The Case for an Institute of Mathematical Biology

Report[1] from an NSF funded workshop held in Washington, D.C., Sept 18-20, 2006

Participants:

Sandy Andelman
Tim Carpenter
Andrew Dobson
John Guckenheimer
Alan Hastings (Chair)
Dennis M. Heisey
Trachette Jackson
John Jungck
Tim Lewis
Sharon R Lubkin
Ellis McKenzie
Carl F. Melius
Aaron Reeves
Lisa Sattenspiel
Tamar Schlick
Andrew R Solow
Jorge X. Velasco-Hernandez
Eberhard Voit
John Wakeley

[1] This report was prepared by the participants of the workshop. The workshop was sponsored by the National Science Foundation through Grant Number DEB-0640021 to the University of California-Davis. Any opinions, findings, conclusions, or recommendations expressed in this report are those of the participants and do not necessarily represent the official views, opinions, or policy of the National Science Foundation.

Table of Contents

Executive Summary

There is a national need for improved understanding and modeling of biological problems that can be gained only by using the approaches of mathematical biology. Examples of these biological problems are:

- Foreign animal disease
- Emerging diseases
- Invasive species
- Cancer and diseases with a genetic basis
- Other biological problems induced by human impacts

One advantage of using ideas from mathematical biology is that common aspects of these problems emerge. In particular, common mathematical frameworks can be used to understand disparate biological questions, ranging from cellular and neural systems to population and ecosystem dynamics. Common mathematical themes include

- Stochastic dynamical systems
- Effects of network architecture on dynamics
- Multiple temporal and spatial scales
- Methods for model reduction
- Methods for fitting models to data

A new institute would play a vital and important role in answering fundamental questions about biology that require the tools and approaches of mathematical biology. A major role of the institute would be the formulation and analysis of models describing biological phenomena, which may require new mathematical approaches. A new institute would overcome many current challenges to progress in mathematical biology. Some important goals would be to

- Shorten timescale to address pressing biological questions
- Focus explicitly on cross-disciplinary questions
- Integrate mathematics and biology
- Transfer methods between different sub-fields of biology

To accomplish these tasks we envision an institute that would be focused on the concept of cross-disciplinary working groups with 5-15 people that would meet at the institute over a period of several days to a week several times over a period of one to two years. These groups would be primarily self assembled and would have their travel and subsistence (but not salary) supported by the institute. This approach would allow mathematicians and biologists from multiple fields to work closely together. Another key function would provide training for more mathematical biologists and modelers at multiple levels (secondary schools to universities). The institute would also serve as the scientific backbone that would help with policy recommendations based on modeling results. A key aspect would be the development of models and software for modeling biological systems, which would require a substantial investment in computer support beyond that typical for an institute. A preliminary discussion of budget suggested initial overall support at the level of $6 million per year.

Introduction and Justification

Mathematical biology is the use of mathematics as a tool for answering biological questions. Today there is unprecedented progress in biology. However, just as progress in physics, engineering, chemistry, and other “hard” sciences accelerated greatly after the development of satisfactory mathematical frameworks and quantitative methods, so too biology will only reach its full maturity and power when it has a foundation of mathematically-based theory. On the other hand, just as the concerns of mathematics have historically been shaped by the physical sciences, it is clear that the future will see major developments in biologically-oriented mathematics (Cohen 2004; May 2004; Bothwell, 2006; Grenfell et al., 2006).

What is frequently missing from biological research is careful, quantifiable mechanism-based theory for studying biological problems. It is relatively easy to engage in empirical curve fitting, and to produce complex simulations that reproduce desired behavior. However, if the dynamics can be derived as a consequence of biological theory that can be expressed as a mathematical model, then the understanding is much greater. Here mathematical models can have many different forms, ranging from very simple descriptions with just a few equations, often describing how a system changes in time, to systems with many equations. These models can then be studied by various means, ranging from analytic solutions to solutions using computers. We can also distinguish between numerical solutions of mathematical models which can be expressed analytically and the alternate approach of simulations which might not even be based on an underlying mathematical model. All approaches are useful in the proper context, but it is important to recognize that simpler models, based only on the essential features of a system, can play a crucial role both in prediction and in developing fundamental understanding.

