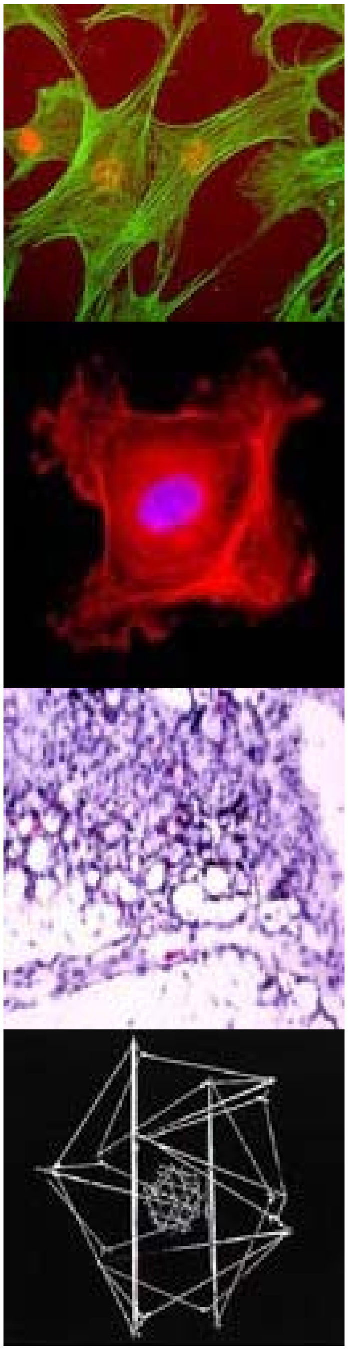

Summary of Research Activities

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Brief Evolution of Research Interests

My research interests in mathematical biology evolved from my training both mathematics (dynamical systems, topology) and biology (biochemistry/molecular biology) in my undergraduate degree, modeling the (pharmaco) kinetics and (pharmaco) dynamics of drugs in my initial graduate studies (honours and masters degree) and modeling digestion and energy regulation in metabolism in my PhD degree. In 2000, I developed and have since coordinated the South African Biomathematics Network (http://www.mth.uct.ac.za/Affiliations/BioMaths/) to bring mathematicians and biologists together to discuss possible collaborative projects and to facilitate the applications of quantitative methods to understanding biological phenomena. In 2001, I was awarded an International Fellowship of the Santa Fe Institute (http://www.santafe.edu) for complex adaptive systems and this has served as a platform for my career and has involved me in a number of different projects, which has stretched my biological and mathematical skills, but has also exposed me to the “grand” questions in biology and the limits of mathematics. Frustrated with the analysis of small biological systems and the quest for explicit solutions of toy mathematical models, and armed with a deeper understanding of key biological questions, I began to rethink both the representation and analysis of large biological systems and the understanding of complex biological systems. I define complex systems research as the studies in different disciplines of how collections of simple components following simple rules produce emergent, collective, and complex behavior, which involve the use and processing of information, the formation of complex dynamic patterns, and learning and adapting to the environment.

My current position as Director for Academic Studies at the African Institute for Mathematical Sciences (www.aims.ac.za) is to develop (leadership) and coordinate (management) both the graduate and research programmes. In addition, I have developed a vibrant research group in epidemiological modeling at the institute and have also developed a research group in host-viral dynamics based at the Stellenbosch Institute for Advanced Study.

In my opinion, complex biological systems should be approached simultaneously from the top down, exploring the macroscopic regularities of systems (for example, as in the statistical properties of large networks, scaling laws in biological systems), and from the bottom up via the development of mechanistic models. This leads one to a central question in science, "*What detail at the level of individual units is essential to understand more macroscopic regularities*", which depends of the particular system under examination and the specific scientific objectives. In my opinion, there are two further requirements to understand complex biological systems:

1. *The need to integrate the information at different time and spatial scales*.

