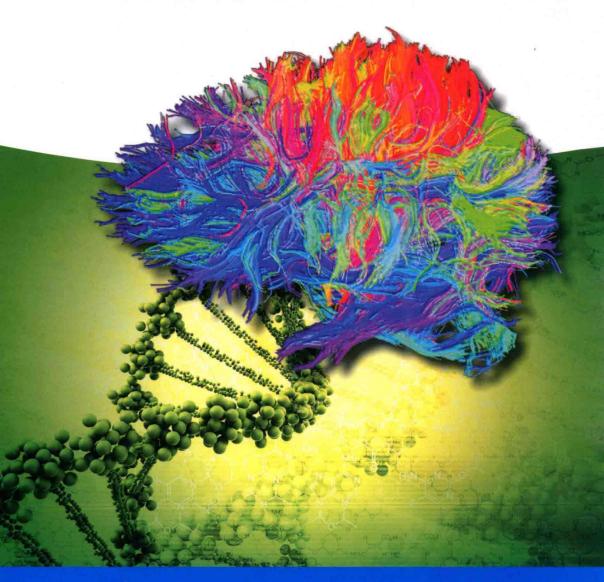
Edited by Misha (Meyer) Z. Pesenson

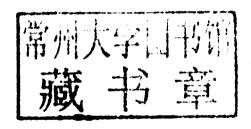
Multiscale Analysis and Nonlinear Dynamics

From Genes to the Brain



Multiscale Analysis and Nonlinear Dynamics

From Genes to the Brain





WILEY-VCH Verlag GmbH & Co. KGaA

The Editor

Dr. Misha (Meyer) Z. Pesenson California Institute of Technology Dept. of Computing & Mathemat. Sciences.

Pasadena, CA, USA mzp@cms.caltech.edu

A book of the Reviews of Nonlinear Dynamics and Complexity

The Series Editor

Prof. Dr. Heinz Georg Schuster Saarbrücken, Germany

Cover Picture

DTI image of the brain by Ashish Raj *et al.* Courtesy Neuron, No. 73, March 2012 produced. Nevertheless, authors, editors, and publisher do not warrant the information contained in these books, including this book, to be free of

All books published by Wiley-VCH are carefully

errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or

other items may inadvertently be inaccurate.

Library of Congress Card No.: applied for

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek The Deutsche Nationalbibliothek lists this

detailed bibliographic data are available on the Internet at http://dnb.d-nb.de>.

publication in the Deutsche Nationalbibliografie;

© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written

permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Print ISBN: 978-3-527-41198-6

ePDF ISBN: 978-3-527-67166-3 ePub ISBN: 978-3-527-67165-6 mobi ISBN: 978-3-527-67164-9 oBook ISBN: 978-3-527-67163-2

Cover Design Grafik-Design Schulz, Fußgönheim Typesetting Thomson Digital, Noida, India

Printing and Binding Markono Print Media Pte Ltd, Singapore

Printed in Singapore Printed on acid-free paper

Edited by Misha (Meyer) Z. Pesenson

Multiscale Analysis and Nonlinear Dynamics

Reviews of Nonlinear Dynamics and Complexity

Schuster, H. G. (ed.)

Reviews of Nonlinear Dynamics and Complexity

Volume 1

2008

ISBN: 978-3-527-40729-3

Schuster, H. G. (ed.)

Reviews of Nonlinear Dynamics and Complexity Volume 2

2009

ISBN: 978-3-527-40850-4

Schuster, H. G. (ed.)

Reviews of Nonlinear Dynamics and Complexity

and Complexity Volume 3

2010

ISBN: 978-3-527-40945-7

Grigoriev, R. and Schuster, H.G. (eds.)

Transport and Mixing in Laminar Flows

From Microfluidics to Oceanic Currents

2011

ISBN: 978-3-527-41011-8

Lüdge, K. (ed.)

Nonlinear Laser Dynamics From Quantum Dots to Cryptography

2011

ISBN: 978-3-527-41100-9

Klages, R., Just, W., Jarzynski (eds.)

Nonequilibrium Statistical Physics of Small Systems Fluctuation Relations and Beyond

2013

ISBN: 978-3-527-41094-1

Pesenson, M. Z. (ed.)

