

Molecular Communication

This comprehensive guide, by pioneers in the field, brings together, for the first time, everything a new researcher, graduate student or industry practitioner needs to get started in molecular communication. Written with accessibility in mind, it requires little background knowledge, and provides a detailed introduction to the relevant aspects of biology and information theory, as well as coverage of practical systems.

The authors start by describing biological nanomachines, the basics of biological molecular communication, and the microorganisms that use it. They then proceed to engineered molecular communication and the molecular communication paradigm, with mathematical models of different types of molecular communication, and a description of the information and communication theory of molecular communication. Finally, the practical aspects of designing molecular communication systems are presented, including a review of the key applications.

Ideal for engineers and biologists looking to get up to speed on the current practice in this growing field.

Tadashi Nakano is an Associate Professor in the Graduate School of Engineering, Osaka University, Suita, Japan. He has authored or co-authored a series of papers on molecular communication, including the very first paper, published in 2005.

Andrew W. Eckford is an Associate Professor in the Department of Electrical Engineering and Computer Science at York University, Toronto, Canada. He has authored over 50 papers in the peer-reviewed literature, and received the Association of Professional Engineers of Ontario Gold Medal.

Tokuko Haraguchi is an Executive Researcher in the Advanced ICT Research Institute at the National Institute of Information and Communications Technology (NICT), Kobe, Japan, and a Professor with the Graduate School of Science and the Graduate School of Frontier Biosciences at Osaka University, Suita, Japan. She has authored 100 papers in biological research.





Molecular Communication

TADASHI NAKANO

Osaka University, Suita, Japan

ANDREW W. ECKFORD

York University, Toronto, Canada

TOKUKO HARAGUCHI

Advanced ICT Research Institute, National Institute of Information and Communications Technology (NICT), Kobe, Japan





CAMBRIDGE UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom

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

Cambridge University Press in part of the University of Cambridge.

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning and research at the highest international levels of excellence.

www.cambridge.org

Information on this title: www.cambridge.org/9781107023086

© Cambridge University Press 2013

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2013

Printing in the United Kingdom by TJ International Ltd. Padstow Cornwall

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

Library of Congress Cataloguing in Publication data

Nakano, Tadashi, 1912-

Molecular communication / Tadashi Nakano, Andrew W. Eckford.

pages cm

Includes bibliographical references and index.

ISBN 978-1-107-02308-6 (hardback)

- 1. Molecular communication (Telecommunication) 2. Molecules.
- 3. Nanotechnology. I. Title.

TK5013.57.N35 2013

620'.5-dc23 2013009571

ISBN 978-1-107-02308-6 Hardback

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party internet websites referred to in this publication, and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.



Contents

	Prefa	ce		page xi
1	Intro	luction		1
	1.1	Molecular c	ommunication: Why, what, and how?	1
		1.1.1 Wh	y molecular communication?	1
		1.1.2 Wh	at uses molecular communication?	2
		1.1.3 Hov	w does it work? A quick introduction	3
	1.2	A history of	molecular communication	6
		1.2.1 Ear	ly history and theoretical research	6
		1.2.2 Mo	re recent theoretical research	8
		1.2.3 Imp	plementational aspects	9
		1.2.4 Cor	ntemporary research	9
	1.3	Application	s areas	11
		1.3.1 Bio	logical engineering	11
		1.3.2 Me	dical and healthcare applications	13
		1.3.3 Ind	ustrial applications	14
		1.3.4 Env	vironmental applications	14
		1.3.5 Info	ormation and communication technology	
		app	lications	15
	1.4	Rationale and organization of the book		15
	Refe	rences		16
2	Natu	e-made biolog	gical nanomachines	21
	2.1	Protein mol	ecules	22
		2.1.1 Mo	lecular structure	22
		2.1.2 Fur	actions and roles	23
	2.2	DNA and R	NA molecules	28
		2.2.1 Mo	lecular structure	28
		2.2.2 Fur	actions and roles	30
	2.3	Lipid memb	oranes and vesicles	31
		-	lecular structure	31
		2.3.2 Fur	actions and roles	33



