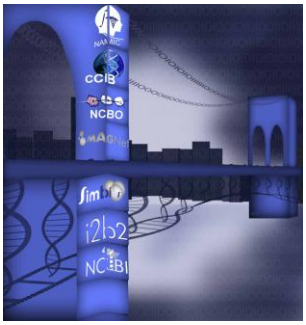

Meeting Report

NIH Roadmap National Centers for Biomedical Computing
2006 All Hands Meeting

July 17- 19, 2006
Bethesda, MD

(Full meeting archive including presentations and posters is at http://www.bisti.nih.gov/ahm2006/)

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EXECUTIVE SUMMARY

Program The NIH Roadmap Initiative on Biomedical Informatics and Computational Biology established four National Centers for Biomedical Computing (NCBCs) in 2004 and three additional Centers in 2005 (see sidebar). An ongoing initiative also promotes collaborations between these Centers and other biomedical and biocomputational research groups (PAR-05-063 and PAR-06-223). The seven Centers, funded via the cooperative agreement mechanism, constitute the core of a 10-year vision to develop a national biomedical computing infrastructure, allowing the biomedical community—including researchers and physicians—to seamlessly integrate, analyze, model, and share data on human health and disease. The 2006 All Hands Meeting offered the first opportunity for the seven NCBCs to meet collectively. The full meeting archive including presentations and posters is at [1].

Focus of Meeting

While offering customary sessions for each Center to report upon individual accomplishments through plenary presentations and posters, the event also emphasized a *prospective focus* on the ten year vision of a national biomedical computing infrastructure, and began to lay the groundwork for the core functions of the NCBCs in building that foundation.

The meeting achieved its prospective focus through the following:

- **Fostering the leadership roles of the NCBCs as core components of a national biomedical computing infrastructure:** The meeting formally launched three cross-cutting NCBC Working Groups [2] focused on areas critical to progress in computational biology and biomedical informatics:

    1. Using science ontologies
    2. Identifying and locating biomedical computing resources
    3. Assuring the relevance of the emerging biomedical computing infrastructure to the research on health and disease.

Funded National Centers for Biomedical Computing

(September 2004 start date)

- **The Physics-Based Simulation of Biological Structures Center (Simbios)**, led by Russ Altman, M.D., Ph.D., and Scott Delp, Ph.D., of Stanford University in Stanford, California
- **The National Alliance for Medical Image Computing (NA-MIC)**, a multi-institutional effort led by Ron Kikinis, M.D., of Brigham and Women's Hospital in Boston, Massachusetts
- **The Center for Computational Biology (CCB)**, led by Arthur Toga, Ph.D., of the University of California, Los Angeles
- **The Informatics for Integrating Biology and the Bedside Center (i2b2)**, led by Boston-based researchers Isaac Kohane, M.D., Ph.D., of Brigham and Women's Hospital and Children's Hospital, and John Glaser, Ph.D., Vice President and CIO at Partners HealthCare System

(September 2005 start date)

- **The National Center for Integrative Biomedical Informatics (NCIBI)**, led by Brian D. Athey, Ph.D., of the University of Michigan in Ann Arbor
- **The National Center for Multi-Scale Analysis of Genetic and Cellular Networks (MAGNet), led by** Andrea Califano, Ph.D., of Columbia University in the City of New York
- **The National Center for Biomedical Ontology (NCBO), led by** Mark A. Musen, M.D., Ph.D., of Stanford University in Stanford, CA

- **Examining the state of the current national biomedical computing infrastructure and exploring the current and potential role of the NCBCs within the framework of a 10 year developmental vision:** A series of "Building Bridges" panels reported on the large number of computing activities supported by the NIH and other federal agencies. A potential for improved coordination among the activities exists, and a web-based compendium of government programs created for this meeting [3] is expected to keep the community aware of funding activities and initiatives.

- **Exploring opportunities for coordination and collaboration:** Discussions with the NCBC Principal Investigators occurred during a public panel session with meeting attendees and the co-chairs of the NCBC Roadmap Implementation Working Group (RIWG), Drs. Jeremy Berg and Donald Lindberg, and a NIH/Centers staff meeting that included the RIWG co-chairs, Drs. Donald Lindberg and Jeremy Berg, the NCBC Principal Investigators, and the NCBC Project Team. The NCBC Principal Investigators frankly discussed needs and opportunities associated with the roles of the NCBCs in building a national biomedical computing infrastructure.

- **Engaging in dissemination, education and outreach activities with NIH staff and other area scientists**: Recognizing that their function as core components of a 10 year national vision must begin with increasing awareness and understanding of their activities and resources, each of the seven Centers elected to remain at the NIH an additional meeting day to engage in outreach activities which they specially developed in conjunction with their NIH Lead Science Officers and other program officials.

Meeting Accomplishments

- "Hot Topics" plenary presentations by each NCBC Principal Investigator, and 37 scientific/technical poster presentations organized into six categories (Modeling, Simulation, Computational Tools , Microarray Data and Pathways in Network Analysis , Ontologies, Natural Language Processing, Translational Medicine, and Imaging) demonstrated NCBC progress in two key respects:

    1. **Advancing translational medicine:** Although only 1-2 years old, the NCBCs reported an impressive collection of scientific/technological accomplishments applying biomedical computing to a broad array of diseases including diabetes, cancer, and brain and behavioral disorders, as well as to research into fundamental biomedical processes.

    2. **Building a biomedical computing infrastructure:** NCBC efforts showed significant momentum in accomplishing a key goal of this Roadmap program: building a national infrastructure for biomedical computing. The NCBCs reported work in computational research in modeling and systems approaches, software tool development for analyzing and accessing data, and developing workflows for multi-step methods needed to process, analyze, access, integrate and store data.

- Demonstration of broad NCBC relevance and interest in the NCBCs through attraction of more than 220 attendees representing 21 NIH components (including four IC Directors, the Director of Intramural Research, the Director of the National Library of Medicine National Center for Biotechnology Information (NCBI), and senior intramural research scientists), other government agencies, national and local academic institutions, international registrants, and representatives from the private sector.

- Progress in advancing national leadership roles of the NCBCs through Working Group activities including:

- Identification of tentative terminologies and biomedical ontologies to be used across Centers, with an eye for adoption by other major national efforts
- Identification of key descriptors to begin an inventory and query framework for biomedical computing resources
- Establishment of a new Working Group to coordinate the NCBC Driving Biological Projects to help define common resource requirements, methodologies, and data resources that could significantly impact the broader research community, and to develop strategies to link these efforts to broader biomedical research efforts.

