



A handwritten signature in black ink that reads "Roderic A. Pettigrew". The signature is written in a cursive, flowing style.

Roderic Pettigrew, M.D., Ph.D.  
NIBIB Director

# THE NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

---

Shu Chien

*Departments of Bioengineering and Medicine, and the Whitaker Institute of Biomedical Engineering, University of California, San Diego, La Jolla, California 92093-0427; email: shuchien@ucsd.edu*

**Key Words** Academy of Radiology Research, American Institute for Medical and Biological Engineering, biomedical engineering, National Institutes of Health, research grants, training

## CONTENTS

SUMMARY .....	2
HISTORY OF DEVELOPMENT OF THE NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING .....	3
Developments in the Biomedical Imaging Community Prior to 1996 .....	3
Developments in the Biomedical Engineering Community Prior to 1996 .....	3
Developments in Biomedical Imaging and Bioengineering Between 1996 and 1999/2000 .....	5
Legislative and Executive Actions to Establish NIBIB in 1999/2000 .....	8
Cooperation of Extramural Communities with the NIH in the Establishment of the NIBIB .....	9
MISSION STATEMENT OF THE NIBIB .....	13
NIBIB DIRECTOR AND ADVISORY COUNCIL .....	14
NIBIB ACTIVITIES .....	18
NIBIB Symposia and Workshops .....	18
NIBIB Requests for Applications in 2002 .....	18
NIBIB Grant Portfolio Areas in 2003 and Initiatives for FY2004 .....	18
NIBIB BUDGET .....	19
REVIEW OF BIOMEDICAL IMAGING AND BIOENGINEERING GRANTS .....	20
Bioengineering Sciences and Technologies IRG .....	21
Surgical Sciences, Biomedical Imaging, and Bioengineering IRG .....	21
NIBIB PARTICIPATION IN NIH ROADMAP ACTIVITIES .....	22
CONCLUSIONS AND PERSPECTIVES .....	24

## SUMMARY

The establishment of the new National Institute of Biomedical Imaging and Bioengineering (NIBIB) has its roots in the organized activities of the biomedical imaging and bioengineering communities beginning around 1970s. The remarkable advances in biomedical engineering and imaging in the past few decades, with strong support from government agencies, especially the National Institutes of Health (NIH) and the National Science Foundation (NSF), and private foundations, particularly the Whitaker Foundation, have led to important contributions to the enhancement of health and the development of new methods for diagnosis, treatment, and prevention of disease. A series of actions in Congress and the presidential signing of Public Law 106–580 led to the establishment of the NIBIB, whose mission is improving health by the promotion of fundamental discoveries, design, and development and the translation and assessment of technological capabilities in biomedical imaging and bioengineering, in coordination with the relevant programs of other agencies and institutes and centers (ICs) of the NIH. The emphasis of the NIBIB is to foster biomedical imaging and bioengineering activities that cut across institutional boundaries and to complement such programs in other NIH ICs. Currently, the NIBIB funds approximately 15% of all NIH grants related to biomedical imaging and bioengineering. Following its formal establishment in April 2001, the NIBIB has made significant progress. Dr. Roderic I. Pettigrew took office as Director in September 2002, and the National Advisory Council for Biomedical Imaging and Bioengineering was formed and held its first meeting in January 2003. The NIH consulted extensively with the extramural community in establishing the NIBIB; Dr. Pettigrew and Dr. Donna Dean, first as Acting Director and later Deputy Director, spoke at more than 70 professional meetings and visited more than 40 academic institutions. The appropriation of a new budget starting in fiscal year (FY) 2002, together with the transfer of grant funds from other ICs, have built up the NIBIB's grant portfolio, which includes grants for R01, the Bioengineering Research Partnership (BRP), small business innovation research (SBIR) and small business technology transfer (STTR) grants, as well as training grants. The FY2003 budget of the NIBIB was nearly 2.5 times that of FY2002, but the proposed FY2004 budget shows only a slight increase over FY2003. The NIH Center for Scientific Review (CSR) is reorganizing integrated review groups (IRGs) and study sections, with a significant emphasis on the review of grants for biomedical imaging and bioengineering. NIH Director Dr. Elias Zerhouni has formulated a new roadmap for the NIH that focuses on new pathways of discovery, research teams for the future, and the re-engineering of the clinical research enterprise. The NIBIB is initiating a series of new activities to realize the vision of the NIH roadmap. The timely establishment of the new institute, with appropriate support for its growth and development, will play a major role in fostering the advancement of biomedical engineering and imaging to improve the health and well-being of people.

---

## HISTORY OF DEVELOPMENT OF THE NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

The establishment of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) in April 2001 was a major event at the National Institutes of Health (NIH) and for the biomedical imaging and bioengineering communities. A summary of the history of these developments is given below. The reader is also referred to an earlier article by Hendee et al. (1).

### Developments in the Biomedical Imaging Community Prior to 1996

In the mid-1970s, the Conjoint Committee on Diagnostic Radiology was formed under the leadership of Drs. Herbert Abrams and Russell Morgan, with sponsorship by the American College of Radiology, the Association of University Radiologists, and the Society of Chairmen of Academic Radiology Departments, to represent the diagnostic imaging community's interests to Congress, the NIH, and other federal agencies. The committee, led by its first two Chairs, Drs. James Youker and Charles Putman, played significant roles in several developments of imaging research at the NIH. The primary focus of NIH-wide imaging research (cancer and noncancer) was transferred from the National Institutes of General Medical Sciences (NIGMS) to the National Cancer Institute (NCI) in 1978, and the intramural Laboratory of Diagnostic Radiology Research (LDRR) was established in 1992. The NIH-sponsored Conference on Developing a Long-Term Plan for Imaging Research was held in 1994, and NIH research funding in this field has increased steadily since (2).

In 1995, the Academy of Radiology Research (ARR) was created as an alliance of 19 (currently 25) scientific and professional societies, with the primary goal of establishing a new institute for imaging research at the NIH. In 1995–1996, the NCI expanded its Diagnostic Imaging Research Branch into a Diagnostic Imaging Program [later renamed the Biomedical Imaging Program (BIP) and, more recently, the Cancer Imaging Program (CIP)], with Dr. Daniel Sullivan as the first Director. Although the success of the CIP demonstrated the potential of imaging research, its limitation to cancer reinforced the imaging community's view that the NIH needed a new institute, with a broad range of applications for all ICs, to support basic research in imaging science (3, 4).

### Developments in the Biomedical Engineering Community Prior to 1996

In 1967–1968, NIH Director James Shannon requested the National Academy of Engineering to conduct a study on how to apply engineering to the pursuit of NIH activities. This led to the formation of the Committee on Interplay of

Engineering with Biology and Medicine, which was chaired by Dr. John Truxell followed by Dr. Robert Marshall, with Dr. Gilbert Devey as Executive Secretary. The establishment of an Institute of Biomedical Engineering was considered, but the final recommendation was to first set up subcontracts with universities to form prototype biomedical engineering departments. In the 1970s, the biomedical engineering research community formed the Alliance for Engineering in Medicine and Biology (AEMB) to organize annual scientific conferences for biomedical engineering and to foster the discipline in the NIH and other federal agencies. In 1991, the American Institute for Medical and Biological Engineering (AIMBE) was formed under the leadership of Dr. Robert Nerem and other key members of the AEMB as a federation of 15 scientific societies<sup>1</sup> to represent the community on public policy issues. AIMBE is also an honorary society that elects outstanding medical and biological engineering investigators and leaders in academia, industry, and other sectors as Fellows. The strong support by the Whitaker Foundation and the AIMBE constituency (including industrial support and generous donations by its Fellows, led by Dr. Jen-Shih Lee), together with excellent leadership and collaboration, have made possible its continued growth and development.

