# Preface

Microbial synthetic biology is a rapidly growing discipline that builds on well-established principles of genetic engineering and biotechnology by integrating computational and engineering approaches into the design and construction of novel biological systems. Although synthetic biology represents a multidisciplinary technology with enormous potential to benefit society, major challenges need to be overcome to achieve a radical step change in our ability to engineer complex multi-scaled biological systems. At the heart of these challenges is a need to understand the enormous complexity that underlies even the simplest of biological entities. This requires a detailed understanding of cell physiology, biochemistry and genetics, as well as that of the sub-cellular molecular machinery that mediates essential biological processes.

The step change in technology that has brought synthetic biology to the fore is our ability to analyse very large datasets generated by high-throughput omics technology. The computational tools and approaches needed for the Computer-Aided Design (CAD) and Computer-Aided Manufacturing (CAM) of complex multi-scaled biological systems (and their constituent molecular machines), although still in their infancy, are already beginning to show their value. The chapters in this volume have been chosen to address the methodology associated with different aspects of synthetic biology.

Responsible innovation must be at the heart of the bioexploitation of biological systems. Calvert and Flow address the issue of responsible innovation and, in particular, the ethical, legal and social implications of synthetic biology. They challenge some of the more familiar ways of addressing these issues by proposing a series of shifts in the framing and language used to discuss the social aspects of synthetic biology.

The Chapter by Hallinan deals with computational intelligence and the design of synthetic microbial systems. It addresses the issue of genome-scale circuit design, one of the ultimate aims of synthetic biology. Critical to the success of synthetic biology is the development of platforms for the automation of genetic design. Myers outlines the standards needed for data representation that facilitates genetic design tasks and discusses the future requirements for genome-scale automated genetic design workflows.

Harwood and colleagues focuses on one of the most widely used synthetic biology chassis, *Bacillus subtilis*. This bacterium is already used extensively for the commercial production of proteins, enzymes and metabolites such as riboflavin. This chapter discusses both the techniques used for genome refactoring and the computational tools and resources required to model its metabolism. In their chapter, Danchin and Sekowska address the constraints on the design of synthetic bacterial chassis, contrasting the top-down and bottom-up approaches to chassis development. They also remind the reader of the importance of time, the fourth dimension of any three-dimensional biological system.

Biological systems are noisy, and individual genetically identical cells in a population subjected to the same environmental conditions exhibit a variety of phenotypes. Girke and colleagues explore the origins, measurement and engineering of noise and its influence on gene expression. As an example of the exploitation of synthetic biology, Goers and colleagues discuss the design, engineering and application of biosensors. Various types of biosensors are described together a range of reporters used to generate an observable signal. This chapter describes how mathematical models can be used to predict the characteristics and performance of biosensors and aid their design.

We sincerely hope that this volume provides the reader with valuable insights into the technology and methods currently being developed for the rapidly expanding discipline of synthetic biology.

**Colin Harwood and Anil Wipat**