STRATEGIC PLAN: DEPARTMENT OF BIOCHEMISTRY AND CELL BIOLOGY

SUMMARY

The goals of the Department of Biochemistry and Cell Biology are to study the underlying biochemical and cellular principles of life and to train the next generation of biomedical scientists. Our plan for the next 10 years is to greatly expand our capabilities through strategic hiring of outstanding new faculty that will allow us to significantly increase our ability to attract extramural funding (in particular in the form of Program Project and Center Grants), enhance the breadth of our *biomedically-relevant* research efforts and expand our teaching mission to keep the curriculum modern. As a result, we seek to move into the top 10% of similar Biochemistry and Cell Biology departments nationwide. Specifically, we seek to hire four new faculty (above and beyond present commitments designed to maintain the *status quo*). In addition, out of the total number of replacement and new hires in the next decade, two should be senior scientists with international reputations. All hires will be focused in a few areas that take advantage of existing strengths and areas that need to grow. This includes two areas of study: Molecular and Cellular Communication and Genomic Regulation, and two methodological initiatives: Structural Biology and Systems Biology. These areas of focus integrate well with President Stanley's research priorities of Cancer, Neurobiology, Infections/Immunity, Bioimaging, Bioinformatics, and Genetics.

RESEARCH MISSION

The research mission of the Department of Biochemistry and Cell Biology (BCB) is to study fundamental biochemical and cellular processes with the goal of applying this knowledge to the development of novel therapeutics for biomedical intervention. This is an unusually broad research mission relative to other medical school and Arts and Sciences departments. The biochemistry mission covers research on the structure and function of biomolecules, while the cell biology mission involves research into cellular and subcellular structure and function. The systems chosen for these studies range widely from molecules to cells and from bacteria to mammals. The key in this regard is that any specific system must be the most powerful to capture all the essential biology for the processes being investigated. The result is that the Department has a very broad, basic research mission that necessitates close ties with both the physical and biomedical sciences, and is reflected in the inclusion of the Department in both the School of Medicine and the College of Arts and Sciences, creating a natural bridge between the East and West campuses.

The quality of our faculty is reflected by the fact that our graduate programs are ranked in the top 50 nationwide (US News and World Report) and that our faculty are quite successful in obtaining external funding from NIH, NSF and other agencies (over $10 million in research expenditures per year). Many of our faculty are internationally recognized scientists, among them a National Academy Member (Dr. William J. Lennarz), recipient of the Presidential Award for Excellence in Science, Mathematics, and Engineering Mentoring (Dr. David Bynum), Distinguished Professors (Drs. William J. Lennarz and Rolf Sternglanz), and leaders of international societies (President of the Society for Glycobiology, Dr. Robert S. Haltiwanger). Areas of research strength in department include the biology, biochemistry and biophysics of membranes, chromatin structure and function, developmental biology, glycobiology, RNA processing, signal transduction, transcriptional regulation, and yeast and plant biology.

Research in the department has links to many diseases, including several types of cancer, neurodegeneartive diseases such as Alzheimer's, infectious diesases, inflammatory states provoked by tissue damage, osteoarthritis, infertility, and birth defects.

TEACHING AND SERVICE MISSION

The Department also has a large and wide-ranging teaching mission relative to other biomedical departments. The Department administers the Biochemistry major, a rigorous degree program with a current enrollment of over 500 students (531 F'08). The Department also collaborates with the Undergraduate Biology Program and the Departments of Ecology & Evolution and Neurobiology & Behavior in offering the Biology major to a total of nearly 2,000 students (1,962 F'08). The Biology major is currently the largest major at Stony Brook. Departmental contributions to the curriculum for the combined Biology and Biochemistry majors (and for the first three years of the Health Sciences curriculum) account for 40% of the nearly 9,000 annual seats in lecture courses. Further, the three upper division laboratory courses overseen by the Department account for over 40% of the 800 seats in upper division laboratory courses offered annually. The Department is also extremely active in sponsoring independent research by undergraduates averaging nearly 50 students per semester that register for BIO487, Research in Molecular and Cellular Biology.

