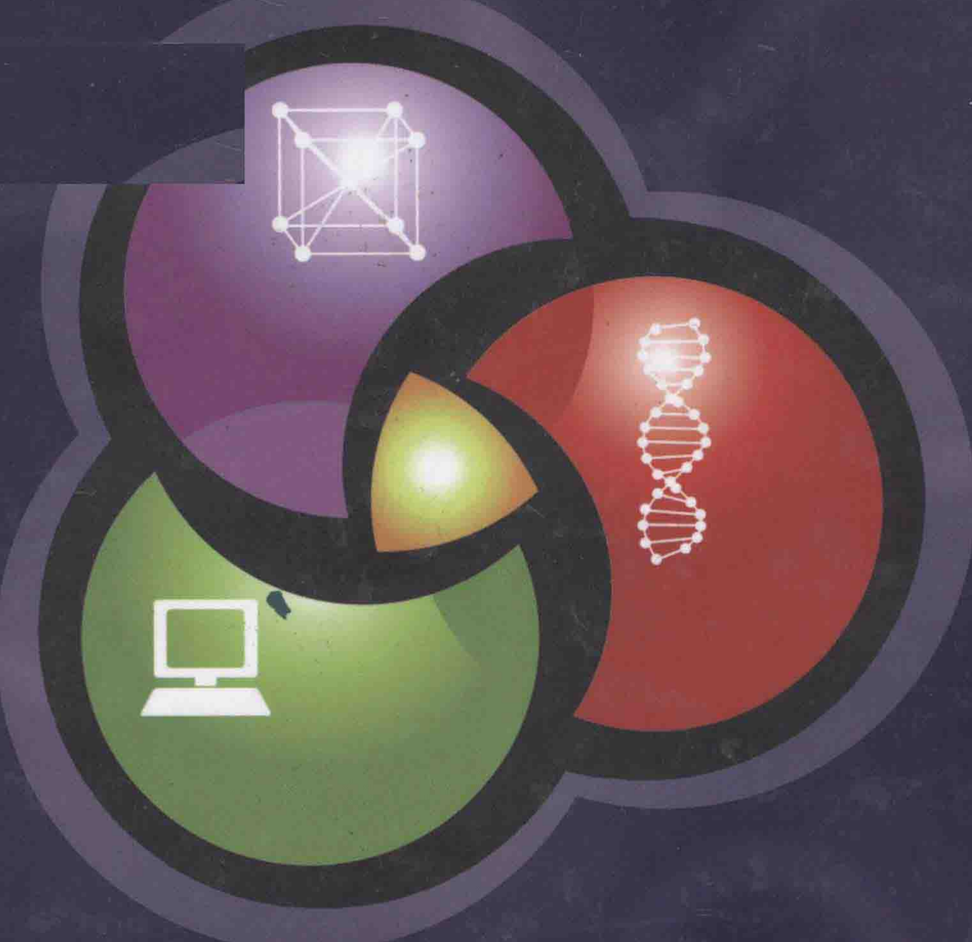

Materiomics

High-Throughput Screening of Biomaterial Properties

Edited by **Jan de Boer**
and **Clemens A. van Blitterswijk**

CAMBRIDGE

Materiomics

High-Throughput Screening of Biomaterial Properties

JAN DE BOER
University of Twente

CLEMENS A. VAN BLITTERSWIJK
University of Twente

CAMBRIDGE
UNIVERSITY PRESS

CAMBRIDGE UNIVERSITY PRESS
Cambridge, New York, Melbourne, Madrid, Cape Town,
Singapore, São Paulo, Delhi, Mexico City

Cambridge University Press
The Edinburgh Building, Cambridge CB2 8RU, UK

Published in the United States of America by Cambridge University Press, New York

www.cambridge.org
Information on this title: www.cambridge.org/9781107016774

First published 2013

Printed and bound in the United Kingdom by the MPG Books Group

A catalogue record for this publication is available from the British Library

Library of Congress Cataloguing in Publication data
Materiomics : high-throughput screening of biomaterial properties / [edited by] Jan de Boer,
Clemens van Blitterswijk.
p. ; cm.
Includes bibliographical references.
ISBN 978-1-107-01677-4 (hardback)
I. Boer, Jan de, 1970– II. Blitterswijk, Clemens A. van.
[DNLM: 1. Biocompatible Materials – chemistry. 2. Biocompatible Materials – analysis. 3. Materials Testing. 4. Regenerative Medicine – methods. 5. Tissue Engineering – methods. QT 37]
610.28′4–dc23

2012038878

ISBN 978-1-107-01677-4 Hardback

Materiomics

This complete, yet concise, guide introduces you to the rapidly developing field of high-throughput screening of biomaterials: materiomics. Bringing together the key concepts and methodologies used to determine biomaterial properties, it will allow you to understand the adaptation and application of materiomics in areas such as rapid prototyping, lithography and combinatorial chemistry. Each chapter is written by internationally renowned experts, and includes tutorial paragraphs on topics such as biomaterial-banking, imaging, assay development, translational aspects and informatics. Case studies of state-of-the-art experiments provide illustrative examples, while lists of key publications allow you to read up easily on the most relevant background material. Whether you are a professional scientist in industry, a student or a researcher, this book is not to be missed if you are interested in the latest developments in biomaterials research.