My research in modelling ecosystems (http://www.mth.uct.ac.za/~hahn/range.html) has taught me that ecosystems are highly adaptive systems, in which properties such as trophic structure and patterns of nutrient flux evolve from interactions among components, and may feed back to influence the subsequent development of those interactions. Elucidating these interactions across scales of time and space is fundamental to resolving the issue of system productivity. Our group has developed a number of quantitative methods (for example, frames-based models) in order to integrate information across temporal and spatial scales.

2. *The need for theoretical frameworks for approaching behavior in spatially extended, hierarchical systems.*

Part of the problem is that mathematical models developed to represent both structure and processes represent phenomena as different types of mathematical objects; for example, muscle fiber orientation is modelled by a tensor, while action potential in a cell can be modelled by solutions of differential equations.

Most of my research involves developing specific mechanistic models to understand the principles of dynamic organization. In my opinion, quantitative approaches should lead to understanding the principles of dynamic organization that involve emergent properties and that resolve the extreme complexity of gene and cellular activities into robust patterns of coherent order. What is needed is a means of reconstructing the behaviour of a system from the detailed knowledge of its components and their interactions – given the baroque complexity of living systems any such reconstruction must be constructive and computational. In addition, I have also explored abstractions of different biological and social systems, for example, examining the effect of rewiring on the dynamics and topology of networks). A number of fundamental mathematical issues cut across all of these challenges: (1) how can we incorporate variation among individual units in nonlinear systems? (2) how do we treat the interaction among phenomena that occur on a wide range of scales or space, time and organizational complexity? (3) what is the relation between pattern and process?

Brief Description of Past and Current Projects

Modelling the cellular-level interactions of the immune system with the human immunodeficiency virus

Our understanding of the dynamics of human immunodeficiency virus (HIV) infection relies largely on the analysis of changes in the viral load in plasma after initiation of treatment with potent antiretroviral drugs. Alan Perelson (Los Alamos National Labs), Rob De Boer (University of Utrecht) and I have been developing a compartmental model to estimate the clearance rates of the human immunodeficiency virus (HIV) from different tissues. In addition, we are interested in the following research topics and questions:

1. Spatial compartmentalization of virus and dynamics with the immune system: What are the effects of the dynamics between the virus and immune system when different tissues are added to existing models?
2. Drug dynamics: What are the effects of drug absorption and bioavailability in different tissues on the interaction between the virus and the immune system?
3. Modelling immune responses: What is the role of CD8+ T cells in determining the viral setpoint of HIV? Developing models of the antiviral immune system response is a substantial challenge and relies on measurements of viral load one needs to characterize the humoral, CTL, and non-cytolytic CD8+ T cell and cytokine responses to viral infections.
4. Dynamics of other viral infections: Can we discern differences in kinetic and immunological factors from existing modelling efforts for different viral infections?

In addition, Alan Perelson and I are parameterising a previously developed model by his collaborators that integrated the spread of HIV and the in-vivo dynamics of HIV using South African data.

A more general control problem involves the defense against pathogens, which is often enhanced after their invasion into the host. Sometimes different options are adopted depending on the identity and the quantity of pathogen. Lee Segal and I have been studying the optimal defense of the host when two or *n* alternative responses are available, which differ in the effectiveness of suppressing the growth of the pathogen, the damage of the host caused by the defense response, and the magnitude of the time delay before the defense response becomes fully effective. We are trying to extend some ideas in optimal control theory to capture the optimal choice of players in the immune system under multiple options.

