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Establishing Research Competitiveness in Biophysical Sciences in Maine

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Investigators
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Establishing Research Competitiveness in Biophysical Sciences in Maine

Project Participants

Senior Personnel

Name: Eckardt, Michael
Worked for more than 160 Hours: Yes
Contribution to Project:
NSF EPSCoR Project Director and Principal Investigator - general oversight over all aspects of the IMB, including personnel, facilities, finances, policy, strategy, and research priorities. Serves on the State EPSCoR committee; Chair of the IMB Institute Policy Committee (IPC).

Name: Knowles, Barbara
Worked for more than 160 Hours: Yes
Contribution to Project:
Co-PI and Co-Director of the IMB, based at The Jackson Laboratory. Directly responsible for IMB activities including personnel, facilities, finances, policy, strategy, and establishing research priorities.

Name: Grunze, Michael
Worked for more than 160 Hours: Yes
Contribution to Project:
Co-PI and Co-Director of the IMB, based at The University of Maine and the University of Heidelberg. Directly responsible for IMB activities including personnel, facilities, finances, policy, strategy, and establishing research priorities. Founding Director of IMB.

Name: Mageean, Deirdre
Worked for more than 160 Hours: Yes
Contribution to Project:
Co-PI and Associate Vice President for Research and Dean of the Graduate School at the University of Maine to June 2005. Responsible for general oversight of the IMB as a research center of the University.

Name: Friesel, Robert
Worked for more than 160 Hours: Yes
Contribution to Project:
Co-PI and primary collaborator from Maine Medical Center Research Institute, one of the three collaborating partners of the IMB.

Name: Kennedy, Robert
Worked for more than 160 Hours: No
Contribution to Project:
President, University of Maine - former Project Director - general oversight of recruitment, facilities development, and communication with state EPSCoR committee.

Name: Woychik, Rick
Worked for more than 160 Hours: Yes
Contribution to Project:
Director, The Jackson Laboratory, and member of the Institute Policy Committee that serves as an advisory board to the IMB Directorate in establishing policies governing the interaction among UM, MMCRI, and JAX.

Name: Ault, Kenneth

Worked for more than 160 Hours: Yes

Contribution to Project:

Director, Maine Medical Center Research Institute, and member of the Institute Policy Committee that serves as an advisory board to the IMB Directorate in establishing policies governing the interaction among UM, MMCRI, and JAX.

Name: Lad, Robert

Worked for more than 160 Hours: No

Contribution to Project:

Director, University of Maine Laboratory for Surface Science Technology - primary collaborator from the University of Maine - serves as their representative on the Executive Committee.

Name: Shopland, Lindsay

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Researcher: Assistant Professor of Molecular Biophysics, University of Maine - gene clustering in primary sequence.

Name: Mason, Michael

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Researcher: Assistant Professor of Chemical and Biological Engineering, University of Maine - development of hybrid optical instruments.

Name: Nohe, Anja

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Researcher: Assistant Professor of Chemical and Biological Engineering, University of Maine - protein aggregation and function in membrane structures.

Name: Eck, Wolfgang

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Visiting Researcher: Visiting Research Associate Professor, University of Maine/University of Heidelberg - nanolithography and generation, and microscopic characterization of new two- and three-dimensional nano- and microstructures for the manipulation of cells and tissue from different mouse phenotypes.

Name: Neivandt, David

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Adjunct Member: Assistant Professor of Chemical Engineering, University of Maine - development of sum frequency vibrational spectrometer and application to synthetic and natural lipid bilayers.

Name: Kim, Carol

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Adjunct Member: Associate Professor of Biochemistry, Microbiology, and Molecular Biology/Cooperating Assistant Professor of Marine Sciences, University of Maine - infection and pathogenesis in zebrafish viral disease model.

Name: Hess, Samuel

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Adjunct Member: Assistant Professor of Physics, University of Maine - optimization of photophysical properties of fluorophores for the investigation of biomembrane organization.

Name: Nadeau, Jay

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Adjunct Member: Assistant Professor of Biomedical Engineering/Associate Member of Physics, Microbiology, & Immunology, McGill University - application of nanoparticles to visualize metabolic processes.

Name: Cremer, Christoph

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Adjunct Member: Visiting Adjunct Professor, University of Maine and Professor, Kirchhoff Institute for Physics, University of Heidelberg - quantitative molecular imaging analysis of nuclear genome sequencing.

Name: Spatz, Joachim

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Adjunct Member: Professor, Institute for Physical Chemistry, University of Heidelberg - programming cell function by nanoadhesive keys that trigger adhesion mediated cell signaling.

Name: O'Brien, Timothy

Worked for more than 160 Hours: No

Contribution to Project:

Former IMB Associate Member: Research Scientist, The Jackson Laboratory - developmental genomic, embryology.

Name: Nemeth, Vicki

Worked for more than 160 Hours: Yes

Contribution to Project:

NSF EPSCoR Associate Project Direcotr, UMaine - general oversight and administration of EPSCoR programs and research development.

Name: Bult, Carol

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Associate member/Collaborating researcher, The Jackson Laboratory - bridging the digital biology divide

Name: Eviskov, Alexei

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Collaborating researcher, The Jackson Laboratory - embryonic genome activation

Name: John, Simon

Worked for more than 160 Hours: No

Contribution to Project:

IMB Asociate member, TJL

Name: Leiter, Edward

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Collaborating researcher, The Jackson Laboratory - diabetes, inflammatory bowel disease

Name: Lindner, Volkhard

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Collaborating researcher, Maine Medical Center Research Institute - immunoreactivity

Name: Millard, Paul

Worked for more than 160 Hours: Yes

Contribution to Project:

IMB Collaborating researcher, University of Maine - biosensors

Name: Prudovsky, Igor

Worked for more than 160 Hours: Yes

Contribution to Project:
IMB Collaborating researcher, Maine Medical Center Research Institute - protein secretion

Name: Vary, Calvin
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Collaborating researcher, Maine Medical Center Research Institute - vascular disease

Name: Burgess, Rob
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Associate Member/Collaborating researcher, The Jackson Laboratory - synaptic membranes

Name: Spicer, Doug
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Collaborating researcher, Maine Medical Center Research Institute - nuclear subdomains

Name: Mills, Kevin
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Collaborating researcher, The Jackson Laboratory - mechanisms for genome stability

Name: Li, Shaoguang
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Collaborating researcher, The Jackson Laboratory - mechanisms of human leukemias

Name: Hutchison, Keith
Worked for more than 160 Hours: No
Contribution to Project:
IMB Associate member, UMaine: Director of the Interdisciplinary Ph.D. in Functional Genomics program (IGERT)

Name: Collins, Scott
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Associate member, UMaine - recently appointed to take over Co-Director position from Michael Grunze (with Rosemary Smith & Barbara Knowles)

Name: Naggert, Juergen
Worked for more than 160 Hours: No
Contribution to Project:
IMB Associate member, TJL

Name: Nishina, Patsy
Worked for more than 160 Hours: No
Contribution to Project:
IMB Associate Member, TJL

Name: Rosen, Cliff
Worked for more than 160 Hours: No
Contribution to Project:
IMB Associate member, TJL

Name: Smith, Rosemary
Worked for more than 160 Hours: Yes

Contribution to Project:
IMB Associate member, Umaine - recently appointed to take over Co-Director position from Michael Grunze (with Scott Collins & Barbara Knowles)

Name: Wojchowski, Don
Worked for more than 160 Hours: No
Contribution to Project:
IMB Associate member, MMCRI

Name: Khalil, Andre
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Associate member, UMaine

Name: Croall, Dorothy
Worked for more than 160 Hours: No
Contribution to Project:
IMB Associate member, UMaine

Name: Ackerman, Susan
Worked for more than 160 Hours: No
Contribution to Project:
IMB Associate member, TJL

Name: Pinz, Ilka
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Associate member, MMCRI

Name: DeVries, Mimi
Worked for more than 160 Hours: Yes
Contribution to Project:
Originally Postdoc with Dr. Barbara Knowles - IMB collaborating researcher

Name: Bewersdorf, Joerg
Worked for more than 160 Hours: Yes
Contribution to Project:
Collaborating research at The Jackson Laboratory

Name: Smith, Rosemary
Worked for more than 160 Hours: Yes
Contribution to Project:

Name: Collins, Scott
Worked for more than 160 Hours: Yes
Contribution to Project:

Name: Gundersen, Robert
Worked for more than 160 Hours: No
Contribution to Project:
IMB Associate faculty, University of Maine

Post-doc

Name: Chada, Gopal
Worked for more than 160 Hours: Yes

Contribution to Project:
Post-doc for IMB Researcher Michael Mason, University of Maine

Name: von Hase, Johann
Worked for more than 160 Hours: Yes
Contribution to Project:
Visiting post-doc for IMB Adjunct Member Christoph Cremer, University of Maine/University of Heidelberg

Name: MacEwan, Kim
Worked for more than 160 Hours: No
Contribution to Project:
Post-doc for IMB Researcher Anja Nohe, University of Maine to December 2004

Name: Haratzi, Tamas
Worked for more than 160 Hours: No
Contribution to Project:
Post-doc with IMB Co-Director Michael Grunze, at the University of Heidelberg

Name: Peaston, Anne
Worked for more than 160 Hours: Yes
Contribution to Project:
Postdoctoral fellow with IMB Co-Director Barbara Knowles, TJL

Name: Gudheti, Manasa
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Associate member Sam Hess, UMaine

Name: Fick, Joerg
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Associate member David Neivandt, UMaine

Name: LeClair, Renee
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Associate member Volkhard Lindner, MMCRI

Name: Terzic, Aleksandra
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Associate member Volkhard Linder, MMCRI

Name: Kirov, Alexander
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Associate member Igor Prudovsky, MMCRI

Name: Pyagay, Peter
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Contribution to Project:
Postdoctoral fellow with IMB Associate member Igor Prudovsky, MMCRI

Name: Graziani, Irene
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Associate member Igor Prudovsky, MMCRI

Name: Fuerst, Peter
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Associate member Rob Burgess, TJL

Name: Kreth, Gregor
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Adjunct Christoph Cremer, UHeidelberg

Name: Birk-Spori, Udo
Worked for more than 160 Hours: No
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Postdoctoral fellow with IMB Adjunct Christoph Cremer, UHeidelberg

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Name: Kepper, Nick
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Postdoctoral fellow with IMB Adjunct Christoph Cremer, UHeideleberg

Name: Glass, Roman
Worked for more than 160 Hours: No
Contribution to Project:
Postdoctoral fellow with IMB Adjunct Joachim Spatz, UHeidelberg

Name: Soldi, Raffaella
Worked for more than 160 Hours: No
Contribution to Project:
Research Fellow with IMB Associate member Igor Prudovsky, MMCRI

Name: Graber, Joel
Worked for more than 160 Hours: Yes
Contribution to Project:
Postdoc with Dr. Barbara Knowles

Name: Nicholson, Anthony
Worked for more than 160 Hours: No
Contribution to Project:
IMB postdoc, The Jackson Laboratory

Name: Wiles, Michael
Worked for more than 160 Hours: No
Contribution to Project:
IMB postdoc, The Jackson Laboratory

Name: Chen, Shiahn
Worked for more than 160 Hours: No
Contribution to Project:
IMB postdoc, The Jackson Laboratory

Graduate Student

Name: Girirajan, Thanu
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student for IMB Researcher Michael Mason, University of Maine

Name: Larkin, Scott
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student with IMB Research Mike Mason, UM

Name: Wolfram, Tobias
Worked for more than 160 Hours: Yes
Contribution to Project:
Visiting graduate student for IMB Adjunct Member Joachim Spatz, University of Maine/University of Heidelberg

Name: Young, Kira
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student for IMB Researcher Anja Nohe, University of Maine

Name: Schmidt, Martin
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student with IMB Co-Director Michael Grunze, at the University of Heidelberg

Name: Doyle, Andrew
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student with IMB Researcher David Neivandt, University of Maine

Name: Staier, Florian
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB researcher Christoph Cremer, at the University of Heidelberg

Name: Bragdon, Beth
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student with IMB Research Anja Nohe, UM

Name: Li, Lei
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Associate member David Neivandt, UM

Name: Sterling, Sarah
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Associate member David Neivandt, UM

Name: Rochira, Jennifer
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Associate member Sam Hess, UM

Name: Mlodzianowski, Michael
Worked for more than 160 Hours: No

Contribution to Project:
Graduate student with IMB Associate member Sam Hess, UM

Name: Gunewardene, Mudalige
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Associate member Sam Hess, UM

Name: Davenport, Glen
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Associate member Joerg Bewersdorf, TJL

Name: Durmus, Tahir
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Associate member Volkhard Lindner, MMCRI

Name: Muller, Marcel
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Co-Director Michael Grunze, UHeidelberg and Edward Leiter, The Jackson Laboratory

Name: Batram, Claudia
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Adjunct Christoph Cremer, UHeidelberg

Name: Stein, Stefan
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Adjunct Christoph Cremer, UHeidelberg

Name: Rinck-Jahnke, Sabine
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student withf IMB Adjunct Joachim Spatz, UHeidelberg

Name: Bahcheli, Daniel
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Adjunct Jay Nadeau, McGill University

Name: Clarke, Samuel
Worked for more than 160 Hours: No
Contribution to Project:
Graduate student with IMB Adjunct Jay Nadeau, McGill University

Name: Craig, Gary
Worked for more than 160 Hours: Yes
Contribution to Project:
Originally undergraduate student with IMB Researcher Mike Mason, UM - graduate student

Name: Snow, Kathy
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student with IMB member Lindsay Shopland and Kevin Mills, TJL

Name: Johnson, Valerie
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student with IMB member Lindsay Shopland, TJL

Name: Fancer, Karen
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student with IMB member Barbara Knowles, TJL

Name: Gould, Travis
Worked for more than 160 Hours: Yes
Contribution to Project:
Graduate student with IMB member Sam Hess, UM

Undergraduate Student

Name: Cook, James
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student worker for IMB Researcher Anja Nohe

Name: Verrill, Joshua
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student worker for IMB Researcher Anja Nohe

Name: Dean, Meigan
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student worker for IMB Researcher Anja Nohe

Name: Hansen, Sawyer
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student with IMB Researcher Mike Mason, UM

Name: Hutchinson, Adrian
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student with IMB Researcher Mike Mason, UM

Name: Tse, Johnny
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student with IMB Researchers Mike Mason & David Neivandt, UM

Name: Veilluex, Dale
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student with IMB Researchers Mike Mason & David Neivandt, UM

Name: Nagpure, Bhupendra
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student with IMB Associate member Sam Hess, UM

Name: Laughlin, Ryan
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student with IMB Associate member Sam Hess, UM

Name: Schoen, Tobias
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student with IMB Researcher Tobias Wolfram, UM/TJL

Name: Belz, Ferdinand
Worked for more than 160 Hours: No
Contribution to Project:
Undergraduate student with IMB Researcher Tobias Wolfram, UM/TJL

Name: Dunham, Jennifer
Worked for more than 160 Hours: Yes
Contribution to Project:
Undergraduate student with IMB Associate Project Director Vicki Nemeth, UM

Technician, Programmer

Name: Lynch, Chris
Worked for more than 160 Hours: Yes
Contribution to Project:
Lab technician with IMB researcher Lindsay Shopland, The Jackson Laboratory

Name: Uvieghara, Mathias
Worked for more than 160 Hours: Yes
Contribution to Project:
Research assistant with IMB Researcher Mike Mason, UM

Name: McOsker, Megan
Worked for more than 160 Hours: Yes
Contribution to Project:
Research Assistant with IMB Researcher Lindsay Shopland, UM/TJL

Name: Lessard, Mark
Worked for more than 160 Hours: No
Contribution to Project:
Research Assistant with IMB Associate member Joerg Bewersdorf, TJL

Name: Wang, Qiaozeng
Worked for more than 160 Hours: No
Contribution to Project:
Research Assistant with IMB Associate member Volkhard Lindner, MMCRI

Name: Carrier, Kathleen
Worked for more than 160 Hours: No
Contribution to Project:
Research Associate with IMB Associate member Volkhard Lindner, MMCRI

Name: Kacer, Doreen
Worked for more than 160 Hours: No
Contribution to Project:
Research Associate with IMB Associate member Igor Prudovsky, MMCRI

Name: Eipel, Heinz
Worked for more than 160 Hours: No
Contribution to Project:
Research fellow with IMB Adjunct Christoph Cremer, UHeidelberg

Name: Ingraham, Betty
Worked for more than 160 Hours: Yes
Contribution to Project:
Technical lab staff with IMB member Anja Nohe, UM

Other Participant

Name: Merritt, Kate
Worked for more than 160 Hours: No
Contribution to Project:
IMB Executive Assistant, UMaine - assistant to Co-Directors until May 2005

Name: Hildreth, Angela
Worked for more than 160 Hours: Yes
Contribution to Project:
Part-time clerical

Name: Michaud, Nathan
Worked for more than 160 Hours: Yes
Contribution to Project:
IMB Coordinator as of Sept. 2005

Name: Mueller, Susan
Worked for more than 160 Hours: Yes
Contribution to Project:
Temporary administrative assistant

Research Experience for Undergraduates

Organizational Partners

Jackson Laboratory

The Jackson Laboratory, in Bar Harbor, Maine, is one of the three collaborating partners in this project, which created the IMB as a virtual institute. TJL has a core of IMB researchers that occupy specific IMB laboratory space and offices that house specialized equipment for the project research. The IMB at TJL receives financial support from the project and contributes in-kind support.

