DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL ADVISORY COUNCIL FOR
BIOMEDICAL IMAGING AND BIOENGINEERING

Summary of Meeting[1]
January 26, 2004

The National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB) was convened for its fourth meeting on January 26, 2004 in Building 31, Room 10, National Institutes of Health, Bethesda, Maryland. Dr. Roderic I. Pettigrew, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), served as Chairperson.

In accordance with Public Law 92-463, the meeting was open on January 26, 2004 from 10:00 A.M. until approximately 1:30 P.M. for the review and discussion of program development, needs and policy, and closed to the public from 1:30 P.M. until 4:30 P.M. for discussion and consideration of individual grant applications.

Council members present:

Dr. Carlo De Luca
Dr. Janie Fouke
Dr. Linda Lucas
Dr. James Zagzebski
Dr. Norbert Pelc
Dr. Robert Grossman
Dr. Rebecca Richards-Kortum

Council members present through teleconference:

Dr. C. Douglas Maynard
Dr. Frank Yin

Council members absent:

Dr. Shirley Jackson
Dr. Barbara McNeil
Dr. Stephen Williams

Ex officio member present:

Dr. Michael Weiner

Ex officio members absent:

Dr. John Brighton
Dr. Arden Bement
Dr. Ann Dellinger
Dr. James Smirniotopoulos

Members of the public present for portions of the open meeting:

Dr. James Duncan, Yale University
Mr. Edward Nagy, Academy of Radiology Research
Ms. Michelle Doose, Academy of Radiology Research
Ms. Marianne Marlowe, Capital Consulting Corporation
Ms. Melissa Murray, American Society of Mechanical Engineering

[1]For the record, it is noted that members absent themselves from the meeting when the Council is discussing applications (a) from their respective institutions or (b) in which a real or apparent conflict of interest might occur.

Dr. Edward Staab, Wake Forest University
Mr. Andrew Hawkins, The Blue Sheet
Ms. Shirley Coney-Johnson

NIBIB employees present for portions of the meeting:

Dr. Roderic Pettigrew
Ms. Yinka Abu
Ms. Taiwo Adeloye
Dr. Prabha Atreya
Ms. Lillian Ashley
Ms. Nancy Curling
Ms. Cheryl Fee
Dr. David George
Dr. Gary Glover
Ms. Yvette Gordon
Ms. Colleen Guay-Broder
Dr. John Haller
Dr. Joan Harmon
Dr. Bill Heetderks
Dr. Christine Kelley
Ms. Mary Beth Kester
Dr. Peter Kirchner
Dr. Peter Lyster
Ms. Ann Mastradone
Dr. Alan McLaughlin
Mr. Todd Merchak
Mr. Nicholas Mitrano
Dr. Peter Moy
Ms. Renee Nowland
Dr. Mary Pastel
Dr. Grace Peng
Ms. Anna Retzke
Dr. Belinda Seto
Ms. Theresa Smith
Ms. Mollie Sourwine
Dr. Richard Swaja
Ms. Sandra Talley
Dr. Meredith Temple-O'Connor
Ms. Florence Turska
Ms. Jennifer Vyskocil
Ms. Stacy Wallick
Dr. Yantian Zhang

Other Federal employees present for portions of the meeting:

Dr. Brenda Korte, National Institute of Justice
Dr. Andrew Watkins, Centers for Disease Control
Dr. Arlene Chiu, National Institute of Neurological Disorders and Stroke
Dr. Robert Archer, Los Alamos National Lab

I. Call to Order and Opening Remarks – Dr. Roderic I. Pettigrew

Dr. Pettigrew welcomed Council members, guests, and staff to the fourth Council meeting, extending a special welcome to those who share the mission of the NIBIB. He thanked Council for attending in such harsh weather conditions, noting that several were unable to make it. He introduced Dr. Robert Grossman, the newest member of NACBIB who was attending his first meeting. Dr. Grossman is Professor and Chairman in the Department of Radiology and Professor of Neurosurgery, Neurobiology, Physiology and Neuroscience at the New York University School of Medicine. He also expressed appreciation to Drs. Rebecca Richards-Kortum and Stephen Williams for agreeing to serve for four more years.

Dr. Pettigrew introduced Dr. James Duncan of Yale University as a speaker for the day. The NIBIB supports Dr. Duncan's pioneering work in neuroimaging. Dr. Pettigrew indicated that this presentation will be the first in an ongoing feature of NACBIB meetings to provide more information to the Council on some of the work that is being supported by the NIBIB.

Dr. Pettigrew introduced Dr. Belinda Seto, the new Deputy Director for the NIBIB. Dr. Seto joins the NIBIB from the NIH Office of the Director where she most recently served as Deputy Director and Acting Director for the Office of Extramural Research.