AIMBE works to enhance the visibility and impact of biomedical engineering in and beyond the NIH, and supports the efforts of biomedical engineers to heighten Congress' awareness of the need for increased support for research in the field. In concert with these efforts, Senator David F. Durenberger (R-MN) inserted language into the NIH Revitalization Act of 1993 (PL 103-43) to direct the Department of Health and Human Services to report on the state of bioengineering research at the NIH. In response to this call from Congress, the NIH prepared a report entitled *Support for Bioengineering Research* (5), for which Dr. John Watson of the National Heart, Lung, and Blood Institute (NHLBI) played a critical role. The NIH also formed the External Consultants Committee, chaired by Dr. Robert Nerem. The committee's report (6), submitted in 1995, made five specific recommendations, including the establishment of a central focus at the highest level in the NIH for basic bioengineering research, with resources for support of extramural research in collaboration with the NIH ICs. Concurrent with these developments, biomedical engineering was making great strides in merging biology, medicine, and engineering to foster tissue engineering, nanoscience and nanotechnology,

---

<sup>1</sup>The 15 founding societies of AIMBE are the American Association of Physicists in Medicine; American College of Clinical Engineering; American Institute of Chemical Engineers: Food, Pharmaceutical, and Bioengineering Division; American Medical Informatics Association; American Society of Agricultural Engineers; American Society for Artificial Internal Organs; American Society of Biomechanics; American Society of Mechanical Engineers: Bioengineering Division; Biomedical Engineering Society; IEEE Engineering in Medicine and Biology Society; Institute of Biological Engineering; Orthopaedic Research Society; Rehabilitation Engineering and Assistive Technology Society of North America; Society for Biomaterials; and SPIE: The International Society for Optical Engineering. They were later joined by the Controlled Release Society, the International Society for Magnetic Resonance in Medicine, and the Surfaces in Biomaterials Foundation.

functional genomics, smart biomaterials, biosensors, molecular imaging, and their applications for the prevention, diagnosis, and treatment of disease (see, e.g., 7, 8). The strong and timely support for biomedical research and training by the Whitaker Foundation has played a pivotal role in the advancement of biomedical engineering as a discipline.

## Developments in Biomedical Imaging and Bioengineering Between 1996 and 1999/2000

The fields of bioengineering and biomedical imaging continued to advance at rapid rates to become frontier areas of biomedical research, making possible earlier detection, improved diagnosis, and more effective treatments for a variety of diseases and, hence, improvements in health care. The remarkable advances in bioengineering and biomedical imaging and the potential of these disciplines to contribute in a profound way to fulfill the mission of the NIH have been presented by Hendee et al. (1) and are not repeated here.

Both ARR and AIMBE grew significantly and began to cooperate in achieving the common goal of enhancing biomedical imaging and bioengineering activities at the NIH and other federal agencies. ARR is currently comprised of 25 societies with a combined membership of over 45,000 radiologists and scientists in the field of biomedical imaging. AIMBE currently has 18 member societies comprised of more than 35,000 engineers, scientists, and clinicians; 83 academic programs in the field; over 700 Fellows; and an industrial council of manufacturers and industries.

Through the efforts of Senator William H. Frist (R-TN), Congress responded to the report on *Support for Bioengineering Research* by including an amendment to the reauthorization legislation for the NIH, which led the Secretary of Health and Human Services (HHS) Donna Shalala to prepare a report to Congress outlining specific plans and time frames for implementing the report's recommendations. The legislation passed in the Senate but was not acted upon by the House. In September 1996, at the urging of the ARR's Dr. Douglas Maynard, Representative Richard M. Burr (R-NC) introduced legislation (HR 4196) to establish the National Institute of Biomedical Imaging at the NIH at the end of the Congressional session, but it did not advance. The bill was reintroduced in the House in 1997 (HR 1715), and a companion bill (SR 990) was introduced in the Senate by Senator Lauch Faircloth (R-NC). These bills also failed to advance. In 1997, Senator Frist introduced SR 1030 to create an NIH Center for Bioengineering Research. Because the proposed center would not have funding authority and would have been located within one existing institute, i.e., the NHLBI, the bill did not receive the broad support of the biomedical engineering community and it did not pass out of committee.

At the NIH, the efforts of NIH Deputy Director for Extramural Research Dr. Wendy Baldwin, Dr. John Watson, and others led to increasing recognition of the role of biomedical engineering as an important discipline in health science and health care. In February 1997, NIH Director Dr. Harold Varmus established the

Bioengineering Consortium (BEACON), with the mission of coordinating bioengineering activities within the NIH and between the NIH and other relevant federal agencies. BECON, which was chaired by Dr. Wendy Baldwin and comprised of senior representatives from each of the NIH ICs, together with representatives from other federal agencies, holds monthly meetings to discuss common interests, problems, and strategies. The first BECON Symposium on Bioengineering, organized by Dr. Dov Jaron of the National Center of Research Resources and Dr. John Watson of the NHLBI, was held in February 1998. As a result of the recommendations of the BECON, NIH developed several major new grant programs, e.g., the Bioengineering Research Partnerships (BRPs) and bioengineering research grants (BRGs). The BRPs, by bringing together investigators from bioengineering, physical sciences, computational fields, and medicine, have contributed greatly to the advancement of interdisciplinary research on bioengineering problems. Dr. Varmus stated in his 1998 plenary lecture at the American Association of the Advancement of Science (9), "We are also fostering new efforts in materials science, bioengineering, instrumentation development, and informatics. In short, biology is not only for biologists." Annual BECON meetings have since been held on specific topics in biomedical imaging and engineering (symposia on biomedical imaging in 1999, nanoscience and nanotechnology in 2000, reparative medicine in 2001, sensors in biological research and medicine in 2002, and catalyzing team science in 2003). The rapid advances in bioengineering, its increasing recognition by the NIH and Congress, and the varied views of how to foster its growth at the NIH are summarized by Agnew (10).

At its annual meeting in March 1999, following considerable discussions, the AIMBE adopted the following resolution: "AIMBE should represent its constituent societies and its Fellows as a unified voice seeking to enhance the identity and support of biomedical engineering at the National Institutes of Health through pursuit of the following objectives: (a) Establishment of a free-standing Center or Institute of Biomedical Engineering with a director with authority equal to that of directors of other NIH centers and institutes. (b) Designation of grant-making authority to the Center or Institute for funds allocated in support of basic science, engineering and mathematics underlying biomedical engineering. (c) Funding the Center or Institute entirely through new appropriations without transfer of funds from existing centers and institutes."

Thus, the biomedical engineering and imaging communities converged on the opinion that the proper support of these rapidly evolving fields required an institute dedicated to these disciplines.

Concurrent with the move to establish a new institute, the biomedical engineering and imaging communities also had concerns that the NIH review process was focused on hypothesis-driven research and rendered it nearly impossible to obtain funding support for research aimed at the design and development of innovative technologies, which are indispensable for the advancement of hypothesis-driven research. In 1999–2000, the NIH took several steps to address these concerns and began to foster design-directed research and technology development.

