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Current Opinion in Biotechnology

Editorial overview: Systems biology: Data, discovery, delivery

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Current Opinion in Biotechnology 2018, **51**:vii–viii

For a complete overview see the Issue

http://dx.doi.org/10.1016/j.copbio.2018.05.002

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Systems biology is growing up. It arose as a framework to deal with the overwhelming complexity of biology, powered by the advent of advanced computing and high-throughput experimental technologies. Now — as big data is sweeping through so many sectors of science, health, industry, and the economy at large — systems biology as a discipline is growing out of its 'startup' phase. Systems biology in 2018 is no longer much of a buzzword, but rather an integral part of modern biology. It is an engine that needs to be put to use in advancing the major challenges that lie in front of us in the biosciences: improving health, reducing disease, advancing renewable energy, improving the environment and so forth. This issue of *Current Opinion in Biotechnology* covers a range of representative topics across systems biology today as this discipline organizes data for discovery and then delivery to address important challenges for society.

One major theme for systems biology is to take large amounts of high-throughput data and convert these into usable knowledge to drive biological and medical discovery. In this issue, Bernhard Palsson *et al.* describe how omics data empowers 'bottom-up' systems biology, built from elucidating molecular mechanisms experimentally. In essence, this integration combines the top down approach that uses global data to try and gain ever increasing resolution and accuracy in representing biological processes, with the bottom-up approach that builds on careful experimentation around components and then stitching these together into more complex models to try and understand how they behave as a system. Adam Deutchbauer *et al.* present a suite of tools for rapidly moving undercharacterized bacteria to model-organism status through expedited strain characterization. Such approaches are critical as the percentage of the microbial world that has been characterized remains exceedingly small — with most of our information about the vast majority of species coming from (meta)genome sequencing alone. Jennifer Reed *et al.* present how genome-scale models can guide iterative experimentation, in this case towards the engineering of microorganisms to carry out desired chemistries. Finally, Jonathan Carr *et al.* discuss how a wide variety of cellular data can be synthesized into a comprehensive whole-cell model and used to predict phenotypes holistically. Such models provide insights into fundamental biology and a framework for understanding how different elements within the cell interact quantitatively.

Another major theme represented in this issue is the application of systems biology to deliver on practical challenges across fields in biotechnology and biomedicine. Nathan Lewis *et al.* report on the emerging role of systems biology for engineering protein production in CHO cells, one of the workhorse platforms for industrial bioprocesses. Jason Papin *et al.* discuss

and experimental scientists in the area of Computational and Systems biology. His group has extensive experience in machine learning, computational biology, probabilistic models, and analysis of heterogeneous high-throughput genomic data. His research focuses on Nutrition, Genetics, Microbiome, and Gene Regulation and their effect on health and disease. His aim is to develop personalized nutrition and personalized medicine. Prof. Segal published over 120 publications, and received several awards and honors for his work, including the Overton prize, awarded annually by the International Society for Bioinformatics (ICSB) to one scientist for outstanding accomplishments in computational biology, and the Michael Bruno award. He was recently elected as an EMBO member and as a member of the young Israeli academy of science.

the use of genome-scale models to identify potential weakness that can be exploited in human pathogens. Such models could be a powerful tool to combat, for instance, antibiotic resistance or to build a digital molecular pathology infrastructure. Finally, Leroy Hood *et al.* report on the use of a systems approach that has led to the successful translation of two multi-parameter protein tests for distinct clinical uses, one for lung cancer and the other for predicting preterm birth. There are hundreds of thousands of candidate biomarkers claimed in papers, but only a handful make it to the clinic in any given year, so repeatable translation to the clinic represents overcoming a highly significant challenge.

Finally, the gut microbiome has recently emerged as a new field of ever-growing complexity, with more and more studies demonstrating its causal role in health and disease. As such, this issue incorporates several perspectives on systems approaches to studying the microbiome, either in its entire complexity, or in isolated studies of its individual bacterial constituents and their interaction with the immune system. Gilbert *et al.* provide an overview of research in the field and lay out the need to include the microbiome and microbial metabolic markers when aiming to diagnose disease, predict treatment outcomes, and identify novel therapeutics. Magnúsdóttir and Thiele describe their studies and those of others to tackle the challenging task of determining the detailed metabolic functions and cross-talk that occurs among different bacterial members, and how metabolites exchange between the different organisms of the microbiome. Their methods are a *tour de force* of *in silico* modeling that constructs biochemically accurate genome scale metabolic networks of microorganisms, and they show how such modeling leads to novel hypotheses on microbial interactions. Reyes and Lahav examine the important layer of non-genetic heterogeneity across microorganisms which can profoundly impact the response of cell populations to therapy, and discuss the technical and analytical breakthroughs in the study of single cells and how this understanding can lead to improved ability to design therapeutic strategies. Meyer-Hermann *et al.* examine the interplay between vaccines against mutating pathogens and why vaccines have poor protectiveness against new evolving strains. This field has also greatly benefited from systems biology *in silico* models which have raised opposing hypotheses for addressing this important question. Finally, Segal and Elinav provide an overview of the emerging field of personalized nutrition, and discuss the evidence that supports the various approaches, some based on human genetics, and others, devised by their own groups, which provide evidence for combining clinical and microbiome data in generating machine learning models for accurately predicting personalized blood glucose responses to meals as well as personalized diets based on these algorithms that are able to successfully normalize blood glucose levels in glucose impaired individuals.

Conflict of interest statement

Nothing declared.