The Society for Mathematical Biology

SMB in USA and UK

The Society for Mathematical Biology

The Society for Mathematical Biology is an "international society which exists to promote and foster interactions between the mathematical and biological sciences communities through membership, journal publications, travel support and conferences"[1] .

Membership

On line live application for research in mathematical and theoretical biology, and/or mathematical biophysics [2]

Governance

- SMB Officers and Directors
- By-laws of the SMB

SMB History

A concise history of The Society for Mathematical Biology co-founded in USA by Dr.George Karreman and Dr. Herbert D. Landahl, is found in Article by Michael Conrad from the September 1996 SMB Newsletter [3]

Past Presidents

- First President of SMB -- Professor George Karreman

Meetings

Held annually[4]

Publications

- *Bulletin of Mathematical Biology*;

the Bulletin is the official journal of SMB.

- The [http://www.smb.org/publications/top_ten.shtml "top ten cited articles from the *Bulletin of Mathematical Biology* "]]

Education

- "Courses in Mathematical Biology" and Mathematical Biophysics.
- Degree Programs in Mathematical Biology: "graduate and undergraduate programs in mathematical biology."
- Instructional Resources: "textbooks, software, manipulatives and other ideas for promoting mathematical biology in the classroom."
- Funding Opportunities in Mathematical Biology Education: "opportunities specifically targeted for mathematical biology education"

Resources

- Book lists "that are of interest to mathematical biology including textbooks and reviews."
- Journals: a "collection of journals that are of interest to mathematical biology" students.
- Grants; links to pertinent grant information.
- Other web-related resources

Prizes

"The Society for Mathematical Biology awards a number of prizes including the Akira Okubo Prize, the Art Winfree Prize, and the Lee Segel Prize."

External links

Mathematical biology: Job Listings

- Studentships in mathematical biology [5]
- Postdoctoral Positions in mathematical biology [6]

References

[1] http://www.smb.org Official Statement of the SMB scientific organization
[2] http://www.smb.org/membership/index.shtml Application form
[3] http://www.smb.org/governance/smb_history.shtml
[4] http://www.smb.org/meetings/annual.shtml Information regarding past, present and future SMB Annual Meetings.
[5] http://www.smb.org/jobs/index.shtml#student
[6] http://www.smb.org/jobs/index.shtml#postdoc

Mathematical biology

Mathematical biology is also called **theoretical biology**,[1] and sometimes **biomathematics**. It includes at least four major subfields: *biological mathematical modeling*, *relational biology/complex systems biology (CSB)*, *bioinformatics* and *computational biomodeling/biocomputing*. It is an interdisciplinary academic research field with a wide range of applications in biology, medicine[2] and biotechnology.[3]

Mathematical biology aims at the mathematical representation, treatment and modeling of biological processes, using a variety of applied mathematical techniques and tools. It has both theoretical and practical applications in biological, biomedical and biotechnology research. For example, in cell biology, protein interactions are often represented as "cartoon" models, which, although easy to visualize, do not accurately describe the systems studied. In order to do this, precise mathematical models are required. By describing the systems in a quantitative manner, their behavior can be better simulated, and hence properties can be predicted that might not be evident to the experimenter.

Importance

Applying mathematics to biology has a long history, but only recently has there been an explosion of interest in the field. Some reasons for this include:

- the explosion of data-rich information sets, due to the genomics revolution, which are difficult to understand without the use of analytical tools,
- recent development of mathematical tools such as chaos theory to help understand complex, nonlinear mechanisms in biology,
- an increase in computing power which enables calculations and simulations to be performed that were not previously possible, and
- an increasing interest in in silico experimentation due to ethical considerations, risk, unreliability and other complications involved in human and animal research.

For use of basic arithmetics in biology, see relevant topic, such as Serial dilution.

Areas of research

Several areas of specialized research in mathematical and theoretical biology[4] [5] [6] [7] [8] [9] as well as external links to related projects in various universities are concisely presented in the following subsections, including also a large number of appropriate validating references from a list of several thousands of published authors contributing to this field. Many of the included examples are characterised by highly complex, nonlinear, and supercomplex mechanisms, as it is being increasingly recognised that the result of such interactions may only be understood through a combination of mathematical, logical, physical/chemical, molecular and computational models. Due to the wide diversity of specific knowledge involved, biomathematical research is often done in collaboration between mathematicians, biomathematicians, theoretical biologists, physicists, biophysicists, biochemists, bioengineers, engineers, biologists, physiologists, research physicians, biomedical researchers,oncologists, molecular biologists, geneticists, embryologists, zoologists, chemists, etc.

Computer models and automata theory

A monograph on this topic summarizes an extensive amount of published research in this area up to 1987,[10] including subsections in the following areas: computer modeling in biology and medicine, arterial system models, neuron models, biochemical and oscillation networks, quantum automata [11], quantum computers in molecular biology and genetics, cancer modelling, neural nets, genetic networks, abstract relational biology, metabolic-replication systems, category theory[12] applications in biology and medicine,[13] automata theory,cellular automata, tessallation models[14] [15] and complete self-reproduction [16], chaotic systems in organisms, relational biology and organismic theories.[17] [18] This published report also includes 390 references to peer-reviewed articles by a large number of authors.[19] [20] [21]

Modeling cell and molecular biology

This area has received a boost due to the growing importance of molecular biology.[22]

- Mechanics of biological tissues[23]
- Theoretical enzymology and enzyme kinetics
- Cancer modelling and simulation [24] [25]
- Modelling the movement of interacting cell populations[26]
- Mathematical modelling of scar tissue formation[27]
- Mathematical modelling of intracellular dynamics[28]
- Mathematical modelling of the cell cycle[29]

Modelling physiological systems

- Modelling of arterial disease [30]
- Multi-scale modelling of the heart [31]

Molecular set theory

Molecular set theory was introduced by Anthony Bartholomay, and its applications were developed in mathematical biology and especially in Mathematical Medicine.[32] Molecular set theory (MST) is a mathematical formulation of the wide-sense chemical kinetics of biomolecular reactions in terms of sets of molecules and their chemical transformations represented by set-theoretical mappings between molecular sets. In a more general sense, MST is the theory of molecular categories defined as categories of molecular sets and their chemical transformations represented as set-theoretical mappings of molecular sets. The theory has also contributed to biostatistics and the formulation of clinical biochemistry problems in mathematical formulations of pathological, biochemical changes of interest to Physiology, Clinical Biochemistry and Medicine.[33] [34]

Population dynamics

Population dynamics has traditionally been the dominant field of mathematical biology. Work in this area dates back to the 19th century. The Lotka–Volterra predator-prey equations are a famous example. In the past 30 years, population dynamics has been complemented by evolutionary game theory, developed first by John Maynard Smith. Under these dynamics, evolutionary biology concepts may take a deterministic mathematical form. Population dynamics overlap with another active area of research in mathematical biology: mathematical epidemiology, the study of infectious disease affecting populations. Various models of viral spread have been proposed and analyzed, and provide important results that

may be applied to health policy decisions.

Mathematical methods

A model of a biological system is converted into a system of equations, although the word 'model' is often used synonymously with the system of corresponding equations. The solution of the equations, by either analytical or numerical means, describes how the biological system behaves either over time or at equilibrium. There are many different types of equations and the type of behavior that can occur is dependent on both the model and the equations used. The model often makes assumptions about the system. The equations may also make assumptions about the nature of what may occur.

Mathematical biophysics

The earlier stages of mathematical biology were dominated by mathematical biophysics, described as the application of mathematics in biophysics, often involving specific physical/mathematical models of biosystems and their components or compartments.

The following is a list of mathematical descriptions and their assumptions.

Deterministic processes (dynamical systems)

A fixed mapping between an initial state and a final state. Starting from an initial condition and moving forward in time, a deterministic process will always generate the same trajectory and no two trajectories cross in state space.

- Difference equations – discrete time, continuous state space.
- Ordinary differential equations – continuous time, continuous state space, no spatial derivatives. *See also:* Numerical ordinary differential equations.
- Partial differential equations – continuous time, continuous state space, spatial derivatives. *See also:* Numerical partial differential equations.
- Maps – discrete time, continuous state space.

Stochastic processes (random dynamical systems)

A random mapping between an initial state and a final state, making the state of the system a random variable with a corresponding probability distribution.

- Non-Markovian processes – generalized master equation – continuous time with memory of past events, discrete state space, waiting times of events (or transitions between states) discretely occur and have a generalized probability distribution.
- Jump Markov process – master equation – continuous time with no memory of past events, discrete state space, waiting times between events discretely occur and are exponentially distributed. *See also:* Monte Carlo method for numerical simulation methods, specifically continuous-time Monte Carlo which is also called kinetic Monte Carlo or the stochastic simulation algorithm.
- Continuous Markov process – stochastic differential equations or a Fokker-Planck equation – continuous time, continuous state space, events occur continuously according to a random Wiener process.

Spatial modelling

One classic work in this area is Alan Turing's paper on morphogenesis entitled *The Chemical Basis of Morphogenesis*, published in 1952 in the Philosophical Transactions of the Royal Society.

- Travelling waves in a wound-healing assay[35]

- Swarming behaviour[36]
- A mechanochemical theory of morphogenesis[37]
- Biological pattern formation[38]
- Spatial distribution modeling using plot samples[39]

Phylogenetics

Phylogenetics is an area of mathematical biology that deals with the reconstruction and analysis of phylogenetic (evolutionary) trees and networks based on inherited characteristics. The main mathematical concepts are trees, X-trees and maximum parsimony trees.

Model example: the cell cycle

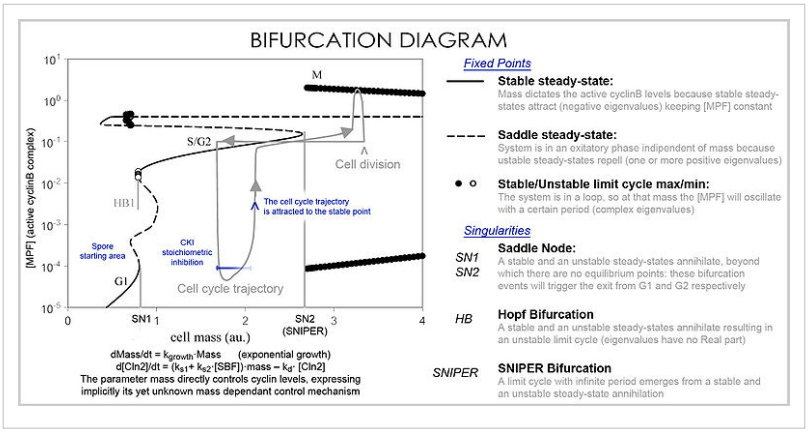
The eukaryotic cell cycle is very complex and is one of the most studied topics, since its misregulation leads to cancers. It is possibly a good example of a mathematical model as it deals with simple calculus but gives valid results. Two research groups [40] [41] have produced several models of the cell cycle simulating several organisms. They have recently produced a generic eukaryotic cell cycle model which can represent a particular eukaryote depending on the values of the parameters, demonstrating that the idiosyncrasies of the individual cell cycles are due to different protein concentrations and affinities, while the underlying mechanisms are conserved (Csikasz-Nagy et al., 2006).

By means of a system of ordinary differential equations these models show the change in time (dynamical system) of the protein inside a single typical cell; this type of model is called a deterministic process (whereas a model describing a statistical distribution of protein concentrations in a population of cells is called a stochastic process).

