5-Year Strategic Plan for the Quantitative and Systems Biology Graduate Track (QSB)
November 2008

I. Overview

Biology is widely believed to be on the brink of a fundamental transformation from a primarily "descriptive" study of individual components of biological systems, to a science based on creating a comprehensive and ultimately predictive understanding of biological systems. This so-called "systems" approach to biology is already dramatically changing how biological research is done, building on foundations of core disciplines and leading to new connections with the physical and computational sciences. This new biology offers the promise of a much more complete understanding of living systems and ultimately new treatments for complex diseases such as asthma, diabetes, and cancer. The central role of multidisciplinary approaches in systems biology provides UC Merced with an excellent opportunity to develop life sciences research and graduate programs at the forefront of this field. The small size and lack of disciplinary barriers at UC Merced have already been fostering a number of multidisciplinary research programs within QSB (see below). Similarly, although many universities are developing academic programs in systems biology, QSB has the advantage of starting its programs from a "blank slate" with no existing institutional barriers. Furthermore, systems biology will be greatly enabled by many of the new or emerging graduate programs and research efforts at UC Merced, such as the applied mathematics and bioengineering programs, and the Center for Computational Biology.

At present the QSB graduate group consists of 27 faculty, 37 Ph.D. students and 7 M.S. students with research projects that fall into five research themes (described below). The size of the graduate group belies a serious need for additional faculty to deepen the research base within these research themes. Indeed, the current QSB faculty would be spread across many departments and schools in a traditionally organized university. While this diversity of disciplinary expertise should be a strength in developing innovative research programs, it is essential that the group develop a critical mass of expertise in a selected set of areas to allow it to recruit top students and faculty and to be competitive for large research and training grants.

Below is the hiring priority for AY 09-10. Currently, less than 28% of the QSB faculty are at the associate of full professor levels. Hence, the priority is for a senior level hire. The QSB GG is requesting a new senior level position to 1) raise our research university to international prominence, and 2) meet the growing teaching needs of our graduate and undergraduate students. Indeed, the QSB GG is the largest graduate group on campus, yet has only a few stand-alone graduate courses. Furthermore, the teaching needs for undergraduate biology courses are growing rapidly. Notably, our hiring priority can meet these goals with the current limitations on laboratory space and startup funds.

<u>Quantitative and Systems Biology Graduate Group Hiring Priority, AY 09-10</u>

Stem Cell Biologist

This position seeks a senior-level hire with training in molecular, cell and developmental biology who applies their expertise to studying stem cell biology. This position will be part of the Stem Cell Consortium group of faculty (http://stemcells.ucmerced.edu/). Areas of particular interest include embryonic and adult stem cell biology, epigenetics, reprogramming, and applications for regenerative medicine using appropriate model organisms. Expertise in human ESC culture and differentiation and humanized mouse models would be a plus. This senior-level hire would provide leadership to junior level faculty, would be expected to lead initiatives such as training grant applications for graduate students in stem cell biology, and also to create and teach upper division and graduate level courses specifically on stem cell biology. The CIRM has been generous to UC Merced faculty in the awarding of over $9M in research and facility grants since 2006. This hire could fall under the SNS hires projected for 2009 and later in cell biology, cancer biology, and developmental biology. This position is synergistic with the stem cell research interests of the BEST Graduate Group.

Justification: The QSB GG is requesting this new senior level position to 1) raise our university to international prominence, and 2) meet the growing teaching needs of our graduate and undergraduate students. The QSB GG proposes to attract an internationally recognized senior

faculty member in stem cell biology for several reasons. First, the $9M awarded to UC Merced from the California Institute of Regenerative Medicine (CIRM) and the new Stem Cell Research Facility will attract the interest of top flight senior investigators, giving QSB an excellent chance to hire someone with international prominence in spite of current space and startup fund limitations. The new Stem Cell Facility and Stem Cell Consortium will significantly reduce the startup and space needs of a senior hire. Second, the senior hire will provide leadership to the many junior faculty in stem cell research. He/She will organize the junior faculty to submit proposals for federally funded training grants, program project grants, and shared instrumentation grants. Finally, this senior hire will help develop needed graduate courses and relieve the growing burden of teaching undergraduate biology courses.

II. Research Themes in the Quantitative and Systems Biology Graduate Group

Research programs

As described in the introduction, there are many exciting research opportunities within the broad area of Quantitative and Systems Biology. The research interests of the founding faculty have fostered a number of initial life sciences research themes for the QSB graduate group. These themes are all examples of the new systems biology described above and have been chosen to leverage special opportunities available to UC Merced and to depend on a common core of facilities and expertise.