Dr. Ellie Ehrenfeld, then Director of the NIH Center for Scientific Review (CSR), formed an ad hoc working group, chaired by Dr. Lee Huntsman (with Linda Engel as Executive Secretary), to recommend ways to make the NIH peer-review process more receptive to the nonhypothesis-driven research that is essential for advancing basic and clinical research (11). As stated in the current version of the PHS 398 grant application instructions (12), “List the broad long-term objectives and what the specific research proposed in this application is intended to accomplish, e.g., to test a stated hypothesis, create a novel design, solve a specific problem, or develop new technology,” as opposed to only “to test a stated hypothesis,” as was specified in the previous version.

The CSR also formed an ad hoc Boundary Panel, chaired by Dr. Bruce Alberts of the National Academy of Sciences, to restructure the NIH peer-review organization into integrated review groups more responsive to the array of research applications received by the NIH (13). In May 2000, using the BECON as a model, the NIH established the Biomedical Information Science and Technology Initiatives Consortium (BISTI), which was aimed at making optimal use of computer science and technology to address problems in biology and medicine.

Although the NIH had been active in fostering biomedical engineering and biomedical imaging during the 1990s, it did not plan to add any new institutes (14). The initial action was to establish the Office of Bioengineering, Bioimaging, and Biocomputing (OB3) in the Office of the NIH Director in response to a Congressional directive in the FY2000 NIH Appropriations Act. OB3 would assume the responsibility of BECON and also work with those ICs in areas of bioimaging and biocomputing, with the goal of coordinating the activities of the various NIH institutes in developing collaborative initiatives and budget in these fields. A search committee, chaired by Dr. Baldwin, was formed to find a scientist with stature in these fields to serve as the OB3 Director, who would report directly to the NIH Director. However, OB3 would not have grant-making authority and its budget would be kept small, in the \$2 million range, mainly for holding the Annual BECON Symposia and for supporting the necessary staff to carry out the coordinating functions. Furthermore, the plan was to terminate the OB3 after ten years; the reasoning was that either it would have succeeded in accomplishing its mission or need to be replaced by some other structure. Although the OB3 was a positive move toward fostering research in bioengineering and bioimaging, the scientific community generally felt that it would fall short of supporting the full potential for these rapidly developing disciplines and that it lacked permanence. As the keynote speaker at the AIMBE Annual Meeting on March 3, 2000, Dr. Baldwin spoke on the NIH plan for biomedical engineering, including the OB3. On March 5, after thorough discussions, the AIMBE Board decided to support the OB3 initiative, but expressed the view that their resolution adopted a year ago was the preferred action.

The evolution of the events during the period of 1996–2000 made it clear to the biomedical imaging and bioengineering communities that it was necessary for them to work together in order to achieve the goal of infrastructure reorganization



**Figure 1** ARR President Douglas Maynard and Shu Chien, May 2000, American Roentgen Ray Society Meeting, Washington, D.C.

at the NIH and to increase the recognition and enhance the activities of these fields. ARR President Douglas Maynard and I met several times to discuss the ways in which ARR and AIBME could collaborate toward our common goal (Figure 1). The establishment of the NIBIB was made possible following the joining of forces of the two communities.

### **Legislative and Executive Actions to Establish NIBIB in 1999/2000**

The remarkable advances in biomedical imaging and bioengineering, the great potential of these disciplines to fulfill the mission of the NIH, and the combined efforts of the two advocacy communities set the stage for a series of extraordinary events, which culminated in the establishment of the NIBIB.

As a result of the AIMBE/ARR coalition, Representative Burr modified his 1996 bill and introduced HR 1795 with Representative Anna Eshoo (D-CA) in 1999, calling for the establishment of a National Institute of Biomedical Imaging and Engineering at the NIH. This bill noted that biomedical engineering and imaging require an identity and research home at the NIH that is independent of the existing structure to ensure the development and transfer of new techniques and technologies that are critical to improving health care for the twenty-first century. Shortly thereafter, majority leader Trent Lott (R-MS) introduced a companion bill (SR1110) in the Senate for the establishment of a National Institute of



**Figure 2** The National Institute of Biomedical Imaging and Bioengineering Establishment Act (Public Law 106–580), signed by President Clinton on December 29, 2000.

Bioengineering and Biomedical Imaging. Introduction of these bills was accompanied by an intense grassroots campaign in the biomedical imaging and bioengineering communities to generate legislative support for their passage. After some debates, the House of Representatives voted to pass HR 1795 on September 27, 2000. The Senate passed the same bill without debate on the last evening (December 15, 2000) of the second session of the 106th congressional session.

On December 29, 2000, then President William J. Clinton signed into law the National Institute of Biomedical Imaging and Bioengineering Establishment Act (Public Law 106–580) (Figure 2). This was the last law signed by President Clinton.

## Cooperation of Extramural Communities with the NIH in the Establishment of the NIBIB

In the processes leading to the establishment of the NIBIB and during the initial years of its operation, the NIH made extraordinary efforts to involve the extramural scientific communities. During the formative years of the NIBIB, the NIH leadership consulted extensively with the relevant scientific communities, especially the two federated organizations in biomedical engineering and

biomedical imaging, i.e., AIMBE and ARR, respectively. Because I was AIMBE President in 1999–2000 and directly involved in these developments, some of the descriptions in this section are written from a personal perspective.

As mentioned above, AIMBE was working with the biomedical imaging community, especially ARR, to facilitate the passage and signing of the bill (HR 1795). Until the final signing of the bill into law, however, it had been uncertain whether the new Institute would become a reality; if President Clinton had not signed it by December 31, 2000, it would have been a pocket veto, which would make all the efforts for naught and everything would have to start from ground zero in the next Congressional sessions.

As the situation unfolded in December 2000, I realized that if the new institute were to become a reality, the major question would be how bioengineering and bioimaging activities at the NIH, especially their funding, would be distributed between the new institute and the existing ones. Most of the members of the bioengineering community felt that, although it would be beneficial to the field to have increased support through the new institute, we should keep most of the current support in the existing institutes.

By the very nature of the interdisciplinary approach in bioengineering research and training, it is critical to have the activities linked to the various institutes focusing on specific diseases and organs. Therefore, I drafted a letter in late December for submission to *Science* (15) to express AIMBE's support of the new institute and the opinion that the transfer of resources from existing NIH institutes to the new institute, as legislatively required, should be done with prudence. That is, our aim was to continue the activities related to bioengineering and bioimaging in the existing institutes, which are very valuable to the growth of these fields. The letter recommended that the new institute focus on fostering activities that cut across institutional boundaries, including fundamental and applied research and training in these fields, and that it should strengthen and complement (not subtract from or substitute for) research programs in the other NIH ICs.

Immediately after the Presidential signing of Public Law 106–580, Dr. Ruth Kirschstein (Figure 3), Acting Director of the NIH, asked me, the AIMBE President, to go to Bethesda to discuss the establishment of the new institute. On January 2, 2001, I met with Dr. Kirschstein and five other high-level NIH administrators, including Dr. Wendy Baldwin and Dr. Donna Dean, who would head the new NIBIB in its transition phase. Dr. Kirschstein told me that the NIH would form an internal working group to draft a mission statement and would welcome the formation of an external advisory group to provide inputs from the extramural scientific community. She and Dr. Dean wanted to work closely with the extramural community for the success of this new institute. We went through various scenarios of how the new institute might function, and the NIH leadership supported what I had drafted in the letter to *Science*.