To obtain these equations an iterative series of steps must be done: first the several models and observations are combined to form a consensus diagram and the appropriate kinetic laws are chosen to write the differential equations, such as rate kinetics for stoichiometric reactions, Michaelis-Menten kinetics for enzyme substrate reactions and Goldbeter–Koshland kinetics for ultrasensitive transcription factors, afterwards the parameters of the equations (rate constants, enzyme efficiency coefficients and Michealis constants) must be fitted to match observations; when they cannot be fitted the kinetic equation is revised and when that is not possible the wiring diagram is modified. The parameters are fitted and validated using observations of both wild type and mutants, such as protein half-life and cell size.

In order to fit the parameters the differential equations need to be studied. This can be done either by simulation or by analysis.

In a simulation, given a starting vector (list of the values of the variables), the progression of the system is calculated by solving the equations at each time-frame in small increments.



In analysis, the proprieties of the equations are used to investigate the behavior of the system depending of the values of the parameters and variables. A system of differential equations can be represented as a vector field, where each vector described the change (in concentration of two or more protein) determining where and how fast the trajectory (simulation) is heading. Vector fields can have several special points: a stable point, called a sink, that attracts in all directions (forcing the concentrations to be at a certain value), an unstable point, either a source or a saddle point which repels (forcing the concentrations to change away from a certain value), and a limit cycle, a closed trajectory towards which several trajectories spiral towards (making the concentrations oscillate).

A better representation which can handle the large number of variables and parameters is called a bifurcation diagram(Bifurcation theory): the presence of these special steady-state points at certain values of a parameter (e.g. mass) is represented by a point and once the parameter passes a certain value, a qualitative change occurs, called a bifurcation, in which the nature of the space changes, with profound consequences for the protein concentrations: the cell cycle has phases (partially corresponding to G1 and G2) in which mass, via a stable point, controls cyclin levels, and phases (S and M phases) in which the concentrations change independently, but once the phase has changed at a bifurcation event (Cell cycle checkpoint), the system cannot go back to the previous levels since at the current mass the vector field is profoundly different and the mass cannot be reversed back through the bifurcation event, making a checkpoint irreversible. In particular the S and M checkpoints are regulated by means of special bifurcations called a Hopf bifurcation and an infinite period bifurcation.

Mathematical/theoretical biologists

- Pere Alberch
- Anthony F. Bartholomay
- J. T. Bonner
- Jack Cowan
- Gerd B. Müller
- Walter M. Elsasser
- Claus Emmeche
- Andree Ehresmann
- Marc Feldman
- Ronald A. Fisher
- Brian Goodwin
- Bryan Grenfell
- J. B. S. Haldane

- William D. Hamilton
- Lionel G. Harrison
- Michael Hassell
- Sven Erik Jørgensen
- George Karreman
- Stuart Kauffman
- Kalevi Kull
- Herbert D. Landahl
- Richard Lewontin
- Humberto Maturana
- Robert May
- John Maynard Smith
- Howard Pattee
- George R. Price
- Erik Rauch
- Nicolas Rashevsky
- Ronald Brown (mathematician)
- Johannes Reinke
- Robert Rosen
- Rene Thom
- Jakob von Uexküll
- Robert Ulanowicz
- Francisco Varela
- C. H. Waddington
- Arthur Winfree
- Lewis Wolpert
- Sewall Wright
- Christopher Zeeman

Mathematical, theoretical and computational biophysicists

- Nicolas Rashevsky
- Ludwig von Bertalanffy
- Francis Crick
- Manfred Eigen
- Walter Elsasser
- Herbert Frohlich, FRS
- Francois Jacob
- Martin Karplus
- George Karreman
- Herbert D. Landahl
- Ilya, Viscount Prigogine
- SirJohn Randall
- James D. Murray
- Bernard Pullman
- Alberte Pullman
- Erwin Schrodinger
- Klaus Schulten

- Peter Schuster
- Zeno Simon
- D'Arcy Thompson
- Murray Gell-Mann

See also

- Abstract relational biology [42][43] [44]
- Biocybernetics
- Bioinformatics
- Biologically inspired computing
- Biostatistics
- Cellular automata[45]
- Coalescent theory
- Complex systems biology[46] [47] [48]
- Computational biology
- Dynamical systems in biology[49] [50] [51] [52] [53] [54]
- Epidemiology
- Evolution theories and Population Genetics
  - Population genetics models
  - Molecular evolution theories
- Ewens's sampling formula
- Excitable medium
- Mathematical models
  - Molecular modelling
  - Software for molecular modeling
  - Metabolic-replication systems [55][56]
  - Models of Growth and Form
  - Neighbour-sensing model
- Morphometrics
- Organismic systems (OS) [57][58]
- Organismic supercategories [57][59] [60]
- Population dynamics of fisheries
- Protein folding, also blue Gene and folding@home
- Quantum computers
- Quantum genetics
- Relational biology [61]
- Self-reproduction[62] (also called self-replication in a more general context).
- Computational gene models
- Systems biology[63]
- Theoretical biology[64]
- Topological models of morphogenesis
  - DNA topology
  - DNA sequencing theory

    For use of basic arithmetics in biology, see relevant topic, such as Serial dilution.
- Biographies
  - Charles Darwin

- D'Arcy Thompson
- Joseph Fourier
- Charles S. Peskin
- Nicolas Rashevsky [65]
- Robert Rosen
- Rosalind Franklin
- Francis Crick
- René Thom
- Vito Volterra

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Lists of references

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- A list of references for applications of category theory in relational biology[72] .
- An updated list of publications of theoretical biologist Robert Rosen[73]

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[68] http://www.springerlink.com/content/w2733h7280521632/
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[70] http://www.bookfinder.com/dir/i/Mathematical_Models_in_Medicine/0080363776/
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[73] Publications list for Robert Rosen http://www.people.vcu.edu/~mikuleck/rosen.htm
[74] http://www.ams.org/notices/199509/hoppensteadt.pdf
[75] http://www.resnet.wm.edu/~jxshix/math490/reed.pdf
[76] http://www.resnet.wm.edu/~jxshix/math490/may.pdf
[77] http://www.resnet.wm.edu/~jxshix/math490/murray.doc
[78] http://eprints.maths.ox.ac.uk/567/01/224.pdf
[79] http://www.biomedcentral.com/content/pdf/1471-2105-7-494.pdf

External links

- Theoretical and mathematical biology website (http://www.kli.ac.at/theorylab/index.html)
- Complexity Discussion Group (http://www.complex.vcu.edu/)
- Integrative cancer biology modeling and Complex systems biology (http://fs512.fshn.uiuc.edu/ComplexSystemsBiology.htm)
- UCLA Biocybernetics Laboratory (http://biocyb.cs.ucla.edu/research.html)
- TUCS Computational Biomodelling Laboratory (http://www.tucs.fi/research/labs/combio.php)
- Nagoya University Division of Biomodeling (http://www.agr.nagoya-u.ac.jp/english/e3senko-1.html)
- Technische Universiteit Biomodeling and Informatics (http://www.bmi2.bmt.tue.nl/Biomedinf/)
- BioCybernetics Wiki, a vertical wiki on biomedical cybernetics and systems biology (http://wiki.biological-cybernetics.de)
- Society for Mathematical Biology (http://www.smb.org/)
- Bulletin of Mathematical Biology (http://www.springerlink.com/content/119979/)
- European Society for Mathematical and Theoretical Biology (http://www.esmtb.org/)
- Journal of Mathematical Biology (http://www.springerlink.com/content/100436/)
- Biomathematics Research Centre at University of Canterbury (http://www.math.canterbury.ac.nz/bio/)
- Centre for Mathematical Biology at Oxford University (http://www.maths.ox.ac.uk/cmb/)

- Mathematical Biology at the National Institute for Medical Research (http://mathbio.nimr.mrc.ac.uk/)
- Institute for Medical BioMathematics (http://www.imbm.org/)
- *Mathematical Biology Systems of Differential Equations* (http://eqworld.ipmnet.ru/en/solutions/syspde/spde-toc2.pdf) from EqWorld: The World of Mathematical Equations
- Systems Biology Workbench - a set of tools for modelling biochemical networks (http://sbw.kgi.edu)
- The Collection of Biostatistics Research Archive (http://www.biostatsresearch.com/repository/)
- Statistical Applications in Genetics and Molecular Biology (http://www.bepress.com/sagmb/)
- The International Journal of Biostatistics (http://www.bepress.com/ijb/)
- Theoretical Modeling of Cellular Physiology at Ecole Normale Superieure, Paris (http://www.biologie.ens.fr/bcsmcbs/)

Theoretical biology

Theoretical biology is a field of academic study and research that involves the use of models and theories in biology.

Many separate areas of biology fall under the concept of theoretical biology, according to the way they are studied. Some of these areas include: animal behaviour (ethology), biomechanics, biorhythms, cell biology, complexity of biological systems, ecology, enzyme kinetics, evolutionary biology, genetics, immunology, membrane transport, microbiology, molecular structures, morphogenesis, physiological mechanisms, systems biology and the origin of life. Neurobiology is an example of a subdiscipline of biology which already has a theoretical version of its own, theoretical or computational neuroscience.

The ultimate goal of the theoretical biologist is to explain the biological world using mainly mathematical and computational tools. Though it is ultimately based on observations and experimental results, the theoretical biologist's product is a model or theory, and it is this that chiefly distinguishes the theoretical biologist from other biologists.

Theoretical biologists

- Pere Alberch
- Anthony F. Bartholomay
- Ervin Bauer
- Ludwig von Bertalanffy
- Jan Charles Biro
- J. T. Bonner
- Jack Cowan
- Francis Crick
- Gerd B. Müller
- Walter M. Elsasser
- Claus Emmeche
- Andree Ehresmann
- Marc Feldman

- Ronald A. Fisher
- Brian Goodwin
- Bryan Grenfell
- J. B. S. Haldane
- William D. Hamilton
- Lionel G. Harrison
- Michael Hassell
- Sven Erik Jørgensen
- George Karreman
- Stuart Kauffman
- Kalevi Kull
- Herbert D. Landahl
- Richard Lewontin
- Humberto Maturana
- Robert May
- John Maynard Smith
- James D. Murray
- Howard Pattee
- George R. Price
- Erik Rauch
- Nicolas Rashevsky
- Ronald Brown (mathematician)
- Johannes Reinke
- Robert Rosen
- Peter Schuster
- Rene Thom
- D'Arcy Thompson
- Jakob von Uexküll
- Robert Ulanowicz
- Francisco Varela
- C. H. Waddington
- Arthur Winfree
- Lewis Wolpert
- Sewall Wright
- Christopher Zeeman

See also

- Journal of Theoretical Biology
- Bioinformatics
- Biosemiotics
- Mathematical biology
- Theoretical ecology
- Artificial life

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External links

- Theory of Biological Anthropology (Documents No. 9 and 10 in English) [1]
- Drawing the Line Between Theoretical and Basic Biology (a forum article by Isidro T. Savillo) [2]

Related Journals

- Acta Biotheoretica [3]
- Bioinformatics [4]
- Biological Theory [5]
- BioSystems [6]
- Bulletin of Mathematical Biology [7]
- Ecological Modelling [8]
- Journal of Mathematical Biology [9]
- Journal of Theoretical Biology [10]
- Journal of the Royal Society Interface [11]
- Mathematical Biosciences [12]
- Medical Hypotheses [13]
- Rivista di Biologia-Biology Forum [14]
- Theoretical and Applied Genetics [15]
- Theoretical Biology and Medical Modelling [16]
- Theoretical Population Biology [17]
- Theory in Biosciences [18] (formerly: Biologisches Zentralblatt)