Research Themes

1) Predictive Understanding of Cell Fate Decisions & Cell Signaling and Response

The ontogeny and maintenance of multicellular life involves an exquisitely complex developmental process in which undifferentiated "stem cells" give rise to specialized cell types. Understanding this process promises to provide new treatments for many complex disease states related to developmental failures. Moreover, because of their ability to generate new specialized cells, stem cells hold the potential to treat a vast array of health problems, including spinal cord injuries, Parkinson's disease, diabetes, and many others. Elucidating the complex mechanisms by which extrinsic and intrinsic signals determine the proliferation or differentiation of stem cells is inherently a systems-level challenge, and will require new technologies for collecting data on cell populations and individual cells, and new methods to build models of cell decision processes. The new California Institute for Regenerative Medicine, which will be awarding hundreds of millions of dollars in stem-cell related research funding over the next several years, makes this area a "special opportunity" for UC Merced.

An ultimate goal of cell biology is to achieve a complete understanding of the biochemical pathways controlling cell sensing and response to outside stimuli. New analytical technologies are allowing genomic, proteomic, and metabolomic characterization down to the single cell level. A combination of experimental investigation and modeling of the interacting pathways and the kinetics of the flow of information in those pathways will provide data to determine the mechanisms of cellular responses to infection, oxidative stress and other environmental factors. This knowledge will allow the development of new therapies to treat diseases, including the potential of chemoprotective agents against environmental toxins and aging.

2) Ecology and Evolutionary Biology

Large-scale, inexpensive DNA sequencing has placed evolutionary approaches at the center of modern biological research. Complete genomic sampling of hundreds of eukaryotic and prokaryotic organisms, coupled with partial genomic sampling of all branches and most twigs on the tree of life, opens unprecedented avenues of research, previously available for only a few model organisms, . Expanding biological inquiry to include many levels of organization and all branches of the Tree of Life raises new analytical challenges in comparative and integrative biology. This new approach necessitates transfer of the infrastructure (computational and molecular) available for model organisms to the developing quantitative research systems of 'non-model' taxa and also among the new systems themselves with the goal of attaining a thorough understanding of evolutionary explanations for ecological and organismal phenomena.

UC Merced faculty, from founding faculty to recent hires, have created a strong foundation for a signature research theme in integrative biology, ecology, and evolutionary biology including the origins of

invertebrate life, symbioses, the emergence of antibiotic resistant microbes, and genetic-, species-, and ecosystem-level conservation of biodiversity, including the processes that link these levels (i.e. biocomplexity). Biocomplexity research particularly applies quantitative systems biology techniques to explore the emergence of self-organized, complex behaviors or structures from the interaction of many simple agents in the environment. Such emergent complexity is a hallmark of life, from the organization of molecules into cellular machinery, through the organization of cells into tissues, to the organization of individuals into communities. The study of biocomplexity in the environment requires novel approaches to understanding pattern and process across multiple temporal and spatial scales, and draws upon interdisciplinary efforts at the interface of biology, physics, chemistry, and mathematics. This research program also has the potential for strong linkages to programs in Earth Systems Science and Environmental Engineering.

3) Complex Disease States

A combination of factors including an aging population, changing diets and lifestyles, as well as unknown, possibly environmental, factors, have led to a dramatic increase in diseases such as diabetes, asthma, and cancer. Such diseases can be described as "complex" because they are influenced by genetic, environmental, behavioral and cultural components and can only be fully understood and effectively treated using multidisciplinary approaches. The Central Valley provides a microcosm of the health challenges of the entire state and nation with high rates of "complex" diseases. A strong research program in this area would foster collaborations with healthcare providers in the Central Valley. Moreover, the local community would provide unique cohorts for studying strategies for treating or reducing the incidence of these diseases.

4) Chemical Biology, Biological Chemistry and Physics

The fields of chemistry and biology have had a long and fruitful partnership, leading to a detailed understanding of many of the chemical processes underlying life. Recently, there has started to be a reciprocal flow of information from biology to chemistry with biology providing "metaphors" for new chemical strategies, such as self-replicating chemicals. Ultimately, biological examples could provide more detailed designs and design principles for practical chemical applications such as catalysts or detectors. Likewise, chemistry informs the biological sciences by providing accurate chemical means of monitoring biological systems. From a physics perspective, studies of biological systems that serve as paradigms of complex, self-assembling, non-equilibrium systems leads to new and interesting physics apart from driving technological innovation. Biophysics for its part is the most rapidly growing area in physics research, attracting both seasoned physicists from several different subfields and large numbers of entering students. Chemical biology could have strong synergies with the bioengineering program and applications in earth systems science and environmental engineering.

