PREFACE

It is most appropriate that *Corrosion Reviews* has chosen to bring out a special issue on the subject of *'Biomaterials Corrosion'* at a time when significant advancements are taking place in the field of materials science and engineering. Biomaterials Science and Technology is evolving nowadays as an important field of interest because it has human value and direct influence on the quality of life. Materials that can survive in the natural ambience of human body with only minor degradation in their physical, chemical and mechanical properties are often referred to as biomaterials. There is a growing demand for manufacturing medical devices from such biomaterials in order to provide important functions of organs and save lives. In this respect, the current developments taking place in the field of materials science and engineering have great influence on the evolution of new biomaterials and manufacturing processes. In spite of these developments, the long-term functionality of any biomaterial implanted in the human body remains a major challenge.

Corrosion is one of the major degradation processes that might occur *in vivo*, and should thus be considered when evaluating new biomaterials and new designs of medical devices. The bioenvironment may be described as 'aggressive and angry,' and is associated with a variety of salts and appreciable changes in the local pH conditions. Metals and alloys, which are extensively used in medical devices, might corrode severely in this bioenvironment in accordance with both thermodynamic and kinetic considerations. This degradation process is undesirable firstly because it limits the functionality and lifetime of medical devices, and secondly because it releases corrosion products that may elicit an adverse biological reaction in the host. Ceramics may also undergo selective leaching, although they more often fail *in situ* due to mechanical processes such as wear.

Corrosion is a complex phenomenon that depends on geometric, metallurgical, mechanical and chemical parameters. Thus, a firm understanding of these parameters and their synergistic effects is required in order to control biomaterials corrosion. In this special issue we have made an effort to put together selected articles from specialists working on various aspects of corrosion of biomaterials. First, Prof. Lotan (Technion, Israel) highlights in Preface 2 the novel areas of activity in the field of Biomaterials. Then, Prof. Blackwood (National University, Singapore) provides an introductory overview of the successes and failures of traditional biomaterials, as well as of the problems that are likely to be encountered before new advanced materials can be successfully used *in vivo*. Subsequently, Dr. Geetha Manivasagam *et al.* (India) review the corrosion and microstructural aspects of titanium and its alloys as orthopaedic devices. Corrosion reactions may be impeded or prevented by kinetic barriers such as passivation, or the formation of a surface oxide film on the metal surface. The reconstruction and regeneration of such films in biological environments are discussed by Prof. Hanawa (National Institute for Materials Science, Japan). The synergistic action of electrochemical and mechanical processes may cause premature failures of metal orthopaedic implants and accelerated release of ionic and particulate debris to the surrounding tissues. Such a phenomenon, known as fretting corrosion, is reviewed by Profs. Hallab and Jacobs (Rush Medical College, USA). These authors also explain in detail the clinical concern about the release and distribution of metallic degradation products in the body. Next, corrosion of contraceptive intrauterine devices (IUDs) made of copper in uterine synthetic solution is evaluated by Prof. Valdez *et al.* (Mexico). Finally, the editors of this special issue and their co-authors (India, Israel) give a survey of failure analyses of stainless steel orthopaedic devices, focusing on localized corrosion phenomena. The authors also discuss the use of advanced stainless steels and the application of nitrogen-ion implantation and bioceramic hydroxyapatite coatings as potential remedies.

We believe that the articles included in this special issue may be of interest to materials specialists, electrochemists, bioengineers, medical doctors, surgeons, and 'modern patients' too. Only through a multidisciplinary effort can the problem of biomaterials corrosion be controlled. We would like to thank Mr. M. Schorr, the Editor of *Corrosion Reviews*, for providing us with the opportunity to serve as the Guest Editors of this Special Issue. We also thank all authors of this Special Issue for their wonderful contributions and cooperation.

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PREFACE 2:
AN OVERVIEW OF BIOMATERIALS – NOVEL APPROACHES AND APPLICATIONS

During the last two decades the field of Biomaterials underwent considerable changes. In the past, the activity was focused on the use of already available materials and attempts were made to accommodate them for the new applications considered. More recently, the trend is towards the "design-for-function" approach, under which molecules and supra-molecular assemblies are first designed for performing the desired task and, subsequently, are synthesized according to the blueprint produced.

