GENETICS, Vol. 210, November 2018, Copyright © 2018

Can deep learning improve genomic prediction of complex human traits?, pp. 809–819

Pau Bellot, Gustavo de los Campos, and Miguel Pérez-Enciso

The current excitement around artificial intelligence and the renewed interest in "deep learning" (DL) have been applied to the genetic analysis of complex traits; however, the performance of DL for genomic prediction of complex human traits has not been comprehensively tested. Here, Bellot, de los Campos, and Pérez-Enciso used data from 100,000 individuals of the UK Biobank and considered several DL configurations. Some DL methods performed comparably to linear models, but in no cases did DL outperform the linear model by a sizable margin. The authors suggest that more research is needed to adapt DL methodology to genetic -based problems.

Birth and death of LTR-retrotransposons in *Aegilops tauschii*, pp. 1039–1051

Xiongtao Dai, Hao Wang, Hongye Zhou, Le Wang, Jan Dvořák, Jeffrey L. Bennetzen, and Hans-Georg Müller

Dai *et al.* employed time-dynamic modeling for the insertion rate (birth) and the deletion rate (death) of long terminal repeat retrotransposons (LTR-RTs) in the *Aegilops tauschii* genome. They found that insertion rates of the 35 most abundant LTR-RT families were not constant and instead formed bursts of amplification that peaked from 0.064 to 2.39 million years ago. The average age of LTR-RTs was negatively associated with recombination rate along a chromosome and with proximity to the closest gene.

Robust genome editing with short single-stranded and long, partially single-stranded DNA donors in *Caenorhabditis elegans*, pp. 781–787

Gregoriy A. Dokshin, Krishna S. Ghanta, Katherine M. Piscopo, and Craig C. Mello

A robust genome editing pipeline is critical to the vitality of a modern genetic laboratory. Previous studies have shown that Cas9 ribonucleoprotein (RNP)-based editing can be highly effective in *Caenorhabditis elegans*, particularly when using single stranded oligodeoxynucleotide (ssODN) donor molecule templates. Dokshin *et al*. find that optimal editing conditions require a balance between DNA cleavage efficacy and RNP-associated toxicity. They report that single stranded overhangs on PCR-generated double stranded DNA donors promote insertion of kilobase size constructs at rates comparable to those observed for ssODNs. These tools should enable most labs to generate a wide array of custom alleles.

Genotyping polyploids from messy sequencing data, pp. 789–807

David Gerard, Luis Felipe Ventorim Ferrão, Antonio Augusto Franco Garcia, and Matthew Stephens

Gerard *et al*. highlight several issues encountered when genotyping polyploid organisms from next-generation sequencing data, including allelic bias, overdispersion, and outlying observations. They present modeling solutions and software to account for these issues and show that their method performs better than competing methods in the presence of allelic bias and overdispersion. Their model uses the known hierarchy present when the sample contains full-sibling organisms; however, their method is more generally applicable to population studies. They also provide calculations for read-depth suggestions.

Transcription promotes the interaction of the FAcilitates Chromatin Transactions (FACT) complex with nucleosomes in *Saccharomyces cerevisiae*, pp. 869–881

Benjamin J. E. Martin, Adam T. Chruscicki, and LeAnn J. Howe

FACT (FAcilitates Chromatin Transactions) is an abundant and conserved complex that is essential for cell viability. FACT binds to highly expressed genes and facilitates transcription while maintaining chromatin structure, but how it is targeted to these regions is unknown. In this study, Martin, Chruscicki, and Howe used high resolution analysis of FACT occupancy in *Saccharomyces cerevisiae* to show that the complex is targeted to transcribed regions through preferential interaction with RNA polymerase-disrupted nucleosomes.

Estimates of the heritability of human longevity are substantially inflated due to assortative mating, pp. 1109–1124

J. Graham Ruby, Kevin M. Wright, Kristin A. Rand, Amir Kermany, Keith Noto, Don Curtis, Neal Varner, Daniel Garrigan, Dmitri Slinkov, Ilya Dorfman, Julie M. Granka, Jake Byrnes, Natalie Myres, and Catherine Ball

Here, Ruby *et al*. analyze an unprecedented amount of public family tree data from Ancestry and determine that the heritability of human longevity was well below 10%, lower than the widely-held belief that lifespan heritability ranged from approximately 15-30%. Their findings suggest that the heritability of human longevity has been historically over-estimated due to assortative mating.

Multiple histone methyl-lysine readers ensure robust development and germline immortality in *Caenorhabditis elegans*, pp. 907–923

Arneet L. Saltzman, Mark W. Soo, Reta Aram, and Jeannie T. Lee

As histone lysine methylation "readers", chromo domain-containing proteins can provide a link between the chromatin landscape and downstream gene regulation. Saltzman *et al.* define new roles for two uncharacterized *Caenorhabditis elegans* chromo domain proteins: CEC-1 and CEC-6. They report interactions between genes encoding chromo domains that recognize distinct histone methylation states. These findings reveal roles for multiple heterochromatin readers in developmental fitness and maintenance of the germline across generations. Their study contributes to a growing understanding of the evolutionary conservation of chromatin readers and the interplay between heterochromatin marks.

Meiotic double-strand break proteins influence repair pathway utilization, pp. 843–856

Nicolas Macaisne, Zebulin Kessler, and Judith L. Yanowitz

Double-strand breaks (DSBs) are purposefully made during meiosis and must be repaired by homologous recombination (HR) to achieve a crossover. In mitotic cells, alternative repair pathways compete with HR for repair; however, little is known about how alternative DSB repair pathways are inhibited during crossover formation during meiosis. Macaisne, Kessler, and Yanowitz report that mutations in *Caenorhabditis elegans* DSB-promoting factors HIM-5 and DSB-2 suppress the formation of chromosome fusions that arise in the absence of RAD-51 by allowing repair through alternative pathways. Their results suggest that the meiotic machinery biases repair by coupling DSB formation to repair pathway choice.

This Month's Perspectives

Caution, overload: the troubled past of genetic load, pp. 747–755

Amir Teicher

To promote a fruitful discussion on our future "genetic load," we should become better acquainted with the concept's own history. Contrary to what most genetic textbooks claim, preoccupation with genetic load did not originate in post-WWII radiation anxieties, but had deep roots in earlier eugenic thinking. In particular, German psychiatrists routinely used the term "hereditary load" to quantify, magnify, and finally eradicate the burden that the mentally ill placed on their families and on the entire nation. In postwar population genetics, the concept evolved into a potentially beneficial one, but many of its earlier connotations remain pertinent to this day.