Related societies

- American Mathematical Society [19]
- British Society of Developmental Biology [20]
- European Mathematical Society [21]
- ESMTB: European Society for Mathematical and Theoretical Biology [22]
- The International Biometric Society [23]
- International Society for Ecological Modelling [24]
- The Israeli Society for Theoretical and Mathematical Biology [25]
- London Mathematical Society [26]
- Société Francophone de Biologie Théorique [27]
- Society for Industrial and Applied Mathematics [28]
- Society for Mathematical Biology [29]
- International Society for Biosemiotic Studies [30]

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[3] http://www.springerlink.com/link.asp?id=102835
[4] http://bioinformatics.oupjournals.org/
[5] http://www.mitpressjournals.org/loi/biot/
[6] http://www.elsevier.com/locate/biosystems
[7] http://www.springerlink.com/content/119979/
[8] http://www.elsevier.com/locate/issn/03043800
[9] http://www.springerlink.com/content/100436/
[10] http://www.elsevier.com/locate/issn/0022-5193
[11] http://publishing.royalsociety.org/index.cfm?page=1058#
[12] http://www.elsevier.com/locate/mbs
[13] http://www.harcourt-international.com/journals/mehy/
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[15] http://www.springerlink.com/content/100386/
[16] http://www.tbiomed.com/
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[19] http://www.ams.org/
[20] http://www.dundee.ac.uk/lifesciences/BSDB/
[21] http://www.maths.soton.ac.uk/EMIS
[22] http://www.esmtb.org/
[23] http://www.tibs.org/
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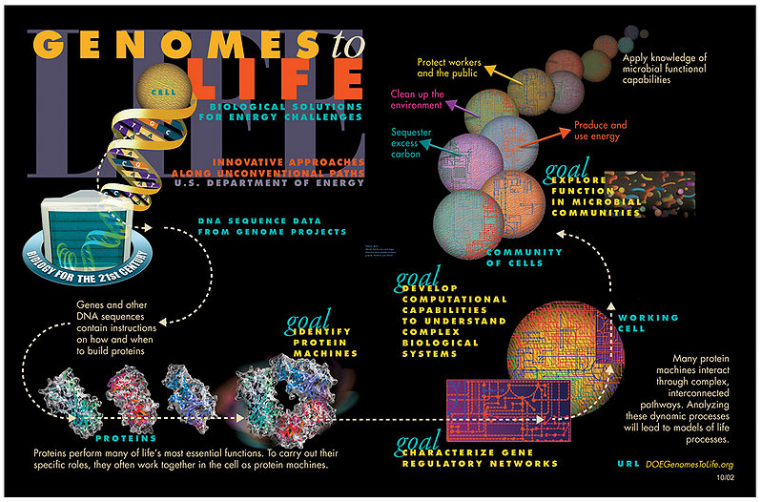
[25] http://bioinformatics.weizmann.ac.il/istmb/
[26] http://www.lms.ac.uk/
[27] http://www.necker.fr/sfbt/
[28] http://www.siam.org/
[29] http://www.smb.org/
[30] http://www.biosemiotics.org/

Complex Systems Biology

Systems biology is a biology-based inter-disciplinary study field that focuses on the systematic study of complex interactions in biological systems, thus using a new perspective (holism instead of reduction) to study them. Particularly from year 2000 onwards, the term is used widely in the biosciences, and in a variety of contexts. Because the scientific method has been used primarily toward reductionism, one of the goals of systems biology is to discover new emergent properties that may arise from the systemic view used by this discipline in order to understand better the entirety of processes that happen in a biological system.



Example of systems biology research.

Overview

Systems biology can be considered from a number of different aspects:

- Some sources discuss systems biology as a **field of study**, particularly, the study of the interactions between the components of *biological systems*, and how these interactions give rise to the function and behavior of that system (for example, the enzymes and metabolites in a metabolic pathway).[1] [2]
- Other sources consider systems biology as a **paradigm**, usually defined in antithesis to the so-called reductionist paradigm, although fully consistent with the scientific method. The distinction between the two paradigms is referred to in these quotations:

  "*The reductionist approach has successfully identified most of the components and many of the interactions but, unfortunately, offers no convincing concepts or methods to understand how system properties emerge...the pluralism of causes and effects in biological networks is better addressed by observing, through quantitative measures, multiple components simultaneously and by rigorous data integration with mathematical models*" Science[3]

  "*Systems biology...is about putting together rather than taking apart, integration rather than reduction. It requires that we develop ways of thinking about integration that are as rigorous as our reductionist programmes, but different....It means changing our philosophy, in the full sense of the term*" Denis Noble[4]

- Still other sources view systems biology in terms of the **operational protocols used for performing research**, namely a cycle composed of theory, analytic or computational modelling to propose specific testable hypotheses about a biological system, experimental validation, and then using the newly acquired quantitative description of

cells or cell processes to refine the computational model or theory.[5] [6] Since the objective is a model of the interactions in a system, the experimental techniques that most suit systems biology are those that are system-wide and attempt to be as complete as possible. Therefore, transcriptomics, metabolomics, proteomics and high-throughput techniques are used to collect quantitative data for the construction and validation of models.

- Engineers consider systems biology as the application of dynamical systems theory to molecular biology.
- Finally, some sources see it as a **socioscientific phenomenon** defined by the strategy of pursuing integration of complex data about the interactions in biological systems from diverse experimental sources using interdisciplinary tools and personnel.

This variety of viewpoints is illustrative of the fact that systems biology refers to a cluster of peripherally overlapping concepts rather than a single well-delineated field. However the term has widespread currency and popularity as of 2007, with chairs and institutes of systems biology proliferating worldwide (Such as the Institute for Systems Biology).

History

Systems biology finds its roots in:

- the quantitative modelling of enzyme kinetics, a discipline that flourished between 1900 and 1970,
- the simulations developed to study neurophysiology, and
- control theory and cybernetics.

One of the theorists who can be seen as a precursor of systems biology is Ludwig von Bertalanffy with his general systems theory, and his book titled "General Systems Theory in Physics and Biology" was published in 1950. One of the first numerical simulations in biology was published in 1952 by the British neurophysiologists and Nobel prize winners Alan Lloyd Hodgkin and Andrew Fielding Huxley, who constructed a mathematical model that explained the action potential propagating along the axon of a neuronal cell.[7] Their model described a cellular function emerging from the interaction between two different molecular components, a potassium and a sodium channels, and can therefore be seen as the beginning of computational systems biology.[8] In 1960, Denis Noble developed the first computer model of the heart pacemaker.[9]

The formal study of systems biology, as a distinct discipline, was launched by systems theorist Mihajlo Mesarovic in 1966 with an international symposium at the Case Institute of Technology in Cleveland, Ohio entitled "Systems Theory and Biology."[10] [11]

The 1960s and 1970s saw the development of several approaches to study complex molecular systems, such as the Metabolic Control Analysis and the biochemical systems theory. The successes of molecular biology throughout the 1980s, coupled with a skepticism toward theoretical biology, that then promised more than it achieved, caused the quantitative modelling of biological processes to become a somewhat minor field.

Since the established of the systems theory, the terms of systems ecology (Van Dyne GM.1966), systems physiology (Sagawa K.1973), system psychology (Edward B. Titchener 1992), system biomedicine (Kamada T.1992), systems biology (Zieglgansberger W, Tolle TR.1993) can be searched from the PubMed of NIH, USA. The concept and model of system medicine (Zeng BJ.) was published at the first national conference on Chinese Traditional

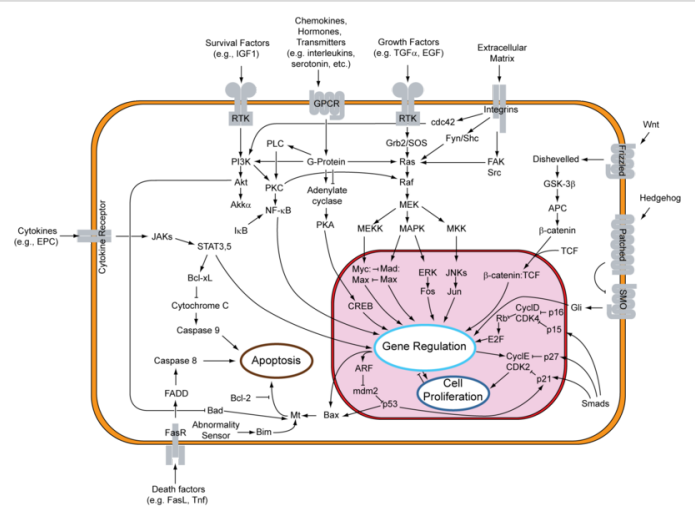
Medicince and west medicine in Guangzhou, China 1992. During 1990s years, Zeng B.J. (Institute of Microbiology, CAS, Beijing) established the concepts of "systems genetics" and "system biological engineering" for the third wave of genetics and engineering of artificial biosystems, and created the genbrain biosystem network of the (world) associates for biosystem science and engineering in Jan. 1999.

However the birth of functional genomics in the 1990s meant that large quantities of high quality data became available, while the computing power exploded, making more realistic models possible. In 1997, the group of Masaru Tomita published the first quantitative model of the metabolism of a whole (hypothetical) cell.

Around the year 2000, when Institutes of Systems Biology were established in Seattle and Tokyo, systems biology emerged as a movement in its own right, spurred on by the completion of various genome projects, the large increase in data from the omics (e.g. genomics and proteomics) and the accompanying advances in high-throughput experiments and bioinformatics. Since then, various research institutes dedicated to systems biology have been developed. As of summer 2006, due to a shortage of people in systems biology[12] several doctoral training centres in systems biology have been established in many parts of the world.

Techniques associated with systems biology

According to the interpretation of System Biology as the ability to obtain, integrate and analyze complex data from multiple experimental sources using interdisciplinary tools, some typical technology platforms are:



Overview of signal transduction pathways

- Transcriptomics: whole cell or tissue gene expression measurements by DNA microarrays or serial analysis of gene expression
- Proteomics: complete identification of proteins and protein expression patterns of a cell or tissue through two-dimensional gel electrophoresis and mass spectrometry or multi-dimensional protein identification techniques (advanced HPLC systems coupled with mass spectrometry). Sub disciplines include phosphoproteomics, glycoproteomics and other methods to detect chemically modified proteins.
- Metabolomics: identification and measurement of all small-molecules metabolites within a cell or tissue
- Glycomics: identification of the entirety of all carbohydrates in a cell or tissue.
- Lipidomics: identification of the entirety of all lipids in a cell or tissue.

In addition to the identification and quantification of the above given molecules further techniques analyze the dynamics and interactions within a cell. This includes:

- Interactomics which is used mostly in the context of protein-protein interaction but in theory encompasses interactions between all molecules within a cell,
- Fluxomics, which deals with the dynamic changes of molecules within a cell over time,
- Biomics: systems analysis of the biome.

The investigations are frequently combined with large scale perturbation methods, including gene-based (RNAi, mis-expression of wild type and mutant genes) and chemical approaches using small molecule libraries. Robots and automated sensors enable such large-scale experimentation and data acquisition. These technologies are still emerging and many face problems that the larger the quantity of data produced, the lower the quality. A wide variety of quantitative scientists (computational biologists, statisticians, mathematicians, computer scientists, engineers, and physicists) are working to improve the quality of these approaches and to create, refine, and retest the models to accurately reflect observations.

