

Progress in Biomedical Engineering, 6

Surface Characterization of Biomaterials

*Edited by
B.D. Ratner*

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Surface Characterization of Biomaterials

**Proceedings of the Symposium on Surface Analysis of Biomaterials,
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Edited by

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Surface Characterization of Biomaterials

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Progress in Biomedical Engineering

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PREFACE

In 1984, C.B. Duke proposed that the surfaces of solids might be considered as a special state of matter, a zone with unique chemistry, organization, dynamics, and electrical properties. Given that the majority of biological reactions occur at surfaces (e.g., cell surfaces, connective tissue surfaces), it is useful to compare a surface scientist's perception of this distinctive outermost layer to that of a biologist's:

- The surface scientist considers a surface as a zone undergoing (or influenced by) a transition from one phase to another.
- The biologist tends to view a surface as an abrupt ending of one phase.
- The surface scientist views surface dynamics as occurring at rates approaching those of atomic vibrations.
- The dynamics of surface change for the biologist are closer to the rate of polymeric (protein) chain translation.
- Contamination at surfaces is a never ending concern for the surface scientist.
- For the biologist, biological surfaces are rarely referred to as being contaminated. Yet, many of the surface interactions that occur with proteins, lipids, and ions might well be described using the same contamination model favored by the surface science community.
- For the surface scientist, surfaces undergo processes that are governed by surface energetics.
- The biologist, on the other hand, rarely explains reactions at surfaces in terms of surface or interfacial energy.
- The surface scientist describes a surface in terms of the geometry and chemistry of its constituents.
- The biologist will use such terminology as "molecular recognition" to explain reactions occurring at a cell surface, but will rarely think of this as a direct manifestation of chemistry and geometry.

- Finally, the surface scientist has access to a variety of tools specifically developed to study surface phenomena at many levels of resolution.
- The biologist studies surfaces either microscopically (optical, SEM, etc.) or via the macroscopic phenomena induced by the surfaces (e.g., reaction rate).

There are, of course, exceptions to these broad generalizations. But, on the whole, biologists will not invoke surface-induced effects in their hypotheses. The surface scientist, on the other hand, will consider the problems of biology as being too complex and disorderly to be dealt with using the theoretical and analytical tools available. There is a wide gap in understanding between these two disciplines, but there are signs that it is narrowing.

I believe we are at a turning point in the appreciation of the role of surfaces in biology. In 1972, I could find only two published papers describing the application of contemporary physical and chemical surface analytical tools to biological problems. In 1978, there were twelve such papers. In 1984, I found nineteen. In 1986, thirty-two papers were published that used these new techniques to study systems of biomedical interest. I believe these numbers will continue to increase as an understanding develops of the wealth of useful information that could be gathered when contemporary surface science methods are used to view biosurfaces.

On June 21-24, 1987, a symposium was held in Ann Arbor, Michigan, that brought together biologists and surface scientists, as well as chemists, physicists, materials scientists, and physicians. The symposium, sponsored by the American Chemical Society, was entitled "Surface Characterization of Biomaterials," and focused on the application of new techniques to analyze complex biological interfaces. A large number of the research groups involved with surface characterization of biomaterials were represented at this symposium, including participants from Canada, Great Britain, Japan, Sweden, and the United States.

This proceedings volume is intended to provide a written record of the important communications that took place at Ann Arbor. An informal survey of the participants indicated that they were enthusiastic about the interdisciplinary nature of the symposium and the perspectives that developed as a result. They also felt that the publication of a proceedings volume would serve to stimulate both thought and research in this evolving field.

At the present time there are no other symposium volumes specifically addressing the surface characterization of biomaterials. It is my hope that the symposium, and this volume based upon it, will act as catalysts for the much needed interaction between surface scientists and biologists and that a mutual understanding in these fields of endeavor will develop.

