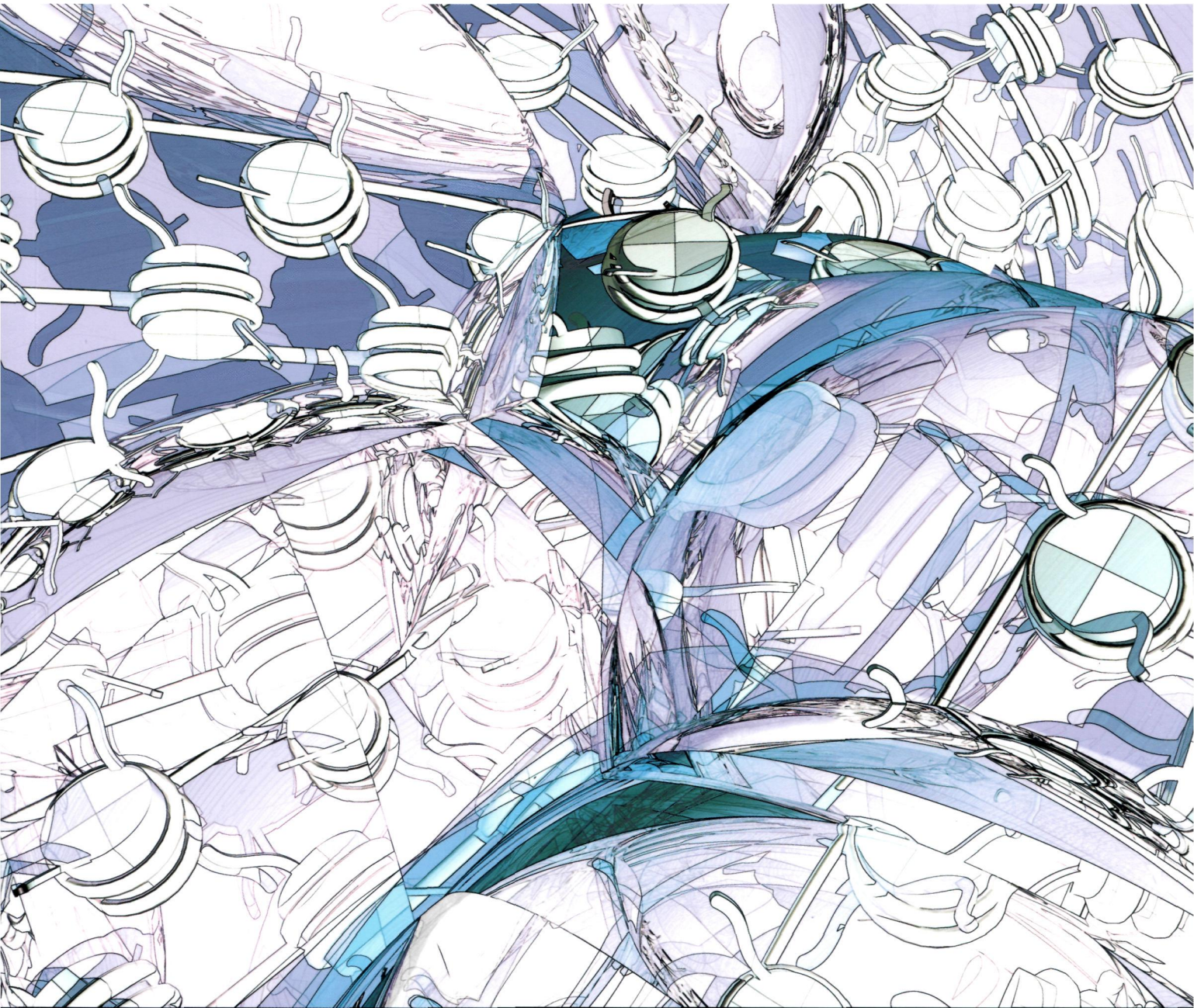


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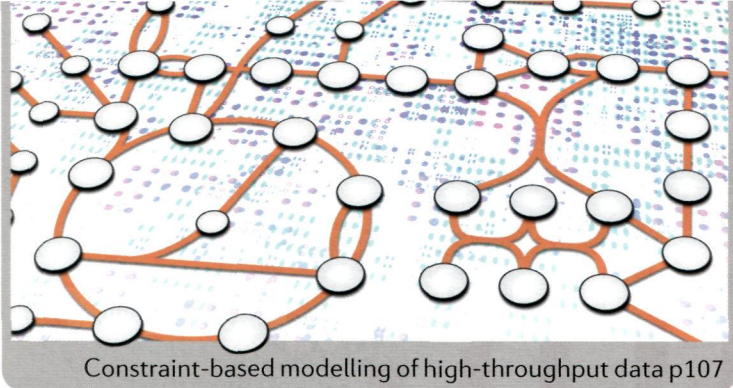


