#### Strategic Academic Vision for Quantitative and Systems Biology at UC Merced

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## A. Executive Summary

UC Merced Mission priorities include discovery of new knowledge and cross-disciplinary inquiry. The best strategic expression of these core values within biology is Quantitative and Systems Biology (QSB). QSB is well-poised to convert UC Merced investments in interdisciplinary science into biological advances. QSB must revamp from an umbrella group for the life sciences with a renewed and sharpened mission to **accelerate biological discovery through innovation**. In its core values, QSB champions the unity of biology, innovation and interdisciplinary science and engineering, quantitative approaches, and integration of models and data to explain and predict biological phenomena, with a focus on information, organization, mechanisms, dynamics and emergent phenomena in living systems. QSB's grand challenge is to fully explain and predict the organization and dynamics of living systems. To get there by 2020, QSB must differentiate its membership, expand transdisciplinary core faculty, and cultivate extramural partnerships and investments to create a Quantitative and Systems Biology Institute (QSBI) and a Department of Quantitative and Systems Biology that offers a unique brand of quantitative and interdisciplinary biology research and education focused on information, organization, dynamics and emergent phenomena in living systems and emergent phenomena in living systems and interdisciplinary biology research and education focused on information, organization, dynamics and emergent phenomena in living systems, and the synthesis of data in integrated models to explain and predict those phenomena.

## **B.** Definition of Thematic Area

#### A Quantitative and Systems Biology that fits UC Merced

Quantitative and Systems Biology is a foundational idea of UC Merced around which many research groups and organizations on campus have organized and invested. The interdisciplinary and forward-thinking themes on which QSB was founded have well served UC Merced undergraduate students, graduate students, and faculty in this 'century of biology' [Venter and Cohen (2004) New Perspectives Quarterly 21(4):73]. QSB also responded adroitly to the National Research Council's recommendations for biological research and education in the 21<sup>st</sup> Century (http://www.ncbi.nlm.nih.gov/books/NBK32500/ and

http://www.nap.edu/openbook.php?isbn=0309085357). With such an auspicious start, QSB helped build UC Merced's largest graduate and undergraduate programs. Upon this solid foundation, QSB is now, with renewed purpose and bold leadership, transitioning from an umbrella for research in the life sciences into a revitalized graduate program. By 2020, QSB aims to develop a Quantitative and Systems Biology Institute (QSBI) ORU and QSB Department centered on a **unique brand of interdisciplinary, quantitative and systems biology** for UC Merced. The strategy outlined below charts a path to renewal and sharpening of a bold mission and vision for QSB that is inclusive, transparent, and enabling, and facilitates new growth and collaboration without being all things to everybody. UC Merced can support QSB's renewed mission, by adding either Quantitative and Systems Biology or Information and Information Systems as a strategic research theme in UC Merced's Strategic Academic Vision. By rallying behind QSB's renewed mission, UC Merced can drive cutting-edge, interdisciplinary innovation and accelerate biological discovery in highly diverse areas of application that matter to UC Merced faculty, the community, and beyond.

#### How the QSB Mission Fits into Campus Thematic Areas

We believe that Quantitative and Systems Biology will prove to be a strategic research theme for our campus. QSB cuts across seven of the nine Themes (themes 3 though 9) suggested by the SAF Working Group. Our stated Mission is to accelerate discovery in *Life Sciences* (theme 9) through innovations in science and technology from other areas, particularly *Information, Computation and Data Sciences and Engineering* (theme 7) and *Matter Science and Engineering* (theme 8). In this way, QSB will stimulate *Innovation and Entrepreneurship* (4) around biotechnologies to benefit *Environmental Sustainability* (5), *Human Health* (3), and *Energy and Energy Systems* (6).

We propose an alternative Thematic Area that would unite QSB with many other SAF Round One proposals: *Information and Information Systems*. This proposed Thematic Area resonates across proposals from all three schools such as: CIS, CHASE, MIST, Applied Philosophy, CCB, MSE, AHA, SpARC, SNRI, ERI, Public Health, AM, CTC, CeQR, CIS, HRRI, AMM, MSE and many others.

