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In this issue . . .

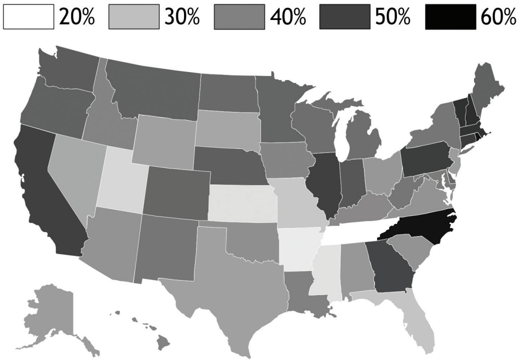
Gradual decline of dinosaurs before extinction

The Chicxulub asteroid impact in Mexico is thought to have driven most dinosaurs to extinction around 66 million years ago, but whether these prehistoric giants experienced a gradual decline toward oblivion or thrived until the cataclysmic impact remains unclear. Using Bayesian phylogenetic analysis of three large dinosaur datasets, Manabu Sakamoto et al. (pp. 5036–5040) explored dinosaur speciation and extinction dynamics before the asteroid impact. The model revealed that extinction rates surpassed speciation rates beginning around 24 million years before the impact; when the three major dinosaur groups were separately considered, extinction rates exceeded speciation rates as early as 48 to 53 million years before impact. Modeling also found a minor but positive effect of sea-level rise on dinosaur speciation, which rose 0.2–0.25% per meter increase in sea level, lending support to a hypothesis that rising seas lead to habitat fragmentation and reproductive isolation. The precise triggers of the speciation decline remain unknown, but Cretaceous phenomena such as the breakup of supercontinents, sustained volcanism, and ecological factors may have possibly influenced the downturn. According to the authors, dinosaurs gradually lost the ability to replace extinct species with new ones, thereby likely favoring the rise of mammals that began to flourish in previously unavailable ecological niches. — P.N.

Dinosaurs were in gradual decline before asteroid impact. Image courtesy of iStockphoto/estt.

Cost-effectiveness of HPV vaccination

In 2014, the US Food and Drug Administration approved Gardasil-9, a human papilloma virus (HPV) vaccine that protects against 80% of cervical cancers, compared with 66% protection from vaccines currently in use, while costing \$13 to \$18 more per dose than existing vaccines. David Durham et al. (pp. 5107–5112) developed a model of HPV transmission and cervical cancer incidence to estimate the health and economic impacts of switching to Gardasil-9 in the United States. The authors found that, at the national level, switching to Gardasil-9 would reduce cancer incidence and mortality by 2050 to a greater extent than continuing to use existing vaccines. The expansion in coverage required to gain an equivalent health benefit from existing vaccines was estimated to cost nearly \$3 billion more than the cost of switching to Gardasil-9. Expanding vaccine coverage would

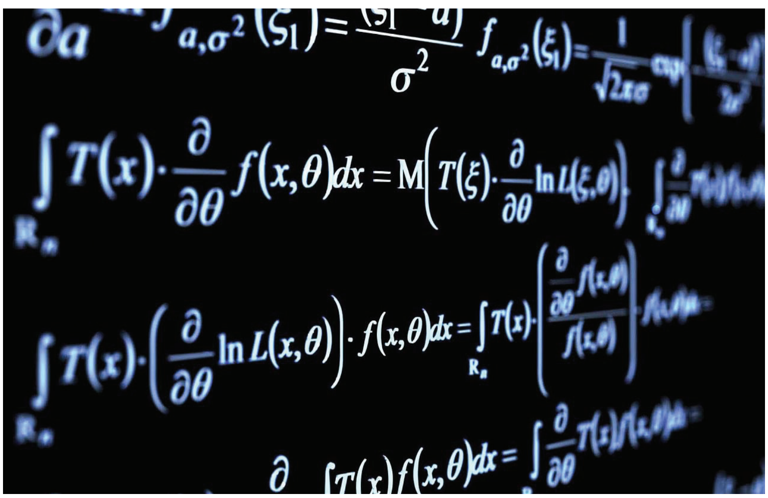


Full-series HPV coverage among adolescents varies across states.

avert the most cancers and deaths in states with the lowest existing coverage, and expanding coverage within a single state would avert a substantial number of cancers beyond that state's borders as a result of interstate migration. The results suggest that coordinating policies to promote expanded coverage and conversion to Gardasil-9 could maximize health benefits and cost savings, according to the authors. — B.D.

Origins of advanced mathematical ability

According to one hypothesis, human mathematical ability is related to language ability, whereas another hypothesis suggests that mathematical ability stems from humans' intuitive knowledge of space, time, and number. Marie Amalric and Stanislas Dehaene (pp. 4909–4917) collected functional MRI scans of 15 professional mathematicians and 15 nonmathematicians of equal academic standing. Both groups were presented with a series of high-level mathematical and nonmathematical statements, and asked to