Jan de Boer is a Professor of Applied Cell Biology at the University of Twente, the Netherlands, at the MIRA Institute for Biomedical Technology and Technical Medicine, where his team performs innovative research on molecular and cellular engineering of bone tissue. He is chair of the Netherlands Society of Biomaterials and Tissue Engineering, and co-founder of the biotech company Materiomics B.V.

Clemens A. van Blitterswijk is Professor of Tissue Regeneration at the University of Twente, and chair of the Department of Tissue Regeneration at MIRA. Clemens has published over 300 papers and is co-inventor on over 100 patents. He is one of only two individuals to have received both the Jean Leray Award and the George Winter Award, the two prestigious prizes of the European Society for Biomaterials. He was recently appointed as a fellow of the Royal Netherlands Academy of Sciences and is a fellow of the Netherlands Academy of Technology and Innovation.

Contributors

Beckham, Haskell
Georgia Institute of Technology, School of Materials Science and Engineering, Atlanta, USA

Beijersbergen, Roderick
The Netherlands Cancer Institute, Division Molecular Carcinogenesis, Amsterdam, The Netherlands

van Blitterswijk, Clemens A.
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

de Boer, Jan
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Bosman, Mirjam
Department of Biomaterials Science and Technology, University of Twente, Enschede, The Netherlands

Bradley, Mark
School of Chemistry, University of Edinburgh, Edinburgh, UK

Buehler, Markus
Department of Civil and Environmental Engineering, MIT, Cambridge, USA

Cranford, Steven
Department of Civil and Environmental Engineering, MIT, Cambridge, USA

Dankers, Patricia
Institute for Complex Molecular Systems and Laboratory of Chemical Biology, Eindhoven University of Technology, Eindhoven, The Netherlands

Danoux, Charlène
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Dechering, Koen
TropIQ Health Sciences, Nijmegen, The Netherlands

Félix Lanao, Rosa
Department of Biomaterials, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Fernandes, Hugo
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Ferreira, Lino
CNC – Centre for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal; Biocant – Centre of Innovation and Biotechnology, Cantanhede, Portugal

Gauvin, Robert
Harvard–MIT Division of Health Sciences and Techology, Boston, MA, USA; Quebec Centre for Functional Materials, Université Laval, Québec City, QC, Canada

Geris, Liesbet
Biomechanics Research Unit, University of Liège, Belgium Prometheus, KU Leuven R&D division for skeletal tissue engineering, KU Leuven, Belgium

Gobaa, Samy
Laboratory of Stem Cell Bioengineering and Institute of Bioengineering, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Gomez, Ismael
Georgia Institute of Technology, School of Chemical and Biomolecular Engineering, Atlanta, USA

Grijpma, Dirk
Department of Biomaterials Science and Technology, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands; Department of Biomedical Engineering, University Medical Centre Groningen, Groningen, The Netherlands

Groen, Nathalie
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Guillemot, Fabien
INSERM, University of Bordeaux, Bordeaux, France

Habibovic, Pamela
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Han, Sangil
Georgia Institute of Technology, School of Chemical and Biomolecular Engineering, Atlanta, USA

Higuera, Gustavo
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Hulshof, Frits
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Hulsman, Marc
Delft Bioinformatics Lab, Delft University of Technology, Delft, The Netherlands

Hunt, John
Clinical Engineering (UK CTE), UKBioTEC, Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK

Khademhosseini, Ali
Harvard–MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, USA

Leeuwenburgh, Sander
Department of Biomaterials, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

Leisen, Johannes
Georgia Institute of Technology, School of Chemistry and Biochemistry, Atlanta, USA

Liu, Er
Department of Biomedical Engineering, La Jolla Bioengineering Institute, San Diego, USA

Lutolf, Matthias
Laboratory of Stem Cell Bioengineering and Institute of Bioengineering, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Mahmood, Tahir
Life Sciences Practice – Commercial Healthcare Group, Booz Allen Hamilton, San Francisco, USA