Multiscale Analysis and Nonlinear Dynamics From Molecules to the Brain

2013

ISBN: 978-3-527-41198-6

Niebur, E., Plenz, D., Schuster, H.G. (eds.)

Criticality in Neural Systems

2013

ISBN: 978-3-527-41104-7

List of Contributors

Danielle S. Bassett

University of California, Santa Barbara Department of Physics 6213 Broida Hall Santa Barbara, CA 93106 USA

Vicente Botella-Soler

Institute of Science and Technology (IST) Austria Am Campus 1 A-3400 Klosterneuburg Austria

Michael X Cohen

University of Amsterdam Department of Psychology Weesperplein 4 1018 XA Amsterdam The Netherlands

Gustavo Deco

University Pompeu Fabra Center of Brain and Cognition Theoretical and Computational Neuroscience Group Roc Boronat, 138 08018 Barcelona Spain

Mathieu Desbrun

California Institute of Technology Department of Computing & Mathematical Sciences MC 305-16 1200 E. California Blvd. Pasadena, CA 91125 USA

Roger D. Donaldson

California Institute of Technology Department of Computing & Mathematical Sciences MC 305-16 1200 E. California Blvd. Pasadena, CA 91125 USA

Elisa Franco

University of California, Riverside Department of Mechanical Engineering 900 University Avenue Bourns Hall A311 Riverside, CA 92521 USA

Conor Houghton

University of Bristol
Department of Computer Science
Merchant Venturers Building
Woodland Road
Bristol BS8 1UB
UK

Etienne Hugues

University Pompeu Fabra Center of Brain and Cognition Theoretical and Computational Neuroscience Group Roc Boronat, 138 08018 Barcelona Spain

Lester Ingber

Lester Ingber Research 545 Ashland Creek Drive Ashland, OR 97520 USA

Jongmin Kim

California Institute of Technology Department of Bioengineering MC 107-81 1200 E. California Blvd. Pasadena, CA 91125 USA

Thomas Kreuz

Consiglio Nazionale delle Ricerche (CNR) Istituto dei Sistemi Complessi (ISC) Via Madonna del Piano 10 50119 Sesto Fiorentino Italy

Jean-Philippe Lachaux

Lyon Neuroscience Research Center Brain Dynamics and Cognition Team INSERM U1028 - CNRS UMR5292 F-69500 Lyon-Bron France

Michel Le Van Quyen

University Pierre et Marie Curie Research Center of the Brain and Spinal Cord Institute (ICM) INSERM UMRS 975 - CNRS **UMR 7225** Hôpital de la Pitié-Salpêtrière 47 Bd de l'Hôpital 75651 Paris Cedex 13 France

Michael Nivala

University of California, Los Angeles David Geffen School of Medicine, Department of Medicine (Cardiology) 650 Charles E. Young Drive South A2-237 CHS Los Angeles, CA 90095 USA

Paul L. Nunez

Cognitive Dissonance, LLC 1726 Sienna Canyon Dr Encinitas, CA 92024 USA

Houman Owhadi

California Institute of Technology Department of Computing & Mathematical Sciences MC 9-94 1200 E. California Blvd. Pasadena, CA 91125 USA

Isaac Z. Pesenson

Temple University Department of Mathematics 1805 N. Broad St. Philadelphia, PA 19122 USA

Misha (Meyer) Z. Pesenson

California Institute of Technology Department of Computing & Mathematical Sciences MC 305-16 1200 E. California Blvd. Pasadena, CA 91125 USA

Raphaël Plasson

Harvard University Department of Earth & Planetary Sciences 100 Edwin H. Land Blvd. Cambridge, MA 02142-1204 USA

Zhilin Qu

University of California, Los Angeles David Geffen School of Medicine, Department of Medicine (Cardiology) 650 Charles E. Young Drive South A2-237 CHS Los Angeles, CA 90095 USA

Yannick Rondelez

LIMMS/CNRS-IIS (UMI 2820) The University of Tokyo Institute of Industrial Science 4-6-1 Komaba, Meguro-ku Tokyo 153-8505 Japan

Felix Siebenhühner

University of Helsinki Neuroscience Center Viikinkaari 4 00014 Helsinki Finland

Friedrich C. Simmel

Technische Universität München Physics Department and ZNN/WSI Systems Biophysics and Bionanotechnology Am Coulombwall 4a 85748 Garching Germany