Dr. Pettigrew recognized two Council members for recent honors. A statue entitled "Triple Helix" was unveiled in October in the Piedmont Triad Research Park on the campus of Wake Forest University in honor of Dr. C. Douglas Maynard's many years of service to the school. Dr. Maynard recently retired after a greater than fifty year association with the University – as student, professor, and finally chairman of the Radiology Department. Dr. Maynard played an integral role in the development of the Research Park that has attracted a number of biotechnology companies to North Carolina.

Dr. Barbara McNeil is one of four radiologists featured in a new exhibit at the National Library of Medicine (NLM) that honors women in medicine. Entitled the "Changing Face of Medicine," the exhibit features women who have contributed significantly to enhancements in the practice of medicine and is designed to inspire another generation of pioneers. The exhibit opened at the NLM in October and closes on April 2, 2004.

Dr. Pettigrew explained that weather caused the delayed start for the meeting. Agenda items would be shortened to permit completion of business by the end of the day.

Dr. Pettigrew drew attention to the calendar of future meeting dates. Council members should contact Dr. Harmon, if there are major conflicts with the following dates. Potential changes will be reviewed by e-mail, if necessary.

May 26-27, 2004
September 13-14, 2004
January 27-28, 2005
May 25-26, 2005
September 14-15, 2005
January 25-26, 2006
May 24-25, 2006
September 13-14, 2006

Council accepted the minutes of the September 2003 meeting without modification.

II. Review of Regulations and Review of Operating Procedures – Dr. Joan T. Harmon

Dr. Harmon summarized the requirements under the Government in the Sunshine Act and the Federal Advisory Committee Act. These Acts require the Department of Health and Human Services (DHHS) to open to public observation as many advisory committee meetings as possible, including the meetings of the National Advisory Councils. The Council meeting, therefore, would be open to public observation except during grant application review, scheduled to begin at 1:30 P.M. and concluding by the end of the day. Notice of the Council meeting was published in the *Federal Register* thirty days prior to the meeting.

Dr. Harmon also reviewed regulations concerning conflict of interest, and Council members were reminded that materials furnished for review purposes and discussion during the closed portions of the meeting are considered privileged information. All Council members present signed a statement certifying that they did not participate in the discussion of, or vote on, an application from any organization, institution, or any part of a university system, except for those which have multi-campus institution waivers or are specifically designated as separate organizations under 18 U.S.C. 208(a), of which they are an employee, consultant, officer, director or trustee, or in which they have a financial interest.

Dr. Harmon asked Council to consider two changes to current Council Operating Procedures. Council approved by unanimous vote the following:

- All applications with concerns relating to involvement of humans or animals in research or inclusion of minorities, women or children are currently brought to Council for discussion. The staff proposes a change to bring only unresolved concerns to Council.
- The staff proposes adding to the Operating Procedures a definition of a "Communication." Currently, it is not defined.

III. Director's Report – Dr. Roderic Pettigrew

Dr. Pettigrew announced transitions for several staff members and staff additions. Dr. Donna Dean, former Deputy Director, NIBIB has accepted a position as Senior Scholar in Residence at the National Academy of Engineering. Former Executive Officer, Mr. Charles Best has also departed. Dr. Brenda Korte, former Program Officer in the Division of Discovery Science and Technology is now a Program Manager with the National Institute of Justice. Ms. Pam Mayer has moved to another Grants Management Office at the NIH and Mr. Steve Green accepted a position at the National Science Foundation.

In addition to Dr. Seto, the new Deputy Director, the NIBIB welcomes Dr. Prabhakara Atreya, to the Office of Scientific Review (OSR). Dr. Atreya was previously with the NIH Center for Scientific Review (CSR). Dr. Yantian Zhang recently came to the NIBIB from the NIH Clinical Center where he was a staff scientist in the intramural imaging research program. He is a Program Director in the Division of Applied Science and Technology. Ms. Theresa Smith, Biomedical Engineer is also in the Division of Applied Science and Technology. In September, Ms. Tinera Fobbs joined the staff of the Office of Extramural Policy, leaving a position in the NIH Intramural labs. The NIBIB Administrative Division benefits from the addition of two Administrative Officers, Ms. Ann Mastradone and Mr. Tony Pirrone.

