# PREFACE

Haem proteins play vital and diverse roles in virtually all life forms. The history of microbiology shows us that respiration, aerobic and anaerobic, was a major focus in the heady early days of bacterial metabolism. In the Third Edition of 'Bacterial Metabolism' (1949)—Marjory Stephenson's classic text first published in 1930—'Respiration' is the first chapter after the Introduction and contains much detail on the components of the 'oxidising system'. Haem proteins and cytochromes, the activation of oxygen, and the diversity of cytochromes were all covered. However, in microorganisms, the research area of $O_2$-binding proteins has now become dominated by studies of globins and globin-related proteins—proteins that get no mention in 'Bacterial Metabolism' (although leghaemoglobin did warrant a brief account).

Now, every 2 years, the amazing progress in this field has been evident by presentations at the Oxygen-Binding Proteins (O2BiP) held across Europe at venues that include Naples, Aarhus, Antwerp and, most recently (2012), Parma. It was this last meeting that led to the idea of a volume to mark some of these achievements. The focus there and here is bacterial and archaeal proteins, where the most dramatic progress has been made.

The first accounts of globins in microbes were those of Keilin in the 1930s, who demonstrated distinctive redox-dependent absorbance bands by use of his hand spectroscope. With no confirmation of the chemical nature of the pigments he observed, he correctly assigned strong bands in yeast, moulds and protozoa to haemoglobin (Keilin, 1953; Keilin & Ryley, 1953; Keilin & Tissieres, 1953). Then, in the 1970s, Oshino, Chance and others investigated in biochemical detail the yeast pigment and showed it to comprise not only a haem domain but also a flavin chromophore (Oshino et al., 1973; Oshino, Oshino, Chance, & Hagihara, 1973); this was the first description of a flavohaemoglobin. Recognition of haemoglobins in bacteria was, however, much later. Webster published many important papers in the 1970s describing a 'soluble cytochrome *o*' in the microaerobic bacterium *Vitreoscilla*. The pigment was observed in intact cells as a stable oxygenated species. Webster and others later published the sequence of this protein (Wakabayashi, Matsubara, & Webster, 1986), showed it was a globin and thus provided the first definitive proof that haemoglobins occur also, and unexpectedly, in bacteria (Perutz, 1986). The first nucleotide sequence of a bacterial globin was that of Hmp, the

bacterial homologue of Keilin's and Chance's yeast protein. The sequence (Vasudevan et al., 1991) clearly revealed the chimeric nature of the protein with an N-terminal monohaem domain and a C-terminal flavin domain. More detailed accounts of the development of our now extensive knowledge of bacterial flavohaemoglobins (Forrester & Foster, 2012) can be found elsewhere. Concomitantly, a shorter than usual 'truncated' globin, GlbN, was observed in the cyanobacterium *Nostoc commune* and related cyanobacteria (Potts, Angeloni, Ebel, & Bassam, 1992) and a haemoprotein with kinase activity, and therefore, sensor function was found in *Rhizobium meliloti* (Gilles-Gonzalez, Ditta, & Helinski, 1991). Additional genomic information revealed the presence of single-domain globins homologous to the globin domain of flavohaemoglobins (Wu, Wainwright, & Poole, 2003) a family of globin-coupled sensors involved in chemotaxis in Archaea and bacteria (Hou et al., 2000) and related single-domain protoglobins (Hou et al., 2001).

These important discoveries paved the way for the advances described in this volume that comprises a selection of illustrative topics and system. The editor asks to be forgiven for omitting other important examples. Here are contributions covering single-domain globins lacking flavin, truncated globins in diverse bacteria including pathogens, as well as cyanobacteria and algae, truncated globins, haem-based sensors and protoglobin. The volume will also highlight the remarkable number of globin (gene) sequences now known but also attempts to discern, predict or guess what function(s) they may fulfil. This task is fraught with uncertainty and difficulty. The number of globin sequences is vast, yet the volume of experimental data on which to base any meaningful prediction of the significance of globin distribution between physiological groups or genera of bacteria is minimal. In my opinion, the 'gold standard' is the exploration of globin function by mutagenesis and phenotypic characterization. Sadly, the frequency of published papers is in overwhelming favour of those describing sequences and structures and studies of function that can be observed when the globin is expressed in another host. Hopefully, this volume will prompt telling experiments that can tell us more about function, that is, physiology.

## REFERENCES

Forrester, M. T., & Foster, M. W. (2012). Protection from nitrosative stress: A central role for microbial flavohemoglobin. *Free Radical Biology & Medicine*, *52*, 1620–1633.

Gilles-Gonzalez, M. A., Ditta, G. S., & Helinski, D. R. (1991). A haemoprotein with kinase activity encoded by the oxygen sensor of *Rhizobium meliloti*. *Nature*, *350*, 170–172.