In terms of biomedical graduate education, we teach both medical and graduate students. Departmental graduate student teaching responsibilities include, among other responsibilities, the majority of core courses common to almost all biomedical graduate programs (Graduate Biochemistry, Molecular Genetics, Biomembranes, Graduate Cell Biology). Our Department is also the home of graduate programs in Molecular and Cell Biology (MCB), and Biochemistry and Structural Biology (BSB). The Department has been successful in obtaining a NIH training grant, which supports both MCB and BSB graduate programs. Both programs are interdepartmental, with the majority of faculty members actually outside the Department. The Department has also played a major role in the interdepartmental Genetics graduate program. This means the Department is carrying out a service mission by providing the graduate students who power the research of a wide variety of labs outside the Department including several at Brookhaven National and Cold Spring Harbor Laboratories.

The Department recently launched a new Master of Science Program that was established to address a recognized deficiency in the educational opportunities available to students at Stony Brook. Development of this new program required the creation of two new graduate courses that specifically address the needs of Masters level students, including an Introduction to Techniques course that will provide exposure and training in cutting edge Imaging and Genomic technologies.

Finally, the Center for Science and Mathematics Education (CESAME) operates as an autonomous unit within the Department led by two tenured Department faculty (Drs. David Bynum and Keith Sheppard). This center has the mission of increasing scientific literacy of teachers and students at all educational levels. CESAME has attracted national attention, reflected in the fact that they have received over $20M in extramural funding.

RECENT HISTORY AND CURRENT STATE OF THE DEPARTMENT

The Biochemistry Department was founded in 1968 with Dr. Melvin Simpson serving as the first chair until 1978. In 1988, Dr. William J. Lennarz was hired (following a nationwide search) to chair of the Biochemistry Department with the task to reinvigorate and expand the Department's mission (Cell Biology was added to the Department name at this time). During Dr. Lennarz's 20-year term as chair, our research-active faculty expanded from 18 to 25. With turnover, 80% of the faculty were replaced between 1988 and 2001. This resulted in a major expansion in grant funding and research activity. As reflected in national rankings, we estimate the Department reached the top 25-30% of Biochemistry departments with a similar mission. However, in recent years this positive if not essential growth has been partly undone. Only one research faculty member has been hired since 2001, and total faculty numbers have dropped by 20%. Our new chair, Dr. Robert S. Haltiwanger, has commitments to hire 3 junior faculty; but unfortunately these three junior recruitment lines will only partially reverse our Department's contraction, which will be further exacerbated by 3-4 anticipated retirements of some of our most experienced faculty in the next few years. Thus, the Department must average one new faculty hire per year for the next 8 years to restore the number of research active faculty to previous levels. These new hires will not only strengthen our research visibility, funding and instructional/teaching capabilities, but the new faculty will be hired in areas that increase the possibilities for synergistic interactions between faculty by building on current areas of strength and expanding the range of experimental approaches being used within the Department (see below). *It must be emphasized that without these additional hires, we predict a rapid erosion of our research activity and funding (especially due to loss of retiring senior faculty), which will be further exacerbated by heavy teaching commitments being concentrated on fewer faculty.*

Among the wide range of research carried out within the Department are two general areas in which we have a nucleus of strength. In terms of biological questions being addressed, one of these areas is the *Genomic Regulation*. This encompasses changes in gene expression and function during development, RNA processing, and the dynamics of chromosomal structure and function. Control of gene expression is fundamental to the regulation of cellular behavior and growth. A second area is *Molecular and Cellular Communication*. All cellular communication involves molecular events happening in or around cell membranes. The membranes that surround cells and delineate their internal organelles are crucial for cell function, as a barrier to pathogenic molecules and agents, and for control of intercellular communication events. Our Department has strength in studies involving structure and function of membrane glycoproteins and membrane lipids. Dysregulation of gene regulation or cellular communication lies at the heart of numerous human diseases, including cancer, neurodegenerative disorders, progressive inflammatory disorders, birth defects, infertility, infection and immunity, and other areas under study by our faculty. As the plan below details, we propose to focus and build upon these Departmental strengths.