Mathematical modeling and simulations are one technique widely used for making predictions about systems where experimentation is not possible, for various reasons - transmission and spread of infectious diseases, forest fires, climate change, extinction, physiological effects of potential new drugs. Some simulations are based on known and tested conceptual frameworks. For example, simulation of blood flow through an artificial blood vessel is based on the well-established physics of fluid flow. The technical details involved in realistic blood flow simulations can be very complex, even though the physics is well characterized. Other types of simulations are based on concepts that are less well understood, but easier to implement in a simulation. For example, a discrete model of a continuous system, such as an age-structured model used to project human population growth, may be easy to program, but may not completely reproduce the biological reality since human age groups are not distinct entities, except by convention. Some simulations are completely outside of the realm of mechanism. For example, an animator wishing to simulate a fern leaf might generate an image of a fernlike fractal using iterated function systems. A plant cannot possibly generate a leaf by that method; it is fortuitous for the animator that a simpler simulation technique is satisfactory, but the simulation provides no biological insight, since it is not based on any real biological mechanisms.

What mathematical biology does best is to translate biological concepts and hypotheses into highly structured, testable mathematical structures: mathematical models. The development, analysis and simulation of such models allows the researcher to

- make qualitative predictions
- make quantitative predictions
- test hypotheses
- determine control and optimization strategies
- express theories clearly

There has been a great increase in activity in mathematical biology in recent years, as explored in a series of workshops run by Hastings, Arzberger and Henson, culminating in two recent publications in BioScience (Hastings et al, 2005; Green et al. 2005). Some ideas from a similar workshop held in 2003, jointly sponsored by NIH and NSF, and the NSF workshops were presented in Hastings and Palmer (2004). Some of these problems require the development of novel mathematical approaches, while others can be approached using existing mathematical tools. In all cases, however, mathematics can provide novel insights and further the development of the biological sciences (Cohen, 2004). Current areas of interest obviously include problems in population biology, ecology and the environment, but also include questions from neuroscience and physiology and cell biology. As covered in the books by Murray (2003a, b), much recent interest has been in using spatial descriptions to study problems ranging from the cellular level to the ecosystem level.

A research institute as we are proposing here allows the integration of experts and expertise for the analysis, modeling, prediction, and control of biological phenomena. By bringing together researchers from distant locations to work together, an institute dramatically increases the productivity of its participants.

- Integration is essential because it brings together a multitude of disciplines, and brings together the individuals that can contribute to problem definition and solution.
- Problem formulation is as important as its solution. Many times, complex problems, such as emergent infectious diseases in animal populations, can be better attacked if correctly formulated in a multidisciplinary approach with an interdisciplinary methodology

There are a number of existing institutes of mathematics (e.g., Institute of Mathematics and Applications, Minneapolis, Minnesota; Mathematical Sciences Research Institute, Berekley, California; Institute for Pure and Applied Mathematics, UCLA, Los Angeles, California; Statistical and Applied Mathematical Sciences Institute, Research Triangle Park, North Carolina; , Pacific Institute for the Mathematical Sciences, British Columbia, Canada), biology (e.g. Marine Biological Laboratory, Woods Hole, Massachusetts; National Center for Ecological Analysis and Synthesis, Santa Barbara, CA,; National Evolutionary Synthesis Center, North Carolina), and other areas of science, and one in mathematical biology (Mathematical Biology Institute, Columbus, Ohio (MBI)). Typical activities are:

- workshops of 1 week
- postdoctoral positions of 2-3 years
- sabbatical positions of 3-12 months
- yearlong programs, which may contain several workshops of varying lengths related to the main theme
- focused, time-limited, self-selected research groups

The existing mathematics and physics institutes occasionally run biological programs, but that is not their primary mission. The MBI's sole area is mathematical biology, but its structure and goals (focused on one time workshops for exchange of information and more on the mathematical aspects of mathematical biology) are very different from the structure and goals we develop here. Notably, the year-long biological themes at the MBI have a development time of two to three years.