# C. Intellectual Components of the Initiative

Importance of Quantitative and Systems Biology

Many of society's fundamental problems and challenges are complex and multifaceted, requiring integrative approaches across disciplines to solve them. The grand challenge QSB will address is to fully explain and predict the organization and dynamics of living systems. Why does life happen in the universe? How do system-level properties like robustness, plasticity, adaptation and cooperation emerge from the dynamics of smaller entities? To answer these questions, we must study the organization and flows of not just matter and energy but information in biological systems. Systems biology offers a framework in which to answer these questions. It requires the integration of experimental data and computational models to explain how salient properties of biological systems, measurements and simulations are guided by iteratively improved models with increasing quantitative accuracy. Scientifically, we must not only disassemble systems and identify their parts — we must also put "Humpty Dumpty back together again" or build and test integrative models of those systems (*Hope for Humpty Dumpty: Systems Biology of Cellular Signaling* 

http://www.plantphysiol.org/content/152/2/470) to test hypotheses and make new predictions about how the systems work as a whole. Quantitative and Systems Biology at UC Merced is important because it challenges biology students of today to train more deeply in quantitative, integrative and interdisciplinary approaches. As a defining focus of a biology graduate program, Quantitative and Systems Biology aims to accelerate the pace at which paradigm-shifting discoveries transform the field.

Key recent achievements in systems biology have shown that information processing and "learning" emerge from the collective behavior of multiple interacting components: whether inside cells in protein and other macromolecular interaction networks, across cells in immune and neural networks, or between individuals in populations. Even in relatively simple biochemical systems, emergent phenomena such as cellular circadian rhythms have an essentially collective basis in molecular interactions, which have recently been mapped in much greater detail and incorporated into synthetic biological circuits. The emergent basis of robustness in cellular and developmental phenotypes against noise and perturbations has been clarified, answering hundredyear old questions in theoretical biology. Comprehensive and quantitative measurements of biological processes have enabled the first high-resolution simulations of entire cells. Advances in synthetic biology have helped whole industries shift from petroleum-based to renewable-resource-based manufacturing processes. Advances in Next Generation Sequencing have laid bare microbial worlds within us and around us - worlds that matter greatly to health and the environment — about which truly nothing was known a decade ago. Innovations in single molecule and single cell analyses have revealed how noise and randomness actually generate order in biological systems. The pace of discovery is so fast that it is the sociological splintering of biology into overspecialized subdisciplines that hinders lateral diffusion of technical and conceptual innovation across the field as a whole. Therefore, our grand challenge going forward is to reunify biology as an indivisible field centered on quantitative and systems approaches. We believe this will enhance the discovery of new generic principles to better explain and predict living systems in general.

#### How will investment in this area make our program distinctive/competitive?

Despite its strong record of success, UC Merced has fallen behind other institutions in building quantitative and systems-oriented biology even though these themes represent the widely recognized future directions of biological research, and even though UC Merced possesses unique structural advantages to lead in those areas. Some of UC Merced's structural advantages are external: California has two of the nation's top biotechnology hubs and at least five prominent universities in the field of systems biology, attracting prominent scholars from around the world. Yet most of these competitor programs are housed in disciplinary programs, often with an exclusively biomedical mission. UC Merced therefore has an opportunity to distinguish itself by promoting systems, quantitative, and interdisciplinary approaches across all areas of biological inquiry. QSB's recruitment strategy further takes advantage of the interdisciplinary make-up of its faculty leadership and membership — which include engineers, physicists, mathematicians, and chemists — by recruiting and co-training students from all fields represented by its faculty.

# D. UC Merced's Role in Quantitative and Systems Biology

The unique and distinctive brand of quantitative and systems biology at UC Merced is summarized by its core values and its revised mission, which is, in short, is to accelerate biological discovery through innovation. More fully, QSB aims to accelerate biological discovery through innovative, interdisciplinary science and engineering of living systems and their properties, which emerge from their information, organization, mechanisms and dynamics.

