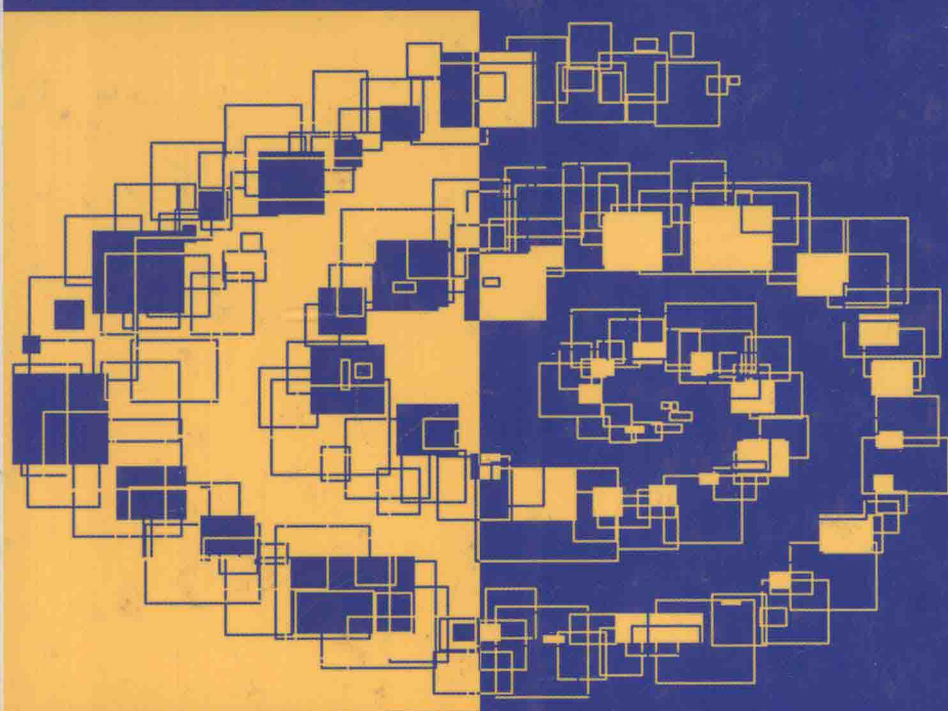
Reflexive Polymers and Hydrogels

Understanding and Designing Fast Responsive Polymeric Systems



Edited by

Nobuhiko Yui, Randall J. Mrsny, and Kinam Park

CRC PRESS

Reflexive Polymers and Hydrogels

Understanding and Designing Fast Responsive Polymeric Systems

江苏工业学院图书馆
藏书章

Edited by
Nobuhiko Yui, Randall J. Mrsny, and Kinam Park

CRC PRESS

Boca Raton London New York Washington, D.C.

Cover image: ***Canon #8*** **by Jennifer C. Hsieh. This work represents changes in a reflexive system over time as it cycles repetitively with an underlying chaotic nature.**

Library of Congress Cataloging-in-Publication Data

Reflexive polymers and hydrogels : understanding and designing fast responsive polymeric systems / edited by Nobuhiko Yui, Randall Mrsny, and Kinam Park.

p. cm.

Includes bibliographical references and index.

ISBN 0-8493-1487-9 (alk. paper)

1. Polymers. I. Yui, Nobuhiko. II. Mrsny, Randall J., 1955- III. Park, Kinam.

TA455.P58.R43 2004

620.1′92—dc22 2003065368

This book contains information obtained from authentic and highly regarded sources. Reprinted material is quoted with permission, and sources are indicated. A wide variety of references are listed. Reasonable efforts have been made to publish reliable data and information, but the author and the publisher cannot assume responsibility for the validity of all materials or for the consequences of their use.

Neither this book nor any part may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, microfilming, and recording, or by any information storage or retrieval system, without prior permission in writing from the publisher.

All rights reserved. Authorization to photocopy items for internal or personal use, or the personal or internal use of specific clients, may be granted by CRC Press LLC, provided that $1.50 per page photocopied is paid directly to Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923 USA. The fee code for users of the Transactional Reporting Service is ISBN 0-8493-1487-9/04/$0.00+$1.50. The fee is subject to change without notice. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

The consent of CRC Press LLC does not extend to copying for general distribution, for promotion, for creating new works, or for resale. Specific permission must be obtained in writing from CRC Press LLC for such copying.

Direct all inquiries to CRC Press LLC, 2000 N.W. Corporate Blvd., Boca Raton, Florida 33431.

Trademark Notice: Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation, without intent to infringe.