Ramesh Srinivasan

University of California, Irvine Department of Cognitive Sciences 2201 Social & Behavioral Sciences Gateway Building (SBSG) Irvine, CA 92697-5100 USA

Mario Valderrama

Universidad de Los Andes Department of Biomedical Engineering Cra 1 Nº 18A-12, Bogotá Colombia

Iuan R. Vidal

Lyon Neuroscience Research Center Brain Dynamics and Cognition Team INSERM U1028 - CNRS UMR5292 69500 Lyon-Bron France

Bradley Voytek

University of California, San Francisco Department of Neurology 1550 4th Street San Francisco, CA 94143-2922 USA

Preface

"Those who study complex adaptive systems are beginning to find some general principles that underlie all such systems, and seeking out those principles requires discussions and collaboration among specialists in a great many fields."

M. Gell-Mann¹⁾

Modern science and engineering deal with problems that involve wide ranges of spatial and temporal scales. Moreover, data-intensive sciences such as Systems Biology and Systems Neuroscience, besides dealing with complex physical, chemical, and biological phenomena, need to handle enormous amounts of high-dimensional data produced by modern high-throughput experimental technologies. All this creates a critical need for modeling sophisticated, natural/artificial systems and analyzing modern high-dimensional data across multiple scales ranging from molecules to macroscales. However, traditional mathematical approaches to modeling/analyzing complex phenomena/data are often limited because of the multiscale nature of the problems. At the same time, it is well known that biological systems solve computationally demanding problems with many scales and process multiscale information deftly. Indeed, in order to resolve a broad range of spatial/ temporal scales present in input signals, perception systems perform sophisticated multiscale encoding, analysis, and decoding in real time. A second example is related to data dimension reduction (which is intimately connected with feature extraction, recognition and learning). In fact, the input signals to all mammalian perception systems, despite their coming from low-dimensional Euclidian space, are transformed internally into extremely high-dimensional representations. This counterintuitive drastic increase in complexity is followed by a concealed, effortless and perpetual nonlinear dimension reduction, that is, converting the complex representations back into low-dimensional signals to be, ultimately, executed by the motor system. Another example comes from Systems Biology where embryonic development is, in fact, an immense information processing task in which DNA sequence data generate and direct the system level spatial deployment of specific cellular functions [2]. These examples indicate that the theoretical understanding of biological computational mechanisms and their experimental implementation can

¹⁾ Cited in Ref. [1].

greatly enhance our ability to develop efficient artificial information processing systems. An important advance in the engineering of biological computing systems has recently been achieved and the first network of artificial neurons made from DNA was created, suggesting that DNA strand displacement cascades could endow biochemical systems with the capability of recognizing patterns [3]. Pattern recognition and multiresolution are quintessential for information processing, which, in turn, is closely connected with learning and adaptivity.

Complex biological systems capable of adaptive behavior and effective information processing are often governed by mechanisms operating simultaneously on multiple spatial and temporal scales. Thus, in order to analyze the machinery that underlies biological information processing and computations in general, this book focuses on modeling multiscale phenomena in Synthetic/Systems Biology and Systems Neuroscience, as well as on mathematical approaches to multiresolution analysis. Because of the inherently interdisciplinary nature of this task, the editor of this book invited experts (theoreticians and experimentalists) in bioengineering, chemistry, cardiology, neuroscience, computer science, and applied mathematics, to provide their perspectives ("seeking out those principles requires . . . collaboration among specialists in a great many fields."). The contributions to this book may broadly be categorized as belonging to mathematical methods, Systems Biology, and Systems Neuroscience. Multiscale analysis is the major integrating theme of this book, as indicated by its title. The subtitle does not call for bridging the scales all the way from genes to behavior, but rather stresses the unifying perspective provided by the concepts referred to in the title. The contributions emphasize the importance of taking into account the interplay between multiscale structure and multiscale dynamics. One of our goals is to attract the attention of scientists working in Systems Biology and Systems Neuroscience by demonstrating that some of the seemingly unrelated problems from these disciplines may be modeled using virtually identical powerful mathematical methods from the inclusive paradigms emphasized here. Each chapter provides a window into the current state of the art in the areas of research discussed. This book is thus intended for advanced researchers interested in recent developments in these areas. It is believed that the interdisciplinary perspective adopted here will be beneficial for all the above-mentioned disciplines. The roads between different sciences, "while often the quickest shortcut to another part of our own science, are not visible from the viewpoint of one science alone" [4].

