Foreword

Biological systems which underpin life itself are continuously yielding their secrets as our ability to isolate processes and analyse their component parts improves. Recent advances have tended to focus on macromolecules – DNA, RNA and proteins – and there is considerable optimism that understanding the make up of our chromosomes and the differential expression of genes will lead to much better understanding of disease. It is also believed that we will soon be able to predict a person's likelihood of developing a disease during their lifetime and tailor curative or preventative treatment more effectively.

Whilst I believe that much of this optimism is well founded, it is clear that study of the behaviour of macromolecules will only give part of the information we need to observe the response of a complex organism, such as man, to a changing environment. To give a more complete picture, we need to be able to observe dynamic markers of biological status – real-time signals which reflect the integrated function of the organism in ways which allow diagnosis and prediction. This is where metabonomics is now demonstrating enormous potential.

Metabonomics was pioneered by a group of scientists now based at Imperial and headed by Jeremy Nicholson. Whilst the technological platform is only now starting to be recognised as a tool of major importance, the foundation studies involving NMR spectroscopy of biological fluids dates back to the mid-1980s. Metabonomics is based on the demonstration that correlation of changes in metabolite pool patterns with changes in the function of integrated biological pathways can lead to ways of predicting outcomes such as the magnitude of response to a drug, potential toxicity or even the path of a disease process.

That the concepts and mathematical algorithms being developed are of major significance is well evidenced by the keen interest being shown by the bio-pharmaceutical industry and regulatory agencies. Both sectors share the goal of identifying surrogate markers of biological or clinical outcome which are well validated and lead to speedier, cheaper ways of identifying which drug candidates may be efficacious or toxic and in which populations. In fact, the management of attrition in the drug discovery–drug development pipeline is one of the most challenging for the industry as development costs and our ability to produce candidate molecules escalate.

The regulators are caught in a difficult position – needing to help important new medicines reach needy patients quickly and also protecting the public at large. Any

tools which can help to predict potential toxicity in particular populations, in speedy cost-effective ways, will undoubtedly be scrutinised closely to see whether they should become a standard part of the drug approval process.

Economic considerations will also raise the potential importance of metabonomic tests in the clinical setting. Huge opportunities exist wherever non-invasive tests costing just a few dollars can be shown to replace invasive tests which are nearly always more expensive.

It would be wrong to leave the impression that metabonomics is only of value in the field of human healthcare. In fact, the technologies are applicable to plant science, animal health and development of model organisms for research (yeast, bacteria or *in vitro* cell systems). The state of the art of metabonomics is now such that some of these possibilities – and more – are verging on being realities. It is thus timely for a comprehensive book on the subject to appear in print. For those closely engaged in the subject, the book will serve as a definitive reference; for those seeking to learn for the first time, the book will open a fascinating new world containing a plethora of possibilities for application.

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