There is a need for an institute where researchers can come together to work on important problems in mathematical biology as soon as they arise, in a setting that fosters productive collaboration.

We believe that such a center would emphasize an interdisciplinary approach truly drawing from both biology and mathematics. The outcome of work at the center on particular problems would lead toward several broad goals:

- Solve biological questions that require a range of mathematical approaches
- Solve mathematical questions appropriate for a range of biological applications
- Promote synthesis through the transfer of different mathematical questions and techniques between different areas of biology, and from mathematics to biology and vice versa.
- Increase overall awareness and research capability at the interface between mathematics and biology, through training and outreach.
- Enable mathematicians and biologists to respond to emerging biological problems in a timely manner.

Organization

Activities

There are two main approaches to mathematical biology. In one, a particular biological problem is the core interest, and whatever mathematical tools that can be productively used are applied to improve understanding of the biological system. Frequently, the mathematical tools used are well understood, but in many cases, new mathematical tools and modeling methods need to be developed. In the other approach, the focus is on the development of mathematical tools, modeling methods, and theoretical concepts which may be essential in addressing a range of biological problems, but where the mathematical basis is sufficiently complicated and poorly understood that a great deal of insight is achieved from the development of the theory.

For example, in the field of epidemiology, typically a researcher would have a particular disease of interest. As dictated by the characteristics of the disease and the available data, and by the purposes of the research (for example developing control strategies), the researcher would use mathematical tools such as differential equations, stochastic models, delay differential equations, integral equations, social network analysis, evolution models, Markov chains, parameter estimation, model reduction, and other tools as needed. This is the approach centered on a biological problem.

An example of an approach centered on the mathematical problems might start from an observation that many very different biological systems exhibit **threshold** effects:

- A disease cannot be maintained in a herd of cattle until its population reaches a certain size; conversely, a disease cannot be eradicated unless the population size is below the threshold.
- A neuron's membrane potential rises slightly in response to a stimulus, then returns to a baseline unless the potential reaches a certain threshold, in which case an action potential in elicited.
- A fishery produces a fine harvest for decades, until the harvest exceeds some threshold, at which point the population collapses.
- An HIV patient lives well until her immune system reaches a threshold, after which her body is in full-blown AIDS, and the previous treatment no longer works.

All of these have the common feature of thresholds, and in order to fully understand what is going on in these diverse biological systems, there needs to be an understanding of the mathematics of thresholds, which falls into the area of dynamical systems and bifurcation theory.

Another example where a focus on the mathematics paradoxically helps the understanding of the biology is the case of **synchrony** (Strogatz, 2003). One researcher observes that certain species of fireflies flash at the same time, whereas others seem to flash at random. Another researcher tries to understand how fish control their muscles in a coordinated undulation that allows them to swim. Another researcher observes that a heart in fibrillation seems to be engaging in inappropriate waves in all directions. An epidemiologist sees that the long term cycles of certain kinds of childhood diseases seem to be in synchrony so that a population is likely to have simultaneous epidemics, while other diseases seem to be desynchronized, so that they rarely occur together. A mathematical biologist builds on the commonalities in all these systems, and begins to develop a conceptual framework for coupled oscillations. Other mathematical biologists develop the theory further, and a neuroscientist realizes that there are parts of the brain where synchronization and desynchronization allow the nervous system to distinguish where a sound is coming from. The research approach of studying the underlying mathematical phenomena rather than the specific biological cases can paradoxically lead to more progress in the specific biological cases, through cross-fertilization of biological flowers by mathematical bees.