- Establishment of a publicly-available permanent archive of a compendium of government programs that covers the major government funding in the field as well as some public private partnerships. These and other resources are located on the Biomedical Information Science and Technology Initiative Committee (BISTIC) page at [4] (http://www.bisti.nih.gov/).

- Implementation of an **NIH NCBC postdoctoral program** to build bridges to other major biomedical informatics and computational projects, with five awards made in FY2006, and two others to be funded in early FY2007.

- Dissemination events for which each of the seven Centers elected to remain at NIH one additional meeting day. These events attracted an impressive attendance and stimulated considerable interactions between the NCBCs and intramural NIH scientists, meeting registrants, and other NIH and local scientists to learn about tools and methodologies available or under development through the NCBCs. These events led to numerous outcomes including:

  - Adoption or exploratory use of NCBC tools including the NA-MIC's 3D Slicer and the MAGNet's geWorkbench by NIH intramural scientists and other academic and business scientists
  - Stimulation of potential new collaborations with non-NCBC attendees
  - Enthusiastic expression of interest by an IC Director to visit NCBCs to learn more about their activities
  - In-depth follow-up discussions with senior NIH intramural leaders exploring mutual interests and coordination efforts
  - Enthusiastic interest in dissemination events manifested through requests by attendees to modify future programs so that all dissemination events are not held concurrently, and attendance at several events is possible

Discussions with NCBC Principal Investigators

During discussions among the NCBC Principal Investigators, RIWG co-chairs Drs. Jeremy Berg and Donald Lindberg, NCBC Project Team, and meeting attendees, the following suggestions were made:

- Foster a biomedical workforce competent in quantitative approaches and analyses, information management and integration, and applications of computational tools
- Consider efforts to link other NIH training initiatives in computing and engineering with the NCBCs

- Address the issue of support for computer scientists in biomedical research. An NCBC Principal Investigator noted that without such support, computer scientists cannot remain in departments to which they are recruited. NIH staff noted efforts to enable multiple PIs on grant applications
- Generate sustained support for programs for which young investigators are encouraged to undertake riskier, more novel career directions
- Use existing funding mechanisms to attract computer scientists to interdisciplinary research
- Expand opportunities beyond the current R01 and R21 PAR announcements to support individual collaborations with NCBCs, such as making supplements to already existing awards
- Build bridges with other major initiatives. The NCBC Principal Investigators suggested creating an NCBC postdoctoral program
- Improve coordination between the NIH extramural and intramural biomedical informatics and computational biology research programs. Coordinate activities of the NIH NCBI with the NCBCs.
- Recognize that although the NCBCs form the core components for building a national biomedical computer infrastructure, completing that infrastructure needs interest, understanding, and support across all ICs to facilitate application and translation of their efforts, to avoid redundant and balkanized efforts, and to promote coordination and interoperability where possible.

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MEETING DEMOGRAPHICS

The meeting was attended by more than 220 registrants, **and accomplished two important goals:**

1. The meeting brought NCBC members of diverse expertise and career levels together as evidenced by the following:

- **High level of NCBC participation:** Sixty seven individuals from 28 organizations and three different countries (the U.S., Canada and the U.K.) represented the seven NCBCs at the meeting. Attendance from each NCBC numbered as follows: the National Center for Integrative Biomedical Informatics (NCIBI), 15; the National Center for Biomedical Ontology (NCBO), 13; the Informatics for Integrating Biology and the Bedside Center (i2b2), 9; the Physics-Based Simulation of Biological Structures Center (Simbios), 9; the Center for Computational Biology (CCB), 7; the National Alliance for Medical Image Computing (NA-MIC), 8; and the National Center for Multi-Scale Analysis of Genetic and Cellular Networks (MAGNet), 6.

- **Diverse NCBC scientific/technical expertise represented:** NCBC attendees included internationally respected experts in diabetes, schizophrenia, cancer, imaging, genetic analysis, model organisms, and numerous other aspects of biomedical research, as well as leaders in informatics, modeling, systems biology, algorithm development, natural language processing, shape analysis, network analysis, information federation, software engineering, computer science, mathematics, and biomedical ontologies.

- **Interdisciplinary representation across multiple career stages**: NCBC participants ranged from the NCBC Principal Investigators and senior Core leaders, to young investigators identified by each Center for special NIH sponsored attendance.

2. The meeting provided an opportunity for NIH staff and the broader biomedical community to learn about the NCBCs, and interact with them as illustrated by the following:

- **Attendance by 21 NIH Components and four IC Directors**: More than 100 NIH staff from 21 NIH components including CIT, CSR, NCI, NCRR, NEI, NHGRI, NHLBI, NIAAA, NIAID, NIAMS, NIBIB, NICHD, NIDA, NIDCR, NIDDK, NIEHS, NIGMS, NIMH, NINDS, NLM, and the OD/NIH attended meeting events. Directors from NCRR, NIBIB, NIGMS, and NLM also attended, as well as the Director of Intramural Research, the Director of NCBI, and senior intramural research scientists.

- **Participation by diverse government agencies**: Besides NIH, attendees represented numerous other government agencies and programs including the National Science Foundation, the National Aeronautics and Space Administration, The U.S. Networking and Information Technology Research and Development Program (NITRD), the U.S. General Services Administration, Tricare Management Activity (The Military Health Plan), the Uniformed Services University of the Health Sciences, the National Institute of Standards and Technology, the Department of Veterans Affairs, and the U.S. Army Telemedicine and Advanced Technology Research Center (TATRC).

- **Attendance by cross-cutting private sector entities:** Participants included representatives from Cray, Inc., Booz Allen Hamilton, Mitre Corporation, Lired Corporation, SRA International, Your Genome Your World, Lewis-Burke Associates, and Information Management Group, L.L.C.

- **International, other academic and non-profit attendees:** The meeting drew attendance from academic, international, and non-profit organizations not formally affiliated with the NCBCs such as the Taipei Medical University, the Japan Biological Information Research Center, MD Anderson Cancer Center, George Washington University, the University of Chicago, Penn State University, George Mason University, Wake Forest University, Indiana University, Universities Space Research Association, the Immune Tolerance Network, and Mindspec (a non-profit applying informatics to autism research).