Visit the CRC Press Web site at www.crcpress.com

© 2004 by CRC Press LLC

No claim to original U.S. Government works

International Standard Book Number 0-8493-1487-9
Library of Congress Card Number 2003065368
Printed in the United States of America 1 2 3 4 5 6 7 8 9 0
Printed on acid-free paper

Preface

Smart materials designed to alter their properties in response to specific stimuli have been important parts of recent advances in the field of material sciences. These materials, typically polymers, can be based upon novel synthetic structures or may use materials obtained from natural sources. Various smart materials have been developed that can respond to even minute environmental changes. While the responsive properties of smart materials are thermodynamic in nature, their spectrum of applications expands dramatically once the component of kinetic control can be incorporated into their response profiles.

Despite significant advances in smart materials and the obvious importance of the kinetic aspects of their responses, only a limited number of studies have addressed the potentially powerful combination of thermodynamic and kinetic regulation of a smart material. This book brings together a collection of works and discussions that consider both thermodynamic and kinetic properties of smart materials. *Instant response* is written in Chinese characters as "瞬發" (pronounced "shun-patsu" in Japanese, "shun-fa" in Chinese, and "soon-bal" in Korean), but English has no equivalent term. For lack of a suitable term to describe materials whose properties can be modified in a rapid, repetitive, and responsive fashion, we have coined the term *reflexive systems*.

The chapters of this book have been organized to examine components of reflexive systems found in nature, to consider the theoretical limitations of reflexive systems, to characterize the current status of artificially prepared materials that may produce both thermodynamic and kinetic response events, and to explore potential future applications of such systems. Chapters in the first section of the book focus on systems found in nature (both in plants and animals) with an emphasis on molecular mechanisms. The second section investigates model systems in which selected interactions of specific reflexive system components are evaluated to determine theoretical limits of response rates and cycle times. The third section recapitulates and focuses on the functions observed in natural systems using synthetic polymers and conditions. Examples of available synthetic systems known to have fast responsive properties or that may benefit greatly by having fast responsive properties are discussed.

We, the editors, are most appreciative of the superb, insightful contributions made by the chapter authors of this book. We would also like to acknowledge the endless support of the staff members at CRC Press, in particular Alice Mulhern and Christine Andreasen for their careful editing of the chapters. It is our hope that this book will serve as a springboard for thought and experimentation toward the identification of novel reflexive systems that more closely emulate natural reflexive systems. We feel that it is only a matter of time for the development of truly biomimetic materials and that progress in the area of reflexive systems will facilitate that goal.

Nobuhiko Yui
Randall J. Mrsny
Kinam Park

Editors

Nobuhiko Yui, Ph.D., is a professor in the School of Materials Science, Japan Advanced Institute of Science and Technology, Ishikawa. Dr. Yui earned his Ph.D. in polymer chemistry from Sophia University, Japan, in 1985. He then joined the Institute of Biomedical Engineering of Tokyo Women's Medical College as an assistant research professor. While at Tokyo Women's Medical College, he spent a year as a doctoral research fellow at the University of Twente, the Netherlands. In 1993, Dr. Yui became an associate professor at the Japan Advanced Institute of Science and Technology; he became a full professor in 1998.

Dr. Yui is a member of the Controlled Release Society (CRS), the American Chemical Society, the New York Academy of Sciences, the Japanese Chemical Society, the Japan Society of Polymer Science, the Japan Society of DDS (Drug Delivery Systems), the Japanese Society for Biomaterials, the Japanese Society for Artificial Organs, and the Japanese Society for Tissue Engineering. He serves as a board member of the Japanese Society for Artificial Organs, the Japan Society of DDS, and the Japanese Society for Tissue Engineering. He is on the Board of Directors of the Japanese Society for Biomaterials, the Board of Scientific Advisors of the CRS, and the Editorial Board of the *Journal of Biomaterials Science, Polymer Edition*.

Dr. Yui served as the general secretary for the first, second, and third Asian International Symposia on Biomaterials and Drug Delivery Systems, which succeeded in strengthening Asian research interests in biomaterials and drug delivery systems (1996–2002). He helped organize the sixth World Biomaterials Congress Workshop entitled "Supramolecular Approach to Biological Functions" in 2000. He edited a book entitled *Supramolecular Design for Biological Applications* for CRC Press in 2002. He received the Award for Outstanding Research from the U.S. Society for Biomaterials in 1985, the 49th Worthy Invention Award from the Science and Technology Agency of Japan in 1990, the Young Investigator Award from the Japanese Society for Biomaterials in 1993, the CRS–Cygnus Recognition Award for Excellence in Guiding Student Research from the CRS in 1997, and the Best Paper Award from the Japanese Society of Artificial Organs in 1997.