University of Washington
Seattle, Washington, USA

Buddy D. Ratner

ACKNOWLEDGEMENTS

Many individuals contributed in time and effort to the organizational and editorial aspects of the symposium and the volume you now hold. In particular, I would like to thank Professor Erdogan Gularli for inviting me to organize a symposium at the Ann Arbor meeting; Dorothy DeCoster, Nancy Mateo, and Thomas Menduni for exceptional editorial efforts; and the speakers and session chairs at the symposium who structured the solid foundation of this volume—namely, its important scientific content.

Buddy D. Ratner

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BIOMATERIALS FROM A SURFACE SCIENCE PERSPECTIVE

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SECTION I

1. INTRODUCTION

A central theme of biomaterials research is the interaction which takes place between the surface atoms of the biomaterial and the biomolecules of the biological system. Very little is known about the basic interactions which determine the biological response. In this paper we discuss techniques for characterizing the biomaterial surface, identify some properties and processes of the biomaterial-biointerface which are expected to be important in the biological response to biomaterials. We then discuss how surface science can contribute to biomaterials research and development. Three important contributions of immediate value are: (i) development of biomaterials via well understood model systems, (ii) surface sensitive analytical techniques for biomaterial characterization, and (iii) methods for well controlled surface preparation. Both attempts are briefly described. A comparison of surface science methods with biological system methods is expected to improve knowledge of biomaterial-biointerface interactions. The main objective for such a developer will be the lack of practical methods for studying biointerfaces at the molecular level.

2. INTRODUCTION

Any biomaterial application involves the creation of at least one interface between the material and the biological system. In an artificial joint one interface is created between bone and the prosthetic material and another interface is created between the prosthetic material and the soft tissue. In a heart valve the material surface is exposed to the blood stream. In a catheter the material surface is exposed to the body fluids. In a contact lens the material surface is exposed to the eye. In a dental prosthesis the material surface is exposed to the oral cavity. In a skin graft the material surface is exposed to the skin. In a bone graft the material surface is exposed to the bone. In a nerve graft the material surface is exposed to the nerve. In a blood vessel graft the material surface is exposed to the blood. In a heart graft the material surface is exposed to the heart. In a lung graft the material surface is exposed to the lung. In a liver graft the material surface is exposed to the liver. In a kidney graft the material surface is exposed to the kidney. In a pancreas graft the material surface is exposed to the pancreas. In a spleen graft the material surface is exposed to the spleen. In a thymus graft the material surface is exposed to the thymus. In a bone marrow graft the material surface is exposed to the bone marrow. In a skin graft the material surface is exposed to the skin. In a heart graft the material surface is exposed to the heart. In a lung graft the material surface is exposed to the lung. In a liver graft the material surface is exposed to the liver. In a kidney graft the material surface is exposed to the kidney. In a pancreas graft the material surface is exposed to the pancreas. In a spleen graft the material surface is exposed to the spleen. In a thymus graft the material surface is exposed to the thymus. In a bone marrow graft the material surface is exposed to the bone marrow.

Since the primary interfacial process is a biomaterial and its biological host occur on the molecular level and it is only by using techniques of high resolution, the surface properties on an atomic scale can be studied. Surface science techniques, therefore, are expected to be important for biomaterials research. We give a brief overview of the most important methods. In the next section we discuss surface science and surface characterization. For a more detailed treatment of some of these topics, see the book edited by R. H. Bailett, *Surface Characterization of Biomaterials*, edited by R. H. Bailett, in this volume (Chapter 1, Surface Characterization and Characterization of Biomaterials).

