

ISSUE HIGHLIGHTS

The effect of recombination on the reconstruction of ancestral sequences, pp. 1133–1139

Miguel Arenas and David Posada

The reconstruction of ancestral nucleotide and amino acid sequences provides a window on molecular evolution. Reconstructed proteins can be resurrected in the laboratory, opening the door for functional studies of ancient proteins. However, ancestral reconstruction methods assume that recombination did not take place in the phylogeny. The authors of this article carried out computer simulations demonstrating that recombination can result in the inference of incorrect ancestral sequences. They show how limiting the ancestral reconstruction to putative recombined fragments can be helpful when the interest is on specific protein domains.

Exact results for the evolution of stochastic switching in variable asymmetric environments, pp. 1113–1119

Bernadett Gaál, Jonathan W. Pitchford and A. Jamie Wood

In populations of genetically identical bacteria, not every one looks the same. Individual bacteria spontaneously switch between phenotypes, seemingly at random. These authors apply ideas from statistical physics and evolutionary biology to ask when random switching can evolve and how it relates to environmental fluctuations. They show that, as environments change, the evolutionary transition between the nonswitching and switching regimes is discontinuous; the optimal switching rate does not smoothly increase from zero but instead makes a sharp change. These mathematical insights transcend academic curiosity, having relevance to medical applications such as combating antibiotic resistance.

Deleterious mutations and selection for sex in finite diploid populations, pp. 1095–1112

Denis Roze and Richard E. Michod

Whence sexual reproduction? is a long-standing question. Deleterious mutations potentially favor the evolution and maintenance of sexual reproduction: Due to chance events, mutations at different loci tend to be found more often in different genomes than combined within the same genome (the Hill-Robertson effect), in which case recombination drives their elimination. The authors of this article show that in diploids chance events tend to generate an excess of heterozygotes, and the effect of this on selection for sex is often much stronger than the Hill-Robertson effect or deterministic forces favoring segregation, even in large populations.

Evolutionary and functional properties of a two-locus β -globin polymorphism in Indian house mice, pp. 1121–1131

Amy M. Runck, Roy E. Weber, Angela Fago and Jay F. Storz

South Asian house mice exhibit intriguing patterns of variation in hemoglobin that are suggestive of balancing selection. The authors of this article conducted a survey of nucleotide variation at two tandemly duplicated β -globin genes and studied functional properties of the encoded hemoglobin protein. Although the population genetic analysis revealed striking evidence for balancing selection, the products of the alternative β -globin haplotypes were functionally identical in terms of oxygen-binding properties. Thus, if the β -globin polymorphism is maintained by balancing selection, the associated effects on fitness are not related to respiratory functions of hemoglobin.

An interspecific plant hybrid shows novel changes in parental splice forms of genes for splicing factors, pp. 975–983

Moira Scascitelli, Marie Cognet and Keith L. Adams

F₁ hybrids of different plant species often show a variety of genetic changes, including alterations in genome structure, methylation patterns, gene expression levels, and gene silencing. The authors of this article add alternative splicing to this list: They found that out of 40 genes examined, two genes encoding splicing factors have novel alternative splice forms in an interspecific *Populus* hybrid compared to the parents.

Epigenetic contribution to covariance between relatives, pp. 1037–1050

Omri Tal, Eva Kisdi and Eva Jablonka

The ubiquity of epigenetic inheritance has implications for disease risk, responses to ecological stresses, and evolutionary dynamics. This article presents a quantitative genetics approach for estimating the heritable epigenetic variation and the extent of epigenetic transmissibility, from covariances between relatives. The authors describe a model that produces “epigenetic transmissibility” and “epigenetic heritability” coefficients for a target phenotype. The ability to quantify transgenerational epigenetic effects can give epidemiologically important information and assist in directing the search domain for molecular epigenetic sequencing.

A genomewide RNA interference screen for modifiers of aggregates formation by mutant Huntingtin in *Drosophila*, pp. 1165–1179

Sheng Zhang, Richard Binari, Rui Zhou and Norbert Perrimon

Protein aggregates are a common yet controversial pathological feature of most neurodegenerative diseases. Over the last decade, *Drosophila* has been used extensively to model many of these diseases. In this study, the authors establish an imaging- and cell-based assay that allows automated quantification of aggregates formation, then identify a diverse group of modifiers of aggregation of Huntingtin protein through a genomewide RNA interference screen in *Drosophila* cells.

This Month in Genetics Research

Integrating pathway analysis and genetics of gene expression for genome-wide association studies, *Am. J. Hum. Genet.* **86**: 581–591

Hua Zhong, Xia Yang, Lee M. Kaplan, Cliona Molony and Eric E. Schadt

Genome-wide association studies (GWAS) have identified genes that contribute to common human diseases, but they generally have not taken advantage of other types of data. This article describes a novel approach that leverages information from gene expression studies to identify pathways enriched for genes associated with disease. The authors identified genes linked to SNPs associated with the expression of genes in metabolically active tissues, and used such eSNPs to identify 16 pathways showing evidence of association with type 2 diabetes. This promises to be a powerful approach for identifying the biological processes underlying GWAS findings.