

of paired sister chromatids) and hence may be resolved by homologous repair (6). Although DNA lesions in GC have not yet been reported, lesion repair during GC is known to be strongly dependent on factors required for homologous repair but not on those for nonhomologous end joining (9). Thus, GC is likely to resemble SHM closely, both in its initiating strand lesion and in its lesion repair pathway (9, 10). CSR, in contrast, is thought to involve a pair of double-strand breaks, which in many (but perhaps not all) cases are repaired by the nonhomologous end joining machinery (8). Interestingly, the junctions formed in CSR are often flanked by point mutations (8), and a defect in the mismatch repair protein Msh2 has similar effects on SHM and CSR (11). It therefore seems possible that CSR, SHM, and GC have a common intermediate (perhaps a common type of DNA lesion) and share mechanistic similarities in the processing and repair of this intermediate.

How AID is involved in these three processes remains a mystery. The puzzle is made all the more tantalizing by the fact that the closest homolog of AID is the RNA-editing enzyme APOBEC-1 (12), which edits the mRNA of the *apoB* gene. The critical catalytic residues of APOBEC-1 are strictly conserved in AID, and like APOBEC-1, AID has the ability in vitro to convert a cytidine nucleotide to a uridine nucleotide through deamination (12). It is not yet known whether AID manifests deaminase activity in vivo—and if it does, what its targets might be.

Experiments thus far have sought to determine whether AID is essential for generating or repairing the DNA lesions of CSR, SHM, and GC. The results have not provided a single, clear answer. One study found that clusters, or “foci,” of repair proteins form in the vicinity of the Ig heavy chain locus when B cells from normal, but not AID-deficient, mice are stimulated to undergo CSR (13). The simplest interpretation is that AID is required for the initial DNA lesions of CSR: no AID, no lesions, and hence no repair foci. Another study came to exactly the opposite conclusion concerning SHM. In the absence of the *AID* gene or AID activity, the double-strand breaks of SHM were not reduced in frequency (14).

One possible, albeit inelegant, conclusion is that AID acts in different ways in CSR and SHM. Perhaps AID edits two different RNA molecules: one encoding a factor involved in generating CSR strand lesions, and the other encoding a protein that operates in the repair phase of SHM and GC. It is tempting to think, however, that AID does not have a split personality.

One possibility is that AID is required for the strand lesions of all three processes, although this would imply that the abundant double-strand breaks associated with SHM are neither intermediates of, nor derived from intermediates of, the SHM reaction. Perhaps most appealing is the notion that AID is essential for the processing and repair phase of all three reactions. In SHM and GC, this could involve shunting homologous repair into an “atypical” pathway, for example, by recruiting error-prone polymerases or facilitating the use of a pseudogene donor rather than the sister chromatid. Recent experiments have demonstrated that “perversion” of error-free homologous repair can indeed induce nucleotide changes that closely resemble those observed in SHM (9). For CSR, one could imagine that AID acts to prevent rapid, nonproductive resealing of the initial DNA lesions, which in turn allows processing of the breaks and the engagement of the two switch partners (and the formation of repair foci).

Whatever turns out to be the case, one

thing is certain: Determining the function of AID—and, if it is an RNA editing enzyme, the identity of its RNA targets—will cast a great deal of light on what is currently a rather murky situation. The results of Arakawa, Harris, and their colleagues tell us that when this happens, not only CSR and SHM but also GC will be under the spotlight.

References

1. M. Muramatsu *et al.*, *Cell* **102**, 553 (2000).
2. P. Revy *et al.*, *Cell* **102**, 565 (2000).
3. H. Arakawa, J. Hauschild, J.-M. Buerstedde, *Science* **295**, 1301 (2002).
4. R. S. Harris *et al.*, *Curr. Biol.*, in press.
5. L. Bross *et al.*, *Immunity* **13**, 589 (2000).
6. F. N. Papavasiliou, D. G. Schatz, *Nature* **408**, 216 (2000).
7. Q. Kong, N. Maizels, *Genetics* **158**, 369 (2001).
8. J. P. Manis, M. Tian, F. W. Alt, *Trends Immunol.* **23**, 31 (2002).
9. J. E. Sale *et al.*, *Nature* **412**, 921 (2001).
10. N. Maizels, *Cell* **83**, 9 (1995).
11. M. R. Ehrenstein, M. S. Neuberger, *EMBO J.* **18**, 3484 (1999).
12. M. Muramatsu *et al.*, *J. Biol. Chem.* **274**, 18470 (1999).
13. S. Petersen *et al.*, *Nature* **414**, 660 (2001).
14. F. N. Papavasiliou, D. G. Schatz, *J. Exp. Med.*, in press.

