Learning from Nature
How to Design New
Implantable Biomaterials:
From Biomineralization Fundamentals to
Biomimetic Materials and Processing Routes

Edited by

R.L. Reis and S. Weiner

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Learning from Nature How to Design New Implantable Biomaterials: From Biomineralization Fundamentals to Biomimetic Materials and Processing Routes
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Learning from Nature How to Design New Implantable Biomaterials: From Biomineralization Fundamentals to Biomimetic Materials and Processing Routes

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# TABLE OF CONTENTS

**CONTRIBUTORS**........................................................................................................................................ vii

**PREFACE**................................................................................................................................................ xi

## 1. STRUCTURE AND MECHANICAL FUNCTIONS IN BIOLOGICAL MATERIALS

1.1. Structure-Mechanical Function Relations in Bones and Teeth  
*S. Weiner and P. Zaslansky*.......................................................................................................................... 3

1.2. Hierarchical Structure and Mechanical Adaptation of Biological Materials  
*P.Fratzl*....................................................................................................................................................... 15

## 2. BIOCERAMICS, BIOACTIVE MATERIALS AND SURFACE ANALYSIS

2.1. Calcium Phosphate Biomaterials: an Overview  
*H. Yuan and K. De Groot*............................................................................................................................ 37

2.2. Nanostructural Control of Implantable Xerogels for the Controlled Release of Biomolecules  
*S. Radin and P. Ducheyne*........................................................................................................................... 59

2.3 Surface Analysis of Biomaterials and Biomineralization  
*B. D. Ratner*.................................................................................................................................................. 75

## 3. BIOMIMETICS AND BIOMIMETIC COATINGS

3.1. Biomimetics and Bioceramics  
*B. Ben-Nissan*.............................................................................................................................................. 89

3.2. New Biomimetic Coating Technologies and Incorporation of Bioactive Agents and Proteins  
*P. Habibovic, F. Barrère and K. De Groot*........................................................................................................ 105
3.3. Learning From Nature How to Design Biomimetic Calcium-Phosphate Coatings  
I. B. Leonor, H. S Azevedo, I. Pashkuleva, A. L. Oliveira, C. M. Alves, R. L. Reis

3.4. Learning from Marine Creatures How to Design Micro-lenses  
J. Aizenberg and G. Hendler

4. TISSUE ENGINEERING OF MINERALIZED TISSUES

4.1. Inkjet Printing for Biomimetic and Biomedical Materials  
P. Calvert, Y. Yoshioka and G. Jabbour

4.2. Stem Cells and Bioactive Materials  
R. C. Bielby and J. M. Polak

4.3. Embryonic Stem Cells for the Engineering and Regeneration of Mineralized Tissues  
L. D. K. Buttery and J. M. Polak

4.4. Tissue Engineering of Mineralized Tissues: the Essential Elements  
A. J. Salgado, M. E. Gomes and R. L. Reis

INDEX
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PREFACE

The development of materials for any replacement or regeneration application should be based on the thorough understanding of the structure to be substituted. This is true in many fields, but particularly exigent in substitution and regeneration medicine. The demands upon the material properties largely depend on the site of application and the function it has to restore. Ideally, a replacement material should mimic the living tissue from a mechanical, chemical, biological and functional point of view. Of course this is much easier to write down than to implement in clinical practice.

Mineralized tissues such as bones, tooth and shells have attracted, in the last few years, considerable interest as natural anisotropic composite structures with adequate mechanical properties. In fact, Nature is and will continue to be the best materials scientist ever. Who better than nature can design complex structures and control the intricate phenomena (processing routes) that lead to the final shape and structure (from the macro to the nano level) of living creatures? Who can combine biological and physico-chemical mechanisms in such a way that can build ideal structure-properties relationships? Who, else than Nature, can really design smart structural components that respond in-situ to exterior stimulus, being able of adapting constantly their microstructure and correspondent properties? In the described philosophy line, mineralized tissues and biomineralization processes are ideal examples to learn-from for the materials scientist of the future.