University of Heidelberg

The University of Heidelberg is an international collaborating partner, and one of the founding IMB Co-Directors holds a faculty position here. Six UH faculty members provide critical support and exchange opportunities for IMB research activities and personnel in Maine.

Maine Medical Center

Maine Medical Center Research Institute is one of the three collaborating partners in this project, which created the IMB as a virtual institute. MMCRI has a core of IMB Associate member researchers that interact with partners at UM, TJL, and UH. The IMB at MMCRI receives financial support from the project and contributes in-kind support.

McGill University

An IMB researcher at McGill University holds an adjunct position with the IMB, and collaborates with partner researchers at UM, TJL, MMCRI, and UH.

l'Ecole Normale Superieure, Lyon, France

An IMB Associate member at the Laboratoire de Physique de l'Ecole Normale Superieure de Lyon, France works with IMB partner researchers at UM, TJL, MMCRI, and UH.

Weizman Institute, Israel

IMB Co-Directors are working on plans for an International Institute for Biophysics with the University of Heidelberg and the Weizman Institute, which would collaborate with the IMB project in Maine.

Other Collaborators or Contacts

There are three major partners in this project: the University of Maine (UMaine), The Jackson Laboratory (TJL), and the Maine Medical Center Research Institute (MMCRI). UMaine is a publicly funded, Carnegie Research I Institution, and TJL and MMCRI are non-profit research institutions in Maine.

The three partners have come together to form the Institute for Molecular Biophysics (IMB), which has been established as a research institute at UM. The IMB Co-Directors reports to the Vice President for Research at UMaine, as do all other Directors of research institutes at the university.

The Institute Policy Committee (IPC) for the IMB is composed of Michael Eckardt (Chair; UM), Kenneth Ault (MMCRI), and Rick Woychik (TJL) and serves as an advisory board to the Directors of the IMB in establishing policies governing the interactions among UM, MMCRI, and TJL. The Institute has an external Board of Scientific Advisors, composed of renowned scientists who are not connected to a Maine institution. The Scientific Advisory Board meets at least once a year and conducts periodic reviews of research performance and overall scientific success of IMB. It also advises the Directors and the IPC on the scientific structure and direction of the IMB.

The three IMB partners also collaborate extensively with the University of Heidelberg, and many faculty members hold dual positions at the institutions, including IMB Co-Director Michael Grunze. Other faculty at McGill University and the Laboratoire de Physique de l'Ecole Normale Superieure de Lyon, France are also integrally involved in collaborations with IMB researchers, providing critical knowledge and tech transfer to Maine

In addition to the extensive collaborations between the partner institutions, the IMB also established a number of scientific collaborations with internationally recognized experts in its first two years, including: Dr. Avi Ulman, Department of Chemistry, Polytechnic University, Brooklyn, NY, Bar Ilan University, Rahovot, Israel û preparation of nanoparticles as probes in cellular imaging; Dr. Chris Jacobsen, Department of Physics, University of NY, Stony Brook, and Dr. Susan Wirzek, NSLS û x-ray microscopy and microspectroscopy on melanosomes to determine mechanisms of glaucoma; Dr. Michael Anderson, Iowa State University û preparation of organelles from different mouse phenotypes, cryo-electron microscopy; Dr. Stefan Hell, Max Planck Institute for Biophysical Chemistry, Gottingen û 4 Pi microscopy; Dr. Gert Schneider, German Synchrotron Bessy, Berlin û x-ray microspectroscopy on cells; Dr. Peter Frtzl, Max Planck Institute for Colloid and Surface Chemistry, Golm, Germany û IR microscopy on cytoskeleton formation; Robert Grober, Yale University (IMB member Michael Mason) - controlled optical/scattering properties of high aspect ratio gold nanowires; Eileen Shore, University of Pennsylvania (IMB member Anja Nohe) û role of BMP signalizing in patients with FOP; Tim O'Brien, Cornell University (IMB member Lindsay Shopland) û nuclear organization of cluster-desert genomic regions; Tom Maniatis and Eugene Makeyev, Harvard University (IMB member Lindsay Shopland) û nuclear organization of mouse and human interferon gene clusters; Ana Pombo and Andre Moeller, MRC, London (IMB member Lindsay Shopland) û ultrastructural analysis fo gene clusters and transcription factories; Daniel Branton, Harvard University (IMB member Wolfgang Eck) û surface coatings of nanopores for DNA sequencing; Armin Golzhauser, University of Bielefeld (IMB Member Wolfgang Eck) û monolayers for ultrathin unimolecular membranes and electronic devices.

In addition, IMB researchers have recently been working with the collaborators: Jeff Merchant, Tufts University; You-Me Kim, Hidde Plough, MIT, Boston, MA; John Wise, University of Southern Maine (metallic nanoparticle toxicity); Peter Allen, Memorial Sloan Kettering Cancer Center (cancer detection using engineered metallic nanoparticle bioconjugates); Alain Arneodo, Ecole Normale Superierure de Lyon; Reiner Heintzmann, Max Planck Institute, Stuttgart, Germany.

The IMB explored the following industry collaborations in its first few years: IMEDCeloNova/Polyzenix - the establishment of a production facility in Maine, requiring access to the University of Maine cleanroom (partially funded by NSF EPSCoR); BASF - the possibilities of collaborative research on the health effects of nanoparticles; and Dr. Kishore Udupi of Medtronic AVE in Santa Rosa, CA. Current on-going industry collaborations include: Evident Technologies (quantum dot development); Brian Bennett of Leica Microsystems CMS, USA; Leica Microsystems CMS, Germany; Stryker Biomedical - image analysis tools for bone implant and growth determination; Richard McAloney, Lynntech Inc.

Activities and Findings

Research and Education Activities:

See the attached Executive Summary for this project.

1. MAJOR RESEARCH AND EDUCATION ACTIVITIES:

The goal of Maine's NSF EPSCoR Research Infrastructure Improvement award is to enhance the state's competitiveness in molecular biophysical sciences through a partnership between the University of Maine and Maine's non-profit research organizations. The primary objective was to create a nationally recognized interdisciplinary center for research and graduate education in molecular biophysical sciences. The result is the Institute for Molecular Biophysics (IMB), which brought together University of Maine (UMaine) faculty in physics, chemistry, biology, mathematics, and spatial engineering, with biomedical researchers at The Jackson Laboratory (TJL) and the Maine Medical Center Research Institute (MMCRI). A correlating objective is to hire additional faculty in the fields of biophysics and advanced optics, biochemistry, structural biology, applied mathematics, computer science, image analysis and visualization, and material science. This will complement and support the research strengths in mammalian physiology, genetics, genomics, and bioinformatics present in Maine's non-profit laboratories.

Once the IMB was established, a third objective was to have interdisciplinary research teams develop new measurement techniques, new sensors, new instruments, and innovative approaches to data processing and interpretation in three focus areas: intracellular structures and dynamics; functional materials as a means to manipulate cellular reactions; and biocomputing.

A fourth objective is to integrate research and education through the development of world-class opportunities for graduate education in biophysical science in Maine, and to provide additional research experiences for undergraduate and high school students that will inspire them to pursue careers in science and engineering.

A fifth objective includes providing mechanisms for Maine's academic, non-profit, and for-profit research institutions to increase their research competitiveness. This includes activities that will assist researchers to acquire new technical skills, develop new collaborations, and access key information.

Year One Activities:

Summary: The major research and education activities of the project in Year One were to (1) establish the Institute for Molecular Biophysics (IMB) as a formal administrative research institute at the University of Maine (UMaine); (2) develop appropriate laboratory and office space for the IMB at The Jackson Laboratory (TJL) and within the Laboratory of Surface Science and Technology at UMaine; (3) recruit a Founding Director; (4) recruit senior, mid-level, and junior scientists; (5) recruit an executive assistant to carry out administrative tasks; (6) identify necessary instruments and insure access to facilities deemed critical; (7) develop a research agenda; (8) educate the research and academic communities of the mission of IMB; (9) formulate an outreach and public education plan; (10) begin the planning process to insure the long-term sustainability of the IMB.

Detailed explanation of activities: (see above summary)

(1) The Institute for Molecular Biophysics (IMB) has been established as a research institute at UMaine, with a formal Memorandum of Understanding signed in March 2002. Its Director reports to the Associate Vice President for Research and Dean of the Graduate School, as do all other Directors of research institutes at the University.

(2) The following space has been committed to the IMB:

The Jackson Laboratory: (subcontracted)
- Three offices (currently occupied)
- 2,300 square feet of laboratory space (completion date of 30 April 2004)
- 436 square feet of confocal microscope space (begin construction May 2004)

University of Maine
- Two offices
- 500 square feet of laboratory space
- Access to 3,000 square feet clean room MEMS microfabrication facility

(3) The status for recruiting a Director:

Dr. Michael Grunze is the Founding Director of the Institute for Molecular Biophysics (IMB), with a fixed-length appointment from April 1,

2003 through August 31, 2004. Recruitment for the Director, IMB consists of a national search, including announcements in Science, Nature, The Chronicle of Higher Education, Association of Women in Science, American Physical Society, American Institute of Physics, Biophysical Society, and National Society of Black Physicists. We expanded the search committee in order to satisfy UM EO concerns and still conform to the Memorandum of Understanding among UM, TJL, and MMCRI. The members of the search committee are Michael Eckardt (Chair) and Robert Lad from UM; Rick Woychik and Barbara Knowles from TJL; and Kenneth Ault and Tom Maciag from the MMCRI. The UM EO Office and the Executive Vice President and Provost have approved the above recruitment plan. The other members of the search committee have also approved the plan. Evaluations of applicants commenced on 31 January 2004 and we hope to make an offer and have received an acceptance for the position of Director, IMB by April 15, 2004, with a formal start date of September 1, 2004. Three men and one woman, all Caucasians have applied: 1) Dr. Paul Agris, Department of Molecular and Structural Biochemistry, North Carolina State University, Raleigh, NC; 2) Dr. Michael Grunze, University of Maine, Orono, ME; 3) Dr. Paul S. O'Shea , School of Biomedical Sciences, Medical School, University of Nottingham, England; 4) Dr. Jordanka Zlatanova, Dept. of Chemical and Biological Sciences and Engineering, Polytechnic University , Brooklyn, NY

(4) Recruitment of senior, mid-level, and junior scientists:
National searches have been conducted for possible hires. In our hiring practices, we strongly encourage women and minorities to apply. In addition, UM's Equal Employment Opportunity Office has funds available to aid in attracting under-represented groups by augmenting salaries.

The following were hired as salaried IMB members: (one male, one female, Caucasian)
- Michael Grunze, Ph.D. (appointment April 1, 2003-August 31, 2004), Founding Director, IMB, Cooperating Professor, Department of Physics and Astronomy, UMaine, Adjunct Scientific Staff Member, TJL
- Lindsay S. Shopland, Ph.D. (appointment December 1, 2003-March 31, 2006), Research Assistant Professor, IMB, Cooperating Assistant Professor, Department of Biochemistry, Microbiology and Molecular Biology, UMaine, Research Associate, TJL

In addition, the following researchers are part of the IMB roster:
- Barbara Knowles, Ph.D., TJL û Principal Investigator
- Thomas Maciag, Ph.D., MMCRI û Principal Investigator
- David Neivandt, Ph.D., UMaine û Adjunct member
- Tim O'Brien, Ph.D., TJL û Adjunct member

The following positions were offered, with Dr. Mason and Dr. Nohe accepting full-time faculty positions, and the other four declining full-time but accepting adjunct status: (three male, three female, one Asian, five Caucasian)
- Michael D. Mason, Ph.D., currently at Yale University, Research Assistant Professor, IMB
Assistant Professor (Tenure Tract), Department of Chemical and Biological Engineering, UMaine, Adjunct Staff Member, TJL
- Anja Nohe, Ph.D., currently at University of Western Ontario, Research Assistant Professor, IMB, Assistant Professor (Tenure Tract), Department of Chemical and Biological Engineering or
Department of Chemistry, UMaine, Adjunct Staff Member, TJL
- Christoph Cremer, Ph.D., currently at University of Heidelberg, Research Professor, IMB,
Research Professor, Department of Physics and Astronomy, UMaine, Adjunct Scientific Staff Member, TJL
- Jay L. Nadeau, Ph.D., currently at Jet Propulsion Laboratory, Research Assistant Professor, IMB Assistant Research Professor, Department of Physics and Astronomy, UMaine
- Joachim P. Spatz, Ph.D., currently at University of Heidelberg, Research Professor, IMB
Research Professor, Department of Physics and Astronomy, UMaine Adjunct Scientific Staff Member, TJL
- Jin Kim Montclare, Ph.D., currently at California Institute of Technology, Research Assistant Professor, IMB, Assistant Professor (Tenure Tract), Department of Chemical and Biological Engineering or Department of Chemistry, UMaine, Adjunct Staff Member, TJL

(5) Recruitment of an executive assistant to carry out administrative tasks: (female, Caucasian, full-time salaried employee of IMB)
- Kate Merritt, Administrative Assistant, IMB (hired February 19, 2004)

(6) Identify necessary instruments and insure access to facilities that are deemed to be critical:
- 3,000 square foot clean room, MEMS microfabrication facility, located on UMaine campus ($820,000; completion û 5/2004))
- Axial tomography ($60,736) PO#U23784-01
- Zeiss microscope ($85,444) PO#U242037
- Spectromicroscopy/Microscopy measurements @ Synchrotron Storage Ring ($52,600)PO#U243289 (12/01/03-06/30/04)
- Computer simulations of mouse nuclear genome (E15,900) PO# U240359 (10/15/03-06/15/2004)

(7) Develop a research agenda:

The general research agenda was described in the original application and included intracellular structures and dynamics, functional materials, and biocomputing. This has been refined further to include: genome architecture in the nucleus; cellular biophysics with focus on nanostructures, biological interfaces, application of nanostructures to cell adhesion and cell mechanics, and biomimetics of cell functions; X-ray microscopy and spectroscopy of cells and tissue; and nanoparticles, quantum dots, and biopolymers to track intracellular processes. A more specific research agenda was influenced by the interests of the scientists who join IMB. Senior scientists associated with IMB developed an NIH Planning Grant (P20), which will result in a detailed plan for implementing specific research projects.