STRATEGIC PLAN FOR RESEARCH: Four Initiatives for the Cost of Two

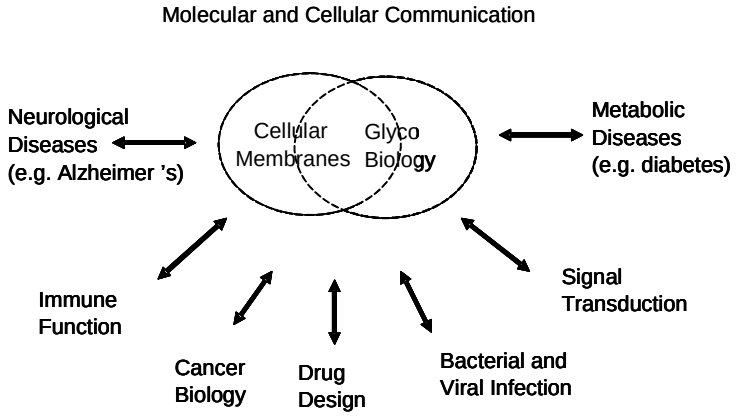
We propose initiatives to develop areas of excellence that build upon Departmental strengths and fill significant gaps. In terms of biological questions, two Centers of Excellence will be developed: **Molecular and Cellular Communication**, and **Genomic Regulation**. These areas fit very well within the proposed research "Topics" targeted for emphasis by President Stanley: Cancer, Neurobiology, and

Infection/Immunity. We propose to build up Departmental strength by key hires in these areas. In particular, we plan to carry this out by hiring faculty as part of **Initiatives in Structural Biology/Bioimaging** and **Systems Biology**, resources that will fill key gaps in our strengths, strengthen biological research at Stony Brook, and align well with the research "Tools" President Stanley has proposed for enhancement: Bioimaging, Genetics, and Bioinformatics. By fulfilling two needs, this plan will provide the most "bang for the buck". Our ultimate goal is to form two "Centers of Excellence" that will synergistically attract top faculty and scientific talent and compete more effectively for individual and group (*e.g.* NIH program project), and other extramural funding.

With these resources, the Department will be able to institute a unique strategy to investigate biological systems and secure additional external funding. Our strategy is based on our ability to do global and simultaneous structure/function analysis at both the molecular and cellular levels in order to define, at the basic level, how a specific biological molecule/system works, and at the translational level, how therapeutic intervention should be designed. These initiatives will allow us to assemble groups that choose specific targets within the area of *Molecular and Cellular Communication* or *Genomic Regulation* and then propose an exhaustive analysis including the atomic structure, conformational and other biochemical properties, cellular assembly, processing and degradation, and finally systems level integration. This global structure/function analysis approach will be unique, play to our unique strengths at Stony Brook, and we will be able to argue that it is the most efficient for both basic understanding of a biological system and design of rational therapeutic approaches. This will put us in a very strong position for Program Project and Center of Excellence funding vehicles at the federal, state and private levels.

A. Centers of Excellence:

1. Molecular and Cellular Communication. Membranes form the lipid and protein barriers that surround the cell and its internal organelles. As noted above, cell membranes serve at the location where cells communicate with the outside world. Thus a firm understanding of cell membranes and their components is essential to most aspects of biology, as shown in the adjacent diagram. It is not surprising that membranes are the site of intervention for most therapeutic agents, and a deeper understanding of the events that are regulated in the complex environment of the membranes is the key to further progress in this regard.



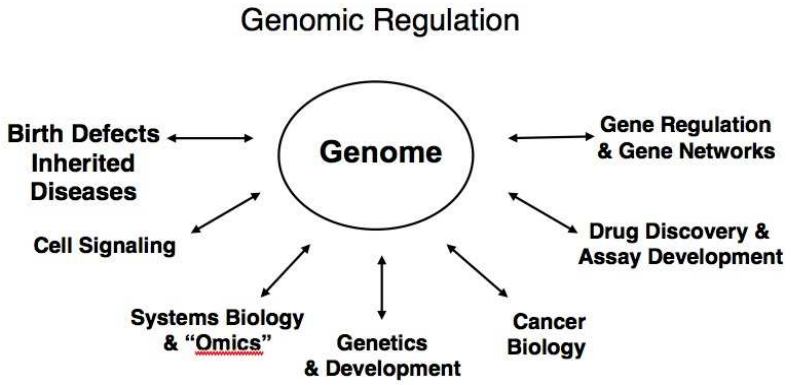
We propose an initiative to enhance the strengths we have in the Department in the areas of membrane structure/function and glycobiology (in particular the study of the structure/function of carbohydrates attached to proteins, frequently membrane proteins) by targeting new hires to allow us to more effectively pursue external program project and center funding. We will focus hiring on investigators with skills in Structural

Biology and Systems Biology (described below) to strengthen these areas. The majority of drugs in use today target membrane proteins, and the most crucial membrane proteins are glycosylated membrane receptor proteins. These versatile receptors interface between the outer membrane of a cell and its environment and are responsible for the control and integration of information (signals) that enable the cell to mount appropriate responses to various signals. Thus, this initiative will focus on receptor glycoproteins, within the context of studies involving a much wider range of membrane components.