SCIENTIFIC/TECHNICAL HIGHLIGHTS

Activities and accomplishments noted in the plenary and poster presentations include the following:

Imaging

- **Automatic image extraction of anatomically meaningful brain fiber bundles:** The National Alliance for Medical Imaging Computing (NA-MIC), in collaboration with computer scientists at MIT, developed a new algorithm to automatically segment white matter fiber tracts in the brain into organized and meaningful fiber bundles. To overcome the burden of quantifying properties of a bundle by analyzing individual fibers, they teamed with collaborators from Brigham and Women's Hospital to develop a novel method to provide a continuous representation of each bundle. NA-MIC now is working to apply these new techniques to study white matter properties in schizophrenia.
- **Visual comparison of activation maps in functional Magnetic Resonance Imaging (fMRI)**: NA-MIC described a method called "Markov Random Fields" which enables detection of brain activation in functional magnetic resonance imaging, as well as providing anatomical information. NA-MIC is translating this work into 3D Slicer, an open software medical image analysis and visualization package developed and supported by NA-MIC through an fMRI Engine module designed to provide a framework for an extensible suite of activation detection algorithms.
- **Computational Atlases for Interactive Integration of Brain Phenotype and Genotype**: The Center for Computational Biology (CCB) developed new 3D integrated segmentation and registration algorithms, new mathematical formulation of biological shape, new computational and visualization tools for imaging, tools for genetic and phenotypic data-mining, and new shape parsing methods based on statistical learning
- **HIV-induced Dementia:** Applying brain mapping algorithms to detect brain changes in dementia, CCB reported the first maps of how HIV/AIDS damages the brain.

- **NA-MIC-toolkit components adopted by large open-source efforts**: Components of the NA-MIC Toolkit have been successfully adopted by other large projects such as KDE (the Linux windows environment), one of the world's largest open source software systems. The NA-MIC toolkit consists of three major types of software technology: programming toolkits (e.g., VTK and ITK), end-user application software (e.g., 3D Slicer, LONI), and system infrastructure (e.g., CMake, CPack, DART). For example, 3D Slicer is an open source, cross-platform application for exploring novel image analysis and visualization techniques, supporting registration, segmentation, 3D model generation, quantification, and real-time integration.

Translational Medicine

- **Redefining human disease based on combined genomic and clinical data**: Through its Integrome Project, the Informatics for Integrating Biology and the Bedside Center (i2b2) aims to redefine the genetics of human disease based on combined genomic and disease phenotypic data. This Center has created and validated a system that identifies and represents phenotypic, environmental, and experimental context for every microarray sample and data set stored in the National Library of Medicine's Gene Expression Omnibus by mapping annotation phrases to phenotypic biomedical concepts in the Unified Medical Language System. The Center's investigators identified a number of genes that were previously not known to be involved in certain disease processes. For example, among the many insights revealed, they discovered that several genes widely known to be associated with inflammation are also associated with other types of diseases. I2b2 is also continuing to integrate further the 2.5 million patient records in the Partners Health Care system into the Center's clinical research electronic charts, to understand how diseases can be reclassified based on their genomic signatures and to determine how individual patients can be recategorized based on their relationship to one another within the Integrome.
- **Beyond monogenic disorders—Computer architecture for analyzing 71 million clinical observations from asthma patients**: i2b2 is working closely with investigators in its Asthma Driving Biological Project (DBP) to develop and implement methods and tools to improve genetic epidemiological and pharmacogenetic research in complex disease. For example, the Asthma DBP created a data mart containing 71 million clinical observations from over 95 thousand patients. Research specific data not routinely available in clinical data sets were loaded into the data mart by running them through a set of web services, designed so that they could be interconnected in multiple, different ways. In this way, data from Semi-Structured Clinical Reports could be wrapped into a web service to process pulmonary reports, which extracted pre and post bronchodilator FEV1, FVC, and patient vital signs. i2b2 also is developing query and visualization tools to provide clear and information visual representations of data.
- **Cancer associated genes in public databases are tumor-specific forms:** CCB reported finding that many of the sequences of cancer-associated genes found in public databases represent tumor-specific forms not found in normal tissue.

Natural Language Processing

- **Challenges in Natural Language Processing for Clinical Data**: i2b2 and partnering institutions have organized the First Shared Task for Challenges in Natural Language Processing for Clinical Data. They have created standardized data sets that will be used as gold standards to evaluate the performance of Natural Language Processing tools for the following two challenges: (1) automatic de-identification of medical discharge summaries and (2) identification of the smoking status of patients based on their medical records. Thus far, 18 teams have committed to participate in the challenges. The competition's results will help evaluate relative strengths of different approaches to addressing the same problem, and be showcased at the American Medical Informatics Association meeting in November in Washington, DC.

Modeling, Simulation, and Computation

- **Physics-based modeling toolkit:** The Physics-Based Simulation of Biological Structures Center (Simbios) is developing a simulation toolkit (SimTK) and its first components are available for download; the dissemination site for Simbios's many software and infrastructure activities (http://simtk.org). The SimTK Core set will contain a full set of tools for simulations, and currently contains high performance numerical methods and multibody dynamics library, all available for download. The design for Simtk.org is based on the open source project management facility GForge (http://gforge.org), but has been extended and tailored to the Biomedical Computation community. Simtk.org was recently redesigned to better serve the user community, capture detailed usage statistics and make it easier for collaborators to host projects, while giving them control on what information is publicly accessible. The work can be explored on the web at https://simtk.org, and the source code that operates the web site is available at simtk.org/home/website. Simtk.org was featured in May in Science Magazine's NetWatch, (www.sciencemag.org/content/vol312/issue5774).

- **Quantifying biomechanical forces in aortic health and disease from the macro to nano-scales:** Investigators at Simbios have developed novel imaging, data analysis, and simulation techniques to describe aortic blood flow, vessel wall dynamics, and structure. A novel "4D" MRI technique was used to quantify aortic wall motion in healthy volunteers. New simulation methods were used to simulate, for the first time, the coupling between pulsatile blood flow and vessel wall dynamics in subject-specific computer models for patients with aortic diseases including aortic coarctation (a narrowing of the aorta) and abdominal aortic aneurysms. A new 3D EM technique was used to describe the three-dimensional micro- and nano-structure of the aorta revealing new anatomic structures (inter-lamellar elastin fibers) not described in prior models and likely important in maintaining aortic strength. Simbios investigators currently are using the aortic modeling work in a study focused on alternate interventions for patients with aortic coarctation. Thus far, more than two dozen patients (children) have been imaged and are currently being modeled before and after interventions. Interestingly, some parents have coined the phrase "virtual catheterization" for this work. These techniques are also being applied in another NIH-funded study investigating the potential for light exercise to slow the progression of small abdominal aortic aneurysms. Image-based patient-specific models will be created and abdominal aortic blood flow will be simulated at rest and during light exercise in a total of 170 patients randomized to exercise or standard therapy.