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69 Dynamic regulation of transcriptional states by chromatin and transcription factors

Ty C. Voss and Gordon L. Hager

To regulate gene expression, transcription factors must access DNA, which is organized in chromatin. This occurs on many timescales; in this Review, the authors discuss the mechanisms that underlie this interaction in regulated and stochastic processes.

82 **Pluripotent stem cells in regenerative medicine: challenges and recent progress**

FEATURED ARTICLE

Viviane Tabar and Lorenz Studer

The derivation of disease-relevant cell types from pluripotent stem cells holds much promise for disease therapy. The recent progress in directed differentiation and the challenges ahead are discussed in this Review.

93 **Chromatin modifiers and remodellers: regulators of cellular differentiation**



Taipeng Chen and Sharon Y. R. Dent

This Review describes the diverse roles for histone-modifying and chromatin-remodelling enzymes in mammalian differentiation. These enzymes are involved in both maintaining pluripotency and specifying cell lineage commitment. Recent progress includes their functional characterization in mouse models *in vivo* and a new appreciation of their multifaceted molecular functions.

107 Constraint-based models predict metabolic and associated cellular functions

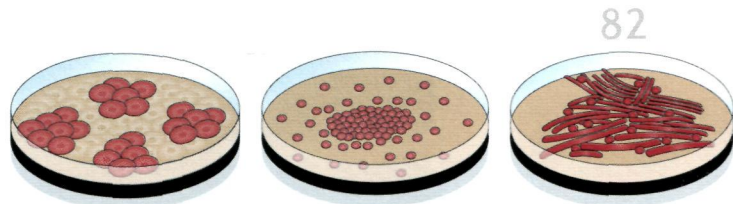
Aarash Bordbar, Jonathan M. Monk, Zachary A. King and Bernhard O. Palsson

Constraint-based modelling methods systematize biochemical, genetic and genomic knowledge into a mathematical framework, which enables a mechanistic description of metabolic physiology. Recent successes in using this approach have implications for microbial evolution, interaction networks, genetic engineering and drug discovery.

121 Sequencing depth and coverage: key considerations in genomic analyses

David Sims, Ian Sudbery, Nicholas E. Illott, Andreas Heger and Chris P. Ponting

Methods that are based on next-generation sequencing technology are used for a range of applications from genome sequencing to transcriptomic and epigenomic studies. Here, the authors discuss the important issue of sequencing depth in the design of such experiments.



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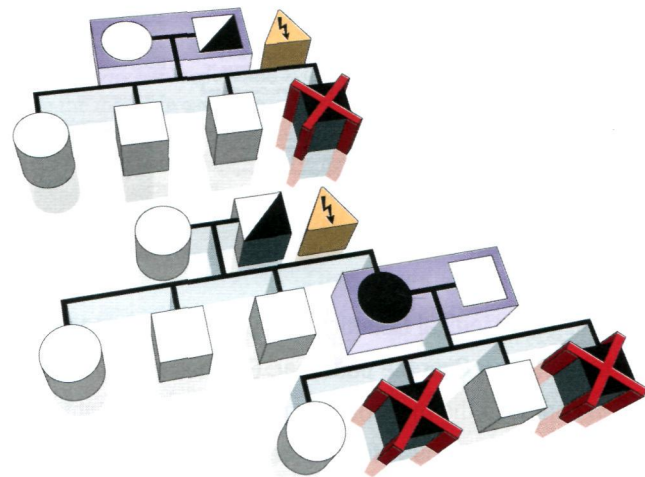
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The role of *de novo* mutations in the genetics of autism spectrum disorders

Michael Ronemus, Ivan Iossifov, Dan Levy and Michael Wigler

In the past few years, there have been rapid advances in the identification of the genetic components of autism spectrum disorders, particularly in the form of *de novo* mutations. Here, the authors review these developments in light of genetic models for autism spectrum disorders.



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