Dr. Pettigrew updated Council on the status of NIBIB fiscal year 2004 appropriations. The President signed the appropriations bill for the Department of Health and Human Services on January 23, 2004. The NIBIB received $288,900,000, reflecting an $8,800,000 increase over fiscal year 2003. Reviewing developments in the NIBIB budget and portfolio, Dr. Pettigrew mentioned the major impact of transfers in fiscal years 2003 and 2004 and the large number of applications received in response to fiscal year 2003 Requests for Applications (RFAs). He

underscored that NIBIB will be challenged to respond to the expected growth in applications anticipated throughout 2004 and beyond given modest budget increases.

The NIBIB has devised a budget management plan to address these issues. To optimize the pay line and maintain a reasonable success rate, the NIBIB will pursue collaborative funding with other Institutes, other government agencies, and industry. The Institute will carefully manage commitments to high-cost grants. Despite the disproportionately large number of high quality SBIR/STTR applications received, funding for this program will be at the statutorily mandated level. As noted at other meetings, the NIBIB aims to achieve a 25 percent annual turnover in competing dollars. Holding research project grants to a maximum of four years, R21s to two years, and bioengineering research project (BRP) awards to five years will support this goal. The NIBIB will also not increase the total budget for Center grants and limit issuance of new initiatives.

Highlighting some recent meetings sponsored by the NIBIB, Dr. Pettigrew mentioned the Biomedical Science Information and Technology Initiative Consortium (BISTIC) symposium, a grantee meeting for awardees leading Bioengineering and Bioinformatics Summer Institutes, and a workshop with industry representatives on collaborative research and training opportunities. The NIBIB has many meetings planned for the next few months, including the following:

- NIBIB/DOE Workshop on Biomedical Imaging: Optical & X-Ray Technologies – Feb. 10-11, 2004
- DOE/NSF/NIH Workshop on Opportunities in Tera Hertz Science – Feb. 12-14, 2004
- NIBIB/NSF Workshop on Transport Processes in Biomedical Systems – Feb. 17-18, 2004.
- Interagency Conference on the Interface of Life Sciences and Physical Sciences – Mar. 2004
- NIDDK/JDRF/NIBIB workshop on Islet Cell Encapsulation – Mar. 29-30, 2004
- NIBIB/NSF Image-guided Interventions Grantee meeting – Apr. 2004

Dr. Pettigrew announces that the NIBIB had joined three Program Announcements led by other Institutes, *Informatics for Disaster Management; Neurotechnology Research, Development and Enhancement;* and *NIH/NSF Collaborative Research in Computational Neuroscience.* The trans-NIH Roadmap continues to progress and the NIBIB has a strong interest in several of the recently issued initiatives. (Information on the Roadmap is available at www.nihroadmap.nih.gov.)

Dr. Pettigrew then provided brief summaries of some of the research being supported by the NIBIB. He highlighted work from the following projects:

- Engineered Self-Assembling scFvs for Piezoimmunosensors *(Xiangqun Zeng, PhD, Oakland University)*
- Integrated Technologies for Polymeric Biomaterials, *(Joachim Kohn, PhD, Rutgers New Jersey Center for Biomaterials)*
- Haptics for Robot-Assisted Minimally Invasive Surgery, *(Allison M. Okamura, PhD, The Johns Hopkins University)*

- Highly Accelerated Parallel MRI on an MR Scanner with 32 Receiver Channels, *(D. Sodickson, Harvard Medical School (HMS), Beth Israel Deaconess Medical Center (BIDMC) and Harvard-MIT Division of Health Sciences and Technology (H-MIT); C. Hardy, GE Global Research Center (GEGRC); Y. Zhu, GEGRC; R. Giaquinto, GEGRC; G. Kenwood, GEGRC; N. Rofsky, BIDMC and HMS; K. Rohling, GEGRC; C. Dumoulin, GEGRC; C. McKenzie, BIDMC and HMS; T. Niendorf, GE Medical Systems; M. Ohliger, BIDMC and H-MIT; J. Willig-Onwuachi, BIDMC and HMS; A. Grant, BIDMC and HMS; E. Yeh, BIDMC and H-MIT; H Kressel, BIDMC and HMS)*

Dr. Pettigrew concluded his report with a brief discussion of the new Intramural Division. Funding for this new Division, in the amount of approximately $3 million has been included in the fiscal year 2004 NIBIB budget. Transfer of the PET Chemistry group from the NIH Clinical Center to the NIBIB is almost complete, with a memorandum of understanding under final review. An agreement for collaboration with the National Institute of Standards and Technology on bioengineering research is under similar review. A planning workshop on potential areas of focus in tissue engineering was held in September. Dr. Pettigrew and Dr. David W. Feigal, Director, Center for Devices and Radiological Health of the Food and Drug Administration signed an agreement on collaborative research in January. Through this arrangement a team will conduct an assessment of medical imaging systems. Specifically these projects are designed to:

- Create an objective assessment of X-ray imaging systems using accurate modeling of image acquisition process, analysis of simulated data, and prediction of clinical performance without lengthy/expensive observer studies
- Perform objective medical image display evaluations to assess the diagnostic impact of such variables as color, viewing-angle, sub-pixel structures, 3D/4D medical image presentations, projection images and stereo and holographic systems

In response to questions from Council, Dr. Pettigrew expanded on the budget management strategy of limiting the duration and size of grants to achieve a 25 percent turnover rate in dollars available for new applications. He clarified that his projection of growth in applications in fiscal year 2004, referred only to investigator initiated applications. He addressed questions on the adequacy of the number of study sections for NIBIB's applications, pointing out that there are two new study sections in the (CSR) with expertise appropriate for applications assigned to the NIBIB. The Institute also has in-house review capability, the OSR that will convene review groups for NIBIB's RFAs. The CSR and NIBIB's OSR successfully completed review of fiscal year 2003 applications, including the very large number received in response to the 10 RFAs. Expansion in the number of CSR study sections devoted to areas of research supported by NIBIB will depend on the quantity of applications received.

Council inquired about the magnitude of the Intramural efforts underway. At Dr. Pettigrew's request, Dr. Peter Kirchner explained that the funding for the PET and Imaging Instrumentation groups is currently included in the budget for the Clinical Center. Transfer of these funds to the NIBIB next year will increase our intramural budget by at least $1.4 million. For the $400,000 - $500,000 cost of the arrangement with the Food and Drug Administration, the NIBIB will gain the expertise of seven scientists examining approaches to imaging, including computer-assisted diagnostics. As the tissue engineering program is still under discussion, a cost estimate is difficult. However, at a minimum, $1.0-$1.5 million would be needed to bring in a lead expert

and ten other scientists. Sharing space and instruments with NIST would reduce start-up costs significantly.

IV. Update on the NIBIB Portfolio – Dr. Mary Pastel

Dr. Pastel stated that she planned to present data on the distribution of NIBIB grants among research areas, as requested by the Strategic Plan Development Subcommittee at the September 2003 Council meeting. Referring to graphics distributed to Council, she showed how transferred grants had declined as a percentage of the portfolio, while the number of new or competing continuation grants increased, as the NIBIB made more funding decisions. She provided a bar chart depicting the distribution of grants across research areas, with additions to the portfolio from the May and September Council review rounds. She noted that the fiscal year 2003 RFAs had resulted in increases in grants in tissue engineering, drug delivery, telemedicine, and image processing and displays. Lastly, Dr. Pastel presented a portfolio distribution by NIH funding mechanism. The R21 mechanism is used for a quarter of the grants funded by the NIBIB, compared to 7 percent on average for the NIH. Only the National Center for Research Resources funds more at 33 percent.

In response to questions from Council, Dr. Pastel clarified how X-ray and CT technologies were represented. She explained that the categories on the final chart were defined by staff to manage the portfolio. Even distribution among categories should not be expected. However, as part of the strategic planning process, staff would examine this distribution and seek to enhance some areas through NIBIB initiatives. Some Council members requested an opportunity to have input to these discussions and decisions. It is critical that a mechanism exists for Council to have ongoing discussions on the distribution of resources among research areas. Referring to discussions at the most recent meeting of the Strategic Plan Development Committee, Council noted the importance of reviewing NIBIB's coverage of a broad range of research areas with sufficient depth to have an impact on the field. Staff agreed, emphasizing that the Strategic Plan Development Subcommittee of Council would be the best vehicle for voicing opinions.

V. Report on Humans and Animals in Research – Dr. Joan Harmon

Dr. Harmon indicated that her report responded to a request by Council at the first meeting in January 2003 to have an annual discussion of humans and animals in research supported by the NIBIB. For both human and animal subjects, Dr. Harmon provided charts showing the percentage of competing applications involving these subjects, percentage of these applications with concerns noted by NIH study groups, and the percentage awarded after resolution of the concerns. She clarified for Council that these numbers reflect the total numbers of applications, including those outside of the NIBIB funding range. Compared to the NIH, the NIBIB has fewer applications involving human subjects, but a similar number using animals. Dr. Harmon underscored the importance of NIH policies on human and animal subjects and NIBIB's expectations of strict compliance with these policies.

Dr. Pettigrew introduced Dr. Jim Duncan, Professor of Biomedical Engineering, Diagnostic

Radiology and Electrical Engineering, Yale University, who directs Yale's interdepartmental Program in Biomedical Engineering within the Faculty of Engineering, as well as the Division of Bioimaging Sciences within the Department of Diagnostic Radiology in the School of Medicine.

