

BOOK REVIEWS

PERSPECTIVES ON MAMMALIAN CELL DEATH

E.d. C S Potten (1987) Oxford University Press
ISBN 0-19-854184-8 £40

It might be supposed that any "perspectives" might abruptly tend to zero with death! Despite its odd title this book brings together a useful set of thirteen contributions that encompasses the multiplicity of processes involved in cell death. Those in the "killing fields" such as radiologists and designers of anti-cancer drugs clearly have different perspectives from developmental biologists or gerontologists. Moreover the death of a cell often means different things to scientists in different disciplines. To the pathologist (*Hume*) cell death has specific morphological meanings whereas the radiologist sees cell death in terms of the loss of ability of cells to divide a prescribed number of times (*Hendry & Scott*). Despite these difficulties, a key concept is that loss of reproductive potential is associated with the normal processes of cell differentiation.

Throughout the book, distinction is made between *necrosis*, the irreversible destruction of cells through injury, and the process of intrinsically programmed self destruction now referred to as *apoptosis*. Although it was only in 1974 that the term apoptosis first appeared in the literature, the biological importance of this phenomenon is considerable. It is now recognised (*Kerr et al*) as a feature of normal embryonic development (*Snow*), of differentiation (*Allen et al*, *von Wagenheim*), of tumour development (*Moore*) and of cell senescence (*Shall*).

Study of the cellular mechanisms involved in apoptosis clearly indicate new gene expression. A characteristic event is double-stranded cleavage of nuclear DNA as a result of the activation of an endogenous endonuclease. A suggestion is that a newly synthesised protein activates this nuclease by mediating an influx of calcium ions into the nucleus. This cleavage of DNA occurs synchronously with a compaction and segregation of chromatin. The functional integrity of plasma membranes nevertheless remains unimpaired and cellular levels of ATP are maintained.

By comparison, necrosis is characterised by a snowballing derangement of most cytoplasmic activities. However many extracellular toxic substances first induce membrane damage. Changes have been detected in membrane permeability, lipid peroxidation, active transport and cell surface morphology (*Sato & Yonei*). Of major significance is the derangement of transport systems for ions which leads to ionic equilibration, osmotic influx and death. Other critical effects occur at the level of the mitochondrial energy generating systems depleting cells of ATP. *Dean* gives specific examples of free radical induced cell death and argues for direct radical attack on membrane transport systems being more critical than effects on lipid peroxidation.

Overall it is surprising what little mention is actually made of free radical mechanisms even in specific chapters on irradiation (*Hendry & Scott*) and immunologically-

mediated cell death (Christian & Moore). Despite this deficiency this is an interesting collation of reviews, but it is unfortunate that the references given only extend to 1985! There has been considerable activity in the free radical field since then.

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**CHEMILUMINESCENCE. PRINCIPLES AND APPLICATIONS IN
BIOLOGY AND MEDICINE**

A.K. CAMPBELL

Ellis Horwood, Chichester (England); VCH Verlagsgesellschaft, Weinheim (FRG)
1988

ISSN 0930-3367; ISBN 3-527-26342-X

559 pages + appendices and index (608 pages incl.)

The wonders of living light certainly have generated enthusiasm in the author, and the book transmits this very well. In the preface, Campbell asks rhetorically: "These fluorescent animals you collect on the beach at night are rather rare, aren't they? Is this something you do just for fun? How on earth are they connected to your investigations into rheumatoid arthritis and multiple sclerosis?" After reading the book, one can see the connection, but one can see the amazing amount of knowledge still to be obtained for a full grasp of this basic and highly interesting biological phenomenon.

The book is a one-author monograph, and this brings advantages and drawbacks. One of the usual drawbacks of multi-author books is the inadvertent redundancy. In this book, however, there is built-in redundancy. For example, from the preface on in almost every chapter one finds the statement that over half of the earth's surface is covered by ocean more than 1,000 m deep and that there the only light is "living light".

The book is organized into 10 chapters, the first one being "A natural history of chemiluminescence", and the basic definitions and history are well presented. The first definition of chemiluminescence was given just over 100 years ago, by the E. Wiedemann (1888) *Ann. der Physik und Chemie* 34, 446-436, "Über Fluoreszenz und Phosphoreszenz", but the history goes back further, for example to the discovery of the Bolognian stone by Cascariola in 1603 and the first observations on luminescence versus incandescence by Boyle in 1668. In chemiluminescence the electronically excited state is generated by a chemical reaction, and the formation of electronically excited states has a typical half-time of 10^{-15} - 10^{-12} seconds. The eye is quite sensitive and can record 30,000 photons/sec per cm^2 of retinal surface. The quantum physics is given in a brief presentation, but of course in-depth explanations are not possible in this context.