By and large, biomaterials are intended to perform medical and biotechnological functions. These include, for example, prosthetic implants, elements in controlled drug delivery and tissue engineering, as well as in biosensors and insoluble biocatalysts. As such, they are used in contact with physiological systems or with physiologically-related ones.

Biomaterials are categorized according to their chemical composition (polymers, ceramics, metals), to their origin (natural or synthetic), as well as to their supramolecular structure (porous, composites). It is this variety that provides us the almost endless opportunities to design and produce the biomaterials we need. Thus, biomaterials science and technology is a most encompassing undertaking. It involves a wide spectrum of disciplines, from physiology to biology, from chemistry to physics, from computer-assisted modeling to engineering, and is dedicated mainly to providing better health care and improved quality of life.

Materials corrosion is of much concern in many areas of science and technology. In the particular case of biomaterials, this process has additional dimensions and must be considered within the much broader context of their biocompatibility. This aspect is of the "two-way-street" type. On the one hand, the biomaterial should stand the physical and chemical characteristics of its environment and should not be affected by the latter in any undesirable manner. On the other hand, the biomaterial should not have any undesired effect on the physiological environment where it performs. Accordingly, biocompatibility is not only a trait of the material itself, but is the interplay between characteristics of the material and those of the particular environment considered. And, while the above definition is rather encompassing, the requirements set forth do not preclude the possibility that some interactions between the biomaterial and the surroundings actually take place. As a matter of fact, in some instances, a well delineated interaction is not only desirable, but may be the very reason for using the biomaterial considered.

Based on the above mentioned concepts, novel areas of activity in the field of Biomaterials emerged. Some of these areas are briefly outlined below.

1. BIOCOMPATIBLE MEDICAL IMPLANTS

Most of the implanted biomaterials are made of polymeric or metallic components. And, while these devices indeed perform their intended function, their biological compatibility with blood and tissues is – in many instances – not appropriate. Activity in this area addresses procedures for improving the biocompatibility of implants by surface modification, using a variety of physical and chemical procedures.

2. SCAFFOLDING MATERIALS FOR TISSUE ENGINEERING

Restoration of damaged or missing tissues in patients with inborn defects or accidental injuries is – in many instances – a life saving medical procedure. However, the supply of donated human organs and tissues, required for transplants, is extremely limited. As such, the laboratory production of viable materials required for such procedures is of very high priority, and it is the area of concern of Tissue Engineering. This activity involves growing the required tissues from human cells, using biocompatible and biodegradable polymeric materials as supporting scaffolds. Much of the related activity addresses the development of appropriate scaffolding materials, as well as of technologies for producing them according to the tissue to be grown.

3. INTERPENETRATING POLYMER NETWORKS AND COMPOSITES

Efforts are made in order to develop biomaterials as insoluble elements, to be used for therapeutic and diagnostic purposes. The applications considered are in biomedical reactors, as scaffolds for tissue engineering and as the biospecific stationary phase in preparative-scale chromatographic systems for biotechnological downstream operations.

4. NANOTECHNOLOGY FOR BIOMEDICAL AND BIOTECHNOLOGICAL APPLICATIONS

Nanotechnology is applied towards development of sub-micron size particulate materials, for use in biomedical/biotechnological areas such as enzyme carriers, controlled release of bioactive molecules and tissue engineering. These materials are made using biodegradable or bioerodible polyesters and polyamino acids. Their design and synthesis involves sound thermodynamic principles related to microphase separation and to self-assembly of supramolecular structures.

5. LARGE-SCALE SEPARATION OF BIOMATERIALS

Biopharmaceutical and biotechnological materials are produced using a variety of techniques, including fermentation, tissue culture, and genetic engineering. Extraction and purification of these materials from their crude mixtures (*i.e.*, downstream processing) account for up to 90% of the production cost. Extensive work is invested towards the development of materials and procedures for carrying out highly efficient, cost-effective and computer-assisted downstream operations. Particular emphasis is placed on multi-functional components intended to serve as insoluble packing materials in chromatographic columns.

