Additions and Corrections

DNA Oxidation as a Source of Endogenous Nucleophiles: Formation of Ethenoadenine Adducts in γ-Irradiated DNA [*J. Am. Chem. Soc.* **1999**, *121*, 9231−9232]. WENDELYN R. JONES AND PETER C. DEDON*

Members of this laboratory have been unable to reproduce the reported radiation dose-response in the formation of 1,N^6-ethenoadenine. While more sensitive detection methods may prove otherwise, we cannot detect ethenoadenine in γ-irradiated DNA at levels measurable by HPLC with a fluorescence detector. However, the formation of ethenoadenine in reactions of 2′-deoxyadenosine with 2-phosphoglycoaldehyde is reproducible and products formed in a similar reaction with 2′-deoxyguanosine will be reported in a forthcoming paper. We deeply regret any inconvenience and confusion caused by this error.

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Book Reviews *

Preparing for FDA Pre-Approval Inspections. Edited by Martin D. Hynes III (Eli Lilly and Co). Marcel Dekker, Inc.: New York. 1998. $165.00. ix + 278 pp. ISBN 0-8247-0218-2.

The generic drug scandal of the 1980s focused attention on the process by which drugs were approved, and this led, ultimately, to the intense pre-approval inspection program currently in force. The implementation of the program, for various reasons, has caused frustration as well as costly delays in the registration of pharmaceutical products. The book under review explains the history of the inspection process, describes a "game plan" for dealing with inspections, and provides minute details on how to best handle the scrutiny of the inspectors. It explains the rights and obligations of the company under review and provides an overall quality approach that will keep the company in a state of equilibrium, preventing panic when an inspection is impending. As such, it is timely and should be required reading for company executives and scientists who will face a pre-approval inspection (PAI).

The initial chapters provide an introduction and adequate history of the PAI process. Chapter 3, on International PAI's, does more than provide advice to International companies. The reader will find much information on the structure and functioning of the FDA (including names, addresses, and telephone numbers of key personnel) as well as general advice that will be useful to international and domestic companies alike. For instance, it is recommended that companies try to schedule daily meetings with the inspection team during the course of the PAI, so that some issues may be resolved immediately.

Chapter 5 gives a detailed review of the consequences of failing a PAI. These range from simply delaying the product approval to exercise of the FDA's "Applications Integrity Policy" (when there is suspicion of fraud), debarment of individuals who participated in fraud, and criminal investigation. Chapter 6 gives a detailed overview of how to manage the actual PAI process. It is full of practical advice on matters ranging from the timing of the inspection up to dealing with 483's. However, practical advice is contained throughout this book. The chapter on international inspections, for instance, provides specific questions to ask the inspection team.

Chapters 4 (Stability Data), 7 (Validation), 8 (Document Standards), 9 (Technology Transfer and Scale-Up), and 10 (Training of Personnel) provide the background for developing a quality organization that has efficient systems in place, thus making it easier to prepare for a PAI. The final chapter deals with cGMP issues and stresses compliance (during the actual manufacture of the batches) with commitments made in the application. Examples of the latter include manufacturing procedures, batch sizes and formulations.

One criticism of the book relates to the fact that the chapter on international inspections appears so early in the book. Had other chapters describing issues pertinent to all inspections appeared first, this chapter could have been devoted solely to items that are peculiar to international inspections, thus eliminating some duplication. The individual chapters are not uniformly well referenced, although the book, as a whole, contains an adequate number of references. The reviewer also felt that the book could have been improved by more careful editing, in some places, to increase the readability and flow of information. A few more examples and selected case studies would help to hold the reader's interest, without necessarily making the book too long. Nevertheless, in its present format, the book is a valuable contribution to the literature and will be useful to drug development scientists and executives at pharmaceutical companies. It may also serve as a valuable addition to university libraries.