Dr. Yui is the author of more than 210 scientific papers. His current major research interests include the molecular designs of biodegradable and/or smart polymers with unique supramolecular structures.

Randall J. Mrsny, Ph.D., is a professor of biology and drug delivery at the Welsh School of Pharmacy in Cardiff, Wales. He earned a B.S. in biochemistry and biophysics from the University of California at Davis (UCD) in 1977. In 1981, he obtained a Ph.D. in cell biology and human anatomy based on studies performed at the UCD School of Medicine. From 1982 through 1987 he was a National Institutes of Health postdoctoral fellow at the Institute of Molecular Biology at the University

此为试读，需要完整PDF请访问：www.ertongbook.com

of Oregon. After postdoctoral training, Dr. Mrsny joined ALZA Corporation where he headed the Peptide Biology Group until 1990. From 1990 through 2001, he headed the drug delivery/biology group at Genentech, Inc. He assumed his current faculty position in 2002 and simultaneously founded a drug delivery company known as Trinity BioSystems, Inc. in California where he holds the position of Chief Scientific Officer.

Dr. Mrsny has held a variety of editorial positions and is currently on the editorial boards of several journals. He has published widely in a variety of areas related to drug delivery. His current research focuses primarily on cellular and molecular events associated with epithelial cell functions in health and disease.

Kinam Park, Ph.D., is a professor in the Department of Biomedical Engineering and Pharmaceutics of Purdue University. He earned a Ph.D. in pharmaceutics from the University of Wisconsin in 1983. After postdoctoral training in the Department of Chemical Engineering at the same university, he joined the faculty at Purdue University in 1986 and was promoted to full professor in 1994. Since 1998, he has held a joint appointment in the Department of Biomedical Engineering.

Dr. Park is currently an associate editor and the book review editor of *Pharmaceutical Research*, and he serves on the editorial boards of various journals. He is the founder of Akina, a company specializing in controlled drug delivery formulations. His current research includes development of novel fast melting tablet formulations, application of the solvent exchange method for microencapsulation, synthesis of hydrotropic polymeric micelles, application of layer-by-layer coating methods for making drug-eluting stents, and elastic superporous hydrogels.

Contributors

Namjin Baek, Ph.D.
Akina, Inc.
West Lafayette, Indiana

Yong Woo Cho, Ph.D.
Akina, Inc.
West Lafayette, Indiana

Mitsuhiro Ebara, Ph.D.
Department of Applied Chemistry
Waseda University
Tokyo, Japan

Hiroshi Frusawa, Ph.D.
Department of Environmental Systems Engineering
Kochi University of Technology
Kochi, Japan

Rupali Gangopadhyay, Ph.D.
Chemical Sciences Division
Saha Institute of Nuclear Physics
Kolkata, India

Stevin H. Gehrke, Ph.D.
Departments of Chemical and Petroleum Engineering and Pharmaceutical Chemistry
The University of Kansas
Lawrence, Kansas

Richard A. Gemeinhart, Ph.D.
Departments of Biopharmaceutical Sciences and Bioengineering
University of Illinois
Chicago, Illinois

Jian Ping Gong, Ph.D.
Graduate School of Science
Hokkaido University
Sapporo, Japan

Chunqiang Guo, M.S.
Department of Biopharmaceutical Sciences
University of Illinois
Chicago, Illinois

Wim E. Hennink, Ph.D.
Department of Pharmaceutics
Utrecht Institute for Pharmaceutical Sciences
Utrecht, the Netherlands

Michio Homma, Ph.D.
Graduate School of Science
Nagoya University
Nagoya, Japan

Kunihiro Ichimuta, Ph.D.
Research Institute for Polymers and Textiles
Science University of Tokyo
Tokyo, Japan

Shin'ichi Ishiwata, Ph.D.
Department of Physics
School of Science and Engineering
Waseda University
Tokyo, Japan

Kohzo Ito, Ph.D.
Graduate School of Frontier Sciences
University of Tokyo
Chiba, Japan

Eduardo Jule, Ph.D.
Graduate School of Engineering
University of Tokyo
Tokyo, Japan

Nobuyuki Kansawa, Ph.D.
Faculty of Science and Technology
Sophia University
Tokyo, Japan

Kazunori Kataoka, Ph.D.
Graduate School of Engineering
University of Tokyo
Tokyo, Japan

Norihiro Kato, Ph.D.
Faculty of Engineering
Utsunomiya University
Utsunomiya, Japan

Akihiko Kikuchi, Ph.D.
Institute of Advanced Biomedical Engineering and Science
Tokyo Women's Medical University
Tokyo, Japan