The second chapter, "Detection and quantification of chemiluminescence" provides useful technical information, and the third "Bioluminescence: living light", provides an excursion into what is dear to the author, namely the description of the different luminous organisms in major habitats on the earth's surface, particularly in

the sea, and one find pictures of the common piddock, *pholad dactylus*, one of the objects of interest in this field. I am not quite sure whether the several pages of photos of different shrimp provide much information, but they are nice to look at. Much is known on the biochemistry of bioluminescent reactions, and the table (p. 228) gives the functions of living light. These are as diverse as obtaining food (illumination to see prey; luring prey; schooling, defence and security, camouflage; decoy; frighten or smoke screen; burglar alarm; warning; blinding; sacrifice lure; vision) and propagation of species (schooling prior to mating; mating ritual; attraction of propagating species; symbiosis). These functions are described in a nice and refreshing way.

The need for chemiluminescence analysis in biology, medicine and biotechnology ranges from the ocean depths to the hospital bed, and a table (p. 240) on the exploitation of chemical light by man includes the applications: "torch, fishing, military, detection, ritual, fun, scientific". Regarding the latter, the most important new developments seem to be the chemiluminescent label in immunoassay and in recombinant DNA technology. These are described in later chapters. Some analytical applications of chemiluminescence include the use of phthalazine diones such as luminol, isoluminol and derivatives for the measurement of reactive oxygen metabolites and to study phagocyte activation and to measure nitric oxide. Similarly, acridinium salts such as lucigenin and acridinium esters have been employed. The bioluminescent reactions of the firefly have an established place in sensitive assays of ATP and related metabolites. Bacterial oxidoreductase-luciferase can measure NADPH, FMN and related metabolites and has been employed for very sensitive detection of low oxygen concentrations. The coelenterate photoproteins such as aequorin or obelin are employed for detecting free calcium (the topic is specially emphasized in chapter 7). The measurement of enzymes and metabolites is given in much detail in chapter 5.

The following chapter is on ultraweak chemiluminescence, a chapter probably most closely related to the field of free radicals. A table on page 380 lists compounds inducing, enhancing or inhibiting ultraweak chemiluminescence and it is well taken to distinguish the ultraweak or inhibiting low-level chemiluminescence from the indicator-dependent chemiluminescence, such as is used by the addition of indicator compounds like luminol or lucigenin. While many aspects are well presented, the contribution of lipid peroxidation is only relatively weakly covered. This is quite surprising, since much of the literature of recent years on ultraweak chemiluminescence utilizes lipid peroxidation as a source. Likewise, the discussion on singlet oxygen is not quite up to date. In contrast, the description on how phagocytes are activated and how the respiratory burst and its associated chemiluminescence is being studied, appears to be well done. Also, the discussion of the use of photoproteins versus the fluorescent compounds from Tsien (fura-2 and related compounds) gives a good overview.

The three final chapters are: "An alternative to radioactive labels", "chemiluminescence energy transfer" and "hills and horizons", with the latter one coming back to the more literary and slightly philosophical trail that was noticeable at the outset. A glossary and some other tables conclude this interesting walk through the world of living light.

Altogether, I have read the book with interest and can recommend it to readers in biology and medicine. As I already mentioned, there are some limitations on a one-author coverage of such divergent areas. In my own field of interest, singlet oxygen and chemiluminescence in lipid peroxidation and in the study of antioxidant

functions, there certainly are some white areas in this treatise. The basic physical chemistry also has some points of criticism. For example, it does not need numerous equations to derive the conclusion that one needs six half-times to measure more than 98% of the photons emitted in an exponential chemiluminescent reaction. One other point of nuisance is the fact that in spite of the enormous work the author has undertaken, apparently there has been not enough time for careful proof-reading. There are numerous misspellings, sometimes in proper names and places, and also in equations. There is some bibliography given, but unfortunately those references that are mentioned in the text are not referred to directly or systematically.

Overall, however, the author is to be congratulated on his effort and on the success in transmitting his enthusiasm on this wonderful biological phenomenon of chemiluminescence. I am sure that each individual reader will take home something new from reading this comprehensive treatise.

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