The draft letter received valuable inputs and was unanimously approved by the AIMBE Board, and ARR President Doug Maynard accepted the invitation to cosign the letter, with approval by the ARR Board. On January 4, 2001, an



**Figure 3** Shu Chien and NIH Acting Director Ruth Kirschstein, January 2001, NIH Director's Office, Bethesda, MD.

AIMBE/ARR Joint Committee was established to provide extramural advice on the new institute as requested by the NIH. The members from AIMBE were Drs. William Hendee, John Linehan, Peer Portner, Buddy Ratner, and Shu Chien. The members appointed by ARR were Drs. Maynard, Stanley Baum, Reed Dunning, Bruce Hillman, and Elias Zerhouni, the current NIH Director. Dr. Baum and I cochaired this joint committee. AIMBE and AAR Executive Directors Kevin O'Connor and Edward Nagy were ex officio members.

On January 8, 2001, Drs. Kirschstein and Dean held a teleconference call with representatives of AIMBE and ARR to discuss the developments of the new institute. Dr. Kirschstein established an internal task force chaired by Dr. Steven Hyman, Director of the National Institute of Mental Health, with four other institute directors: Dr. Stephen Katz (National Institute of Arthritis, Musculoskeletal and Skin Diseases), Dr. Richard Klausner (NCI), Dr. Claude Lenfant (NHLBI), and Dr. Lawrence Tabak (National Institute of Dental and Craniofacial Research).

In January 2001, the AIMBE-ARR Joint Committee proposed the mission statement and goals for the NIBIB, which were sent to Drs. Kirschstein and Dean on January 30. In February 2001, the joint committee representatives met on several occasions with Dr. Dean and Dr. Hyman, who said that the NIH internal task force

used the letter to *Science* (15), among other documents, as content for the mission statement for the NIBIB. The statement was quite congruent with that drafted by the joint committee. The joint committee stressed the importance of a significant budget base and pointed out the importance of R01 funding, together with other funding mechanisms, and training support, as well as the need for an intramural program in the NIH on biomedical imaging and bioengineering.

The NIH internal task force formed a working group composed of program officials from several ICs with experience on relevant research areas to work with the task force to review their existing research grant portfolio for the identification of grants that are appropriate for transfer to the NIBIB. The amount transferred was \$67 million (see FY2002, below).

On March 1, 2001, Dr. Kirschstein gave the keynote address at the AIMBE Tenth Anniversary Meeting on "Partnerships for the New Millennium," in which she outlined the plans for the new NIBIB and invited the medical and biological communities to provide input. Her address was followed by active and constructive discussions. On March 2, AIMBE held a forum on "NIH and Bioengineering." At the forum, Dr. Dean gave a speech on the current developments and future directions of NIBIB and served with Drs. Baum (ARR) and Linehan (AIMBE) as panelists in an open forum, where I served as the moderator. The discussions were very fruitful, with active participation by the audience, on issues related to the operation of NIBIB, e.g., grant funding mechanisms, areas of emphasis, transfer of grants from other institutes, etc.

On March 19, 2001, representatives of ARR and AIMBE met with Drs. Kirschstein and Dean at the NIH. Dr. Kirschstein was pleased with the publication of the letter in *Science* on March 2, 2001 (15). The NIH had just sent the plans and timelines for establishing the NIBIB to Secretary Tommy Thompson, Department of HHS, for approval. Dr. Kirschstein encouraged the bioimaging and bioengineering communities to submit nominations for members of the NIBIB Director Search Committee and candidates to be considered as NIBIB Director, as well as members of the Advisory Council. Dr. Kirschstein stated that the new Institute would start with an appropriate budget that would be ramped up over a five-year period, as in the case of the National Human Genome Research Institute, and that the NIBIB would foster training as well as research in bioimaging and bioengineering.

On April 20, 2001, Secretary Thompson approved the NIBIB Establishment Plan, which described the initial infrastructure, organization, budget requirements, and mission of the NIBIB.

On April 26, 2001, Dr. Donna Dean was designated as Acting Director of the NIBIB (Figure 4). She initiated the internal implementation steps: recruiting scientific and administrative staff, organizing program areas, establishing referral guidelines for grant applications, finalizing transfer of funded grants into the NIBIB, establishing a Web site (<http://www.nibib.nih.gov>), setting up NIBIB's central offices in the NIH's building 31, and extending outreach and communications to the potential research constituencies. On April 29, 2001, Dr. Dean spoke about



**Figure 4** Shu Chien and NIBIB Acting Director (2001–2002) Donna Dean, May 2001, NIBIB Acting Director’s Office, Bethesda, MD.

the NIBIB at the American Roentgen Ray society annual meeting in Seattle and met with the Board members of ARR and AIMBE.

## MISSION STATEMENT OF THE NIBIB

The mission statement of the NIBIB was first developed by the NIH task force and was made public on March 5, 2001:

“The mission of the National Institute of Biomedical Imaging and Bioengineering is to improve health by promoting fundamental discoveries, design and development, and translation and assessment of technological capabilities in biomedical imaging and bioengineering, enabled by relevant areas of information science, physics, chemistry, mathematics, materials science, and computer sciences. The Institute plans, conducts, fosters, and supports an integrated and coordinated program of research and research training that can be applied to a broad spectrum of biological processes, disorders and diseases and across organ systems. The Institute coordinates with the biomedical

imaging and bioengineering programs of other agencies and NIH Institutes to support imaging and engineering research with potential medical applications and facilitates the transfer of such technologies to medical applications.” (An abbreviated version is shown on the home page of <http://www.nibib.nih.gov>)

In support of its mission, the institute will perform the following:

- Support research and research training through existing NIH funding mechanisms, and take the lead in exploring novel approaches for funding technology development and interdisciplinary research
- Form partnerships with NIH ICs to translate fundamental discoveries into research and applications for specific diseases, disorders, or biological processes
- Coordinate with other government agencies to translate fundamental or cross-cutting discoveries and developments in imaging, engineering, and related areas of information science and technology assessment into biomedical applications
- Encourage and support the development of relevant standards and guidelines that will enable widespread adaptability for biomedical imaging, bioengineering, and related information science and technology and computation, by taking a leadership and coordinating role for the NIH.

The principles outlined above form the basis of the congressional budget justifications for the NIBIB.

## NIBIB DIRECTOR AND ADVISORY COUNCIL

At the end of August 2001, the NIH advertised the position of the Director of the NIBIB in many scientific and professional publications, as well as on a number of Web sites. A search committee was formed, which was cochaired by Drs. Lawrence Tabak and Stephen Katz of the NIH, with seven members from the biomedical imaging and bioengineering communities and four other members from the NIH. The cochairs solicited qualified applicants from over 20 relevant professional organizations. The requirements included having a doctoral degree, senior-level research expertise and knowledge in relevant areas, outstanding scientific competence respected nationally and internationally, demonstrated leadership of an interdisciplinary research program, a track record of resolution of operational problems, and experience in management of financial and human resources.

