

# iPlant Systems Biology (iPSB): An International Network Hub in the Plant Community

The *Arabidopsis thaliana* genome (120 Mb) was the third fully sequenced genome of a multicellular organism ([Arabidopsis Genome, 2000](#)) completed just after those of the nematode *Caenorhabditis elegans* ([C. elegans Sequencing Consortium, 1998](#)) and the fruit fly *Drosophila melanogaster* ([Adams et al., 2000](#)). Availability of a full whole-genome sequence for the reference plant opened to plant biologists what is commonly called the post-genomic era. Nowadays, the democratization of sequencing, together with the diversification of “omics techniques,” has led to an avalanche of data across biological systems, several orders of magnitude above daily data accumulating in astronomy or social network platforms such as Twitter and YouTube ([Stephens et al., 2015](#)). Capturing and analyzing genetic diversity of plants is at the forefront of international sequencing efforts, with the most emblematic ones including the 1001 Genomes project ([1001 Genomes Consortium. Electronic address: magnus.nordborg@gmi.oeaw.ac.at and 1001 Genomes Consortium, 2016](#)), the Big Plant Phylogenomic Tree ([Lee et al., 2011](#)), and the ongoing 10KP (10 000 Plants) genome sequencing project ([Cheng et al., 2018](#)). A recent evaluation reports that transcriptome datasets for more than 1000 different plant species have been generated using RNA-seq ([Rai et al., 2017](#)). This situation triggered a great interest of the plant biology community for data analysis and integrative tools. Some of the classic and most heavily used tools include MapMan ([Thimm et al., 2004](#)), Virtual Plant ([Katari et al., 2010](#)), ePLant ([Fucile et al., 2011; Waese et al., 2017](#)), and Plaza ([Van Bel et al., 2012, 2018](#)). All these tools build on the concept that new properties emerge from data integration both within and across species. To make sense of such a treasure trove of data and to synthesize new ideas, modeling these data through the mindful use of mathematics and computational science is now a *sine qua non* condition to reach an important level of understanding of (plant) biology.

Our motivation for starting the International Plant Systems Biology (#iPSB) conference series and summarizing the most exciting developments in this special issue of *Molecular Plant* is to promote systems approaches as an exciting way to advance plant biology in the post-genomic era and handle the emerging complexity with omics and modeling. Despite the increasing importance of Systems Biology over the last 15 years, we realized at ICAR2015 (International Conference on Arabidopsis Research) in Paris that plant systems biologists never get together as a community to discuss and learn about the latest advances in their field. We decided that the time was ripe for a plant systems biology conference and joined forces to organize the first International Plant Systems Biology (iPSB) Conference, which was held in Roscoff (France) in September 2018 and funded as a prestigious Jacques Monod Conference.

Incidentally, Jacques Monod (Nobel Prize Laurent, 1965) has pioneered, among others, the central dogma of molecular biology by demonstrating that RNA was the link between DNA and proteins, as well as the role of the first transcription factors (TFs) ([Jacob and Monod, 1961](#)). As such, his pioneer discoveries opened the door toward reductionist approaches. However, we discovered in an interview that Monod gave to a British journalist (short montage available at <https://youtu.be/rIEfqrFFbY?t=28>) that more than 50 years ago Monod had a very clear vision of the system of interactions (termed “Network”) operating inside a cell. He also envisioned one of the ultimate goals of applied biology approaches: the *de novo* creation of living organisms from raw materials, nowadays called “synthetic biology.” Often described as one of the fathers of reductionist approaches in molecular biology, Monod, was clearly aware of the “obvious complexity” of the cell as an integrated system. We think that it is such a symbol then that the first iPSB meeting was endorsed and funded to be a Jacques Monod Conference.

The first iPSB2018 held in Roscoff (FR) gathered 100 attendees with a common interest in applying modeling techniques to problems in plant biology. It was meant to mix active researchers in the Plant Systems Biology (PSB) field as well as researchers looking to adopt these approaches. Sessions, as well as this issue, were organized around key themes in systems biology and aimed to reflect, albeit incompletely, the breadth of this emerging and exciting field. Historically, the first networks built in biology even before the post-genomic area, were Metabolic Networks (Session 1) that graphically displayed the complex interconnectivities of metabolites and metabolic pathways. Nowadays, the computational power coupled with the latest metabolomics technologies is revolutionizing metabolic network analysis. The session was designed to explore the relationships that exist between metabolomics approaches coupled with genomics and other sources of information to understand coordination between different levels of information within an organism. One particular important goal of PSB, as well as in other organisms, is to infer transcriptional Gene Regulatory Networks (GRNs) (Session 2) using transcriptomic data as a readout of their activity. This session was dedicated to the different approaches used to (1) experimentally probe GRNs and (2) model them using transcriptomics and other sources of information. Beyond bulk approaches, it is not only recognized, but today can be addressed experimentally that tissues and organs are not homogeneous assemblies but consist of heterogeneous and partially specialized single cells. From Single Cell Genomics to Tissue