(8) Educate the research and academic communities of the mission of IMB:
Numerous lectures and seminars have been given by the Founding Director to national and international audiences. A national and international position solicitation was posted in the spring, and applications were evaluated in July 2003. All of the scientists being offered positions have given lectures at UMaine, TJL, and MMCRI. This has resulted in great visibility for IMB and its research mission.

The Founding Director and members of the IMB collaborated on the 'Advances in Nanostructural Genomics III' conference, which took place October 16-18, 2003 (http://www.jax.org/courses/nano 03.html).

(9) Formulate an outreach and public education plan:
(please see section 4. Outreach Activities)

(10) Sustainability of IMB:
Grants management officials from MMCRI, TJL, and UM have developed standard operating procedures for including cooperating institutions into grant proposals originating from a sponsoring (host) institution (e.g., subcontracts). Written procedures have been developed, approved by the Institute Policy Committee (IPC), and provided to Drs. Michael Grunze and Deirdre Mageean. The intent is to insure that grant-related expenses of cooperating institutions are appropriately reimbursed by the granting agency. Concerns over finding adequate space for IMB have been discussed. It was decided to use the Maine Biomedical Research Coalition/University of Maine System Committee to advance this issue. UM has made IMB its primary space priority to this group, and TJL and MMCRI are supportive.

A meeting was scheduled for members of IPC, IMB Executive Committee members, and Drs. Michael Grunze and Deirdre Mageean on March 11, 2004 in order to develop operational amendments to clarify the original MOU and to begin to lay-out the sources of revenue to support IMB after completion of the EPSCoR (April 2006). These recommendations were forwarded to the Executive VP and Provost and President of UM for approval.

Year Two Activities:

Summary: The major research and education activities of the project in Year Two were to (1) develop the administrative infrastructure of the IMB and hire Co-Directors; (2) renovate laboratory and office space for the IMB in the Department of Chemical and Biological Engineering at UMaine; (3) recruit senior, mid-level, and junior scientists; (4) continue to develop and implement a research agenda focusing on intracellular dynamics and structure, functional materials, and biocomputing; (5) apply for external funding to support the continuing mission of the IMB; (6) continue the planning process to insure the long-term sustainability of the IMB; (7) establish national and international collaborations; (8) provide training opportunities for undergraduate and graduate students and for postdoctoral fellows; (9) equip the individual laboratories of the newly-hired scientists for cutting-edge research; (10) mentor the newly-hired scientists as they establish their laboratories, write individual and group grants and papers, and take on teaching and training activities; (11) establish a weekly work-in-progress seminar series on interactive TV between UMaine, TJL, MMCRI, and the University of Heidelberg; (12) establish biennial meetings of the entire IMB staff; (13) conduct the annual meeting of the Scientific Advisory Board; (14) establish an IMB-funded position at MMCRI; (15) continue to develop and expand outreach activities; (16) disseminate research findings.

Detailed explanation of activities: (see above summary)
(1) Develop the administrative infrastructure of the IMB and hire Co-Directors:
The IMB Memorandum of Understanding between the three organizations (UMaine, TJL, MMCRI) was revised and updated in June 2004. Criteria and policies for IMB membership were drafted in September 2004. Dr. Michael Grunze (UMaine & University of Heidelberg) and Dr. Barbara Knowles (TJL) were offered, and accepted, concurrent positions as co-Directors of the IMB in August 2004. Their four-year appointments began September 1, 2004. Vicki Nemeth, UMaine Research Programs Administrator and EPSCoR Project Administrator, was hired July 1, 2004, and has worked with the Project Director, Co-Directors, and the IMB Executive Assistant to ensure that administrative procedures are effectively in place for all aspects of the new organization.

(2) Renovate laboratory and office space for the IMB:
The research facilities of the Institute have grown steadily since its inception. The laboratory space at The Jackson Laboratory was officially

opened in May 2004, and was well received by the general public and representatives of the Congressional Delegation. It includes a fully outfitted cell culture facility, six lab areas for faculty and visiting scientists, an internal high-capacity computing network, and two microscopy rooms. The recently acquired super-high resolution 4pi prototype nanoscope (Leica) will be housed in one of these rooms. Research collaborations to unlock the architecture of the mouse genome and to explore the transition of stem cells to tumor cells are already underway, and will be the first projects to challenge the power of the nanoscope. The other room is occupied by the prototype microaxial tomograph, developed through collaboration between one of our geneticists and one of our optical physicists. This novel instrument can image the nucleus of whole cells at high resolution, and allows scientists to examine areas of interest within a cell without distorting its contents.

The facilities at the University of Maine were completed in August 2004 and house a 2-photon confocal microscope, a prototype spectromicroscope, and fluorimetry, synthetic chemistry, and biochemistry laboratories. Our physical sciences faculty are currently developing novel instrumentation that combines Raman and fluorescence imaging to provide simultaneous structural and dynamic information of samples of interest. Our biosciences faculty are using high-resolution techniques to examine the location and clustering of proteins in cell membranes to better understand how cell receive and convert the signals that determine what type of cell they will become.

The Jackson Laboratory, (subcontracted)
- Three offices (all currently occupied)
- 2,300 square feet of laboratory space (completed and opened May 2004)
- 436 square feet of confocal microscope space (completed March 2005), with an additional 500 square feet of space set to be renovated in Year3

University of Maine
- Four offices (three currently occupied)
-500 square feet of laboratory space dedicated to biological imaging and prototype instrument development (completed August 2004)
- 400 square feet of additional laboratory space for wet lab and cell culture preparation and experiments (completed August 2004)
- access to 3,000 square feet clean room MEMS microfabrication facility in the Department of Chemical and Biological Engineering

(3) Recruit senior, mid-level, and junior scientists:
The following researchers were salaried members of the IMB:
- Michael Grunze, Ph.D., IMB Co-Director and Co-Principal Investigator (1/2 time appointment September 1, 2004ûApril 30, 2006); Cooperating Professor, Dept. of Physics and Astronomy, UMaine; Adjunct Scientific Staff Member, TJL; Professor of Physical Chemistry, University of Heidelberg.
- Barbara Knowles, Ph.D., IMB Co-Director and Co-Principal Investigator (1/3 time appointment from September 1, 2004 û August 31, 2007), VP for Training, Education and External Scientific Collaborations, TJL, University Professor, UMaine
- Wolfgang Eck, Ph.D., IMB Visiting Research Associate Professor, UMaine; University of Heidelberg.
- Michael D. Mason, Ph.D., IMB and Assistant Professor of Chemical and Biological Engineering, UMaine
- Anja Nohe, Ph.D., IMB and Assistant Professor of Chemical and Biological Engineering, Cooperating Assistant Professor, Dept. of Biochemistry, Microbiology and Molecular Biology, UMaine
- Lindsay S. Shopland, Ph.D., IMB Research Assistant Professor, Cooperating Assistant Professor, Dept. of Biochemistry, Microbiology and Molecular Biology, UMaine; Research Associate, TJL

National searches have continued to be conducted for possible hires. In our hiring practices, we strongly encourage women and minorities to apply. In addition, UMaine's Equal Employment Opportunity Office has funds available to aid in attracting under-represented groups by augmenting salaries

In addition, the IMB membership includes the following researchers in the specified roles:
- Robert Friesel, Ph.D., MMCRI û Co-Principal Investigator & Executive Committee member
- David Neivandt, Ph.D., UMaine û Adjunct member
- Tim O'Brien, Ph.D., Cornell University û Adjunct member
- Christoph Cremer, Ph.D., University of Heidelberg û Adjunct member
- Sam Hess, Ph.D., Physics, UMaine û Adjunct Member
- Carol Kim, Ph.D., Biochemistry, Microbiology, and Molecular Biology, UMaine û Adjunct Member
- Jay Nadeau, Ph.D., McGill University û Adjunct Member
- David Neivandt, Ph.D., Chemical and Biological Engineering, UMaine û Adjunct Member
- Joachim Spatz, Ph.D., University of Heidelberg û Adjunct Member
- Rob Burgess, Ph.D., TJL û Collaborating Researcher
- Alexei Eviskov, Ph.D., TJL û Collaborating Researcher
- Igor Prudovsky, Ph.D., MMCRI û Collaborating Researcher
- Doug Spicer, Ph.D., MMCRI û Collaborating Researcher

- Calvin Vary, Ph.D., MMCRI û Collaborating Researcher
- Volkhard Lindner, Ph.D., MMCRI û Collaborating Researcher
- Robert Lad, Ph.D., LASST, UMaine û Executive Committee member, Collaborating Researcher
- Paul Millard, Ph.D., UMaine û Collaborating Researcher
- Ed Leiter, Ph.D., TJL û Collaborating Researcher
- Simon John, Ph.D., TJL û Collaborating Researcher
- Carol Bult, Ph.D., TJL û Collaborating Researcher
- Gopal Chada, Ph.D., UMaine û postdoc
- Kim MacEwan, Ph.D., UMaine û postdoc
- Johann von Hase, Ph.D., University of Heidelberg û visiting postdoc at TJL
- Andre Kahlil, Ph.D., McGill University û postdoc
- Tamas Haratzi, Ph.D., University of Heidelberg û postdoc
- Kevin Mills, Ph.D., TJL û Collaborating Researcher
- Shaoquang Li, M.D., Ph.D., TJL û Collaborating Researcher

Administrative participants include:
- Michael Eckardt, Ph.D., V.P. for Research, UMaine û IMB Principal Investigator and IPC member
- Deirdre Mageean, Ph.D., Associate V.P. for Research and Dean of the Graduate School, UMaine û IMB Co-Principal Investigator
- Rick Woychik, Director, TJL û IPC Committee member
- Kenneth Ault, Director, MMCRI û IPC Committee member
- Robert Kennedy, President, UMaine û administrative oversight
- Vicki Nemeth, Research Programs Administrator/EPSCoR Project Administrator, UMaine
- Kate Merritt, Executive Assistant to the Directors, IMB, UMaine
- Angela Hildreth, Administrative Assistant (22% of time) (contracted as of August 1, 2004)

(4) Develop and implement the research agenda:
(please also see section 2. Major Findings from Activities)
The general research agenda was described in the original application and included intracellular structures and dynamics, functional materials, and biocomputing. This was refined further to include: genome architecture in the nucleus; cellular biophysics with focus on nanostructures, biological interfaces, application of nanostructures to cell adhesion and cell mechanics, and biomimetics of cell functions; X-ray microscopy and micro-spectroscopy of cells, organelles, and tissue; and nanoparticles, quantum dots, and biopolymers to track intracellular processes.

Our projects have not only increased the research at each participating institution, but they have also increased the level of cooperation between these institutions. Currently, members of the Institute at each location are developing a program to study the nanoscale architecture of the cell and a second, parallel program to synthesize nanoprobes specific to cellular proteins to increase the efficiency and resolution of current imaging techniques (NSF NIRT). Additionally, Institute members are using high resolution spectromicroscopy to explore genetic markers of glaucoma. Moreover, some of our members are working in cooperation with Evident Technologies to develop novel nanoprobes for detecting the onset of cancer.

(5) Apply for external funding to support the continuing mission of the IMB:
IMB members collaborated to submit two grants: NIH COBRE: 'Nanotags for Nuclear & Membrane Architecture' (not funded) and NSF NIRT: 'Probes for Subcellular Nano-architecture' (pending). These grants sought to combine the research focus areas above under the umbrella of developing nanoscale tools to investigate cell surfaces and genome architecture.

Drs. Knowles, Grunze, and Cremer submitted a grant to NSF and a matching grant to the Keck Foundation to obtain a 4-Pi confocal laser scanning microscope and a multiphoton microscope, and to fund an optical physicist to work with the biologists using the 4-Pi microscope. These grants were awarded, the multiphoton microscope has been installed in TJL's microscopy core service, Dr. Joerg Bewersdorf, a young optical physicist, has been hired to arrive June 15, 2005, and the scheduled delivery date for the 4-Pi microscope is June 1, 2005.

Several grants were submitted in January 2005: Drs. Mason, Hess, Neivandt, and Grunze submitted a collaborative grant to NSF for the development of a hybrid scanning multiphoton fluorescence and sum-frequency spectroscopy imaging microscope (pending); Dr. Lindsay Shopland submitted an NSF grant for 'Relating Gene Clustering in Primary Sequence with 3-D Nuclear Structure and Function' (pending) and two NIH 1 R01 grants, one for 'Chromatin Structure during Spermatogenesis' and the other for 'Functional Organization of Gene Clusters in Nuclei'; and Dr. Anja Nohe submitted an NIH grant for the 'Role of CK2 and Endoglin in Bone Morphogenetic Protein Signaling' (pending). In addition, an NIH K08 grant application by Dr. Samuel Hess was favorably reviewed and is expected to be funded during the next granting period. Dr. Jay Nadeau transferred a grant from Cal Tech to TJL, which is currently supporting her IMB work. Drs. Grunze and Leiter submitted a proposal to the Juvenile Diabetes Foundation to build a novel instrument to measure non-invasive glucose in mice and rats

(pending).

IMB members have at least five more planned grant submissions in the coming year. The directorate is currently establishing a peer review committee for Institute members who wish to submit individual or collaborative grants affiliated with the IMB.

(6) Continue the planning process to insure the long-term sustainability of the IMB:
In addition to an overall and on-going strategy process addressing IMB sustainability, several specific actions are being considered: discussion is underway regarding operating the 4 Pi scope as a user facility, providing access to outside scientists; space considerations are being looked at, as current facilities are at maximum usage; strategies to teach joint courses with the University of Heidelberg via the Internet are being looked at.

(7) Establish national and international collaborations:
(please also see Project Participants, item #3)
The Institute has developed a key collaboration with our international partner, the University of Heidelberg. With scientists from the laboratories in Germany, we are developing nanoprobes to study the oocyte-to-embryo transition, creating nanostructured surfaces to investigate the development of the neuromuscular junction, and modifying, adapting, and enhancing current high resolution imaging techniques for biological samples. Researchers from Maine have traveled to Germany for specific training, and several visiting researchers and students from Germany have been placed at TJL to work with IMB members. Other collaborations include McGill University,

(8) Provide training opportunities for undergraduate and graduate students and for postdoctoral fellows: (please see section 3. Opportunities for Training & Development)

(9) Equip the individual laboratories of the newly-hired scientists for cutting-edge research:
In addition to basic lab equipment, the following major equipment has been purchased and is housed either at UMaine or TJL: a 2û photon confocal microscope; a single photon time-correlated fluorescence Raman spectromicroscope (custom built); Langmuir Blodgett trough and plasma etcher for nanoparticle synthesis & structured surfaces research; Zeiss axioplan two-fluorescence microscope custom-equipped for microaxial tomography; 4-Pi confocal scanning microscope.

(10) Mentor the newly-hired scientists as they establish their laboratories, write individual and group grants and papers, and take on teaching and training activities. Our new teaching and research faculty have been actively participating in regular IMB meetings, and have begun numerous internal and external collaborations. Some of these collaborations have resulted in grant submissions; others are related to cooperative efforts to expand knowledge and development of new laboratory techniques. IMB members have expressed a great deal of enthusiasm in learning beyond their field, and sharing their knowledge, abilities and equipment with other interested members.

(11) Establish a weekly work-in-progress seminar series:
The IMB has held regular weekly inter-institutional faculty meetings and seminars by videoconference since July 2004. This encompasses IMB members at UMaine, TJL, MMCRI, and the University of Heidelberg.

(12) Establish biennial meetings of the entire IMB staff;
A conference entitled 'Advances in Nanostructural Genomics IV' took place at The Jackson Laboratory, September 9-12, 2004 and was organized by IMB faculty. Additionally, IMB members organized a colloquium entitled 'Nanotechnological Approaches for Studying the Neurobiology of the Laboratory Mouse,' which was held March 2-4, 2005.

