## SCIENCE'S COMPASS

text falls short of what might be expected of an encyclopedia-the author's lack of expertise in several aspects of meteoritics has resulted in errors. The straightforward text takes the traditional approach of systematically describing stones, stony-irons, and iron meteorites in terms of their classification and properties. The book is not the sort that a nonspecialist would read in order to learn about meteorites; it is much too technical for that. However, it is beautifully and lavishly illustrated with many pictures of meteorites in thin section as well as of hand specimens. These images should help the work fulfill another of its goals, providing a "guide to assist searchers in the field to recognize the many classes of meteorites."

Meteoritics has come a long way in the 208 years since Chladni's publication. Bevan and de Laeter devote their final chapter to looking to the future, in which they consider missions to Mars, comets, and asteroids, along with efforts to retrieve interstellar dust. Much remains for the next 200 years; we are still looking for meteorites that are indubitably from Mercury, Venus, a cometary nucleus, and a Kuiper belt object. Part of the excitement of meteoritics is knowing that any of these extraterrestrial rocks might already be here on Earth, just waiting to be found, identified, and written about. In their different ways, both of these books convey the message that meteoritics is a fast-moving field, one in which we still have much to learn.



## BROWSINGS

Earth from Above. Revised and Expanded Edition. *Yann Arthus-Bertrand*. Abrams, New York, 2002. 462 pp. \$45.00. ISBN 0-8109-3495-7. Earth From Above. An exhibit at Millennium Park, Chicago, IL, through 30 September 2002.

With a helicopter as his preferred tripod, Arthus-Bertrand specializes in composing images on the fly. Ranging from an intimate glimpse at a worker resting on cotton in the Côte d'Ivoire to a spectacular panorama of the Himalayan crest, the 190 photographs in this oversize volume capture the beauty of natural landscapes and human settlements alike. Many depict strikingly abstract patterns, such as these formed by crystallized salts on the surface of Kenya's Lake Magadi (above). Arthus-Bertrand's project was supported by UNESCO, and the book includes 14 new short essays on our beleaguered world and steps towards an "eco-economy." The exhibit, with 120 large (1.2 m by 1.8 m) prints, opened in Paris in May 2000 and has appeared in 40 cities and 15 countries.

SCIENCE'S COMPASS



# PERSPECTIVES

### PERSPECTIVES: GENOMICS

# Vertebrate Genomes Compared

### S. Blair Hedges and Sudhir Kumar

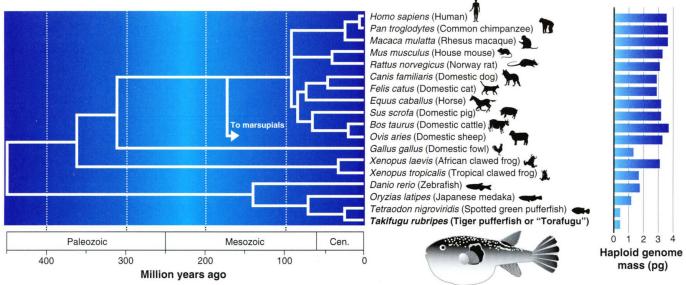
t takes two of anything to make a comparison. With the publication of the draft genome sequence of the tiger pufferfish (*Fugu rubripes*) by Aparicio *et al.* on page 1301 of this issue (1), we are now able to compare the genomes of two vertebrates. Measuring 365 million base pairs in length, the *Fugu* genome is only one-ninth the size of the human genome (2) yet contains approximately the same number of genes. Shorter introns and a smaller amount of repetitive DNA in the pufferfish genome account for this difference. Its unusually small genome size, combined with a faster method of sequencing (whole-genome shotgun), has yielded a much lower price tag-a mere \$12 million compared with the hundreds of millions of dollars spent on sequencing the human genome. The primary incentive for sequencing this and other vertebrate genomes lies in better identification and characterization of human genes and their regulatory elements, especially those that are mutated in human diseases. For example, nearly 1000 putative human genes have been discovered by comparing the Fugu and human genomes (1). Beyond biomedical applications, the extent of conservation and divergence among the pufferfish and human genomes will shed light on the underlying evolutionary and genetic mechanisms that shape them.

