitate its survival and proliferation (*13*). Volkman *et al*. show that beyond altering its intracellular environment, this pathogen harbors a sinister scheme to remodel its tissue environment as well.

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CLIMATE

Drylands in the Earth System

A study of one of the world's driest forests elucidates the climatic effects of drylands.

David S. Schimel

Arid regions (or drylands) cover about 45% of Earth's land surface; in most classifications of ecosystem types, they constitute the largest biome on the planet. Yet the global change literature is dominated by other ecosystems, particularly the humid tropics, with high deforestation rates and high biodiversity levels, and the Arctic regions, with high rates of warming and huge stocks of vulnerable carbon. Drylands are less studied because they seem to have low rates of biological activity and sparse biota. On page 451 of this issue, Rotenberg and Yakir (*1*) present evidence that contradicts this received wisdom. The dryland Yatir Forest in Israel takes up carbon at rates similar to those of pine forests in continental Europe.

For the past decade, Yakir and co-workers have studied carbon, water, and energy exchange in one of the world's driest forests. Rotenberg and Yakir now analyze how the Yatir Forest maintains productivity despite severe temperature and water stress. They argue that an adjustment of forest metabolism to ambient conditions reduces the impact of climate on carbon flux. Yatir's net carbon uptake [2.3 metric tons per hectare (t/ha)] is slightly higher than that of the average European pine forest (2 t/ha) and only slightly lower than the mean for all pine forests globally (2.5 t/ha).

How does a forest growing in a hot, dry environment sustain such high rates of carbon uptake? Several mechanisms contribute to the high levels of activity. First, although photosynthesis rates in this system are moderate relative to the range of fluxes observed globally, respiration is low (possibly because low soil moisture inhibits decomposition), resulting in a carbon storage efficiency 60% higher than the average of global data.

A second explanation lies in the timing of biological activity. The rates of carbon exchange in the Yatir Forest peak early in the spring, when temperatures are far below their midsummer highs. The local vegetation is adapted to achieve peak photosynthesis rates at springtime temperatures around 14°C and to be relatively dormant during the midsummer highs of 25°C and above. A series of sites from high northern latitudes through southern Europe also had peak carbon exchange rates at similar temperatures (16° to 18°C) [data cited in (*1*)]. However, in most ecosystems, peak photosynthesis rates occur near maximal temperatures.

Peak rates of carbon uptake are a key control over annual uptake; the other key control is the length of the growing season (when the system gains carbon) relative to the dormant season (when the system loses carbon) (*2*). The displacement of peak growth to early spring in the Yatir Forest results in a growing season length similar to other coniferous forest ecosystems, also contributing to Yatir's carbon uptake.

Rotenberg and Yakir expose an important set of emergent controls over carbon metabolism globally. The work reinforces the need to conduct research in extreme and marginal envi-

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The Yatir Forest from space. The dark color of the forest contrasts with the surrounding, desertified landscapes. The Yatir, which covers about 30 km^2, warms its local environment by absorbing incoming solar radiation, whereas the surrounding bright desert landscapes reflect more of the incoming radiation to space. Today, the Yatir shows up as a green anomaly in a vast desert landscape, but in biblical times, this entire region was forested.

ronments to expand the scale over which processes are observed.

The authors extend their analysis to consider other pathways through which forests influence climate and to elucidate the role of drylands in the overall surface energy budget of Earth's land surface. Since Bonan *et al.*'s seminal 1992 study (*3*), it has been known that tree cover affects the local radiation balance, with important consequences for climate. Forests are dark and absorb incoming solar radiation, converting it into energy for photosynthesis and heat and thereby causing local warming. Bonan *et al.*'s computer simulation explored eliminating the dark boreal forest cover and thereby exposing the bright, highly reflective snow. The bright surface reflects more of the incoming sunlight, cooling the surface. Rotenberg and Yakir now report a real-world analog to this computer-enabled thought experiment.

Desertification exposes the bright soil surface, which reflects sunlight, much as in the boreal simulation. At the same time, increased convection over dryland forests such as the Yatir cools the surface, reducing outgoing thermal radiation but increasing the radiative forcing on the overlying regional atmosphere and likely increasing air temperatures aloft. Whereas desert surfaces are hotter than vegetated ones, the atmosphere overlying the desert cools with altitude more quickly and is cooler overall. Paradoxically, desertification has thus likely contributed local cooling to offset the global warming from the carbon release that occurs when dryland forests are cleared.

Although modern humanity has a hard time realizing it, the climate system has never been unchanging. Human activities have long been a driver of change in the Earth system and will continue to be for the foreseeable future (*4*). Rotenberg and Yakir's study of the arid Yatir Forest shows how recent desertification has affected local temperatures and global climate. It also provides a perspective on how humans and the climate system have interacted over millennia.

More than 3000 years ago, at the dawn of the human modification of the Earth system, the Israelites entered Canaan (modern-day Lebanon, Israel, and the Palestinian territories) and were commanded by Joshua to "go up into the forest country and clear an area for yourselves there" [Joshua 17:15; see also (*5*)]. Those early settlers released carbon as they cleared forests, thereby changing the albedo, affecting the surface energy balance, and altering the local climate. The modern-day Yatir Forest was planted in 1964 by the Jewish National Fund and—as Rotenberg and Yakir document—has substantially modified the local climate. A global program of dryland reforestation may initially cause regional warming as these new forests modify the surface energy balance, but will pay dividends in the long term as these forests become substantial global carbon sinks.

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SYSTEMS BIOLOGY

Amoeba-Inspired Network Design

Wolfgang Marwan

Computational models of biological self-organizing systems may have real-world applications for optimizing dynamic technological networks.

The ability to self-optimize is one of the fundamental properties of living organisms. Adaptive self-optimization in the course of biological evolution is an obvious phenomenon, although it occurs on a time scale of millions of years. On page 439 of this issue, Tero *et al.* (*1*) describe a model system where self-optimization of cell morphology in response to a chosen experimental situation can be directly observed and mathematically quantified as it occurs on a time scale of hours to a few days. These living cells display adaptive behavior of the sort that may be desired for scalable, multicomponent networks that are supposed to function robustly in the absence of central control mechanisms. Self-organization, self-optimization, and self-repair as it naturally occurs in the slime mold *Physarum polycephalum* are capabilities that may be required for technological systems such as mobile communication networks or networks of dynamically connected computational devices.

The *Physarum* microorganism (a plasmodium) used by Tero *et al.* is a multinucleate single cell that continually grows as long as nutrition is available. During growth, multiple nuclear divisions occur but the growing cell does not divide, so that all nuclei remain suspended in a single contiguous cytoplasmic volume. When the plasmodium grows on a nutrient-rich substratum, it covers the surface as a coherent layer (like a pancake). If nutrition becomes limited, it forms fenestrae and finally transforms into a network of interconnected veins that enclose the entire cytoplasmic volume (see the figure). Each vein is a gel-like tube covered by a cell membrane and contains a core of fluid cytoplasm.

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