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BIOMATERIALS FROM A SURFACE SCIENCE PERSPECTIVE

B. Kasemo and J. Lausmaa

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SUMMARY

A central issue in biomaterials research is the interaction which takes place between the surface atoms of the biomaterial and the biomolecules of the biological system. Very little is known about the basic interactions which give rise to a particular tissue response. In this paper we first formulate some elementary questions which presently lack satisfactory answers, and identify some properties and processes of the biomaterial-tissue interface which are expected to be important for the biological response to biomaterials. We then discuss how surface science can contribute to biomaterials research and development. Three important contributions of immediate value are: (i) development of concepts via well understood model systems, (ii) surface sensitive analytical techniques for biomaterial characterization, and (iii) methods for well controlled surface preparation. Some examples are briefly described. A combination of surface science methods with biological evaluation methods is expected to rapidly advance the understanding of biomaterial-tissue interactions. The main obstacle for such a development is the lack of biological methods for interface characterization at the molecular level.

INTRODUCTION

Any biomaterial application involves the creation of at least one interface between the material and the biological system. In an artificial joint one interface is created between bone and the anchoring part of the prosthesis and another between the two articulating surfaces. In a vascular graft, interfaces are created between the biomaterial and blood, and between the biomaterial and the walls of the blood vessel. And so on. At such interfaces the molecular constituents of the biological system meet and interact with the molecular constituents of the biomaterial. The effects of this molecular interaction will eventually be observable on a macroscopic scale, e.g. in an optical microscope. Depending on the details of the interaction, the nature of the tissue, and the properties of the biomaterial, the overall response may be functional or non-functional.

Since the primary interactions between a biomaterial and its biological host occur on the molecular level and in a very narrow interface zone of width < 1 nm (ref.1), the surface properties on an atomic scale take a central position when discussing biomaterials (refs.1,2). The purpose of this paper is to identify and discuss surface properties and processes that are expected to be important for biomaterial-tissue interactions. We also shortly discuss some of the most important methods, in this context, for surface analysis and surface preparation. For a more extensive treatment of some of these issues, see e.g. refs.1-3 concerning inorganic biomaterials, and the article by B.D. Ratner in this volume concerning polymer materials and references in these articles.

FORMULATION OF QUESTIONS

Fig.1 schematically illustrates the situation at the biomaterial-tissue interface. The biomaterial surface is in contact with the extracellular fluid of the biological system. At some distance from the surface cellular components appear. The composition of the extracellular fluid, the distance between the biomaterial surface and the cells, and the exact composition of the biomaterial surface are all functions of the time that has elapsed after the first moment of contact between the biomaterial and the biosystem (ref.1), as schematically illustrated in Fig.2. Very little is known about what mechanisms that govern the biomaterial-tissue interactions. Many elementary questions which presently lack an answer may be formulated:

- (i) Which type of biomolecules are adsorbed in the first monomolecular layer on the biomaterial surface?
- (ii) What type of bonding keeps the biomolecules to the surface?
- (iii) Is the conformation of these molecules changed and if so, is the conformational change reversible or irreversible?
- (iv) Is there a continuous change, with time, of the molecules adsorbed on the surface? If the answer is yes, what is the time scale for such exchange?
- (v) How close to the surface can cells come? Is there always a layer of extracellular components that separate cells from the surface?
- (vi) How is water structured at the interface and how does it bind to the surface?
- (vii) How is information communicated between cells and biomaterial surfaces in vivo?
- (viii) How does the chemical composition of the surface influence the biological response? What is the role of surface contamination?
- (ix) How important is the microstructure of the surface at different scales of dimension?

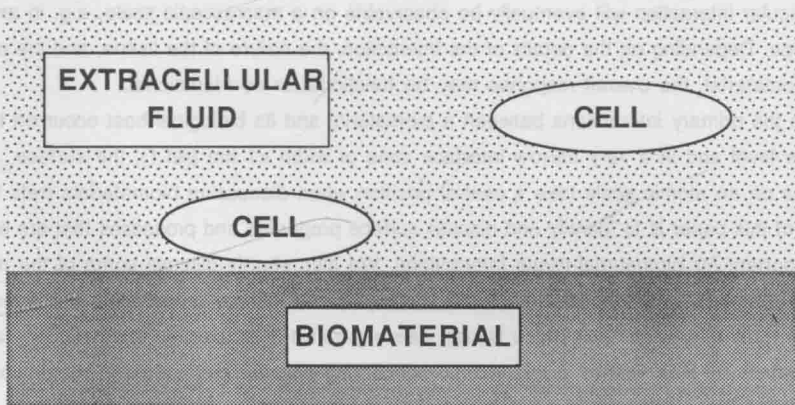


Fig.1. Schematic illustration of the biomaterial-tissue interface. The biomaterial surface is in contact with extracellular components with cells at some distance away from the surface.