The tiger pufferfish is a good example of how the concept of "model organism" has changed. Growing up to 70 cm in length, it is a relatively large marine fish known for its taste, not a laboratory workhorse like the fly or mouse. It was introduced as a "genomic model" organism (3) specifically because of its compact genome, permitting efficient comparison with the human genome. Other genomic models include human parasites, such as Plasmodium and Trypanosoma, and species of interest to agriculture, such as rice and corn. Fugu's relative, the spotted green pufferfish (Tetraodon nigroviridis), is a much smaller (up to 17 cm in length) freshwater species with a similarly small genome, and is more accessible to experimental research requiring laboratory breeding. The Tetraodon genome, one of at least 18 vertebrate genomes being sequenced, is almost complete (see the figure).

A major motivation behind genome-sequencing projects is to generate a better

S. Blair Hedges is at the NASA Astrobiology Institute and Department of Biology, 208 Mueller Laboratory, Pennsylvania State University, University Park, PA 16802–5301, USA. S. Kumar is in the Department of Biology, Life Sciences 351, Arizona State University, Tempe, AZ 85287–1501, USA.

# SCIENCE'S COMPASS



Evolution of vertebrate genomes. The evolutionary tree shows relationships, times of divergence, and genome sizes (in picograms of DNA, pg) of vertebrates whose genomes have been selected for sequencing. Classically, 1 pg of DNA has been considered equivalent to roughly 1 billion base pairs, although the conversion factor for both human and Fugu is 0.91 ×10<sup>9</sup> base pairs. The position of marsupials is indicated to illustrate their potential importance in filling an evolutionary gap in genome projects (12). The relationships and divergence times are largely from a molecular clock study of 658 proteins (8), although reflecting current uncertainty in the position of some orders of mammals (9) and supplemented with data on fishes and genome sizes of vertebrates (www.genomesize.com/) (12-15). "Takifugu" is considered by ichthyologists to be the correct genus instead of the more popular "Fugu" (www.fishbase.org/).

understanding of the genetics of human diseases (4). Sequencing of the complete Fugu genome, a distant relative of humans, provides an opportunity to compare these two genomes at the level of exons, introns, and the protein sequence. The much shorter length of Fugu introns will enable sequence stretches important for regulating gene expression (5) to be identified, and the role of noncoding DNA (which makes up most of the human genome) to be clarified. The Fugu genome carries a handful of "giant" genes containing long introns, which should provide insight into what has driven the change in genome size during evolution. Understanding the genome structure of Fugu also will foster a clearer picture of the master control genes directing vertebrate development (6).

The amino acid changes causing certain human disorders are more likely to occur at conserved (invariant) sites in the protein sequence, and such sites are best identified by comparison with a distant species, such as Fugu (7). In contrast, it is difficult to distinguish functionally conserved sites in the protein sequence from less constrained sites among close relatives, such as two species of mammal, because insufficient time has elapsed for changes to occur at the variable sites. Why are amino acid changes in conserved sites associated with human disease? Sites that are less variable usually are more crucial for survival of the organism, and therefore changes at those sites are more likely to cause disease. In fact, disease-associated amino acid changes are overabundant

at evolutionarily conserved positions of the protein sequence, and the alteration in chemistry is more extreme than that permitted by natural selection (7). Thus, comparison of nonmammalian genomes with the human genome will be crucial for understanding the genetic basis of many human diseases.

Evolutionary biology also has benefited greatly from genome-sequencing projects. The wealth of new genome data is helping to better resolve the tree of life, particularly its major branches. This has been especially true for prokaryotes, where more than 80 genomes have been sequenced so far and the results have greatly improved our view of the early history of life. For vertebrates, many thorny issues remain to be resolved, such as the phylogeny of families and other major groups in the tree of life. For example, it is not yet known whether humans are closer to mice or to cattle because different results have been obtained with different gene analyses (8, 9). On the other hand, there is no guarantee that complete genome sequences will immediately solve all phylogenetic questions, as evidenced by the continuing debate over the relationships among humans, flies, and nematodes (10). We will need to develop new statistical methods and bioinformatics tools to handle the greater volume of data and to unravel the complexities of molecular evolution.