- **Cadherin Binding Specificity understood at the molecular level**: Cadherins mediate cell-cell adhesion and are important in the development of multicellular structures in animals. A subtle difference between N and E cadherin appears to be responsible for the separation of neural tube cells from ectoderm cells during early stages of vertebrate embryogenesis. How can small changes between proteins at the molecular level have such profound consequence at the cellular level? Investigators affiliated with the National Center for Multi-Scale Analysis of Genetic and Cellular Networks (MAGNet) have discovered the molecular basis of this cellular behavior by comparing homology models of cadherin heterodimers that fail to form (e.g. the N/E heterodimer) to those of the known E-E and N-N homodimers. Remarkably, the only apparent differences between the failed and actual complexes involved two amino side chains that have the capability of forming cross-dimer hydrogen bonding interactions. This raised a further question: Could the secret of cell-cell adhesive specificity be encoded in the identity of just two amino acid side chains? Experiments designed to test this seemingly improbable prediction confirmed the result: Structure-guided mutations of these amino acids showed that cells expressing N-cadherin mutants adhere to cells expressing E-cadherins, but not to cells expressing wild type N cadherin. Thus, experiments carried out in cells were used to confirm the results of modeling studies at the detailed atomic level. These results are important because they provide the first atomic-level

explanation of cell-cell adhesive behavior and of how adhesive specificity might have evolved. Some of the most interesting applications of this new approach will be found in studies of the nervous system where specific adhesion proteins, including cadherins, help define the wiring of the neural networks of the brain.

- **Evaluating potential biomechanical effects of surgical treatments**: Through dynamic simulations, investigators at Simbios quantified how muscles contribute to walking, enabling them to identify the potential causes of abnormal motion in individual subjects, and to evaluate the likely biomechanical effects of surgical and non-surgical treatments.
- **Nanoscale simulation of molecular motors and RNA folding**: Studies from Simbios reported applying novel computational models to study distributions among complex, branching kinetic pathways through which biomolecules convert chemical to mechanical energy. This work showed that that the power stroke in the molecular motor, myosin, is coupled to the conformational changes in the ADP-bound state. In another study using hydroxyl radical footprinting techniques that probe the solvent exposure of molecular sites, Simbios researchers found that the commitment of an RNA molecule to a particular folding pathway depends upon the initial conformation of the molecule. Furthermore, the rate at which the molecule traverses the pathway is highly dependent on the reaction conditions.

Microarray Data and Pathways in Network Analysis

- **Identifying Diabetic End-Organ Damage:** At the National Center for Integrative Biomedical Informatics (NCIBI), Bayesian network modeling has been used to create models to identify transcriptional regulatory networks controlling expression and regulation of kidney glomerular filter proteins. Coupled with gene/protein annotation information, this Center has identified putative co-regulated proteins which might elucidate causal mechanisms related to complications of diabetic nephropathy.
- **Predicting stability of mRNA:** Studies from the MAGNet showed that dedicated methods for measuring genome-wide mRNA decay rates are not necessary for screening hundreds of conditions for dynamic regulation of mRNA stability. The Center's computational work suggests that regulation of mRNA stability is not a special case phenomenon, but rather a pervasive regulatory mechanism that rapidly adapts cellular processes to a changing environment.
- **The DREAM Project and Reverse Engineering:** MAGNet and IBM are collaborating on the "Dialogue on Reverse Engineering Assessment Methods" (DREAM) project which aspires to collect data and techniques that researchers can use to understand how well their reverse engineering methods can infer the nature of the underlying biochemical networks in the cell. The first open meeting for DREAM was held September 7 and 8, 2006, and jointly sponsored by the Center for Discrete Mathematics and Theoretical Computer Science (DIMACS) in New Jersey.
- **Bipolar Genetic Repository Linked to Michigan NCBC:** The National Center for Integrative Biomedical Informatics (NCIBI) at the University of Michigan will participate with the Prechter Bipolar Genetic Repository to host genome-wide microsatellite data from Johns Hopkins University and NIMH samples; to expand and improve data presentation and analysis, and to host the CHR 8q24 SNP data and allow the searching of results.
- **New Tools for HapMap Project:** Investigators associated with NCIBI are developing and applying tools such as a SNP Function Portal (for annotating and identifying related SNPs) and MarkerInfoFinder (a web-based Medline abstract search engine that supports the use of genetic marker IDs and flexible positional/linkage disequilibrium criteria) to accelerate research in the international diabetes research FUSION project. These tools are now available on the NCIBI.org website for use by the life and health sciences research communities.

- **Building upon Oncomine**: Oncomine (www.oncomine.org) is a resource for examining gene expression in cancer. In particular, it has been an important resource for prostate cancer research, demonstrating the value of computational biology, statistics, and related techniques. The goal of the Oncomine project is to collect, standardize, analyze, and deliver published cancer gene expression data to the research community. Oncomine enables investigators to probe the expression of a gene across thousands of cancer samples or to explore genes, processes and pathways deregulated in a particular type of cancer. Investigators at NCIBI reported building upon Oncomine, creating additional tools and methods which do similar work, and which can be joined into easily used workflows. They presented several resources and tools forming the core of tools needed to create such workflows.
- **geWorkbench:** MAGNet described further development of genomics Workbench, a Java-based open-source platform for integrated genomics. Using component architecture, it allows individually developed plug-ins to be configured into complex bioinformatics applications. More than 40 available plug-ins supporting the visualization and analysis of gene expression and sequence data are available. geWorkbench version 1.0 was released May 31, 2006 and may be downloaded from the project's web site at geworkbench.org. A companion GForge site has also been set up to support collaborative development.
- **An Algorithm for the Genome-Wide Discovery of Modulators of Transcriptional Interactions:** MINDY, a new information-theoretic method to identify multivariate statistical dependencies between a transcription factor and one or more of its targets, conditional on the presence (or absence) of a candidate modulator gene (e.g. a kinase or a co-transcription factor) has been developed by MAGNet at Columbia University. This has lead to the genome-wide identification of kinases capable of modulating each transcription factor in a human B-cell.