There are many central questions in biology where progress in answering the questions is currently limited by the lack of fundamental work at the interface between mathematics and biology, which in many cases must be driven by specific biological problems. These questions include applied issues, such as

- preparing for and responding to threats of emerging diseases
- design of programs for the maintenance of ecosystem services
- design of efficient systems of drug delivery

Similarly, there are basic questions requiring new advances in mathematical biology such as understanding issues in

- evolution
- growth and development
- dynamics of cells
- transport in tissues
- structure of and dynamics in random media
- structure and dynamics of biological networks

Advances in understanding of fundamental biological questions, such as the dynamics of networks, would naturally increase understanding of, and ability to answer, applied questions such as optimal ways of dealing with emerging diseases and basic questions such as how cells use signaling networks to control cell growth.

There are also deep issues in methods of mathematical modeling which would benefit from focused research, such as:

- parameter identification
- multiple scales
- model identifiability
- model complexity
- dimension reduction
- stochastic dynamic systems
- heterogeneity in space, time, state, structure, and parameters
- advanced sampling methods for large configurational spaces of complex biological systems
- development of mesoscale models for complex biological systems that have an appropriate level of detail

The kind of interdisciplinary approach which we believe is essential could be achieved in a variety of ways. We believe that a focus on workshops, defined as one-time gatherings of scientists, would not achieve the kinds of sustained interdisciplinary efforts needed to answer the questions we have posed. Also, grants to individual investigators, or even small groups of investigators, are highly unlikely to bring together investigators from the needed range of mathematical and biological topics in a way that would allow substantial progress in the areas we have found to be most compelling.

We developed several principles to guide the formation of an institute as a way to achieve substantial progress in answering both basic and fundamental applied questions in mathematical biology:

- The time scale from the identification of a particular problem to convening a group for beginning investigation needs to be relatively short, on the scale of months rather than years.
- Solutions will require true interdisciplinary teams with substantial representation from both biologists and mathematical scientists.
- Identification of appropriate problems can be done well using a bottom-up approach relying on members of the community to identify problems, and to initiate the formation of appropriate teams of interdisciplinary researchers. A center could also serve as a focal point for gathering researchers to work on specific national needs as they arise (e.g., foreign animal diseases).
- The range of biological questions and mathematical approaches is broad enough that a center primarily consisting of permanent scientific staff or long term scientific visitors will not have the necessary breadth.
- Identification of common themes, such as the importance of spatial descriptions, will foster the transfer of techniques between sub-fields of biology and contribute to the rapid solution of biological questions.
- A single center could effectively deal with both basic and applied questions.
- Educational issues are central to develop future generations of researchers, but having graduate students or large numbers of postdoctoral scholars in residence will not be appropriate since adequate mentoring would not be available.
- Strong support for computing with on-site permanent computing staff that would actively support research through coding of algorithms, GUIs, I/O and other functions is essential, since this would greatly increase progress by scientists focusing on the mathematical and biological issues.

Existing centers focused on various areas of mathematics or biology do not currently meet the needs we have outlined here. Additionally, many of the traditional models for centers, based primarily either on permanent scientific staff or on workshops would not meet the goals outlined here. We expect that there are several ways to meet these goals, but note that one model (with suitable modifications) that could achieve the goals outlined here is that used at the very successful National Center for Ecological Analysis and Synthesis (NCEAS, www.nceas.ucsb.edu). NCEAS has in residence postdoctoral scholars and sabbatical visitors, but the most important aspect for our purposes here is the working group, which we now describe in more detail.

Most of the activity at NCEAS takes place through working groups that are independently developed by self-assembled groups of researchers. These researchers identify a problem or problem area that is ready for a new approach, and apply to NCEAS for support. Proposals are reviewed by an advisory board of scientists, and then funding is awarded to the best proposals. The funding pays for the researchers to come to NCEAS to work on the problem, typically for three or four meetings of 3 days to one week duration each, spread out over 1 to 2 years. Thus, NCEAS serves as a place where scientists who would not normally interact are provided with an environment with appropriate support where work can take place. Note that the only costs paid are for travel and subsistence, not salary or time. This model is in contrast to one focused on workshops which primarily serve as venues for exchange of information. Instead, working groups aim to develop new syntheses or new approaches. These groups are best with about 5 to 12 participants, including graduate students and postdoctoral scholars, and the time from proposal to first meeting can be as short as a few months. The advantage provided by having topics arise from the broader community can be substantial, as demonstrated by the huge impact of the research accomplishments facilitated by NCEAS.