Comparative genomics, with its large numbers of genes and proteins, provides better estimates of when different species diverged. These "molecular clocks" tell time by applying known rates of sequence change from one part of the tree to other

parts where times are unknown (8). Accurate species divergence times are needed to link biological events with Earth's geological history and the appearance of characteristic life forms. Such genomic clocks might determine with better precision whether the orders of mammals began splitting from one another in the Mesozoic era (80 to 100 million years ago) when continents were breaking apart, or later in the Cenozoic era (65 million years ago) after the dinosaurs disappeared, vacating ecological niches (8). Robust estimation of the timing of gene-duplication events enables reliable predictions of gene content in unsequenced genomes and estimation of the rate of gene content increase over time (11). Also, better estimates of when genes and species diverged will make it possible to investigate the relationship (if any) between genome expansion (especially of developmentally important genes) and adaptation of species to their environments.

Historically, studies of biomedicine and evolutionary biology have sought separate goals, yet comparative genomics (or more precisely evolutionary genomics) is begin-ing to blur traditional boundaries. A symbi-otic relationship has developed in which evo-lutionary biologists are answering fundamental questions using sequence data generated through public health projects. Simultaneous-ly, biomedical researchers are using trees, time scales, and the methodology of evolutionary biology to investigate human diseases and gene function. The future should see a greater effort by the scientific community #

# SCIENCE'S COMPASS

and funding agencies to further recognize the mutual benefits of comparative genomics.

#### References

- S. Aparicio et al., Science 297, 1301 (2002); published online 25 July 2002 (10.1126/science.1072104).
- 2. J. C. Venter et al., Science 291, 1304 (2001).
- 3. S. Brenner et al., Nature **366**, 265 (1993).
- 4. E. D. Green, in The Metabolic and Molecular Basis of
- Inherited Disease, C. R. Scriver, A. L. Beaudet, W. S. Sly, D. Valle, Eds. (McGraw-Hill, New York, 2000), vol. 1, pp. 259–298.
- 5. B. S. Abrahams et al., Genomics 80, 45 (2002).
- M. S. Clark, L. Shaw, A. Kelly, P. Snell, G. Elgar, *Immunogenetics* 52, 174 (2001).
- 7. M. P. Miller, S. Kumar, Hum. Mol. Genet. 10, 2319 (2001).
- 8. S. Kumar, S. B. Hedges, Nature 392, 917 (1998).
- 9. W. J. Murphy et al., Science 294, 2348 (2001).
- PERSPECTIVES: MATERIALS SCIENCE

# **Dynamics in Ceramics**

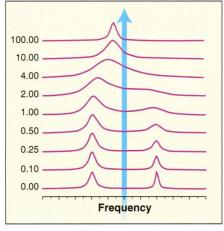
## Jonathan F. Stebbins

n a macroscopic scale, oxide ceramics are hard, rigid materials. It is therefore tempting to think of them as rigid at the atomic scale as well. In particular, the oxide  $(O^{2-})$  ions that take up much of the space in these materials seemingly ought to stay put in the crystal lattice.

It is therefore a bit surprising that these ions can be quite mobile in some ceramics. This mobility is exploited, for example, in the zirconia-based ( $ZrO_2$ ) oxygen sensors that monitor the catalytic converters in most cars in the United States. The anionic electrical conductivity supplied by oxide ions is also crucial to many solid electrolytes for fuel cells, which promise more efficient use of fossil fuel and hydrogen energy resources.

Detailed knowledge of the microscopic processes underlying ionic conductance is, however, lacking. On page 1317 of this issue, Kim and Grey (I) bring a powerful technique to bear on this problem. They show that solid-state nuclear magnetic resonance (NMR) not only can directly determine the rate at which oxide ions hop from site to site in ionic conductors, but also can identify the sites involved in this process.

High-resolution NMR has long been an everyday tool for identifying organic molecules in liquid solutions. Since the early 1980s, NMR has also been used widely for structural studies of organic and inorganic solids. Solid-state NMR uses high-resolution methods such as magic angle spinning, in which small samples are rapidly spun at an angle of 54.7° to the external magnetic field to average out some or all orientationdependent spectral line broadening. For oxide and silicate materials, <sup>17</sup>O NMR provides a wealth of structural detail (2, 3) but requires enriched samples with ~1000 times their natural <sup>17</sup>O abundance. Enrichment sometimes necessitates tricky syntheses, but in refractory materials with mobile oxide



**Merging peaks.** Hypothetical NMR spectra for a material that has two distinct sites with a 2:1 occupancy ratio. The spectra were calculated at increasing ratios of site exchange frequency to frequency separation (as labeled), as expected with increasing temperature.

ions, it can readily be accomplished by high-temperature gas exchange (1).

