Modellierung dynamischer Prozesse in der Zellbiologie

Freie Universität Berlin, Fachbereich Mathematik und Informatik, SS2005

Modellierung dynamischer Prozesse in der Zellbiologie

Do 16-18 Uhr
SR 046, Informatik
Wilhelm Huisinga, Illia Horenko

Aktuelle Information

Allgemeines

Inhalt: Mathematische Modelle zur Beschreibung dynamischer Phänomene werden in der Biologie mit großem Erfolg angewandt. Es gibt Beispiele, wie die Modellierung des Ca(2+) Einflusses auf die elektrische Aktivität einer Zelle (Chay und Keizer 1983), bei denen die theoretischen Vorhersagen der experimentellen Überprüfung Jahre im voraus waren - auch wenn dies sicherlich nicht die Regel ist. Grob kann man zwischen deterministischen Modellen, wie z.B. Reaktions-Diffusions-Gleichungen und stochastischen Modellen, wie z.B. Markov-Prozessen unterscheiden. In diesem Seminar wollen wir uns schwerpunktmäßig mit der stochastischen Modellierung dynamischer Phänomene befassen. Zu Beginn erarbeiten wir uns die notwendigen mathematischen Grundlagen und setzen uns mit der Frage auseinander, was unter stochastischer Modellierung überhaupt zu verstehen ist. Anschließend betrachten wir je nach Neigungen und Vorkenntnissen der Seminarteilnehmer/innen verschiedene Anwendungsklassen: stochastische Brückenbindung von Ionen-Kanälen, Theorie der Molekülmotoren, Simulation von Zellzyklen sowie mechanochemische Modelle. Dabei wollen wir neben der Modellierung und algorithmischer Beschreibung herausarbeiten, welche mathematischen Eigenschaften in die jeweiligen Modelle eingehen. Grundlegende Phänomene sollen mit Simulationen am Computer illustriert werden.
Zielgruppe: Studierende der Mathematik , Biologie und (Bio-)Informatik sowie verwandter Fächer ab dem 5. Semester.
Voraussetzungen: Elementare Wahrscheinlichkeitstheorie und Statistik (Stochastik I); Vertrautheit im algorithmischen Denken und Grundkenntnisse über Markov-Ketten sind empfehlenswert
Schein/Credits: Gemäß Prüfungsordnung
Perspektiven: Ergänzende Seminare im Grenzbereich von Stochastik und Numerik mit Möglichkeit zur Abschlussarbeit in verschiedene Richtungen

Kontakt

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Zeitplan

Datum	Vortragende(r)
17. 04.03	Wilhelm Huisinga Modellierung dynamischer Prozesse in der Zellbiologie. (http://compphysiol.math.uni-potsdam.de/pub/SemCellBioIntro-SS03 Überblicksvortrag und Verteilung der bisher noch nicht vergebenen Themen. Literatur: Some remarks concerning "deterministic and stochastic models", Jason Kastner and Jerry E. Solomon, California Institute of Technology.
24.04.03	Wilhelm Huisinga **Einfürung in die stochastischen Modellierungsansätze**
08.05.03	Illia Horenko Einfürung in die deterministischen Modellierungsansätze (http://compphysiol.math.uni-potsdam.de/pub/SemCellBioDeterm-SS Matlab-Demoprogramme: Michaelis.m, reaktion1.m, reaktion2.m.
	Themenkomplex Insulin: Alex Finck, Adrian Schuster, Eric Wolski. Vorbereitungstreffen: Fr. 02. Mai, 14:15-16:00 (SR126, Pi) und Mi 07. Mai, 16:15-18:00 (SR126, Pi). Literatur: Christopher P. Fall, Eric S. Marland, John M. Wagner und John J. Tyson "Computational Cell Biology", sections 2.2-2.4, 5.4. James Keener und James Sneyd "Mathematical Physiology", section 19.3
15.05.03	Adrian Schuster: Insulin - biologische, physiologische und medizinische Grundlagen (http://compphysiol.math.uni-potsdam.de/pub/InsulinIntro_Schuster. Eryk Wolski: **Voltage gated ionic currents (http://compphysiol.math.uni-potsdam.de/pub/Wolski_VoltageG** Matlab-Demoprogramme: sovo.m (Hauptprogramm), volt.m, voltclamp.m
22.05.03	Eryk Wolski: **Interaction ion channels: the Moris-Lecar model** Alex Finck: **The pancreatic beta cell: Chay-Keizer model (http://compphysiol.math.uni-potsdam.de/pub/Finck_ChayKeize**
	Themenkomplex Zellzyklus: Roland Börenz, Tim Conrad. Vorbereitungstreffen: Fr. 16 Mai, 14:15-16:00 (SR126, Pi) und Do. 22. Mai, 14:15-16:00 (SR108, Pi). Literatur: Albert Goldbeter "A Minimal Cascade Model for the Mitotic Oscillator Involving Cyclin and cdc2