VI. Bioimaging and Intervention in Neocortical Epilepsy– Dr. James Duncan

The average annual incidence of epilepsy in the USA ranges from 31 to 57 cases per 100,000 people. Thus, there are 70,000 to 130,000 new cases per year and up to 69 percent are felt to be symptomatic, e.g., with a discoverable cause. Medial temporal lobe epilepsy (MTLE) has been the subject of intense research over the last two decades and although the epileptogenic mechanism remains obscure, this brain region has been well characterized electrophysiologically and biochemically with numerous PET and MRS studies. Medically intractable MTLE may also be successfully treated with a limited anteromedial resection, yielding cure rates of approximately 70 percent across many studies.

However, the majority of medically refractory seizures originate in the remaining neocortex and our present ability to treat these epileptogenic substrates is far inferior to the medial temporal lobe syndrome. Three critical issues must be considered. First, surgery still remains the only potential cure in this group, with success rates ranging from 30 to 50 percent. Improving these statistics requires a much better method of defining the epileptogenic substrate, its volume, and the *in vivo* relationship between the primary excitatory and inhibitory neurotransmitters. Second, outcome studies point out that quality of life is best improved with total seizure control and this is accomplished by removing the total epileptogenic substrate, both the electrical and the anatomical/metabolic substrate. Third, additional research is addressing non-ablative approaches to regional seizure control in the symptomatic epilepsies using perfusion and/or electrical stimulation when ictal areas overlap functional brain. These critical future steps will also necessitate the clear three-dimensional definition of epileptogenic substrate and functional cortex.

A team of Yale engineers, scientists, physicians and their colleagues whose efforts are centered in the Departments of Diagnostic Radiology and Biomedical Engineering have been funded by the NIBIB to conduct advanced bioimaging research that will provide neurosurgeons with a wealth of new information that could dramatically change the treatment of patients suffering from severe epilepsy. This project, entitled "Bioimaging and Intervention in Neocortical Epilepsy" aims to characterize the biochemical signature of brain tissue that causes severe epileptic seizures and understand its relationship to surrounding normal tissue. It involves the use of high field Magnetic Resonance Spectroscopy (MRS) and functional Magnetic Resonance Imaging (fMRI) to image the brain as well as mathematical modeling strategies to analyze the properties and position of the brain prior to and during the surgical procedure.

Magnetic resonance functional and spectroscopic imaging (fMRI, MRS) of the brain provide tremendous opportunities in the study and treatment of epilepsy. In neocortical epilepsy, where the epileptogenic region is highly variable in size, structure, and location, deeper insight into the biochemical and functional characteristics of the region and surrounding tissue may provide critical data to assist the neurosurgeon and neurologist in localization and treatment. To fully

utilize the multiple forms of available information (MR and EEG), these data must be transformed into a common space and integrated into the intra-operative environment. The work being performed will develop high resolution MRS and fMRI at 4T and advanced analysis and integration methods to better define the epileptogenic tissue and surrounding regions, and enhance our understanding of the biochemical mechanisms underlying the dysfunction in neocortical epilepsy. The team will validate these measurements against the gold standard of intracranial electrical recording.

These goals will be achieved in this Bioengineering Research Partnership by bringing together six partners from three academic institutions (Yale (lead institution), Albert Einstein and the University of Minnesota) and one industrial partner (BrainLAB, Inc.) to carry out four integrated programs of scientific investigation and bioengineering development in the area of bioimaging and intervention: 1) development of high resolution fMRI and MRS at 4T for the study of epilepsy; 2) investigation with MRS of the relationship between neuronal damage or loss through the measurement of N-acetylaspartate (NAA), alterations in neurotransmitter metabolism through the measurement of gamma amino butyric acid (GABA) and glutamate, and abnormalities in electrical activity in the epileptogenic region and surrounding tissue; 3) investigation of the relationship between fMRI activation amplitude and the cognitive task, underlying cortical structure, cortical metabolic state, and physiology, and the impact of epilepsy on these factors; and 4) development of integration methodologies for fusing multimodal structural and functional (image- and electrode-derived) information for the study and treatment of epilepsy.

The information integration will be centered on an image-guidance platform that uses light-striping technology to register the patient's physical facial features (in the operating room) to those found by segmenting the same information from a pre-operative MRI scan. The neurosurgeon can now point to physical areas on the patient's exterior and see on a 3D display what the 3D MR information is in that region within the brain. However, after an initial surgery is performed that includes a ten to twelve centimeter craniotomy and removal of the dura, the brain deforms non-rigidly within this rigidly-registered coordinate system, throwing off the image guidance platform by as much as one centimeter. The research team is addressing this challenge by developing a system that uses stereo cameras mounted in the ceiling of the operating room to track the movement of the surface of the portion of the brain exposed during the craniotomy and combining this with an elastic model to predict the deformation of the entire brain volume.