The investigations of a single level of biological organization (such as those listed above) are usually referred to as Systematic Systems Biology. Other areas of Systems Biology includes Integrative Systems Biology, which seeks to integrate different types of information to advance the understanding the biological whole, and Dynamic Systems Biology, which aims to uncover how the biological whole changes over time (during evolution, for example, the onset of disease or in response to a perturbation). Functional Genomics may also be considered a sub-field of Systems Biology.

The systems biology approach often involves the development of mechanistic models, such as the reconstruction of dynamic systems from the quantitative properties of their elementary building blocks.[13] [14] For instance, a cellular network can be modelled mathematically using methods coming from chemical kinetics and control theory. Due to the large number of parameters, variables and constraints in cellular networks, numerical and computational techniques are often used. Other aspects of computer science and informatics are also used in systems biology. These include new forms of computational model, such as the use of process calculi to model biological processes, the integration of information from the literature, using techniques of information extraction and text mining, the development of online databases and repositories for sharing data and models (such as BioModels Database), approaches to database integration and software interoperability via loose coupling of software, websites and databases[15] and the development of syntactically and semantically sound ways of representing biological models, such as the Systems Biology Markup Language (SBML).

See also

Related fields

- Complex systems biology
- Complex systems
- Complex systems biology
- Bioinformatics
- Biological network inference
- Biological systems engineering
- Biomedical cybernetics
- Biostatistics
- Theoretical Biophysics
- Relational Biology
- Translational Research
- Computational biology
- Computational systems biology
- Scotobiology
- Synthetic biology
- Systems biology modeling
- Systems ecology
- Systems immunology

Related terms

- Life
- Artificial life
- Gene regulatory network
- Metabolic network modelling
- Living systems theory
- Network Theory of Aging
- Regulome
- Systems Biology Markup Language (SBML)
- SBO
- Viable System Model
- Antireductionism

Systems biologists

- Category:Systems biologists

Lists

- Category:Systems biologists
- List of systems biology conferences
- List of omics topics in biology
- List of publications in systems biology
- List of systems biology research groups

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Further reading

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978-1-60566-076-9

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- BMC Systems Biology (http://www.biomedcentral.com/bmcsystbiol) - open access journal on systems biology
- Molecular Systems Biology (http://www.nature.com/msb) - open access journal on systems biology
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External links

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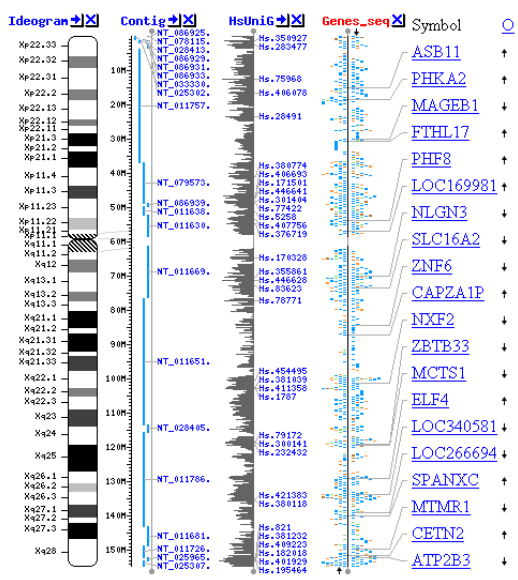
- Systems Biology Portal (http://www.systems-biology.org/) - administered by the Systems Biology Institute
- Semantic Systems Biology (http://www.semantic-systems-biology.org)
- SystemsX.ch (http://www.systemsx.ch/) - The Swiss Initiative in Systems Biology
- Systems Biology at the Pacific Northwest National Laboratory (http://www.sysbio.org/)

Bioinformatics

Bioinformatics is the application of information technology to the field of molecular biology. The term *bioinformatics* was coined by Paulien Hogeweg in 1978 for the study of informatic processes in biotic systems. Bioinformatics now entails the creation and advancement of databases, algorithms, computational and statistical techniques, and theory to solve formal and practical problems arising from the management and analysis of biological data. Over the past few decades rapid developments in genomic and other molecular research technologies and developments in information technologies have combined to produce a tremendous amount of information related to molecular biology. It is the name given to these mathematical and computing approaches used to glean understanding of biological processes. Common activities in bioinformatics include mapping and analyzing DNA and protein sequences, aligning different DNA and protein sequences to compare them and creating and viewing 3-D models of protein structures.



Map of the human X chromosome (from the NCBI website). Assembly of the human genome is one of the greatest achievements of bioinformatics.

The primary goal of bioinformatics is to increase our understanding of biological processes. What sets it apart from other approaches, however, is its focus on developing and applying computationally intensive techniques (e.g., data mining, machine learning algorithms, and visualization) to achieve this goal. Major research efforts in the field include sequence alignment, gene finding, genome assembly, protein structure alignment, protein structure prediction, prediction of gene expression and protein-protein interactions, genome-wide association studies and the modeling of evolution.

Introduction

Bioinformatics was applied in the creation and maintenance of a database to store biological information at the beginning of the "genomic revolution", such as nucleotide and amino acid sequences. Development of this type of database involved not only design issues but the development of complex interfaces whereby researchers could both access existing data as well as submit new or revised data.

In order to study how normal cellular activities are altered in different disease states, the biological data must be combined to form a comprehensive picture of these activities. Therefore, the field of bioinformatics has evolved such that the most pressing task now involves the analysis and interpretation of various types of data, including nucleotide and amino acid sequences, protein domains, and protein structures. The actual process of analyzing and interpreting data is referred to as computational biology. Important sub-disciplines within bioinformatics and computational biology include:

a) the development and implementation of tools that enable efficient access to, and use and management of, various types of information. **b)** the development of new algorithms (mathematical formulas) and statistics with which to assess relationships among members of large data sets, such as methods to locate a gene within a sequence, predict protein structure and/or function, and cluster protein sequences into families of related sequences.

Major research areas

Sequence analysis

Since the Phage Φ-X174 was sequenced in 1977, the DNA sequences of hundreds of organisms have been decoded and stored in databases. The information is analyzed to determine genes that encode polypeptides, as well as regulatory sequences. A comparison of genes within a species or between different species can show similarities between protein functions, or relations between species (the use of molecular systematics to construct phylogenetic trees). With the growing amount of data, it long ago became impractical to analyze DNA sequences manually. Today, computer programs are used to search the genome of thousands of organisms, containing billions of nucleotides. These programs would compensate for mutations (exchanged, deleted or inserted bases) in the DNA sequence, in order to identify sequences that are related, but not identical. A variant of this sequence alignment is used in the sequencing process itself. The so-called shotgun sequencing technique (which was used, for example, by The Institute for Genomic Research to sequence the first bacterial genome, *Haemophilus influenzae*) does not give a sequential list of nucleotides, but instead the sequences of thousands of small DNA fragments (each about 600-800 nucleotides long). The ends of these fragments overlap and, when aligned in the right way, make up the complete genome. Shotgun sequencing yields sequence data quickly, but the task of assembling the fragments can be quite complicated for larger genomes. In the case of the Human Genome Project, it took several days of CPU time (on one hundred Pentium III desktop machines clustered specifically for the purpose) to assemble the fragments. Shotgun sequencing is the method of choice for virtually all genomes sequenced today, and genome assembly algorithms are a critical area of bioinformatics research.

Another aspect of bioinformatics in sequence analysis is the automatic search for genes and regulatory sequences within a genome. Not all of the nucleotides within a genome are genes. Within the genome of higher organisms, large parts of the DNA do not serve any obvious purpose. This so-called junk DNA may, however, contain unrecognized functional elements. Bioinformatics helps to bridge the gap between genome and proteome projects--for example, in the use of DNA sequences for protein identification.

See also: sequence analysis, sequence profiling tool, sequence motif.

Genome annotation

In the context of genomics, **annotation** is the process of marking the genes and other biological features in a DNA sequence. The first genome annotation software system was designed in 1995 by Dr. Owen White, who was part of the team that sequenced and analyzed the first genome of a free-living organism to be decoded, the bacterium *Haemophilus influenzae*. Dr. White built a software system to find the genes (places in the DNA sequence that encode a protein), the transfer RNA, and other features, and to make

initial assignments of function to those genes. Most current genome annotation systems work similarly, but the programs available for analysis of genomic DNA are constantly changing and improving.

Computational evolutionary biology

Evolutionary biology is the study of the origin and descent of species, as well as their change over time. Informatics has assisted evolutionary biologists in several key ways; it has enabled researchers to:

- trace the evolution of a large number of organisms by measuring changes in their DNA, rather than through physical taxonomy or physiological observations alone,
- more recently, compare entire genomes, which permits the study of more complex evolutionary events, such as gene duplication, horizontal gene transfer, and the prediction of factors important in bacterial speciation,
- build complex computational models of populations to predict the outcome of the system over time
- track and share information on an increasingly large number of species and organisms

Future work endeavours to reconstruct the now more complex tree of life.

The area of research within computer science that uses genetic algorithms is sometimes confused with computational evolutionary biology, but the two areas are unrelated.

Measuring biodiversity

Biodiversity of an ecosystem might be defined as the total genomic complement of a particular environment, from all of the species present, whether it is a biofilm in an abandoned mine, a drop of sea water, a scoop of soil, or the entire biosphere of the planet Earth. Databases are used to collect the species names, descriptions, distributions, genetic information, status and size of populations, habitat needs, and how each organism interacts with other species. Specialized software programs are used to find, visualize, and analyze the information, and most importantly, communicate it to other people. Computer simulations model such things as population dynamics, or calculate the cumulative genetic health of a breeding pool (in agriculture) or endangered population (in conservation). One very exciting potential of this field is that entire DNA sequences, or genomes of endangered species can be preserved, allowing the results of Nature's genetic experiment to be remembered *in silico*, and possibly reused in the future, even if that species is eventually lost.[1]

Analysis of gene expression

The expression of many genes can be determined by measuring mRNA levels with multiple techniques including microarrays, expressed cDNA sequence tag (EST) sequencing, serial analysis of gene expression (SAGE) tag sequencing, massively parallel signature sequencing (MPSS), or various applications of multiplexed in-situ hybridization. All of these techniques are extremely noise-prone and/or subject to bias in the biological measurement, and a major research area in computational biology involves developing statistical tools to separate signal from noise in high-throughput gene expression studies. Such studies are often used to determine the genes implicated in a disorder: one might compare microarray data from cancerous epithelial cells to data from non-cancerous cells to determine the transcripts that are up-regulated and down-regulated in a particular population of cancer

cells.

Analysis of regulation

Regulation is the complex orchestration of events starting with an extracellular signal such as a hormone and leading to an increase or decrease in the activity of one or more proteins. Bioinformatics techniques have been applied to explore various steps in this process. For example, promoter analysis involves the identification and study of sequence motifs in the DNA surrounding the coding region of a gene. These motifs influence the extent to which that region is transcribed into mRNA. Expression data can be used to infer gene regulation: one might compare microarray data from a wide variety of states of an organism to form hypotheses about the genes involved in each state. In a single-cell organism, one might compare stages of the cell cycle, along with various stress conditions (heat shock, starvation, etc.). One can then apply clustering algorithms to that expression data to determine which genes are co-expressed. For example, the upstream regions (promoters) of co-expressed genes can be searched for over-represented regulatory elements.