(13) Conduct the annual Scientific Advisory Board meeting:
The following members were recruited for the IMB Scientific Advisory Board (SAB), which reviews scientific progress and make recommendations on the scientific structure and direction of the IMB:
- Daniel Auerbach, Ph.D. (General Physics and Computation), IBM
- Benjamin Geiger, Ph.D. (Cellular Biophysics), Weizman Institute
- Peter Goodfellow, Ph.D. (Genetics & Industry Liaison), SmithKline/Glaxo
- R³diger Iden, Ph.D., BASF
- Janos Kirz, Ph.D. (Synchrotron Radiation Research), SUNY at Stony Brook
- Buddy Ratner, Ph.D. (Biomaterials), University of Washington
- Gabor Somorjai, Ph.D. (Surface Physics and Spectroscopy), UC Berkeley
- Roel van Driel, Ph.D. (Imaging), University of Amsterdam
- Viola Vogel, Ph.D. (Molecular Motors), ETH Zurich
- Horst Weller, Ph.D. (Nanoparticles and Quantum Dots), Hamburg
- George Whitesides, Ph.D. (Biological Chemistry), Harvard

The first meeting of the SAB was held by telephone on October 30, 2003 (all members attending), to discuss hiring of IMB faculty and administrative matters. This was followed by a meeting at the new IMB facilities at TJL on September 12-14, 2004, with seven of the members attending. Our faculty presented their current research, and the SAB toured our facilities at TJL and UMaine. Their report was presented to UMaine's Vice President of Research and Project Director, Michael Eckardt, and indicated that 'Overall the SAB had a very favorable impression of the quality of the work we heard. There was evidence of excellent science and novel instrumentation, and strong collaborations are already established. We were also impressed with the high quality of the recent hires to the IMB and its related positions. Strong international involvement exists and is being effectively leveraged.' The SAB noted that there were still administrative issues involved in establishing the IMB between three separate places, and cautioned that the institutions involved should guarantee stability for the faculty for at least four years. They also advised the Co-Directors to focus the mission of the institution more narrowly.

(14) Establish a funded position at MMCRI:
Negotiations are currently underway to fund an IMB position at MMCRI under a sub-contractual arrangement in Year 3.

(15) Continue to expand outreach activities:
(please see section 4. Outreach Activities)

(16) Disseminate research findings:
IM faculty organized a conference entitled 'Advances in Nanostructural Genomics IV' at TJL, September 9-12, 2004. In addition, our faculty have presented at many national and international meetings this year. In addition to 28 presentations throughout the year, Dr. Grunze gave a major presentation at the annual meeting of the American Society for Science and Technology in the fall of 2004, where he featured work done by IMB faculty.

Dr. Nohe has presented at the following: Feb. 2005, Biophysical Society, Long Beach, CA - Dynamics of Caveolin-1 isofomrs; Nov. 2004, CHI signal transduction, Boston - Dynamics of BMP receptors on the cell surface and implication to signal transduction; Sept. 2004, Structural Nanogenomics at the Jackson laboratory - Dynamics of Caveolin 1 isoforms; Aug. 2004, University of Wuerzburg, Germany -Role of BMPs in heterotopic ossification, Radiation Therapy; Aug. 2004, Semasopht, Lausanne, Switzerland - Single Particle Tracking. She has also been involved with:
Organizing Committee, Canadian Chemical Biophysical Symposium, Toronto, Canada; Organizing Committee, 'Expanding you Horizons' Women in Engineering, UMaine; Co-Chair of the Platform 'Membrane Dynamics and Bilayer Probes, ' Biophysical Society, Long Beach, U.S.A. She has also been invited to write a paper for Science STKE, and a book chapter on the effect of radiation on bone formation.

Dr. Shopland has presented at the following: MBMSS, Mount Desert Island Biological Laboratory, April 2004, poster, 'Linking primary sequence with 3-D structure: nuclear organization of gene clusters and deserts'; Nanostructural Genomics IV, The Jackson Laboratory, September 2004, invited speaker, 'Linking primary sequence with 3-D structure: nuclear organization of gene clusters and deserts'; Dynamic Organization of Nuclear Function, Cold Spring Harbor Laboratory, October 2004, speaker, 'Linking primary sequence with 3-D structure: nuclear organization of gene clusters and deserts.'

Year Four Activities:

Summary:
The major research and education activities of the project in Year four were to (1) further develop the administrative infrastructure of the IMB to provide for long term sustainability; (2) Recruit senior and junior membership to strengthen the focus areas of excellence of the IMB. (3) renovate the IMB laboratories at UMaine in the department of Chemical and Biological Engineering, (4) apply for external funding to promote intra institute collaborations and support, (5) implement and strengthen three focus areas of excellence, (6) plan for the long term, sustainability of the IMB, (7) provide training opportunities for young scientists, both student and post graduate, (8) disseminate research activities and add technical significance to the scientific database.

Detailed explanation of activities: (see above summary)
(1) Further develop the administrative infrastructure of the IMB: In September of 2007, with Michael Grunze retirement as co-director of the IMB due to health reasons, Professors Rosemary L. Smith and Scott D. Collins (UMaine) were appointed as co-directors of the IMB to assist Barbara Knowles (TJL). The co-directors, in consultation with the Institutional Policy Committee, developed a strategic plan for the future sustainability of the IMB and to facilitate a smooth transition from the NSF EPSCoR grant to alternative funding sources. This plan outlines three strategic imperatives to foster the IMB's continued growth as an internationally recognized institution: I. Establish a seamless, interactive research/training team within Maine, II. Build a critical mass in our areas of excellence: microscopy and spectroscopy, functional materials and

probe development, biocomputing, and bioengineering to establish the IMB as a unique, well-funded research identity, III. Expand formal collaborations beyond Maine to solidify the IMB's international research reputation.
I. Interactive research/training team. The IMB has made significant strides in creating a cohesive and interactive research team. The fourth year finds a solidification of the interdisciplinary and inter-institutional research collaborations initiated in years 1-3 resulting in tremendous growth in productivity (see sections below on publications and grants). The administrative policies which produced these results are a). active recruitment of eager and highly qualified researchers and b). individual mentoring of new hires by established faculty on issues such as grant and publication submissions and interdisciplinary opportunities. The interactive weekly seminar series at which IMB members present current research and discuss grant opportunities has been a key administrative tool in educating members, promoting collaborations and creating cohesion in the group. These seminars educate the IMB membership in divergent fields and produce active discussions on problems and unique applications in biology and biophysics. These weekly meetings in combination with the winter colloquium and summer international scientific meeting brings all IMB scientists together
II. Three focus areas of excellence.
The IMB administration has selected three focus areas of excellence to enhance. a). High Resolution Microscopy, b). Nanoscale Spectroscopy, and c). Nanosystems Development. (for a complete description see below). These are current strengths of the IMB and the administration has targeted them for further growth with international recognition. The IMB focus areas have already produced fruit. One technique developed at the IMB, high resolution microscopy (FPALMùHess and Mason), has been cited by Science magazine as one of the ten most promising optical techniques of 2007.
III. Expand international collaborations.
The IMB has successful, established collaborations with researchers at McGill University, L'Ecole Superiure de Lyon, and University of Heidelberg, who actively collaborate with IMB members on specific research projects and participate in the IMB functions. McGill University adds an expertise in nanoparticles; L' Ecole Normale Superieure de Lyons expands IMB's capabilities in data and imaging processing, while the University of Heidelburg has been invaluable in providing expertise in optical microscopy. Currently, the IMB is in discussion with the Weismann Institute in Israel to further enhance its expertise resources.

(2) Recruit senior and junior membership: An extensive recruitment effort has produced an increase in the active membership of the IMB, with the following recent additions:
-Susan Ashworth, Research Scientist, Dept. of Chemical and Biological Engineering, UMaine, Kidney membrane functions.
-Rosemary Smith, Professor, Dept. of Electrical and Computer Engineering, UMaine, Micro and Nanosystems.
-Scott Collins, Professor, Dept. of Chemistry, UMaine, Micro and nanosystems
-Alain Arneodo, Professor, l'Ecole Superiure de Lyon, Image analysis
-Michael Wiles, Associate Research Scientist, TJL
-Anne Peaston, Research Scientist, TJL
-Anthony Nicholson, Associate Research Scientist, TJL, behavioral physiologist
-Robert Burgress, Staff Scientist, TJL, Axonal growth
-Joerg Brewersdorf, Research Scientist, TJL, Optical microscopy, 4pi.
-Robert Gunderson, Professor, Dept of Biochemistry, Microbiology, and Molecular Biology, UMaine, Membrane phenomena.

(3) Renovate the IMB laboratories: The IMB facilities located within the Department of Chemical and Biological Engineering were completed in the four year. This included and new DI water supply and renovation of the laboratories of Anja Nohe and Mike Mason. Currently, discussion are under consideration to expand the facilities resources of the IMB by affiliation with the recently established Graduate School of Biological Sciences at UMaine and/or the Laboratory for Surface Science and Technology.

(4) Apply for external funding: Members of the IMB have actively applied for external funding to support the interests of the institute. In the fourth year of the grant, IMB members had 14 active grants totaling $3,192,865.00, and submitted 25 proposals 15 of which are still pending. Of particular importance is the submission of several large multi investigator, multi-institutional proposals that unite the IMB with a single goal.

The following is the list of active grants during Year 4:
PI Nohe, A. R56, NIH, Role of CK2 and Endoglin in Bone Morphogenetic Protein Signaling. Total $79,091, August 2006- July 2007.
PI Nohe, A. Preventive & Therapeutic Effects of Vitamin D3 in Neoplastic Cells Maine Cancer Foundation Total: $76,206, July 2006 - June 2007.
PI Wesley Beamer, Co-PI Nohe, A. NIH, Genetic and Dynamic Analyses of Peak Bone Density. $209,000. August 2006 - July 2010.
PI Mayer G. Co-PI's Nadeau J., Smorodin V. and Nohe, A. EPA. Nanoparticle Toxicity in Zebrafish US Award anticipated. Total $399,000, April 2007 -March 2010.
PI Nohe, A. In Vivo Models to Study IGF-1.Receptor Dynamics in Bone Stem Cells, American Society for Bone and Mineral Research. Total $38,500, July 2007 - June 2008.
Stryker Orthopaedics. (I. Dickey, D. Donohue, A. Nohe, M. Mason, & A. Khalil (PIs)). 6/1/06-6/1/07 Artificial Bone Implant Research. Total

155,843.82 Nohe $22,922. July 2006 - January 2007
PI: S. Hess, The Role of Rafts in Virus- Induced Membrane Remodeling National Institutes of Health (NIAID), The grant is a 5-year award for $662,730.
PI: Mason, CoPI: Grunze, CoPI: Hess, CoPI: Neivandt, National Science Foundation 'MRI: Development of a Hybrid Scanning Fluorescence and Sum-Frequency Spectroscopy Imaging Microscope' $728,102.
PI: Lindsay Shopland, Role of Chromosome Rearrangement in Lymphoma Nuclei, Maine Cancer Foundation, $75,000, 2006-2008
PI: Mason, CoPI: Allen, CoPI: Eck, Sloan Kettering Cancer Center 'Pancreatic Cancer Detection using Engineered Metallic Nanoparticle Conjugates' $63,564.
PI: Donahue, CoPI: Mason, CoPI: Khalil, Stryker Biomedical 'Foam Metal bone transplant ingrowth image analysis' $155,843.
Co-PI Nadeau, Nanoparticle Toxicity in Zebrafish, EPA, $398,298, 10/06-9/08
Co-PI Nadeau, Bioavailability and Fates of CdSe and TiO2 Nanoparticles in Eukaryotes and Bacteria, EPA, $399,986, 10/06-9/09
PI Nadeau, Selected targeting and destruction of malignant cells using redox-sensitive quantum dots, CIHR, $150,000, 02/07
PI Cremer 3D Genome and Function (STREP), European Union, 265,075 Ç, 01/01/2003 û 11/30/2006
PI Cremer Extension of a Spatially Modulated Illumination Microscope for the Optical Analysis of Active Chromatin Complexes, Deutsche Forschungsgemeinschaft (DFG)
Total support ca. 900,000Ç. 04/01/2003 û 03/31/2009
PI Cremer (Project Coordinator) Coordination of the DFG-Priority Programme 1128 'Optical Analysis of the Structure and Dynamics of Supramolecular Biological Complexes' Deutsche Forschungsgemeinschaft (DFG), ca. 15 Mio Ç, 04/01/2003 û 03/31/2009
PI Cremer Light Optical Nanoscopy of Cellular Structures using 4Pi-Microscopy,
Deutsche Forschungsgemeinschaft (DFG), 950,000 Ç, 12/07/2004 - present
PI Cremer Integrated Technologies for in-vivo Molecular Imaging, European Union 408,530 Ç, 01/01/2004 û 12/31/2008
PI Cremer Biocomputing of radiation risk on the basis of nuclear genome structure data, European Union, 200,000 Ç, 01/01/2004 û 31/07/2008

PI Cremer (associated) Cellular Networks: From Molecular Mechanisms to Quantitative Understanding of Complex Functions, Deutsche Forschungsgemeinschaft 30 Mio Ç, 01/01/2007 û 12/31/2011
PI Knowles A Consortium for the Acquisition of a 4Pi-Confocal Laser Scanning Microscope National Science Foundation, $685,580 9/01/04-8/31/07
Co-PI Knowles Comparative Functional Genomics INBRE in Maine, NIH/NCRR, 7/1/04-6/30/09
Co-PI Knowles Cancer Center Support (Core) Grant , NIH/NCI, 1/1/07-1/31/12
PI Knowles Translation and Transposons in Mammalian Development, NIH/NICHD, $986,755 1/1/04-12/31/08
PI Knowles IGERT: Predoctoral Training in Functional Genomics of Model Organisms, National Science Foundation, 12/1/02-11/30/07
PI: Knowles REU Site: Functional Genomics Research Projects for Undergraduates National Science Foundation, $261,300, 05/15/05-04/30/08
PI Knowles Methods in ES Cell Research, NIH/NHLBI, $277,594 7/01/06-6/30/09
PI Knowles Experimental Genetics of the Laboratory Mouse In Cancer Research, NIH/NCI, $448,737, 07/01/06 û 06/30/11
PI Grunze Neutron Reflectometer for in situ characterization of biological interfaces BMBF 1,304,660.00Ç 7/1/07-6/30/10
PI Grunze X-ray in line holography for cell biology BMBF 411,668.00Ç 7/1/04-6/30/07
PI Grunze Digital In-Line holography on biological samples BMBF 629,400.00Ç 7/1/07-6/30/10
PI Grunze X-ray spectroscopy on biological samples BMBF 183,442.00Ç 4/1/04-6/30/07
PI Grunze 'Neutronenreflektrometrie zur Struktur-/Funktionsanalyse biomedizinisch relevanter Grenzflõchen' 212,557.00Ç 7/1/04-12/31/07
PI Grunze CeloNova BioSciences Matterials Research DFG 46,215.58Ç 10/1/06-9/30/07
PI Grunze Computer-Simulation Hydration forces in phospholipid bilayers DFG 264,700.00Ç 5/1/07-1/1/10
PI Grunze Computer-Simulation Hydration forces in phospholipid bilayers DFG 75,400.00Ç 6/1/06-5/31/07
PI Grunze Co-operation MPI Berlin IR Microscopy on whole cells 39,200.81Ç 1/1/04-7/1/07
PI: Burgess ALS Association Mitochondrial Involvement in SOD1 Mediated Neuron Loss $39,660 8/1/06 - 7/31/07 Active.
PI: Burgess A. Parseghian Med Research Fdn Characterization and Development of a new mouse model of Niemann-Pick Type C (NPC) Disease $5,000 5/1/06 - 4/30/07 Completed.
PI: Burgess NINDS A Mouse Mutation Causing Progressive Cerebral Ischemia $251,114 4/6/05 - 2/28/08 Active.
PI: Burgess NINDS Genetics of the Neuromuscular Junction: Mechanisms and Disease Models $900,000 9/5/06 - 8/31/10 Active.
PI: DeVries ACS Determining Disease Progression with Loss of Beta-Catenin in a Mouse Mammary Tumor Model $30,000 3/1/07 - 2/29/08 Active.
PI: Eck Volkswagen Fdn Preparation, Characterization and Applications of Free-Standing Unimolecular Nanosheets $188,361 8/1/06 - 7/31/09 Active.
PI: Mills ELLIS New Scholar in Aging Award $200,000 12/1/06 - 11/30/10 Active.
PI: Mills NCI Molecular Mechanisms of Lymphomagenesis $710,000 8/1/06 - 7/31/10 Active.
PI: Mills VFOUN Homologous Recombination in Genome Stability and Tumor Suppression $100,000 12/1/05 - 11/30/07 Active.
PI: Peaston KOMEN Mammary Cancer Stem Cells $200,000 5/1/06 - 4/30/08 Active.
PI: Bult NIH Biochemical Database for the Mouse $145,650 04/01/06-01/31/09