Jong-Duk Kim, Ph.D.
Department of Chemical and Biomolecular Engineering
Korean Advanced Institute of Science and Technology
Daejeon, South Korea

Seiji Kurihara, Ph.D.
Faculty of Engineering
Kumamoto University
Kumamoto, Japan

Randall J. Mrsny, Ph.D.
Welsh School of Pharmacy
Cardiff University
Cardiff, Wales

Teruo Okano, Ph.D.
Institute of Advanced Biomedical Engineering and Science
Tokyo Women's Medical University
Tokyo, Japan

Tooru Ooya, Ph.D.
School of Materials Science
Japan Advanced Institute of Science and Technology
Ishikawa, Japan

Yoshihito Osada, Ph.D.
Graduate School of Science
Hokkaido University
Sapporo, Japan

Kinam Park, Ph.D.
Departments of Pharmaceutics and Biomedical Engineering
Purdue University
West Lafayette, Indiana

Nicholas A. Peppas, Ph.D.
Departments of Chemical, Biomedical Engineering and Pharmaceutics
University of Texas
Austin, Texas

Kiyotaka Sakai, Ph.D.
Department of Applied Chemistry
Waseda University
Tokyo, Japan

Teruo Shimmen, Ph.D.
Graduate School of Science
Himeji Institute of Technology
Hyogo, Japan

Madoka Suzuki, M.Sc.
Department of Physics
School of Science and Engineering
Waseda University
Tokyo, Japan

Takahide Tsuchiya, Ph.D.
Faculty of Science and Technology
Sophia University
Tokyo, Japan

Cornelus F. van Nostrum, Ph.D.
Department of Pharmaceutics
Utrecht Institute for Pharmaceutical Sciences
Utrecht, the Netherlands

Jan Hein van Steenis, Ph.D.
Department of Pharmaceutics
Utrecht Institute for Pharmaceutical Sciences
Utrecht, the Netherlands

Toshiharu Yakushi, Ph.D.
Graduate School of Science
Nagoya University
Nagoya, Japan

Seung Rim Yang, Ph.D.
Department of Chemical and Biomolecular Engineering
Korean Advanced Institute of Science and Technology
Daejeon, South Korea

Etsuo Yokota, Ph.D.
Graduate School of Science
Himeji Institute of Technology
Hyogo, Japan

Ryo Yoshida, Ph.D.
Graduate School of Engineering
University of Tokyo
Tokyo, Japan

Nobuhiko Yui, Ph.D.
School of Materials Science
Japan Advanced Institute of Science and Technology
Ishikawa, Japan

Contents

此为试读，需要完整PDF请访问：www.ertongbook.com

Section I

Learning from Natural Systems

1 Learning from Nature: Examples of Rapid, Repetitive, Responsive Biological Events

Randall J. Mrsny

CONTENTS

INTRODUCTION

A wide range of potential biomedical applications of polymers have been described in the literature. One very exciting subset of these applications involves efforts to mimic some of the rapid, repetitive, responsive biological events (RRRBEs) observed in various tissues and organs of the body. Such events allow the body to perform critical tasks associated with homeostasis as well as adaptation. For example, the body must maintain a constant supply of critical nutritive factors to all of its areas yet must be able to increase or decrease the levels of these factors systematically or locally in accordance with changes in the demand for these factors.

Complex systems regulate hemodynamic parameters and allow the body to adapt to changing needs. Other RRRBEs can be observed in systems where the body must react to stimuli as well as filter responses to specific external signals. Olfactory events serve as examples of such systems.[1] A new odor is easily detected initially, but with time that odor stimulus is filtered (even muted) to provide for increased acuity to new odors even in the continued presence of the initial odor. Both systems, blood flow and odor sensation, are extremely complex. Fortunately, studies have been able to break down such complex systems into incremental biological functions

0-8493-1487-9/04/$0.00+$1.50
© 2004 by CRC Press LLC

of individual RRRBEs. Such simplified systems may be potentially mimicked by polymeric processes.

The success of current and future applications of polymeric systems that mimic RRRBEs will require overcoming a number of challenges. One challenge is that these systems sufficiently portray a desired biological event. It may not be necessary to match the RRRBE exactly; rather it may be sufficient to emulate its critical functions. Identifying the critical parameters of such events demands an appreciation of not only the biological principles of the event in question but also, and maybe more importantly, an understanding of the intent of the RRRBE function. It is the goal of this chapter to discuss both of these issues — the critical factors of such events in light of the action that the event is acting to achieve.