Maniura-Weber, Katharina
Empa – Swiss Federal Laboratories for Materials Science and Technology, Laboratories for Materials–Biology Interactions, St Gallen, Switzerland

Meredith, Carson
Georgia Institute of Technology, School of Chemical and Biomolecular Engineering, Atlanta, USA

Moghe, Prabhas
Department of Biomedical Engineering, Rutgers University, Piscataway, New Jersey, USA; Department of Chemical & Biochemical Engineering, Rutgers University, Piscataway, New Jersey, USA

Mollet, Björne
Institute for Complex Molecular Systems and Laboratory of Chemical Biology, Eindhoven University of Technology, Eindhoven, The Netherlands

Moroni, Lorenzo
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Negro, Andrea
Laboratory of Stem Cell Bioengineering and Institute of Bioengineering, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Oreffo, Richard
Bone and Joint Research Group, Centre for Human Development, Stem Cells and Regeneration, Human Development and Health, Institute of Developmental Sciences University of Southampton, Southampton, UK

Pape, Bram
Institute for Complex Molecular Systems and Laboratory of Chemical Biology, Eindhoven University of Technology, Eindhoven, The Netherlands

Pernagallo, Salvatore
School of Chemistry, University of Edinburgh, Edinburgh, UK

Reinders, Marcel
Delft Bioinformatics Lab, Delft University of Technology, Delft, The Netherlands

Smith, James
Bone & Joint Research Group, Centre for Human Development, Stem Cells and Regeneration, Human Development and Health, Institute of Developmental Sciences University of Southampton, Southampton, UK

Tare, Rahul
Bone & Joint Research Group, Centre for Human Development, Stem Cells and Regeneration, Human Development and Health, Institute of Developmental Sciences University of Southampton, Southampton, UK

Truckenmüller, Roman
Department of Tissue Regeneration, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

Unadkat, Hemant
Mechanobiology Institute, National University of Singapore, Singapore

Zant, Erwin
Department of Biomaterials Science and Technology, University of Twente, Enschede, The Netherlands

Zhang, Rong
School of Chemistry, University of Edinburgh, Edinburgh, UK

Preface

It's that sense of unease when you step out of the airport terminal building and onto the streets of Kathmandu. Or the moment when you open the door to your new office to see unfamiliar faces waiting for you. Step out of your comfort zone and discover how exciting, thrilling and liberating it can be: a new world is waiting for you. This book is about stepping out of the comfort zone of your own scientific discipline and about exposing yourself to something new. Embrace all the scientific disciplines that build modern-day biomaterials research, in the cultural hotpot of materiomics. Don't let the jargon and three-letter abbreviations of cell biology hold you back, nor the abracadabra of statistical models, nor the Latin terms for body parts and diseases. Learn a new language and a whole new culture is waiting for you.

The compilation of this book was initiated after an exciting conference termed 'High throughput screening of biomaterials: shaping a new research area', held beside the Amsterdam canals in April 2011. The meeting was attended by 50 selected scientists from all over the globe and across all the disciplines of biomaterials research, and the format of the conference took away that sense of unease. Chemists talked to clinicians, biologists listened to information scientists, engineers brainstormed with policy makers. We decided to bring this open and inviting atmosphere to the public through this book. Therefore, each chapter contains a tutorial on the topic for non-experts, gives an overview of the current status of that field and discusses how this technology will further shape the future of materiomics. The result of this exciting journey is presented here and was made possible only with the help of all the authors and those who contributed to the organization of the conference (Anouk Mentink), the editing of the book (Ruben Burer) or the chapters (Kristen Johnson). We hope that this book will be a scientific passport which lets you travel across the border of your discipline and helps you to learn to appreciate that of others. You won't be disappointed. Enjoy your journey!

Jan de Boer

'The adventurous spirit of this book, and indeed the field of materiomics, is excellently prefaced by Jan de Boer in this thorough compilation of concise chapters produced by an international cast of experts. It succeeds in its aim to be of use to both the student and the experienced practitioner in the multi-faceted emerging discipline of materiomics, containing both useful information and thought-provoking discussion and future perspectives. I would recommend it both to those interested in and to those already immersed in this rapidly evolving field.'

Morgan Alexander, The University of Nottingham

'By dissecting the contribution of various disciplines of diverse nature, ranging from chemistry to informatics or from advanced imaging to rapid prototyping, the book organically defines Materiomics as a field of its own. The reader is ultimately left with the awareness that the field of Materiomics will play a central role in future approaches to design complex material systems with predictable properties, for biomedical or industrial applications.'