Analysis of protein expression

Protein microarrays and high throughput (HT) mass spectrometry (MS) can provide a snapshot of the proteins present in a biological sample. Bioinformatics is very much involved in making sense of protein microarray and HT MS data; the former approach faces similar problems as with microarrays targeted at mRNA, the latter involves the problem of matching large amounts of mass data against predicted masses from protein sequence databases, and the complicated statistical analysis of samples where multiple, but incomplete peptides from each protein are detected.

Analysis of mutations in cancer

In cancer, the genomes of affected cells are rearranged in complex or even unpredictable ways. Massive sequencing efforts are used to identify previously unknown point mutations in a variety of genes in cancer. Bioinformaticians continue to produce specialized automated systems to manage the sheer volume of sequence data produced, and they create new algorithms and software to compare the sequencing results to the growing collection of human genome sequences and germline polymorphisms. New physical detection technology are employed, such as oligonucleotide microarrays to identify chromosomal gains and losses (called comparative genomic hybridization), and single nucleotide polymorphism arrays to detect known *point mutations*. These detection methods simultaneously measure several hundred thousand sites throughout the genome, and when used in high-throughput to measure thousands of samples, generate terabytes of data per experiment. Again the massive amounts and new types of data generate new opportunities for bioinformaticians. The data is often found to contain considerable variability, or noise, and thus Hidden Markov model and change-point analysis methods are being developed to infer real copy number changes.

Another type of data that requires novel informatics development is the analysis of lesions found to be recurrent among many tumors .

Prediction of protein structure

Protein structure prediction is another important application of bioinformatics. The amino acid sequence of a protein, the so-called primary structure, can be easily determined from the sequence on the gene that codes for it. In the vast majority of cases, this primary structure uniquely determines a structure in its native environment. (Of course, there are exceptions, such as the bovine spongiform encephalopathy - aka Mad Cow Disease - prion.) Knowledge of this structure is vital in understanding the function of the protein. For lack of better terms, structural information is usually classified as one of *secondary*, *tertiary* and *quaternary* structure. A viable general solution to such predictions remains an open problem. As of now, most efforts have been directed towards heuristics that work most of the time.

One of the key ideas in bioinformatics is the notion of homology. In the genomic branch of bioinformatics, homology is used to predict the function of a gene: if the sequence of gene *A*, whose function is known, is homologous to the sequence of gene *B,* whose function is unknown, one could infer that B may share A's function. In the structural branch of bioinformatics, homology is used to determine which parts of a protein are important in structure formation and interaction with other proteins. In a technique called homology modeling, this information is used to predict the structure of a protein once the structure of a homologous protein is known. This currently remains the only way to predict protein structures reliably.

One example of this is the similar protein homology between hemoglobin in humans and the hemoglobin in legumes (leghemoglobin). Both serve the same purpose of transporting oxygen in the organism. Though both of these proteins have completely different amino acid sequences, their protein structures are virtually identical, which reflects their near identical purposes.

Other techniques for predicting protein structure include protein threading and *de novo* (from scratch) physics-based modeling.

See also: structural motif and structural domain.

Comparative genomics

The core of comparative genome analysis is the establishment of the correspondence between genes (orthology analysis) or other genomic features in different organisms. It is these intergenomic maps that make it possible to trace the evolutionary processes responsible for the divergence of two genomes. A multitude of evolutionary events acting at various organizational levels shape genome evolution. At the lowest level, point mutations affect individual nucleotides. At a higher level, large chromosomal segments undergo duplication, lateral transfer, inversion, transposition, deletion and insertion. Ultimately, whole genomes are involved in processes of hybridization, polyploidization and endosymbiosis, often leading to rapid speciation. The complexity of genome evolution poses many exciting challenges to developers of mathematical models and algorithms, who have recourse to a spectra of algorithmic, statistical and mathematical techniques, ranging from exact, heuristics, fixed parameter and approximation algorithms for problems based on parsimony models to Markov Chain Monte Carlo algorithms for Bayesian analysis of problems based on probabilistic models.

Many of these studies are based on the homology detection and protein families computation.

Modeling biological systems

Systems biology involves the use of computer simulations of cellular subsystems (such as the networks of metabolites and enzymes which comprise metabolism, signal transduction pathways and gene regulatory networks) to both analyze and visualize the complex connections of these cellular processes. Artificial life or virtual evolution attempts to understand evolutionary processes via the computer simulation of simple (artificial) life forms.

High-throughput image analysis

Computational technologies are used to accelerate or fully automate the processing, quantification and analysis of large amounts of high-information-content biomedical imagery. Modern image analysis systems augment an observer's ability to make measurements from a large or complex set of images, by improving accuracy, objectivity, or speed. A fully developed analysis system may completely replace the observer. Although these systems are not unique to biomedical imagery, biomedical imaging is becoming more important for both diagnostics and research. Some examples are:

- high-throughput and high-fidelity quantification and sub-cellular localization (high-content screening, cytohistopathology)
- morphometrics
- clinical image analysis and visualization
- determining the real-time air-flow patterns in breathing lungs of living animals
- quantifying occlusion size in real-time imagery from the development of and recovery during arterial injury
- making behavioral observations from extended video recordings of laboratory animals
- infrared measurements for metabolic activity determination
- inferring clone overlaps in DNA mapping, e.g. the Sulston score

Protein-protein docking

In the last two decades, tens of thousands of protein three-dimensional structures have been determined by X-ray crystallography and Protein nuclear magnetic resonance spectroscopy (protein NMR). One central question for the biological scientist is whether it is practical to predict possible protein-protein interactions only based on these 3D shapes, without doing protein-protein interaction experiments. A variety of methods have been developed to tackle the Protein-protein docking problem, though it seems that there is still much work to be done in this field.

Software and tools

Software tools for bioinformatics range from simple command-line tools, to more complex graphical programs and standalone web-services available from various bioinformatics companies or public institutions. The computational biology tool best-known among biologists is probably BLAST, an algorithm for determining the similarity of arbitrary sequences against other sequences, possibly from curated databases of protein or DNA sequences. BLAST is one of a number of generally available programs for doing sequence alignment. The NCBI provides a popular web-based implementation that searches their databases.

Web services in bioinformatics

SOAP and REST-based interfaces have been developed for a wide variety of bioinformatics applications allowing an application running on one computer in one part of the world to use algorithms, data and computing resources on servers in other parts of the world. The main advantages lay in the end user not having to deal with software and database maintenance overheads. Basic bioinformatics services are classified by the EBI into three categories: SSS (Sequence Search Services), MSA (Multiple Sequence Alignment) and BSA (Biological Sequence Analysis). The availability of these service-oriented bioinformatics resources demonstrate the applicability of web based bioinformatics solutions, and range from a collection of standalone tools with a common data format under a single, standalone or web-based interface, to integrative, distributed and extensible bioinformatics workflow management systems.

See also

Related topics

- Biocybernetics
- Bioinformatics companies
- Biologically inspired computing
- Biomedical informatics
- Computational biology
- Computational biomodeling
- Computational genomics
- DNA sequencing theory
- Dot plot (bioinformatics)
- Dry lab
- Margaret Oakley Dayhoff
- Metabolic network modelling
- Molecular Design software
- Morphometrics
- Natural computation
- Pharmaceutical company
- Protein-protein interaction prediction
- List of nucleic acid simulation software
- List of numerical analysis software
- List of protein structure prediction software
- List of scientific journals in bioinformatics

Related fields

- Applied mathematics
- Artificial intelligence
- Biology
- Cheminformatics
- Clinomics
- Comparative genomics
- Computational biology
- Computational epigenetics
- Computational science
- Computer science
- Cybernetics
- Ecoinformatics
- Genomics
- Informatics
- Information theory
- Mathematical biology
- Molecular modelling
- Neuroinformatics
- Proteomics
- Pervasive adaptation
- Scientific computing
- Statistics
- Structural biology
- Systems biology
- Theoretical biology
- Veterinary informatics

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- Computational Biology: Genomes, Networks, Evolution Free MIT Course (http://ocw.mit.edu/OcwWeb/Electrical-Engineering-and-Computer-Science/6-895Fall-2005/CourseHome/index.htm)
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External links

- Major Organizations
  - Bioinformatics Organization (Bioinformatics.Org): The Open-Access Institute (http://bioinformatics.org/)
  - EMBnet (http://www.embnet.org/)
  - European Bioinformatics Institute (http://www.ebi.ac.uk/)
  - European Molecular Biology Laboratory (http://www.embl.org/)
  - The International Society for Computational Biology (http://www.iscb.org/)
  - National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/)
  - National Institutes of Health homepage (http://www.nih.gov)
  - Open Bioinformatics Foundation: umbrella non-profit organization supporting certain open-source projects in bioinformatics (http://www.open-bio.org/)
  - Swiss Institute of Bioinformatics
  - Wellcome Trust Sanger Institute
- Major Journals
  - Algorithms in Molecular Biology (http://www.almob.org/)
  - Bioinformatics (http://bioinformatics.oupjournals.org/)
  - BMC Bioinformatics (http://www.biomedcentral.com/bmcbioinformatics)
  - Briefings in Bioinformatics (http://bib.oxfordjournals.org/)
  - Journal of Advanced Research in Bioinformatics (http://www.i-asr.org/jarb.html)
  - Evolutionary Bioinformatics (http://www.la-press.com/evolbio.htm)
  - Genome Research (http://www.genome.org)
  - The International Journal of Biostatistics (http://www.bepress.com/ijb/)
  - Journal of Computational Biology (http://www.liebertpub.com/publication.aspx?pub_id=31)
  - Cancer Informatics (http://la-press.com/journal.php?pa=description&journal_id=10)
  - Journal of the Royal Society Interface (http://publishing.royalsociety.org/index.cfm?page=1058)
  - Molecular Systems Biology (http://www.nature.com/msb/index.html)
  - PLoS Computational Biology (http://compbiol.plosjournals.org)
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  - International Journal of Bioinformatics Research and Applications (http://www.inderscience.com/browse/index.php?journalcode=ijbra)
  - List of Bioinformatics journals (http://www.bioinformatics.fr/journals.php) at Bioinformatics.fr
  - EMBnet.News (http://www.embnet.org) at EMBnet.org
  - International Journal of Computational Biology and Drug Design (IJCBDD)
  - International Journal of Functional Informatics and Personalized Medicine (IJFIPM)
- Other sites
  - The exhaustive bioinformatics information resource directory including servers, tools, database links and bioinformatics companies (http://bionet.awardspace.info/)

  - The Collection of Biostatistics Research Archive (http://www.biostatsresearch.com/repository/)
  - Human Genome Project and Bioinformatics (http://www.ornl.gov/TechResources/Human_Genome/research/informatics.html)
  - List of Bioinformatics Research Groups (http://www.bioinformatics.fr/laboratories.php) at Bioinformatics.fr
  - List of Bioinformatics Research Groups (http://www.dmoz.org/Science/Biology/Bioinformatics/Research_Groups//) at the Open Directory Project
- Tutorials / Resources / Primers
  - Bioinformatics - A Science Primer (http://www.ncbi.nlm.nih.gov/About/primer/bioinformatics.html) — by NCBI
  - A bioinformatics directory (http://bioinformatics.co.nr/)

See also

- International Society of Intelligent Biological Medicine (ISIBM)

Quantum Biology

Quantum chemistry is a branch of theoretical chemistry, which applies quantum mechanics and quantum field theory to address issues and problems in chemistry. The description of the electronic behavior of atoms and molecules as pertaining to their reactivity is one of the applications of quantum chemistry. Quantum chemistry lies on the border between chemistry and physics, and significant contributions have been made by scientists from both fields. It has a strong and active overlap with the field of atomic physics and molecular physics, as well as physical chemistry.