V١	Co	ntents	,

	2.4	Whole cells	34	
	2.5	Conclusion and summary	35	
	Refe	35		
3	Molecular communication in biological systems			
	3.1	Scales of molecular communication	36	
	3.2	Modes of molecular communication	37	
	3.3	Examples of molecular communication	38	
		3.3.1 Chemotactic signaling	40	
		3.3.2 Vesicular trafficking	41	
		3.3.3 Calcium signaling	42	
		3.3.4 Quorum sensing	44	
		3.3.5 Bacterial migration and conjugation	45	
		3.3.6 Morphogen signaling	46	
		3.3.7 Hormonal signaling	47	
		3.3.8 Neuronal signaling	47	
	3.4	Conclusion and summary	49	
	Refe	References		
4	Mole	52		
	4.1	Molecular communication model	52	
	4.2	General characteristics	54	
		4.2.1 Transmission of information molecules	54	
		4.2.2 Information representation	56	
		4.2.3 Slow speed and limited range	56	
		4.2.4 Stochastic communication	57	
		4.2.5 Massive parallelization	57	
		4.2.6 Energy efficiency	58	
		4.2.7 Biocompatibility	58	
	4.3	Molecular communication network architecture	58	
		4.3.1 Physical layer	60	
		4.3.2 Link layer	61	
		4.3.3 Network layer	64	
		4.3.4 Upper layers and other issues	65	
	4.4	Conclusion and summary	67	
	Refe	rences	67	
5	Math	71		
	5.1	Discrete diffusion and Brownian motion	71	
		5.1.1 Environmental assumptions	71	
		5.1.2 The Wiener process	72	
		5.1.3 Markov property	74	



			Contents	vii
		5.1.4	Wiener process with drift	75
		5.1.5	Multi-dimensional Wiener processes	76
		5.1.6	Simulation	77
	5.2	Molec	cular motors	78
	5.3	First a	urrival times	80
		5.3.1	Definition and closed-form examples	80
		5.3.2	First arrival times in multiple dimensions	82
		5.3.3	From first arrival times to communication systems	82
	5.4	Conce	entration, mole fraction, and counting	83
		5.4.1	Small numbers of molecules: Counting and	
			inter-symbol interference	84
		5.4.2	Large numbers of molecules: Towards concentration	85
		5.4.3	Concentration: random and deterministic	87
		5.4.4	Concentration as a Gaussian random variable	89
		5.4.5	Concentration as a random process	90
		5.4.6	Discussion and communication example	92
	5.5	Model	ls for ligand–receptor systems	93
		5.5.1	Mathematical model of a ligand–receptor system	93
		5.5.2	Simulation	94
	5.6	Concl	usion and summary	95
	Refe	rences		95
6	Com	nunicatio	on and information theory of molecular communication	97
	6.1	Theore	etical models for analysis of molecular communication	97
	0.1	6.1.1	Abstract physical layer communication model	97
		6.1.2	Ideal models	99
		6.1.3	Distinguishable molecules: The additive inverse	
			Gaussian noise channel	99
		6.1.4	Indistinguishable molecules	100
		6.1.5	Sequences in discrete time	102
	6.2	Detect	tion and estimation in molecular communication	104
		6.2.1	Optimal detection and ML estimation	104
		6.2.2	Parameter estimation	106
		6.2.3	Optimal detection in the delay-selector channel	108
	6.3		nation theory of molecular communication	109
		6.3.1	A brief introduction to information theory	109
		6.3.2	Capacity	110
		6.3.3	Calculating capacity: A simple example	112
		6.3.4	Towards the general problem	115
		6.3.5	Timing channels	116
	6.4		nary and conclusion	120
		rences	•	121