Ivan Martin, University Hospital Basel

Contents

1 Introducing materiomics

Nathalie Groen, Steven W. Cranford, Jan de Boer,
Markus J. Buehler and Clemens A. Van Blitterswijk

1.1 Introduction to materiomics

The ability to regenerate and repair tissues and organs – using science and engineering to supplement biology – continuously intrigues and inspires those hoping that the frailty of our bodies can be ultimately avoided. From ancient times, a surprising range of unnatural materials have been used to (partially) substitute human tissues for medicinal purposes. For example, in the era of the Incas (*c.* 1500), moulded materials such as gold and silver were used for the 'surgical' repair of cranial defects. In addition, archaeological findings reveal a wide range of materials, such as bronze, wood and leather, being used to replace and repair parts of the human body. Continuous refinement led to the first evidence of materials successfully implanted *inside* the body, reportedly used to repair a bone defect in the seventeenth century (see Further Reading).

Even earlier than this, the relationships between anatomy (i.e. structure) and function of living systems had been explored by Leonardo da Vinci and Galileo Galilei, who were among the first few to apply fundamental science to biological systems. In the current age of technology, new materials for biomedical and clinical application have undergone a modern Renaissance, resulting in a surge in design and successful application (1–5). The concepts of tissue repair and substitution are constantly improving and becoming more accessible, as proven for example by the widespread occurrence (and popular approval) of total hip and knee replacements. But rather than replacement with synthetic analogues, can biological tissue(s) be directly engineered?

The first biomaterials arose to solve specific clinical problems, and it was only later that this became a field of research in itself. Polymers and ceramics (and other effective biomaterials) were not developed for implants *per se*, but rather were used because of their availability and proven (known) material properties. This need not be the case. The field of biomaterials has witnessed exciting and accelerating progression, partly owing to the emergence of physical-science-based approaches in the biological sciences. Consequently, developments have led to a number of blockbuster materials which currently play a substantial part in modern healthcare, with various clinical applications ranging from degradable intraocular lenses and sutures to coronary stents, heart valves and orthopaedic implants. But ultimately, where does this field lead?

Materiomics: High-Throughput Screening of Biomaterial Properties, ed. Jan de Boer and Clemens van Blitterswijk. Published by Cambridge University Press.

1.2 The challenge of 'living' materials science

Hitherto, the field of biomaterials has largely been characterized by trial-and-error experimentation, practical intuition and low-throughput research (6). As a result, identification and development of successful biomaterial candidates has frequently been iterative, employing *ad hoc*, piece-wise or one-off approaches to design and characterize materials for a specific application (7). Currently lacking is a single set of 'design parameters' that can satisfy more than the most rudimentary system – there is neither a standard 'code' for biological systems nor a standard 'toolset' for analysis.

Despite continuous advances both in the understanding of the natural function of biological materials and systems and in the synthesis and regeneration of certain tissues (such as bone), a cohesive and systematic approach is still wanting. What is the primary impediment? Biological tissues, organs and materials exploit multiple structures and functions across scales – they are universally hierarchical (8, 9). Such multiscale *hierarchies* consequently make any single-scale analysis and prediction a hypothesis at best. While studies have successfully characterized components at specific scales (e.g. the molecular structure of DNA or the sequence of a multitude of proteins), superposition of the structure or the functional properties of individual components (defined differently according to scale) is insufficient to understand the complete system (10). In simpler terms, '$1 + 1 \neq 2$'. We utterly fail in the 'design' and 'construction' of such material systems – we cannot accurately or reliably predict behaviour of the final product. Indeed, whether through a lack of critical system variables or understanding of system response, we are unable to model larger (living) multiprotein systems and networks, let alone the structural role that such materials play in a cellular tissue. This is the exact opposite of the definition of engineering, where it is necessary to prescribe the performance of system components with reliable and repeatable accuracy.

Conversely, understanding the interaction of materials with biological ('living') tissues across all scales – from atoms and molecules to tissues and eventually at the organism level – remains a crucial hurdle in tissue engineering and biomaterial development. The challenge is intrinsically double-sided, yet highly intertwined. The scientific complexity at both sides of the interface – the material on the one hand and the organism on the other – needs to be considered (Figure 1.1). The fundamental problem of combining living (biological) and non-living (synthetic) components can be encapsulated by the popular adage, 'The whole is greater than the sum of its parts' (commonly attributed to Aristotle, who probably was not referring to the interface of biology and materials). The complex interactions between materials and biological systems require a certain flair to analyse deterministic (or predictive) behaviours and material properties. Nature, through meticulous trial and error over centuries of optimization and refinement, has intricately combined material structure, properties and functionality (9). Structure and function are so intimately linked that one-to-one substitution of other potential materials is currently not possible – but need this be the case?