Once the initiative is operational, we will be able to study the full range of membrane glycoprotein structure and function. These studies will include high-resolution structure of the isolated proteins, how they function in the natural cellular environment, how glycosylation affects their function, how the control of their biosynthesis and degradation regulates function, how they impact the global functions of the cell, and how they are affected by potential drug candidates (the latter to be performed in collaboration with the Institute of Chemical Biology and Drug Design, ICB&DD). This will give Stony Brook the *unique* ability to perform comprehensive structure/function analysis at a level that will directly impact the development of novel therapeutic approaches. This Center fits well with several of the President's research initiatives, including Cancer, Neurobiology, and Infection/Immunity.

The University and BCB Department are natural homes for this initiative for good reasons. Stony Brook has a particularly strong reputation in membrane biology and glycobiology that can be easily built by recruitment. Furthermore, as noted above, biological membranes and glycobiology form an internationally-recognized focus of research in the BCB Department. Nevertheless, it is important to note that the members of this center will not solely be within the BCB Department. There will be obvious interactions with faculty in this and related areas in other departments where overlaps in interest and expertise exist. Examination of the diagram above shows obvious interactions with the Molecular Genetics and Microbiology, Pharmacology, Physiology and Biophysics and Pathology Departments. Issues of drug design and action will lead to strong collaborations with the ICB&DD.

2. Genomic Regulation. A major goal in the realm of human health and translational medicine is to understand how gene mutations and abnormalities affect gene products (RNAs and proteins). We all understand that mutations in genes cause diseases and developmental abnormalities. Learning how such genes are regulated and how gene defects might be corrected is a central pursuit of modern medicine. We propose to grow our core of faculty who work on gene organization, regulation and expression into a center of Excellence in Genomic Regulation.



Research under this initiative would be aimed at discovery of fundamental molecular and biochemical mechanisms governing gene expression, as well as research into how abnormal genes and gene regulation affect cellular dysfunction and disease. Faculty within this initiative would be studying how any organizational unit of a genome (*e.g.* chromosome, gene, regulatory element), or gene products (RNA and protein) are acted upon by biochemical, cellular and developmental processes. Fields of research under this umbrella would include any that interface with DNA or chromosome structure, organization, replication, and production and regulation of gene products. Areas of faculty expertise in the Department include signal transduction to the nucleus, chromatin structure, transcription factors, transcriptional mechanisms, post-transcriptional mechanisms (*e.g.* RNA processing, splicing and transport) and translational regulation. The Genomic Regulation initiative will build upon our core strength in this area through new hires in Systems Biology and Structural Biology (described below), which should allow us to define the molecular and cellular basis of defects in genomic regulation, and greatly enhance the value of collaborative research grants among existing and new faculty.

Understanding how genes and other components of prokaryotic or eukaryotic genomes are regulated will foster breakthroughs in basic and translational medicine. For example, small organic molecules are fast becoming fertile ground for discovery of agents that inhibit or activate genes by affecting cell signaling, DNA-binding proteins, gene transcription, chromatin structure and production or translation of mRNA. Synthesis and screening of small molecules, particularly ones based upon "rational" (structure-based) design, is a major endeavor of modern drug discovery (as done in ICB&DD). Another example of translational potential is research on how gene mutations are caused by chemicals (*e.g.* environmental toxins) or mistakes in DNA replication, meiosis or mitosis, and how drugs might be used to correct or compensate for these errors. Genomic Regulation research would also encompass gene therapy, animal models of human genetic diseases (*e.g.* fly, worm or mouse mutants), and "functional genomics", a research area that investigates the broad phenotypic outcomes resulting from dysfunction of a particular gene or pathway.

