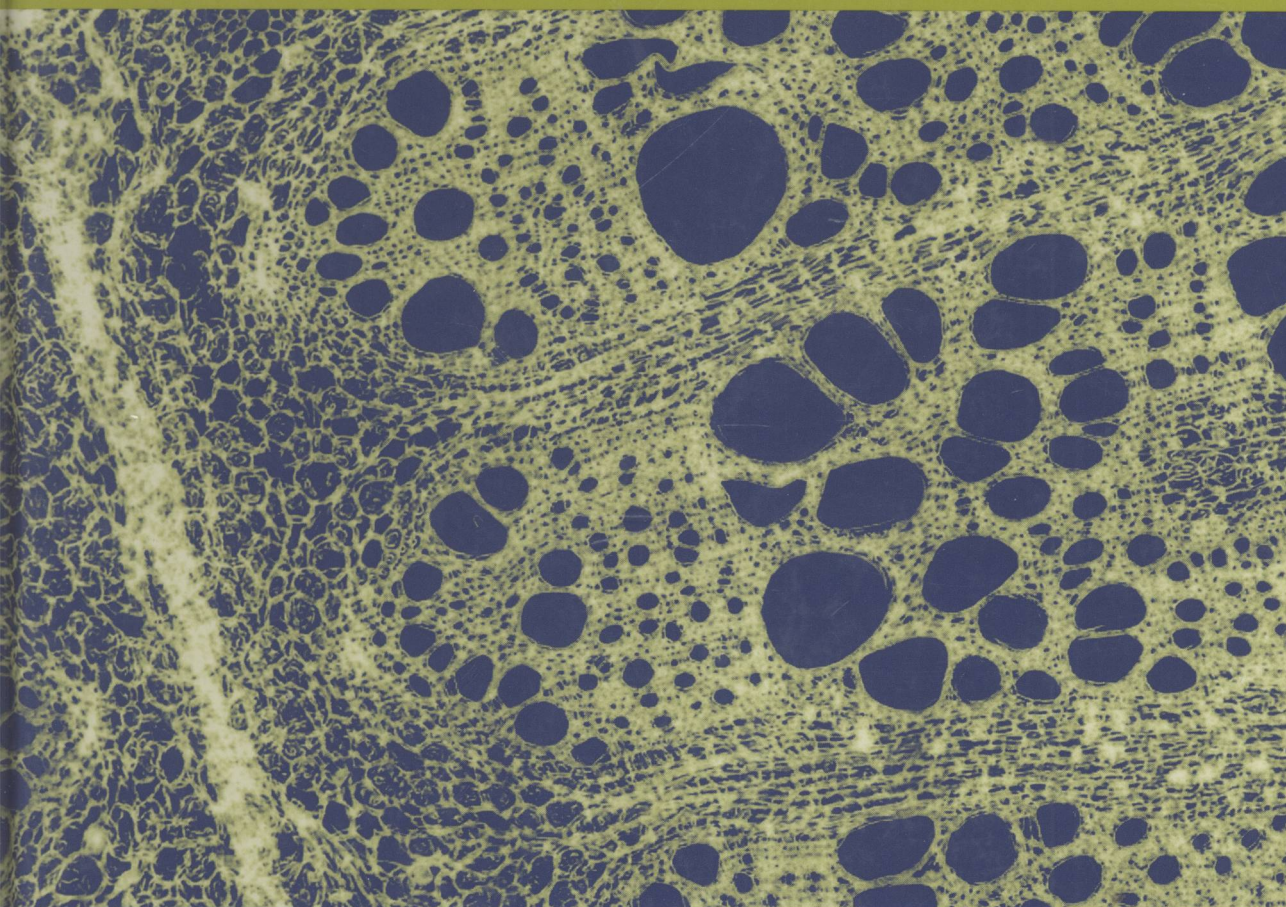




ENGINEERING IN MEDICINE & BIOLOGY

Jeremy Ramsden

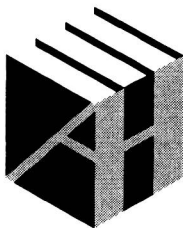


Biomedical Surfaces

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Jeremy Ramsden



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*“Es ist alles viel einfacher als man denkt, aber auch verschränkter,
als man sich vorstellen kann.”*