PERSPECTIVES: ECOLOGY

Species Diversity—Scale Matters

Katherine J. Willis and Robert J. Whittaker

As predictions of the loss of global biodiversity grow increasingly pessimistic, identifying the factors that determine species richness has become a hot topic. The best-known pattern in species diversity is the gradient ranging from low at the poles to high at the equator. This pattern is so general across so many taxa that it

suggests the existence of an equally general explanation. Much attention, therefore, has been given to finding the mechanism that explains patterns of species richness, with the underlying assumption that whatever scale the relationship is measured at can be scaled up or down in simple fashion. If this were so, a model that successfully accounts for local patterns in richness could be scaled up to account for variations seen at a coarser regional or even global scale. This reasoning resembles that used to explain evolutionary change, where variations manifest

over decades or centuries can be scaled up to describe the more dramatic patterns of macroevolutionary change over geological time. But, as some evolutionists have argued (1), biological and environmental systems are more complex than this. It is becoming increasingly apparent that the factors best accounting for patterns of biodiversity seem to be delimited by scale. This finding needs to be taken into account when assessing present or predicting future worldwide patterns of species richness.

Rahbek and Graves (2) have examined the geographic range of 2869 species of birds breeding in South America. By analyzing the same species data set over 10 spatial scales, ranging from 12,300 to 1,225,000 km², the authors were able to make direct comparisons of patterns of numbers of species as a function of scale. The number of species was statistically analyzed against a suite of environmental variables including climate, ecosystem diversity, topography, and latitude. The investigators found that the order in which the explanatory variables entered the statistical models varied with scale: Whereas precipitation was the most influential fac-

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tor at finer spatial scales, cloud cover and area (2) were more important predictors of species richness at coarser spatial scales.

Two recent studies of British plants (3) and birds (4), have produced similar insights. The first study analyzed species-area curves for vascular plants, using sampling units of 0.01 m² up to 100 km² in size. The investigators demonstrated that the slope of the log-species/log-area plot is not constant, but varies systematically with spatial scale (3). The authors conclude that different processes are likely to determine plant diversity at different spatial scales. The second study, which analyzed the distributions of British bird species, found that the location of richness hotspots varies radically depending on the scale of observation. The authors discovered that the most species-rich areas underwent a shift northwards as the scale coarsened (4). The richness pattern at the finest scale (10-km resolution) was statistically unrelated to the pattern at the coarsest scale (90-km resolution). They point out the serious implications of this finding for conservation policy: The location of a reserve selected according to maximum species richness may change considerably depending on the size of the reserve or the scale of the analysis.

This complexity in the relation between species richness and scale is not confined to the terrestrial realm. The distributions



The beauty of diversity. *Phyllica pubescens*, a member of the species-rich plant genus *Phyllica* (Kirstenbosch Botanic Garden, Cape Town, South Africa).

of bryozoans (marine invertebrates) in the North Atlantic (5) indicate that different factors account for species richness at different scales. At the finest scale (a single bryozoan assemblage) there was no apparent variation in species richness with latitude, whereas at a regional scale, there was a strong latitudinal trend indicating a peak in species richness between 15° and 30°N.

Similarly, factors driving variations in diversity over time may manifest themselves at different spatial scales. At the broadest spatial scale, for example, the distributions of mammal families between



continents, fundamental differences in biogeographical realms have been driven by historical processes acting over tens to hun-

dreds of millions of years. These processes include environmental variables such as tectonic plate movements and variations in sea level (6). In comparison, at regional spatial scales (variations within continents), environmental factors acting over time scales of 1 to 10 million years have had the strongest influence on species richness of particular lineages. For example, in the South African Cape, Richardson *et al.* (7) found from their molecular analysis of the species-rich plant genus *Phyllica*, that the diversity of this genus resulted from a series of rapid speciation events that began about 7 to 8 million years ago (see the figure). Similarly, rapid speciation events have been recognized in the molecular record of the Neotropical rainforest genus *Inga* over the last 3 million years (8). Both studies concluded that these events contributed significantly to the biotic character and biodiversity of these regions and were driven by environmental factors operating over time scales of 1 to 10 million years. The South African speciation event appears to have been associated with an extensive aridification episode caused by changes in ocean currents. Similarly, the diversification of *Inga* in forests of the Neotropics can best be explained by climate changes associated with the late Tertiary uplift of the Andes and Quaternary cycles of glaciation (8). Finally, on a local scale, numerous studies suggest that environmental events—such as fires, storms, hurricanes, and landslides—operating over periods of 1 to 1000 years, markedly influence species richness patterns at a local-to-landscape scale (9).