We believe that the approach exemplified by NCEAS, with some modifications, can be used to meet the challenges we have posed. In particular, it may be advisable for the director of the center or board to play a larger role in suggesting new expertise to be added to groups. Also, some of the calls for proposals or funding may be targeted to achieve some of the goals of dealing with specific problems, such as understanding the progress of a particular animal disease, or the environmental impact of an invasive species. The particular implementation should not be specified now, as many variations on the approach we have described could certainly be successful.

Educational Aspects

One of the most fundamental issues that an institute needs to address is education. Here, as well, we do not think it appropriate to specify all the details, but there are a number of principles that emerged from our discussions. As recognized in previous reports (such as the one from the joint NSF-NIH workshop organized by Palmer in 2003), progress at the interface between mathematics and biology has been hindered by the lack of appropriately trained scientists. Also, the real need is for individuals who are at least truly conversant in both mathematics and biology. This leads to the following two major principles:

- Educational activities need to be targeted at all levels, beginning with K-12 and going through at least the postdoctoral level.
- Individuals being trained need active guidance and exposure to both mathematical and biological training.
- The institute needs to be national and international in scope and to disseminate both specific results and a culture of research to a broad community.

We first consider the training of postdoctoral scholars, as this is an immediate need. The second concept of active mentoring suggests that full time residence at the institute might not be best for many postdoctoral scholars or graduate students. Instead, the institute could provide partial support for postdoctoral scholars or graduate students with matching or primary support from mentors running working groups. Postdoctoral scholars and graduate students could have a “home” with mentor institutions, but spend long visits at the institute coordinated with the timing of working group meetings (and/or related working groups). This would work even better if groups with similar themes are coordinated to run sequentially for postdoctoral scholar and other visitor overlap.

We recognize the difficulty of combining active mentoring with the development of independent scientists. Perhaps, postdoctoral scholars would spend more time with the mentor at the beginning of their tenure and more time at the institute later. The way the split occurs could be determined by postdoctoral scholars depending on their and their mentor's comfort level.

Training for undergraduates and for many graduate students and at the K-12 level would depend on developing methods to transfer knowledge and approaches to a national audience. This would clearly require staff to coordinate and help with repository of developed educational resources. The working groups described above could do this to some extent, but would need assistance.

Bringing in faculty from the NSF sponsored Undergraduate Biology and Mathematics (UBM) programs or similar programs would be one way to get information out to a larger audience. Special attention should be paid to involving faculty from community colleges, small liberal arts colleges and regional universities since many biologists and mathematicians begin training at this type of institution. Special attention needs to be paid to incorporate education of minorities, first generation college students, transfer students, and students who have had little exposure to mathematical biology. There could also be ways to get faculty in Math and Biology Education to follow a working group tenure at center in order to get educators to pass on excitement of mathematical biology to high school and junior high teachers. It is important to get high school students excited about mathematical biology before they get to college so that they realize its importance and begin taking appropriate classes like introductory biology and college level mathematics classes like calculus early in their undergraduate education.

In general, the institute needs to be a focal point for innovation in mathematical biology education. We have highlighted some points, but would expect that actual proposals would need to develop these ideas in much greater depth. Specific resources would need to be devoted to education.

Computational Aspects

Computer Support Staff with expertise in Mathematical Biology.

Computation is central to progress in mathematical biology. One aspect of an institute that would really excite potential participants would be "expert" computer support staff that could actively participate in the working groups. These highly trained and skilled individuals would have expertise in biological systems, numerical analysis, mathematics, and have excellent programming skills. While these staff members would take part in the scientific aspects of working groups, their primary role would be to help working groups develop and maintain computer code. These individuals would be particularly valuable for projects that spanned several years, ensuring the stability, quality and coherence of the computer programs.