QSB core values are 1) the unity of biology, 2) innovation and interdisciplinarity in science and engineering, 3) quantitative approaches, 4) a focus on information, organization, dynamics and emergent phenomena in living systems, and 5) integration of data with models to explain and predict biological phenomena. In developing a unique and distinctive brand of Quantitative and Systems Biology that promotes an integrative and interdisciplinary vision for biological research and education, QSB will play a leading role in shaping biology in the 21<sup>st</sup> century.

All UC campuses have strengths in quantitative or systems biology but QSB at UC Merced will be unique in how it unifies biology around the interdisciplinary perspectives of quantitative, systems, and informationoriented approaches. As a biology graduate program, QSB will also be rather unique in taking advantage of its faculty from diverse disciplines to recruit and uniquely co-train students from engineering, physics, computer science and math as well as biology backgrounds. Current strengths in QSB at UC Merced include Molecular and Microbial Systems Biology, Quantitative and Computational Biology, Bioinformatics, Biochemistry, Biophysics and Biomathematics. QSB proposes to continue to strengthen Biology, Theoretical Biology, Cellular and Developmental Systems Biology, Organismal and Integrative Systems Biology, and Systems Ecology. Growing the systems interface across biology subdisciplines not only helps create a unique brand of systems biology at UC Merced, it takes advantage of our interdisciplinary mission to leapfrog other campuses in the reunification of biology as a field.

#### **Enabling Biology through QSB**

To maximally capitalize on current investments, UC Merced biology must define an interdisciplinary group of **affiliated QSB faculty** and additionally expand its **core QSB faculty** who demonstrate the application of interand transdisciplinary QSB approaches to biological problems both individually and in collaborative teams (for more on transdisciplinary science please see e.g. [*Gray (2008) Enhancing Transdisciplinary Research Through Collaborative Leadership. Am J Prev Med. 2008 35(2 Suppl): S124–S132]).* Newly hired core QSB faculty will share common motivations and approaches, and address research questions about the information, organization and dynamics of biological systems in general. In order to hire transdisciplinary core QSB faculty, QSB will assemble **interdisciplinary QSB search committees.** This will help ensure the hiring of core QSB faculty who actively and intrinsically promote interdisciplinary research not only through collaboration, but individually. **QSB should have an open door policy with a low-barrier to membership for affiliated faculty.** Faculty need not "opt-out" even if they don't share all core values or fully identify with the QSB mission.

### E. What bylaw units/grad groups might participate, and how?

#### QSB and the Organization of Biology at UC Merced

QSB faculty are members of the MCB, LES, Math, Chemistry, Physics, and Engineering bylaw units. According to its current recruitment and curriculum strategies, biology faculty will have more options to recruit and train students from non-biology fields through QSB and *vice versa*, giving QSB a unique role that is complementary to that of other graduate groups. Another complementarity of the QSB, MCB, ES, and CCB graduate groups lies in their distinct missions (Figure 1, left). In addition, we advocate for undergraduate instruction in quantitative, systems, and synthetic biology at UC Merced. We propose that a QSB-themed emphasis for the UCM Biology major should be introduced, with optional subemphases be as shown in Figure 1 (right).



Figure 1. Mission Foci of UCM Biology Graduate Groups and Emphases/Subemphases of UCM Biology Major. The MCB Graduate Group is anticipated to start in January, 2015. A "Department of QSB," described below, is proposed for September, 2017.