Emerging from these findings is the realization that a variety of factors over different spatial and temporal scales contribute to an understanding of biodiversity. A hierarchical approach, as argued for evolutionary change (1), may be more appropriate for accurately modeling the distribution of species richness (9, 10). In a hierarchical model, processes can be nest-

A HIERARCHICAL FRAMEWORK FOR PROCESSES INFLUENCING BIODIVERSITY

Spatial scale	Scale of species richness	Environmental variables predominantly responsible	Temporal scale at which processes occur
Local scale	Species richness within communities, within habitat patches	Fine-scale biotic and abiotic interactions, e.g., habitat structure, disturbance by fires, storms	Processes occurring on time scales of ~1–100 years
Landscape scale	Species richness between communities; turnover of species within a landscape	Soils, altitude, peninsula effect	Processes occurring on time scales of ~100–1000 years
Regional scale	Species richness of large geographical areas within continents	Radiation budget and water availability, area, latitude	Processes occurring over the last 10,000 years, i.e., since end of last glacial
Continental scale	Differences in species lineages and richness across continents	Aridification events, glacial/interglacial cycles of the Quaternary, mountain-building episodes, e.g., Tertiary uplift of the Andes	Processes occurring over the last 1–10 million years
Global scale	Differences reflected in the biogeographical realms, e.g., distribution of mammal families between continents	Continental plate movements, sea-level change	Processes occurring over the last 10–100 million years

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ed according to both spatial and temporal scales (see the table). There will be some transmission of signal from one scale to the next, but different variables should emerge at different scales. Thus, variables that best account for species richness on a local spatial scale or recent time scale may not be the same as those accounting for richness at regional spatial scales or longer time scales. We should take this into ac-

count during future attempts to model and assess species diversity for conservation purposes.

References and Notes

1. S. J. Gould, *Philos. Trans. R. Soc. London Ser. B* **353**, 307 (1998).
2. C. Rahbek, G. R. Graves, *Proc. Natl. Acad. Sci. U.S.A.* **98**, 4534 (2001). This analysis was based on latitude-longitude grids, and thus unfortunately is not strictly equal to area. Accordingly, quadrat area was used as a variable, which is a commonly used "fix" in this type of analysis.
3. M. J. Crawley, J. E. Hurrell, *Science* **291**, 864 (2001).
4. J. J. Lennon et al., *J. Anim. Ecol.* **70**, 966 (2001).
5. A. Clarke, S. Lidgard, *J. Anim. Ecol.* **69**, 799 (2000).
6. J. C. Briggs, *Global Biogeography* (Elsevier Science, Amsterdam, 1995).
7. J. E. Richardson et al., *Nature* **412**, 181 (2001).
8. J. E. Richardson, R. T. Pennington, T. D. Pennington, P. M. Hollingsworth, *Science* **293**, 2242 (2001).
9. R. J. Whittaker, K. J. Willis, R. Field, *J. Biogeogr.* **28**, 453 (2001).
10. H. C. J. Godfray, J. H. Lawton, *Trends Ecol. Evol.* **16**, 400 (2001).

PERSPECTIVES: THERMOELECTRIC MATERIALS

Smaller Is Cooler

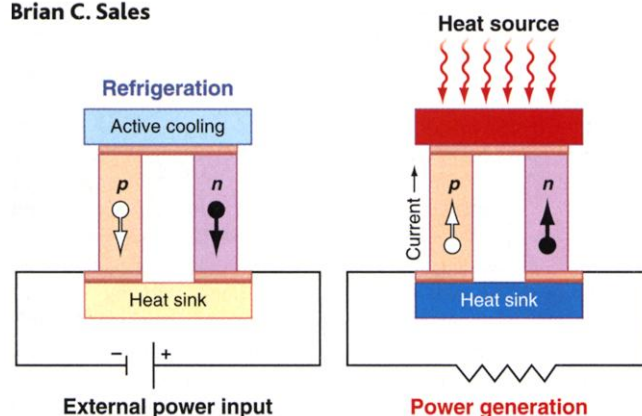
Brian C. Sales

To most people, the word "semiconductor" is associated with modern electronics such as the personal computer. In the early 1950s, however, most semiconductor research focused on using semiconductors not in integrated circuits but in thermoelectric modules for home refrigeration. The latter never became practical because of poor cooling efficiency. New materials and synthesis techniques have reawakened interest in the use of semiconductors in refrigeration and power generation. Some of the most promising new thermoelectric structures contain carefully arranged films or clusters on nanometer length scales.