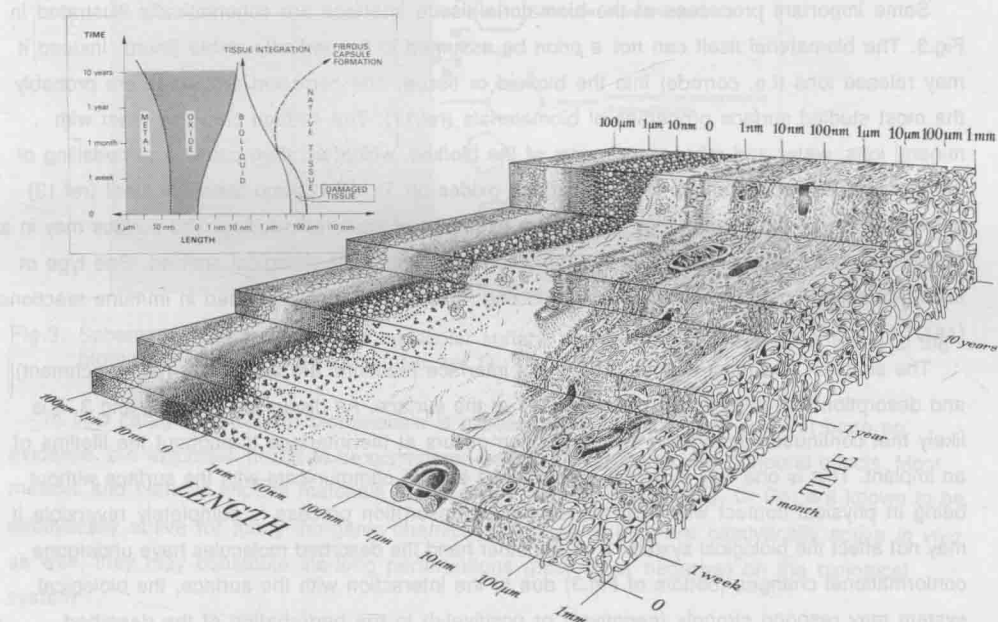


Fig.2. Schematic illustration of the development in time of the interface between a metal implant and tissue. At the moment of implantation, the implant surface is surrounded by a biological fluid containing e.g. water, ions and proteins. With time, cells and tissue approach the surface, and the oxide grows in thickness. In favourable cases a close integration between implant and tissue may result, while in unfavourable cases a capsule of fibrous tissue develops (from ref.1).

Several attempts have been made to theoretically address these questions, both from the biological viewpoint (see e.g. refs.4-7, 27) and from the biomaterial point of view (refs.1,3,8-10). This work has resulted in valuable working hypotheses, but the hard facts to answer the questions above are still lacking. To improve this situation it is necessary to perform systematic experimental studies to evaluate the various parameters that may be important and not the least to develop sensitive biological methods for such evaluation. Such systematic studies are underway in several laboratories, including our own.

In the following we focus our attention on the surface properties that may be important for the function of biomaterials, and on methods that can be used to analyze surface properties and to systematically vary them. We restrict the treatment to inorganic biomaterial surfaces. Polymer surfaces are treated in several other papers in this volume.