PI: Bult NIH Computational Biology Resources $192,007 03/01/05-02/28/09
Project Leader: Bult NIH Mouse Genome Informatics $477,362 08/01/06-07/31/11

Proposals Pending or Denied in Fourth Year:
PI Smorodin, Co - PI Nohe A. NSF, Surface Thermodynamics of Domains in Lipid Films, Total 788,432,$315,373. Pending
PI Nohe, Co-PIs Calvin Vary and Wesley Beamer NIH., RO1 A2. Role of CK2 and Endoglin in Bone Morphogenetic Protein Signaling. Total $1.858,609, 1.858,609, Denied
PI Smorodin, V. Co-PI Nohe A. Structural-Functional Aspects of Heterogeneity of Lipid Membranes. US Dept of Health & Human Services. Total $1.838,167 $459,542. Pending
PI's: Ian Dickey, Anja Nohe, Darrell Donahue, Scott Collins, Robert Lad, Rosemary Smith. Emerging Area Grant, University of Maine. Soft tissue in-growth in highly porous foam metals (Foam Metals Implant Group). $1.250.000. Pending
PI: B B. Knowles, Probing Stem Cell Reprogramming at the Nanoscale US Dept of Health & Human Services through Co- PI 20 $3,316,583 35 9/14/2006 Denied
PI: S. Hess, Quantification of Membrane Organization Induced by Viral and Cytoskeletal Protei, US Dept of Health & Human Services, $1,804,873 59 Pending
PI: Igor Prudovsky, Release of FGF1 and pathology of angiogenesis, NIH, R01, 1,250,000 Pending
PI: Igor Prudovsky, Oncogenic potential of Notch-regulated FGF1 release, Maine Cancer Foundation, $86,147 Pending
PI: Samuel Waxman Co-PI: Igor Prudovsky, Nuclear envelope and chromatin composition in myeloid leukemia Cancer Research Foundation, 345,000 Pending
PI: Igor Prudovsky, Mechanism and angiogenic effect of thrombin-induced FGF release, NIH, R21, 250,000, 2006, Denied.
PI: Joerg Brewersdorf, MRI: Development of a Fast Three-Dimensional Particle-Tracking Fluorescence Microscope for Live-Cell Imaging, NSF, $1,115,137, Pending
PI: Joerg Brewersdorf, NIH-Director's New Innovator Award Program: 03-Challenging Microscopy Limitations: Molecular 3D Resolution in Space and Time, NIH, $1,500,000, Pending
PI:Ng (PI), CoPI: Mason, National Institutes of Health 'R01: Immunotoxicological studies of noble-metal Nanoparticles' $501,350. Pending
PI: Mason, CoPI: Khalil, Stryker Biomedical 'Foam Metal bone transplant ingrowth image analysis' $201,000. Pending
PI: Wise, CoPI: Mason, National Institutes of Health 'R01: Silver and Gold Nanoparticle Genotoxicity and Carcinogenicity in Human Lung and Skin Cells', $501,350. Pending.
PI: Mason, CoPI: Grunze, CoPI: Hess, CoPI: Neivandt, National Science Foundation 'MRI: Development of a Hybrid Scanning Fluorescence and Sum-Frequency Spectroscopy Imaging Microscope' $728,102. Denied
PI: Wise, CoPI: Mason, Department of Defense 'Depscor: Genotoxicity and Carcinogenicity of Metal Nanoparticles' $544,252. Pending
PI: Ng, CoPI: Mason, National Institutes of Health 'Effects of nanoparticles on immune and respiratory systems' $275,000. 2006, Denied.
PI: Ng, CoPI: Mason, Environmental Protection Agency 'Cytotoxic and Proinflammatory Effects of Gold Nanoparticles on Immune and Lung Cells' 2006, $200,000. Denied.
PI: Wise, CoPI: Mason, Environmental Protection Agency 'Genetic Toxicology of Gold Nanoparticles in Human Lung Cells' $400,000, 2006. Denied
PI: Wise, CoPI: Mason, Department of Defense 'Genotoxicity and Carcinogenicity of Metal Nanoparticles' $500,000, 2006 . Denied
PI: Mason, CoPI: Eck, National Institutes of Health 'Single nanoparticle Localization and dynamics by Time-Resolved Spectral Imaging' $551,807, 2006. Denied
PI: Grunze, CoPI: Hess, CoPI: Mason, CoPI: Neivandt, National Science Foundation 'MRI: Development of a Hybrid Scanning Fluorescence and Sum-Frequency Spectroscopy Imaging Microscope' $964,730, 2006. Denied
PI: Nadeau, Quantum dot conjugates as sensors of intracellular processes, NIH, $500,000, 2006. Denied
PI: Evsikov NICHD Visualizing Embryonic Genome Activation $800,000 12/1/07 - 11/30/11 Pending.
PI: Shopland ACS Role of Genome Instability in Regional Deregulation of Gene Expression in Lymphoma $27,500 2/1/07 - 1/31/08 Denied.
PI: Evsikov NICHD Visualizing Embryonic Genome Activation $800,000 4/1/06 - 3/31/10 Denied.
PI: Burgess NINDS Genetics of the Neuromuscular Junction: Mechanisms and Disease Models $1,250,000 12/1/05 - 11/30/10 Denied.
PI: Bewersdorf NIBIB Frontiers in Microscopy II Meeting $10,000 7/1/07 - 6/30/08 Denied.
PI: Burgess NIH Adhesion and Matrix Molecules in the Neuronal Development of the Retina $1,250,000 12/1/07 - 11/30/12 Denied.
PI: Burgess NIH Agrin in Synapse Formation $1,250,000 7/1/06 - 6/30/11 Denied.
PI: Burgess NIH Agrin in Synapse Formation $1,000,000 4/1/05 - 3/31/10 Denied.
PI: Burgess JMR Barker Neurodevelopment and Neurodegeneration $50,000 7/1/04 - 6/30/05 Denied.
PI: Burgess Amer. Fed. For Aging Research A Mouse Mutation Causing Progressive Cerebral Ischemia $60,000 7/1/04 - 6/30/06 Denied.
PI: DeVries NICHD Signaling in Follicular- and Early Embryo Development $1,000,000 7/1/07 - 6/30/12 Denied.
PI: DeVries NICHD Signaling in Follicular- and Early Embryo Development $1,000,000 7/1/05 - 6/30/10 Denied.
PI: DeVries NSF Beta-catenin and Wnt Signaling in Mammalian Follicular- and Preimplantation Embryo Development $618,559 1/1/04 - 12/31/07 Denied.

(5) Implement and strengthen focus areas: Three focus areas of excellence were strengthened in the fourth year of the IMB to further expand the national and international reputation of the IMB. These areas are: (I).High Resolution 3D Microscopy, (II). Nanoscale Spectroscopy, and (III). Nanosystems Development.
(I). High Resolution Microscopy.
In a successful bid to the Keck Foundation and NSF, the IMB acquired funding to purchase the first 4Pi confocal microscope in the US (TJL). The 4Pi sets the standard in optical resolution and provides an unprecedented view of cellular systems at the 100nm level in three dimensions. The IMB researchers at TJL, UMaine, and Heidelberg have developed technologies to further increase the resolution of the 4Pi system to <100nm (Brewsdorf, Hell). Additionally, researchers at UMaine IMB (Hess and Mason) have recently developed a new technique, Fluorescence Photo Activated Localization Microscopy (FPALM), which provides 3D imaging resolution at the 20nm scale. This technique has been identified by Science Magazine as one of the ten most significant imaging developments of the year. (http://www.sciencemag.org/cgi/content/full/314/5807/1850a). A scanning Electron Microscope (SEM) with Focused Ion Beam (FIB) and a cryogenic sample preparation and visualization stage were also purchased. This instrument allows the electron or ion beam imaging of biological samples at the 1-2nm scale. Using the FIB to section the sample in situ at the 2-4nm scale, provides 3D reconstruction of biological samples with molecular resolution. Elemental mapping of the cell can also be accomplished with the SEM/FIB making it an extremely powerful and unique tool in biological investigations.
(II). Nanoscale Spectroscopy
Researchers at the IMB have developed two unique analytical techniques in spectroscopy and have applied them to the study of cellular processes: a). Multi channel Raman Spectroscopy and b). Sum Frequency Spectroscopy. IMB researchers (Mason) have pioneered an improvement in Raman spectroscopy that allows the simultaneous measurement/visualization of up to ten chemical species at 20nm resolution. Using Raman spectroscopy with ten tags provides a revolutionary new venue to track the mutual interaction of multiple biologically functional sites and determine their mutual biochemical interactions. Sum Frequency Spectroscopy (Neivandt) is another spectroscopy technique that is unique to IMB and provides a method to map the structure and dynamics of interfaces, particularly biological membranes processes.
III. Nanosystems Development
Nanotechnology is a critical focus area for the 21st century over virtually all disciplines. The IMB capitalizes on the research excellence at LASST in surface science and the recent addition of nano/micro fabrication technology to augment its biological research mission. Researchers with the IMB (Smith and Collins) have expertise in the design and fabrication of micro/nano instrments for biological research and worked together with IMB researchers to bring nanotechnology to the IMB. This technology assisted in the application for several patents and proposals. Several nanoscience projects are currently underway including: Membrane structural analysis of oestiocytes through AFM (Nohe, Collins), microfluidic systems for axonal growth and inhibition (Smith, Burgress, Collins), Microscope on a chip with nanometer resolution (Hess, Smith, Collins), microsystems for in vitro fertilization of mouse oocytes (Wiles, Smith, Collins, Malcom).

(6) Plan for long-term sustainability: To provide sustainable funding, in 2007 the directors of the IMB approached the David Mann Foundation for a $50M endowment to the IMB. Negotiations with the Foundation are still in progress. Additionally, the IMB actively seeks funding opportunities at extramural funding agencies. Of particular importance are multi investigator proposals that encompass large sections of the IMB membership such as the recently submitted $7M NIH BioEngineering Partnership Research center proposal to the NCI.

(7) Provide training opportunities: Training is a significant aspect of the mission of the IMB and the three participating organizations. The IMB provides excellent training and education opportunities for students and junior researchers in the biological and biophysical sciences. By the end of this project, the IMB had been involved in the training of 33 graduate students, 22 postdoctoral associates, and 16 undergraduate students. The approach of the IMB is to involve the junior researchers and students in an apprentice-like environment, where they are mentored by several IMB in a rotation scheme. Typically, a student will train under three mentors/labs in divergent fields before choosing a permanent laboratory, although there is considerable lateral migration of junior researchers across IMB collaborating labs and institutions. Several IMB-associated Ph.D. students expected to graduate in the next few years.

(8) Disseminatation and technical significance: To disseminate IMB result to the general research community, IMB members have published in reputable journals in their appropriate fields, attended and presented critical emerging research in respected national and international conferences, published book and book chapters, as well as organized and sponsored IMB relevant conferences. IMB hosted a colloquium in March 2007 on nanoprobe development; over 38 IMB researchers attended. In June 2007, over 100 scientists attended an IMB-organized international conference on high-resolution microscopy. In addition, patents are currently being prosecuted for IMB research discoveries. During the fourth year of the NSF grant, IMB members published 68 peer reviewed journal articles, presented 51 conference papers both national and international, produced 5 book chapters, and 6 patent applications.

Conference and Professional Presentations:
Alexei Evsikov, 'Maternal molecules mediating development and speciation'. Platform presentation, 'Stem Cells V' conference, October 2006, Cold Spring Harbor, NY.
Ben Harwood, Sophia K. Cross, Emily E. Radford, Barbara B. Knowles, and Wilhelmine N. de Vries 'Members of the Wnt signaling pathways

are widely expressed in ovaries and preimplantation embryos.' Highlighted Poster at the 1st Biennial National IDeA Symposium of Biomedical Research Excellence (NISBRE); Washington, DC
Anne Peaston Genomic Impact of Eukaryotic Transposable Elements. Poster presentation: 'Retrotransposons in mouse oocytes and cleavage-stage embryos'. March 2006. Asilomar CA.
Anne Peaston Workshop on Endogenous Retroviruses & Retroelements. Poster presentation 'Retrotransposons in mouse oocytes and cleavage-stage embryos'. September 2006. Mystic CT.
Barbara Knowles, Speaker, National Institutes of Health Human Embryonic Stem Cell Infrastructure/Training Meeting, Toronto Canada, June 2006.
Barbara Knowles seminars 'Oocyte to Embryo Transition':Tokai University, Japan, June 2006;
Barbara Knowles; Co-Organizer, Workshop on Current Protocols in Stem Cell Biology, The Jackson Laboratory, Bar Harbor, Maine, August 2006.
Barbara Knowles: Co-Organizer, Mount Desert Island Stem Cell Symposium, Salisbury Cove, Maine, August 2006.
Barbara Knowles: Co-Organizer, Experimental Genetics of the Laboratory Mouse in Cancer Research, The Jackson Laboratory, Bar Harbor, Maine, September 2006.
Lindsay Shopland ,Chromosome structure, Short Course in Medical and Experimental Genetics, TJL, July 2006
Lindsay Shopland, Dynamic Organization of nuclear function, September 2006, Cold Spring Harbor
Lindsay Shopland, Signal transduction in the nucleus, March 2007, Ventura, CA
Lindsay Shopland, Chromosome Biology, April 2007, NCI, NIH
Joerg Brewersdorf, Super-Resolution Optical Imaging Mini-Symposium, UCLA, November 2006
Joerg Brewersdorf, Keystone Symposium 'Physics of Quantum Electronics', Snowbird, UT, January 2007
Bragdon B*, Young K, Horton L, Ackert-Bicknell C, Beamer W, Rosen C, Nohe A (2006). Mouse genetic models of bone stem cells and nano scale receptor dynamics. Nanomedicine. 2(4) 277-8.
Young KA*, Cook J, Bragdon B, Vary C, Nohe A (2006. Protein receptor interaction studied on the nanoscale. Nanomedicine. 2(4) 314.
Bragdon B*, Johnson A, Cook J, Young K, Nadeau J, Mayer G, Nohe A (2006). Semiconductor nanoparticle uptake and toxicity correlates with particle size and core degradation. Nanomedicine. 2(4). 318.
A.N. Johnson*, G. D. Mayer, B.E. Bragdon, A. Nohe (2006). SETAC North Atlantic Chapter Semiconductor Nanoparticle Uptake and Toxicity correlates with Particle Size and core degradation.
Smorodin V. Y*. and Nohe A (2006). Conceptual Approach in Theory of Lipid Bilayer Domains. Biophysical Journal
K.A. Young*, J. Cook, B. Bragdon, C. Vary and A. Nohe (2006). Investigation of novel signaling proteins for BMPs. Biophysical Journal.
B. Bragdon*, A. Johnson, J. Cook, K. Young, J. Nadeau, V. Smorodin, C. Vary, G. Mayer and A. Nohe. (2006) In Vivo Model For Nanoparticle Toxicity. Biophysical Journal.
A. Nohe and C. Rosen* (2006). NIA RFA Assays of Stem Cell Function in Clinical Aging Research, Wahsington, DC.
Samuel J. Clarke, C. Annette Hollmann, and Jay L. Nadeau, 'Visualization of quantum dot-electron donor conjugate uptake and processing by living cells,' NSTI-NanoTech, Boston, May 2006
S. Clarke, D. Bahcheli, C.A. Hollmann, J. Nadeau, 'Surface characterization of QD-dopamine conjugates and specific uptake in mammalian cells,' CeNS Workshop, Venice, Italy, September 2006
J. L. Nadeau, S. J. Clarke, C. A. Hollmann, D. M. Bahcheli, 'Quantum dot-FRET systems for imaging of neuronal action potentials,' Engineering in Medicine and Biology Society, 2006. EMBS '06. 28th Annual International Conference of the IEEE, Aug. 2006, pp. 855 - 858
A.N. Johnson*, G. D. Mayer, B.E. Bragdon, A. Nohe (2006). SETAC North Atlantic Chapter Semiconductor Nanoparticle Uptake and Toxicity correlates with Particle Size and core degradation.
Nohe A , Nanotech Investor Forum, Boston, MA, Delivery of Nanoparticles and Proteins into the Cytoplasm and Nucleus of Living Cells, Nov. 2006, Invited Speaker.
Nohe A, American Academy of Nanomedicine, Washington, Mouse genetic models and nanoscale receptor dynamics, Aug. 2006, Invited Speaker
Nohe A, McGill University, Montreal, Canada. Implication of Bone Morphogenetic Protein Receptor Dynamics to Signal Transduction, Mar. 2006, Invited Speaker.
Wolfgang Eck, FNano Conference 2006, Snowbird, Utah, April 2006, Presentation: 'Generation of two- and three-dimensional nanostructures by electron beam lithography on self-assembled monolayers'
Michael Grunze, 7.03.2006, 94. Bunsen-Kolloquium 'Controlling Protein Adsorption at Materials Surfaces', Bayreuth, Germany, New results on the mechanism of protein-resistant surfaces
Michael Grunze, 8.04.2006, 5th Brazilian German Workshop on 'Applied Surface Science', Mangaratiba/Brasilien Biology meets surface science
Michael Grunze, 17.06.2006, 8th International School and Symposium on ynchrotron Radiation in Natural Sciences Zakopane/Polen Scanning Transmission X
Michael Grunze, Ray Microscopic Analysis of Purified Melanosomes of the Mouse Iris
Michael Grunze, 11.8.2006, Science of Adhesion, Gordon Research Conference, Tilton, New Hampshire To stick or not to stick, that is the question