Acknowledgments

First of all, I would like to thank the General Editor of the Series, Heinz Georg Schuster, for inviting me to edit this volume and for his inspiration and help. I am especially grateful to Michael Egan and Mathieu Desbrun whose steady, strong encouragement and support made this book possible. I would like to acknowledge Joel Tropp for his support during the initial stage of this project.

This collection is the result of the combined work of many people. I am grateful to the contributors for the effort they invested in this endeavor, for the time dedicated to cross reviewing the chapters, and for their flexibility and patience during the editing process.

My deep appreciation goes to the people who directly or indirectly influenced me and my work on this book: my parents Leah and Zalman Pesenson; my children Dina, Igor, and Liza Pesenson; Andrey E. Borovik, Victor Shrira, Lev Mogilevich, Lev I. Katz, Valentin L. Izrailevich, Elena D. Khomskaya, Uekuma Sensei, and my dear friends. My very special thanks go to Michèle Pedrini for her encouragement, unfailing support, inspiration, and light.

I would like to thank the technical editors, Vera Palmer and Ulrike Werner, of Wiley for their prompt, professional editing of the manuscripts. I am grateful to the staff of the Caltech Libraries led by University Librarian Kimberly Douglas, and especially to Viet Nguyen, Judy Nollar, Dana Roth, Kristin Buxton, George Porter, Marie Noren, Bertha Saavedra, Jason Perez, and Christine Ngo for their technical help and dedication to books and information dissemination in general. I gratefully acknowledge the funding provided by NGA NURI the grant number HM1582-08-1-0019 and partial funding by AFOSR MURI Award FA9550-09-1-0643 that made this project possible.

Pasadena, 2013

Misha Z. Pesenson

References

- 1 Schuster, H. (2001) Complex Adaptive Systems, Scator Verlag.
- 2 Davidson, E. (2010) Emerging properties of animal gene regulatory networks. Nature, 468, 911-920.
- 3 Qian, L., Winfree, E., and Bruck, J. (2011) Neural network computation with DNA strand displacement cascades. Nature, 475, 368-372.
- 4 Anderson, P. (1972) More is different. Science, 177, 393-396.

Contents

List of Contributors		XIII
Preface	XVII	

1	Introduction: Multiscale Analysis – Modeling, Data, Networks, and
	Nonlinear Dynamics 1
	Misha (Meyer) Z. Pesenson
1.1	Multiscale Modeling 5
1.1.1	Domain-Specific Modeling 6
1.1.2	Analysis 7
1.1.3	Model Interpretation and Verification: Experimental/Simulation
	Data 9
1.2	Multiresolution Analysis and Processing of High-Dimensional
	Information/Data 10
1.3	Multiscale Analysis, Networks, and Nonlinear Dynamics 11
1.4	Conclusions 14
	References 14
Part One	Multiscale Analysis 19
2	Modeling Across Scales: Discrete Geometric Structures in
	Homogenization and Inverse Homogenization 21
	Mathieu Desbrun, Roger D. Donaldson, and Houman Owhadi
2.1	Introduction 21
2.2	Homogenization of Conductivity Space 23
2.2.1	Homogenization as a Nonlinear Operator 24
2.2.2	Parameterization of the Conductivity Space 26
2.3	Discrete Geometric Homogenization 31
2.3.1	Homogenization by Volume Averaging 32
2.3.2	Homogenization by Linear Interpolation 33
2.3.3	Semigroup Properties in Geometric Homogenization 37
2.4	Optimal Weighted Delaunay Triangulations 39
	Construction of Positive Dirichlet Weights 40