As in the case of Molecular and Cellular Communication, the BCB Department is a natural home for this initiative. The Department has a core faculty strength in this area, and our Resource Initiatives in Structural Biology and Systems Biology (described below) will expand our abilities to engage in cutting edge Genomic research, as well as foster interactions and collaboration between our own faculty and those of other departments where overlaps in interest and expertise exist. Cancer, Genetics and Bioinformatics are key areas of research that President Stanley has identified as a field for significant future investment by Stony Brook. Our Initiative will feed into and synergize with these goals.

B. Resource Initiatives

1. Structural Biology and Bioimaging. One key area of proposed faculty/research expansion within the Department is in Structural Biology. Structural biology is a field whose aim is the determination of high-resolution structures of biological molecules and their complexes. These structures provide the foundation for 1) understanding the mechanisms of normal cellular processes and the molecular basis of disease, 2) the design of therapeutic agents and 3) engineering of novel bioactive molecules. The four major approaches in structural biology are crystallography, NMR

spectroscopy, computation and high-resolution imaging. Our close proximity and relationship with Brookhaven National Laboratory (BNL) and the unique access we have to the National Synchroton Light Source (NSLS) provides a strong rationale for why Stony Brook should be a world leader in x-ray crystallography. The current construction of NSLSII at BNL, which will be the brightest light source in the country, is a very strong recruiting tool that can be used to attract outstanding crystallographers here. By way of analogy, completion of Advanced Light source in Lawrence Berkeley Lab helped UC-Berkeley to recruit top-flight structural biologists: Dr. Jennifer Doudna from Yale and Dr. John Kuriyan from Rockefeller, both National Academy members. In addition, Stony Brook scientists have access to the New York Structural Biology Center (NYSBC) located in Manhattan. The NYSBC is one of the premier facilities for NMR spectroscopy in the world.

The Department of Biochemistry and Cell Biology is the natural home for Structural Biology at Stony Brook for several reasons. First, biochemistry is the study of biology at the atomic and molecular levels, and most biochemistry faculty require access to the tools that structural biology offers at some level in their research. In recognition of this fact, we are the departmental home of the interdepartmental Center for Structural Biology. Second, we are in charge of the Biochemistry and Structural Biology graduate program, which trains Structural Biology graduate students. Third, we have a growing departmental effort in this area with two structural biologists of international reputation (in NMR, Dr. Steve Smith, and imaging, Dr. Huilin Li) already on the departmental faculty, and we are presently carrying out a search for a third junior faculty member in this area (in crystallography). The proximity and access to top-notch structural biology facilities at Brookhaven National Lab should aid in attracting stellar scientists, and it would be a missed opportunity for the Department and university if we were not able to achieve and maintain a national reputation in Structural Biology. Of course, our effort to establish and maintain high caliber research and facilities in Structural Biology also fits with the proposed campus-wide Bioimaging Initiative since the high-resolution side of bioimaging encompasses technology (cryo-electron microscopy, atomic force microscopy, transmission electron microscopy) that falls under the umbrella of Structural Biology and is currently overseen by Departmental faculty.

Finally, it is important to stress that Structural Biology represents a collection of tools that allow one to address a wide diversity of biological and biomedical problems. Faculty recruits with expertise in different areas of Structural Biology can also complement or strengthen the proposed research initiatives described above (Molecular and Cellular Communication, Genomic Regulation), and will provide technical expertise that extends beyond Departmental boundaries in order to strengthen the Center for Structural Biology as a university resource. Structural Biology also forms an essential interface with computational biology, a growing area of expertise on campus with the recent recruitment of Dr. Ken Dill as director of the Laufer Center.

2. Systems Biology. The completion of the human genome project along with technological advances in DNA sequencing, mass spectrometry, and nucleic acid hybridization techniques have led to the emergence of an important new methodological approach to biological questions termed Systems Biology. In Systems Biology, rather than focus on individual molecules, all of the genes, proteins, lipids,

carbohydrates, or metabolites, *etc.* of a cell are monitored during the course of an experiment. This type of study provides a global view of changes occurring within a cell in response to different conditions. Results from this type of approach are used to inform computational studies that attempt to predict cellular behavior. Mass spectrometry is a major method used in many of these types of studies (*e.g.* proteomics, lipidomics, glycomics, or metabolomics) because of its ability to detect and quantify many components of a complicated system. Although some expertise in mass spectrometry exists in the Department and University, this is an area that needs to be greatly expanded. Microarray technology and high-throughput DNA sequencing is used for genomic studies. Some expertise in microarrays already exists on campus with more at Cold Spring Harbor. Systems Biology requires expertise in these methodologies as well as Bioinformatics to deal with the large amounts of data generated. Thus, Systems Biology fits well with the President's emphasis on Genetics and Bioinformatics.