Thermoelectric devices are extremely simple, have no moving parts, and use no greenhouse gases (see the first figure). The devices use two types of semiconductor "legs" that are connected in series. Negatively charged electrons carry electrical current in the *n*-type leg, whereas positively charged holes carry the current in the *p*-type leg.

Refrigeration is possible because electrons and holes carry heat as well as electrical charge. An external battery forces the hot electrons and holes away from the cold side of the device (left panel in the first figure), resulting in cooling. In some multistage thermoelectric modules, temperatures as low as 160 K can be achieved. Today, spot cooling of electronics is the primary application for thermoelectric refrigerators.

If heat is applied to only one side of the device, a voltage develops across the *n* and *p* legs that can be used to convert part of the heat into electrical power (right panel



Thermoelectric refrigeration and power generation. A single thermoelectric couple is shown, configured for refrigeration (left) or power generation (right). The labels *p* (positive) and *n* (negative) refer to the sign of the charge carriers in each leg; open circles correspond to holes and filled circles to electrons. The copper-colored regions depict electrical connections.

in the first figure). NASA has used this principle to provide hundreds of watts of electrical power for deep space probes such as Voyager I and II and the Cassini mission to Saturn.

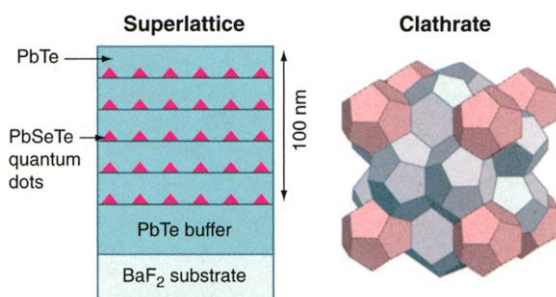
The major problem with thermoelectric devices is poor efficiency. The efficiency of a thermoelectric module is fundamen-

tally limited by the material properties of the *n*- and *p*-type semiconductors—regardless of how cleverly the module is engineered. The inherent efficiency of any thermoelectric material is determined by a dimensionless parameter ZT , where T is the temperature and Z characterizes the material's electrical and thermal transport properties. Effective thermoelectric materials have a low thermal conductivity but a high electrical conductivity (1, 2).

The best thermoelectric materials commercially available today have $ZT \approx 0.9$. This is acceptable for certain specialized applications, but to be economically competitive with the refrigerators in our kitchens, a thermoelectric refrigerator would require $ZT \approx 3$ at room temperature.

At the recent Materials Research Society meeting in Boston (3), several materials with $ZT > 1$ for both refrigeration and power generation applications were reported. Particularly exciting were results obtained by Venkatasubramanian (Research Triangle Institute), who showed $ZT = 2.4$ for *p*-type superlattices of $\text{Bi}_2\text{Te}_3/\text{Sb}_2\text{Te}_3$ at room temperature and $ZT = 1.2$ for *n*-type superlattices (4). The superlattice is produced by alternately depositing thin (1 to 4 nm) films of Bi_2Te_3 and Sb_2Te_3 . Harmon (Lincoln Labs, MIT) reported $ZT \geq 2$ just above room temperature for quantum dot superlattices (see the left panel in the second figure) (5).

The studies of Venkatasubramanian and Harmon imply an increase in ZT when either the layer thickness or the size of the quantum dot is near 1 nm. The results confirm some of the earlier ideas of Dresselhaus and collaborators (6), who suggested that nanoengineering of thermoelectric materials could result in higher values of ZT .



Promising new materials. (Left) Nanoengineered thermoelectric materials of this kind are prepared with molecular beam epitaxy. (Right) In this model clathrate crystal structure, the cubic crystal structure is composed of two types of polyhedra that consist of clusters of 20 or 24 atoms. In self-assembled structures of this type, nature does the nanoengineering.

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