 2.4.2 Weighted Delaunay and <i>Q</i>-Adapted Triangulations 43 2.4.3 Computing Optimal Weighted Delaunay Meshes 44 2.5 Relationship to Inverse Homogenization 47 2.6 Electrical Impedance Tomography 49 2.6.1 Numerical Tests 52 2.6.1.1 Harmonic Coordinate Iteration 53 2.6.1.2 Divergence-Free Parameterization Recovery 55
 2.4.3 Computing Optimal Weighted Delaunay Meshes 44 2.5 Relationship to Inverse Homogenization 47 2.6 Electrical Impedance Tomography 49 2.6.1 Numerical Tests 52 2.6.1.1 Harmonic Coordinate Iteration 53
 2.5 Relationship to Inverse Homogenization 47 2.6 Electrical Impedance Tomography 49 2.6.1 Numerical Tests 52 2.6.1.1 Harmonic Coordinate Iteration 53
 2.6 Electrical Impedance Tomography 49 2.6.1 Numerical Tests 52 2.6.1.1 Harmonic Coordinate Iteration 53
2.6.1 Numerical Tests 522.6.1.1 Harmonic Coordinate Iteration 53
2.6.1.1 Harmonic Coordinate Iteration 53
,
References 61
Multiresolution Analysis on Compact Riemannian Manifolds 65
Isaac Z. Pesenson
3.1 Introduction 65
3.2 Compact Manifolds and Operators 66
3.2.1 Manifolds without Boundary 66
3.2.2 Compact Homogeneous Manifolds 67 3.2.3 Bounded Domains with Smooth Boundaries 68
3.3 Hilbert Frames 69
3.4 Multiresolution and Sampling 70
3.5 Shannon Sampling of Band-Limited Functions on Manifolds 72
3.6 Localized Frames on Compact Manifolds 73
3.7 Parseval Frames on Homogeneous Manifolds 76
 3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79
 3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81
 3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79
 3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81
 3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89 4.3.1 A Two-Node Molecular Oscillator 90
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89 4.3.1 A Two-Node Molecular Oscillator 90 4.3.2 Analysis of the Oscillatory Regime 91
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89 4.3.1 A Two-Node Molecular Oscillator 90 4.3.2 Analysis of the Oscillatory Regime 91 4.3.3 Experimental Implementation and Data 95
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89 4.3.1 A Two-Node Molecular Oscillator 90 4.3.2 Analysis of the Oscillatory Regime 91
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89 4.3.1 A Two-Node Molecular Oscillator 90 4.3.2 Analysis of the Oscillatory Regime 91 4.3.3 Experimental Implementation and Data 95 4.4 Scaling Up Molecular Circuits: Synchronization of Molecular Processes 96
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89 4.3.1 A Two-Node Molecular Oscillator 90 4.3.2 Analysis of the Oscillatory Regime 91 4.3.3 Experimental Implementation and Data 95 4.4 Scaling Up Molecular Circuits: Synchronization of Molecular Processes 96 4.4.1 Analysis of the Load Dynamics 97
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89 4.3.1 A Two-Node Molecular Oscillator 90 4.3.2 Analysis of the Oscillatory Regime 91 4.3.3 Experimental Implementation and Data 95 4.4 Scaling Up Molecular Circuits: Synchronization of Molecular Processes 96 4.4.1 Analysis of the Load Dynamics 97 4.4.1.1 Quasisteady State Approximation of the Load Dynamics 99
3.7 Parseval Frames on Homogeneous Manifolds 76 3.8 Variational Splines on Manifolds 79 3.9 Conclusions 81 References 81 Part Two Nonlinear Dynamics: Genelets and Synthetic Biochemical Circuits 83 4 Transcriptional Oscillators 85 Elisa Franco, Jongmin Kim, and Friedrich C. Simmel 4.1 Introduction 85 4.2 Synthetic Transcriptional Modules 86 4.2.1 Elementary Activation and Inhibition Pathways, and Simple Loops 87 4.2.2 Experimental Implementation 88 4.3 Molecular Clocks 89 4.3.1 A Two-Node Molecular Oscillator 90 4.3.2 Analysis of the Oscillatory Regime 91 4.3.3 Experimental Implementation and Data 95 4.4 Scaling Up Molecular Circuits: Synchronization of Molecular Processes 96 4.4.1 Analysis of the Load Dynamics 97 4.4.1.1 Quasisteady State Approximation of the Load Dynamics 99