—JOHANN WOLFGANG VON GOETHE

Preface

The subject of biomaterials—from which biomedical surfaces are made—has grown up in a very ad hoc manner. There is no universal agreement about the definition of biomaterials. Some authors restrict the term to describing the materials from which prostheses and other medical implants are made—that is, materials with distinctively medical applications. Others includes materials for drug delivery, biosensors, protein separations and so forth—anything indeed that comes into contact with biomolecules, hence also including ex vivo applications for analysis and production. If this definition is extended to biomatter in general, then even textiles touching the skin would qualify to be called biomaterials. Yet others include the living matter itself in the definition—even biomolecules like DNA. Adding to the confusion is the fact that most biomaterials in use at present have been adapted from other, nonmedical and nonbiological purposes. For example, titanium was initially developed for rocket motors, silicone rubbers for industrial adhesives, polytetrafluoroethylene textiles for heavy-duty water repellent clothing. All these novel materials were subsequently exapted for medical use. During this exaptation a great deal has of course been learned about interfacing synthetic materials with living tissue. The time is now ripe for exploiting this knowledge in combination with the unprecedented control over the constitution of materials now being enabled by nanotechnology. Hence, for the first time, the fully rational design of biomaterials becomes a possibility. This book is conceived to usher in this new age of rational biomaterials design.¹

¹“Synthetic materials that must dwell safely, effectively, and intimately in contact with living systems to fulfil the goals of medical and dental device designs and therapies” will be used as a working definition in this book. Note also the definition in PAS 132

The surface of any component in a device destined for *in vivo* implantation or for being placed in contact with biomolecules *ex vivo* (note that some applications, such as the tubing of hemodialysers, fall between these two categories) plays a crucial role in its performance. It is through its surface that the component interacts with the biological world in which it finds itself. This book focuses on those surfaces.

One of the core premisses is that whenever an artificial material is brought into contact with living tissue or fluid containing dissolved proteins, adsorption of proteins on the surface of the material is the first significant event to occur. Deep understanding of this adsorption phenomenon is therefore essential. Therefore, after the Introduction, Chapter 1 deals with the fundamentals of the interaction of biomacromolecules with surfaces. This knowledge will be used directly in later chapters (3 and 4) dealing successively with biofluids in contact with materials and with the interaction of living cells and tissues with surfaces. Chapter 2 is also of a fundamental nature, dealing with the attributes of biomedical surfaces from a somewhat abstract viewpoint. Lubrication and wear, often leading to the release of inflammatory particles, which can become immunogenic, into the body, are discussed in Chapter 5. The processes of manufacturing biomedical devices places certain constraints on their surface finishes, and an extensive body of expertise has been built up in order to find suitable compromises between the demands of fabrication and the demands of biocompatibility; this knowledge is summarized in Chapter 6. The metrology of surfaces (Chapter 7) is particularly important for controlling their quality during manufacture (dealt with in Chapter 6), but it is also an essential research tool for advancing fundamental understanding of how surface attributes are correlated with biological responses.

Despite numerous attempts, as yet the science appears to be some considerable distance from a proper theory of these responses, and overall mastery of the field has not been helped by premature assertion of propo-

“Terminology for the Bio-Nano Interface” (London: British Standards Institute, 2007): (1) any material produced using a biological system, or any material produced *in vitro* that could be made by biological system; (2) any substance, synthetic or natural, that can be used as a system or part of a system that treats, augments, or replaces any tissue, organ, or function of the body.

sitions whose basis is in fact rather weak. Just as that most excellent of biomaterials, bone, is fashioned through the concerted action of the bone-constructing osteoblasts and the bone-destroying osteoclasts, so should we also remember that the biomaterials field also has need of constant destruction of erroneous ideas in order to become a strong edifice. The final Chapter 8 of the book is oriented towards the future and includes a discussion of promising directions for smart materials of various kinds, such as bioactive and biodegradable surfaces. Nanotechnology applied to biomaterials is a particularly important development for biomedical materials, since the possibilities for achieving unusual combinations of material attributes are greatly enhanced. This should enable a more perfect practical realization of desirable design principles than has hitherto been achievable.

It is already well appreciated that many disciplines are needed for work in biomedical surfaces. Materials science and engineering are obviously essential, but a good knowledge of biology is also required. Almost everything in biomaterials depends on the interface between the living and the nonliving—the bio/abio interface, which may simply be called the problem of biocompatibility, and which in turn fundamentally depends on the biomolecular interactions dealt with in Chapter 1. A complicating feature of biomaterials is the fact that the living matter is constantly modifying the nonliving, as well as itself, and useful insight can be gained by considering the process as being driven by an active flow of information between the living and the nonliving components. This aspect is briefly touched upon in Chapter 8.