Michael Grunze, 17.12.2006, Biomaterials from 2D to 3D and Beyond, Biointerfaces and Surface Analysis, The Westin Maui, USA
Towards quantifying biomolecule/surface interactions 'Non-equilibrium Lipid Distributions in a Simulated Three-Species Biomembrane,' A.P. Paradis, S.R. McKay, and S.T. Hess, presented at the American Physical Society Annual Meeting, Denver, CO, March, 2007.
Sam Hess, 'Sub-diffraction Imaging of Protein Distributions in Live Cells by Fluorescence Photoactivation Localization Microscopy,' presented by proxy (Joerg Bewersdorf) at the Deutsche Forschungsgemeinshaft-sponsored symposium 'High-Performance Fluorescence Imaging in the Life Sciences,' University of Ulm, Germany, April, 2007.
Sam Hess, 'Quantifying intracellular dynamics: Evolution of fluorescence methods and probes,' Seminar for 'Probing Biological Structures on the Nanoscale,' Jackson Laboratory, Bar Harbor, ME, March 2007.
Sam Hess, 'Nanoscale Imaging of Intracellular Protein Distributions by Fluorescence Photo-Activation Localization Microscopy (FPALM),' American Society for Cell Biology, San Diego, CA, December, 2006.
Sam Hess, 'Nanoscale Imaging of Intracellular Fluorescent Proteins: Breaking the Diffraction Barrier,' CIRCS Seminar, Department of Physics, Northeastern University, Boston, MA, December, 2006.
Sam Hess, Ultra-High Resolution Imaging by Fluorescence Photoactivation Localization Microscopy (FPALM),' CNSI Mini-symposium on Super-Resolution Optical Imaging, University of California at Los Angeles, Los Angeles, CA, November, 2006.
Sam Hess, 'Ultra-High Resolution Views of Intracellular Proteins: Can the Diffraction Barrier Be Broken?' Physics Department Colloquium, Colby College, Waterville, ME, November, 2006.
Sam Hess, 'Imaging Nanoscale Protein Distributions in Live Cell Membranes with Fluorescence Photoactivation Localization Microscopy (FPALM),' plenary talk presented at the Spring meeting of the New England Section of the American Physical Society and American Association of Physics Teachers, University of Maine, Orono, ME, April, 2007.
Sam Hess, 'Lipid rafts in biomembranes: From giant unilamellar vesicles (GUVs) to living cells', M.V. Gudheti, and S.T. Hess, Colloquium for the Department of Physics & Astronomy Colloquium, University of Maine, Orono, ME, May, 2006.
Eck, W. 'Fluorescence microscopy for in situ life detection,' AAAS-SWARM, Houston, April 2007
J. L. Nadeau, S. J. Clarke, C. A. Hollmann, D. Bahcheli, R. Khatchadourian, A. Bachir, P. Wiseman, 'Quantum dot systems for specific biosensing applications,' Photonics West, San Jose, 2007, Proc. SPIE 6448

Patents and Intellectual Property:
- Provisional Patent, Method and Kit for Intracellular Delivery' Number 60/868,178 December 1, 2006. Inventor A. Nohe and J. L. Nadeau
- Polypeptides as Therapeutics for Osteoporosis Treatment December 5th 2006. Inventor A.Nohe. (Provisional patent in preparation)
- Maciag, T., Mandinova, A., Mandinov, L., Prudovsky, I., Bellum, S., Soldi, R., Bagala, C. U.S. non-provisional application no. 10/786,223. Filed Feb. 23, 2004. 'Copper-Dependent Non-Traditional Pro-Inflammatory Cytokine Export and Methods, Composition and Kits Relating Thereto.'
- Prudovsky, I., Kolev, V., Kacer, D., Duarte, M., Maciag, T. U.S. provisional application no. 60/681,612. Filed May 17, 2005. 'Compositions and Methods Related to Biological Effects of Intracellular Domains of Delta 1 and Jagged 1.'
- 'Stoichiometric antibody bioconjugation of noble metal nanoparticles', W. Eck; M. Mason
- 'Metallic nanoparticle bioconjugates as high resolution taget specific CT contrasting agents', W. Eck; M. Mason; P. Allen; A. Nicholson.

Findings:

2. MAJOR FINDINGS AND RESULTS FROM ACTIVITIES:
The general research agenda was described in the original application and included intracellular structures and dynamics, functional materials, and biocomputing. This was refined further to include: genome architecture in the nucleus; cellular biophysics with focus on nanostructures, biological interfaces, application of nanostructures to cell adhesion and cell mechanics, and biomimetics of cell functions; X-ray microscopy and spectroscopy of cells, organelles, and tissue; and nanoparticles, quantum dots, and biopolymers to track intracellular processes. The following are examples of some of the results from activities:

Intracellular Dynamics and Structure: The Axial tomography and Zeiss microscopes were combined into the development of the microaxial tomograph, a prototype microscope that was designed and built in collaboration with the University of Heidelberg (completed October30, 2004). It is currently being used to take measurements related to genome architecture in the nucleus of the mouse embryo (Dr. Cremer, Dr. Eviskov, Florian Steier, in progress).

During 2004, experiments were performed at the National Synchrotron Light Source (NSLS, Brookhaven National Laboratories, NY) using the scanning transmission X-ray microscope at beam line X1A (built by Professor Janos Kirz and Professor Chris Jacobsen from Stony Brook University, NY). We have been carrying out studies on melanosomes from the eyes of mice strains developed at TJL. Melanosomes are specialized intracellular membrane bound organelles that produce and store melanin pigment. The composition of melanin and distribution of melanosomes determine the color of many mammalian tissues, including the hair, skin, and iris. However, the presence of melanosomes within a tissue carries potentially detrimental risks related to the cytotoxic indole-quinone intermediates produced during melanin synthesis. In order

to study melanosomal molecules, including melanin and melanin-related intermediates, we have refined the preparation methods allowing for spectromicroscopic analysis of purified melanosomes using a Scanning Transmission X-ray Microscope. We measured for the first time absorption spectra of melanosomes at the carbon absorption edge. The high-resolution images of melanosomes at discrete energies demonstrate that fully melanized mature melanosomes are internally non-homogenous, suggesting the presence of an organized internal sub-structure. The spectra of the purified melanosomes are complex, partially described by a predominating absorption band at 288.4 eV with additional contributions from several minor bands. Differences in these spectra were detectable between samples from two strains of inbred mice known to harbor genetically determined melanosomal differences, DBA/2J and C57BL/6J, and are likely to represent signatures arising from biologically relevant and tractable phenomena. Our measurements show for the first time that different mouse phenotypes may be distinguished by the spectra of single melanosomes. A detailed publication is being submitted .Further studies on other mice strains and different organelles than melansosomes are planned in the future.

In collaboration with Dr. Leiter of TJL, Dr. Grunze designed a novel instrument to measure non-invasively the glucose levels in mice. The use of animal models of diabetes carries with it the obligation to minimize discomfort to the experimental animals. The presence or absence of Type 1 diabetes in a mouse or rat model can be non-invasively assessed by testing for urine glucose. However, this semi-quantitative assessment cannot replace blood glucose determination when anti-hyperglycemic therapies are being implemented (islet or stem cell transplantation, immunotherapies, etc.). For rodent models of Type 2 diabetes developing complications of chronic hyperglycemia, ability to monitor blood glycemic changes over time is essential. Because current methods of obtaining multiple samples of blood from mice is limited by their small blood volume, and is stressful to both the investigator and the mice, it is desirous of fostering development of a methodology allowing non-invasive blood glucose determination. We designed an instrument that will use ellipsoid optics to enhance detection of the infrared radiation signal emanating from the tail of conscious mice. The basic premise is infrared detection of glucose by elliptical mirrors and filters that exploit the thermal gradient established by higher infrared radiation absorption in the dermis which is vascularized, versus the epidermis, which is not. Dr. Grunze will supervise instrument construction and refinement both in Heidelberg and Bar Harbor, while Dr. Leiter will supervise calibration and field testing using his many mouse models that transit from normoglycemia to hyperglycemia in a reasonably standardized time frame. The results from the non-invasive monitor will be compared to glucometer readings taken from the same mice shortly afterward. If we are successful in accurate measurement of glycemia changes in our mouse models of diabetes, we will determine whether the instrumentation will allow the same measurements from the tail of BB rats. Our goal is to make this instrumentation universally available.

Functional Materials: space at The Jackson Laboratory has been outfitted to produce biocompatible and bioselective structured surfaces and nanoparticles. Production will begin in early May 2005. Additionally, IMB has access to the new 3,000 square foot clean room, MEMS microfabrication facility, located on UM campus, which will also be used for collaborative work.

Biocomputing: the project 'Computer simulations of mouse nuclear genome' was completed and has proven effective at modeling the folding of chromatin in the mouse nucleus. These data have been submitted for publication (Shopland, et al). This research has supported the development of additional research projects that bridge the divide between mathematical modeling and real-life dynamics.

New projects have been initiated between Andre Kahlil, a postdoctoral fellow with Dr. Jay Nadeau, and Dr. Kevin Mills at TJL, focusing on the proximity of translocation break points in the interphase nucleus.

The following is a summary of on-going and prospective IMB research projects and collaborations:
-Michael Grunze, Ph.D., UMaine/University of Heidelberg - IMB Co-Director and Co-Principal Investigator: x-ray microscopy and spectroscopy applied to melanosomes, synchrotron based IR microscopy on intracellular networks, non-invasive glucose measurements on mice using IR emission, drug delivering microparticles, sum frequency generation on membrane models and Monte Carlo simulations on water in phospholipids membranes, and optimization of photophysical properties of fluorphores for the investigation of biomembrane organization.
-Barbara Knowles, Ph.D., TJL - IMB Co-Director and Co-Principal Investigator: systems approaches to the oocyte-to-embryo transition and to mammary tumorigenesis.
-Michael D. Mason, Ph.D., UMaine - Assistant Professor of Chemical and Biological Engineering: time-resolved simultaneous PL/Raman imaging spectroscopy of single molecules/single nanoparticles in vivo; using a combination of single molecule spectroscopic and imaging techniques to characterize and quantify the underlying photophysics of a range of new nanoprobes which exhibit potential as fluorescent single molecule reporters for applications in the biological and materials sciences.
-Anja Nohe, Ph.D., UMaine - Assistant Professor of Chemical and Biological Engineering, Cooperating Assistant Professor, Dept. of Biochemistry, Microbiology and Molecular Biology: family of image correlation spectroscopy (FICS) to analyze the distribution aggregation and clustering of membrane proteins on the cell surface; seek to develop tools that allow the examination of intermolecular interactions and reactions directly on the cell surface, particularly on live cells in culture or in tissue.
- Lindsay S. Shopland, Ph.D., UMaine/TJL - Research Assistant Professor, Cooperating Assistant Professor, Dept. of Biochemistry, Microbiology and Molecular Biology: three-dimensional genome structure and function in nuclei.
- Wolfgang Eck, Ph.D., UMaine/University of Heidelberg - Visiting Research Associate Professor: development of magnetic nanoparticles

with biomolecularly defined coatings, free-standing phospholipids membranes on nanostructured artificial cytoskeletons, two-dimensional models for cell membranes.
- David Neivandt, Ph.D., UMaine û Adjunct member: phospholipid membrane order and deformation studied by sum frequency generation vibrational spectroscopy (SFS).
- Christoph Cremer, Ph.D., University of Heidelberg û Adjunct member: quantitative molecular imaging and analysis of specific nuclear genome structures, modeling of the dynamic structure in the nucleus.
- Sam Hess, Ph.D., Physics, UMaine û Adjunct Member: optimization of photophysical properties of fluorphores for the investigation of biomembrane organization.
- Carol Kim, Ph.D., Biochemistry, Microbiology, and Molecular Biology, UMaine û Adjunct Member: innate immunity in the zebrafish.
- Jay Nadeau, Ph.D., McGill University û Adjunct Member: application of nanoparticles to visualize metabolic processes, electrophysiology, neural stimulation.
- Joachim Spatz, Ph.D., University of Heidelberg û Adjunct Member: programming cell function by nanoadhesive keys that trigger adhesion mediated cell signaling.
- Rob Burgess, Ph.D., TJL û Collaborating Researcher: utilization of high-resolution microscopy for the localization and distribution of agrin in the synaptic membrane
- Doug Spicer, Ph.D., MMCRI û Collaborating Researcher: the role of nuclear subdomains in Rb-mediated transcription.
- Calvin Vary, Ph.D., MMCRI û Collaborating Researcher: application of 4Pi confocal microscopy and image correlation spectroscopy in elucidation of mechanisms in vascular disease.
- Carol Bult, Ph.D., TJL û Collaborating Researcher: bridging the digital biology divide, integrating sequence and biology in the Mouse Genome Informatics (MGI) database, the Mouse Tumor Database (MTB), informatics for large-scale phenotyping, unraveling the transcriptional logic of early mammalian development.
- Alexi Evsikov, Ph.D., TJL û Collaborating Researcher: visualizing embryonic genome activation.
- Simon John, Ph.D., TJL û Collaborating Research: genetics of pressure- and nonpressure-induced neurodegenerations, causes of high IOP, genetics of glaucoma in DBA/2J mice, neurobiology of pressure-induced damage in glaucoma, anterior segment of dysgenesis and developmental glaucoma.
- Ed Leiter, Ph.D., TJL û Collaborating Researcher: genetics and pathogenesis of diabetes and inflammatory bowel disease in mice, new leptin receptor mutation in NOD/LtJ, role of nicotine adenine dinucleotide metabolizing enzymes in autoimmune diabetes, pharmacogenetics of rosiglitazone responsiveness, identifying a major modifer of inflammatory bowel disease in mice.
- Volkhard Lindner, Ph.D., MMCRI û Collaborating Researcher: function of the novel gene Cthrcl, characterization of FGF2-related immunoreactivity in normal plasma.
- Paul Millard, Ph.D., UMaine û Collaborating Researcher: biosensors for microbial pathogens, amplification of molecular beacon fluorescence, screening of physiologic mutations in embryonic zebrafish.
- Igor Prudovsky, Ph.D., MMCRI û Collaborating Researcher: non-classical protein secretion as a flexible mechanism of cytokine delivery.
- Tamas Hartzi, Ph.D., University of Heidelberg û postdoc working with Dr. Grunze on x-ray microscopy and spectroscopy.
- Martin Schmidt, Ph.D. student, University of Heidelberg û working with Dr. Grunze on synchrotron-based infrared spectroscopy on living cells.
- Kevin Mills, Ph.D., TJL û molecular mechanisms that maintain genome stability.
- Shaoguang Li, M.D., Ph.D., TJL û molecular mechanisms of human leukemias, identification of Src family kinases as key signaling molecules in BCR-ABL-Induced B-lymphoid leukemia, role of adhesion molecules in the development of BCR-ABL-induced chronic myeloid leukemia.