The examples presented were selected specifically to provide a perspective of several types of RRRBEs observed in the body. Some of these events have already been modeled in various ways using polymeric systems. Others have not yet been solved. However, from the discussion of these systems, it is hoped that the reader will obtain a better understanding of how nature has solved problems related to RRRBEs and possibly how to apply these principles in instances where polymeric systems may find applications.

GENERAL PRINCIPLES

The body performs such a wide range of tasks that it would be impossible to even begin to describe them here. These events occur inside cells, outside cells, and even between cells, and they occur at every possible level of sophistication. Many events appear simple and thus quite direct, i.e., rising glucose levels result in the increased release of insulin from the beta cells of the pancreatic islets. Thus, such events might be readily modeled using a polymeric system that can respond to a glucose signal with the release of insulin. However, this superficial assessment of the role of islet beta cells does not accurately describe the true complexity of the system in which the cells participate.[2]

Glucose recognition by islet beta cells initiates an extensive network of intracellular signaling events that leads to outcomes much more complex than simply secreting insulin.[3] From a pharmaceutical perspective, the connection of glucose to insulin secretion can be sufficient for a therapeutic application.[4] Thus, a polymeric system that primarily emulates such an outcome may not need to follow the entire pathway of the events required to achieve that outcome in the body. With this in mind, we wish to introduce a new descriptor of polymeric systems designed to emulate RRRBEs. In essence, such systems should be able to respond to a stimulus to provide a simple response rather than the complex and interactive network of events that typically occurs in the body. Therefore, the term *multi-reflexive* was introduced to describe polymeric systems that produce the rapid, repetitive, and responsive events similar to those observed in the body, yet work in the absence of more complex networks of events that commonly occur following such stimuli.

The term *multi-reflexive* was selected due to connotations of the root components that discriminate function and capabilities of these types of polymers. Reflex events involve direct outcomes that occur in the absence of a higher level of responding network or cognitive events. Since it is highly unlikely that current polymeric technologies would be able to respond more elaborately than in a purely reflexive fashion, *reflexive* seemed a more accurate term than *responsive*. The term *multi* refers to the desired action of such systems to potentially affect specific types of events at several levels of responses. In some instances, it may be desirable for the system to transition repeatedly between two physical states — rapidly producing multiple all-or-none events. In other cases, the system may provide the desired action through a graded response rather than an all-or-none outcome. Such a system could allow a stimulus to provide varied levels of responses through opening one to many portals of release for a substance to be delivered. Although these two types of responses are not mutually exclusive, and it is likely that combinations of such events would be attractive in certain cases, each represents the concept that polymers can provide multiples of release and/or modification events. These are only a few examples of how multi-reflexive polymeric systems might function. The types of polymer systems being developed are likely to provide a tremendous variety of polymer-based delivery systems that might be used to emulate RRRBEs.

In order to emulate RRRBEs through the use of multi-reflexive polymeric systems, it is important to understand the critical elements of the desired outcome. Further, it is important to establish a system that responds only to a desired stimulus and at a threshold where premature, undesirable events will not occur. These two issues represent difficult challenges for multi-reflexive polymeric systems because they do not typically have the sophistication of RRRBEs where networks of events can act to guard against subthreshold activation events and where a combination of low-level stimuli can provide an augmented, and thus sufficient, stimulus for system activation. For example, nerves can discriminate varied levels of stimuli that might be simultaneously delivered from several factors.[5] The release of a neurotransmitter from an adjacent cell may be insufficient to activate an action potential in a nerve unless it is of a certain magnitude or it is presented in the presence of another stimulus such as heat or another neurotransmitter, etc.[6] Additionally, a response to factors that normally induce an action potential may be completely muted in the presence of another type of neurotransmitter whose function is to evaluate the stimulus in another way and to determine signal validity. Nerves are constantly modulating their synaptic interactions to provide a very complex level of cell function modification.[7] These types of responses are frequently bidirectional to provide feedback information.[6] As one might imagine, a multi-reflexive polymeric system may never be able to achieve such levels of complexity. Therefore, the remainder of this chapter will be devoted to examples of RRRBEs that are deconstructed in an effort to find situations where multi-reflexive polymeric systems might be applicable and, more importantly, successful. The intent of this approach is to highlight mechanisms used to achieve the speed and sophistication of responses observed for many RRRBEs of the body.

LESSONS FROM NERVES

Nervous tissue is comprised of a number of cell types with very different phenotypes and functions.[6] At the heart of nervous tissue is one cell type — the neuron — although, here again, a wide range of subtypes of such cells exist that relate primarily

此为试读，需要完整PDF请访问：www.ertongbook.com