Ontologies

- **The BioPortal:** The National Center for Biomedical Ontology (NCBO) has produced an early-stage web portal for researchers to access biomedical ontologies and related tools. The portal will provide methods for accessing ontologies and their contents; navigating large, complex ontologies; using ontology content in applications; relating different ontologies and terminologies to one another and for creating mappings among them. It will also provide ontology metadata and services to support peer-review and ontology development. Ongoing research on the Degree of Interest Modeling for Ontology Navigation and Development (DIaMOND) is helping users more effectively and efficiently navigate ontologies through the presentation of adaptive visualizations
- **The Open Biomedical Ontologies (OBO) Foundry:** NCBO reported progress in developing the Open Biomedical Ontologies Foundry which seeks to create a set of best-practices, standards-based, reference ontologies. Using community input, the team has developed the Protein and RNA ontologies, and the Functional Genomics Investigation Ontology. Additionally, a number of candidates for the Foundry are under review.
- **The Open Biomedical Database (OBD):** Ontologies are important to biomedical research for sharing a common understanding of the entities in a given domain and for enabling reuse of data and information. In the field of computer science, an ontology is a representation of the entities, and the relationships among those entities, within a defined application domain. Ontologies are explicit models that drive modern information technology and thereby support the development of systems designed for purposes such as data mining, decision support, and data integration. NCBO reported progress in developing the OBD. This is test, or 'instance,' database that will allow expert scientists to store, visualize, and analyze experimental data that is fully described (annotated) using the Open Biomedical Ontologies Foundry (see next highlight). NCBO also has developed a software tool called "Phenote" to facilitate annotation of phenotype data.

- **NCBO Driving Biological Trial Bank:** The objective of the Trial Bank Project is to drive the development and use of ontologies and ontology-based services to augment the computational reasoning in randomized controlled clinical trials.
- **Ontologies that Link Human Diseases to Animal Models:** Researchers funded under NCBO are developing resources and syntax of the Phenotype and Trait Ontology (PATO) to design a set of orthogonal ontologies to describe mutant phenotypes and diseases. They expect to extend this to annotate phenotypes in all species, thus providing a means to link human diseases to model organisms.
- **The PhenGO database system:** MAGNet has developed an early-stage database that adds phenotypic contextual information (cell types) to existing association between gene products and terms in the established Gene Ontology (GO).

Dissemination and Education

- **Building a collaborative environment for physics-based modeling:** Simbios reported establishing Simbiome.org, a repository of advanced algorithms and modeling applications with easy-to-use graphical user interfaces as a curated portal to all available simulation related resources.
- **Biomedical Computation Review:** Simbios researchers have published five issues of the highly popular and award winning *Biomedical Computation Review* (BCR), with a mission to build community amongst the highly varied audience of researchers interested in developing and utilizing biomedical computation. BCR covers the broader area of biomedical computing and is freely available in print and on the web (http://biomedicalcomputationreview.org). Each issue is mailed to over 2,500 researchers and includes two feature articles along with regular columns such as Editorial, News Bytes, Editor's Picks, Book Review, Featured Lab, Under the Hood (tutorial), and Seeing Science (scientific imagery). Past feature article topics have included: Top 10 advances/challenges, NCBC Round 1, Education, Computer-Brain Interfaces, NCBC Round 2, Visualization-Driven Science, Multiscale Modeling, Women in Biomedical Computing, Human vs. Machine and Infectious Disease modeling. Plans for future feature articles include Terascale Computing, Microarrays, Public Databases and Proteomics.

HIGHLIGHTS OF DISCUSSIONS WITH NCBC PRINCIPAL INVESTIGATORS

Numerous views relevant to building a national biomedical computing infrastructure emerged during discussions with the RIWG co-chairs, NCBC Project Team, and meeting attendees. Highlights of those discussions are the following:

- **Build a computationally competent biomedical workforce:** Participants emphasized the need to foster a biomedical workforce competent in quantitative approaches and analyses, information management and integration, and applications of computational tools.
- **Link NIH training efforts with NCBCs:** A national leader in informatics suggested NIH consider efforts to link other NIH training initiatives in computing and engineering with the NCBCs**.**
- **Support computer scientists:** The issue of support for computer scientists in biomedical research persists. An NCBC Principal Investigator noted that without such support, computer scientists cannot remain in departments to which they are recruited. NIH staff noted efforts to enable multiple Principal Investigators on grant applications.

- **Promote sustainability to retain young scientists:** An NCBC Principal Investigator observed that young scientists cannot be expected to commit to major initiatives of unknown sustainability. He noted that it is appropriate for individual funded components to undergo reviews for competitive renewal, but the overall major initiative should represent a viable and sustainable venue to risk careers.
- **Create interdisciplinary research opportunities:** Existing funding mechanisms should be used to attract computer scientists to interdisciplinary research.
- **Improve the program for fostering collaborations with NCBCs:** The NCBCs are developing collaborations with outside researchers using the current announcements, PAR-05-063 (R01) and PAR-06-223 (R21). This is a slow and time-consuming process. This initiative should be improved. One possibility would be to supplement other existing NIH awards.
- **Build bridges to major biocomputing/informatics Initiatives:** In their role as National Centers, the NCBCs are seeking collaborations with other major initiatives. To promote this, the Roadmap NCBC initiative is providing support for a postdoctoral position for each of the seven Centers to build bridges to other biocomputing and informatics efforts.
- **Improve coordination between the NIH intramural and extramural research programs**: Meeting attendees noted the importance of improved coordination between the NIH extramural and intramural biomedical informatics and computational biology research programs. This includes coordinating activities of the NIH NCBI with the NCBCs.
- **Address Preservation of Digital Data:** Dr. Donald Lindberg, Director of NLM and RIWG co-chair, noted the ever growing critical need for the preservation of digital data, and its potential to change the face of medicine, and reduce costs; however, to realize this potential, many technical issues remain with assuring access to varied and changing data formats.
- **Attend to need for anonymizing data**: Dr. Lindberg also mentioned the growing, national need for a "cast iron" method for anonymizing data. He emphasized the importance for NIH to establish such a process.
- **Involve NIH Program Officers of Driving Biological Projects**: An NCBC Principal Investigator suggested that the NIH NCBC Project Team exert more proactive efforts to involve and inform NIH program officers of NCBC Driving Biological Projects about the NCBC Roadmap efforts.
- **Involve NIH ICs:** Recognizing that although the NCBCs form the core components for building a national biomedical computer infrastructure, completing that infrastructure needs interest, understanding and support across all ICs to facilitate application and translation of their efforts, to avoid redundant and balkanized efforts, and to promote coordination and interoperability where possible.

  The following are based on written comments read during the public session because a late-breaking scheduling conflict prevented Dr. Zerhouni from his previously planned participation. His full comments are included at the end of this report.

- **NCBCs not Business as Usual**: Dr. Zerhouni reminded the Centers they are about boldness, not business as usual.
- **NCBC cooperation and unconventional leadership**: Because of his concern about artificial silos and barriers in research, Dr. Zerhouni commended the Centers on creating Working Groups to explore areas of mutual interest, cooperation and interaction, indicating they represent the bold, broad-based, unconventional leadership he expects from the NCBCs and the Roadmap efforts.