	Kinase", Proc. Natl. Acad. Sci. USA. 1991; 88: 9107-9111
28.05.03	Roland Börenz: **Biologie des Zellzyklusses, Michaelis-Menten-Kinetik** Tim Conrad: **Goldbeter's Modell des Zellzyklusses und Erweiterungen (http://compphysiol.math.uni-potsdam.de/pub/Conrad_Cellcycl**
	Themenkomplex Bakteriophagen: Christof Dehmel, Reiner Mattiesen, Stephan Menz. Vorbereitungstreffen: Fr. 23. Mai, 14:15-16:00 (SR126, Pi) und Fr. 30. Mai, 14:15-16:00 (SR126, Pi). Literatur: Michael Gibson "Computational Methods for Stochastic Biological Systems", PhD thesis, California Institute of Technology, April 2000. R. Srivastava, L. You, J. Summers and J. Yin "Stochastic vs. Deterministic Modeling of Intracellular Viral Kinetics" J. theor. Biol. 218 (2002) 309-321.
05.06.03	Reiner Mattiesen, Stephan Menz: Bakteriophagen: Biologische Einführung und mathematische Modellierung (T7, incl. Vergleich determinsitisch vs. stochastisch) (http://compphysiol.math.uni-potsdam.de/pub/BakterioPhagen.pdf) Matlab-Demoprogramme: stochastisches Modell (Next Reaction): stochSimNextReacT7.m; deterministisches Modell: T7_detMain.m (Hauptprogramm), T7_RHS.m
12.06.03	Stefan Menz, Christof Dehmel: Ein detailliertes Modell des Bakteriophagen Lambda: Biologie und stochastische Simulation (http://compphysiol.math.uni-potsdam.de/pub/LambdaPhageTeil2.p
	Themenkomplex Wechselwirkung zwischen Zellen: Jonas Heise, Utz Pape, Andrea Weiße, Jorge Numata. Vorbereitungstreffen: Fr. 06. Juni, 12:15-14:00 (SR126, Pi) und Fr. 13. Juni, 14:15-16:00 (SR126, Pi). Literatur: A.S. Mikhailov, V. Calenbuhr "From Cells to Societies", Sections 2.1, 2.2 and Chapter 6. Matlab-Dateien: diffusion_2d.m (Hauptprogramm), num_laplace.m, RHS_diffusion.m
19.06.03	Zwei Vorträge zum Themenkomplex Wechselwirkung zwischen Zellen
26.06.03	Jorge Numata: **Wechselwirkung zwischen Zellen (http://compphysiol.math.uni-potsdam.de/pub/NumataInterZelle** Matlab-Demoprogramme: *.mat, Movies *.avi, *.mpeg
	Themenkomplex Ionenkanäle und molekulare Motoren: Heval Benav, Marko Briesemann, Gernot Faulseit: Fr. 27. Juni, 15:15-17:00 (SR126,

	Pi) und Do, 03. Juli, 16:15-18:00 (SR046, Inf). Literatur: Christopher P. Fall, Eric S. Marland, John M. Wagner und John J. Tyson "Computational Cell Biology", Chapters 11, 12 and 13.2, 13.4.
10.07.03	Gernot Faulseit: **Molekulare Maschinen als Brownsche Motoren (http://compphysiol.math.uni-potsdam.de/pub/Faulseit_Molecul** Matlab-Demoprogramme: *.m, Java-Applets: *.java
17.07.03	Zwei Vorträge zum Themenkomplex Ionenkanäle und molekulare Motoren