Biological Networks

Current work in networks has been motivated to a high degree by empirical studies of real world networks. Some of the empirical studies focus on the statistical properties of networks including the average path length, clustering coefficient, and degree distribution and resilience of networks. Interaction networks of agents, for example, species in ecosystems and metabolites in signaling networks, frequently re-wire themselves to other agents. Our current conceptual framework of networks is based mostly on the assumption of a fixed network. The aim of this project is to examine the effect of rewiring on the “local” network and the interpolation towards a “global” network by (randomly) rewiring some of the links, that is, by replacing some of the connections with connections between pairs of nodes chosen at random. Preliminary simulations have shown that the average path length between pairs of nodes, when measured as a function of the average number of rewirings, exhibits a cutoff so that the small world effect arises before the clustering property is lost. It seems as though rewiring plays an important role in the criteria for phase transitions. I think that percolation theory may shed some light on this phenomenon with implication that a network may have a number of phase transitions depending on the nature of the self-rewiring.

Modeling Energy Regulation

Current experimental research focuses on how substrates are absorbed in digestion and the consequent use of energy by different tissues in metabolism. Under different conditions of the supply of nutrients, energy gets partitioned to different tissues. Understanding the mechanisms governing this partitioning of energy has important implications for the management of undernutrition and obesity. I met Dr George Biltz, a pediatrician, during my second visit to SFI in October 2002. We started collaborating on a project to develop a model to understand human energy regulation. The broad objectives of the project are to develop dynamic mechanistic elements representative of the growth process that will enable:

1. The simulation of the change of body weight and composition (including specific organs) of children on different diets.
2. The simulation of body composition (and specific organ) changes of children

during different physical activities.

3. The understanding of the physiological mechanisms involved during energy partitioning to different tissues.

Some broader questions include:

- Of what consequence is the flexibility and inflexibility of metabolism during energy regulation?
- What does metabolic inflexibility tell us about the evolution of metabolism?
- Why is the evolution of diabetes mellitus in children much quicker that in adults?

Summary of Teaching Portfolio

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Contents

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1. Teaching Philosophy

I take teaching to be the **purposeful** creation of situations from which learners should not be able to escape without learning or developing.

In this definition I emphasise the importance of the existence of a purpose and the pursuit of one. This (for me) distinguishes education as a process from other situations in which learning occurs. Education (for me) is a process which involves and uses teachers and hence is distinct from the natural (and valuable) learning or development, which will often happen incidentally or accidentally, yet is totally tutor-less and learner-directed. I link learning and development because I believe that the highest cognitive learning is about the development of cognitive skills rather than the incidental exercise for students to master particular content within individual subject contexts. I, therefore, see and hope for the real possibility of an active, and even proactive, role for the facilitative teacher. My questions and comments in a structured learning activity are purposefully intended to be constructive, although I may not know in which direction they will lead. I believe that there are situations in which the influence of the teacher in achieving purpose is restricted to the particular structures and tasks, and there are those in which the engagement of the teacher continues throughout the student's pursuit of learning.

It is my goal to adopt a reflective (or self-reflective) approach to teaching and to emphasise that the process of learning about the world involves successive approximations and flexible models that are not necessarily true but instead useful for the questions being considered and the level of understanding that is desired. I believe that such an attitude offers a better account of the actual learning process and encourages students to question aspects of models and be active learners and sceptics instead of passive absorbers of "knowledge and truth". Scientific methods are usually evaluated and judged based on outcomes, data generated, percentage yields, accuracy and precision. I have included an approach that involves a more sceptical approach to the scientific process itself: an excursion within the details that support each step of the scientific method.

My expectations for my students' education have been shaped by the Mission Statements of the University of Cape Town and the Department of Mathematics and Applied Mathematics: "to lay a foundation of skills, knowledge and versatility that will last a life-time, despite a changing environment; critical enquiry in the form of the search for new knowledge and better understanding; promote the love of learning, the skill of solving problems, and the spirit of critical enquiry and research". These statements provide the foundation on which all my courses have been built.

