molecular functions of individual components of the assembly machinery. So far, three major mechanisms have been proposed for insertion of the β-barrel precursors into the outer membrane. BamA and Sam50, which are β-barrel proteins themselves, form channels (*9*, *14*), but it is not yet clear whether the precursors are inserted into a pore formed within a monomer or whether oligomeric forms of BamA and Sam50 form a channel. A third possibility is that the precursor proteins are not inserted into the outer membrane via a protein channel, but that BAM/SAM function as a scaffold that facilitates insertion of β-barrel proteins at the protein-lipid interface.

What are the functions of the further components of the β-barrel assembly pathway? When Hagan *et al*. altered the composition of the accessory lipoproteins in their reconstituted system; they found that most subcomplexes were unstable. The stability of two subcomplexes—BamAB and BamACDE—was similar to that of the full BAM complex, but they had low activity in β-barrel assembly upon reconstitution into liposomes. Thus, all four accessory lipoproteins are required for full activity of the BAM complex. The results of Hagan *et al*. further suggest that multiple copies of SurA bind to a precursor protein and that the chaperone-precursor complex directly delivers the β-barrel polypeptides to the outer-membrane assembly machinery in a folding-competent state (*8*). The authors found no evidence for an external energy source driving precursor transfer and insertion into the outer membrane. The transport pathway may be driven by the free energy released during folding and insertion of the β barrels into the lipid phase of the outer membrane.

The core processes of β-barrel biogenesis have been conserved during evolution (*1*), but the machineries acquired further functions. The mitochondrial SAM complex is not only required for the biogenesis of β-barrel proteins, but is also a dynamic platform for the assembly of α-helical proteins of the outer membrane. Several forms of the SAM complex, differing in subunit composition, serve distinct functions in the biogenesis of different classes of precursor proteins (*12*). The SAM complex is associated with a multifunctional organizing center that is involved in lipid transport, maintenance of mitochondrial shape, and the connection of mitochondria to the endoplasmic reticulum (*10*–*12*, *15*). Future studies will address whether the BAM complex is dedicated to β-barrel assembly only or whether it may play further roles in outer-membrane biogenesis. The reconstruction of the BAM complex as a stable, active, and homogeneous complex by Hagan *et al*. will also greatly aid in solving the high-resolution structure of an outer-membrane assembly machinery.

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ECOLOGY

Are Lizards Toast?

Warming is held responsible for a rash of extinctions of global lizard populations.

Raymond B. Huey,[1] Jonathan B. Losos,[2] Craig Moritz[3]

Lizards should be relatively invulnerable to warming: They are very good at evading thermal stress, tolerate high body temperatures, and resist water loss. Nevertheless, on page 894 of this issue, Sinervo *et al*. (*1*) document extinctions of lizard populations on five continents and argue that global warming is responsible. They use a simple biological model, validated against observed extinctions, to predict that warming will drive almost 40% of all global lizard populations extinct by 2080. If their prediction is even close to correct, lizards may be "the new amphibians" (*2*) in a race toward extinction.

A stark result for a genus of lizards in México leads off their paper: 12% of 200 previously validated *Sceloporus* populations (all with intact habitats) went extinct in recent decades. Moreover, extinction probability was correlated with magnitude of warming at that site in spring, but not in other seasons. This correlation suggests that extinction is driven by energetic shortfalls during spring (when reproductive energy demands are highest), rather than by summer heat stress. Lizard natural history is instructive here: On hot days, lizards seek cooler refuges, such as burrows. With warming, lizards will spend longer periods in refuges, reducing foraging time, such that net energy gain becomes insufficient for reproduction; extinction ensues.

To test this mechanistic hypothesis, Sinervo *et al*. examined four *S. serrifer* populations, two of which have recently gone extinct (see the first figure). Using field estimates of maximum available body temperatures of lizards (operative temperatures) at these sites in spring and of body temperatures acceptable for activity, they predicted the number of hours per day that operative temperatures exceeded a lizard's thermal preferences, thus forcing retreat (see the second figure). At sites where the lizards are now extinct, predicted time restrictions exceeded 3.85 hours; but at sites where lizards persist, predicted restrictions were shorter. Sinervo *et al*. then used air temperature data from weather stations to estimate time restrictions at all Méxican sites. *Sceloporus* populations with predicted restrictions above 3.85 hours in spring had higher extinction rates than did populations with shorter restrictions.

To predict future extinctions, Sinervo *et al*. applied their history-validated approach to current and future warming scenarios across the globe, using 1216 lizard populations on four continents. First, by resurveying known lizard populations and conducting literature surveys, they detected many extinctions; for example, 21% of Madagascar lizard populations in nature reserves have gone extinct. Estimated activity-time restrictions (with critical thresholds tuned to the thermal biology of each lizard family) effectively predicted populations that had gone extinct. Based on these data, the authors estimate that by 2080,

[1]Department of Biology, University of Washington, Seattle, WA 98195, USA. [2]Museum of Comparative Zoology, Harvard University, Cambridge, MA 02138, USA. [3]Museum of Vertebrate Zoology, University of California, Berkeley, CA 94720, USA. E-mail: hueyrb@uw.edu

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No escape from warming. The lizard *Sceloporus serrifer* has gone locally extinct at several warmed sites in México.