- **NCBC Dissemination:** Dr. Zerhouni expressed concern that scientists need to find effective ways of communicating the importance and value of their work to the public. He said he was heartened by the enthusiasm by which the NCBCs embraced and organized "Dissemination Events" to explain their work while at the NIH. He noted such efforts are absolutely critical to the NCBC mission as a Roadmap endeavor, and to helping him explain as NIH Director the value of the NIH investment.

NCBC WORKING GROUPS

Background: Since their inception, all NCBCs have engaged in scientific and technical discussions of common interests under the auspices of the NIH Software and Data Integration Working Group (SDIWG). Using remote, collaborative technologies (Web Wiki, Breeze, and teleconference) prior to the All Hands Meeting (AHM), the SDIWG developed three working groups which then met in person for the first time during the AHM. The regular meeting minutes and other discussions have been entered in a common Wiki site [2]. The following provides a summary of the two hour working group meetings, which occurred on July 18, and links to Workgroup Wiki sites:

Science Ontologies

Mission: The mission of this group is to recommend a minimal and simple set of biomedical ontologies that can be followed by investigators within the various NCBCs who are in the process of building databases, or annotation engines, or catalogs relevant to diverse enterprises of biomedical research. The working group is adopting a pragmatic approach and is avoiding rigorous debates about the definition of what constitutes ontology, a terminology, or a nomenclature. The group will provide broad guidance and leadership by promoting the adoption of its own recommendations within the NCBCs.

Meeting Outcome: Based on several virtual meetings attended by representatives from all NCBCs, as well the July 19 meeting, the group provided a draft list of biomedical ontologies on its Wiki site [2].

Future Directions: The draft list of biomedical ontologies serves only as a point of initial discussion rather than a final set of recommendations. The group's next steps will be to move discussion forward by adding detail about the chosen categories, and to continue further vetting. These steps should allow the NCBCs to provide a public, pragmatic set of guidelines regarding this increasingly important set of resources. A longer term goal is for this activity to provide infrastructure, whereby the larger biocomputing community will adopt a common minimal set of ontologies, as well as a process for adopting new ontologies.

Software Yellow Pages and Resourceome

Mission: This Workgroup aims at developing an extensible repository describing the wide spectrum of tools, databases, services and resources being produced by the seven NCBCs. The repository will enable biomedical researchers to identify NCBC software tools and resources to facilitate their work. Ultimately, Resourceome will engage the broader community of biomedical software developers to contribute descriptions of their tools, and could eventually provide a "one-stop" searchable resource for researchers looking for needed computational and informatics resources.

Meeting Outcome: The group began defining the framework for this resource. The group focused on creating a Web-based infrastructure (the "Resourceome") for describing resources and searching for them (including software tools, data, and services). The group proposed a minimal set of required meta-data descriptors for tools and resources created, maintained, and distributed by the seven NCBC Centers—a

prototype is available on the Wiki site [2]. They also proposed a set of optional parameters. Some group members already are implementing open software tools to support web-based collection and maintenance of resource descriptions. For example, the Simbiome, a resourceome for physics-based simulation software, is currently in use and the underlying code was made available on Simtk.org, so that other Centers can follow a similar model. These tools may be useful to create the Resourceome.

Future Directions: Moving forward, this working group will finalize the specification of data descriptors for tools and resources, populate these descriptors for the tools/resources of each NCBC, and adapt existing open software tools to implement Resourceome, compiling these descriptions and providing the research community with Web based search functionality to find the resources and tools appropriate to their work. A longer term goal for the "Resourceome" is to provide the infrastructure whereby the larger biocomputing community will adopt a common set of methods to access, use, and compose valuable computational resources and tools and avoid unnecessary efforts.

NCBC Driving Biological Project (DBP) Biomedical Impact Workgroup

Mission: An increasing number of biologists and biomedical researchers in the NCBC program and in the broader community are beginning to rely on genome-wide knowledge about molecular and cellular interactions to dissect specific biological mechanisms and processes. For instance, coupling Quantitative Trait Loci (QTL) and genetic pathway data has been shown to help in the identification of low-penetrance susceptibility genes. Similarly, the study of differential gene expression analysis in normal vs. diseased tissue can benefit from the knowledge of the underlying genetic interaction networks, for instance to filter out downstream effects related to the dysregulation of a specific pathway. Finally, modeling is not limited to cellular networks, but includes computational nano-biology as well as macroscale modeling such as whole-body modeling that will lead to improved pharmacokinetics for drug discovery or computational support for the operating room of the future, to name just a few. The ability to integrate, model, and analyze heterogeneous data in a controlled and reproducible way has emerged as a major challenge for biomedical research. Several NCBCs and their partners are actively working to enable and accelerate this process.

The goal of this new workgroup, is to coordinate the NCBC DBPs to help define common resources requirements, methodologies, and data resources, such as those discussed above, that have the potential to significantly impact the broader research community. The output of the discussions is on the Wiki site [2]. This coordination will help define which NCBCs will provide or require specific tools and data integration capabilities in this area. This is especially important given the variety of existing and future DBPs and collaborative R01 (PAR-05-063) and R21 (PAR-06-223) initiatives that may benefit from such activities. A major goal of this workgroup is to synthesize the various efforts ongoing within the NCBC community, including strategies to link these efforts into the work being done in the broader community. The working group will also develop plans to evaluate the biomedical impact of the NCBCs, as well as the associated DBPs and the collaborating R01/R21 program.

Meeting Outcome: The group met to discuss its mission, acknowledging it faces very significant challenges. The group concluded it must leverage and interact with the “Software Yellow Pages and Resourcome” and the “Science Ontology” workgroup products. It expressed interest in understanding the needs and approaches identified and being currently implemented in the various DBPs in the full complement of the NCBCs. It also expressed interest in exploring DBP areas that span many NCBCs (e.g. Diabetes, Schizophrenia) or pathways/approaches that are shared by several DBPs. It reported on a recent NCBC-lead activity, focused on harmonization efforts: the organization of the DREAM workshop and database. The DREAM project aspires to collect data and techniques that researchers can use to understand how well their reverse engineering methods can infer the nature of the underlying biochemical networks in the cell. This initiative has been broadly supported by the international reverse engineering

community. A document [5] summarizes the planning activities and conclusions of the DREAM planning meeting, which was held on March 9th and 10th, 2006 at the New York Academy of Sciences.

