Cool mint. Mildly cool temperatures (25° to 15°C) and the cooling agent menthol activate the TRPM8 ion channel. This channel is expressed by sensory neurons in the mouth that project to the trigeminal ganglia (TG) in the brain, and by sensory neurons in the skin that project to the dorsal root ganglia (DRG) of the spinal cord. When activated, TRPM8 channels open, allowing Ca^{2+} and Na^+ ions into neurons, which then become depolarized. TRPM8, like other TRPM channels, is a tetramer with each subunit containing six transmembrane domains and unusually long amino and carboxyl termini.

amino acids in length, is in the class of TRP channels that has extremely long amino and carboxyl termini rather than in the vanilloid class of temperature-sensing TRPs containing ankyrin repeat domains. This class of long or melanostatin-related TRPs was thought to be involved in cell division, although the best-characterized TRP channels are all sensory: The *Drosophila* TRP channel is involved in vision, and the vanilloid TRPs sense temperature or osmotic changes.

It is intriguing that although TRPM8 was already identified, its sensitivity to temperature and menthol remained undiscovered. First, the classification of TRPM8 in the TRPM family may have been somewhat misleading because it does not bear close homology to TRPM class members. Also, presumably due to low levels of mRNA, TRPM8 did not show up in commercially available Northern blots of nervous tissue. Finally, because most cells in patch-clamp recordings are equilibrated at ~22°C, the TRPM8 current would have been only weakly activated.

The two studies are in reasonable agreement about the threshold for activation of TRPM8 (22° to 26°C), and the ~5°C shift induced by subactivating concentrations of menthol. Also, both studies agree that the channel is expressed in small-diameter neurons, consistent with the known sensitivity to temperature of unmyelinated C and thinly myelinated Aδ primary afferent sensory neurons. However, the papers do come to some different conclusions. In cultures of mouse trigeminal sensory neurons, McKemy *et al.* found that ~50% of neurons expressing TRPM8 also expressed TRPV1 (VR1). This suggests that some neurons are both heat and cold sensors, potentially explaining the confusing sensations that we humans can have with hot and cold stimuli. As McKemy *et al.*

point out, simultaneous contact with warm and cool surfaces (such as a thermal grill) evokes a sensation of burning pain. Also, mild cold can induce a feeling of burning pain after elimination of large nerve fibers by nerve block or injury. Using in situ hybridization in trigeminal ganglia from adult mice, Peier *et al.* found that TRPM8 was not expressed in TRPV1 (VR-1)–containing neurons, suggesting that there exist distinct subpopulations of neurons expressing either TRPM8 or TRPV1. Peier *et al.* also propose that the TRPM8 channel is uniquely associated with neurons that express the TrkA growth factor receptor; indeed, TRPM8 mRNA was not present in newborn mice lacking TrkA. The issue of whether heat and cold sensors are in the same neurons could be efficiently resolved in further studies of freshly isolated human and mouse nerve tissue.

Besides the complex road ahead for determining how neurons recognize and evaluate temperature, another set of interesting mysteries remains to be solved. The thermosensors TRPV1, TRPV2, and TRPM8 are expressed not only in neurons but also in nonneuronal cells. What could these receptors be doing in such tissues as the prostate? Finally, it will be intriguing to learn the native chemical messengers in neurons that open these channels.

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PERSPECTIVES: ECOLOGY

Of Predators, Prey, and Power Laws

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Power laws, in which one quantity can be expressed as some power of another, are ubiquitous in physical and social systems. They have been used to describe phenomena as diverse as the frequency of earthquakes of different magnitudes (the Gutenberg-Richter law), the distribution of income among individuals

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(Pareto's law), and the rank-frequency distribution of city sizes, or words in natural languages (Zipf's law) (*1*, *2*). Power laws in the form of scaling or allometric relationships are used by biologists to express how physiological, ecological, and life-history attributes relate to body size (*W*) raised to a power, usually a multiple of 1/4 (*3*). Among the vast number of biological power laws, those related to energy acquisition, transformation, and delivery are of fundamental importance, because energy sustains life. Thanks to the work of Max

Kleiber in the 1930s, we know that the amount of energy organisms need to extract from their environments to sustain themselves, metabolism (*M*), scales with body mass according to $M \propto W^{3/4}$ (Kleiber's law) (*4*). This simple power law represents a fundamental first principle whose consequences for the structure and operation of ecological systems we are just beginning to appreciate. On page 2273 of this issue, Carbone and Gittleman (*5*) demonstrate that the interaction between metabolic requirements and locally available energy can account for the observed power law relation between carnivore population density and body size. Their approach illustrates the importance of incorporating local ecological information if we are to understand large-scale patterns in biodiversity.