4.4.2.2	Nonconsumptive Coupling and Retroactivity 100
4.4.3	Insulation 102
4.4.3.1	Reduction of Perturbations on the Oscillator Dynamics 103
4.4.3.2	Signal Transmission to the Insulated Load 104
4.5	Oscillator Driving a Load: Experimental Implementation and Data 105
4.6	Deterministic Predictive Models for Complex Reaction Networks 105
4.7	Stochastic Effects 107
4.8	Conclusions 110
	References 110
5	Synthetic Biochemical Dynamic Circuits 113
,	Raphaël Plasson and Yannick Rondelez
5.1	Introduction 113
5.2	Out-of-Equilibrium Chemical Systems 114
5.2.1	A Short Historical Overview 114
5.2.1.1	Discovery of Nonlinear Chemical Systems 114
5.2.1.2	Unexpected Oscillating Chemical Systems 115
5.2.2	Building Nonequilibrium Systems 116
5.2.2.1	Energetic Requirements 116
5.2.2.2	System Closure 116
5.2.2.3	Instabilities and Dynamic Stability 118
5.2.3	Design Principles 119
5.2.3.1	Dynamism 119
5.2.3.2	Interacting Feedbacks Processes 121
5.2.3.3	Modularity 122
5.3	Biological Circuits 123
5.3.1	Biological Networks Modeled by Chemistry 123
5.3.2	Biosystems: A Multilevel Complexity 124
5.3.3	A First Example of a Biological Reaction Circuit 124
5.3.4	Biological Networking Strategy 125
5.3.4.1	GRNs Are Templated Networks 125
5.3.4.2	Regulation and Feedback Loops 125
5.3.4.3	Nonlinearities in Genetic Regulation 127
5.3.4.4	Delays 128
5.3.4.5	Titration Effects 129
5.3.5	Higher Level Motifs and Modularity of Biochemical Networks 129
5.4	Programmable In Vitro Dynamics 130
5.4.1	Enzymatic Systems 130
5.4.1.1	DNA–RNA Sequence Amplification 131
5.4.1.2	The Genelet System 131
5.4.1.3	The PEN Toolbox 132
5.4.2	Nonenzymatic Networks: Strand Displacement Systems 134
5.4.3	Numerical Modeling 135
5.4.3.1	Mathematical Descriptions 135
5122	ISA and Rifurcation Analysis for Design 137

VIII	Contents

5.4.3.3	Time Evolutions 138	
5.4.3.4	Robustness Analysis and In Silico Evolutions	138
5.5	Perspectives 139	
5.5.1	DNA Computing 140	
5.5.2	Self Organizing Spatial Patterns 140	
5.5.3	Models of Biological Networks 141	
5.5.4	Origin of Life 141	
	Peferences 142	

Part Three Nonlinear Dynamics: the Brain and the Heart 147

6	Theoretical and Experimental Electrophysiology in Human Neocortex:
	Multiscale Dynamic Correlates of Conscious Experience 149
	Paul L. Nunez, Ramesh Srinivasan, and Lester Ingber
6.1	Introduction to Brain Complexity 149
6.1.1	Human Brains and Other Complex Adaptive Systems 149
6.1.2	Is "Consciousness" a Four-Letter Word? 150
6.1.3	Motivations and Target Audiences for this Chapter 151
6.1.4	Brain Imaging at Multiple Spatial and Temporal Scales 151
6.1.5	Multiple Scales of Brain Dynamics in Consciousness 153
6.2	Brief Overview of Neocortical Anatomy and Physiology 154
6.2.1	The Human Brain at Large Scales 154
6.2.2	Chemical Control of Brain and Behavior 155
6.2.3	Electrical Transmission 156
6.2.4	Neocortex 156
6.2.5	The Nested Hierarchy of Neocortex: Multiple Scales of Brain
	Tissue 158
6.2.6	Corticocortical Connections Are Nonlocal and "Small World" 159
6.3	Multiscale Theory in Electrophysiology 160
6.3.1	Characteristic EEG and Physiological Time Scales 160
6.3.2	Local versus Global Brain Models and Spatial Scale 161
6.3.3	A Large-Scale Model of EEG Standing Waves 162
6.3.4	Relationships between Small, Intermediate, and Large Scales: A Simple
	Mechanical Analog 164
6.4	Statistical Mechanics of Neocortical Interactions 166
6.4.1	SMNI on Short-Term Memory and EEG 166
6.4.1.1	SMNI STM 167
6.4.1.2	SMNI EEG 168
6.4.2	Euler–Lagrange Equations 168
6.4.2.1	Columnar EL 169
6.4.2.2	Strings EL 170
6.4.2.3	Springs EL 171
6.4.3	Smoking Gun 171