A typical long-term project that involved creating extensive computer code would require approximately ½ FTE. The number of "expert" computer support staff members would depend on the number of on-going projects and how much of the work is being conducted by the staff member. Some funding for these individuals could come from external sources (e.g. from grants of researchers in working groups or from funding agencies sponsoring specific projects), but we expect that the core support would have to come from the institute. These positions could potentially be filled by post-doctoral fellows, but ideally the positions would be filled by permanent employees who have PhDs and choose not to pursue independent research programs/tenure-track positions.

Development of open source software and maintain software database.

One mission of the institute could be to foster the development of open source software and maintain a software database (i.e., act as archivist of software). This would enable the software developed by working groups to be transferred not only to other working groups but to the larger scientific community. Participants of the workshop agreed that this would be a major attraction for the institute and would be a valuable part of the the institute's educational and outreach aspects.

Working groups would be encouraged to develop models and provide algorithms. Professional staff would then be responsible for maintaining a database of this software, helping to write appropriate documentation for software, improving program structure and commenting code. The programming help mentioned above will increase the stability and quality of the software.

Could the Institute act as a Repository for Biological Data?

Assuming that the institute would cover a wide range of general biological topics, the feasibility of the center acting as a data repository is questionable. However, if specific funding was supplied for databases in one specific area (e.g. infectious disease), then this could be possible but would likely require at least 2 permanent FTEs.

Overall Computational Support

The program we have outlined here clearly would require a large number of highly trained professionals, and, as we note below, would therefore require a substantial budget. However, this level of support (6 or more FTE Ph.D. level staff) would be a key part of an institute, both in reaching the goals set out above, and as a real incentive for participation in working groups. We have not given a detailed discussion of hardware issues as these are much more standard. Support for hardware at the institute and for the use of laptops by participants would be required. In particular, maintenance of databases of software would also require appropriate backup capability as well. Additionally, other aspects of computer support required have been discussed under education.

Knowledge Transfer

Assuring that the results from investigations at the proposed institute reach appropriate audiences outside the institute will require concerted efforts on the part of individual working groups and the institute as a whole. Dissemination of research results and ways of approaching problems both to a larger research community and to answer specific applied questions is another important part of a proposed institute. Working groups may take care of part of this themselves, but this would need to be explicitly included as a responsibility. Another way to do this would be to have a working papers series or technical reports available electronically. Working groups could be required to produce some type of summary materials that could be disseminated. Permanent staff would be needed to help with dissemination of these materials online.

Also, dissemination and advertising more generally would be required to reach a broader audience, essentially those who may not yet know they would and should be interested. Again, staff support would be needed to make available online this material (e.g., interviews with researchers, movies, podcasts) and to publicize this material.

Budget

General issues of budget were discussed to get an understanding of the scope of resources needed. One principle that emerged was that the funding may have to be larger than some other institutions of comparable size, given the substantial ongoing computer support needs described above. We briefly describe and justify estimated expenses under broad categories.

First, the center would need scientific leadership, equivalent to a full time director and a full time deputy director. There also needs to be an administrative support staff. A center in which many working groups come for short to intermediate stays will require a larger support staff than a more vertically-oriented institute would require. The vision here is for a more horizontally-structured operation, driven by the presence of working groups discussed above. The success of a horizontally-organized institute will depend on the ease with which working groups can come together without logistical hurdles. A projected cost for the academic leadership and administrative staff is about one million dollars per year.

The working groups will be a major part of the center. These are roughly ten individuals who bring together a broad range of expertise to tackle a problem in mathematical biology. A realistic duration of stay is about one week. A very rough estimate is that 30 groups per year would cost roughly $2 -2.5 million per year of direct support.

There will be one time and ongoing costs for computer hardware, but much more significant will be ongoing costs for computer support as we discussed above. We estimate that a reasonable figure is $1 million per year for the support functions.