PROCESSES AT THE INTERFACE

Some important processes at the biomaterial-tissue interface are schematically illustrated in Fig.3. The biomaterial itself can not *a priori* be assumed to be perfectly stable (inert). Instead it may release ions (i.e. corrode) into the biofluid or tissue. The corrosion properties are probably the most studied surface properties of biomaterials (ref.11). The surface can also react with mineral ions, water and other constituents of the biofluid, which will then cause a remodelling of the surface. The observations that the surface oxides on Ti (ref.12) and stainless steel (ref.13) grow and incorporate mineral ions *in vivo*, are examples of such remodelling. The surface may in a similar way react with and remodel by interaction with organic or biological species. One type of such interaction could be reactions with oxidizing radicals which are released in immune reactions (ref.14).

The simplest and most elementary type of interface reactions are adsorption (i.e. attachment) and desorption (i.e. release) of (bio)molecules at the surface. As discussed in refs.1 and 3, it is likely that continuous adsorption and desorption occurs at the interface throughout the lifetime of an implant. This is one way by which cells may be able to communicate with the surface without being in physical contact with it. If the adsorption-desorption process is completely reversible it may not affect the biological system. If on the other hand the desorbed molecules have undergone conformational changes (bottom of Fig.3) due to the interaction with the surface, the biological system may respond strongly (negatively or positively!) to the perturbation of the desorbed species. Surface induced conformational and chemical changes of biomolecules is an important channel by which biomaterial surfaces may affect the biological response.

Another central issue is how the surface interacts with the water molecules of the biofluid and with the water shells surrounding e.g. the proteins. Several possibilities can be distinguished. The surface may keep a strongly bound layer of water which does not affect the water shell of the proteins. In this case there is always at least a double layer of water between the virgin biomaterial surface and the biomolecules. The opposite extreme is that the interaction is such that water molecules are repelled away and that no separating water molecules are left between the surface and the protein. In view of the large variety of biomaterials that exists, and the even larger variety of biomolecules, it seems plausible to assume that both extremes and all possible intermediate cases occur in real *in vivo* systems.

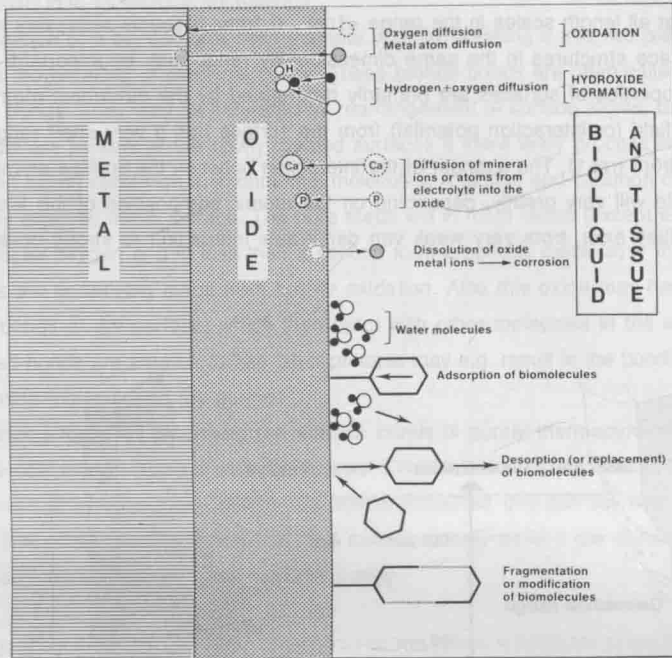


Fig.3. Schematic illustration of some molecular surface processes that are likely to occur at the biomaterial-tissue interface (from ref.1).

In vivo catalytic activity of biomaterials is a possibility for which there has yet been no evidence, but which still needs to be considered because of its potentially profound effects. Most metallic and ceramic implant materials in use today (e.g. Ti/TiO₂, Al₂O₃, Cr-Co) are known to be catalytically active for many inorganic chemical reactions. If they are catalytically active *in vivo* as well, they may constitute life-long perturbations (positive or negative) on the biological system.