S. Indiran Pather, D. Pharm., *CIMA Labs, Inc.*

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Phosphoinositides. Chemistry, Biochemistry, and Biomedical Applications. ACS Symposium Series 718. Edited by Karol S. Bruzik (University of Illinois at Chicago). Oxford University Press: New York. 1998. xii + 300 pp. $115.00. ISBN 0-8412-3628-3.

This book, the result of collaborations between cellular biologists, biochemists, and chemists, brings together the latest developments in the study of inositol phospholipids and covers inositol signaling pathways at both the cellular and molecular levels. The 18 papers are drawn from a symposium sponsored by the Division of Carbohydrate Chemistry at the 214th National Meeting of the American Chemical Society held in Las Vegas, Nevada, September 7−11, 1997.

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The Molecular Origins of Life: Assembling Pieces of the Puzzle. Edited by André Brack (Centre Biophysique Moléculaire, CNRS). Cambridge University Press: Cambridge, U.K. 1998. viii + 417 pp. $85.00. ISBN 0 521 56475 1.

While all living creatures are conscious of or "involved" in the present, only *Homo sapiens* exhibit a strong tendency for exploring

*Unsigned book reviews are by the Book Review Editor.

and trying to understand the past (as well as for trying to predict the future). Undoubtedly the most extreme manifestation of this is our growing efforts to understand the origins of life itself. It is intriguing that we should try to wrap our minds around such a complex and immense puzzle. *The Molecular Origins of Life*, edited by André Brack, spreads on the table numerous pieces of this four-dimensional space−time puzzle as seen through the eyes of leading researchers delving into all aspects of the origin-of-life question. Each contributor gives us extensive, up-to-date references to the work in their area. The key pieces of the puzzle are intrinsically molecules that must be fit together by understanding the chemistry of their formation and interactions.

We usually start assembling a puzzle by finding the edge pieces or boundary conditions. For this origin-of-life puzzle, the past century has revealed the cosmic abundance of elements as the boundary condition for starting materials and biomacromolecules as one—but not necessarily the only—boundary condition for products. Now comes the hard part—filling in the puzzle from edge to edge. How can we do this when so many pieces of the puzzle were lost billions of years ago? *The Molecular Origins of Life* reveals how careful observation and experimentation have allowed us to recover remnants of these pieces and speculate what they originally looked like.

In the first two chapters, Tobias Owen and James Kasting/Lisa Brown refine the cosmic elements into a plausible atmosphere of starting materials by examining both observational data and chemical models. Before starting Chapter 3, I would suggest that the reader jump to Chapter 17, in which Francois Raulin discusses our expanding knowledge of Titan, a moon of Saturn that has an atmosphere containing an orange smog, rich in hydrocarbon and cyano compounds. The Titan pieces mesh better with the pieces from the first two chapters.

Stanley Miller then describes how these simple molecules may be transformed in the atmosphere or on the Earth's surface into biological building-block molecules, amino acids, purines/pyrimidines, etc. under reasonable primitive Earth conditions. In the past two decades, the complexity of the puzzle has increased with the discovery of hydrothermal vent chemistry/biology. Nils Holm/Eva Andersson explore this as a possible venue for life's origin. Karl Stetter expands this theme, describing a zoo of hyperthermophiles and other seemingly strange microorganisms that broaden the chemical context in which life may have arisen. These findings make more plausible the origin of life in an iron−sulfur world (as postulated by Gunter Wachterhauser), possibly involving a thioester-based protometabolism (as described by Christian DeDuve).

Another controversy that has made the origin-of-life puzzle yet more fascinating is the exogenous delivery of organic matter to the Earth by comets, meteorites, and especially micrometeorites. This idea has been gathering additional support in recent years. Armand Delsemme, Michel Maurette, and John Cronin give evidence of the extraterrestrial formation of "useful" organic materials and the delivery of substantial quantities of these to the primitive—as well as the modern—Earth.