6.4.3.1	Neocortical Magnetic Fields 172
6.4.3.2	SMNI Vector Potential 172
6.5	Concluding Remarks 173
	References 174
7	Multiscale Network Organization in the Human Brain 179
	Danielle S. Bassett and Felix Siebenhühner
7.1	Introduction 179
7.2	Mathematical Concepts 181
7.3	Structural Multiscale Organization 182
7.4	Functional Multiscale Organization 187
7.5	Discussion 191
7.5.1	Structure and Function 191
7.5.2	Hierarchical Modularity 193
7.5.3	Power-Law Scaling 194
7.5.4	Network Models of Multiscale Structure 194
	References 195
8	Neuronal Oscillations Scale Up and Scale Down
	Brain Dynamics 205
	Michel Le Van Quyen, Vicente Botella-Soler, and Mario Valderram
8.1	Introduction 205
8.2	The Brain Web of Cross-Scale Interactions 206
8.3	Multiscale Recordings of the Human Brain 208
8.4	Physiological Correlates of Cross-Level Interactions 210
8.5	Level Entanglement and Cross-Scale Coupling of Neuronal
	Oscillations 212
8.6	Conclusions 213
	References 214
9	Linking Nonlinear Neural Dynamics to Single-Trial Human
	Behavior 217
	Michael X Cohen and Bradley Voytek
9.1	Neural Dynamics Are Complex 217
9.2	Data Analysis Techniques and Possibilities Are Expanding
	Rapidly 218
9.3	The Importance of Linking Neural Dynamics to Behavior
,,,	Dynamics 219
9.4	Linear Approaches of Linking Neural and Behavior
	Dynamics 220
9.5	Nonlinear Dynamics and Behavior: Phase Modulations 221
9.6	Cross-Frequency Coupling 224
9.7	Linking Cross-Frequency Coupling to Behavior 226

x	Contents	
	9.8	Testing for Causal Involvement of Nonlinear Dynamics in Cognition and Behavior 228
	9.9	Conclusions 229
		References 229
	10	Brain Dynamics at Rest: How Structure Shapes Dynamics 233 Etienne Hugues, Juan R. Vidal, Jean-Philippe Lachaux, and Gustavo Deco
	10.1	Introduction 233
	10.2	Model 234
	10.3	Results 236
	10.3.1	Neural Dynamics 236
	10.3.1.1	Case of Infinite Conduction Velocity 236
	10.3.1.2	Case of Finite Conduction Velocity 238
	10.3.2	BOLD Dynamics 238
	10.4	Comparison with Experimental Data 239
	10.5	Discussion 240
		References 242
	11	Adaptive Multiscale Encoding: A Computational Function of Neuronal
		Synchronization 245
		Misha (Meyer) Z. Pesenson
	11.1	Introduction 245
	11.2	Some Basic Mathematical Concepts 247
	11.3	Neural Synchronization 247
	11.3.1	Connections with Some Existing Approaches to MRA 253
	11.4	Concluding Remarks 253
		References 254
	12	Multiscale Nonlinear Dynamics in Cardiac Electrophysiology:
		From Sparks to Sudden Death 257 Zhilin Qu and Michael Nivala
	12.1	Introduction 257
	12.1	
	12.2	Subcellular Scale: Criticality in the Transition from Ca Sparks to Ca Waves 258
	12.3	Cellular Scale: Action Potential and Ca Cycling Dynamics 260
	12.3.1	Intracellular Ca Alternans 260
	12.3.2	Fast Pacing-Induced Complex APD Dynamics 262
	12.3.3	EAD-Mediated Nonlinear Dynamics at Slow Heart Rates 264
	12.4	Excitation Dynamics on the Tissue and Organ Scales 266
	12.4.1	Spatially Discordant APD Alternans 266
	12.4.2	Spiral and Scroll Wave Dynamics 267
	12.4.3	Chaos Synchronization 269
	12.5	Conclusions 271
		References 271