One ultimate goal of this work is to illustrate that MRS can be used to define the epileptogenic zone without the use of attached electrodes. Thus a 3D display of a biochemically-indicated zone via MRS and surrounding brain function mapped out by fMRI would now more efficiently and precisely point the surgeon to the tissue that should be resected to eliminate the seizures. This integrated, detailed map of the structure and function of the brain will help surgeons both plan and perform the procedure more precisely and efficiently. Thus, the approaches being developed on this project could significantly enhance understanding of neocortical epilepsy and provide revolutionary new treatment paradigms by shortening the time necessary to perform these extensive surgeries (typically two four-to-eight hour procedures). Furthermore, at some point, it is intended that MRS/fMRI information alone could guide the implantation of small

biochemical sensors and delivery systems that may eliminate the need for surgery altogether.

Dr. Duncan listed other members of the team. Dennis Spencer, M.D., Professor and Chair of Neurosurgery and the Acting Dean of the School of Medicine is a key co-investigator of the grant. Other lead members of the Yale team include: Drs. Douglas Rothman, Professor of Diagnostic Radiology and Biomedical Engineering; Todd Constable, Associate Professor of Diagnostic Radiology, Biomedical Engineering and Neurosurgery; and Lawrence Staib, Associate Professor of Diagnostic Radiology, Biomedical Engineering and Electrical Engineering. Primary members of the teams from outside of Yale include: Drs. Hoby Hetherington and Julie Pan from the Albert Einstein College of Medicine in New York; Thomas Vaughan from the University of Minnesota; and Rainer Birkenbach from BrainLAB, AG, an image-guided surgery company based in Munich, Germany. Other key Yale investigators on the project include: Drs. Susan Spencer, Professor of Neurology; Hemant Tagare, Associate Professor of Diagnostic Radiology and Electrical Engineering; Steven Zucker, Professor of Computer Science and Electrical Engineering; Xenios Papademetris, postdoctoral fellow in diagnostic radiology; Robin de Graaf, Assistant Professor of Diagnostic Radiology; and Ognen Petroff, Associate Professor of Neurology.

Dr. Pettigrew thanked Dr. Duncan for his outstanding presentation and remarked on how representative this project is of the type of interdisciplinary work that the NIBIB supports and how beneficial these collaborations can be to advancing health research in the nation. In response to questions from Council, Dr. Duncan described how communications are managed by the geographically disperse group. This potential challenge has been resolved nicely through informal weekly meetings, formal quarterly meetings and regular e-mail with the collaborator in Munich. Council also suggested that publicizing this presentation on the NIBIB website would inform others in the extramural community of Dr. Duncan's progress and a very successful model of interdisciplinary bioengineering research. Dr. Pettigrew agreed.

Dr. Pettigrew concluded that a similar presentation from an NIBIB grantee would be included in all future Council meetings.

VII. Report from the Strategic Plan Development Subcommittee – Dr. Carlo De Luca

On behalf of Dr. Frank Yin, Chair of the Strategic Plan Development Subcommittee, Dr. De Luca provided a summary of a meeting held on January 14, 2004 at the Bethesda Marriott. In attendance at the meeting were: Drs. Yin, De Luca, Maynard, Grossman and Pelc and several members of the staff of the NIBIB. At the request of the Director, NIBIB, at this meeting Council members commented on several points related to the strategic directions of the Institute. Dr. De Luca outlined the remarks of each presenter.

Dr. Yin's presentation: Dr. Yin drew parallels between the goals of the NIBIB and the elements of the NIH roadmap. He suggested several strategic issues for consideration in developing the plan, including distinguishing characteristics of the NIBIB mission, the balance between hypothesis-driven and design-driven projects, the need for interdisciplinary training, and the marriage of discovery and applied research. He encouraged the staff to find ways of leveraging

the unique aspects of the NIBIB, pointing to partnerships with non-profits as an avenue to be explored. The fiscal year 2004 budget was discussed with a proposal of limiting grant size and award duration as a tool for managing limited resources. He raised the question of whether NIBIB should have an intramural division, given the current projected outlook for the budget. After significant discussion throughout the day, the group generally concluded that, if created, this division should focus on unique areas of research not underway in universities that would contribute to the establishment of an NIBIB identity.