Year Three Additional Research Activities and Findings

- Michael Grunze: X-ray microspectroscopy, IR microscopy, non invasine glucose measurements, Sum Frequency Generation. Findings: Published (in print) the first x-ray microscopy study of melanosomes, and the realization of a micriofluidic cell to study live cells with IR microscopy.
- Barbara Knowles: Exploring the molecular mechanisms driving reprogramming of the egg and sperm nuclei between fertilization and activation of the newly formed, combined embryonic genome. Findings: Computational and molecular approaches to identify common cis-elements (3'UTRs) of mRNAs.
- Mimi de Vries is collaborating with Joel Graber, to examine the 3'UTRs of specific maternal messages for common cis-element motifs.
- Dr. Alexei Evsikov: found a series of known and suspected RNA-binding proteins are very abundantly expressed in the fully grown oocyte. These proteins protect the maternal mRNAs from degradation by binding to cis-elements in their 3'UTR. When these bound proteins are modified, by signal transduction mechanisms, as the result of hormonal stimulation, the mRNAs can be polyadenylated and translated. We identified an oocyte-specific form of the translation factor, Eif4E, which plays a central role in the initiation of translation of specific proteins providing the changing biochemical environment necessary for the full grown oocyte to complete maturation, meiosis, fertilization, and formation of a totipotent embryonic blastomere.
-Dr. Anne Peaston, in conjunction with Dr. Alexei Eviskov, found that MaLR retroviral transcripts are transcribed in the growing oocyte and

are extremely abundant during the oocyteûto-embryo transition. Furthermore, when these LTRs integrate into host genes they coordinate host gene expression, in some cases upregulating transcription of normal host genes, in some cases providing de novo oocyte expression and in some cases providing new start sites for transcription resulting in truncated proteins. Interestingly these retroviral transcripts, from both the sense and anti-sense direction, are present before the first round of host gene transcription suggesting they may inform about the mechanisms shaping the first embryonic transcriptome.

-Lindsay Shopland: 3-D chromosome structure in the nucleus, and how this is established by primary sequence organization. Examining chromosome regions with 'gene deserts,' which contain highly conserved sequences that may regulate gene expression via structural mechanisms. Findings: Mapped the spatial relationships between sequences across a gene desert and the Dach1 gene. Data indicate that these sequences, up to 800 kb away from the gene, are very closely (< 300 nm) and non-randomly associated with Dach1 in the nucleus. This nuclear organization is cell type specific. Found that gene deserts in general preferentially associate with the edge of the nucleus, a region typically involved in gene silencing. Desert association with the nuclear edge plays a role in establishing the 3-D organization of a large chromosome region containing multiple gene deserts. The end result of these structures is that the genes between the deserts are also brought close together in the nucleus.

- Wolfgang Eck: Development of biocompatible and biologically targeted nanoparticles for high resolution imaging and cancer diagnostics. Findings: Developed biocompatible semiconductor quantum dots and gold nanoparticles that show extremely high stability in colloidal dispersion. These particles bear novel organic shells based on heterobifunctional polyethylene glycol that make them highly biocompatible and directable to specific biological locations by attachment of biological signal molecules.

- Michael Mason: Research is focused on two complimentary but distinct efforts: developing techniques for imaging chemical dynamics at the single molecule level within complex (biological) systems, and the design and optimization of organic, semiconductor, and metallic nanoprobes to be used as locally sensitive nanoprobes. As is typical when establishing a new laboratory based on an emerging instrumental technology much of the effort over this past year has been devoted to organization, design, acquisition, construction, and optimization. Findings: Now have a working multifunctional scanning spectroscopic imaging microscope capable of single molecule imaging. Developed novel chemistries for the synthesis of hybrid Raman/Fluorescence active nanoparticles. Currently extending these systems to include >10 unique nanoparticles, well beyond the limitations of fluorescence techniques.

- Anja Nohe: The Family of Image Correlation Spectroscopy (FICS) Dynamics of Membrane Domains, Signal Transduction of Bone Morphogenetic Proteins, Signal Transduction of EGF Receptors. Findings: Analyzed in detail the aggregation, clustering and dynamics of receptors on the plasma membrane and analyzed the influence of these dynamics on signaling. Found the aggregation and localization for receptors on the plasma membrane in a certain area is crucial for the initiation of the signal pathway. Signaling systems of interest: Vitamin D, BMP, EGF, IGF-1.

- David Neivandt: Application of Sum Frequency generation vibrational Spectroscopy to the study of membrane structure and its relevance to biological function.

Development of new spectroscopies and microscopies. Findings: Work this past year has focused on laying the theoretical foundation for the development of a physiologically relevant model membrane system amenable to study via SFS. This has led to several publications on the physics of thin film interference effects in non-linear optics, both from theoretical and applied viewpoints. Neivandt is currently in the process of fabricating lipid membranes suspended on hydrogel supports and correlating their SF response with theory. Additionally collaboration with Igor Prudovsky on the study of non-classical protein transport has continued with linear infrared and fluorescence leakage work probing FGF1 induced vesicle deformation.

- Andre Khalil: Use and development of image analysis formalisms based on Topology, Fractals, and Wavelets. Applications on the cell nuclear structure, surface cell membrane, and in astrophysics. Findings: Characterization of the non-spherical nature of chromosome territories; characterization of the change of lipid rafts morphology as a function of temperature; characterization of the filamentary distribution of galaxies in the Universe.

- Joerg Bewersdorf: Development of new 4Pi microscopy techniques and application of 4Pi microscopy to biological projects. Findings: Successful application of one-photon excitation in 4Pi microscopy. First successful application of 4Pi microscopy to imaging of tissue sections and mouse embryos in an early stage of development.

- Christoph Cremer: Quantitative molecular imaging analysis of specific nuclear genome structures. Findings: In collaboration with Dr. Lindsay Shopland we have started to contribute to quantitative far field light optical analysis of nanostructures in mouse cell nuclei. Presently, the following methods are being established; Quantitative image analysis of conventional light microscopical data, establishment of micro-tomography at IMB/TJL, 4Pi-microscopy measurements of nuclear specimens prepared by Dr. Shopland, and biocomputing of large-scale mouse nuclear genome structure and of the Piebald region.

- Manesa Gudheti (post-doc Hess Lab): Effect of unsaturated trans-lipids on membrane properties; the role of membrane rafts in the pathogenesis of influenza virus.

Findings: Trans-lipids alter bilayers membrane properties in giant unilamellar vesicles.

- Gopal Chada (post-doc Mason Lab): Synthesis, characterization of gold and silver nanoparticles with well-defined size, shape, crystal structure and surface properties has been investigated. Findings: The purpose of our current research is to build up the multidisciplinary research effort devoted to the development of functionalized nanoparticles for advanced imaging techniques in novel applications. Different size, shapes of Gold, Silver nanoparticles have been synthesized using documented methods involving the reduction of gold, silver solution by reducing agent with and without a stabilizing agent in aqueous and organic medium. Characterization of these materials based on size has been

determined using Transmission Electron Microscopy, Atomic Force Microscopy, Zetasizer and UV-Visible spectroscopy. Modification of these inorganic materials with organic molecules to functionalize systems with molecular/biomolecular recognition elements such as thiols, 1,2-bis (4-pyridyl)ethylene (BPE), and pyridine etc. has been explained with surface enhanced Raman scattering (SERS) technique. SERS allows for in situ real time measurements, non-destructive and non-intrusive sampling, remote sampling through fiber optics, and detection of analytes in aqueous solvents by adsorbing the analyte onto nanostructured gold and silver surfaces. This can lead to Raman spectra that are a million times more intense than ones without surface enhancement. Gold nanoparticles also used for thin films of membrane separation. Multiple Langmuir-Blodgett depositions of 15 nm gold nanoparticles onto a mesoporous silica membrane resulted in a membrane with a significantly modified gas permeance and a decreased number of active pores of radii 40 ? and less.

- Thanu Prabha Girirajan (graduate student, Mason lab): The objective is to develop the instrumentation for Time resolved simultaneous Single Molecule Fluorescence and Raman spectroscopy to image the position and dynamics (leading to thermodynamics and kinetic) of the Novel Nanoprobes in a variety of systems like films, cells etc., using simultaneous Fluorescence and Raman Spectroscopy. This requires the development of a time-resolved versatile specific software control program capable of operation across multiple data acquisition modalities (involves the use of Labview). Research focus is on building a Raman/PL spectral imaging microscope which includes integrating in imaging format the following things 1. Time-resolved single photon counting in multiple channels synced with pulsed laser system (time-stamping and inter-photon counting); 2. Pixel-by-Pixel Raman Spectroscopy; 3. 3D Scanning; 4. Image/Data Acquisition software. Findings: Image Acquisition (Fast scan) Time-stamp measurement by selecting different points in the image; 2. Spectral Acquisition at different points in the image; 3. Simultaneous measurement of time-stamps and spectra.
- Tobias Wolfram (graduate student, Grunze lab): Nanostructured surfaces, nanoparticles, bio-functionalization, molecular cell biology, differentiation of neuronal cellular systems. Findings: Establishment of micellar nanolithography at the IMB, differentiation impairment via substrate stiffness.
- Martin Schmidt (graduate student, Grunze Lab): The investigation of intracellular structures of single living mammalian cells and to probe their dynamic nature by means of infrared spectroscopy. The research involves the development of new instrumentation for fast and sensitive dichroic studies and of a methodology for cell handling in a micro-flow cuvette with nano-patterned substrates suitable for infrared spectroscopy. Findings: Developed and tested a polarization modulation apparatus on an infrared microscope for dichroitic measurements with high spatial and temporal resolution. In order to make possible measurements of single living cells by infrared microspectroscopy in aqueous culture medium we designed and implemented a demountable and temperature-controlled micro-fluidic IR cuvette. In preliminary experiments we succeeded in measuring single living fibroblast and osteoblast cells by means of infrared microspectroscopy. Further needs for instrumental and methodological improvements were identified and are targeted.
- Beth Bragdon (graduate student, Nohe Lab): The importance of caveolin and IGF-1R (insulin-like growth factor-1 receptor) interactions that may affect the pathway of IGF-1. Currently looking at the interactions within two mice lines from Jackson Labs. Using confocal microscopy to visualize co-localization as well as reporter gene assay to examine gene activity. Nanoparticle toxicity using zebra fish as a model. The zebra fish embryos are incubated with quantum dots (various sizes of dots) and the affects are observed using confocal microscopy and various other techniques. Findings: The quantum dots are entering the zebra fish embryos and definitely having an effect on the health and life span of the embryos. Embryos incubated with the dots are killed with in a few hours to a couple of days depending on the existence of a shell and the size of the shell of the quantum dots.

Year Four Additional Research Activities and Findings:

During the four years of NSF support, IMB has developed robust programs that occupy the cutting-edge of research in 1) biological applications of ultra-high resolution microscopy & spectroscopy 2) development of nanoprobes 3) biocomputing and 4) bioengineering.

Ultra-high resolution microscopy and spectroscopyù The application of ultra high-resolution microscopy to resolving nuclear and membrane structures within cells has started bearing fruit on a technical level, and we are using this technology to tackle a series of challenging biological questions. Our 4Pi confocal laser scanning microscope (CLSM), acquired with NSF and Keck funding, is the only 3D super-resolution microscope in the United States. We have developed techniques to image biological samples such as cell nuclei, mouse blastocysts and mouse brain and nerve cells that were previously believed to be unsuitable for 4Pi imaging. Research using the 4Pi to investigate the role of free and phosphorylated H2AX in DNA repair mechanisms and the structure of the presynaptic CaV2.2 channel-transmitter release site core complex has recently been published. Projects that will use the 4Pi CLSM to examine 3D chromatin structure, nuclear compartments and neural cell organization are currently in progress.

Last year, IMB scientists developed a revolutionary new microscopic technique, Fluorescence Photo-Activated Localization Microscopy (FPALM), which provides resolution at the 20 nm scale and can be used to image single molecules in living cells. We are currently working to apply these techniques to biological samples and to combine FPALM with the 4Pi to create a 3D version of FPALM. 3D FPALM would provide 30 nm resolution in all dimensionsùa significant step toward the ultimate goal of single molecule localization. Researchers are also designing and developing a 3D participle-tracking microscope (3D PTM). This microscope will allow researchers to track the movement of single molecules (1 nm) in live cells in real time. 3D FPALM and 3D PTM are seminal breakthroughs in modern microscope development; more importantly, taken together they hold the promise of revolutionizing our view of sub-cellular structure and function.

IMB researchers have developed sum frequency spectroscopy for biological applications. This technique probes chemical processes at surfaces and provides unique structural, directional, and functional information about biological processes in membranes. It is critical technique for improving our understanding of membrane structure and cross-membrane transport mechanisms.

IMB researchers are also expanding the biological applications of Raman spectroscopy, which can locate biological structures with 20 nm resolution. Prior to our work, use of Raman spectroscopy in examining complex cellular processes was limited because only two fluorescent labels could be imaged simultaneously. IMB researchers have shattered this barrier by developing techniques which allow for the simultaneous labeling and measurement of up to ten species with 20nm resolution. This work has transformed the utility of Raman spectroscopy in identifying and tracking biological structures and biochemical interactions and has the potential to localize components of molecular machines.

IMB houses this unique set of microscopic and spectroscopic techniques for biological imaging, an array of complementary, one-of-a-kind instruments. In addition, IMB has assembled the expertise and fostered the interdisciplinary collaborations necessary to exploit these technologies to tackle fundamental biological questions. Thus, IMB is a powerful resource that provides our researchers, and scientists worldwide, new windows into the world of gene expression, nuclear structure and membrane function. New research opportunitiesùpathways to examine functioning neurons and neural networks, tracking single proteins, and elucidate the connection between epigenetic changes and gene expression depend on the emerging research synergies and techniques developed by IMB technologists, biologists and chemists.

