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Promoting Collaborative Interdisciplinary Research at the Duke Center for Systems Biology

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Systems biology is the science of how interactions between biological components–genes, pathways, cells, and so forth–give rise to complex biological systems. The systems biology approach is an iterative interplay between experimentation and computational analysis that strives to explain the data in terms of these interactions. The comprehensive nature of systems biology requires not only integration of data from a variety of approaches and sources but also integration of scientists from diverse experimental, computational, and theoretical disciplines.

In the Duke Center for Systems Biology (DCSB) we have strived to create an academic culture of free and open discussions across scientific disciplines, which has generated synergy on multiple levels. Beyond the obvious value of collaborations between experimentalists and theorists, the Center has been an incubator for the cross-pollination of ideas among experimentalists working on different systems and among modelers approaching problems from different perspectives. Productive interactions have been formed between scientists at all levels of training, from undergraduate students to faculty. These interactions have led to research that never would have occurred without the DCSB. Our goal in this article is to share some insights into the development of a Center, and moreover of a collaborative culture, that continues to stimulate interdisciplinary science.

THE EVOLUTION OF THE CENTER

At Duke, the discussion of systems biology was initiated in 2003 when a meeting with a systems engineer prompted now-Director of the DCSB, Philip Benfey, to organize the "Biological Networks Group" (BNG). Over the next two years this group grew to include graduate students, postdocs, and faculty from a wide range of departments and backgrounds. The bimonthly meetings featured a mix of research presentations, mini-tutorials, and journal clubs designed to make sure everyone could speak a common language. From the beginning, so-called "dumb questions" were not only accepted, they were encouraged. This open and questioning environment continues to be key in educating and stimulating discussions across disciplines.

For many of the experimentalists in the group, one of the striking realizations that emerged was that they would need to become much more sophisticated about choosing quantitative approaches for addressing biological problems. The experimentalists had previously believed that if they could find one computationally trained scientist willing to work with them, that person could handle all of their modeling needs. Over the course of the BNG meetings it became clear that this was as naive as expecting that a microbiologist could answer all questions of biological interest to a computational scientist.

In the fall of 2004, the BNG began considering future directions and decided it was time for a more unified approach. A central research theme of network dynamics across different time-scales was identified. Ongoing projects focused on three time scales in a variety of model organisms: the cell cycle in yeast and human cells, with a scale of minutes to hours; development in plant roots and sea urchin embryos, with a scale of hours to weeks; and evolution of networks in yeast and sea urchins, with a scale of millions of years. Initially, each group focused on mapping the connections of the gene regulatory networks involved in the various processes.

Beginning by renaming itself the "Systems Biology Group" in fall 2005, the group evolved considerably over the next three years (Box 1). In 2006, a number of the faculty were part of an initiative that received Howard Hughes Medical Institute funding to develop undergraduate courses focusing on interdisciplinary approaches to systems biology. Soon thereafter, the Duke provost granted a request to create an official University Center for Systems Biology with a mission to "nurture interactions between experimental scientists and theorists with a common interest in biological systems." This support allowed for the Center to sponsor the first Systems Biology Symposium at Duke, a tradition maintained annually to date. After achieving these milestones, the DCSB applied for and was granted NIH support to become a NIGMS National Center for Systems Biology in the summer of 2007. Along with expanding the research capacity of this Center, NIH support allowed for the development of new education, outreach, and diversity initiatives, which are further described below.

As of 2012, the DCSB has grown to include 19 faculty and their research groups from the departments of biology, biomedical engineering, cell biology, computer science, mathematics, physics, statistical science, and others. Figure 1 illustrates the web of interactions among DCSB faculty, with links indicating a substantial continuing or proposed research connection. These links are highly dynamic because the structure of the Center encourages creation of new links based on emerging experimental and quantitative directions and methodologies. The emphasis of the Center research has also evolved: we are now characterizing how the dynamics of gene regulatory networks mediate the connection between genotype, environment, and phenotype. An exciting research theme of responses to environmental stress has also been

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Box 1. DCSB Milestones

2003
Biological Networks Group formed
2004
Regular meetings and mini-tutorials held
2005
Renamed to "Systems Biology Group"
First collaborative NIH proposal submitted
2006
HHMI initiative supports development of undergraduate systems biology courses
Became University-level Center for Systems Biology
First Duke Systems Biology Symposium
2007
Named NIGMS National Center for Systems Biology
2008 – 2010
New members, new activities, and more research
sysbionetwork.org created
2011
First Duke Synthetic Biology Symposium
Sixth Annual Duke Systems Biology Symposium, including workshop on international collaborations

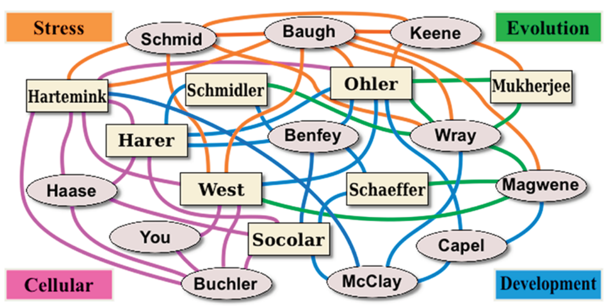

Figure 1. Substantive interactions between DCSB faculty. Ovals indicate experimental research groups, and rectangles indicate groups that are computational or theoretical. Colors are used to indicate the four primary areas of research interest.

added, as a result of recruitment of young investigators Amy Schmid and Ryan Baugh.