# F. General description of special programmatic needs

QSB 2020: QSBI and a Department of Quantitative and Systems Biology for UC Merced By 2020 QSB proposes to establish the Quantitative and Systems Biology Institute (QSBI) as an ORU to manage campus-wide partnerships in furtherance of its mission. For example, QSBI will synergize activities with other graduate groups, HSRI, SNRI, ERI, the Center for Statistical and Quantitative Research (CeQR), the newly proposed Center for Human Adaptative Systems and Environments ORU (CHASE) and the newly proposed Center for Theory and Computation CRU (CTC). QSBI can provide support for interdisciplinary research consortia with QSB affiliate faculty in SoE and SSHA for initiatives like complex systems neuroscience, strengthening a connection between QSB and the Cognitive and Information Sciences unit. Additionally, QSBI will manage relationships with state, federal and private entities vested in UC Merced's quantitative and systems biology programs. Examples include QB3, biotech companies including Contract Research Organizations and incubators, fostering extramural public-private partnerships and capital investments on campus. In addition, the UC Merced Mission meshes graduate and research programs with high-quality undergraduate programs and interdisciplinary research as a nourishing foundation for undergraduate learning. By 2020, a UC Merced Department of Quantitative and Systems Biology will serve the current and growing demand for an interdisciplinary undergraduate degree in quantitative and systems biology. There is pent-up demand for undergraduate training in computational and systems biology at UC Merced. Informally from a poll in BIO 2, about 10% of Bio majors are hobby programmers interested in computational biology. But this is probably an underestimate, as today quantitatively-minded students choose other programs besides the BIO major. Also UC Merced has, since 2012, fielded teams to iGEM (http://igem.org/) even without a campus unit for synthetic biology. With its proximity to world-leading tech industries, a new undergraduate Quantitative and Systems Biology emphasis of the Biology Major would create new opportunities for our student population and drive a unique recruiting brand for UC Merced.

### Getting to QSB 2020

In **Phase I** (completed AY13-14), a **renewed QSB mission** must be negotiated to lead this effort with all UC Merced faculty who support it. QSB further needs **reorganization into core and affiliated QSB faculty in seven different emphasis areas**. Affiliated faculty gain the opportunity to train and support students through QSB. Affiliated QSB faculty need *not* do exclusively QSB-style research in order to affiliate with QSB or gain its benefits. On the other hand, core QSB faculty commit to the QSB Mission and Core Values and help build and run QSB directly through QSB research, teaching and service. The renewed mission and organization of QSB is being defined through a dialogue of interested faculty parties during Phase I in a transparent, accessible and accountable process.

In **Phase II** (starting AY14-15), QSB will lead hiring of additional core QSB faculty. QSB will court campus partnerships and extramural strategic capital investment and funding around its core Mission.

In **Phase III** (starting AY15-16), QSB will propose a Quantitative Science Biology Institute ORU and lay foundations to create an interdisciplinary Department of Quantitative and Systems Biology with degree programs for undergraduates.

The Core QSB Program. QSB will be organized into seven proposed emphasis areas of 1) Molecular Systems Biology, Biochemistry and Biophysics (MSB<sup>3</sup>), 2) Cellular and Developmental Systems Biology (CDSB: including cellular networks, systems neuroscience, systems immunology and developmental systems biology and cancer systems biology), 3) Microbial Systems Biology (MicroSB), 4) Organismal and Integrative Systems Biology (OISB: including physiology and evolution), 5) Systems Ecology (SysEco http://www.nature.com/news/systems-ecology-biology-on-the-high-seas-1.13665), 6) Quantitative and Theoretical Biology (QTB) and 7) Synthetic Biology (SynthBio). Through these emphasis areas, QSB will address problems in astrobiology, biomedicine, and environmental science, contributing to many of the core research themes in UC Merced's Strategic Vision. In Table 1, all current QSB faculty are listed by estimated fit to one or more of these seven emphasis areas of QSB. (many faculty fit more areas than listed).

#### What We Need to Attain QSB 2020

1. Adoption of QSB strategic theme, flexible graduate programming, and liberation from 'umbrella' status. UC Merced should make Quantitative and Systems Biology a strategic research theme in its Strategic Academic Vision. Internally, refocusing and sharpening its identity around a renewed mission and vision will be a dynamic process for QSB that cannot be expected to emerge by strict consensus among all its current