Typically, the main characteristics of the route by which the mineralized hard tissues are formed is that the organic matrix is laid down first and the inorganic reinforcing phase grows within this organic matrix/template. Bone, tooth, lobster and crabs exoskeletons, oyster shells, coral, ivory, pearls, sea urchin spines, cuttlefish bone, are just a few of the wide variety of biomineralized materials engineered by living creatures. Many of these biological structural materials consist on inorganic minerals combined with organic polymers. The study of these structures has generated a growing awareness that the adaptation of biological processes may lead to significant advances in the controlled fabrication of novel and better-engineered smart-materials. To date, neither the elegance of the biomineral assembly mechanisms nor the rather complex composite microarchitectures could be duplicated by non-biological methods. This is true in spite of the fact that substantial progress has been made in understanding how biomineralization occurs. However, most of this knowledge is yet to be used on relevant industrial applications, namely on the design of appropriate biomimetic routes that will lead to the development of a new generation of implantable biomaterials.

Biomimetics is a new very important field of science that studies how Nature designs, processes and assembles/disassembles molecular building blocks to fabricate high performance mineral-polymer composites (e.g., mollusc shells, bone, tooth) and/or soft materials (e.g., skin, cartilage, tendons) and then applies these designs and processes to engineer new molecules and materials with unique properties. Studies can focus on: the
development of methods to reveal the mechanisms through which organic assemblies such as proteins/peptides can determine the biomineral structure of tooth and bone; the determination of tooth and bone hierarchical structure; deciphering of biological basis of biomineralization using paradigms from marine invertebrates; understanding fundamentals of dental enamel proteins self-assembly; the design of a new generation of tooth and bone structure materials based on lessons from the marine mussel and spider silk proteins; and the development of "mineral delivery vehicles" based on phospholipids self-assembly for the repair or re-mineralization of enamel, dentin as well as bone defects. For instances, bone formation is a particularly complex process, on which hydroxylapatite precipitation seems to be associated, initially, with matrix vesicles and subsequently with collagen fibres. Very small crystals are formed, parallel to one another, under the influence of the collagen fibrils structure, as a result of the composition of the inorganic salts present in the body fluids. Bone is synthesized as a complex composite and the organization and interfacial chemistry of the components are optimised for functional use by means of cell-mediated processes.

Furthermore, in the last few years it is becoming well established that the essential requirement for an artificial material to exhibit a bone-bonding behaviour is the formation, on its surface, of a calcium phosphate (Ca-P) similar to bone apatite. In fact, the presence of an apatite like layer on the surface of an orthopaedic biomaterial is considered as a positive biological response from the host tissues. So, it is expected that any material coated with such a bone-like apatite layer might show a bioactive behaviour when implanted. Several works have been trying to learn from the natural processes and to develop synthetic in-vitro methodologies, whereby a mineral phase is deposited in a particular polymer matrix or on the surface of a polymeric substrate. In all these works, a very important issue is to generate the chemical conditions at the interface that induce precipitation of mineral phase. Many works have already introduced the term biomimetic (related to the formation of a Ca-P layer on the surface of an implant material) into the biomaterials community.

We have decided to organize a NATO Advanced Study Institute on “Learning from Nature How to Design New Implantable Biomaterials: From Biomineralization Fundamentals to Biomimetic Materials and Processing Routes”, when we realized that there was a clear need for a course that would address all the above referred to topics. In fact it was our deep believe that there was a necessity for a course that addressed, in an integrated way, topics that go from understanding biomineralization processes of different mineralized tissues (that means: not only bone, tooth, etc.) to the use of that science to engineer new biomimetic processes and materials. In fact only an understanding of the relevant fundamentals and a simultaneous application oriented view will lead to the design of new biomimetic materials and processing routes (including production of biomimetic coatings). However the biomineralization and biomaterials research communities have not been working side by side in the past few years. In fact, to our knowledge, no course has addressed before this topic in such an integrated and ‘looking forward’ perspective. The only meeting on which both communities regularly meet is the Gordon research Conference on Biomineralization. However there is almost no training content on that has most of the talks are aimed at presenting new breakthroughs on biomineralization science to best scientists (most of them well established) in the field. So we thought that an ASI could be a
complementary tool as it seemed to us to be the best forum to educate and brainstorming on this area of such strategic importance. This was in our opinion achieved with success. The ASI also helped to integrate the NATO Partner countries in this moving edge technology by means of inducing joint activities and student exchanges with NATO countries Institutions.