Quantum chemistry mathematically describes the fundamental behavior of matter at the molecular scale.[1] It is, in principle, possible to describe all chemical systems using this theory. In practice, only the simplest chemical systems may realistically be investigated in purely quantum mechanical terms, and approximations must be made for most practical purposes (e.g., Hartree-Fock, post Hartree-Fock or Density functional theory, see computational chemistry for more details). Hence a detailed understanding of quantum mechanics is not necessary for most chemistry, as the important implications of the theory (principally the orbital approximation) can be understood and applied in simpler terms.

In quantum mechanics the Hamiltonian, or the physical state, of a particle can be expressed as the sum of two operators, one corresponding to kinetic energy and the other to potential energy. The Hamiltonian in the Schrödinger wave equation used in quantum chemistry does not contain terms for the spin of the electron.

Solutions of the Schrödinger equation for the hydrogen atom gives the form of the wave function for atomic orbitals, and the relative energy of the various orbitals. The orbital approximation can be used to understand the other atoms e.g. helium, lithium and carbon.

History

The **history of quantum chemistry** essentially began with the 1838 discovery of cathode rays by Michael Faraday, the 1859 statement of the black body radiation problem by Gustav Kirchhoff, the 1877 suggestion by Ludwig Boltzmann that the energy states of a physical system could be discrete, and the 1900 quantum hypothesis by Max Planck that any energy radiating atomic system can theoretically be divided into a number of discrete energy elements ε such that each of these energy elements is proportional to the frequency ν with which they each individually radiate energy, as defined by the following formula:

$$\epsilon = h\nu$$

where h is a numerical value called Planck's Constant. Then, in 1905, to explain the photoelectric effect (1839), i.e., that shining light on certain materials can function to eject electrons from the material, Albert Einstein postulated, based on Planck's quantum hypothesis, that light itself consists of individual quantum particles, which later came to be called photons (1926). In the years to follow, this theoretical basis slowly began to be applied to chemical structure, reactivity, and bonding.

Electronic structure

The first step in solving a quantum chemical problem is usually solving the Schrödinger equation (or Dirac equation in relativistic quantum chemistry) with the electronic molecular Hamiltonian. This is called determining the **electronic structure** of the molecule. It can be said that the electronic structure of a molecule or crystal implies essentially its chemical properties. An exact solution for the Schrödinger equation can only be obtained for the hydrogen atom. Since all other atomic, or molecular systems, involve the motions of three or more "particles", their Schrödinger equations cannot be solved exactly and so approximate solutions must be sought.

Wave model

The foundation of quantum mechanics and quantum chemistry is the **wave model**, in which the atom is a small, dense, positively charged nucleus surrounded by electrons. Unlike the earlier Bohr model of the atom, however, the wave model describes electrons as "clouds" moving in orbitals, and their positions are represented by probability distributions rather than discrete points. The strength of this model lies in its predictive power. Specifically, it predicts the pattern of chemically similar elements found in the periodic table. The wave model is so named because electrons exhibit properties (such as interference) traditionally associated with waves. See wave-particle duality.

Valence bond

Although the mathematical basis of quantum chemistry had been laid by Schrödinger in 1926, it is generally accepted that the first true calculation in quantum chemistry was that of the German physicists Walter Heitler and Fritz London on the hydrogen (H_2) molecule in 1927. Heitler and London's method was extended by the American theoretical physicist John C. Slater and the American theoretical chemist Linus Pauling to become the **Valence-Bond (VB)** [or **Heitler-London-Slater-Pauling (HLSP)**] method. In this method, attention is primarily devoted to the pairwise interactions between atoms, and this method therefore correlates closely with classical chemists' drawings of bonds.

Molecular orbital

An alternative approach was developed in 1929 by Friedrich Hund and Robert S. Mulliken, in which electrons are described by mathematical functions delocalized over an entire molecule. The **Hund-Mulliken** approach or **molecular orbital (MO) method** is less intuitive to chemists, but has turned out capable of predicting spectroscopic properties better than the VB method. This approach is the conceptional basis of the **Hartree-Fock method** and further post Hartree-Fock methods.

Density functional theory

The **Thomas-Fermi model** was developed independently by Thomas and Fermi in 1927. This was the first attempt to describe many-electron systems on the basis of electronic density instead of wave functions, although it was not very successful in the treatment of entire molecules. The method did provide the basis for what is now known as **density functional theory**. Though this method is less developed than post Hartree-Fock methods, its lower computational requirements allow it to tackle larger polyatomic molecules and even macromolecules, which has made it the most used method in computational chemistry at present.

Chemical dynamics

A further step can consist of solving the Schrödinger equation with the total molecular Hamiltonian in order to study the motion of molecules. Direct solution of the Schrödinger equation is called *quantum molecular dynamics*, within the semiclassical approximation *semiclassical molecular dynamics*, and within the classical mechanics framework *molecular dynamics (MD)*. Statistical approaches, using for example Monte Carlo methods, are also possible.

Adiabatic chemical dynamics

In **adiabatic dynamics**, interatomic interactions are represented by single scalar potentials called potential energy surfaces. This is the Born-Oppenheimer approximation introduced by Born and Oppenheimer in 1927. Pioneering applications of this in chemistry were performed by Rice and Ramsperger in 1927 and Kassel in 1928, and generalized into the RRKM theory in 1952 by Marcus who took the transition state theory developed by Eyring in 1935 into account. These methods enable simple estimates of unimolecular reaction rates from a few characteristics of the potential surface.

Non-adiabatic chemical dynamics

Non-adiabatic dynamics consists of taking the interaction between several coupled potential energy surface (corresponding to different electronic quantum states of the molecule). The coupling terms are called **vibronic couplings**. The pioneering work in this field was done by Stueckelberg, Landau, and Zener in the 1930s, in their work on what is now known as the Landau-Zener transition. Their formula allows the transition probability between two diabatic potential curves in the neighborhood of an avoided crossing to be calculated.

Quantum chemistry and quantum field theory

The application of quantum field theory (QFT) to chemical systems and theories has become increasingly common in the modern physical sciences. One of the first and most fundamentally explicit appearances of this is seen in the theory of the photomagneton. In this system, plasmas, which are ubiquitous in both physics and chemistry, are studied in order to determine the basic quantization of the underlying bosonic field. However, quantum field theory is of interest in many fields of chemistry, including: nuclear chemistry, astrochemistry, sonochemistry, and quantum hydrodynamics. Field theoretic methods have also been critical in developing the ab initio Effective Hamiltonian theory of semi-empirical pi-electron methods.

See also

- Atomic physics
- Computational chemistry
- Condensed matter physics
- International Academy of Quantum Molecular Science
- Physical chemistry
- Quantum chemistry computer programs
- Quantum electrochemistry
- QMC@Home
- Theoretical physics

Further reading

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- Pauling, L., and Wilson, E. B. *Introduction to Quantum Mechanics with Applications to Chemistry* (Dover Publications) ISBN 0-486-64871-0
- Atkins, P.W. *Physical Chemistry* (Oxford University Press) ISBN 0-19-879285-9
- McWeeny, R. *Coulson's Valence* (Oxford Science Publications) ISBN 0-19-855144-4
- Landau, L.D. and Lifshitz, E.M. *Quantum Mechanics:Non-relativistic Theory* (Course of Theoretical Physics vol.3) (Pergamon Press)
- Bernard Pullman and Alberte Pullman. 1963. *Quantum Biochemistry.*, New York and London: Academic Press.
- Eric R. Scerri, The Periodic Table: Its Story and Its Significance, Oxford University Press, 2006. Considers the extent to which chemistry and especially the periodic system has been reduced to quantum mechanics. ISBN 0-19-530573-6.
- Simon, Z. 1976. *Quantum Biochemistry and Specific Interactions.*, Taylor & Francis; ISBN 978-0856260872 and ISBN 0-85-6260878 .

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[1] http://cmm.cit.nih.gov/modeling/guide_documents/quantum_mechanics_document.html|"Quantum Chemistry". *The NIH Guide to Molecular Modeling*. National Institutes of Health. http://cmm.cit.nih.gov/modeling/guide_documents/quantum_mechanics_document.html. Retrieved on 2007-09-08.

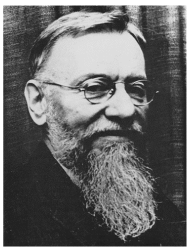
External links

- The Sherrill Group - Notes (http://vergil.chemistry.gatech.edu/notes/index.html)
- ChemViz Curriculum Support Resources (http://www.shodor.org/chemviz/)
- Early ideas in the history of quantum chemistry (http://www.quantum-chemistry-history.com/)

Nobel lectures by quantum chemists

- Walter Kohn's Nobel lecture (http://nobelprize.org/chemistry/laureates/1998/kohn-lecture.html)
- Rudolph Marcus' Nobel lecture (http://nobelprize.org/chemistry/laureates/1992/marcus-lecture.html)
- Robert Mulliken's Nobel lecture (http://nobelprize.org/chemistry/laureates/1966/mulliken-lecture.html)
- Linus Pauling's Nobel lecture (http://nobelprize.org/chemistry/laureates/1954/pauling-lecture.html)
- John Pople's Nobel lecture (http://nobelprize.org/chemistry/laureates/1998/pople-lecture.html)

Nicolas Rashevsky

Nicolas Rashevsky	
 Nicolas Rashevsky	
Born	9 November, 1899 Chernigov, Ukraine
Died	January 16, 1972 Michigan, United States
Residence	US
Nationality	US and Russian
Ethnicity	Russian
Fields	Theoretical physicist, Mathematical biology
Institutions	University of Chicago, Ann Arbor, Michigan
Alma mater	Kiev University, University of Chicago
Religious stance	Orthodox

Nicholas Rashevsky (1899-1972) was a Ukranian-American theoretical biologist who pioneered mathematical biology.[1] [2] [3] [4]

He was trained as a theoretical physicist in Russia and immigrated to the USA in 1924, where he worked for Westinghouse Research Labs in Pittsburgh where he got interested in the physics of cell division. In 1934 he went to the University of Chicago on a Rockefeller Fellowship and became an assistant professor in the Department of Physiology. In 1938 he published the first edition of his magnum opus *Mathematical Biophysics* and in 1939 founded the first mathematical biology international journal entitled the *Bulletin of Mathematical Biophysics*.

His later efforts focused on topology of biological systems and the formulation of fundamental principles in biology and hierarchical organization of organisms and human societies[5] [6] . He also introduced the concept of "organismic sets", that was later developed by other authors[7] through applications of category theory to relational biology [8] , organismic supercategories and Complex Systems Biology[9] .

However his ideas found little support amongst practicing experimental or molecular biologists, and in 1954 the budget for his Committee of Mathematical Biology was drastically cut; however, this was at least in part politically, rather than scientifically, motivated.