Molec. SB, Biochem, Biophys (MSB <sup>3</sup> )	Cell and Dev. SB (CDSB)	Microbial SB (MicroSB)	Organismal and Integrative SB (OISB)	Systems Ecology (SysEco)	Quantitative and Theoretical Biol (QTB)	Synthetic Biology (SynthBio)
Ardell	Cleary	Ardell	Blois	Beman	Ardell	Chin
Choi	Filipp	Barlow	Dawson	Blois	Colvin	Escobar
Cleary	Hoyer	Beman	Escobar	Chin	Gopinathan	McCloskey
Colvin	Garcia-Ojeda	Choi	Fogel	Dawson	Huerta-Sanchez	Muñoz
Filipp	Kitazawa	Frank	Forman	Fogel	Leiderman	Tsao
Forman	Loots (LLNL)	Hart	Frank	Frank	Moran	Viney
Gopinathan	Manilay	Nobile	Hart	Hart	Sindi	
Hirst	McCloskey	Ojcius	Ortiz	Moran	Wang (LBNL)	
LiWang, A.	Ojcius		Sexton	Sexton		
LiWang, P.	Oviedo		Wolf			
Nobile	Saha					
Saha	Wolf					
Visel (LBNL)						
Xu						

Table 1. Current QSB Faculty by Emphasis Areas of Systems/Synthetic Biology (alphabetically)

members. Therefore, most immediately, QSB needs the approval of the Molecular and Cell Biology Graduate Group at UC Merced to accommodate faculty who may indeed support QSB yet for whom QSB does not express their highest research priorities. The four Biology Graduate Groups have distinct mission foci (Figure 1, left) that serve different markets for funding dollars as well as student and employer demands. Although health, biomedical and environmental research are now strongly served, the growing demand for biologistprogrammers and interdisciplinarily and quantitatively trained biology students will be better served by QSB 2020. By diversifying and sharpening its biology portfolio, UC Merced will gain prestige, winning students and diversifying its funding streams. By providing flexibility for faculty to self-organize around diverse missions, UC Merced can make room for a renewed QSB as described here.

2. Core FTEs in QSB. QSB needs core QSB faculty who will commit to building QSB directly through research, teaching and service. The research programs of these core faculty need to be intrinsically interdisciplinary, quantitative and systems-oriented, yet address diverse basic and applied questions in biological science and engineering. QSB itself needs to oversee the hiring of core faculty committed to. The identification of a home bylaw unit for core QSB faculty recruits is secondary and can potentially occur late in the recruitment process. Table 2 below shows a suggested plan of QSB recruitment to 2020.

3. A Quantitative and Systems Biology emphasis in the UC Merced Undergraduate major. QSB should form a Department to develop and deliver a new **Quantitative and Systems Biology emphasis** with additional subemphasis options in **computational biology** and **synthetic biology and biotechnology**. This new emphases will offer an interdisciplinary approach to biology education with a curriculum that consistently integrates programming and modern statistics, integrative biology, bioinformatics, biochemistry, biomathematics and biophysics. The new Quantitative and Systems Biology emphasis will meet future job market demands and open new academic and biotech career opportunities for UC Merced undergraduates.

3. A Department of Quantitative and Systems Biology. Besides delivery of the QSB major, a Department of Quantitative and Systems Biology can oversee hiring and promotion of transdisciplinary QSB core faculty who may not be as easily evaluated and mentored in disciplinary bylaw units. Departments do not yet exist at UC Merced. They could be just bylaw units or something slightly different. For example, suppose core faculty of the Graduate Program automatically become voting members of the Department, even if they already belong to another bylaw unit. Other core faculty might belong exclusively to a new QSB bylaw unit as their only voting unit for hiring and promotion. By this or some other formal arrangement, an administrative structure must be made to reward and support participating faculty and units for fulfilling QSB undergraduate and graduate teaching needs and carrying out hiring, promotion, and governance in its service.

4. An affiliated ORU in systems biology to cultivate partnerships with state agencies, federal funding agencies and companies for capital investments. QSB would like to strengthen and focus the existing QSB program into a **Quantitative Systems Biology Institute ORU, QSBI**. QB3 Director Regis Kelly expressed interest in extending QB3 benefits to UC Merced as part of an extended "QB North Consortium" — this would provide resources for individual faculty to transfer technology related to systems and synthetic biology to biotechnology and other companies. As industry relationships strengthen through the hiring of core QSB faculty such as Clarissa Nobile (hired into MCB AY 12-13 who has started a biotech company through QB3), QSB can cultivate private investment for buildings, instrumentation and other resources.