The broader view of cellular systems provided by Systems Biology is an important complement to the reductionist approaches of traditional biochemistry and cell biology that often focus on single molecules. Though still a young discipline, a large number of significant advances have already flowed from Systems Biology approaches. Currently, Systems Biology is not well represented in either the BCB Department or at Stony Brook. Thus, the hiring of new faculty in this area represents an opportunity to turn a perceived weakness into a strength. Importantly, as for Structural Biology, Systems Biology is a methodology that can be applied to any number of questions of biological interest. Thus, new Systems Biology faculty can also contribute to the Centers for Excellence in Molecular and Cellular Communication and Genomic Regulation.

Faculty Hiring to Carry Out the Strategic Plan for Research

To carry out this strategic plan it will be necessary to both maintain Department strengths and build up Departmental excellence in the areas outlined above. The aging of the Department (one hire in the last decade) is severe, and coupled with recent and upcoming retirements, we are entering a period in which Department strength will rapidly deteriorate unless something is done soon. The three junior faculty hires committed to Dr. Haltiwanger, as well as replacing upcoming retirements, may be sufficient to maintain the Department at its present status, but not to strengthen the Department. Just filling gaps left by retirement with some of the new areas outlined above will result in new gaps in areas that will be of "former expertise" thus defeating our proposed initiatives.

To cover the areas of weakness without cannibalizing areas of strength, we propose an expansion of the Department **by four additional faculty, two in Structural Biology and two in Systems Biology (see Table below)**. These hires would be in addition to the three junior faculty lines and retirement replacement lines already promised to Dr. Haltiwanger. In each case, resources in terms of start-up packages that are competitive with those of the top 10% of universities should be provided. To move the Department into the top 10% of Biochemistry Departments in the country, we recommend that two hires (either as part of the expansion, or replacements for retirements) be for endowed chairs in Biochemistry and Cell Biology, occupied by faculty of international reputation (*e.g.* National Academy Members or Howard Hughes Investigators).

It is important to point out the synergy implicit in this hiring plan. First, the number of hires needed is greatly reduced by having the new faculty will each fit into two initiatives (see Table below). Second, the hires in the new areas will have synergy in terms of expertise to the extent that methods with different strengths can be combined, equipment can be shared, and graduate student research will be enhanced by a stronger pool of expertise for thesis committees. It cannot be emphasized enough that overlapping and complementary expertise greatly enhances the value and power of the advice of a thesis committee for graduate students.

How Each Expansion Hire Will Strengthen the Two Initiatives		
	Systems Biology	Structural Biology
Genome Regulation	Hire A	Hire C
Molecular and Cellular Communication	Hire B	Hire D

STRATEGIC PLAN FOR TEACHING AND SERVICE

Our strategic plan is to carry out and enhance our teaching activities. This requires a critical mass in terms of faculty to shoulder the teaching burden. The central component of this plan must be to reverse the 20% contraction of Department faculty so as to bring the Department to its recent steady-state level. This is crucial for preventing the teaching mission from overwhelming the research mission, and of course dovetails perfectly with our strategic plan in terms of research mission. It should allow us to extend the scope of the MCB/BSB NIH training grant. It should also allow us to firmly establish a large and successful MS program, which can be an aid to research if we recruit a sufficiently large stream of students, who can carry out research without requiring support from external funding, and/or who may often decide to enter Ph.D. studies at Stony Brook as highly proficient researchers at the end of their MS studies. Reversing faculty contraction will also allow us to expand summer and winter teaching offerings, thus increasing flexibility/opportunities for undergraduate students to graduate on-time, which has direct impact upon the reputation of the university and its ability to recruit top-notch undergraduates. New faculty hires with unique expertise will also allow us to offer new courses in new areas, keeping the curriculum at the forefront of science.