Much of the recent dramatic progress in the life sciences has been driven by quantitative approaches and a molecular-level understanding of complex biological systems. Experimental, computational and theoretical methods and techniques from Physics and Chemistry have played a significant role in these advances. Cutting-edge imaging techniques have provided snapshots of biological molecules and their complex assemblies in action and have also led to dramatic improvements in medical imaging. The ability to control matter at the smallest scales, using for example optical and magnetic tweezers, has allowed us to study and manipulate biological processes at the single molecule level. The result of advances in biological physics and chemistry will be a better understanding of normal and pathological processes at both the molecular and systems level, which is key for the design of rational approaches to diagnosis and treatment.

5. Gene-Environment Interaction

An interdisciplinary group composed of faculty and students in QSB and ES has formed a center that focuses on the interaction of the environment on gene expression. A major focus is on oxidants and other electrophiles in both damage to organisms and in normal physiology; however, many other environmental variables will be investigated. The present and proposed work includes studies of photobleaching of coral, how Hepatitis C infection is modulated through redox signaling, how elephant seals avoid injury in extreme environments to which they are adapted, how growth factors act through redox signaling, and understanding the recognition of oxidants important to inflammation with the goal of designing anti-inflammatory pharmaceuticals. Reactive oxygen and nitrogen species (which includes free radicals, such as superoxide and

nitric oxide) play essential and ubiquitous roles in biology but they are only part of the complex interactions of the environment with gene expression that is the focus of this group.

Resource needs for the QSB Graduate Group

There are very large funding sources for life sciences research. Federal agencies provide approximately $30 billion per year and research funding is also available from many foundations and private companies. Nevertheless, these funding sources are all highly competitive and successfully acquiring funding requires a strong research program. The five research themes described above build on excellence in the foundational sciences but also are well aligned with the newest academic and research priorities of the funding agencies and foundations. Most major research universities are also creating research programs in quantitative and systems biology, but their natural advantages in having already established research programs and facilities may be somewhat offset by having larger institutional barriers to building multidisciplinary research efforts.

Faculty

The QSB critically needs new faculty hires to enable the research programs described above. The QSB faculty are presently drawn from the Schools of Natural Sciences and Engineering. Many of the QSB priorities for faculty hires are represented in the strategic plans from these two schools. Specifically, the QSB faculty endorse the hiring requests for the life-sciences and bioengineering research programs, including the areas of biomedicine, integrative biology, evolutionary biology, environmental effects of human health, biochemistry, chemical biology, and bioengineering-related nanotechnology. The QSB would also place a special emphasis on future faculty recommendations in areas that bridge traditional disciplines and faculty whose research involves integrating multiple techniques to solve problems in the life sciences and bioengineering.

Core Facilities

The QSB research programs require continued development of research facilities. Good progress has been made over the past year in developing life sciences research resources; however, the facilities require continued development, and several facilities are needed that have yet to be developed. The vivarium opened for animals in Summer 2007 and is used by several QSB faculty utilizing rodent and frog models. CIRM awarded UC Merced a facilities grant to build the Stem Cell Instrumentation Foundry (SCIF) which will contain Class 100 cleanrooms suitable for microfabrication that will be open to the entire UCM faculty. Construction of the SCIF is expected to begin in 2009. Shared instrumentation has been purchased by several groups of faculty that are intended to be part of proposed cores, such as the Genomic Center of Excellence and Quantitative Cytometry Core Facility. These instruments have been purchased through the awarding of equipment grants from NSF, and UCM Graduate and Research Council grants, as well as with faculty start-ups. Formal procedures for recommendation of core facilities as official University research cores was discussed by Graduate and Research Council in AY 2008-09, and are still under review. As current core equipment has been purchased and is now maintained by current faculty start-up funds, new faculty start-up packages could include funds for salary support for core managers and maintenance agreements. University financial support for the salary of core managers, and improved administration, such as recharge set up for UC and non-UC affiliates is key for the success of any research core. The full establishment of core facilities is crucial for the success of research progress, recruitment and retention of faculty and should be a high priority for the School and the Office of Research, under the direction of the Vice Chancellor for Research.

Table 1: Summary of facilities required for QSB research programs. Facilities shown in bold are already under development.

	Cell Fate	Evolution & Biocomplexity	Complex Diseases	Chemical Biology/ Biochemistry	Gene-Environment Interactions
Genomics	√√	√√	√	√	√
Cell Imaging	√	√	√	√	√
Proteomics (Mass Spec.)	√√	√	√	√	√√
Proteomics (Microarray)	√	√	√√	√	√
Animal (Vivarium)	√√	√	√√		√
Animal (Transgenic)	√		√√		√
High-field NMR			√	√√	

III. QSB Academics

Overview

In AY2008-2009, there are 37 Ph.D. Students in the Quantitative and Systems Biology Graduate Group (QSB). Based on the growth in QSB faculty over the past year and the concomitant growth in research funding awarded to UC Merced, we expect to admit at least 15 doctoral students in AY09-10. Another source of growth in the life sciences graduate programs will be M.S. students. We currently have 7 M.S. students and there have been many inquiries about the MS program being offered through QSB, so it may be reasonable to assume that 5% of the graduating Biological Sciences seniors would go on to this program. The evidence from existing programs is that UC Merced has the opportunity to create a substantial graduate program in the life sciences. Nationwide, the pool of biology doctoral students is very large. In 2002 nearly 4,500 life sciences Ph.D.s were conferred—by comparison in the same year 3,800 were conferred in all of the physical sciences combined. [http://nces.ed.gov/programs/digest/d03/tables/dt254.asp].

