

Preface

The ability to control the rates of metabolic processes in response to changes in the internal or external environment is an indispensable attribute of living cells that must have arisen with life's origin. This adaptability is necessary for conserving the stability of the intracellular environment which is, in turn, essential for maintaining an efficient functional state. The remarkable advances in molecular genetics that have occurred over the past several decades have somewhat eclipsed areas of traditional biochemistry such as protein chemistry, enzymology and metabolic control. With many genomes sequenced and others nearing completion, the next step is the less straightforward task of analysing the expression and function of gene products (proteins), as well as more thoroughly elucidating metabolism and its control. The task of completing the picture of all cellular proteins, their actions and reactions, is one of the biggest challenges facing life science researchers today. Although molecular biology has generated a host of impressive techniques (i.e., protein over-expression, site-directed mutagenesis, metabolic engineering, cDNA microarrays, etc.) for assessing various aspects of protein/enzyme structure-function and regulatory control, one cannot deduce the properties of a functional protein or the kinetic and regulatory properties of an enzyme solely from genetic information. Furthermore, recent genome sequencing projects have revealed a plethora of gene sequences that encode proteins having unknown functions, and many organisms whose genomes are currently being sequenced have not had their metabolism extensively studied. Where feasible, their metabolic phenotype is determined using annotated genome sequence data. Thus there appears to be a resurgence of interest in protein, enzymological and metabolic research for understanding biological processes in the post-genome era. Efficient approaches are needed for determining (a) the function of unknown gene products, (b) protein expression and corresponding metabolite levels in different cells and in different sub-cellular compartments under various developmental and environmental conditions, (c) covalent modifications of proteins in response to different stimuli, (d) protein:protein interactions, (e) the relationship between protein structure and protein function, (f) membrane transporter proteins that selectively translocate specific metabolites between different sub-cellular compartments and (g) the sophisticated mechanisms that serve to control the flux of metabolites through specific metabolic pathways *in vivo*.

Although biochemists frequently employ the terms 'regulation' and 'control' interchangeably, the need to discriminate between these terms has been emphasised by David Fell [1]. *Metabolic control* refers to adjusting the output of a metabolic pathway in response to an external signal. By contrast, *metabolic regulation* occurs when an organism maintains some variable which remains relatively constant over time, despite fluctuations in external conditions. Homeostasis is therefore a consequence of

metabolic regulation, which itself may be a result of metabolic control. For example, the regulation of mammalian blood glucose is largely due to the secreted peptide hormones glucagon ('starved' signal) and insulin ('fed' signal) controlling intracellular metabolism within the liver. In this case, the concentration of blood glucose is regulated (kept constant) mainly by controlling (varying) fluxes of metabolic pathways (i.e., glycogen breakdown versus synthesis, glycolysis and gluconeogenesis) in hepatocytes. Regulation and control are properties of highly elaborate metabolic systems. An ongoing challenge is to link our knowledge of molecular, reductionist-based, enzyme control mechanisms to organismal-level explanations of metabolic regulation.

The advent of genomics, proteomics and metabolomics has revolutionised the study of plant development and is now having a significant impact on the study of plant metabolism and its control. In the last few years, significant advances have been made as enzyme gene families are elucidated, and new proteinaceous and allosteric regulators are identified. Enzyme activity is the major factor influencing the magnitude of metabolic fluxes in any cell. Metabolic control may occur at several levels, beginning with gene transcription and proceeding through various stages of protein synthesis and turnover. More rapid alterations in metabolic flux occur through activation and inhibition of pre-existing key enzymes along the major metabolic pathways, particularly by mechanisms such as reversible covalent modification and by the actions of allosteric effector molecules that reflect the cell's adenylate energy charge, oxidation/reduction potential and/or the accumulation of metabolic end products. Discoveries concerning plant metabolic control continue to be made at a rapid rate, particularly in the field of signal transduction. Each discovery adds to the view that plant signal transduction and metabolic control networks have remarkable intricacy. Although great advances have been made in our understanding of the mechanisms that contribute to the control of plant metabolism, our comprehension of why plant metabolic systems behave as they do *in vivo* is incomplete. However, the tools to address these questions are rapidly evolving, and advances in the theory of metabolic control and in computing power to analyse metabolism have kept pace with experimental developments. This holds great promise for those plant molecular geneticists who wish to reap a harvest via the process of metabolic engineering. A volume that reviews this progress and can point out the major research areas for the future, therefore, is very timely.

In this volume, a group of international specialists present their ideas and interpretations of specific subject matter relevant to plant primary metabolism and its control. Each chapter is written by an acknowledged expert or group of experts and provides an informed discussion on how the problem of metabolic control may be evaluated using the wide assortment of sophisticated techniques available to the modern researcher. The chapters are interrelated in order to provide the reader with an integrated view, reviewing information from the current literature and developing novel hypotheses based upon data acquired from extensive and diverse research activities.

For the purposes of this volume, primary metabolism is defined as the primary auxotrophic pathways in plants (CO_2 fixation and assimilation; sucrose and starch

synthesis) and those in common with the primary pathways in mammalian cells (i.e., glycolysis and respiration). However, Part I of the volume (the first six chapters) is devoted to more generic aspects of metabolic control, with chapters on plant enzyme control by reversible covalent modification (i.e., protein-kinase mediated phosphorylation and dithiol-disulfide interconversions), metabolite transporters and the emerging roles of genomics, proteomics and metabolomics for informing the study of plant metabolic control. The chapters in Part I provide a basis for full appreciation of the information in the seven chapters of Part II. The latter focus on the control of specific pathways and enzymes of primary plant metabolism.

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Reference

- [1] D. Fell (1997) *Understanding the Control of Metabolism*. Portland, London.