Dr. De Luca's presentation: In his own presentation at the meeting, Dr. De Luca raised three issues for consideration in formulating the plan: (1) the creation of an NIBIB identity; (2) the need for the NIBIB to be responsive to it's unique mission of bringing forth new technologies; and (3) a strategy for the NIBIB to facilitate the introduction of new technologies into societies. The plan should provide the framework for the NIBIB to have a major impact on health care over the next decade in the view of the Congress and more importantly the public. On the third point there was much discussion of the multiple stages in the technology development process and the most appropriate point for NIBIB financial intervention to facilitate the movement of technologies into society. The group agreed that NIBIB should not become a "cash cow" for industry, committing large sums to fund the high-cost later stages of device development.

Dr. Pelc's presentation: In his presentation, Dr. Pelc noted that the focus of the Institute should be technology development, with a balance between longer- and shorter-term projects that may have an immediate impact on healthcare. He emphasized the importance of early success for the Institute, brought about by appropriate selection of projects. Thus far, the Institute has performed well; the staff should build upon this foundation.

Dr. Pelc added to Dr. De Luca's summary of Dr. Pelc's remarks. Careful attention should be given to the effect of the budget on the pay line for NIBIB. Having attracted so many new investigators to the NIH, the NIBIB should ensure a reasonable pay line to encourage their continued interest and to guard against friction among the wide range of research interest served by the Institute. In partnering with other Institutes, the NIBIB should bring a unique contribution that is well recognized. Limited resources dictate careful consideration of high-cost projects such as Research Resource Centers (P41s) that were previously in the portfolio of the National Center for Research Resources (NCRR). In the long term, NCRR may be the more appropriate home for these. Agreeing with previous comments, the Intramural Division should be non-duplicative of existing research, focused on work that could only be done at the NIH, and a way of defining the NIBIB identity. To ensure that applications received by the Institute reflect its priorities, the Institute should publicize its goals to the extramural community and to the peer reviewers sitting on the study sections within the CSR at the NIH. NIBIB should not fund large clinical trials, but should support projects to demonstrate the feasibility of an application.

Dr. Maynard's presentation: Dr. Maynard strongly endorsed the idea of NIBIB spending greater than the NIH average proportion of dollars on training. Training of more clinical investigators in radiology is critically needed. He called upon the NIBIB to address the void in training support that will occur with the closing of the Whitaker Foundation, an organization that has created tremendous excitement for research in bioengineering. An intramural division that draws upon

the unique resources of the NIH research environment could contribute to these training goals. On the question of depth versus breadth, Dr. Maynard encouraged the Institute to lend significant support to a few promising areas for high impact. He also suggested that the Institute take steps to address the aging research infrastructure in universities.

Dr. Maynard added to Dr. De Luca's summary of Dr. Maynard's remarks that NIBIB training programs should be innovative, multi-disciplinary, programs that prepare investigators for the team approaches that will likely be the model for much future research. Expanding on innovation, Dr. Maynard cautioned the staff to not be constrained by programs that exist in other Institutes; instead, take risks and be creative.

Dr. Grossman offered highlights of his presentation at the January 14th meeting. He noted that there is a paradox in defining the research interest of the NIBIB as technology development and the desire to create public support for the Institute through significant health care result. The NIBIB must support not only technology development, but also projects that address the application of this technology to disease prevention, diagnosis and treatment. NIBIB should not necessarily fund large clinical trials, but the Institute should support projects at the interface between the development and the application of technology, that will permit the NIBIB to lead advances in health care practices. The Council should play an active role in helping the NIBIB identify applications that may be risky but have the potential to significantly alter the health care landscape. Modifications to the typical review process should be considered to allow the Council to examine all applications that may fit within these priorities, not just those recommended by NIH study sections.

Dr. Yin further addressed the review process. Projects that are not hypothesis-driven do not fare well in NIH study sections that may deliberately or subconsciously downgrade application-driven research. Educating study sections on NIBIB priorities may alleviate the problem somewhat, but other measures are needed.

Dr. De Luca concluded by mentioning some of the major issues that were discussed throughout the day, including the role of the strategic plan in creating an identity for the NIBIB, the critical role of training in accomplishing the mission of the NIBIB, and the question of depth versus breadth in the NIBIB portfolio. As agreed at other meetings, the staff has responsibility for developing the plan with ongoing input from the Council Subcommittee.

VIII. BISTI Symposium – Drs. Peter Lyster and Grace Peng

Dr. Lyster began by defining bioinformatics as research, development or application of computational tools and approaches for expanding the use of biological, medical, behavioral or health data, including those to acquire, store, organize, archive, analyze or visualize such data. Computational biology is the development and application of data-analytical and theoretical methods, mathematical modeling and computational simulation techniques to the study of biological, behavioral, and social systems.