Notes & References

This article incorporates material from Nicholas Rashevsky on PlanetMath, which is licensed under the GFDL.; the article also incorporates additonal data from planetphysics.org [65]

[1] http://planetphysics.org/encyclopedia/NicolasRashevsky.html Nicolas Rashevky's Biography
[2] http://www.smb.org/ The Society for Mathematical Biology
[3] Robert Rosen *Essays on Life* (2004).
[4] Evelyn Fox Keller *Making Sense of Life* pp. 82-89
[5] http://planetphysics.org/encyclopedia/NicolasRashevsky.html Nicolas Rashevsk's biography
[6] http://planetphysics.org/encyclopedia/BiographiesOnPlanetPhysicsOrg.html
[7] Planet Math page (http://planetmath.org/encyclopedia/NicolasRashevsky.html)
[8] http://planetphysics.org/encyclopedia/AbstractRelationalBiologyARB.html Abstract Relational Biology and Category Theory Representations of Functional Organisms and Societies
[9] http://planetphysics.org/encyclopedia/OrganismicSupercategoriesAndSuperComplexSystemBiodynamics.html Organismic Supercategories and Complex Systems Biology

Links

- Books by Rashevsky (http://openlibrary.org/a/OL2010564A/Nicolas-Rashevsky)

George Karreman

George Karreman	
 George Karreman	
Born	9 November, 1921 Rotterdam, Netherlands
Died	January 23, 1997 Philadelphia, United States
Fields	physics, Mathematical biology
Institutions	University of Pennsylvania
Academic advisors	Nicolas Rashevsky, Hendrik Anthony Kramers
Known for	Quantum biology

George Karreman, PhD, MA (Hon) (4 November, 1920 in Rotterdam, Netherlands – 23 January, 1997 in Philadelphia, USA) was a Dutch-born US physicist, mathematical biophysicist and mathematical/theoretical biologist, first President of the Society for Mathematical Biology[1] (SMB).

George Karreman's father, from whom he may have inherited many of his mathematical skills, was Chief Engineer for the Dutch Merchant Marine. He studied at Leiden University. He received his B.S. in Physics and Mathematics in 1939. He obtained his M.S. [Doctorandus(Drs.)] in Theoretical Physics in 1941 under professor Kramers one month before the University was closed.

Career

George Karreman earned his B.S. in Physics and Mathematics in 1939. He completed in 1941 his M.S. (*Doctorandus(Drs.)*) in Theoretical Physics under professor Hendrik Anthony Kramers one month before Leiden University was closed during WWII. For the remainder of the second World War he kept food on the table of his family by tutoring students in physics and mathematics[2]

He was awarded a University of Chicago Fellowship that allowed him financially to complete a Ph.D. in Mathematical Biology in 1951 under the supervision of the Founder of Mathematical Biophysics and Mathematical Biology, professor Nicolas Rashevsky[3] . Dr. Karreman worked as a scientific research Advisor to Dr. Albert Szent-Gyorgi at the Institute for Muscle Research at the Marine Biological Laboratory in Woods Hole. To follow his keen interest in mathematics applied to physiology and medicine in 1957 he moved to Philadelphia, where he was appointed to Senior Medical Research Scientist at the Eastern

omonth after his second child was born he was appointed Associate Professor of Physiology at the University of Pennsylvania School of Medicine. He also worked at the Bockus Research Institute at the Graduate Hospital. In 1970 he was appointed full Professor of Physiology at the same university, where he held this position until his retirement in 1983, when he was named the first Professor of Emeritus of Mathematical Biology. He continued to be active in research. Among his interests were: mathematical biology and mathematical biophysics, membrane biophysics, photsynthetic mechanisms, quantum biochemistry and quantum biophysics, biological energy transfer; quantum biology, physiological irritability, mathematical and systems analysis of cardiovascular and other biosystems; cooperative and threshold phenomena in biomembranes, adsorption mechanisms at membrane surfaces.

Dr. George Karreman was Co-Founder (together with drs. H. Landahl and A. Bartholomay) and the first president of the Society for Mathematical Biology. He was also a member of: the American Physiological Society, the New York Academy of Sciences, the Franklin Institute, the Society for Supramolecular Biology, Sigma Xi, the Physiological Society of Philadelphia, and the Society for Vascular System Dynamics.

Biography

After having seen a book on Mathematical Biophysics by Nicholas Rashevsky, in August 1948 he came to Chicago with a ten day visitor's visa and $100 in his pocket and he contacted Rashevsky at the University of Chicago, where he became Rashevsky's PhD student in Mathematical Biophysics. In 1950 he was only the third cardiac patient to undergo successful coarctation surgery at the University of Chicago. In 1953 he married Anneke Halbertsma and they moved to Cape Cod, Massachusetts where their first child, Grace, was born in 1954. His first son, Frank Karreman was born in 1958, and in 1962 his second son, Hubert-Jan was born. George Karreman was an exceptionally devoted educator, an inspiration to his students, research associates, family, and friends; he was also a generous man, obviously having not forgotten Rashevsky's generosity to him in his early life in Chicago. All of his children received advanced degrees from the University of Pennsylvania in several fields. He had a wide interest in his readings, a keen interest in the fine arts, such as paintings, an advanced chess player, and a most devoted husband and father. In his later years, he further developed his interests in painting and sculpture, and was also a frequent traveller to the Pacific Northwest where his son and daughter lived with their families.

Dr. Karreman passed away on February 27, 1997 at the age of 76. He is survived by his wife Anneke, his children Grace, Frank and Hubert-Jan, Daughter-in-law Jennifer, Grand-daughter Nancy, his brother Herman, and his sister-in-law Erna.

Honours

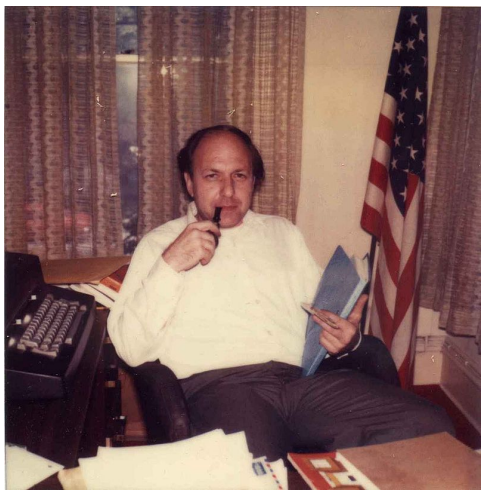
- 1974 – first president of the Society for Mathematical Biology

References

[1] http://www.smb.org/
[2] In Memory of GEORGE KARREMAN, Communicated by the Chairman of Dr. Karreman's department, Paul De Weer (http://www.smb.org/governance/karreman.shtml)
[3] http://planetphysics.org/encyclopedia/NicolasRashevsky.html Nicolas Rashevsky's Biography, by I.C. Baianu, PhD.

Robert Rosen

See also arts and entertainment celebrity producer-writer-performer: Robert M. Rosen, Robert Ozn


Robert Rosen

Robert Rosen (27 June, 1934, - 28 December, 1998, Rochester, New York) was an American theoretical biologist and professor of Biophysics at Dalhousie University.

Biography

Robert Rosen was born on June 27, 1934 in Brownsville (a section of Brooklyn), in New York City. He studied biology, mathematics, physics, philosophy, and history-- especially the history of science-- and eventually became a student of physicist and theoretical biologist, Professor Nicholas Rashevsky at the University of Chicago. He received his PhD in Relational Biology from the University of Chicago in 1959 and remained there until 1964.[1] In 1964 Rosen was offered a full professorship with tenure at the University of Buffalo, now known as the State University of New York (SUNY) at Buffalo, holding a joint appointment at the Center for Theoretical Biology. In 1970, he took a sabbatical and spent a year as a Visiting Fellow at Robert Hutchins' Center for the Study of Democratic Institutions, in Santa Barbara, California. It was a seminal year for him, leading to the conception and development of what he later called Anticipatory Systems Theory, a corollary of his larger theoretical work on relational complexity, in which it is embedded. In 1975, he left Buffalo and accepted a position at Dalhousie University, in Halifax, Nova Scotia, as a Killam Research Professor in the Department of Physiology & Biophysics, where he remained until he took early retirement in 1994.[2]

He was president of the Society for General Systems Research, (now the ISSS), in 1980-81.

Work

Rosen's research was concerned with the most fundamental aspects of biology, specifically the question "What is life?" or "Why are living organisms alive?". Major themes in the work of Robert Rosen were:

- developing a specific definition of complexity that is based on relations and, by extension, principles of organization
- developing a rigorous theoretical foundation for living organisms as "anticipatory systems"

Rosen came to realize that the contemporary model of physics - which is still based on the Cartesian/Newtonian world of mechanisms - was inadequate to explain or describe the behavior of biological systems; that is, one could not properly answer the question "what is life?" from within a scientific foundation that is entirely reductionistic. Approaching organisms with reductionistic scientific methods and practices always sacrifices the whole in order to study the parts, but what Rosen discovered was that the whole could not be recaptured once the organization had been destroyed. His conclusion was that the very thing about living organisms biologists should be studying, the organization, was the first aspect of all biological systems to be thrown away in scientific analysis. This is a limitation of contemporary science when science regards the machine as a model for all systems in the universe. Rosen came to regard the machine metaphor as the single biggest impediment to scientific exploration of questions in biology and concluded that the paradigm needs to be expanded beyond purely reductionist capabilities. In order to do this properly, he said there must be a sound theoretical foundation underlying the expansion and that relational complexity provided such a foundation. So it was that, rather than biology being a mere subset of already-known physics, it turned out that biology had profound lessons for physics, and science in general.[3]

Notion of the scientific model

The clarification of the notion of the scientific model: Rosen maintained that modeling is the essence of science and of thought. His book *Anticipatory Systems* describes, in detail, what he termed the modeling relation. He showed the deep differences between a true modeling relation and a simulation, which is not based on such a relation. In biology he is known by some for a class of relational models called "(M,R)-Systems" that he devised, which he said capture the minimal capabilities a material system would have to manifest to justify calling it a "alive". In this class of system, M stands for metabolism and R stands for Repair. Thus, his mode for determining life or defining life in any given system is a functional one, not a material one.

Relational biology

Rosen's work proposes a methodology he calls "relational analysis" which needs to be developed in addition to the current capability of reductionistic science. ("Relational" is a term he attributes to Nicholas Rashevsky.) Rosen’s "relational biology" maintains that organisms, indeed all systems, have a distinct quality called "organization" not captured by the language of reductionism. It has to do with more than purely structural or material aspects. For example, organization includes all relations between material parts, relations between the effects of interactions of the material parts, and relations with time and environment, to name a few. Many people sum up this aspect of complex systems by saying

that "The whole is more than the sum of the parts". Relations between parts and between the effects of interactions must be considered as additional parts, in some sense. Organization, Rosen says, must be independent from the material particles which seemingly constitute a living system. As he put it: "The human body completely changes the matter it is made of roughly every 8 weeks, through metabolism and repair. Yet, you're still you--with all your memories, your personality... If science insists on chasing the particles, they will follow them right through an organism and miss the organism entirely," (as told to his daughter, Judith Rosen).

He goes very far in this direction claiming that when studying a complex system, we can "throw away the matter and study the organization" to learn essential things about an entire class of systems, in general. He supports this claim (actually it is a quote which he also attributes to Rashevsky) based on the fact that living organisms are a class of systems with an extremely wide range of material "ingredients", different structures, different habitats, different modes of living and reproducing, and yet we are somehow able to recognize them all as "living". In contrast, a study of the specific material details of any given organism, or even of a whole species, will only tell us about how that type of organism "does it". Such a study doesn't approach what is common to all living organisms, i.e.; life. Relational approaches in biology allow us to study organisms in ways that preserve the qualities we are trying to learn about.

