

Opportunities of Mathematical Biology in William and Mary

Mathematical Biology

- **Mathematical biology** or **biomathematics** is an <u>interdisciplinary</u> field of academic study which aims at modeling natural, <u>biological</u> processes using <u>mathematical</u> techniques and tools. It has both practical and theoretical applications in biological research.
- 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 <u>genomics</u> revolution, which are difficult to understand without the use of analytical tools,
- recent development of mathematical tools such as <u>chaos theory</u> to help understand complex, nonlinear mechanisms in biology,
- an increase in <u>computing</u> power which enables calculations and <u>simulations</u> to be performed that were not previously possible, and
- an increasing interest in <u>in silico</u> experimentation due to the complications involved in human and animal research.

Basic courses in math and bio

- Math 131, 132 (Calculus for Life Sciences, I, II)
- Biol 203 (Principle of biology: Molecules, cells, development)
- Biol 204 (Organisms, ecology, evolution)
- Math 302 (Differential Equations)

Study math biology and research opportunity

- Math 345 (Introduction to Mathematical Biology) every fall semester
- Math 410 (Biol 404) (Ecology and evolution of metapopulation) every spring semester
- National Science Foundation Grant: UBM: Undergraduate Research in Metapopulation Ecology (2004-2009) summer research program (Dan Cristol, John Swaddle, Randy Chambers (Biology); Sebastian Schreiber, Junping Shi, Tim Killingback (Math)).

Degree/concentration

- Major/minor in mathematics (scientific application in biology)
- Major/minor in biology
- Minor in applied sciences (computational biology)
- Honor thesis in biology/mathematics

Other related courses

- APSC 451 Cellular Biophysics and Modeling
- APSC 452 Networks in the Brain and Biology
- APSC 453 Introduction to Bioinformatics
- MATH 351 Applied Statistics
- MATH 441/442 Introduction to Applied Mathematics
- CHEM 341 Principles of Biophysical Chemistry

Goal of the course:

Learn basic models in biology and related mathematical methods

Motivation of Math Biology

Most technology innovations in 20th century were based on physics, and it is expected that most technology innovations in 21th century will be based on biology

A branch of sciences is considered mature and reliable if a mathematical theory of this branch is established and matches with experiments (physics is, and biology is not) What role does mathematics play in biology?

What are central questions in biology (or science)?

At what level is mathematics involved in biological sciences?

Some answers from a distinguished "panel":

James Murray (Oxford University, University of Washington) Ian Stewart (Warwick University) a panel of National Science Foundation Robert May (Oxford Univ., President of Royal Society)

Mathematical models in biology (from Murray's Preface)

Why use mathematics to study something as intrinsically complicated and ill understood as development, angiogenesis, wound heeling, interacting population dynamics, regulatory networks, marital interaction and so on? We suggest that mathematics, rather theoretical modelling, must be used if we ever hope to genuinely and realistically convert an understanding of the underlying mechanisms into a predictive science. Mathematics is required to bridge the gap between the level on which most of our knowledge is accumulating (in development biology it is cellular and below) and the macroscopic levels of patterns we see.

The aim in all these applications is not to derive a mathematical model that takes into account every single process because, even if this were possible, the resulting model would yield little or no

insight on the crucial interactions within the system. Rather the goal is to develop models which capture the essence of various interactions allowing their outcome to be more fully understood. As more data emerge from the biological system, the models become more sophisticated and the mathematics increasingly challenging.

In development (by way of example) it is true that we are a long way from being able to reliably simulate actual biological development, in spite of the plethora of models and theory that abound. Key processes are generally still poorly understood. Despite these limitations, I feel that exploring the logic of pattern formation is worthwhile, or rather essential, even in our present

state of knowledge. It allows us to take a hypothetical mechanism and examine its consequences in the form of a mathematical model, make predictions and suggest experiments that would verify or invalidate the model; even the latter casts light on the biology. The very process of constructing a mathematical model can be useful in its own right. Not only must we commit to a particular mechanism, but we are also forced to consider what is truly essential to the process, the central players (variables) and mechanisms by which they evolve. We are thus involved in constructing frameworks on which we can hang our understanding. The model equations, the mathematical analysis and the numerical simulations that follow serve to reveal quantitatively as well as qualitatively the consequences of that logical structure.

Mathematical models in biology

(from Murray's Preface)

Models can provide biological insight and be very useful in summarizing, interpreting and interpolating data.

There is no "right" model: producing similar temporal or spatial patterns to those experimentally observed is only a first step and does not imply the model mechanism is the one which applies.

Mathematical descriptions are *not* explanations. Mathematics can never provide the complete solution to a biological problem on its own.

Modern biology is certainly not at the stage where it is appropriate for mathematicians to try to construct comprehensive theories.

Life's other secret (from Stewart's Preface)

Until the middle of the twentieth century, it was totally unclear whether life had any kind of inorganic basis. The discovery of the first secret of life, the molecular structure of DNA (deoxyribonucleic acid), solved that particular riddle. Life is a form of chemistry, but chemistry unlike any that ever graced a test tube, chemistry is so complex that it makes an industrial city look like a village. Inside every living creature on Earth—and we know of none off it—a complex molecular code, a Book of Life, prescribes the creature's form, growth, development, and behavior. Our fate is written in our genes.

Without any question, this discovery was one of the most significant ever made. It irrevocably changed our views about the living world: it opened up entirely new ways to unravel many of life's secretsbut not all of them.