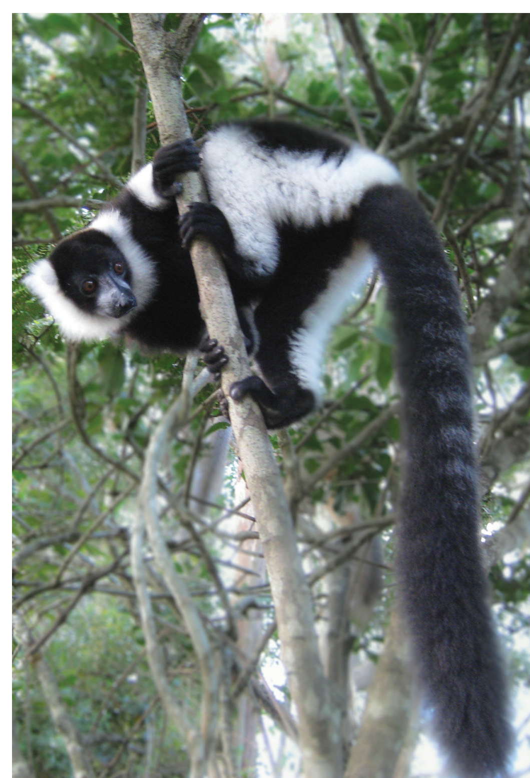


Neural basis for advanced mathematical thinking. Image courtesy of Wikimedia Commons/Wallpoper.

evaluate each statement as true, false, or meaningless. Statements pertaining to mathematical analysis, algebra, geometry, and topology activated a particular set of bilateral intraparietal, inferior temporal, and prefrontal brain regions in mathematicians, but not in nonmathematicians. These brain regions were distinct from those associated with language processing and semantics, which were activated by nonmathematical statements in both mathematicians and nonmathematicians. The regions activated by high-level mathematical statements in mathematicians were also activated by numbers and simple arithmetic calculations in mathematicians and nonmathematicians alike. The results support the hypothesis that high-level mathematical thinking deploys the same neural network as basic number sense, which is distinct from the language network. According to the authors, the findings might explain why number sense in early childhood can help predict subsequent mathematical performance. — B.D.

Lemur extinction and Madagascar's forest health

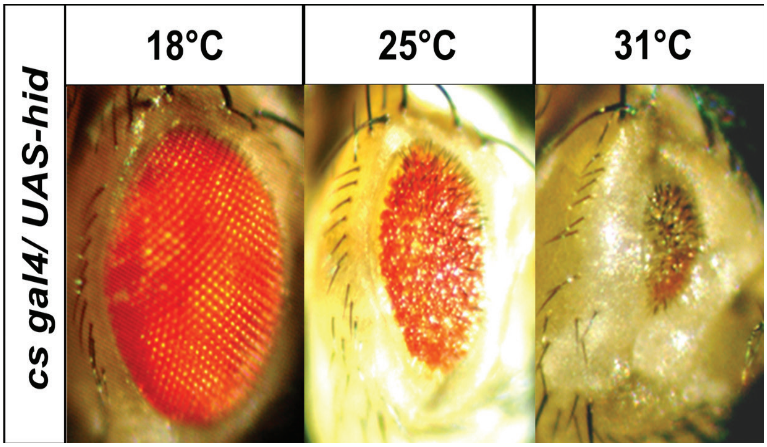
Lemurs in Madagascar serve an important role as seed dispersers, and it is unclear how lemur extinctions have affected the health of Madagascar's forests. Sarah Federman et al. (pp. 5041–5046) analyzed the dietary strategies of living and recently extinct lemurs, as well as the effects of the extinctions on the survival of Malagasy plants. At least 17 lemur species have gone extinct over the past few thousand years, and evidence from tooth morphology, dental wear, and isotope studies indicates that several of the species likely enabled seed dispersal. The authors found that the extinction of large-bodied lemurs significantly reduced the number of lemurs associated with the dispersal of large seeds. The authors identified several "orphaned" large-seeded plants that did not appear to have any existing animal seed dispersers, but the seeds of which could have been consumed and spread by extinct lemur species. The authors suggest that these plant species persist due to their long generation times and inefficient seed dispersal by rodents or cyclonic winds, and that the extinction of large lemurs could endanger their long-term survival. The authors also identified living lemur species, including several endangered species, that occupy essential dispersal niches. According to the authors, conservation efforts should take into account the effects of seed dispersers on the structure and function of Madagascar's forests. — S.R.



Black and white ruffed lemur (*Varecia variegata*).

Generating cold-sensitive mutants

Cold-sensitive mutants behave normally above a certain temperature but like loss-of-function mutants below that temperature. Such mutants, which can be used to probe gene function in living organisms, are rare, and the molecular mechanisms behind cold sensitivity are unclear. Chetana Baliga et al. (pp. E2506–E2515) developed a method to rationally design cold-sensitive mutants. The authors used an algorithm to predict amino acids that could be mutagenized to destabilize a protein. When the authors mutagenized such sites in four test proteins in the bacterium *Escherichia coli* and the yeast *Saccharomyces cerevisiae*, the mutagenesis resulted in the partial loss of function of these proteins. Next, the authors used heat-inducible promoters to selectively increase the expression levels of these proteins at higher temperatures. The authors found that the increased expression could overcome the effects of the partial loss-of-function mutations at higher temperatures, whereas the lower levels of expression of these proteins at lower temperatures resulted in a cold-sensitive loss-of-function phenotype. The authors could also transfer the cold-sensitive phenotype of Gal4 mutants from yeast to *Drosophila*, and the technique was effective even when amino acid sequences of proteins with unknown structures were used to design the mutants. According to the authors, destabilizing mutations can be combined with selective protein overexpression to generate cold-sensitive mutants. — S.R.



Cold-sensitive mutant of Gal4 is used to drive expression of a toxic gene in fruit fly eye.