viii Contents

7	Desi	gn and engineering of molecular communication systems	122	
	7.1	Protein molecules	123	
		7.1.1 Sender and receiver bio-nanomachines	123	
		7.1.2 Information molecules	124	
		7.1.3 Guide and transport molecules	125	
	7.2	DNA molecules	129	
		7.2.1 Sender and receiver bio-nanomachines	129	
		7.2.2 Information molecules	129	
		7.2.3 Interface molecules	130	
		7.2.4 Guide and transport molecules	131	
	7.3	Liposomes	132	
		7.3.1 Sender and receiver bio-nanomachines	133	
		7.3.2 Interface molecules	134	
		7.3.3 Guide molecules	135	
	7.4	Biological cells	136	
		7.4.1 Sender and receiver cells	136	
		7.4.2 Guide cells	142	
		7.4.3 Transport cells	144	
	7.5	Conclusion and summary	147	
	Refe	erences	147	
8	Appl	Application areas of molecular communication		
	8.1	Drug delivery	152	
		8.1.1 Application scenarios	153	
		8.1.2 Example: Cooperative drug delivery	153	
		8.1.3 Example: Intracellular therapy	154	
	8.2	Tissue engineering	156	
		8.2.1 Application scenarios	156	
		8.2.2 Example: Tissue structure formation	157	
	8.3	Lab-on-a-chip technology	158	
		8.3.1 Application scenarios	160	
		8.3.2 Example: Bio-inspired lab-on-a-chip	160	
		8.3.3 Example: Smart dust biosensors	161	
	8.4	Unconventional computation	162	
		8.4.1 Application scenarios	162	
		8.4.2 Example: Reaction diffusion computation	162	
		8.4.3 Example: Artificial neural networks	164	
		8.4.4 Example: Combinatorial optimizers	165	
	8.5	Looking forward: Conclusion and summary	166	
	Refe	erences	166	



			Contents	ix
9	Conc	lusion		169
	9.1	Toward practical implementation		169
	9.2	Toward the future: Demonstration projects		170
Appendix	Review of probability theory			172
	A.1	Basic probability		172
	A.2	Expectation, mean, and variance		173
	A.3	The Gaussian distribution		174
	A.4	Conditional, marginal, and joint probabilities		175
	A.5	Markov chains		175
	Index	;		177





Preface

As early researchers in molecular communication, we have been amazed by the rapid expansion of the field. A decade ago, virtually nobody worked in this area; today, dozens of researchers form a multi-national research community, and over a hundred papers have been published. At the frontiers of the field, there are fundamental questions to be answered such as the relationship between information theory and biology; and disruptive innovations to be developed, such as direct manipulation of structures in the human body at a microscopic level.

Given the advances over the past few years, we believe the time is right to take stock of the field and publish a complete overview of the state of the art. In an interdisciplinary field such as this one, we hope this book can provide a needed common point of reference. Moreover, in an evolving field such as this one, we recognize that our book should not be considered the final word on the field. Indeed, in writing it we have become fully aware of the many important open problems and research questions that need to be addressed for this field to reach its potential, and we hope our book is viewed as an invitation to further research, to expand upon this exciting new discipline.

Finally, we would like to thank the many people whose work, discussions, and encouragement over the years have made this book possible: in no particular order, Akihiro Enomoto (Qualcomm), Ryota Egashira (Yahoo! Inc.), Yasushi Hiraoka (Osaka University/National Institute of Information and Communications Technology), Satoshi Hiyama (NTT DoCoMo), Takako Koujin (National Institute of Information and Communications Technology), Shouhei Kobayashi (National Institute of Information and Communications Technology), Jian-Qin Liu (National Institute of Information and Communications Technology), Michael Moore (Pennsylvania State University), Yuki Moritani (NTT DoCoMo), Kazuo Oiwa (National Institute of Information and Communications Technology), Yutaka Okaie (Osaka University), Jianwei Shuai (Xiamen University), Tatsuya Suda (Netgroup Inc.), Nariman Farsad (York University), Lu Cui (York University), Peter Thomas (Case Western Reserve University), Raviraj S. Adve (University of Toronto), K. V. Srinivas (Samsung), Sachin Kadloor (University of Illinois at Urbana-Champaign), Chris Rose (Rutgers), and Chan-Byoung Chae (Yonsei University).