Biochemistry and Genetics

Rosen also questioned many aspects of mainstream interpretations of biochemistry and genetics. He objects to the idea that functional aspects in biological systems can be investigated via a material focus. One example: Rosen disputes that the functional capability of a biologically active protein can be investigated purely using the genetically encoded sequence of amino acids. This is because, he said, a protein must undergo a process of "folding" to attain its characteristic three-dimensional shape before it can become functionally active in the system. Yet, only the amino acid sequence is genetically coded. The mechanisms by which proteins fold are not completely known. He concluded, based on examples such as this, that phenotype cannot always be directly attributed to genotype and that the chemically active aspect of a biologically active protein relies on more than the sequence of amino acids, from which it was constructed: There must be other factors at work.

Questions about Rosen's arguments were raised in a paper authored by Christopher Landauer and Kirstie L. Bellman which claims that some of the mathematical formulations used by Rosen are problematic. (Note, by Judith Rosen, who owns the copyrights to her father's books: Some of the confusion is due to known errata introduced into the book, "Life, Itself," by the publisher. For example, the diagram that refers to "(M,R)-Systems" has more than one error; errors which do not exist in Rosen's manuscript for the book. These errata were made known to Columbia University Press when the company switched from hardcover to paperback version of the book (in 2006) but the errors were not corrected and remain in the paperback version as well. The book "Anticipatory Systems; Philosophical, Mathematical, and Methodological Foundations" has the same diagram, correctly represented.)

See also

- Autopoiesis
- system theory
- philosophy of science

Publications

Rosen has written several books and articles. A selection: [4]

- 1970, *Dynamical Systems Theory in Biology* New York: Wiley Interscience.
- 1970, *Optimality Principles*, Rosen Enterprises
- 1978, *Fundamentals of Measurement and Representation of Natural Systems*, Elsevier Science Ltd,
- 1985, *Anticipatory Systems: Philosophical, Mathematical and Methodological Foundations*. Pergamon Press.
- 1991, *Life Itself: A Comprehensive Inquiry into the Nature, Origin, and Fabrication of Life*, Columbia University Press

Published posthumously:

- 2000, *Essays on Life Itself*, Columbia University Press.
- 2003, "Anticipatory Systems; Philosophical, Mathematical, and Methodolical Foundations", Rosen Enterprises
- 2003, *Rosennean Complexity*, Rosen Enterprises.
- 2003, *The Limits of the Limits Of Science*, Rosen Enterprises

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[1] (http://www.rosen-enterprises.com/RobertRosen/rrosenautobio.html)
[2] In Memory Dr. Robert Rosen (http://communications.medicine.dal.ca/connection/feb1999/rosen.htm), feb 1999, retrieved Oct 2007.
[3] Robert Rosen - Biology, Complexity and Physics (http://www.panmere.com/rosen/rosensum.htm)
[4] A complete Bibliography (http://users.viawest.net/~keirsey/rosenbiblio.html) of Robert Rosens publications.

External links

- Rosen Enterprises (http://www.rosen-enterprises.com) Judith Rosen's website providing biographical information, discussion of, and reprints of the work of Robert Rosen.
- (http://www.rosen-enterprises.com/RobertRosen/rrosenautobio.html) Autobiographical Reminiscences of Robert Rosen; about his educational background, his philosophy of science, and his general point of view.
- Rosen: Complexity and Life (http://www.panmere.com/''Robert) A website exploring the work of Rosen.
- Robert Rosen: June 27, 1934 — December 30, 1998 (http://www.people.vcu.edu/~mikuleck/Rosenreq.html) by Aloisius Louie.
- *Robert Rosen: The well posed question and its answer: why are organisms different from machines?* (http://www.people.vcu.edu/~mikuleck/PPRISS3.html) An essay by Donald C. Mikulecky.
- Paper (http://content.aip.org/APCPCS/v627/i1/59_1.html) by Christopher Landauer and Kirstie L. Bellman criticising some of Rosen's mathematical formulations, followed by

attempts to improve the formulations.

Anatol Rapoport

Anatol Rapoport (Russian: Анато́лий Бори́сович Рапопо́рт, born May 22 1911-January 20 2007) was a Russian-born American Jewish mathematical psychologist. He contributed to general systems theory, mathematical biology and to the mathematical modeling of social interaction and stochastic models of contagion.

Anatol Rapoport, from “Paradoxical Effects of Social Behavior”, 1986.

Biography

Rapoport was born in Lozovaya, Russia. In 1922, he came to the United States, and in 1928 he became a naturalized citizen. He started studying music in Chicago and continued with piano, conducting and composition at the Vienna Hochschule für Musik where he studied from 1929 to 1934. However, due to the rise of Nazism, he found it impossible to make a career as a pianist.[1]

He shifted his career into mathematics, getting a Ph.D. degree in mathematics under Nicolas Rashevsky at the University of Chicago in 1941. According to the *Toronto Globe and Mail*, he was a member of the American Communist Party for three years, but quit before enlisting in the U.S. Army Air Corps in 1941, serving in Alaska and India during World War II.[2]

After the war, he joined the Committee on Mathematical Biology at the University of Chicago (1947-1954), publishing his first book, *Science and the Goals of Man,* co-authored with semanticist S. I. Hayakawa in 1950. He also received a one-year fellowship at the prestigious Center for Advanced Study in the Behavioral Sciences (Stanford, California).

From 1955 to 1970 Rapoport was Professor of Mathematical Biology and Senior Research Mathematician at the University of Michigan, as well as founding member, in 1955, of the Mental Health Research Institute (MHRI) at the University of Michigan. In 1970 Rapoport moved to Toronto to avoid the war-making ways of the Vietnam-era United States. He was appointed professor of mathematics and psychology at the University of Toronto, 1970-1979. He lived in bucolic Wychwood Park overlooking downtown Toronto, a neighbour of Marshall McLuhan. On his retirement from the University of Toronto, he became director of the Institute of Advanced Studies (Vienna) until 1983.

In 1954, Anatol Rapoport cofounded the Society for General Systems Research, along with the researchers Ludwig von Bertalanffy, Ralph Gerard, and Kenneth Boulding. He became president of the Society for General Systems Research in 1965.

Anatol Rapoport died of pneumonia in Toronto. He is survived by his wife Gwen, daughter Anya, and sons Alexander and Anthony.

Work

Rapoport contributed to general systems theory, mathematical biology and to the mathematical modeling of social interaction and stochastic models of contagion. He combined his mathematical expertise with psychological insights into the study of game theory, social networks and semantics.

Rapoport extended these understandings into studies of psychological conflict, dealing with nuclear disarmament and international politics. His autobiography, *Certainties and Doubts: A Philosophy of Life*, was published in 2001.

Game theory

Rapoport had a versatile mind, working in mathematics, psychology, biology, game theory, social network analysis, and peace and conflict studies. For example, he pioneered in the modeling of parasitism and symbiosis, researching cybernetic theory. This went on to give a conceptual basis for his lifelong work in conflict and cooperation.

Among many other well-known books on fights, games, violence and peace, Rapoport was the author of over 300 articles and of Two-Person Game Theory (1966) and N-Person Game Theory (2001). He analyzed contests in which there are more than two sets of conflicting interests, such as war, diplomacy, poker or bargaining. His work led him to peace research (see below), including books on *The Origins of Violence*' *(1989) and* 'Peace, An Idea Whose Time Has Come (1993), both written at the University of Toronto.

He won a computer tournament in the 1980s, based on Robert Axelrod's *The Evolution of Cooperation*. This sought to understand how cooperation could emerge through evolution. Rapoport's entry, *Tit-For-Tat* has only four lines of code. The program opens by cooperating with its opponent. It then plays exactly as the other side played in the previous game. If the other side defected in the previous game, the program also defects; but only for one game. If the other side cooperates, the program continues to cooperate. According to *Peace Magazine* author/editor Metta Spencer, the program "punished the other player for selfish behaviour and rewarded her for cooperative behaviour—but the punishment lasted only as long as the selfish behaviour lasted. This proved to be an exceptionally effective sanction, quickly showing the other side the advantages of cooperating. It also set moral philosophers to proposing this as a workable principle to use in real life interactions."

His children report that he was a strong chess player but a bad poker player because he non-verbally revealed the strength of his hands.[3]

Social network analysis

Anatol Rapoport was an early developer of social network analysis. His original work showed that one can measure large networks by profiling traces of flows through them. This enables learning about the speed of the distribution of resources, including information, and what speeds or impedes these flows—such as race, gender, socioeconomic status, proximity and kinship.[4] This work linked social networks to the diffusion of innovation, and by extension, to epidemiology. Rapoport's empirical work traced the spread of information within a school. It prefigured the study of Six degrees of separation, by

showing the rapid spread of information in a population to almost all—but not all—school members (see references below).

Conflict and peace studies

According to Thomas Homer-Dixon in the *Toronto Globe and Mail*, Rapoport "became anti-militarist quite soon after the war. [WWII]. The idea of military values became anathema." He was a leading organizer of the first teach-ins against the Vietnam War at the University of Michigan, a model that spread rapidly throughout North America. He told at a teach-in: "By undertaking the war against Vietnam, the United States has undertaken a war against humanity.... This war we shall not win." (*Ann Arbor News*, April 1967). He said he was an abolitionist, rather than a total pacifist: "I'm for killing the institution of war".

Rapoport returned to the University of Toronto to become the founding (and unpaid) Professor of Peace and Conflict Studies programme, working with George Ignatieff and Canada's Science for Peace organization. As its sole professor at the start, he used a rigorous, interdisciplinary approach to the study of peace, integrating mathematics, politics, psychology, philosophy, science and sociology. His main concern was to legitimize peace studies as a worthy academic pursuit. The Trudeau Centre for Peace and Conflict Studies continues to flourish at the University of Toronto, under the leadership of Thomas Homer-Dixon. When Rapoport began, there were one (unpaid) professor and twelve students. Now, there are three (paid) professors and ninety students.[5]

Rapoport's students report that he was an engaged and inspiring professor who captured their attention, imagination and interest with his wide-ranging knowledge, passion for the subject, good humor, kind and generous spirit, attentiveness to student concerns and animated teaching style. [6]

In 1981, Rapoport co-founded the international NGO *Science for Peace*, and in 1984 he created the famous tit for tat strategy for the iterated prisoner's dilemma tournament held by Robert Axelrod that year. He was recognized in the 1980s for his contribution to world peace through nuclear conflict restraint via his game theoretic models of psychological conflict resolution. He won the Lenz International Peace Research Prize in 1976.

Publications

Rapoport's books and articles include:

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- 1975, *Semantics*, Crowell, 1975. [7]
- 2000, *Certainties and Doubts : A Philosophy of Life*, Black Rose Books, Montreal, 2000: His autobiography.

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[4] Harrison White, *Identity and Control*, 2nd ed., Princeton, NJ: Princeton University Press, 2007
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[6] Chesmak Farhoumand-Sims, "Memories of Anatol Rapoport," *Peace Magazine*, April 2007, p. 14
[7] This book about general semantics along the lines of S.I. Hayakawa's *Language in Thought and Action* and more technical (mathematical and philosophical) material. A valuable survey.

External links

- Science for Peace website (http://scienceforpeace.sa.utoronto.ca/)
- History of Science for Peace (http://www.peacemagazine.org/archive/v03n5p27.htm)
- Profile of Anatol Rapoport (http://www.isss.org/lumrapo.htm)
- "Memories of Anatol Rapoport" (http://www.peacemagazine.org), Cheshmak Farhoumand-Sims, *Peace Magazine*, April 2007
- Farhoumand-Sims, Cheshmak (April 2007). "http://archive.peacemagazine.org/v23n2p14.htm|Memories of Anatol Rapoport". *Peace Magazine*: p14. http://archive.peacemagazine.org/v23n2p14.htm. Retrieved on 2008-05-03.

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