SUMMARY OF
NIH BISTIC PLANNING GRANTS:
ATIONAL PROGRAMS OF EXCELLENCE IN BIOMEDICAL COMPUTING
AWARDS
FOR PROGRAM ANNOUNCEMENT PAR-00-102
FY 2001

The following text provides a summary of grant awards from BISTIC member institutes and centers for planning grants that will lead to national centers of excellence in biomedical computing in response to program announcement PAR-00-102. The objective of this program is to support planning grants for centers of excellence that will promote bio-informatics and bio-computational research that enables the advancement of biomedical research; develop useful and interoperable informatics and computational tools for biomedical research; establish mutually beneficial collaborations between biomedical researchers and informatics and computation researchers; and train a new generation of bio-informatics and bio-computation scientists.

Funded grants are listed below in alphabetical order by the principal investigator's (PI's) last name. Other information provided for each grant includes PI affiliation, grant title, application number, funding organization, and a brief summary of the project.

1. **PRINCIPAL INVESTIGATOR:** **ALTMAN, RUSS B**
   AFFILIATION: Stanford University
   PROJECT TITLE: Planning the Stanford Center for Biomedical Computation
   GRANT NUMBER: 1P20GM064782-01
   SUMMARY:
   Stanford University has demonstrated excellence in biology, medicine, computer science, engineering and the other basic contributing disciplines that comprise biomedical computation. In the last two years, faculty from the schools of Medicine, Engineering and Humanities & Sciences have begun a grass-roots effort to organize biomedical computation so that the greatest scientific challenges facing modern biomedical research can benefit from the power of information technologies. In this project, we will outline a planning process for the Stanford Center for Biomedical Computation (CBMC) with joint leadership from the Schools of Medicine and Engineering. The CBMC comprises structures that will allow Stanford scientists to create new methodologies in biomedical computation and apply these to the most difficult unsolved problems in biomedicine. The CBMC mission includes the creation of shared computational infrastructure, joint training of young scientists, and interdisciplinary collaborations falling outside traditional departmental boundaries. We outline a plan for continued and accelerated activities in this area. These activities include continuing a very successful biomedical computation research symposia, creation of new courses and curricula, and assessment of student and post-doctoral fellow trajectories in biomedical computing careers. We further define three development projects which will focus on (1) distributed database design and integration, (2) creating biomechanical models from image data and (3) simulation-based surgical training. These projects all involve interdisciplinary teams from multiple departments, and create the basic set of users for the proposed core support--including professional staff to help target, acquire and maintain large computational resources in support of this planning and research development process.

2. **PRINCIPAL INVESTIGATOR:** **CHRISTOPHER, JOHNSON R**
   AFFILIATION: University of Utah
   PROJECT TITLE: Program for Computational Functional Imaging and Visualization
   GRANT NUMBER: 1P20HL068566-01
   SUMMARY:
   The University of Utah is developing a”Program of Excellence for Computational Bioimaging and Visualization" that will have a pair of interrelated scientific goals. The first goal is to support interdisciplinary research that relies on the important relationship between computing and bioimaging. The second goal is to educate scientists who are capable of contributing to such interdisciplinary computational biomedical research. We propose to develop three technical core areas that support two biomedical research projects. Topics of the technical cores are image acquisition, image and signal processing, and scientific computing and visualization. These are areas of existing

strength and the University of Utah, and we will pursue new topics within this existing framework and also develop the interdisciplinary infrastructure required for enhanced collaboration. The research projects are: multimodal cardiac imaging and subject-specific functional neuro-imaging. These projects address important scientific questions and also share a set of technological challenges that demand better methods for imaging and better tools for utilizing and combining the data that are generated by various imaging modalities. We will also develop an interdisciplinary training program for graduate students and postdoctoral fellows. The program will consist of a rotation of courses that include: basic physiology, cell biology, computational science, and image/signal processing, and radiology. Many of these courses are already offered to inter-disciplinary audiences, and we also imagine modifying existing courses or adding new ones to accommodate this new program. This sequence of courses will culminate in a project course where students work in interdisciplinary teams on projects that better reflect the true nature of research problems computational imaging. Upon completion, each student will receive the certificate in Computational Bioimaging as well as the degree from their home department.

3. PRINCIPAL INVESTIGATOR: HONIG, BARRY
AFFILIATION: Columbia University
PROJECT TITLE: Center for Compuational Biology and Bioinformatics
GRANT NUMBER: 1P20LM07276-01
SUMMARY:

Columbia University is working to establish a Center for Computational Biology and Bioinformatics that will serve as a focal point for research and education at the university. The center will facilitate the integration of computational methods into different areas of biomedical research through the fostering of collaborations between laboratory and computational scientists, through training programs, workshops and seminars, and by providing the computational infrastructure and support that is necessary for cutting-edge research in this area. In-house research will include areas such as DNA and protein sequence analysis, SNP analysis and its relationship to human disease, protein structure analysis, tile analysis of microarrays, tile analysis and comparison of complete genomes, functional annotation of proteins, the study of networks of interacting proteins, and the 3D structure based design of new pharmaceuticals. The center will play a central role in education through the development of joint courses and degree programs with participating departments. An industrial outreach program will also be established in which industrial scientists will be able to attend center lectures, symposia and workshops, spend mini-sabbaticals at the center, and establish research contacts with center scientists.