Many excellent candidates were nominated and applied for the position. The search committee selected the seven most qualified candidates for interviews, and three finalists were presented to the NIH. Following further interviews with the NIH leadership, Dr. Roderic I. Pettigrew (Figure 5), who had superb expertise in biomedical imaging and bioengineering and outstanding leadership ability, was selected and appointed as the first permanent Director of the NIBIB in May 2002.



**Figure 5** NIBIB Director Roderic Pettigrew and Shu Chien, July 2002, Medical Imaging Meeting at Imperial College, London.

Dr. Pettigrew received his Ph.D. degree in applied radiation physics from the Massachusetts Institute of Technology and his M.D. from the University of Miami School of Medicine. He did his internship and residency in internal medicine at Emory University and completed his residency in nuclear medicine at the University of California, San Diego. Prior to assumption of the NIBIB Directorship in September 2002, he was Professor of Radiology, Medicine (Cardiology), and Bioengineering at Emory University School of Medicine in Atlanta, and Director of the Emory Center for MR Research.

Dr. Dean was appointed as Deputy Director of NIBIB, a position she held until November 2003. In December 2003, Dr. Belinda Seto (Figure 6), previously serving as Acting Deputy Director for Extramural Research at the NIH, was appointed as the NIBIB Deputy Director.

The National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB) was established by HHS Secretary Tommy Thompson under the Public Health Service Act to advise, assist, consult with, and make recommendations to the Secretary and the NIBIB Director on matters related to the activities carried out by and through the Institute and the policies related to these activities. The advisory council has 12 scientific members composed of scientists, engineers, physicians, and other health professionals. Of these, six represent disciplines in biomedical engineering and imaging; the other six represent other disciplines and



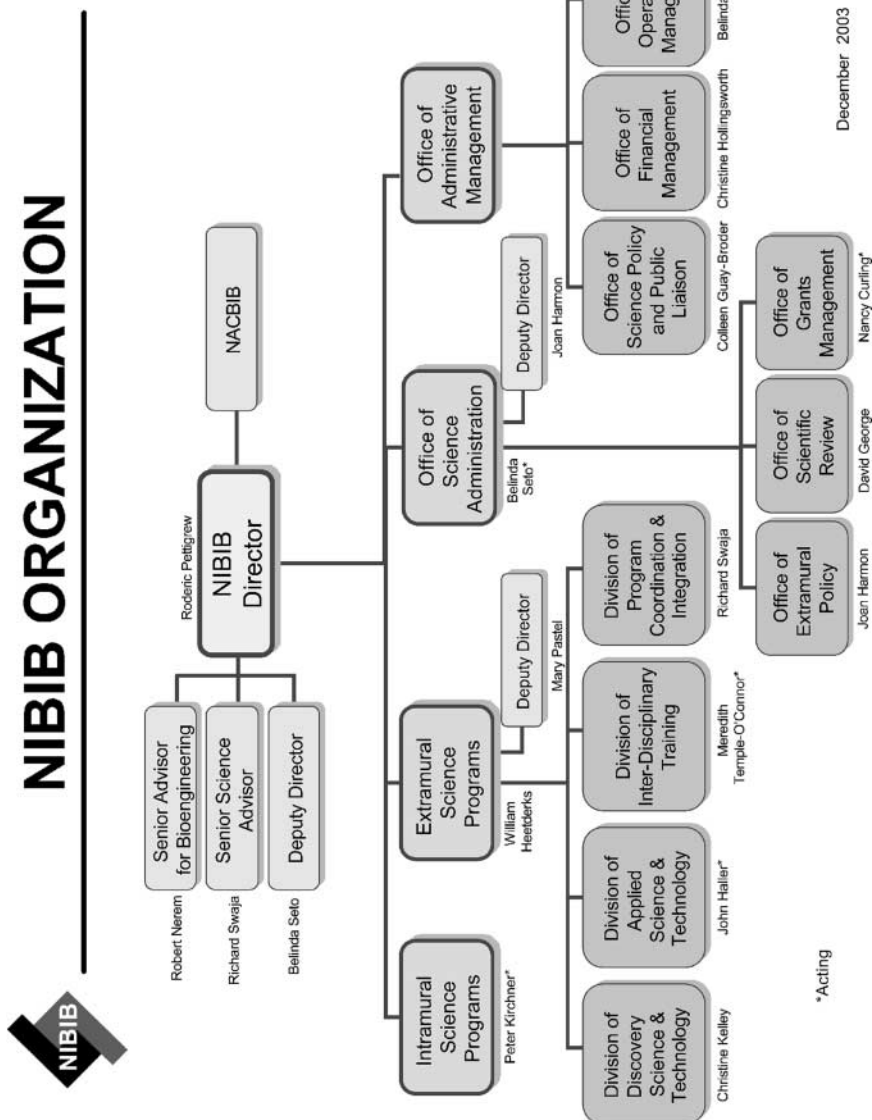
**Figure 6** Shu Chien and NIBIB Deputy Director Belinda Seto, February 2004, NIBIB Office, Bethesda, MD.

are knowledgeable about the applications of biomedical engineering and imaging in medicine. Ex officio members of the advisory council include the Director of the Centers for Disease Control and Prevention, the Director of the NSF, and the Director of the National Institute of Standards and Technology (or their designees). The advisory council held its first meeting on January 16–17, 2003, and meets three times a year. The roster of the advisory council and the minutes of past meetings can be found at <http://www.nibib.nih.gov/about/NACBIB/NACBIB.htm>.

Under the excellent leadership of Dr. Pettigrew, assisted by Dr. Dean and other very capable staff members, the NIBIB has made remarkable advances in less than three years. The leaders of various programs and divisions in the NIBIB, together with its organizational chart, are provided in Figure 7.

Drs. Pettigrew and Dean made unprecedented efforts to communicate with extramural communities, reaching out for input and providing information on developments at the NIBIB. In 2002 and 2003, they spoke at more than 70 scientific and professional society meetings and visited more than 40 academic institutions. These interactions between the NIBIB leadership and the biomedical imaging and bioengineering communities have been very valuable in the development of the NIBIB in concert with the opportunities and challenges of the frontiers of these disciplines.

To enhance the participation of bioengineering leaders in the NIBIB policy matters, Dr. Pettigrew appointed Dr. Robert M. Nerem of the Georgia Institute of Technology and Emory University as a part-time senior advisor for bioengineering in January 2003. The other senior advisor is Dr. Richard Swaja.



December 2003

\*Acting

Figure 7 NIBIB organizational chart.

## NIBIB ACTIVITIES

### NIBIB Symposia and Workshops

The NIBIB has organized, sponsored, or cosponsored many symposia and workshops. The most recent ones held between August 2002 and August 2003 are given below:

- NIBIB Workshop on Biomedical Imaging and Bioengineering Training
- NIH/NSF Workshop on Image-Guided Interventions
- BMIS Medical Implant Information, Performance, and Policies Workshop
- Third Inter-Institute Workshop on Diagnostic Optical Imaging
- NIBIB Workshop on Future Research Directions
- Symposium on Defining the State of the Art in Biomedical Imaging: Research for the Future
- Symposium on Imaging the Pancreatic Beta Cell
- BECON 2003 Symposium: Catalyzing Team Science [the sixth in a series of annual BECON meetings (see Developments in the Biomedical Engineering Community Prior to 1996)]
- Symposium on Modeling of Complex Biological Systems

### NIBIB Requests for Applications in 2002

The NIBIB held several workshops (see previous section) to identify the highest priority research focus areas that are appropriate in relation to its mission and national priorities, as well as promising emerging technologies or high-impact projects. The research focus areas thus identified led to the issuance in early 2003 of ten requests for applications (RFA) on development of advanced biomaterials, development of novel drug and gene delivery systems and devices, image-guided interventions, improvements in imaging methods and technologies, research opportunities in tissue engineering, low-cost medical imaging devices, telehealth technologies development, research and development of systems and methods for cellular and molecular imaging, systems and methods for small animal imaging, and operation of sensors in vivo.