Literatur

- Christopher P. Fall, Eric S. Marland, John M. Wagner und John J. Tyson, **"Computational Cell Biology"**, Springer Serie "Interdisciplinary Applied Mathematics", New York, 2002 online material
- James P. Keener and James Sneyd, **"Mathematical Physiology"**, Springer Serie "Interdisciplinary Applied Mathematics", New York, 1998
- A. S. Mikhailov and V. Calenbuhr, **"From cells to societies"**, Springer, Berlin, 2002
- Pierre Bremaud, **"Markov Chains"**, Springer, Cambridge 1999
- W. Huisinga, Skript zur Vorlesung "Markov Ketten", WS2002/03 (ps)
- **Nature's Insight on Computational Biology**. Besonders empfehlenswert: Computational Biology Insight. "A collection of reviews showing how sophisticated mathematical concepts can illuminate the principles underlying biology at a genetic, molecular, cellular and even organismal level."
- **The Metabolic Control Analysis**. "Metabolic control analysis (MCA) is a phenomenological quantitative sensitivity analysis of fluxes and metabolite concentrations. In MCA one studies the relative control exerted by each step (enzyme) on the system's variables (fluxes and metabolite concentrations). This control is measured by applying a perturbation to the step being studied and measuring the effect on the variable of interest after the system has settled to a new steady state."
- **Biophysics Textbook**. On-line, collaborative biophysics textbook
- **Channels, Ions and Excitable Membranes**. A historical perspective of the biophysics of excitability in neurons
- ***Life: The Science of Biology***, 5th Ed. by William K. Purves, Gordon H. Orians, H. Craig Heller, and David Sadava, Sinauer Associates, Inc./W. H. Freeman and Co., 1998
- ***Links to Selected Biology Sources on the Web*** by Robert J. Huskey, University of Virginia Information Technology & Communication
- **ExPASy** (Expert Protein Analysis System) proteomics server of the Swiss Institute of Bioinformatics (SIB). Many, many links and useful information
- **The Silicon Cell**: computing the living cell by BioCentrum Amsterdam, CWI, Institute for Informatics of the University of Amsterdam

Weitere Informationen

Software

BioSpice. *Aim*: cellular pathways. *Features*: pathways are graphically represented, access to databases. *Models*: 3D fluid-mechanical systems. *Language*: Matlab/Java - open source software. *People*: Adam Arkin, project director of Berkeley BioSpice Network Representation and Modeling System (NRMS), see also here

Cellerator. *Aim*: interacting signal transduction networks. *Features*: biological modeling via automated equation generation. *Models*: (ordinary) differential equations. *Language*: Mathematica. *"People"*: Jet Propulsion Laboratory, California Institute of Technology

E-Cell. *Aim*: Modeling and simulation environment for biochemical and genetic processes. *Features*: functions of proteins, protein-protein interactions, protein-DNA interactions, regulation of gene expression, other features of cellular metabolism. *Models*: deterministic ODEs, discrete stochastic systems, many components driven by multiple algorithms with different timescales. *Language*: C++. *People*: Masaru Tomita at the Institute for Advanced Biosciences, Keio University

FluxAnalyzer. *Aim*: A graphical interface for Metabolic Flux Analysis (MFA). *Features*: Stoichiometric analysis and determination of flux distributions in metabolic networks *Models*: abstract (symbolic) network representation, network graphics visualizing the metabolic network (metabolic maps). *Language*: MATLAB - free for academic users. *People*: Steffen Klamt, Systems Biology group of Ernst Dieter Gilles, MPI "Dynamics of Complex Technical Systems", Magdeburg

Gepasi. *Aim*: Modeling biochemical systems. *Features*: many compartments with different volumes, tools to fit models to data, optimize any function of the model, metabolic control analysis, linear stability analysis, parameter studies, SBML support *Models*: matrices and differential equations*Language*: source code in C, user interface using Microsoft Windows - free software. *People*: Pedro Mendes at Aberystwyth Quantitative Biology and Analytical Biotechnology Group, University of Wales Aberystwyth