Life's other secret (from Stewart's Preface)

Some secrets lie deeper than the genetic code. Genes are fundamental to earthly life, but their role in determining form and behavior tends to be overstated—especially in the media. Genes are not like engineering blueprints; they are more like recipes in a cookbook. They tell us what ingredients to use, in what quantities, and in what order-but they do not provide a complete. accurate plan of the final result. Every cook knows that a recipe is not the same as a meal: Between the cook and the dining table lie the intricacies of ovens, grills, pots and pans, seasoning to taste. and the maddeningly obtuse behavior of ingredients. Last week, the recipe for bread worked perfectly, but this week's bread is as flat as a pancake. You won't find out why by studying the recipe, or the oven, or even both; you must also take

account of the physical and chemical laws that govern water, bicarbonate of soda, hot air, and sticky dough—and a thousand other things.

In trying to understand life, however, it is so tempting just to look at life's recipe book—its DNA code sequences. DNA is neat and tidy; organisms are messy. DNA can be captured by little more than a list of symbols; the laws of physics require sophisticated mathematics even to state them. Also, the amazing growth in our understanding of genetics has opened up so many fruitful lines of research that it will take decades to follow up the most obvious ones, let alone the more elusive ones.

Life's other secret (from Stewart's Preface)

As a consequence, we are in danger of losing sight of an important fact: There is more to life than genes. That is, life operates within the rich structure of the physical universe and its deep laws, patterns, forms, structures, processes, and systems. Genes do their work within the context o physical laws, and if unaided physics or chemistry can accomplish a task then the genes can safely leave them to it. Genes nudge the physical universe in specific directions, to choose this chemical, this pattern this process, rather than that one, but the mathematical laws of physic; and chemistry control the growing organism's response to its genetic instructions.

The mathematical control of the growing organism is the other secret—the second secret, if you will—of life. Without it, we will

novel solve the deeper mysteries of the living world-for life is a partnership between genes and mathematics, and we must take proper account of the role of both partners. This cognizance of both secrets has run like a shining thread through the history of the biological sciences—but it has attracted the mavericks, not the mainstream scientists. Instead of thinking the way most biologists think, these mavericks have been taking a much different approach to biology by thinking the way that most physical scientists and mathematicians think. This difference in working philosophy is the main reason why understanding of the deeper aspects of life has been left to the mavericks.

Models to study in this class:

population biology (animal group(s) or humans) biochemical model (bacteria, microorganism) epidemiology (influenza, malaria, AIDS, SARS, bird flu) natural resource management (fishery, forestry) chemical reaction model (autocatalytic reactions) neural conduction (Hodgkin-Huxley, FitzHugh-Nagumo equation) genetics and evolution

Biological Systems of current interests

A Workshop at the National Science Foundation March 14 and 15, 1996

http://www.nsf.gov/bio/pubs/mobs/mobs.htm

I. MOLECULAR AND CELLULAR BIOLOGY

1. GENOME

2. PROTEIN STRUCTURE AND FUNCTION

3. SIMULATIONS

4. BIO-INSPIRED MATERIALS

- II. ORGANISMAL BIOLOGY
- 1. CELL SIGNALING
- 2. MECHANICS AND EMBRYOLOGY
- 3. BIOFLUID DYNAMICS
- 4. IMMUNOLOGY AND VIROLOGY
- 5. NEUROSCIENCES

III. ECOLOGY AND EVOLUTIONARY BIOLOGY

- 1. Conservation biology, the preservation of biodiversity
- 2. Global change
- 3. Emerging disease
- 4. Resource management

Other areas

- A. POPULATION GENETICS
- **B. CONSERVATION BIOLOGY**
- C. MANAGEMENT OF NATURAL SYSTEMS
- D. GLOBAL CHANGE AND BIODIVERSITY
- E. THE DYNAMICS OF INFECTIOUS DISEASES

An article by Robert May (Feb 6, 2004, Science):

A paradigmatic account of the uses of mathematics in the natural sciences comes, in deliberately oversimplified fashion, from the classic sequence of Brahe, Kepler, Newton: observed facts, patterns that give coherence to the observations, fundamental laws that explain the patterns.

Tycho Brahe (1546-1601) made the most precise instruments available before the invention of the telescope. The instruments of Brahe allowed him to determine the detailed motions of the planets. In particular, Brahe compiled extensive data on the planet Mars.

Johannes Kepler (1571-1630), Brahe's assistant. By using Brahes data, he formulated the correct theory of the Solar System: Three Laws of Planetary Motion. But he was not able to prove them mathematically.

Isaac Newton (1642-1727) is the greatest scientist ever. He demonstrated that the motion of objects on the Earth could be described by three new Laws of motion, and then he went on to show that Kepler's three Laws of Planetary Motion were special cases of Newton's three Laws. In fact, Newton went even further: he showed that Kepler's Laws of planetary motion were only approximately correct, and supplied the quantitative corrections that with careful observations proved to be valid.

Consider the role played by applications of mathematics in sequencing the human and other genomes. This adventure began with the recognition of the doubly helical structure of DNA and

its implications, an oft-told tale in which classical mathematical physics played a central role. Brilliant biochemical advances, allowing the 3 billion-letter-long human sequence to be cut up into manageable fragments, were a crucial next step. The actual reassembling of the sequence fragments, to obtain a final human genome sequence, drew on both huge computational power and complex software, itself involving new mathematics. The sequence information, however, represents only the Tycho Brahe stage. Current work on various genomes uses pattern-seeking programs to sort out coding sequences corresponding to individual genes from among the background that is thought to be noncoding. Again, elegant and sometimes novel mathematics is

involved in this Keplerian stage of the work in progress. We are only just beginning, if that, the Newtonian stage of addressing the deeper evolutionary questions posed by these patterns.

In this Newtonian quest, mathematical models will help in a different way than in earlier stages. Various conjectures about underlying mechanisms can be made explicit in mathematical terms, and the consequences can be explored and tested against the observed patterns.