Table 2. Proposed QSB Core Faculty Hires by AY,	<b>Corresponding Emphasis Areas and Collaborative</b>
Beneficiaries ("dry lab" hires are shown in <i>italics</i> )	

AY	Type of recruitment	Emphasis Area	Potential Beneficiaries
2014 15	1) Computational Dynamics of Whole Cells	CDSB, MicroSB, QTB	MCB, LES, BEST, CTC
2014-15	2) Computational Developmental Sys. Biol.	CDSB, QTB	MCB, LES, CTC
2015-16	1) Computational Protein Regulatory		MCB, HSRI, CTC, CeQR
	Networks	MSB, QTB	ES, LES, SNRI, CTC,
	2) Computational Systems Ecology	SysEco, QTB	CeQR
2016-17	1) Comparative Systems Physiology	OISB	MCB, LES, HSRI
	2) Community Microbial Physiology	MicroSB, OISB, SysEco	MCB, LES, HSRI, BEST
	3) Synthetic Biology (Biofuels)	MicroSB, SynthBio	MCB, BEST, ERI
	4) Genomic/Epigen. Regulatory Networks	MSB, MicroSB	MCB, HSRI
2017-18	1) Computational Systems Neuroscience	CDSB, QTB	MCB, CHASE, CIS, CTC
	2) Neuroinformatics	MicroSB, SysEco,	MCB, CHASE, CTC
	3) Community Synthetic Biology (Biotech)	SynthBio	MCB, LES, BEST
	4) Systems Ecology	SysEco	ES, LES, SNRI
2018-19	1) Theoretical Systems Astrobiology		
	2) Comparative Systems Biol of	MSB, MicroSB, SysEco	MCB, LES, CIS, CTC
	Multicellularity	CDSB, MicroSB, OISB	MCB, LES, ES, SNRI
2019-20	1) Protein Interaction Networks	MSB, CSDB	MCB, HSRI
	2) Developmental Systems Biology	MSB, CSDB	MCB, LES

CHASE: proposed Center for Human Adaptive Systems and Environments ORU.

CTC: proposed Center for Theory and Computation CRU.

CeQR: Center for Statistical and Quantitative Research

ERI: Energy Sciences Institute

CIS: Cognitive and Information Sciences

#### **Resource Implications**

Future space needs of QSB to be procured through public-private partnerships include co-located space in a dedicated building for core QSB faculty, core facilities for high-throughput data generation and computation, and a conference-scale auditorium. To add 15 full-time faculty will require offices and research space for about five additional theoretical/computational "drylab" faculty and about ten "wetlab" faculty. Reaching a 3:1 to 4:1 student-to-faculty ratio in QSB (assuming a present day 2:1 average) implies capacity to seat 45 to 60 additional graduate students and 15-25 postdoctoral researchers by 2020. Working space for "drylab" students and postdocs should ideally place 2-4 group members in quiet offices adjoining group meeting and discussion space. Increased server room space and expanded access to the microfluidics and fabrication facility will be necessary. A DNA synthesis and other core facilities as described in the MCB proposal will be needed. The new undergraduate programs proposed will require expanded access to linux servers and teaching laboratories for both experimental and computational biology and biotechnology. Additional staff support including one for research computing, and 2-3 full-time administrative assistant equivalents for the Dept. of QSB and QSBI.

#### **Metrics of Success**

QSB metrics of success will include 1) the attainment of extramural funding to build interdisciplinary QSB-style graduate and undergraduate degree programs through training grants, 2) improvement in merits of student applicants to QSB programs, 3) the breadth (diversity) and volume of extramural grants, publications and intellectual property enabled by QSB core faculty, QSB-funded students, and QSB research infrastructure, and 4) public-private partnerships for fellowships and capital investment to build core QSB research infrastructure.