Teaching Objectives

Of greatest importance to me is that my students can think critically, become independent learners and, above all, can respect and appreciate learning. It is of paramount importance that students are made clear of my commitment to their learning and that I treat each one openly and fairly in my efforts to stimulate that learning. Specifically, I strive to

- **Encourage and inspire students to become independent learners**
  By independent learners I mean that students are able to reflect on their own learning and evaluate their learning process. I have attempted to design the structure of my courses so that students can individually reflect on the content and on their learning process. For example, in the MAM251F class I have asked students to write an "open-ended" essay that would integrate some area of their major subject/s (for example, chemistry) with mathematics and/or statistics. One of the reasons for this task (and one of the three objectives of the MAM251F course) was to develop student's ability to quantitatively analyse problems arising in their own field. I have also designed projects that use technology to prompt

students to individually discover certain key concepts. This also provided students with the opportunity to reflect on what they had done. In the future, I would like to explore better uses of technology in the teaching of mathematics.

- **Promote the development of critical-thinking skills**

I structure tutorial activities so that students are challenged and at the same time are able to reflect on and also analyse their answers critically. I take this type of analysis to be a cognitive process in which students can explore patterns and generalities, and look for noteworthy exceptions. I use discussion groups as a means for students to test their understanding of key concepts; and sometimes I even play devil's advocate. I found that such intellectual challenges force students to understand, to integrate what they are doing into a broader context and to communicate their understanding to others.

- **Respect each student as an individual.**

Developing a hypothesis involves the framing of a question or set of questions and also the determination of what is to be asked. I believe that the questions one asks may be constrained by one's beliefs that in turn may be shaped by, among other things, social, cultural and economic contexts. In addition, students take in and process information in different ways. It is for these reasons that I pay particular attention to my teaching style in order to address as many different learning styles as possible.

- **Foster a sense of cooperation and community in the classroom.**

I have used informal and formal collaborative learning techniques to assist students to become interdependent and practice their communication and problem-solving skills. Some informal collaborative learning exercises that I have used is to divide students into groups of two or three at the beginning of a lecture and ask them to recall the previous lecture, or to divide students into groups of two or three towards the end of a lecture and ask them to summarize the lecture. Formal collaborative learning activities include setting team projects: a single project is done and handed in by teams and only one mark is given per team (and may be adjusted for individual contributions)(see ASPECT, 1997 report)

- **Recognize the use of technology to enhance the teaching-learning process.**

Before technology played a role in education, the demands of humdrum tasks left no time for the teaching and learning of higher-level abilities. I structure course activities so that students can make use of technology to think more deeply about concepts and to explore (usually on their own) and (hopefully) to discover important patterns and abstractions. I use technology as a tool for students to analyse problems effectively and to formulate decisions. I have found that the use of computers in the classroom reinforces the need for an appreciation of the diversity of mathematics tools that are applied to various areas. More than that, the use of computers actually makes it feasible to expose students to a breadth of topics, both within other courses and within courses in their programmes. The use of computers and modelling increases the need for mathematics although many think the opposite! Because many "real-world" problems do not lend themselves to easy pen-and-paper solutions, the ability to use computers to visualize and analyse solutions is critical. No matter which way a solution is obtained, one's intuition as to whether the result makes sense is important, and doing this effectively may even require some pen-and-paper ability.

- **Demonstrate an excitement about teaching and learning.**

I have attempted to make my lectures very interactive: engaging students by asking questions and to give (where possible) interesting and current examples. Because I love what I do, this seems to flow from my enthusiasm for science and learning quite easily.

- **Maintain high standards in a caring, supporting environment.**

I have always adopted an open-door policy to students and have given students the opportunity to fully express themselves. This has lead to me being awarded a counselling honorarium in 1996 while working in ASPECT. I also ran career development workshops for students and tutors (see ASPECT, 1997 report).

Most importantly for me is to acknowledge that each course I teach will require a different balance between process and structure, depending on my course objectives. I will continue to learn from my mistakes by reflecting on my teaching, personal and professional development, and to actively seek better ways to transform and extend my teaching scholarship.