39% of all lizard populations and 20% of all lizard species will be extinct.

These observations and projections are disturbing, and concordance between predicted and observed extinctions on different continents suggests that they should be taken seriously. Other studies also warn that reptiles are vulnerable to warming (*3*–*5*). Even so, cautious skepticism is prudent, and some aspects of the study warrant further investigation.

How strong is the evidence of local extinctions? Lizard populations rise and fall over time, and failure to detect individuals during short surveys may indicate transient rarity rather than extinction. The conspicuousness of *Sceloporus* and other highlighted species argues against such "pseudo-extinction," but only follow-up surveys can resolve whether these are true local extinctions.

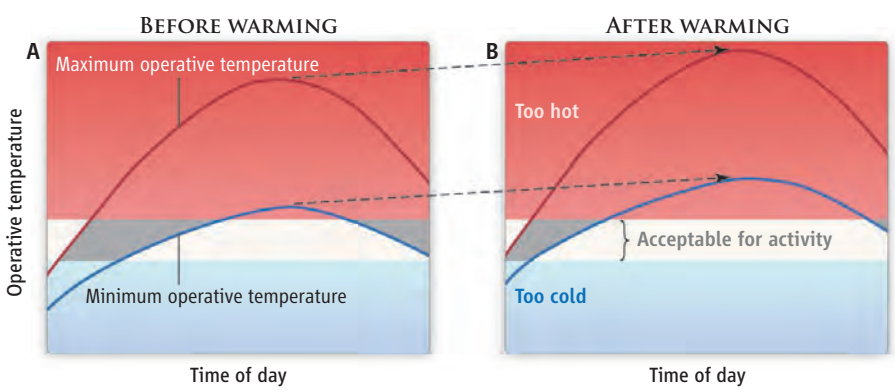
How strong are the analytical approaches? The global scale of this study demanded methodological compromises, but more robust ecophysiological approaches are available (*5*–*7*). The prediction of widespread extinctions should encourage studies using more complex biophysical, energetic, and demographic models.

How reasonable is the assumption that warming causes extinction through energetic shortfalls during the reproductive period? This proposition is supported by independent studies (*6*, *8*). For example, Dunham's individual-based model for *Sceloporus merriami* in Texas predicted that even a 2°C increase in air temperature will severely restrict activity time, reducing energy gain and rates of population growth, and thus precipitate extinction (*6*).

Might lizards be able to escape this toaster oven? Rapid genetic responses to climate warming have been documented in insects (*9*), but seem less likely in organisms like lizards with longer generation times (*10*). Using genetic models, Sinervo *et al*. conclude that genetic adaptation is not feasible. Some species may evade extinction by retreating uphill or to higher latitudes, where operative temperatures are lower (*11*, *12*). However, human-induced habitat fragmentation may block such moves, and montane species may eventually run out of space (*1*). Moreover, observed extinctions of several montane *Sceloporus* populations appear related to increased interspecific competition from upward movements of lowland species (*1*).

Lizards are remarkably diverse in geography, physiology, behavior, and habitat (*13*). Are Méxican *Sceloporus* reliable models for lizards? We think that they are: Most lizards are also diurnal, thermoregulate carefully, and are active at high body temperatures, and most lineages show limited variation in thermal physiology between species. However, tropical forest lizards are different (*4*), because they do not thermoregulate carefully and are active at low body temperatures; and some lineages—most famously *Anolis* lizards (*14*)—show marked variation in thermal physiology between species. Whether they have the genetic capacity to outrun global warming (*10*) remains to be evaluated, but biophysical and physiological data suggest that even these species are at risk (*4*).

Global warming is expected to drive widespread extinctions, but predictions are rarely validated against actual extinctions and by knowledge of causal mechanisms (*15*). Sinervo *et al*. deliver a disturbing message: Climate-forced extinctions are not only in the future but are happening now. Moreover, the authors provide an effective framework for exploring organismal susceptibility to climate change. The steps involve documenting extinctions, evaluating underlying biophysical and eco-physiological mechanisms, considering the potential for adaptive evasion, and then building projection models based explicitly on established mechanisms. This should be the logical framework even as more complex and sophisticated methodologies are applied.



Time is of the essence. Warming will shorten activity times of lizards, potentially reducing energy gains below levels required for reproduction and thus causing extinction. (**A**) Maximum (red lines) and minimum (blue lines) operative temperatures of lizards during a spring day before global warming. Lizards are active whenever the operative temperatures are within an acceptable range (gray fill). (**B**) Operative temperatures rise after warming, shortening lizard activity time.

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