At this point, we might direct our attention to the pieces of the puzzle such as molecular aggregates (David Deamer discusses research on membrane compartments) and biopolymer formation that contain much more complex patterns. In the 1960s and 1970s, scientists focused their efforts on the condensation of amino acids to polypeptides. Based on the discovery of ribozymes, which have both catalytic and information-bearing properties, in the 1980s chemical evolution research was dominated by work to substantiate the "RNA world" as the environment in which life arose. Four chapters are devoted to the RNA world: its origins (Alan Schwartz), possible models for RNA synthesis (James Ferris), ribozyme catalysis (Kenneth James/Andrew Ellington), and self-replication (Jens Burmeister). This area of the puzzle depicts a less alien landscape.

On another edge of our puzzle, we are able to build a fairly intricate picture of the fossil record, greatly expanded by the detection of Precambrian microfossils as described by William Schopf. Probes to comets, moons, and planets in our solar system such as Titan and Mars (contributed by Christopher McKay) are bringing new jigsaw pieces to the table.

We step back and look at the progress with our puzzle but are dismayed by the fact that there is an immense gulf between our monomeric building blocks on one side of the puzzle and the RNA world on the other. Key parts of the puzzle are missing, such as, a plausible synthesis of the RNA sugar ribose and the formation in the ancient oceans of polynucleotides with phosphate ester linkages or proteins with polyamide linkages. Indeed, those authors that do discuss the "biopolymer problem" bring isolated pieces to the puzzle that do not fit very well into the picture; i.e., they require special conditions that seem unlikely on the early Earth.

Despite these frustrations, humanity keeps playing with the puzzle, finding missing pieces and carefully placing each, certain that the picture that emerges will be incredibly beautiful. It is predicted that completing this origin-of-life puzzle will be a major human endeavor in the next millennium. *The Molecular Origins of Life* provides a detailed look at many of the pieces scientists have started to assemble.

Robert D. Minard, *Penn State University*

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Industrial Catalysis: Optimizing Catalysts and Processes. By R. J. Wijngaarden (Shell Chemical Co., Geismar, LA), A. Kronberg, and K. R. Westerterp (University of Twente). Wiley-VCH: Weinheim. 1998. $185.00. 268 pp. ISBN 3-527-28581-4.

Most chemicals today are produced with at least one catalytic process which can be homogeneous or heterogeneous. Homogeneous catalysts are usually well-defined chemical species and are in solution together with the reactants. Their study is in the realm of chemistry, and there is not much needed from the engineer for an industrial catalyst design. The situation is quite different for heterogeneous catalysts, where the engineering aspects are critical components. These catalysts are porous solids, and due to their high specific surface area (for example, 300 $m^2\ g^{-1}$), they pack a very high density of active sites per unit volume, deep inside nanometer-sized pores. For this reason, the *transport of chemical species and of heat* is a major consideration in the design of a heterogeneous catalyst and also in the measurement of kinetics in the laboratory. To avoid these transport problems in chemical research, there are a number of procedures, including using special types of reactors and crushing the catalysts into a fine powder. In industrial practice, this is not possible, and the catalyst is shaped into pellets with the dimension of a few millimeters, for example, to keep the pressure drop in the reactor to a manageable level. Thus, interference of transport phenomena in the kinetics (catalysis) is unavoidable in industrial processes and in many cases is even used as a design tool. The objective of this book is to demonstrate how to calculate the effect of transport phenomena on the overall performance of the catalyst. Engineers designing heterogeneous catalytic reactors will find this book very useful. Researchers in the laboratory working with heterogeneous catalysts will also need to understand this subject, although the amount of material covered is beyond what is necessary, and the readers may not be willing to distill the relevant information for themselves.

The book includes the following chapters: 1. Introduction; 2. Kinetics; 3. Production and Physical Characteristics of Solid Catalysts; 4. Catalysis and External Transfer Processes; 5. Experimental Methods; 6. Calculation of Effectiveness Factor; 7. Complex Situations; 8. Design of Catalyst Pellets; and 9. Examples. There are also six appendices and a subject and author index.