Presentation at the Third Southern Hemisphere Symposium on Undergraduate Mathematics Teaching Kruger National Park, South Africa 01- 05 July 2001. "Targeted Intervention: A Mathematics course for Geology and Chemistry students."

2. Teaching

a. Summary of courses taught at UCT

Course	Year	Semester	Convenor	Number of students
END 107W /MAM103W	1996/1997	1 AND 2	NO	80-100
MAM 280W	1996/1997	1 AND 2	NO	30-40
STA 101H	1998	1	YES	80

STA 220S	1999	2	YES	150
MAM204S LS	1999	2	YES	4
MAM 251F	2000	1	YES	57
MAM 251F	2001	1	YES	59
MAM 251F	2002	1	YES	72
MAM 252F	2003	1	YES	70
MAM 380F	2003	1	YES	60
MAM 106H	2004	1 AND 2	YES	180
MAM 200W	2004	2	YES	220

3. Brief Description of Projects (Research) in Mathematics Education

a. Integrating Quantitative skills for chemistry and geology students

Many mathematics departments usually teach a variety of courses for students from different science departments and even different faculties. These “service” courses are usually taught in the same way as the courses for mathematics major students. However, in science, because of the need to better analyse and interpret experimental data and the increased use of mathematical tools in chemistry and geology textbooks, it is becoming necessary to teach these science students quantitative skills beyond the scope of first year mathematics courses. I designed a one-semester second year mathematics course, mainly for chemistry and geology students, with three specific objectives: to develop students’ ability to quantitatively analyse problems arising in their own field, to illustrate the great utility of mathematical models to provide answers to key chemistry and geology problems, to develop students’ appreciation of the diversity of mathematical approaches potentially useful in the chemical and geological sciences. I have developed techniques to assist students to transfer their quantitative skills to their particular major courses.

b. Examining student beliefs of a service mathematics course

My goal is to develop a framework/model for student beliefs in mathematics. This project started with a number of questionnaires that attempted to determine what student's value in their learning of mathematics. The next step of this project is to elucidating the paths (beliefs) to achieving those values and how we as teachers can change certain beliefs in our structured activities.

4. Publications (as related to teaching and education)

- Witten G.Q. (2004). A Mathematics course for Geology and Chemistry majors. (To appear in *Educational Studies in Mathematics*, 2004)

- Witten GQ (2003). Reflecting on the design of a mathematics course for Chemistry and Geoscience students (Accepted for publication as a short paper in the Proceedings of the AMESA '03 conference, July 2003). http://www.sun.ac.za/MATHED/AMESA/AMESA2003/Index.htm

- Witten GQ (2004). The Cardiovascular System, *Maths For All* Textbook chapter (Submitted in November, 2003)

- Witten GQ (2001). Targeted Intervention: A Mathematics course for Geology and Chemistry majors. (Published in the *Communications* of the Warthog Delta conference, July 2001).

- Witten GQ (2001). Career Development Process: 6 Key lessons. (Careering Magazine, U.C.T., February 2001)

- Report: MAM 251F Quantitative skills for scientists (2001)
- Mathematics Education Project (UCT) publications:

Modelling Biological Systems - The Mathematics of Animal Growth (May, 1998)

The Mathematics of Markets (August, 1998)

- Teaching Mathematics in the Academic Support Programme in Engineering of Cape Town at UCT (1997)

- Book Review for the Centre for Research in Engineering Education (1996)

Other Activities and publications related to education and scholarship

- Nominated for the Distinguished Teacher Award (2002 & 2003), University of Cape Town.

- Consultant for Schools Development Unit, University of Cape Town (2003-)

- First Year handbook for all first year mathematics and applied mathematics students (2000, 2001)

- Assisting Mr Iegsaan Isaacs from the Science Faculty office to promote science by giving talks at schools in the Western Cape (2000, 2001)

- Consult with School's Development Unit (UCT) on financial mathematics content for textbooks (2001 - 2004)

References

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