

recombination events between nonallelic copies. The finding of a recombinogenic motif within the repeats may therefore help to explain the observation that the breakpoints of nonallelic recombination events are often clustered (12). The overall influence of mobile DNA elements on recombination remains unclear, however, with some over- and some underrepresented within hotspots.

The seven-nucleotide motif is not among those previously associated with recombination in other species. However, its role in influencing recombination is supported by sperm-typing experiments, as is the role of another nine-nucleotide motif (CCCCACCCC) identified by the authors. Indeed, at a subset of hotspots in humans, mouse, and yeast, variation in hotspot intensity among individuals has been shown to depend on particular alleles, with recombination events occurring more often initiating on the background of the “hot” variant. When Myers *et al.* examined the sequence context of two human hotspots whose intensity has been shown to vary

among alleles, they found that the “hot” alleles were their top-scoring seven and nine oligomer motifs and that in both cases, the “colder” alleles were a mutation away from that motif. This result strongly suggests that these sequences modulate hotspot activity (see the figure). Further evidence will come from sperm-typing studies of other hotspots polymorphic at the same motifs, as well as at other candidate sequences.

In light of recent reports that hotspot locations are largely discordant in humans and chimpanzees (9, 13), the discovery of human motifs that appear to influence hotspot activity raises a number of additional questions: Can changes to sequence motifs explain most of the interspecies differences, or do other genomic features, such as chromatin accessibility or transposable element activity, explain their rapid evolution? Given that most recombination events take place within hotspots, and hotspot locations appear to be rapidly evolving, is there any constraint on recombination rates below that of a chromosomal arm? For

example, are the density and intensity of hotspots constrained within circumscribed regions of the genome? With more sperm-typing experiments and extensive linkage disequilibrium data collection in close evolutionary relatives of humans, answers to these questions should no longer be elusive.

References

1. T. Hassold, P. Hunt, *Nat. Rev. Genet.* **2**, 280 (2001).
2. A. Lynn, T. Ashley, T. Hassold, *Annu. Rev. Genomics Hum. Genet.* **5**, 317 (2004).
3. S. Myers, L. Bottolo, C. Freeman, G. McVean, P. Donnelly, *Science* **310**, 321 (2005).
4. N. Arnheim, P. Calabrese, M. Nordborg, *Am. J. Hum. Genet.* **73**, 5 (2003).
5. L. Kauppi, A. J. Jeffreys, S. Keeney, *Nat. Rev. Genet.* **5**, 413 (2004).
6. T. D. Petes, *Nat. Rev. Genet.* **2**, 360 (2001).
7. D. C. Crawford *et al.*, *Nat. Genet.* **36**, 700 (2004).
8. G. A. McVean *et al.*, *Science* **304**, 581 (2004).
9. S. E. Ptak *et al.*, *Nat. Genet.* **37**, 429 (2005).
10. D. A. Hinds *et al.*, *Science* **307**, 1072 (2005).
11. P. Fearnhead, N. G. C. Smith, *Am. J. Hum. Genet.*, www.journals.uchicago.edu/AJHG/home.html.
12. J. R. Lupski, *Genome Biol.* **5**, 242 (2004).
13. W. Winckler *et al.*, *Science* **308**, 107 (2005).

10.1126/science.1120154

ATMOSPHERIC SCIENCE

Weather Forecasting with Ensemble Methods

Tilmann Gneiting and Adrian E. Raftery

A radical change has occurred in the practice of numerical weather prediction over the past decade. Until the early 1990s, atmospheric scientists viewed weather forecasting as an intrinsically deterministic endeavor: For a given set of “best” input data, one “best” weather prediction is generated. Armed with sophisticated computing resources (including supercomputers), weather centers ran carefully designed numerical weather prediction models to produce deterministic forecasts of future atmospheric states. Although this is still the case today, weather prediction has been transformed through the implementation of ensemble forecasts. An ensemble forecast comprises multiple (typically between 5 and 100) runs of numerical weather prediction models, which differ in the initial conditions and/or the numerical representation of the atmosphere, thereby addressing the two major sources of forecast uncertainty.

Realizing the full potential of an ensemble forecast requires statistical postprocess-

ing of the model output, in that model biases, insufficient representations of forecast uncertainty, and the differing spatial scales of model gridboxes and observations need to be addressed. In concert with statistical postprocessing, ensembles provide flow-dependent probabilistic forecasts in the form of predictive probability distributions over future weather quantities or events. Probabilistic forecasts allow one to quantify weather-related risk, and they have greater economic value than deterministic forecasts in a wide range of applications, including electricity generation, aircraft and ship routing, weather-risk finance, and disease modeling (1).

A maturing area is that of medium-range probabilistic forecasting at prediction horizons up to 10 days, which involves ensembles of global numerical weather prediction models (1, 2). Three operational methods for the generation of medium-range initial condition ensembles have been developed. The U.S. National Centers for Environmental Prediction (NCEP) and the European Centre for Medium-Range Weather Forecasts (ECMWF) seek directions of rapid error growth in selective sampling procedures, known as the bred-vector per-

turbation method (3) and the singular-vector technique (4), respectively. The Meteorological Service of Canada (MSC) uses the Monte Carlo–like perturbed-observation approach (5), in which the model physics parameterizations vary as well. Ensemble forecasting and atmospheric data assimilation (the melding of weather observations into a numerical model) can mutually benefit from each other, and there are promising options for a linked system (6). A recent comparative study suggests that the ECMWF data assimilation, numerical modeling, and ensemble generation system has the best overall performance, with the NCEP system being competitive during the first few days, and the MSC system during the last few days, of the 10-day forecast period (7). The successful operation of forecast ensembles on the global scale has motivated the development of limited-area short-range ensembles driven by initial and boundary conditions supplied by different weather centers, such as the University of Washington ensemble system (8–10) over the North American Pacific Northwest (see the figure).

Probabilistic forecasting has become an integral part of seasonal prediction as well (1, 11). Forecasts on seasonal to interannual time scales rely on comprehensive global coupled ocean-atmosphere models and have become feasible with an improved understanding of the coupling between sea surface temperature anomalies and atmospheric circulation patterns. A recent special issue of *Tellus* (12) is dedicated to results from the European Union–spon-

The authors are in the Department of Statistics, University of Washington, Box 354322, Seattle, WA 98195, USA. E-mail: tilmann@stat.washington.edu