Modeling (Session 3) was pioneered in particular in the *Arabidopsis* root (Birnbaum et al., 2003; Brady et al., 2007). Since then, several attempts to model the plant tissue have been made, unraveling for instance the crucial role of cell pressure and tissue constraints in the control of organogenesis. This session was meant to present the important and exciting results ranging from single cell studies to cell networks and tissue modeling in plants. Session 4, Evolutionary Networks and Systems, was on a different spatial scale and timescale: “Nothing in Biology Makes Sense Except in the Light of Evolution” (Theodosius Dobzhansky). Gene networks of all kinds have been shaped by evolution. Thus, understanding the determinants that lead to the selection of such complex systems is key to solving the system itself. During this session, results concerning cross species and natural variation (within a single species) research was presented in order to highlight this concept. Session 5, Integrative Systems Genomics, discussed that the functioning of a plant as a system is not the result of a simple network but rather a combination of multiple, intertwined, dynamic, and linear or nonlinear interactions between very diverse molecular elements. Information is thus delivered through the confrontation of different levels of integration. This session was dedicated to such concepts where data integration is a predominant avenue to understand the complexity of the system and to pinpoint emerging properties. Lastly, the more practically oriented sister of systems biology, Synthetic Biology (Session 6), is intimately entangled with systems biology. Where systems biology tries to understand the emerging properties of a complex organism, synthetic biology tries to define new functions or pathways, often for sustainable commercial applications.

In this Special Issue on Plant Systems Biology, we showcase some of the research presented at iPSB2018 and others. This special issue includes research as well as review articles illustrating a diversity of approaches and important biological topics. Iain G. Johnston (2018) reviews the current knowledge of the systems-level response coordination by organelles (chloroplasts and mitochondria) in the context of the plant cell. A very interesting hypothesis aims to explain which and how many of the genes are retained in organelle genomes. The author highlights the use of mathematical modeling to understand the basic principles shaping organelle populations. The increasing abundance of genome and transcriptome data for a variety of organisms begs for an understanding of the underlying molecular regulatory networks. Limiting the theoretical modeling of this is the lack of experimental data for TF-DNA interactions. Lai et al. (2018) review progress in filling this important gap by mathematical and structural modeling of these interactions. A new approach toward understanding multicellular organisms, and especially organ and tissue architecture, is the use of network science for cell-cell connectivity and analysis of tissue and cell functions. Bassel (2019), a pioneer of this approach, reviews the application of network science to cell network connectivity and provides a vision of how these analyses will foster the understanding of emergent properties of tissues.

Auxin is among the most important plant signaling molecules and has been the prime system for mathematical modeling of plant processes. Three articles in this issue illuminate different aspects

of auxin signaling. Quantitative modeling of auxin distributions, especially in the root lead, has paved the way to an increasingly good understanding of the underlying regulatory factors. Teixeira and Tusscher (2019) review how computational modeling is helping our understanding of auxin regulatory modules and how these mediate specific functions in different stages of lateral root development. The diverse effects of auxin are mediated by physical protein-protein interaction networks, and extended families of TFs and regulatory factors then interpret the incoming signals and translate them into specific transcriptional responses. Stigliani et al. (2018) demonstrate how the inherent combinatorial control of auxin response factors (ARFs) and interacting IAA-regulatory proteins is even further enhanced by different ARF binding modes. The fact that auxin is central for a wide variety of plant processes and requires integrated systems biological approaches is exemplified by Xin-Ran Li and colleagues who study auxin gradients during fruit ripening (Li et al., 2019). These three articles together illustrate how much progress plant systems biology has already made and the magnitude of the even greater challenge of integrating the diverse complexity of models ahead of the community.

Besides the increasing push toward understanding plants as complex and nonlinear systems, a parallel revolution emerges in the analysis of the microbial world associated with higher eukaryotes. Only a minority of microbes are harmful and many can have profound beneficial effects for the plant host. Rodriguez and colleagues (Rodriguez et al., 2019) review the important topic of plant interactions with beneficial and pathogenic microbes and outline how systems biology is required to answer some of the fundamental questions in this area. Understanding how plants encourage beneficial and fend-off pathogenic microbes will be not only an intellectually exciting, but also practically relevant field in plant systems biology. Lagunas and colleagues (Lagunas et al., 2019) illustrate how integrated systems biological approaches are required to investigate and understand the complex interplay of host and microbial symbiont with environmental factors and how microbes can fundamentally alter plant resource allocation.

The avalanche of genome sequence data across the evolutionary tree allows asking and answering fundamental questions about the gradual evolution of complex systems. In an exciting report, Han et al. (2019) demonstrate how the complex light perception system of plants evolved in response to light conditions in habitats that changed from the deep sea to increasingly shallow waters and finally land. Finally, we would like to highlight that this issue features the latest update (MapMan4) of the classic and widely used MapMan resource, a fully updated and synchronized set of this central tool for analysis of primary and secondary metabolism (Schwacke et al., 2019). As mentioned above, MapMan (Thimm et al., 2004) was one of the first integrative tools made available to the plant biology community.

We are happy and proud to be the modest catalysts promoting growth of the International Plant Systems Biology Community. Building a community is important not only for discussion, learning, and training but also fundamental for well-spirited data sharing, replication, and defining standards for research. The

sharing of information on studies and discussing the data underlying findings allows researchers to verify, extend, and generalize findings. Healthy and vibrant scientific communities are beacons for attracting talent that can act as a positive feedback force on the community. Moreover, scientific communities can also help identify and articulate grand challenges that can only be undertaken by collaborative groups of researchers across the globe. We hope this international community of scientists in the field of Systems Biology will continue to grow and thrive to resolve important outstanding questions in (Plant) Biology.

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