The intention of the authors in writing Chapters 1−3 was probably to provide an introduction and short description of the material that is needed in later chapters. Chapter 2 should have been a key chapter since the objective of this book is to describe how the kinetics will be affected by transport processes. The authors, however, give a brief description of this subject with most of the references coming from their own work. It would have been useful to at least provide guidance to the general literature available. Chapter 3 gives a description of how catalysts are made and tested with references to some of the classical work in the field. The last section of Chapter 3, "Mass and Heat Transfer in Porous Catalysts", shows where the main interest of the authors resides and starts to describe the transport characteristics on porous media, including the dusty gas model and binary friction model. The treatment on transport processes continues in Chapter 4 with a discussion of how the outer surface of the catalyst pellet exchanges heat and mass with the surrounding fluid.

In Chapter 5, the special experimental techniques necessary to obtain the parameters to be used in the calculations dealing with industrial catalysts are described. Chapters 6 and 7, together with the appendices, form the core of the book. Here the authors review the literature on transport processes and conclude that there are a large number of results described, but that these results cannot be easily compared and generalized. A general theory is proposed by the authors based on what

they call the zeroth and first Aris numbers. The authors develop the theory in Chapters 6 and 7 and include examples to problems with an increasing number of variables. Chapter 8 shows how the developed theory can be used to design an optimal catalyst pellet. These chapters, together with Chapter 9, allow the reader to learn how to apply the method to his or her own specific problem.

A chapter dealing specifically with the task of how to avoid transport limitations when one is trying to measure catalytic rates would have been a good addition. Here the target reader would have been the researcher trying to avoid heat and mass transfer problems and willing to use special reactors and special testing procedures to avoid these pitfalls. This chapter would also have put in one place experimental procedures and negligibility criteria for transport limitations for this special application.

In summary, understanding heat and mass transfer limitations is of extreme importance for anyone working with heterogeneous catalysts. This book will be a good addition to the field and should be on the shelves of engineers and chemists.

Fabio H. Ribeiro, *Worcester Polytechnic Institute*

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Imaging of Surfaces and Interfaces. Edited by Jacek Lipkowski (University of Guelph) and Philip N. Ross (National Institutes of Health). J. Wiley & Sons: New York. 1999. 338 pp. $125.00. ISBN 0-471-24672-7.

This book provides a comprehensive summary of progress in the imaging of electrode surfaces ex situ or in electrolyte and is addressed to a wide audience of scientists interested in electrochemistry, surface science, material science, and electrodeposition technologies. According to the editors, the intent of this book is "to provide sufficient background so that it can be read by a specialist and a nonspecialist alike." The book contains seven chapters written by leading international researchers on different applications of various surface-imaging techniques that advance our understanding of the thermodynamics and structures of surfaces and the dynamics of interfacial processes. References included in most chapters are well updated to the late 1990s, with a considerable number of references given to earlier reviews in related fields. However, the references are not exhaustive by any means.

The book begins with an excellent introduction on electrochemical phase formation and growth. The first topic of this chapter is the theoretical and experimental results of low-dimensional metal phase formation on foreign substrates. Thermodynamics, structures, and dynamics of low-dimensional metal phase formation are discussed in both quantitative and qualitative ways. The second topic is the current status of nanostructuring and nanomodification of solid surfaces under defined electrochemical conditions. Several interesting experiments are illustrated by using in situ scanning probe microscope (SPM) techniques carried out on surfaces of metal single crystals, highly oriented pyrolytic graphite, epitaxial thin films of high-T_C superconductors, and semiconductor single-crystal surfaces. The site specificity of electrode processes is well elucidated with the help of these surface-imaging techniques and theoretical models.

The chapter dealing with ex situ studies of surfaces by electron diffraction and electron microscope is well written and includes a fair amount of well-selected, high-quality images and schematic diagrams. In the main body of this chapter, the authors present a few case studies that illustrate most of the methods being used. Personally, I find this chapter a wonderful resource for any specialist or nonspecialist who is interesting in ex situ structural characterization of bare and adsorbate-covered single-crystal surfaces. Readers may also find the flame treatment specimen preparation method and the electrode- emersion under potential control technique to be quite interesting.