6. PHYSIOLOGICALLY-CONTROLLED DRUG DELIVERY SYSTEMS

Currently available drug-releasing systems usually achieve a controlled and constant rate of delivery and rely mainly on physical processes (*i.e.*, diffusion and dissolution). For cases requiring a variable rate of release these systems are not only inappropriate, but even detrimental. The activity in this area is intended to study and develop the advanced class of materials and devices from which the drug release process and release rate are not constant, but controlled by the physiological status of the disease. The operation of these devices relies on bioerosion (*i.e.*, enzymic degradation) of the drug-carrier hybrid.

7. BIOMATERIALS FOR MOLECULAR ELECTRONICS

Molecular Electronics and, particularly, its most novel area of Molecular Bio-Electronics is here considered as a broad, multi-disciplinary effort. As part of this activity, enzyme-based molecular switches which are operated by outside signals are designed by molecular engineering approaches, using computerized molecular modeling. Using such switches, enzyme-based logic gates are designed, experimentally assembled and operated. The research is extended to also include biochemical neural networks. As a related topic, the synthesis of novel electro-conducting polymers (the "molecular wires") and the study of their interaction with redox enzymes are considered.

8. METABOLIC ASSIST WITH ENZYMIC BIOREACTORS IN CONTACT WITH BLOOD

The normally-functioning organism disposes of endogenous and exogenous toxic materials by eliminating them as such (*e.g.*, through the kidney), or by first transforming them - in the liver - into disposable metabolites. The related activity is intended to develop extracorporeal modalities for the supplementation of the impaired vital functions. The key elements of these devices are bioreactors containing detoxifying enzymes immobilized on biocompatible polymers or ceramics. Related systems are intended for use in local therapeutic procedures involving prodrugs.

9. ENZYME-BASED HYBRID SYSTEMS FOR CANCER THERAPY

In this context, enzyme-based procedures are considered, by which blood is treated in bioreactors in order to remove metabolic elements that are critically required for the growth and multiplication of tumor cells (the "selective starvation" approach). These systems are supplemented by controlled drug delivery units, and the two are combined in a fully-implanted or extracorporeal hybrid system of concerted action.

10. ENZYMIC REACTORS FOR MULTI-COMPONENT PROCESSES

A wide variety of biotechnological and therapeutical processes take place in enzymic reactors, in which multi-component interactions occur. Particular emphasis is given to diffusion limitations, enzyme inhibition and interactions of substrates and products with a ligand. For the design and operational analysis of these systems, extensive use is made of the compartmental analysis approach. When considering bioreactors as therapeutical devices, this approach is extended to also include the reactor-patient interaction.

11. BLOOD- AND BLOOD PLASMA SUBSTITUTES

Blood- and blood plasma substitutes are required in cases of medical emergencies, such as mass disasters (*e.g.*, wars or earthquakes) and individual needs (*e.g.*, surgery, severe hemorrhaging). They can be stockpiled without refrigeration, and do not pose limitations related to the blood type of the recipient. An intensive effort is invested for developing such materials.

12. MOLECULAR ENGINEERING

This is a rather novel engineering discipline by which molecules and supramolecular assemblies are designed, produced and operated in order to perform a predetermined function. The design procedure relies on computer-assisted, molecular-level mechanics, dynamics and modeling, as well as on sound thermodynamic principles. The methodologies developed are implemented mainly in the areas of controlled drug delivery, molecular logic systems, and molecular robotics.

To conclude, the field of biomaterials science and technology faces most challenging goals. In order to reach them, research and development rely on a variety of materials and on a broad spectrum of disciplines. It is this multi-face activity that provides the wide and solid base required for developing new and better biomaterials, as well as safer and more efficient devices and modalities.

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* The author gratefully acknowledges the partial support of the L.&D. Sherman Research Fund, the Fund for the Promotion of Research at the Technion, and the Technion V.P.R. Fund-R.L. Kohns Eye Research Fund.