The Biomedical Information Science and Technology Initiative (BISTI) was launched at the NIH

in the late 1990's after Dr. Harold Varmus, the then Director, NIH commissioned a study on how to bring informatics and computational science into the NIH extramural portfolio. At this time, NIH study sections were also given the go-ahead to favorably consider non-hypothesis-driven research. A trans-NIH consortium (BISTIC) has responsibility for implementing BISTI, currently under the leadership of Dr. Eric Jakobsson of the Center for Bioinformatics and Computational Biology, National Institute of General Medical Sciences. The BISTIC issues initiatives, the first three of which aimed to:

- Build informatics centers
- Encourage appropriate R21/R33 and SBIR applications
- Support development of software

The first BISTI symposium, "Digital Biology: the Emerging Paradigm" occurred last fall. The staff of the NIBIB had a major role in planning the meeting and leading the breakout sessions, three of which were entitled: (1) Quantitative Science and Biology; (2) Data Integration; and (3) Network Science. In 2004, BISTIC will join the NIH Bioengineering Consortium (BECON) in organizing a symposium in June, "Biomedical Informatics for Clinical Decision Support: Toward the 21st Century."

The NIH Roadmap has produced a number of initiatives in these research areas. A very large number of applications have been received for *National Centers for Biomedical Computing*, an RFA issued in the fall. NIH will likely fund four to eight of these through the U54 mechanism. Another RFA, *Dynamic Assessment of Patient-Reported Chronic Disease Outcomes* has not closed. It is anticipated that initiatives will be forthcoming in the areas of "Building Blocks, Biological Pathways, and Networks" and the "National Electronic Clinical Trials and Research Network." A trans-NIH Informatics Committee has been established to coordinate all informatics activity under the Roadmap. Informatics is currently represented in the NIBIB portfolio and the staff anticipates future support for work in (1) systems biology/tissue engineering; (2) imaging informatics; (3) data integration; and (4) large-scale databases. NIBIB is also the lead Institute for the Interagency Modeling and Analysis Group (IMAG).

Dr. Peng expanded on NIBIB's specific informatics activities. The Institute participates in three neuroinformatics initiatives:

- Human Brain Project
- Collaborative Research in Computational Neuroscience
- Neuroimaging Informatics Technology Initiative

The IMAG mentioned by Dr. Lyster includes thirteen Institutes at the NIH, three National Science Foundation Directorates, two research agencies of the Department of Defense, and NASA. A trans-agency initiative on multi-scale modeling is under development. Dr. Peng emphasized that informatics is well represented in the NIBIB portfolio as a component of all major research areas; however, in five areas, it is the dominant focus, although the portfolios are small.

1. Mathematical Models and Computational Algorithms
2. Bioinformatics
3. Image Processing
4. Remote Diagnosis and Therapy

5. Surgical Tools and Techniques

Dr. Peng reviewed the four areas for future directions presented by Dr. Lyster, noting that NIBIB anticipates much future growth in all of these areas.

Keying on the list of future directions, Council asked if the strategic planning process would be the primary mechanism for determining these priorities. Council also questioned how NIBIB could use any of the listed broad research areas to help define the NIBIB identity, a major goal articulated by Council at the recent Strategic Planning meeting, considering that so many Institutes already have such large portfolios in these areas. Council also suggested that future presentations such as this should include specific examples of projects to facilitate an understanding of NIBIB's unique role in advancing the science. Responding, Dr. Pettigrew emphasized that BISTIC is a trans-NIH effort, and that NIBIB will continue to define its identity through support of projects that will have a high impact on health care.

IX. Closing Remarks – Dr. Roderic Pettigrew

Dr. Pettigrew thanked everyone for their participation. He recognized staff for all the work involved in putting on the meeting, especially with the severe weather complications. The meeting closed for review of applications at approximately 1:30 P.M.

X. Closed Session

This portion of the meeting, involving specific grant review, was closed to the public in accordance with the provisions set forth in Section 552b (c) (4) and 552b (c) (6) Title 5, U.S. Code and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2).

We certify that, to the best of our knowledge, the foregoing minutes and attachments are accurate and complete.

/s/

Joan T. Harmon, Ph.D.
Executive Secretary
National Advisory Council for Biomedical Imaging and Bioengineering
Director, Office of Extramural Policy

National Institute of Biomedical Imaging
and Bioengineering

/s/
Roderic I. Pettigrew, Ph. D., M.D.
Chairperson,
National Advisory Council for Biomedical
Imaging and Bioengineering
Director
National Institute of Biomedical Imaging
and Bioengineering

The Council will consider these minutes at its next meeting. Corrections or notations will be incorporated in the minutes of that meeting.