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Preface

Phytochemistry and the new technologies: Tackling the critical barriers to advancing systems biology

Since 2000, the Regional Editors of Phytochemistry have been committed to publishing Special Issues directed at breakthrough technologies and to the identification of critical research barriers in selected/specific areas of science and technology. Recent examples of Special Issues have included Metabolomics (2003), Proteomics (2004) and Genomics (2005). In addition, a workshop entitled "Realizing the Vision: Leading Edge Technologies in Biological Systems" drew together various leading researchers from all areas of science (plant, mammalian and bacterial), including the two Phytochemistry Regional Editors (G.P. Bolwell and N.G. Lewis) and several of the contributors to this Special Issue. The purpose of the workshop, held at the Cosmos Club, Washington DC, was also to identify key critical barriers in the biological sciences. The present volume, Dynamic Metabolic Networks, guest edited by Professor George Radcliffe and Dr. Nick Kruger (University of Oxford), builds further on this vision by addressing one such critical barrier – namely that of dynamic metabolic networks, colloquially known as fluxomics— using various plant systems. This Special Issue on Fluxomics thus "networks" the visions of the Phytochemical Society of Europe (Richard Robins, ex-President), Phytochemistry (via Regional Editors, G.P. Bolwell, N.G. Lewis and D. Strack), and the NSF-funded workshop. The organization of the Special Issue mainly evolved from conversations between G.P. Bolwell and R. Robins, who solicited both George Ratcliffe and Nick Kruger as guest editors. They, in turn, have drawn together a number of important contributions from experts worldwide in this Special Issue. The critical barriers in this area of science are large, but scalable. Just to include three examples, they include areas such as: how to address rational metabolic engineering by developing methodologies/approaches to understand how control is exercised over compartmentalized metabolic networks; in defining, in mathematical model terms, the dynamic nature of flux (forward, reverse, branch point redirection, etc.) and of the inputs/outputs associated with the same in the generation of meaningful metabolic flux maps that emphasize the dynamic nature of metabolic networks.

The achievement of such aims in the application of systems biology to particular problems in plants will necessitate refinement of the basic post-genomics technologies. Early applications tended to be very qualitative and comparative and have rapidly had to adapt to being semi-quantitative and now quantitative. The approach from 'something changes' to 'what changes and by how much' has enabled the technologies to impact considerably on our understanding of the integrated and interactive manner in which cells and tissues function. Now that pathways are studied *in silico* we can at last simulate and model the complex flow through the pathways, redrawing them along the way. Nevertheless, to be useful, the models need to be built on real data, which is obtained by the traditional means of experimentation. Furthermore, different experimenters have different approaches and different approaches can, all too frequently, lead to opposed interpretations. Thus, the rational for this special issue was to draw together contributions from those who study how enzyme regulation is integrated into metabolic flux analysis, how fluxes are determined correctly by a variety of methods, how experimental demand can push methodological developments forward and, finally, how all this data can be drawn together to provide testable mathematical models to advance our understanding of dynamic metabolic networks. The commissioning editors recognised that George Ratcliffe and Nick Kruger have long been in the forefront of this field in plants and would be able to persuade many leaders to contribute who are carrying out work essential to developing the subject. The commissioning editors wish to express their gratitude to all involved for publishing their work in this special issue.

However a simple scan of the contributions will show that with the exception of two papers, all of the applications presented are in primary metabolism: so, we see this as a seminal starting point for applications in secondary metabolism. Therefore we fervently hope, since this is Phytochemistry, that this collection of papers will stimulate broadening of the application of fluxomics to defining dynamic metabolic networks in the production of natural products. We can foresee future applications of the tech-

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nology in studying the switching of primary to secondary metabolism in development, and in response to biotic and abiotic stresses. This may be most easily accomplished in single cells such as can occur in tissue cultures, but the next logical level of organisation to put under the microscope is the inter-tissue integration of plant metabolism and regulation and signalling at a distance. Examples from the proteomics and genomics world already show a degree of specialisation in gene and protein expression within different cell types that might not have been previously anticipated and the consequent challenges to systems biology to unravel the integration of metabolism throughout the plant are immense. To take just a few examples of specific questions that interest one of us (R. Robins) and to illustrate these challenges and critical barriers: Why and how when a tobacco leaf is attacked by a pest does the synthesis of nicotine in the roots increases? How are some pathways regulated partly in one tissue and partially in another (e.g. scopolamine biosynthesis)? Why do some plants accumulate defence compounds when never stimulated but others only in response to an exogenous effector? Why do some groups of compounds respond to stimulation but others do not? We hope to answer many of these types of questions in Phytochemistry in the coming years. Undoubtedly the special issue superbly put together by George Ratcliffe and Nick Kruger will be constantly quoted in this future work and recognised as stimulating another quantum leap in enabling technology. Most probably, contributions in future special issues in proteomics and genomics in Phytochemistry will be increasingly quantitative to address these critical barriers. It is hoped that in their preparation the present special issue will be referred to as a paradigm in quantitative metabolomics technologies applied to systems biology.

Therefore we are greatly appreciative of the work of the guest editors, and of the contributors to this fascinating international, interdisciplinary, special issue from the global scientific community. We thus encourage the reading of the special issue from cover to cover to learn about the rapid progress being made. Plants are special forms of all living systems which enable us to study flux from individual living cells to more specialized tissues/organs. More importantly, the insights gained apply to all other living systems as well. So read on and enjoy!

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