Most graduate programs in the life sciences are very discipline-oriented, e.g. biochemistry, cell biology, etc. This restricts the type of students entering the program and limits the training opportunities for students in the program. In contrast, the QSB brings together faculty from a wide range of disciplines with broad expertise to investigate the complex systems and networks responsible for the biological functions of cells, tissues and organisms. The current QSB faculty is drawn from both the Schools of Natural Sciences and Engineering covering disciplines including molecular and cell biology, evolutionary biology, genomics, proteomics, signal transduction, experimental technologies, and computational biology. QSB students are involved in a wide range of life sciences research projects, and this will continue to grow as new faculty join the graduate group. The doctoral program emphasizes quantitative analyses at multiple levels of biological systems, development and use of novel model systems, and computational and analytical approaches for the study of biological processes.

Academic Resource Needs

A central part of a successful graduate program are a diversity of advanced courses. The QSB graduate track requires 5 full graduate courses for its Ph.D. program, and it is expected that many students will take more than this minimum. In its first few years, the QSB track has offered just one specialized graduate course each semester (QSB 290, Topics in Quantitative and Systems Biology). To provide other necessary graduate training, the QSB faculty have led individualized study sections (QSB 299) or taught graduate classes that "piggybacked" on upper division courses. Although this was a necessary expedient due to the large undergraduate teaching commitments of QSB faculty, this is neither ideal nor sustainable. Therefore, starting in AY07-08, the QSB graduate track plans to offer at least 1-2 stand-alone graduate courses per semester. The exact course offering will depend on the student needs and faculty availability.

Besides QSB290 and QSB299, the following QSB courses have been approved and are in the catalog:
QSB 200: Advanced Molecular and Cellular Biology
QSB 212: Advanced Signal Transduction and Growth Control
QSB 214: Tissue Engineering Design
QSB 215: Principles of Biological Technologies
QSB 217: Lab on a Chip: Developing 3rd World Diagnostics for Global Health
QSB 220: Cellular microbiology
QSB 227: Virology
QSB 241: Advanced Genomic Biology
QSB 242: Genome Biology
QSB 244: Phylogenetics: Speciation and Macroevolution
QSB 247: Advanced Theory in Ecology and Evolution
QSB 250: Embryos, Genes and Development
QSB 252: Cancer Genetics and Tumor Biology
QSB 261: Human Physiology
QSB 280: Advanced Mathematical Biology
QSB 281: Advanced Computational Biology
QSB 283: Population Genetics

QSB 294: Ethics
QSB 296: Professional Skills Development

IV. Milestones and Assessments for the QSB Graduate Group

Research Programs

The success of the UC Merced QSB Graduate Group involves many components. First and foremost, is the success of the individual life sciences faculty in producing important research results leading to recognition, high-impact publications and continued research support. However, another metric for success will be UC Merced's effectiveness in developing unique, multidisciplinary research programs based on the cross-disciplinary principles of the university. Success in this metric will make the program competitive for special funding for research centers and training programs, and will also help attract strong faculty, post-docs and graduate students to UC Merced. Another long term metric will be the impact of the life sciences programs at UC Merced on the community, both in economic development and in partnering with healthcare providers and health-related community organizations.

Academic Programs

An important metric in evaluating the success of our academic life sciences programs will be the graduate and undergraduate enrollments. In AY08-09, there are 37 graduate students in the QSB, of whom 8 have advanced to candidacy. Graduate enrollment at two of the smaller UC schools (UC Santa Cruz and UC Riverside) represents approximately 10% of the student body. UC Merced will probably be most similar to graduate enrollments at the smaller UC campuses. However, we anticipate that life sciences will be well-represented in the graduate student body because of the strong growth to date of the QSB graduate program at UC Merced. In the long run, we anticipate the percentage of graduate students enrolled in life sciences to at least track the figure for the UC Davis campus (17%).

Assessment of the success of the QSB program will involve monitoring both the competitiveness of the graduate student applicants to the programs and the long term career success of its graduates. Despite its newness and small size, the QSB graduate group at UC Merced is attracting academically strong students.