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Preface

Functional Redox Radicals in Proteins

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Our knowledge of catalysis in biological systems involving or being proposed to involve protein radicals has increased dramatically within the last 10-15 years. While there have been several very excellent general reviews on this subject recently, an entire issue of a scientific journal devoted to bringing together a collection of specific reviews covering a range of biological systems and different spectroscopic methods has been lacking. I hope with this special issue of BBA-Bioenergetics to cover a range of such topics and techniques together in a single issue. The articles presented here range from dedicated reviews on stable and transient proteins radicals including their detailed characterisation with biophysical techniques through to the attempts to theoretically calculate complex mechanisms of catalysis in biology and to explore such radical chemistry by means of protein engineering and de novo design. Of course when mentioning radical intermediates one immediately can think of techniques such as electron spin resonance (ESR) spectroscopy and Fourier transform infra-red (FTIR) spectroscopy. This is indeed the case here and I have included several articles whose central theme is the application of modern ESR methods to identify, characterise and localise radical species. ESR is a technique that, although still largely based in the hands of the expert, is becoming far more commonplace in the vocabulary of the biochemist and molecular biologist and, as an ESR spectroscopist myself; I hope that the articles presented here will further motivate this trend.

One of the first protein radicals to be observed spectroscopically was found to arise from an oxidised tyrosine residue and although since then several other stable and transient amino acid radicals have been localised on other amino acids, tyrosine remains the most commonly studied species as will become quite apparent in this issue.

Fortunately in recent years an increasing number of research groups at the forefront of methodological development in biophysical spectroscopy have taken up the challenge of studying such species in great detail especially in complex biological matter such as membrane proteins. For example the pioneering studies using high-field ESR of small organic molecules such as semiquinones and tyrosines have led to an ever increasing and detailed study of such species in proteins. Currently well-known "fingerprints" of tyrosine, tryptophan, glycine or cysteine radical species are known.

It is the prime purpose of this special thematic issue to give an overview of the different approaches and the remarkable progress that has been made in these fields in recent years. Gunnar Jeschke gives an introduction to the ESR techniques that have and may be employed to study radical enzymes and in particular radical amino acids. While it is now clear that many systems exist which involve for example amino acid radicals, there are as yet only really a couple of systems where they have been studied in great depth, namely Ribonucleotide reductase and photosynthesis (or more especially photosystem II). Thus two articles cover important aspects of these fields. The first by Friedhelm Lendzian reviews the application of high-field ESR spectroscopy to the study of amino acid radicals in class1 Ribonucleotide reductase while the second by Catherine Berthomieu and Rainer Hienerwadel demonstrates the power of vibrational spectroscopy to the study the properties of redox-active tyrosines in Photsystem II and other proteins.

Not only radicals but also the presence of radical pairs, especially in photosynthesis, had led to the use of this subject for the development of spectroscopic techniques to elucidate structural information over large distances. These investigations, reviewed by Robert Bittl and Stefan Weber can provide additional constraints for structure determination in large multi-subunit membrane proteins. Stefan Weber has also done an excellent job summarising the field of light-driven catalysis of DNA repair. There are a couple

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of articles related to resolving mechanisms in radical enzymes. Fahmi Himo reviews the mechanism of C-C bond formation in radical enzymes from a theoretical point of view, while Matthias Boll discusses the mechanism of anaerobic aromatic metabolism.

An article relating to the technical advantages of time resolution in the detection of short-lived transient radical species in electron transfer proteins, e.g. cytochrome *c* oxidase, has also recently been published in BBA (Microsecond freeze-hyperquenching: development of a new ultrafast micro-mixing and sampling technology and application to enzyme catalysis by Alexey V. Cherepanov & Simon de Vries; *Biochem. Biochim. Acta* (2004) 1656, 1-31). This article, which was originally planned for this special issue, can thus be considered as cognate to this collection of reviews. It describes the technique of fast mixing and freeze-quenching of reactions (freeze hyperquenching) at time resolutions at least two orders of magnitude higher than that currently commercially available. I am convinced that this technique when applied together with some of the detailed spectroscopic techniques described here (e.g. modern pulsed EPR techniques) will be of increasing and significant importance in the future when trying to elucidate the complex mechanisms of the many different electron transfer processes in bioenergetics.

Finally the issue is completed by two further articles; one by Kristina Westerlund, Bruce Berry, Heidi Privett and Cecilia Tommos covering amino-acid radical chemistry from a protein engineering and de novo design point of view. The final article by Dimitri Svistunenko discusses the reactions of haem containing proteins from a radical perspective.

While the list of articles is not comprehensive (it was never intended to be!) I hope that the selection of topics in this special issue covers a range of systems and techniques that will not only be useful for the experts in the field as a "state of the art" reference but will also be attractive for colleagues from outside the field, who may now find an alternative "Ansatz" to address mechanistic or functional questions arising in the many membrane proteins (bioenergetic or otherwise) that are still waiting to be studied in such great depth.