Future Plans: This group intends to provide a forum to begin to further organize and leverage the NCBC DBPs, look for opportunities for interaction, explore potential new DBPs, and to help generally ensure that the impact(s) of the NCBCs on their target biological and biomedical research areas are maximized in relation to the science, software and data dissemination, and building bridges between the NCBC DBPs and beyond to the lager NIH research community. The first DREAM meeting was held on September 7th and 8th, 2006 in the Wave Hill Convention Center, New York NY.

BUILDING BRIDGES OUTREACH

Background: The suggestion for biomedical computing National Centers of Excellence came from the 1999 Smarr-Botstein report on Biomedical Information Science and Technology Initiative (BISTI) [4]. This report also recommended programs in training, increased capability in information storage curation archival and retrieval (ISCAR), as well as non-hypothesis based computational research covering a broad range of domain sciences from molecular biology to bioengineering. The NIH Roadmap for biomedical informatics and computational biology has envisioned a hub-and-spoke model for the national Centers program with the seven NCBCs augmented by research funded through independent collaborative R01 (PAR-05-063) and R21 (PAR-06-223) grants responding to announcements dedicated to this purpose.

The Building Bridges Compendium [3] emanating from the AHM identified a wide-ranging set of government programs with significant efforts in biomedical informatics and computational biology.

Meeting Activity: During the meeting, three one-hour panels comprised of twenty two government program leaders representing a cross-section of the compendium addressed the meeting to promote interaction among the seven NCBCs and their respective programs. The panels represented seven areas: NIH Roadmap, Networked Science, Federal Government, Interagency, NIH Intramural Science, Modeling, and Imaging.

Building Bridges Accomplishments: The open discussions represented the first known aggregate of such a large cross section of government leaders in biomedical informatics and computational biology. Numerous connections were made during the panel discussions and in subsequent direct discussions between panelists and attendees following the sessions. For example, a common theme of the Roadmap panel is the difficulty of managing and evaluating collective interactions of the large-scale efforts, beyond just the local scientific research that is funded. Quite a number of Roadmap Networks were formed by peer-review of independently-written applications for funding. In effect, these are networks whose connections are being formed after the core components are set in place. Discussions focused on the collaborating R01/R21 initiatives (or 'spokes') and the use of administrative supplements to focus on building bridges and connections among the NCBCs as well as with the broader community of government efforts in biomedical informatics and computational biology. A significant outcome of the AHM is the establishment of a publicly-available permanent archive [3] of this compendium that covers at least 90% of government funding, as well as some public private partnerships. Also, a decision was made to initiate the NIH NCBC postdoctoral supplements to build bridges to other major biomedical informatics and computational biology programs.

DISSEMINATION EVENTS

A robust national biomedical computing infrastructure requires effective and efficient distribution of its tools and technologies. For this reason, the NIH Roadmap NCBC program expects its participating Centers to inform and instruct the broader biomedical community about their resources. In response, each NCBC, in conjunction with their NIH Lead Science Officers and other staff, voluntarily organized and held a special dissemination event unique to its research interests while in Bethesda at the NCBC AHM. These events—all held concurrently on July 19—varied in content and format. Beyond those who attended the general plenary sessions of the AHM, the dissemination events attracted numerous additional local and NIH scientists just to these special sessions, including one IC Director and senior NIH intramural scientists, seeking more in-depth discussions and interactions than those possible at the plenary events.

Event Summaries and selected related outcomes are the following:

- **The National Center for Integrative Biomedical Informatics (NCIBI)**

  Workshop on "Tools and Technologies for Studying Prostate Cancer and Diabetes Complications": Approximately 55 participants representing NIH extramural and intramural staff from nine ICs (including senior intramural scientists from NCI, NIDDK and NIMH), as well as local academic, Department of Defense, and private sector scientists attended a half-day dissemination workshop with presentations by representatives from The National Center for Integrative Biomedical Informatics (NCIBI), including the University of Michigan, Carnegie Mellon, and the Broad Institute. Part I of the Workshop addressed tools and technologies for studying the severity of prostate cancers and their potential applications to other diseases. Part II examined tools and technologies for studying cellular and organ-specific complications of Type I Diabetes and their potential application to the study of other complex diseases. Following the workshop, extended discussions continued over lunch with the intramural Chief of the Diabetes Division at NIDDK. Another senior intramural scientist expressed interest in hearing the Center's progress in proteomics as it moves into its second year.

- **The Informatics for Integrating Biology and the Bedside Center (i2b2):**

  Seminar and Discussion on "Harnessing the Health Care Enterprise for Translational Research in the Genomic Era": NCBC Principal Investigator Dr. Isaac Kohane presented the work of his Center, focusing on (1) extracting robust phenotypic information from narrative clinical records; (2) assembling an array of analytic packages in a useful clinical research chart; and (3) mobilizing patients and clinical researchers to conduct research in a way that meets ethical/consent guidelines. Approximately 40 individuals from nine NIH components, academic and the private sector attended. Discussion focused on critical topics such as enforcing NIH data sharing requirements, patient-owned health records, assuring data security, and the relationship between the NCBC efforts and the DHHS Health Information Technology Initiative.

- **The Center for Computational Biology (CCB)**

  "Methods and Tools for Analyzing Biological Shape, Form and Size": This 3-hour event focused on presenting the efforts of the Center for Computational Biology in the critical area of analyzing biological shape, form, and size. Presenters compared and contrasted the Center's approaches to other current techniques, and solicited critical feedback on the Center's methods and tools. Thirty-five participants from NIH, FDA and the VA, as well as other NCBCs and the broader biomedical academic community attended. Productive discussions which stimulated possible future projects and collaborations followed the formal presentations.

- **National Alliance for Medical Image Computing (NA-MIC)**

  A hands-on, **3D Slicer Training workshop focused on "Diffusion Weighted Image (DWI) Analysis"**: Twenty-four attendees evenly divided between intramural participants (representing 11 different laboratories within NIH) and extramural participants (representing 7 different universities and companies) attended this day-long, software training event. Ninety-five percent of the participants were computer scientists, a large majority with PhD degrees. All participants had successfully completed the preparation steps prior to the workshop. The Diffusion Weighted Image analysis workshop, organized in four hands-on sessions, guided the participants through a logical progression of tasks, from loading and visualizing data, to clustering fiber tracts. Various exercises provided the trainees with practical experience of image analysis and visualization with 3D Slicer. At the end of each session, all the participants successfully obtained the results expected. The dissemination event tutorials are available on the Slicer 101 web page which has been accessed 7,700 times. This workshop was led by Sonia Pujol (Brigham and Women's Hospital), with the participation of Steve Pieper (Isomics, Inc.).