4. PRINCIPAL INVESTIGATOR: LAKE, GEORGE
AFFILIATION: Institute for Systems Biology
PROJECT TITLE: Intelligent Information Systems for Systems Biology
GRANT NUMBER: 1P20GM064361-01
SUMMARY:

This Center at the Institute for Systems Biology (ISB) will attack the challenges created by the large quantity of data generated from new high throughput technologies. We have teamed biologists, computer scientists and computational scientists from several universities to build an experienced and distinguished team. Our first major tool building project will be an Object Oriented Framework for the integration of data and tools for genomics, proteomics, DNA arrays and protein-protein interactions. This tool will follow the data from the source through model building. It will build on existing open source tools such as a data acquisition package from particle physics (ROOT), a public database system (MYSQL or PostgreSQL), statistics tools ("R"), graphics libraries, a variety of software tools that have been developed at ISB and new tools needed for the new technologies. We stress the use of an open source system as a means to build the community, creating a functioning system that can be tailored for research and education. We then propose to augment this system with tools for analysis, visualization and model building. We will use yeast as a model system owing to the wide range of data that it available for it. Finally, we propose some novel educational programs designed to put graduate students together into interdisciplinary teams for problem solving.

5. **PRINCIPAL INVESTIGATOR: LEVY, RONALD M**
AFFILIATION: Rutgers University
PROJECT TITLE: Biocomputing: Regulation of Gene Expression
GRANT NUMBER: 1P20GM064375-01
SUMMARY:

A group of investigators with complementary expertise in molecular biology, structural biology, statistical physics, control theory, computer modeling, and computer science, will work to develop computational models for complex systems involved in the regulation of gene expression. Two initial research projects are proposed: Project I will focus on the structural and mechanistic basis of the first, and most highly regulated, step in gene expression: i.e., transcription. A combination of high-resolution structural methods, biophysical and biochemical methods, and molecular modeling will be used to construct structural models of the nanometer-scale supramolecular assembles involved in transcription initiation, elongation, and regulation. Computational-chemistry methods will be used to infer equilibrium and dynamic properties of assemblies, and statistical-mechanical methods will be used to incorporate information about all structural and reaction-state microstates important for transcription initiation, elongation, and regulation. Small-molecule inhibitors of protein-DNA interactions occurring in individual structural microstates will be designed, synthesized, and characterized. Project II, which will be tightly integrated with Project I, will focus on comprehensive quantitative simulation of two model biological regulatory networks: i.e., regulation of lactose and galactose assimilation in bacteria, and regulation of lytic and lysogenic developmental pathways in bacteriophage lambda. For each regulatory network, a multi-step analysis will be performed, with the first step involving simulation of the central circuitry of the regulatory network, and with successive steps involving simulation of first step involving simulation of the central circuitry of the regulatory network, and with successive steps involving simulation of sensory components that mediate transfer of information among the central circuitry, the cell, and the cellular environment. Inputs for simulations will include structural and mechanistic information from Project I, and quantitative data from systematic population and single-cell measurements of RNA levels, protein levels, small-molecule-effector levels, promoter activities, and protease activities. Simulations will be tested by comparing predicted and observed effects of perturbations of regulatory networks. The results to be obtained will contribute to understanding transcriptional regulation, will contribute development of approaches to simulate complex biological regulatory networks, and will contribute to development of approaches to predict effects of small-molecule agents on complex biological systems. The organizational infrastructure of the effort will be closely affiliated with the Rutgers University Initiative for Research and Education at the Biological/Mathematical/Physical-Sciences Interface (BioMaPS), which provides for establishment of a graduate courses, summer research internships, and seminars at the BioMaPS interface, and for recruitment of additional faculty members in biological computing and modeling.

6. **PRINCIPAL INVESTIGATOR: MILLER, PERRY L**
AFFILIATION: Yale University
PROJECT TITLE: Planning a Biomedical Computing Center of Excellence
GRANT NUMBER: 1P20LM007253-01
SUMMARY:

Yale University is working to plan and develop a Biomedical Computing Center of Excellence. The overall theme of the Center will be: "Harnessing Advanced Computing Technologies for Biomedicine." The Center will provide a focus for highly collaborative research and training involving many academic units and research support units within Yale University as a whole. The initial focus will be on four research themes: a) heterogeneous biomedical database design, b) multilevel approaches to facilitate interoperation among biological databases and software tools, c) integrative genomic database analysis, and d) high performance distributed biocomputing. These themes each build upon particular research strengths at Yale. The proposed activities include the following: 1) A central component will involve planning for the establishment of the Center of Excellence. 2) A set of ongoing activities will promote interaction and collaboration among the academic units participating in the Center. 3) A Biomedical Computing Education Committee will plan for a full spectrum of educational activities. 4) Three pilot projects will be carried out: a) developing a flexible pilot EAV/CR database for describing heterogeneous microarray expression experiments, b) integrative data mining to relate protein characteristics to gene expression patterns, and c) computational and statistical analysis of gene expression as a dynamical system using high performance computing techniques. Although the pilot projects will focus on different computational research themes, they all focus on the challenges posed by the analysis of experimental microarray data. 5) A Biomedical Computing Core will support the activities of the three pilot projects.