Complementing the high-resolution structural data, NMR can also provide unique and quantitative insights into site-specific dynamics. Many such studies have been performed on polymers (4), but site-specific dynamical data for inorganic materials remain limited. Spin-lattice relaxation rates are most commonly measured for nuclides such as <sup>1</sup>H, <sup>7</sup>Li, and <sup>19</sup>F, whose ions often diffuse rapidly even in solids. Such studies can be informative but are generally not site-specific. Furthermore, data analysis can be highly model-dependent, and relaxation can be strongly affected by local "rattling" within sites, which is often relatively unimportant to macroscopic transport properties.

The clearest sign of diffusive dynamics in NMR spectra is the merging of two spectral peaks, assigned to ions or molecules in distinct chemical environments, with increasing temperature (see the figure). The merging process or "coalescence" is often attributed to chemical exchange between the sites. The exchange rate is slow at low tem-

- J. E. Blair, K. Ikeo, T. Gojobori, S. B. Hedges, BMC Evol. Biol. 2, 7 (2002).
- 11. M. Lynch, J. S. Conery, Science 290, 1151 (2000).
- 12. J. W. Thomas, J. W. Touchman, *Trends Genet*. **18**, 104 (2002).
- C. A. Bisbee, M. A. Baker, A. C. Wilson, I. Hadji-Azimi, M. Fischberg, *Science* **195**, 785 (1977).
- B. Venkatesh, P. Gilligan, S. Brenner, *FEBS Lett.* **476**, 3 (2002).
  J. Wittbrodt, A. Shima, M. Schartl, *Nature Rev. Genet.*
  - **3**, 53 (2001).

perature, but with increasing temperature it becomes faster than the frequency separation of the peaks. The peak separation, typically 10 to  $10^6$  Hz, defines the time scale of the site exchange (0.1 to  $10^{-6}$  s).

Few studies of this kind have been performed in inorganic materials, primarily because ions of the most commonly observed nuclides (such as <sup>29</sup>Si, <sup>27</sup>Al, and <sup>17</sup>O) start hopping around at the required rates only at elevated temperatures. Alkali metal cations are more mobile but often occupy only a single site in a given crystal structure, also frustrating attempts at exchange spectroscopy, although there are exceptions (5, 6). Fluoride anions can also be remarkably mobile, and high-resolution solid-state <sup>19</sup>F NMR has recently revealed F- site hopping (7). The fast ion conductors described by Kim and Grey (1) are unusual, with oxide site exchange rates rapid enough to be observed by NMR below about 250°C (the current upper limit of fast magic angle spinning technology).

In the ionic conductive ceramic  $\alpha$ -Bi<sub>4</sub>V<sub>2</sub>O<sub>11</sub>, Kim and Grey (1) report rapid exchange of oxide ions among distinct sites within the vanadium oxide layers. The latter are rich in the oxygen vacancies that promote diffusive motion. No exchange is seen with the more rigid, fully occupied bismuth oxide layers. In a related, Ti-doped phase that is an even better oxide ion conductor, the authors report oxygen site hopping that is not frozen out until well below room temperature.

With some modifications, solid-state NMR can be used to observe exchange dynamics in a greater variety of materials. Slower hopping rates can be observed by two-dimensional exchange experiments (5, 7). Magic angle spinning NMR can be done with special probes capable of reaching above 600°C, but with slower spinning rates and reduced resolution (6). Spectra can be acquired at temperatures above 2000°C on nonspinning ("static") samples (8) and can show distinct sites and site exchange for nuclides such as <sup>27</sup>Al, <sup>29</sup>Si, and  $^{17}$ O (9). Static spectra of single crystals often have high resolution and can again be collected at high temperatures (10).

The prospects are thus bright for elucidating mechanisms of ionic mobility in oxide materials with high-resolution

The author is in the Department of Geological and Environmental Sciences, Stanford University, Stanford, CA 94025–2115, USA. E-mail: stebbins@stanford.edu