### NIBIB Grant Portfolio Areas in 2003 and Initiatives for FY2004

Analysis of the NIBIB research grants portfolio in 2003 using program class codes has identified the following subject areas: biosensors; biomaterials; biomechanics; bioinformatics; computational biology; drug and gene delivery; image-guided therapies; medical devices/implants; magnetic resonance imaging and spectroscopy; nanotechnology; nuclear medicine; optical imaging; platform technology; rehabilitation engineering; surgical tools and techniques; tissue engineering; ultrasonics; and X ray, electron microscopy, and ion beam.

The NIBIB has been working on identifying concept areas for exploration in FY2004. Examples of these research areas include the following:

- Data integration
- Quantum projects
- Tissue engineering
- Multiscale modeling
- Computer-assisted image-guided surgery
- Microimaging of pancreatic islets
- Chemistry of imaging agents and molecular probes
- Brain computer interface
- Translational research in nanotechnology-based diagnoses and therapy

Currently, the NIH is operating under a continuing resolution, as indicated below, and an approved budget is needed for the initiation of new projects.

## NIBIB BUDGET

The legislation establishing the NIBIB was not passed until the end of 2000, thus precluding the NIBIB's inclusion in the FY2001 NIH budget, which had been developed almost a year earlier. However, the NIH FY2001 appropriation contained \$1.975 million originally designated for the OB3 within the Office of the NIH Director, and this amount was used to support the administrative activities necessary to create the new institute.

The FY2002 operating budget totaled \$111.7 million, which included \$67 million in grants and funds that were transferred from other ICs of the NIH (see above). The majority of the funds over and above the transfer, approximately \$40 million, were used to support the NIBIB's mission, which included research grants and contracts, training grants, and operations (Table 1).

The transfer of funds from the existing ICs to the NIBIB was not an easy process. It is often difficult to clearly differentiate grants that are crosscutting versus those that are organ/disease-specific. As a result of the cooperative efforts between NIH leadership and the scientific community in a working group examining the grant

**TABLE 1** NIBIB operating budget figures for fiscal years 2002 and 2003 (million \$)

	Training	RMS <sup>a</sup>	Contracts	Other res.	Centers	RPG <sup>b</sup>	Total
FY2002	0.2	11.7	1.3	2.9	1.3	94.3	111.7
FY2003	2.8	13.8	7.3	4.5	23.6	226.2	278.2

<sup>a</sup>RMS: Research management and support funds.

<sup>b</sup>RPG: Research project grants including BRP and SBIR/STTR. SBIR funds were \$0.89 million in 2002 and \$10.9 million in 2003.

portfolios, a solution was attained with the transfer of an additional \$150 million from the various NIH ICs to the NIBIB. The extramural members of the working group were Drs. Don P. Giddens, Peer M. Portner, and Matthew Tirrell from AIMBE and Drs. Stanley Baum, Reed Dunnick, and Etta Pisano from ARR. The intramural members were Drs. Robert Balaban, Suzanne Fisher, and King C.P. Li, with staff support from Dr. Mary Pastel and Ms. Stacy Wallick. Kevin O'Connor (AIMBE), Edward C. Nagy (AAR), and Dr. Dean were ex officio members.

The FY2003 budget appropriation was passed in February 2003. The total operating budget was increased to \$278.2 million, which included the \$150 million in grants and funds transferred from other ICs. The approximately \$128.2 million over and above the transfer was used to carry out the NIBIB's mission, including a significant increase in its funding of research and training, especially research project grants and center grants. In FY2003, the NIBIB funded 38 BRP grants with \$30 million, which constitute approximately 30% of all BRPs in the NIH (130 grants with an annual budget of \$106 million). For all biomedical imaging- and bioengineering-related NIH grants, approximately 15% were supported by the NIBIB and the remainder by other ICs.

The budget appropriation for FY2004 is yet to be passed. The president's budget and the House mark both have \$282 million for the NIBIB, whereas the Senate mark is slightly higher at \$289 million. The FY2004 president's budget provides only a 1.4% increase over FY2003.

## REVIEW OF BIOMEDICAL IMAGING AND BIOENGINEERING GRANTS

As mentioned above (see Developments in the Biomedical Engineering Community Prior to 1996, above), the CSR has implemented its reorganization of the peer review system at the NIH (13). The reorganization of the review system involves (a) the establishment of IRGs, each with approximately six to eight study sections, to replace the initial review groups and (b) the realignment of study sections. The CSR is proceeding with implementation plans for the IRGs that were approved in January and May 2003. Descriptions of the IRGs and their study sections can be found on the CSR's IRG description page located at <http://www.csr.nih.gov/review/irgdesc.htm>. Lists of the scientific review administrators (SRAs) and provisional membership rosters are available on the CSR study section roster index page at <http://www.csr.nih.gov/Committees/rosterindex.asp>. Investigators are encouraged to read these Web pages to identify the IRG and study section most suited for the review of their applications. With each grant application, the principal investigator may submit a cover letter to suggest an IRG or study section, as well as the areas of science and engineering needed for appropriate peer review.

As a result of the reorganization of the review system, two new IRGs related to biomedical imaging and bioengineering, namely, Bioengineering Sciences and

Technologies (BST) and Surgical Sciences, Biomedical Imaging, and Bioengineering (SBIB), have been formed in place of the previous Surgery, Radiology, and Bioengineering (SRB) IRG. These two new IRGs are described below. The study sections in these IRGs review the applications for research project grants (R01, R21, R15, etc.) and SBIR and STTR grants.

## Bioengineering Sciences and Technologies IRG

The BST IRG reviews grant applications that focus on fundamental aspects of bioengineering and technology development in the following areas: gene and drug delivery systems, imaging principles for molecules and cells, modeling of biological systems, bioinformatics and computer science, statistics and data management, instrumentation, chips and microarrays, biosensors, and biomaterials. Although biological context is important in bioengineering, a central premise in organizing this IRG is the need for effective review of bioengineering and technology development in early stages before specific practical uses are proven. The current BST IRG includes the following study sections:

- Gene and Drug Delivery Systems (GDD)
- Microscopic Imaging (MI)
- Modeling and Analysis of Biological Systems (MABS)
- Biodata Management and Analysis (BDMA)
- Instrumentation and Systems Development (ISD)
- Biomaterials and Biointerfaces (BMBI)

## Surgical Sciences, Biomedical Imaging, and Bioengineering IRG

The SBIB IRG reviews applications for research grants that address topics in a variety of areas at the interface between a physical science or engineering and biomedical or clinical research. Major areas include the following: (a) Development of molecular probes and contrast agents; development of molecular imaging techniques; and basic, applied, and preclinical aspects of the design and development of medical imaging systems (including hardware, software, and mathematical methods of image analysis) for studying organs or whole animals (including humans). (b) Application of computational sciences to knowledge and information in biological and clinical medicine, healthcare, and their integration. (c) Development of biomedical sensing and measurement instrumentation; diagnostic instrumentation creating knowledge to enhance organ system function and recovery; innovative biologics, materials, processes, implants, devices; and informatics approaches to prevent, diagnose, and treat disease. (d) Surgery and anesthesiology, host response to sepsis and injury, surgical and microsurgical therapies, surgical critical care and emergency medicine, treatment of trauma; multi-organ responses to surgery.