- **The National Center for Multi-Scale Analysis of Genetic and Cellular Networks (MAGNet)**

  "geWorkbench—The Bioinformatics Platform of the National Center for the Multi-scale Analysis of Genomic and Cellular Networks": NCBC Principal Investigator Dr. Andrea Califano provided an overview to approximately 20 attendees of the application design of geWorkbench, including its interoperability and workflow frameworks. The Center showcased how the application can address actual biological problems, and demonstrated some of the tools developed by The National Center for Multi-Scale Analysis of Genetic and Cellular Networks (MAGNet).

- **The National Center for Biomedical Ontology (NCBO)**

  "An Overview of Biomedical Ontologies": In a half-day session, world-renowned ontology experts Dr. Mark Musen, Director of the National Center for Biomedical Ontology, and Dr. Barry Smith, Distinguished Professor of Philosophy in the University at Buffalo, presented an overview of how the term 'ontology' has been used in recent history, of the powerful tools that are now available for ontology developers, and how ontologies are being used in health information systems and in informatics-based biomedical research. They spoke to a capacity audience eager to learn more about the Center's proposed solution to the growing heterogeneity of terminologies in biomedicine. The speakers discussed the National Center for Biomedical Ontology's efforts to solve this problem by creating a family of interoperable gold standard reference ontologies. They showed how this solution can address the problems of data retrieval and reuse, and enhance terminology resources. Representatives from the NIH, the DHHS Office of the National Coordinator for Health Information Technology (ONC), the Center for Disease Control, the National Institute of Standards and Technology, the Veterans Administration, and the National Science Foundation attended the session.

- **The Physics-Based Simulation of Biological Structures Center (Simbios)**

  "Physics-based Simulation of Biological Structures": The Physics-Based Simulation of Biological Structures Center (Simbios) offered a morning workshop presenting the software features, functionality, availability, documentation, user testing, and accuracy of its SimTK toolkit, including features offering advanced capabilities for modeling the geometry and physics of biological systems (such as RNA folding, and myosin, cardiovascular, and neuromuscular biomechanics), and for integrating and comparing simulation results with experimental data. The Center's Director, Dr. Russ Altman, and Co-PI Scott Delp, also discussed the function and success of the Center's distributed software development system at www.simtk.org. A Roundtable discussion followed about the Dissemination, Training & Collaboration Efforts of the

Center, including Biomedical Computation Review, a magazine it produces devoted to biocomputational science and tools, Simbiome, an inventory of high-quality commercial and academic bio-simulation tools, curriculum and training material for biomedical scientists and students, and opportunities for collaborating with Center.

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NCBC POJECT TEAM
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ALL HANDS MEETING PLANNING GROUP
The Planning Team for the 2006 NCBC All Hands Meeting consisted of various representatives from the NCBC Project Team, Science Officers associated with the NCBCs and the Lead Science Officer for each of the seven NCBCs.

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Graphic Development

The AHM Planning Team gratefully acknowledges the contribution of Dr. Nancy Freeman (NIH/NIDCD) for development of the 2006 NCBC AHM graphic.

WEB REFERENCES

[1] The Roadmap National Centers for Biomedical Computing 2006 All Hands Meeting web site and permanent archive: http://www.bisti.nih.gov/ahm2006/

[2] The Software and Data Integration Working Group Wiki: http://na-mic.org/Wiki/index.php/SDIWG:Software_and_Data_Integration_Working_Group

[3] The Compendium of government and private programs with significant components of biomedical informatics and computational biology: http://www.bisti.nih.gov/ahm2006/Building%20Bridges%20Compendium.htm

[4] The BISTIC Consortium Web Page: http://www.bisti.nih.gov/ and Report of the Working Group on Biomedical Computing of the Advisory Committee to the Director National Institutes of Health (June 3, 1999) http://www.nih.gov/about/director/060399.htm

[5] Summary of DREAM kick-off meeting March 9-10, 2006 http://na-mic.org/Wiki/images/a/a1/Summary_DREAM_Kickoff_Meeting.pdf

ATTACHMENT I: COMMENTS FROM DR. ZERHOUNI: Read to panel of Principal Investigators of the National Centers for Biomedical Computing by NIGMS Director, Dr. Jeremy Berg (07/18/2006)

As you know, this meeting has been on my schedule for some time, and I've looked forward to the opportunity of interacting with you, the Principal Investigators of the Roadmap National Centers for Biomedical Computing. I recall a cold December day in 2002 at one of the earliest Roadmap planning meetings when I was reminded by some of your colleagues of the 1999 BISTI report, and emphatically pressed to "get on" with the creation of National Programs of Excellence in Biomedical Computing. I also remember being at the first Digital Biology symposium in the Fall of 2003. Much of the excitement centered upon announcement that week of one the earliest Roadmap initiatives, which enabled – for the first time – a truly cross-cutting program in Biomedical Computing, broader than any single NIH domain. Thus, this program has been a pioneer in all respects. You are among the first of our Roadmap pioneers, but more important, you are pioneers in the critical quantitative, analytical, informational and integrative issues defining new frontiers in biomedical research and pre-emptive medicine. It is time we all talk about the next steps in transforming a shared vision into a true national infrastructure for biomedical computing.

Your Centers are part of the Roadmap process through which NIH serves emerging areas of science, incubates research concepts, and experiments with leading-edge issues. Your Centers are about boldness, not business as usual. I worry about what I call "sclerosis:" artificial silos and barriers in research. For that reason, I commend you on creating Working Groups to explore areas of mutual interest, cooperation and interaction. The efforts you are exerting through your Work Groups in developing systems for identifying and characterizing computational tools, tackling the data and resource needs for systems biology, and addressing the complicated issues associated with scientific ontologies represent the bold, broad-based, unconventional leadership we expect from you and the Roadmap efforts.

I also remain concerned that scientists need to find effective ways of communicating the importance and value of their work to the public. For these reasons, I also am heartened by the enthusiasm by which you all have embraced and organized tomorrow's Dissemination events while you are here. Such efforts are absolutely critical to your mission as a Roadmap endeavor, and to helping me explain as NIH Director the value of the NIH investment.

With its theme of "Building Bridges," this All Hands Meeting represents the innovation we anticipated from you. It has become organic, in that it is not a gathering in time, but the beginning of new thinking, new efforts and new relationships. I regret that a last minute scheduling conflict kept me from being with you, but I assure you that I will follow the reports of your comments during this panel discussion and activities here with great interest, and look forward to future opportunities for more direct dialogues.