The technologically important field of electrocrystallization/electrodeposition is discussed in Chapter 3. There is some repetition with Chapters 1 and 3 that could have been avoided, although the major part of Chapter 3 discusses the use of in situ SPM methods in studying the growth processes of the bulk metal phase from the initial stages. This chapter contains a table that lists recent publications of the applications of local probe methods in studying metal deposition processes. Readers may find this table one of the most useful resources in this book. Impressive images of the progressive growth of electrodeposits were obtained using real-time in situ SPM methods. However, as the authors frankly point out, one should realize that the deposition conditions in such in situ SPM experiments might be significantly different from those occurring during "conventional" metal plating due to the "hindrance effect" of the probe. As such, in situ SPM may not be suitable for reliable quantitative measurement of microscopic growth rate for electrodeposition, although it may still yield significant qualitative information if the experimental limitations are realized and understood. This chapter also contains a nice discussion on the influence of metal plating bath additives and strain at the metal−foreign substrate interface as a result of misfit between the deposit and substrate lattice.

In Chapter 4, the authors focus mainly on several optical methods used to image reaction fronts at surfaces and interfaces. It provides the readers with quite detailed discussions on the scanning photoemission microscope, photoemission electron microscope, ellipso-microscope, reflection anisotropy microscope, and the infrared microscope for imaging reaction fronts in heterogeneous catalysis. The potential probe technique and surface plasmon microscope, used for imaging in electrochemical environments, are also discussed. However, other important optical techniques, such as the second harmonic generation microscope, are only surveyed very briefly at the end of this chapter. The techniques discussed here could possess the advantage of real-time imaging and the potential of observing fast dynamic processes at surfaces.

Chapters 5 and 6 describe the advances of SPM to study organic films on metal electrodes and to image potential-dependent phase transitions in organic monolayers. Chapter 5 focuses on adsorption, nucleation/growth, structural phase transitions, and electrochemical reactions in organic monolayers at the electrode−electrolyte interface. The effects of different substrates on the adsorbate−substrate interactions in the molecular packing structures of the adsorbed monolayers are discussed for several heterocyclic molecules. In Chapter 6, the authors have divided the review into two sections: one focusing on the scanning tunneling microscope (STM) and the other on the scanning force microscope (SFM). Both sections begin with a brief discussion on the instrumentation and operational principles for each technique. The next part of each section highlights several examples of characterizations of organic monolayers and polymer films. Some of the applications discussed herein demonstrate the potential of SPM techniques for mapping interfacial physicochemical properties on a molecular-length scale. The authors clearly understand that the challenge of these techniques is to harness their power and to interpret data and images both quantitatively and qualitatively, especially in addressing issues related to the local structure and spatial distribution of specific sites at electrode surface with high levels of reactivity.

These advances in the applications of SPM have rekindled interest in the theoretical treatments dealing with the interfacial processes because theory plays a central role in understanding images and data obtained. Progress in the theory of the operation of STM in an electrolyte solution is carefully reviewed in the last chapter, helping readers to interpret STM images of electrode surfaces. This chapter provides the readers with a nice theoretical background on electron tunneling in a solution, as compared to that in the vacuum. Several spectroscopic applications, e.g., the measurement of current−distance and current−voltage relations are also discussed but demonstrated only with a limited number of case studies.

Overall, this is an excellent resource for imaging techniques of surface and interface based on SPM, electron diffraction/electron microscopy, and optical methods. The book fulfills the goal of making the information interesting to a wide audience of scientists. However, the readers should be aware that this is not an exhaustive review for all of the SPM and surface imaging techniques. For example, little discussion, if any, is given about near-field scanning optical microscopy, scanning electrochemical microscopy, scanning Kelvin probe microscopy, etc. Readers interested in these related techniques will have to rely on other scientific literature. Nevertheless, I would recommend this book for both researchers and graduate students who are interested in surface imaging techniques.

Fu-Ren F. Fan, *The University of Texas at Austin*

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