The following scientific review groups are included within this IRG:

- Biomedical Imaging Technology (BMIT)
- Medical Imaging (MEDI)
- Biomedical Computing and Health Informatics (BCHI)
- Bioengineering, Technology, and Surgical Sciences (BTSS)
- Surgery, Anesthesiology, and Trauma (SAT)
- Small Business Biomedical Imaging (SBMI)
- Small Business Bioengineering, Surgical Sciences, and Technology (SBTS)
- Small Business Biomedical Sensing, Measurement, and Instrumentation (SSMI)
- Small Business Bioelectromagnetics Special Emphasis Panel

Deliberations are under way on the development of recommendations for other IRGs that may share interests in areas of research with these IRGs. Tentative proposals on shared-interest guidelines are being developed for each of the study sections, pending further input from the remaining study section design teams, the scientific community, the CSR Advisory Committee to the Director, and the CSR.

For the most part, all grant applications are reviewed by the CSR; however, training grant applications, program project grants, and applications in response to RFAs are mainly reviewed by the institutes. The review administrators receive the applications, set up the reviews, and compile the summary statements. The program administrators give guidance to the applicants before submission and after review. In September 2003, the NIBIB Special Emphasis Panel was established, which enables the institute's Office of Review to hold special review meetings. The first review meetings in November 2003 encompassed reviews of applications of institutional training grants and research career-development awards.

## NIBIB PARTICIPATION IN NIH ROADMAP ACTIVITIES

Following his appointment as the Director of the NIH in May 2002, Dr. Elias Zerhouni initiated the creation of a new research vision for the NIH that focused the attention of the biomedical research community on three main themes: new pathways of discovery, research teams for the future, and the re-engineering of the clinical research enterprise (the Web site for the NIH roadmap is located at <http://nihroadmap.nih.gov>). This roadmap strategy was developed after extensive discussions involving the directors of NIH's 27 ICs. The three main themes include the following nine implementation groups:

- New Pathways to Discovery
  - Building Blocks, Pathways, and Networks Implementation Group
  - Molecular Libraries and Imaging Implementation Group
  - Structural Biology Implementation Group

- Bioinformatics and Computational Biology Implementation Group
- Nanomedicine Implementation Group
- Research Teams of the Future
  - Interdisciplinary Research Implementation Group
  - High-Risk Research Implementation Group
  - Public-Private Partnerships Implementation Group
- Re-Engineering the Clinical Research Enterprise
  - Clinical Research Implementation Group

The aim of these roadmap activities is to improve health by providing researchers with tools and capabilities to make innovative, novel, and multidisciplinary discoveries in science, engineering, and technology, and to ensure that these basic research discoveries are translated quickly into new approaches for diagnosis, treatment, and prevention of disease. Because the broad mission of the NIBIB is to improve health by leading the development and application of emerging and breakthrough biomedical technologies based in the physical and engineering sciences, there is a direct tie between the NIBIB's mission and the roadmap initiatives. The NIBIB is designated as a participant in all the roadmap initiatives.

Under New Pathways to Discovery, a key focus at the NIBIB is individualized molecular medicine. Technologies will be developed to evaluate specific diseases and their presentation in individual patients, with the goal of enabling physicians to obtain personalized profiles of molecular and genetic disease markers. Using this information, treatments can be tailored to each patient.

The goals of the initiatives under the Building Blocks, Pathways, and Networks Implementation Group include developing a network of research centers to create new tools to describe the dynamics of protein interactions, developing novel technologies to study cellular metabolites, establishing standards for proteomics and metabolomics, and assessing critical reagents for proteomics.

For the initiatives on Molecular Libraries and Imaging, an emphasis will be placed on the development of high-resolution probes for cellular imaging. The goals are to support multidisciplinary teams for the development of new technologies that enable higher-sensitivity biological imaging in living cells; to encourage and facilitate novel, high-risk strategies to create fundamentally new probes with enhanced spectral characteristics; to improve detection schemes by a factor of 10–100; and to develop probes that can be used to routinely achieve single-molecule sensitivity for imaging dynamic processes in living cells.

The NIBIB will participate in the initiative of the Bioinformatics and Computational Biology Implementation Group through the activities of the trans-NIH BISTI. The goals of this initiative include providing key building blocks for the national biomedical computing environment, the formation of single or multisite consortia, and the establishment of National Centers for Biomedical Computing.

For the initiative on Nanomedicine, the NIBIB focuses on nanoscience and nanotechnology. The goals are to obtain quantitative measurements on biological

molecular system components and their interactions, and to combine these measurements using mathematical and analytical tools for the fundamental understanding of biological circuits/processes and their precise interactions, with the aim of effecting desired changes in human health.

Under Research Teams of the Future and Re-Engineering the Clinical Research Enterprise, the NIBIB focuses on the implementation of interdisciplinary research. The goals are to supplement existing programs to promote research training experiences and to create new initiatives for the (a) promotion of curriculum development and short course development and (b) revitalization of clinical research scientist training for M.D.s and Ph.D.s.

## CONCLUSIONS AND PERSPECTIVES

The establishment of the NIBIB is a timely event that allows the NIH to capitalize on the remarkable advances in these fields to realize its mission to improve the health and well-being of our citizens. The establishment of the Institute was the result of the outstanding accomplishments of the scientists and engineers in the fields; the sustained and coordinated efforts of the relevant communities; the timely and generous support by the Whitaker Foundation; and the increasing recognition of the importance of these disciplines by the NIH, the public, and Congress.

The extraordinary cooperation between the NIH and the extramural communities has played a significant role in the establishment of NIBIB. The visionary leadership at the NIH and the NIBIB has led to its significant growth and development in a short period of time. The NIBIB now funds 800 grants in biomedical imaging and bioengineering. In addition to this active extramural program, we look forward to the establishment of an intramural program in these important frontier areas.

Because of the suddenness of its formation, however, the NIBIB started with a relatively limited budget. The budget for FY2003 did show a healthy increase over that of FY2002, but the proposed FY2004 budget does not provide much of an increase. For this new institute to further enhance its activities and to fully implement its mission, it is necessary to have a progressive increase in funding with a relatively steep slope for several years before attaining a quasi-steady state. The extramural community and the individual investigators need to reflect this need to our congressional and administrative leaders, emphasizing the vital importance of biomedical engineering and imaging in contributing to the infrastructure essential to advances in biomedical sciences and critical to the improvement of health care. By fostering biomedical imaging and biomedical engineering, the NIBIB will synergize with the other ICs at the NIH to elucidate the mechanisms underlying health at all levels of biological hierarchy; the diagnosis, treatment, and prevention of diseases; and the training of future generations of biomedical engineers and biomedical imagers. NIBIB is still in its beginning phase. To accomplish these important missions, it is essential that it grow to become at least a

medium-sized institute among the NIH ICs and to have a high-quality intramural program.