It follows from Kleiber's law that a lim-

ited amount of available energy per unit area will sustain a larger number of individuals of a small-sized species than of a bigger species. Thus, assuming energy limitation, population densities (N) of large species are expected to be lower than those of smaller ones because of their higher total metabolic demands, and both are expected to conform to a power law of the form $N \propto W^{-3/4}$. Available estimates, based on the compilation of data from different ecosystems worldwide, show that mammalian primary consumers (herbivores) conform well with this expectation (6). Furthermore, because the energy available to secondary consumers (those feeding on other animals) is less than that available to primary consumers (7), it is expected that carnivores will reach lower population densities than similar-sized herbivores. Available data for mammalian species also support this expectation (8, 9). However, what has puzzled ecologists for a long time is that the allometric exponent of this power law is considerably smaller (that is, steeper slopes in the range −1.0 to −0.8) than −3/4 (see the figure). Explanations for this discrepancy have been elusive, and are usually based on presumed systematic (allometric) variations in prey biomass and productivity with predator body mass (8). However, Carbone and Gittleman present data showing that the relation between population density and size in mammalian carnivores (species of the order Carnivora) is constrained by metabolic rate and by variability in their resource base (prey species) such that the −3/4 power law only emerges if the local productivity of prey species, experienced by a carnivore population, is taken into account. Thus, the answer to the anomalous scaling of mammalian secondary consumers is found in local resource availability.

Carbone and Gittleman incorporate resources available to carnivore species into allometric equations by assuming that under energy limitation, the maximum density N_{max} that a species can attain is related to the rate of resource supply per unit area (R) and to the average rate of resource use per individual (M) by $R \propto N_{max} \times W^{3/4}$, which amounts to $N_{max}/R \propto W^{-3/4}$ (Equation 1) (10). Most studies, however, have implicitly or explicitly assumed that the rate of resource supply in different environments is constant and bounded within similar levels, reducing the previous equation to $N_{max} \propto W^{-3/4}$. But, as Carbone and Gittleman show, this is not a safe assumption for secondary consumers, carnivores in particular,

because there is a positive relation between available resources and carnivore population density, which (assuming energy limitation) renders misleading comparison across secondary consumer species using data from populations experiencing environments that differ in the availability of resources. These authors demonstrate that density estimates should first be made comparable by standardizing them by the amount or rate at which they become available to each population. To accomplish this, Carbone and Gittleman standardize carnivore density according to their available resources, estimated as biomass and productivity of available prey. Thus, using
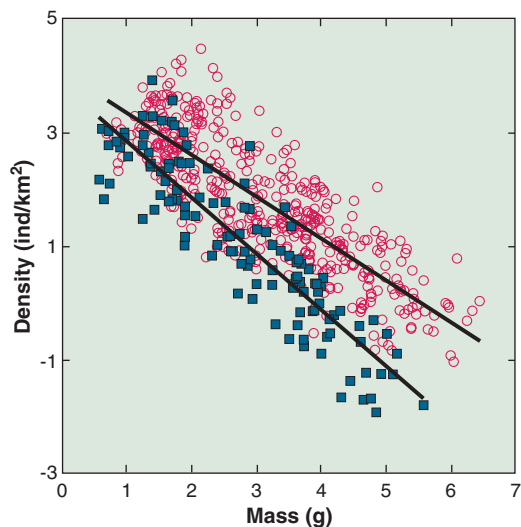
Carnivores on a slippery slope. The power law in mammalian population densities. The relation between the logarithms of population density and body mass in mammalian primary (open circles) and secondary (filled squares) consumers. The relation for primary consumers (herbivores) has a slope of −3/4, whereas the slope for secondary consumers (such as carnivores) is much steeper. Population density and body mass data are from a worldwide compilation by Damuth (11).

Equation 1 and assuming that carnivore density does in fact scale with carnivore mass as $W^{-3/4}$, they accurately predict the allometry of carnivore numbers per 10,000 kg of prey and per unit productivity of prey, accounting for a larger proportion of the variance in carnivore population density. This result lends support to the energy limitation hypothesis and underscores the importance of prey density for the persistence of carnivore populations.

The study by Carbone and Gittleman raises several questions with important implications. In particular, why do herbivore populations show a −3/4 power allometric scaling without the need for standardizing by resource availability? The wide variability observed in the density of similar-sized species of herbivorous mammals suggests

that they might be affected by local resource availability, but that this variability is averaged out when considering a large number of species and populations. This would imply that small samples of herbivorous species might show steeper slopes, similar to the one observed for secondary consumers. A simple bootstrap analysis of a data set reported by Damuth (11) reveals that the slopes characterizing secondary consumers are significantly steeper ($P = 0.0005$) than expected from sampling alone (see the figure) (12), suggesting that the density-size power law for herbivores reflects the scaling of their metabolic demands (6). Considering that plant species density follows the same −3/4 power law (13) as do the herbivores that feed on them, a related question is why the power law in herbivore density does not map onto one with a similar allometric exponent for carnivores such that it is necessary to correct for prey abundance? The answer to this question probably lies in constraints upon the prey size spectrum available to predators of different body sizes, competition for prey species, and ecosystem productivity. A definitive answer to this and related questions, however, will benefit from detailed allometric studies of food webs within local communities.

Finally, Carbone and Gittleman illustrate that our understanding of power laws, and other macroecological patterns in ecosystems, can be enhanced by going beyond the compilation of published data devoid of local ecological context. As has been demonstrated (14), power laws are ubiquitous within local ecosystems and may hold the clue to understanding large-scale patterns in the structure and function of biodiversity.

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