The main aims of this Advanced Study Institute were to review, in a tutorial and comprehensive manner, the actual scientific knowledge and recent R&D achievements on biomimetic and mechanical functions in Biological Materials. To understand the fundamentals involved. To comprehend the present state of the art on the use of bioactive ceramics and glasses and other mineralized materials on bone, cartilage and tooth (and other human tissues) regeneration and replacement. To discuss what can be learned from Nature in order to develop new biomaterials. To use the understanding of biomimetic processes on the development of new biomimetic materials and processing routes. To review the present status of research and industrial activities in the development of biomimetic and mechanical functions in Biological Materials. To discuss all the most important areas related to these multidisciplinary fields, trying to help on creating new collaboration and new multidisciplinary hybrid researchers that can also be involved in technology transfer. The main aim is to give the students tools to play a key leading role, guiding research and industrial spin-offs, on the evolution of this particular area in the coming decades. In fact, biomimetics is believed to be, together with tissue engineering one of the most challenging and promising areas on biological driven materials research in the coming decades.

The present book summarizes most of the information delivered during the different lectures and mimics the scientific quality that was presented in the meeting. It is organized in four different sub-topics:

- Structure and mechanical Functions in Biological Materials
- Bioceramics, Bioactive Materials and Surface Analysis
- Biomimetics and Biomimetic Coatings
- Tissue Engineering of Mineralized Tissues

It is composed by 13 chapters by 10 different groups. The book is mainly what will remain from the NATO-ASI course that was held from the 13th to the 24th of October 2003 in Alvor, Algarve, Portugal. Its structure reflected the integrated and multidisciplinary approach needed in this particular field. The course addressed a wide range of topics, joining together the world-leaders on most of the relevant fields. The Faculty not only gave tutorial lectures, but was always very interactive with the participants trying to open their minds for the future of the field. The lecturers also tried to maximize discussion between themselves and with the participants. The course was organized in several topics and was complemented by short presentations and posters delivered by the participants. The best works presented by the participants have been invited to submit a full manuscript to be considered for publication in a special issue of Materials Science & Engineering: Part C Biomimetic and Supramolecular Systems of which I will be the Guest Editor.
Finally, I must say that, as most of you know, nobody can organize a course without the help of hard working people and support from several institutions. I would of course first of all like to thank the NATO Scientific Division for their support that made possible for me to organize another NATO-ASI course and the publication of the present book. I would like also to acknowledge the contributions of my co-director Steve Weiner that really needs no introduction in this field. He was a great support whenever I needed it. The members of the scientific committee and several of lecturers made a lot of useful suggestions. All the invited speakers that accepted our invitation and made the course and the book possible are gratefully acknowledged. The contributions of several of the speakers to this book made possible to produce a state-of-the-art volume to be used by researchers all around the world in the coming years.

But the course, and its program, was also made by the ASI students and their contributions. As said before the best contributions from the ASI students will be published in a special issue of *Materials Science & Engineering: Part C Biomimetic and Supramolecular Systems*. All the supporting institutions, namely the Foundation for Science and Technology of Portugal (FCT), are grateful acknowledged. University of Minho and the Department of Polymer Engineering that have supported me, and my students, in so many ways also deserve a word of appreciation. But I am especially grateful to all of my Post-doc fellows, PhD Students and staff colleagues, not forgetting my personal executive assistant, that work daily on the 3B’s Research Group – Biomaterials, Biodegradables and Biomimetics (www.dep.uminho.pt/3bs) that I have the pleasure of directing. We are now more than 40 people of which only 5 are staff members, all the others are young, bright and ambitious students. The outcome of the ASI was mainly the result of their hard work, devotion, commitment, and of their own ambitions and aspirations. They have put a great number of hours on the enterprise or organizing the course and realized that this was an important organization for all of us. Several of them also supported me on preparing this book. I cannot refer all the names herein, but if you find one of the members of the 3B’s Research Group – Biomaterials, Biodegradables and Biomimetics (that I have the pleasure of directing) in one of the meetings you attend, please just speak with her/him and you will see how fortunate I am for being able to advise such a wonderful group of young and bright researchers!

Please enjoy the science and the lessons contained in this book. We really hope the book will be a useful research and education tool and that it can give the readers the same degree of satisfaction we could experience when preparing it for publication.

Rui L. Reis
(Director of the NATO-ASI Course)