To encourage existing faculty from within Duke to try systems biology approaches, the Center has found success with seed grants. The time it takes the seed grant awardees to complete the project is generally sufficient to decide whether a relationship with the Center will be beneficial long-term. One of the seed grant success stories is Blanche Capel, Professor of Cell Biology, who studies sex differentiation in mouse gonads. While no one else in the Center works on a mouse model, her group has found common ground with Center scientists studying regulatory networks that drive development in other model organisms.

■ DEVELOPING COLLABORATIONS THAT WORK

Developing a common language that allows scientists to communicate is key to interdisciplinary collaborations. At the DCSB, this starts in our weekly seminars and lunches and extends into the efforts of each research team. We have found that the most successful collaborations begin before any experiments or modeling. While this is by no means the only approach to a fruitful collaboration, it does give the team the time needed to appreciate the realities of each other's skill set, establish common goals, and overcome scientific language barriers. This approach is exemplified in a recent article by the DCSB's Haase and Hartemink groups, in which they describe what they learned during a collaborative study of the dynamics of cell cycle oscillation in yeast.[1] In brief, they recommend meeting early and often, using the goals of the biological question to determine the experimental and computational approaches, and including all members of the team when making decisions about experimentation, analysis, and validation. We encourage those interested to read their article for an in depth discussion.

■ FOSTERING SCIENTIFIC EXCHANGE AT DUKE AND BEYOND

Much like the networks we study, the DCSB is effective because it fosters a synergistic, cohesive network of collaborations between experimentalists, computational modelers and theorists. To do this, the DCSB has developed outreach programs that promote the exchange of scientific ideas and resources within Duke as well as in the broader national and international systems biology communities. Our scientific exchange program includes a weekly seminar series with visiting lecturers, topic-focused lunch discussions, annual symposia and retreats, as well as support for sabbatical visits and conference travel.

In addition, the DCSB provides a context to promote and nurture growth of related fields. For example, over the past 10 years, synthetic biology has emerged as a vibrant field that has implications for both practical applications and for defining a new approach to address basic biological questions. At Duke, much of the synthetic biology effort has grown due to the participation of several young faculty members associated with the DCSB. The first Duke Synthetic Biology Symposium was recently co-organized by three of these faculty members (Buchler, Schmid, and You) and was cosponsored by the DCSB. Such activities represent a logical extension of the scope of DCSB and directly reflect the Center's commitment to nurture new collaborations relevant to our scientific mission.

To broaden our global reach, the DCSB has led an effort to create an international consortium of systems biology institutes that are working together to share ideas and resources. This effort began with the creation of sysbionetwork.org, a Web site designed to help share ideas and resources. We are now focusing on bringing scientists together for face-to-face discussions and training, because we believe that this is the most effective way to stimulate creative solutions to common problems. For example, a workshop on the challenges of international collaborations was held in conjunction with the 2011 Duke Systems Biology Symposium.

■ TRAINING

Training the next generation of scientists to integrate biological context with computational analysis and modeling approaches is essential for systems biology. Moreover, biology as a whole is becoming more and more tightly intertwined with quantitative analysis as high-throughput methods become pervasive. The DCSB is involved in a number of education initiatives that aim to excite and train scientists at all levels about the potential for combining biology and computational analysis.

DCSB faculty members have developed three undergraduate courses designed to introduce biological modeling approaches to Duke students. The DCSB also partners with North Carolina Central University (NCCU), a historically black university located minutes from Duke. Each fall, DCSB scientists team teach an interactive course on complex genetic traits at NCCU. Research opportunities for undergraduates are offered both ad hoc and as part of an annual summer internship program managed by the Duke Institute for Genome Science and Policy.

We see it as a hopeful trend that quantitative methods have been incorporated into the curriculum of many of the graduate programs in the biological sciences at Duke in the past few years. Of these, the Computational Biology and Bioinformatics (CBB) program has been a particularly successful model for integrative training. Coursework is designed to respond to the ever-evolving spectrum of statistical and computational approaches to biological questions. For their research projects, CBB students have two mentors, one from the biological sciences and the other from a quantitative field, such as computer science, engineering, or statistics. The dual-mentor approach is also proving to be useful to DCSB postdoctoral fellows and graduate students from other programs.

■ ONGOING CHALLENGES

During the workshop on international collaborations held in 2011, we identified several challenges the systems biology field needs to overcome as it moves forward. The foremost of these is the need for integration on a number of fronts: integration of technology, biology, and computational analyses, integration of data from different sources and genomics approaches, integration of modeling approaches across groups and institutions, and integration and training of cross-disciplinary scientists. While advances have been made in many of these areas over the past decade, it is clear that work is still needed. To accomplish this, the systems biology community must continue to promote open discourse across research groups, disciplines, and institutions.

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Notes

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■ REFERENCES

(1) Mayhew, M. B., Guo, X., Haase, S. B., and Hartemink, A. J. (2012) Close encounters of the collaborative kind. *Computer 45* (3), 24−30.