We are indeed at a very exciting time. The NIBIB, if provided an adequate budget, will be able to seize the unprecedented opportunity presented by the rapid advancements of biomedical engineering and imaging and meet the grand challenge of taking the research frontiers of these disciplines to new heights, with the ultimate goal of enhancing the health and well-being of people in the United States and throughout the world.

## ACKNOWLEDGMENTS

The author wishes to express his gratitude to the valuable advice, comments, and provision of information by officials in NIBIB and other components of the NIH, especially Drs. Roderic Pettigrew, Donna Dean, Wendy Baldwin, Robert Nerem, Elliot Postow, Donald Schneider, Richard Swaja, John Watson, Cheryl Fee, Christine Kelley, and Peter Moy. I would like to thank many friends and colleagues in biomedical imaging (Dr. Douglas Maynard and Edward Nagy) and bioengineering (Dr. William Hendee, Dr. Jack Linehan, Patricia Horner, and Kevin O'Connor) for their valuable input and critiques. I am grateful to all the friends and colleagues with whom I have had the pleasure and privilege to work with toward the common goal of establishing the NIBIB for enhancing the health and well-being of people.

**The Annual Review of Biomedical Engineering is online at  
<http://bioeng.annualreviews.org>**

## LITERATURE CITED

1. Hendee WR, Chien S, Maynard CD, Dean DJ. 2002. The National Institute of Biomedical Imaging and Bioengineering: history, status and potential impact. *Ann. Biomed. Eng.* 30:2–10; *Radiology* 222:12–18
2. Putman CE, Frank JA. 1993. Enhancement of diagnostic radiologic research and education. *Invest. Radiol.* 28(Suppl. 2):552–56
3. Holman BL, Nagy EC. 1998. Why we need a National Institute of Biomedical Imaging. *Acad. Radiol.* 5:211–14
4. Academy of Radiology Research. 1998. Imaging Research and the Federal Government: A White Paper. Washington, DC, September
5. National Institutes of Health Report on Support for Bioengineering Research. 1994. National Institutes of Health, Bethesda, MD, <http://www.becon1.nih.gov/nihreport.htm>
6. Nerem RM, Taylor KD, Arnold F, Chien S, Katona PG, et al. 1995. Support for Bioengineering Research, Department of Health and Human Services, Public Health Service, National Institutes of Health, <http://www.becon1.nih.gov/externalreport.htm>
7. Bronzino JD. 2000. *The Biomedical Engineering Handbook*. Boca Raton, FL: CRC Press
8. Griffith LG, Grodzinsky AJ. 2001. Advances in biomedical engineering. *JAMA* 285:556–61

9. Varmus H. 1998. *New directions in biology and medicine*. AAAS Plenary Lecture, <http://www.nih.gov/about/director/021398.htm>
10. Agnew B. 1998. Multidisciplinary research. Biology by design: from software to skin. *Science* 280:1516–18
11. Huntsman LL, Chien S, Davis RW, Griffith LG, Hendee WR, et al. 1999. Expanding opportunities. *NIH Work. Group Rep., Rev. Bioeng. Technol. Instrum. Dev. Res.* Natl. Inst. Health, Bethesda Md. <http://www.drg.nih.gov/bioopp1/select.htm>
12. U.S. Department of Health and Human Services. *Public Health Service Grant Application (PHS 398 Instructions) Rev. 05/2001* (<ftp://ftp.grants.nih.gov/forms/phs398.pdf>)
13. Alberts BM, Ayala FJ, Botstein D, Frank E, Holmes EW, et al. 2000. Recommendations for change at the NIH's Center for Scientific Review. *Phase 1 Rep.*, Panel Sci. Bound. Rev, Natl. Inst. Health, Bethesda, Md. <http://www.csr.nih.gov/bioopp/select.htm>
14. Varmus H. 2001. Proliferation of National Institutes of Health. *Science* 291:1903–5
15. Chien S, Maynard CD. 2001. Newest member of the NIH family. *Science* 291: 1701–2



## CONTENTS

---

FRONTISPIECE, <i>Roderic Pettigrew</i>	xii
THE NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING, <i>Shu Chien</i>	1
TISSUE ENGINEERING APPLICATIONS OF THERAPEUTIC CLONING, <i>Anthony Atala and Chester J. Koh</i>	27
BIOMATERIALS: WHERE WE HAVE BEEN AND WHERE WE ARE GOING, <i>Buddy D. Ratner and Stephanie J. Bryant</i>	41
TISSUE GROWTH AND REMODELING, <i>Stephen C. Cowin</i>	77
BREAST TISSUE ENGINEERING, <i>Charles W. Patrick, Jr.</i>	109
TISSUE ENGINEERING OF LIGAMENTS, <i>G. Vunjak-Novakovic, Gregory Altman, Rebecca Horan, and David L. Kaplan</i>	131
ADVANCES IN HIGH-FIELD MAGNETIC RESONANCE IMAGING, <i>Xiaoping Hu and David G. Norris</i>	157
MICRO-COMPUTED TOMOGRAPHY—CURRENT STATUS AND DEVELOPMENTS, <i>Erik L. Ritman</i>	185
OPTICAL PROJECTION TOMOGRAPHY, <i>James Sharpe</i>	209
MECHANICAL BIOEFFECTS OF ULTRASOUND, <i>Diane Dalecki</i>	229
OCULAR BIOMECHANICS AND BIOTRANSPORT, <i>C. Ross Ethier, Mark Johnson, and Jeff Ruberti</i>	249
MECHANOTRANSDUCTION AT CELL-MATRIX AND CELL-CELL CONTACTS, <i>Christopher S. Chen, John Tan, and Joe Tien</i>	275
FUNCTIONAL EFFICACY OF TENDON REPAIR PROCESSES, <i>David L. Butler, Natalia Juncosa, and Matthew R. Dressler</i>	303
FLUID MECHANICS OF HEART VALVES, <i>Ajit P. Yoganathan, Zhaoming He, and S. Casey Jones</i>	331
MOLECULAR MACHINES, <i>C. Mavroidis, A. Dubey, and M.L. Yarmush</i>	363
ENGINEERING SYNTHETIC VECTORS FOR IMPROVED DNA DELIVERY: INSIGHTS FROM INTRACELLULAR PATHWAYS, <i>Charles M. Roth and Sumati Sundaram</i>	397
FRACTAL ANALYSIS OF THE VASCULAR TREE IN THE HUMAN RETINA, <i>Barry R. Masters</i>	427

ADVANCES IN QUANTITATIVE ELECTROENCEPHALOGRAPH ANALYSIS METHODS, <i>Nitish V. Thakor and Shanbao Tong</i>	453
ROBOTICS, MOTOR LEARNING, AND NEUROLOGIC RECOVERY, <i>David J. Reinkensmeyer, Jeremy L. Emken, and Steven C. Cramer</i>	497
INDEXES	
Subject Index	527
Cumulative Index of Contributing Authors, Volumes 1–6	549
Cumulative Index of Chapter Titles, Volumes 1–6	552
ERRATA	
An online log of corrections to <i>Annual Review of Biomedical     Engineering</i> chapters may be found at <a href="http://bioeng.annualreviews.org/">http://bioeng.annualreviews.org/</a>	