With the exceptions of corrosion and conformational changes of proteins, there is a lack of experimental studies of the type of processes mentioned above. At present we can only identify possible processes, but not rank them with regard to their biological importance.

SURFACE PROPERTIES AT THE INTERFACE

It is appropriate to consider separately the structural and the chemical surface properties of biomaterials.

The microstructure of surfaces can vary on all length scales from the atomic scale up to the macroscopic scale. Fig.4. illustrates some of the structural surface features that are relevant in this context and also some of the biological elements that geometrically may match the surface structures. For example, atomic defects and surface roughness on the nanometer scale may interact with functional groups in proteins. At the macroscopic end of the length scale, surface irregular-

arities or deliberately produced structures on the 10 μm scale, may influence the behaviour of cells (for an example, see the paper by D. Brunette in this volume). The importance of surface structural features of biomaterials has not yet been established but since there exists biological structural elements at all length scales in the range $<1\text{nm} - 0.1\text{mm}$, it seems necessary to assume that biomaterial surface structures in the same dimensionality range may be important.

The chemical properties of surfaces are primarily determined by the outermost atomic layer. The chemical force field (or interaction potential) from the surface has a very short range, of the order of a few Ångström (ref.1). The strength of the interaction between the surface atoms and a particular biomolecule will vary greatly, depending on the atomic composition of the former. In principle all possibilities exist, from very weak van der Waals interaction to strong covalent and

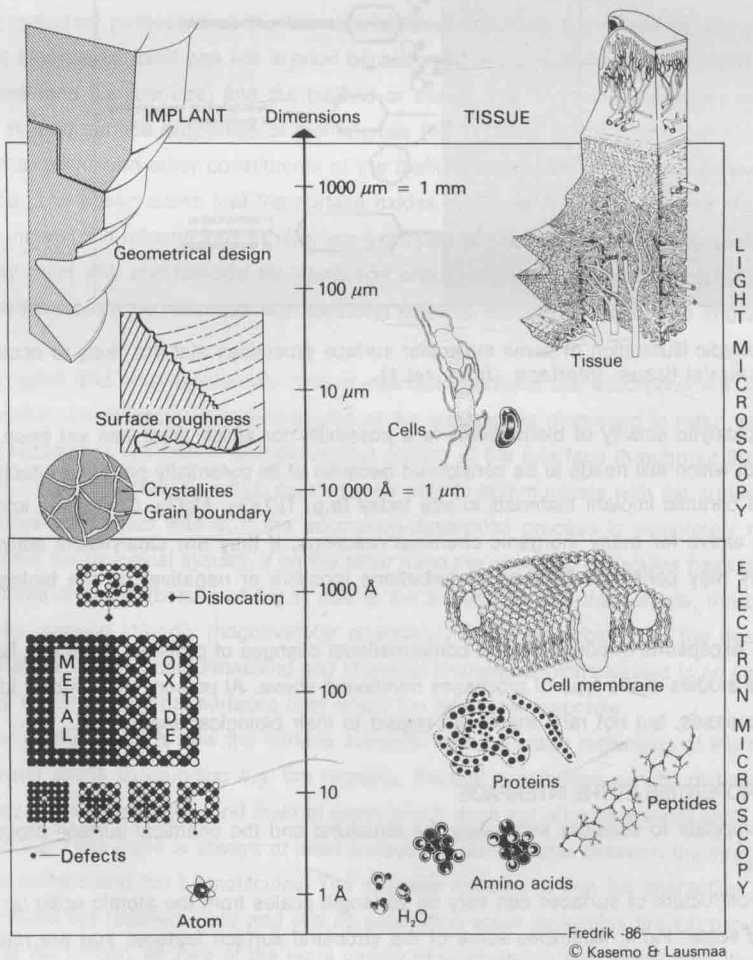


Fig.4. Schematic illustration of the approximate dimensions of some geometrical structures and elements that occur at the biomaterial and biological sides of the interface (from ref.1)