There are, I suppose, two ways in which to write a book such as this. One is to start from the viewpoint of the engineer or materials scientist, who will be well acquainted with materials and how to modify them but may have only a rudimentary knowledge of biology, even its more chemical aspects, such as the structure and dynamics of biological macromolecules; and the other is to start from the viewpoint of the biologist, or the medical scientist, who may have a great deal of knowledge about living organisms and their molecular constituents, but whose knowledge of materials is likely to be based on a few elementary notions propagated heuristically in the literature, and not always based on solidly demonstrable principles. On the basis of the time-honored Principle of Sufficient Reason, one may suppose

that the field is divided roughly equally between these two camps, and thus it would appear to be a hopeless task to attempt to cover the ground in such a way that both sides will be equally engaged. I have set out to do so by maintaining an abstract overview as far as is possible, focusing on fundamental aspects and underlying concepts that may be unfamiliar to both sides. For detailed, specific facts the reader is invited to consult some of the encyclopedic texts available elsewhere, such as the monumental *Biomaterials Science* edited by Buddy Ratner and colleagues, or the enormous research and review literature that is too vast to be reviewed other than superficially in a book of this size. This book is therefore not a how-to manual; in contrast, it seeks to uncover the general principles that lie beneath the vast web of facts, which should thereafter be understood in more compact form. In other words, it provides a framework with which the already vast accumulation of facts can be made more intelligible. It is also hoped that fruitful lines of future research will become apparent.

To reiterate, a very important guiding principle developed in this book is that all materials are modified by protein deposition once they are inserted into a living body. Much of the science and technology of biomaterials has been developed simply for dealing with that. Another pervasive concept is that the environment of a biomaterial is very much a system, in the sense of being constituted from inseparable interacting components that must be considered in their entirety in order to be able to formulate a proper description of the body's response to the biomaterial, and the biomaterial's response to the body.

This book could well have been subtitled "The Principles of Biocompatibility," but biocompatibility itself has no unique, consensus definition in the literature. The most compact definition of biocompatible is "tolerant of life," but one very often finds vaguer definitions (of biocompatible) such as "the ability of a material to perform with an appropriate host response in a specific application" (from the *Williams Dictionary of Biomaterials*). Now, as Sommerhoff has so clearly explained, "the notion of adaptation when applied to living nature refers to the widespread and striking *appropriateness* which organic activities show in relation to the needs of the organism, and to the *effectiveness* with which organisms meet the demands made upon them by their environment." Thus adaptedness implies

appropriateness, but goes beyond it because the response must not only be appropriate for the particular set of concrete circumstances with which the practitioner is inevitably engaged in any particular instance, but also appropriate had the initial circumstances been somewhat different. Given the variability inherent in the living environment, this is an extremely important point. For example, a stent might be designed to perform very well under a particular set of environmental variables including temperature, chemical composition of the blood, and flow rate. Very often, indeed, stent performance is optimized in the laboratory under a rather narrowly defined set of conditions. Clearly, if the stent malperforms whenever one or more of these variables are changed, such as is very likely to happen during the life of a patient, the stent cannot be said to be adapted. This is a particular challenge for the designer of biomedical surfaces, and which may well exceed the challenges to engineers in other fields, in which environmental variation tends to be more constrained and predictable.

A note about referencing: under the Further Reading sections that end each chapter will be found a list of books and review articles that have either been consulted during the preparation of the chapter, or contain useful additional material for the reader. References to the primary literature are chiefly given in footnotes directly where they are relevant, and are mostly restricted to important recent research papers that are not yet discussed elsewhere or papers that can be recommended in order to fill a gap in coverage, inclusion of which the available space does not permit. In this age of highly effective Internet search engines and specialized electronic databases of the scientific literature and reference data, the reader should have no difficulty in gathering more information on most of the topics brought up in the book. The index at the end of the book should be used not only as a way to locate topics identifiable by their key words, but also as a cross-referencing tool, since in this interdisciplinary topic many chapters presuppose or will be enhanced by careful reading of material in other chapters. Note that words from the section or subsection headings that appear in the table of contents are usually not indexed.

I owe a great debt of gratitude to my colleagues at Cranfield—David Allen and David Stephenson for discussions about the manufacture of surfaces, Jeff Alcock for discussions about lubrication, and Stephen James

about far-field optical techniques—and Gert Goch and Stephan Patzelt from the Universität Bremen for having called my attention to photoacoustic microscopy as a useful method for surface characterization, and for having explained speckle to me. A collaboration with Danish Malik from Loughborough University and his circle of colleagues, including Nicholas Hoenich from the University of Newcastle, resulted in numerous discussions, which have been invariably enjoyable, and, as with the tales of Scheherazade, invariably leave one with an appetite for more. It is also a pleasure to thank my colleagues at Artech House Publishers, especially Wayne Yuhasz for unfailingly stimulating discussions, Jessica Thomas for her indefatigable reminders and ever helpful responses concerning all matters relating to production, and also the anonymous reviewers of the draft manuscript for their thoughtful and much appreciated comments, which have without doubt greatly improved it, although I must add the customary statement that any remaining deficiencies are my sole responsibility.

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