MCell. *Aim*: A General Monte Carlo Simulator of Cellular Microphysiology. *Features*: so far the focus has been on one aspect of biological signal transduction, namely the microphysiology of synaptic transmission. *Models*: Simulations are positioned at a biological scale above molecular dynamics but below whole cell and higher level studies; Diffusion of individual ligand molecules by Brownian dynamics random walk algorithm, and bulk solution rate constants are converted into Monte Carlo probabilities so that the diffusing ligands can undergo stochastic chemical interactions with individual binding sites such as receptor proteins, enzymes, transporters, etc.*Language*: obtained as a machine-specific executable program - free software (copying and/or editing of MCell without the authors' consent is expressly forbidden). *People*: Tom Bartol at Computational Neurobiology Laboratory (CLN) at Salk Institue and Joel R. Stiles at Biomedical Applications, Pittsburgh Supercomputing Center

Metabolizer. *Aim*: Simulation of complex biological systems *Features*: Integration of deterministic and stoachastic simulation techniques of metabolic networks into a hybrid simulator, SBML support. *Models*: Gillespie's first reaction method; ODEs and PDEs models are planed. *Language*: Java *People*: Markus Schwehm Department of Computer Architecture, University of Tübingen

ProMoT/DIVA. *Aim*: Structured dynamic simulation models *Features*: symbolic transformations, optimization. *Models*: differential and algebraic rate equations. *Language*: Lisp/Java - free software under Linux/Unix. *People*: Virtual Biological Laboratory: Martin Ginkel, Andreas Kremling, Torsten Nutsch at MPI "Dynamics of Complex Technical Systems", Magdeburg

ScrumPy. *Aim*: biochemical modelling. *Features*: steady-state determination, time-course simulation, MCA functions, determination of Elementary Modes and enzyme subsets. *Language*: Python - open-source . *People*: Metabolic Control Analysis Research Group, Oxford Brookes University, UK

Stochastirator. *Aim*: chemical and biological reaction networks. *Features*: stochastic mathematical framework. *Language*: C++. *People*: Eric Lyons, Larry Lok

StochSim. *Aim*: general purpose biochemical simulator *Features*: individual molecules or molecular complexes

are represented as individual software objects; reactions between molecules occur stochastically (employing "pseudo-molecules"). Multiple states of molecules (conformational state, ligand binding, phosphorylation, methylation, or other covalent modification). *Models*: random selection of two molecules. *Language*: platform-independent core simulation engine *People*: Carl Firth (formerly Carl Morton-Firth), Computational cell biology group at the Department of Zoology of the University of Cambridge (USA)

STOCKS. *Aim*: STOChastic Kinetic Simulation of biochemical processes to simulate time evolution of the system composed of large number of first and second order chemical reactions. *Features*: several cellular generations using linearly growing volume of reaction environment and simple model of cell division. Substance in equilibrium modelled as random pools with Gaussian distribution. *Models*: Gillespie's direct method *Language*: C++ under Unix/Linux - public domain (GNU GPL) software. *People*: Andrzej M. Kierzek, Institute of Biochemistry and Biophysics, Warszawa

Virtual Cell. *Aim*: remote user modeling and simulation environment to create biological models of various types and run simulations on a remote server. A transparent general purpose solver is used to translate the initial biological description into a set of concise mathematical problems. *Features*: mathematical simplification using pseudo-steady approximations and mass conservation relationships. *Language*: Java based graphical interface. *People*: Jim Schaff (Virtual Cell Developer) at National Resource for Cell Analysis and Modeling, NRCAM

SBW. "The Systems Biology Workbench (SBW) is a modular, broker-based, message-passing framework for simplified application intercommunications." by ERATO Kitano Systems Biology Project. Contains a good list of links

Other programs are **Jarnac** (Herbert Sauro). **STODE** (Carel van Gend, Ursula Kummer). Furhtermore, **METACON** and **EMPATH** are no longer being developed, maintained or supported

Guide to Available Mathematical Software. "A cross-index and virtual repository of mathematical and statistical software components of use in computational science and engineering."

Sonstige Internet-Ressourcen

BioMedNet a portal to live sciences. **PubMed** PubMed, a service of the National Library of Medicine, provides access to over 12 million MEDLINE citations back to the mid-1960's and additional life science journals. PubMed includes links to many sites providing full text articles and other related resources

 http://compphysiol.math.uni-potsdam.de/