We have not explicitly included costs yet for sabbatical visitors, expenses explicitly for education, other expenses for research dissemination and to meet other contingencies, and for the hardware aspects of computing. We will estimate this part of the budget to be approximately $1 million per year.

Our very rough calculations suggest an overall budget of approximately $6 million per year would support an institute of the size required to deal with the challenges we describe above.

Workshop Participants

Sandy Andelman, Senior Director, TEAM Initiative, Conservation International
Tim Carpenter, Professor/Epidemiologist, Department of Medicine and Epidemiology, University of California, Davis, CA
Andrew Dobson, Professor, Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ
John Guckenheimer, Department of Mathematics, Cornell University, Ithaca, NY
Alan Hastings (Chair), Professor, Department of Environmental Science and Policy, University of California, Davis, CA
Dennis M. Heisey, CWD Researcher, United States Geological Survey, Madison, WI
Trachette Jackson, Associate Professor; Department of Mathematics, University of Michigan, Ann Arbor, MI
John Jungck, Mead Chair of the Sciences and Professor of Biology, Biology Department, Beloit College, Beloit, WI
Tim Lewis, Associate Professor, Department of Mathematics, University of California, Davis, CA
Sharon R Lubkin, Associate Professor, Department of Mathematics, North Carolina State University, Raleigh, NC
Ellis McKenzie, Senior Scientist, Fogarty International Center, National Institutes of Health Bethesda, MD
Carl F. Melius, Lawrence Livermore National Laboratory, Livermore, CA
Aaron Reeves, Research Associate, Animal Population Health Institute, College of Veterinary Medicine & Biomedical Sciences, Colorado State University, Fort Collins, CO
Lisa Sattenspiel, Professor, Department of Anthropology, University of Missouri-Columbia, Columbia, MO
Tamar Schlick, Professor of Chemistry, Mathematics, and Computer Science, New York University, New York, NY
Andrew R Solow, Scientist, Woods Hole Oceanographic Institution, Woods Hole, MA
Jorge X. Velasco-Hernandez, Coordinador, Programa de Matematicas Aplicadas y Computacion, Instituto Mexicano del Petroleo, Mexico City, Mexico
Eberhard Voit, Professor and Georgia Research Alliance Eminent Scholar in Systems Biology, Wallace H. Coulter Dept. of Biomedical Engineering, Georgia Institute of Technology, Atlanta, GA
John Wakeley, Professor, Department of Organismic & Evolutionary Biology, Harvard University, Cambridge, MA
Colleen T. Webb. Assistant Professor, Department of Biology, Colorado State University, Fort Collins, CO

References

Bothwell, J. H. F. (2006). "The long past of systems biology." New Phytologist **170**(1): 6-10.

Cohen, J. E. (2004). "Mathematics is biology's next microscope, only better; Biology is mathematics' next physics, only better." Plos Biology **2**(12): 2017-2023.

Green, J. L., A. Hastings, et al. (2005). "Complexity in ecology and conservation: Mathematical, statistical, and computational challenges." Bioscience **55**(6): 501-510.

Grenfell, B. T., C. S. Williams, et al. (2006). "Simplifying biological complexity." Nature Physics **2**(4): 212-214.

Hastings, A., P. Arzberger, et al. (2005). "Quantitative bioscience for the 21st century." Bioscience **55**(6): 511-517.

Hastings, A. and M. A. Palmer (2003). "Mathematics and biology: A bright future for biologists and mathematicians?" Science **299**(5615): 2003-2004.

May, R. M. (2004). "Uses and abuses of mathematics in biology." Science **303**(5659): 790-793.

Murray, J. D. (2003). Mathematical Biology I. An Introduction. New York, Springer-Verlag.

Murray, J. D. (2003). Mathematical Biology II. Spatial Models and Biomedical Applications. New York, Springer-Verlag.

Strogatz, S. *Sync: the Emerging Science of spontaneous Order*. Hyperion Press. New York. 2003.