Nanoprobe DevelopmentùThis cutting-edge program in functional materials complements our advances in biological imaging and spectroscopy. IMB scientists have been working with gold nanoparticles and Raman fluorescent probes. They are developing new methods to synthesize these probes and fine-tuning their characteristics including, brightness, bleaching, blinking, and toxicity. Our scientists are also working on ways to direct these probes to specific sites within cells using unique sol-gel coatings and antibody conjugation techniques. These gold and Raman probes are also at the center of a breakthrough in developing contrast agents for CT scanning. In addition, our researchers have devised a way to get quantum dots to enter the nucleus of living cells, which was previously considered impossible. This technique has huge implications for nuclear imaging and chromatin structure elucidation. The contrast agents and nuclear staining technique are the subjects of preliminary patents as are several other developments by IMB researchers (see 6).

BiocomputingùBiocomputing and sequence analysis is a critical aspect of the IMB research portfolio. The methods provide key links between microscopic and spectroscopic images and biochemical and structural data that allows the images to be correctly interpreted and integrated into solutions to biological questions. Our researchers are combining sequence-specific analysis of DNA with an understanding of 3D chromatin nanostructure by using advanced image analysis and biocomputing techniques. IMB researchers have demonstrated the direct association between genome features in the primary sequence and a higher-order organization in the interphase nucleus. They also have made new discoveries by using image analysis techniques to investigate the proximity of translocation break points in the interphase nucleus. Affiliated IMB researchers have developed wavelet transform techniques to evaluate the structural nature of DNA across different scales. These approaches are particularly useful for detecting possible long-range correlations among structural features of the genome that may also correlate to chromatin conformation, in particular, the positioning and dynamics of nucleosomes.

BioengineeringùThis is our newest research focus. It has literally exploded within the last year through key collaborations between IMB technologists, bioengineers, neurobiologists and geneticists. IMB scientists are currently devising and applying remote sensing of physiological parameters within mice or within cages of mice. A pilot program for these devices is ongoing in TJL's animal facilities. In addition, IMB scientists have created a microchamber to determine the factors involved in nerve growth and synaptogenesis in vivo; the prototype chamber is currently being tested. IMB collaborators are also working on nanopatterned surfaces, which may provide a method to understand cell migrations during development.

Training and Development:

3. OPPORTUNITIES FOR TRAINING AND DEVELOPMENT:

Year One

The IMB is being staffed by world-class scientists who are in the process of procuring state-of-the-art equipment and facilities. All of those scientists involved in negotiations or who have been offered a position have expressed an interest in training graduate students, postdoctoral fellows, and being involved in teaching academic courses related to their research interests. Furthermore, they have indicated a willingness to share their expertise and instruments with colleagues unfamiliar with the methodology used by molecular biophysicists and by working with local high school students, undergraduates at the University of Maine, and with visiting high school and undergraduate students in the

residential summer programs at TJL and MMCRI.

IMB provided funds to Dr. David Neivandt, Department of Chemical and Biological Engineering, UM and a graduate student to travel to the University of Heidelberg to gain additional technical training in specific biophysical methodology. Dr. Lindsay Shopland is currently at the University of Heidelberg receiving additional training.

Year Two

The three IMB partner organizations were awarded a National Science Foundation IGERT grant, which assisted in the implementation of a new Functional Genomics Ph.D. program at the University that has been successfully attracting graduate students with its integrated approach to the field. While taking core courses in the biological, computational, and physical sciences, students in the program rotate through labs at the three institutions in order to gain experience in multiple disciplines, and culminate their efforts with a thesis research topic that has two co-advisors from different fields. Six graduate students are enrolled in the program, with an additional seven more pending admission.

In acknowledgement of how critical it is to cross-train top-quality students who can then perform research at institutions such as those in the IMB, the University of Maine has created a new Graduate School of Biomedical Sciences. Set to premiere in the fall of 2005, the school is currently admitting students and will encompass four tracks: functional genomics; cellular and molecular biology; neurosciences; and nanotechnology. These students will have the opportunity to gain valuable experience by studying and working with researchers at the IMB partner institutions.

Three post-docs, seven graduate students, and three undergraduate research students have participated directly with IMB personnel in their research. Several students in the University's masters degree program for science teachers have also had the opportunity to intern with IMB researchers, and a collaboration with the University of Heidelberg has resulted in opportunities for research exchanges that involve IMB faculty, a post-doc, and a graduate student. At the Jackson Laboratory, six high school and undergraduate students have also interned with IMB researchers over the past two years with the support of various programs such as NIH INBRE and NSF REU. The Jackson Laboratory's 75th year Summer Program in 2004 brought 34 high school and undergraduate students together in a residency program.

Undergraduate & graduate students and postdocs participating in research activities include:
Gopal Chada: Post-doc with IMB Researcher Michael Mason, UMaine
Johann von Haase: Visiting post-doc with IMB Adjunct Member Christoph Cremer & IMB Member Lindsay Shopland, UMaine/University of Heidelberg
Kim MacEwan: Post-doc with IMB Researcher Anja Nohe, UMaine
Andre Kahlil: Post-doc with IMB Adjunct Member Jay Nadeau, McGill University
Thanu Girirajan: Graduate student with IMB Researcher Michael Mason, UMaine
Scott Larkin : Graduate student with IMB Researcher Michael Mason, UMaine
Mathias Uvieghara : Graduate student/lab technician with IMB Researcher Michael Mason, UMaine
Tobias Wolfram : Visiting graduate student with IMB Adjunct Member Joachim Spatz, University of Heidelberg, and Collaborating Researcher Rob Burgess, TJL
Kira Young: Graduate student with IMB Researcher Anja Nohe, UMaine
Jon Moyer: Graduate student with IMB Member Barbara Knowles, TJL (M.S. program in teaching high school science)
Andrew Doyle: Graduate student with IMB Member David Neivandt, UMaine
Karen Faucher: Graduate student with IMB Co-Director Barbara Knowles, TJL
Florian Steier: Graduate student with IMB Members Christoph Cremer, University of Heidelberg, and Lindsay Shopland, TJL (microaxial tomography project)
James Cook: Undergraduate student worker with IMB Researcher Anja Nohe, UMaine
Joshua Verril: Undergraduate student worker with IMB Researcher Anja Nohe, UMaine
Meigan Dean: Undergraduate student worker with IMB Researcher Anja Nohe, UMaine
Six graduate students in the Functional Genomics program serve rotations in the various IMB labs.

As the IMB continues to grow in its third year, additional programs for both graduate and undergraduate student programs are being developed. By taking advantage of the interdisciplinary nature of the IMB and its researchers, NSF EPSCoR will provide a very valuable infrastructure that allows for the direct integration of educational programs with state-of-the-art facilities and researchers on the cutting edge of science.

Members of the IMB have been actively participating in training and mentorship roles. Dr. Nohe and Dr. Mason were involved in the development of a new course entitled 'Physical Aspects of Chemical and Biological Engineering,' which will be taught this summer semester. This junior/senior level course was designed to present many of the fundamental concepts typically taught in a physical chemistry class but with emphasis on engineering applications. During the spring semester, Dr. Nohe has begun development for a hands-on course in molecular

biology, which could be implemented in fall. In addition, Dr. Shopland participated in team-teaching a Functional Genomics course, and was a guest lecturer for a Molecular Genetics course.

In her new lab, Dr. Nohe has spent a considerable amount of time introducing her one graduate and three undergraduate students to molecular biology and single particle tracking, utilizing the strategy of identifying solid, challenging projects and leading them through the results so that they begin to gain an understanding of the experimental, theoretical and conceptual relations.

Dr. Mason, UMaine, has been rapidly expanding his new lab over the past several months, with Dr. Chada joining his group in August 2004 and assisting in establishing their nanoparticle synthesis and wet chemistry lab facility. Also at that time Thanu Girirajan joined his group as a masters student in ECE. Her ongoing project involves developing the electronic timing and software integration of the individual components of our microscope system. Later in the fall semester Mathias Uvieghara joined as a Lab Technician, to aide in the acquisition process necessary to establish a working lab. Recently, Mathias has been admitted into the Biological Engineering MS program and will continue to work with Dr. Mason on a bio-sensing collaboration with Doug Bousfield. This spring Scott Larkin was hired as a Research Assistant to help Dr. Chada with the expanding effort to synthesize novel optical nanoprobes. Scott is a PhD candidate in the Chemistry Department and has considerable expertise in inorganic synthesis.

A considerable amount of Dr. Mason's effort has gone into hands-on training within the lab, with direct involvement of all members of his group in each phase of the project. This is being accomplished by direct interaction in the optics lab, the machine shop, the wet chemistry lab, and on the chalkboard discussing the physical concepts behind the techniques, and during informal group meetings and discussions. All members of his group are encouraged to review one relevant literature article each day, and Dr. Mason makes himself available to discuss their findings and questions.

Dr. Neivandt's graduate student, Andrew Doyle, was able to spend significant time with researchers at the University of Heidelberg, studying the transfer of proteins across membranes using sum frequency generation vibrational spectroscopy. His research resulted in a publication.

Dr. Shopland sponsored Laura Brenner, a TJL summer student who worked on probing for organizational motifs in the Dach cluster-desert region.

All teaching and research faculty have been actively participating in the weekly IMB work in progress meetings, and as a result, have begun numerous internal and external collaborations. Some of these collaborations have resulted in grant submissions; others are related to cooperative efforts to expand knowledge and development of new laboratory techniques.

The EPSCoR Project Administrator has been working with UMaine's Office of Research and Sponsored Programs to develop and implement the following strategies for increasing outreach to other Maine research institutions:
- sponsor an NSF EPSCoR Outreach Conference in October 2004
- assist researchers in finding funding by creating a Funding Opportunities database that will shortly become available for use by anyone in the state
- begun presenting Grantwriting workshops to targeted groups of researchers and graduate students
- initiated an e-mail notification service to researchers throughout the state for major funding opportunities.

Additional Year 3 Training & Development

The following postdocs, graduate, and undergraduate students were integral participants in Year 3 research activities, working closely with IMB mentors at UM, TJL, and MMCRI, as well as at other partner institutions.

Postdoctoral fellows:
Gopal Chada: with IMB Researcher Michael Mason, UMaine and IMB Researcher Wolfgang Eck, TJL
Manesa Gudheti: with IMB Associate member Sam Hess, UMaine
Joerg Fick: with IMB Associate member David Neivandt, UMaine
Renee le Clair: with IMB Associate member Volkhard Linder, MMCRI
Aleksandra Terzic: with IMB Associate member Volkhard Linder, MMCRI
Alexander Kirov: with IMB Associate member Igor Prudovsky, MMCRI
Peter Pyagay: with IMB Associate member Igor Prudovsky, MMCRI
Irene Graziani: with IMB Associate member Igor Prudovsky, MMCRI
Peter Fuerst: with IMB Associate member Rob Burgess, TJL
Gregor Kreth: with IMB Adjunct Christoph Cremer, University of Heidelberg

Udo Birk-Spori: with IMB Adjunct Christoph Cremer, University of Heidelberg
Jutta Finsterle: with IMB Adjunct Christoph Cremer, University of Heidelberg
Johann von Hase: with IMB Adjunct Christoph Cremer, University of Heidelberg
Nick Kepper: with IMB Adjunct Christoph Cremer, University of Heidelberg
Roman Glass: with IMB Adjunct Joachim Spatz, University of Heidelberg

Graduate Students:
Thanu Girirajan: Graduate student with IMB Researcher Michael Mason, UMaine
Kira Young: Graduate student with IMB Researcher Anja Nohe, UMaine
Beth Bragdon: Graduate student with IMB Researcher Anja Nohe, UMaine
Andrew Doyle: Graduate student with IMB Associate member David Neivandt, UMaine
Lei Li: Graduate student with IMB Associate member David Neivandt, UMaine
Sarah Sterling: Graduate student with IMB Associate member David Neivandt, UMaine
Jennifer Rochira: Graduate student with IMB Associate member Sam Hess, UMaine
Michael Mlodzianowski: Graduate student with IMB Associate member Sam Hess, UMaine
Mudalige Gunewardene: Graduate student with IMB Associate member Sam Hess, UMaine
Glen Davenport: Graduate Student with IMB Researcher Joerg Bewersdorf, TJL
Tahir Durmus: Graduate student with IMB Associate member Volkhard Lindner, MMCRI
Tobias Wolfram : Visiting graduate student (TJL) with IMB Adjunct Joachim Spatz, University of Heidelberg
Martin Schmidt: Visiting graduate student (TJL) with IMB Co-director Michael Grunze, University of Heidelberg
Marcus M³ller: Visiting graduate student (TJL) with IMB Co-director Michael Grunze, University of Heidelberg
Stefan Stein: graduate student with IMB Adjunct Christoph Cremer, University of Heidelberg
Sabine Rinck-Jahnke: graduate student with IMB Adjunct Joachim Spatz, University of Heidelberg
Daniel Bahcheli: graduate student with IMB Adjunct Jay Nadeau, McGill University
Samuel Clarke: graduate student with IMB Adjunct Jay Nadeau, McGill University

Undergraduate Students: (research positions or internships)
Gary Craig: Undergraduate student with IMB Researcher Michael Mason, UMaine
Sawyer Hansen: Undergraduate student with IMB Researcher Michael Mason, UMaine
Adrian Hutchinson: Undergraduate student of IMB Researcher Michael Mason, UMaine
Johnny Tse: Undergraduate student with IMB Researchers Michael Mason and David Neivandt, UMaine
Dale Veilluex: Undergraduate student of IMB Researchers Michael Mason and David Neivandt, UMaine
James Cook: Undergraduate student with IMB Researcher Anja Nohe, UMaine
Joshua Verrill: Undergraduate student with IMB Researcher Anja Nohe, UMaine
Meagan Dean: Undergraduate student with IMB Researcher Anja Nohe, UMaine
Bhupendra Nagpure: Undergraduate student (College of the Atlantic) with IMB Associate member Sam Hess, UMaine
Ryan Laughlin: Undergraduate student with IMB Associate member Sam Hess, UMaine
Tobias Schoen: Undergraduate student mentored by Tobias Wolfram, TJL
Ferdinand Belz: Undergraduate student mentored by Tobias Wolfram, TJL

Other:
Chris Lynch: Research Assistant with IMB Researcher Lindsay Shopland, TJL
Megan McOsker: Research Assistant with IMB Researcher Lindsay Shopland, TJL
Mark Lessard: Research Assistant with IMB Researcher Joerg Bewersdorf, TJL
Qiaozeng Wang: Research Assistant with IMB Associate member Volkhard Lindner, MMCRI
Kathleen Carrier: Research Associate with IMB Associate member Volkhard Lindner, MMCRI
Raffaella Soldi: Research Fellow with IMB Associate member Igor Prudovsky, MMCRI
Doreen Kacer: Research Associate with IMB Associate member Igor Prudovsky, MMCRI
Heinz Eipel: Research fellow with IMB Adjunct Christoph Cremer, University of Heidelberg

In addition, graduate students in the Functional Genomics Ph.D. program and the University of Maine's new Graduate School of Biomedical Sciences continue to take core courses from IMB faculty and rotate through faculty research labs at the three IMB institutions.

Project administrators, researchers, and state legislators attended the National NSF EPSCoR conference in Puerto Rico in September 2005. Andrew Doyle, graduate student of David Neivandt, was selected to also attend and present a poster of his research.

The Project Administrator presented several grant workshops throughout the year; continued hosting the University's web-based funding

opportunities database to encourage increased proposals; expanded the Maine EPSCoR website; attended NSF EPSCoR and other workshops and conferences and disseminated relevant information to the rest of the state; produced the Maine EPSCoR newsletter; and consulted with researchers to enhance proposal submissions.

Additional Year Four Training & Development:

The following additional students and post doctoral associates were trained/mentored by IMB members during the fourth year:

Post Doctoral Associates:
IMB Mentor Igor Prudovsky:
Alek Kirov, MD, Non-classical protein release
Raffaella Soldi, PhD, Non-classical protein release
IMB Mentor Mike Mason:
Dr. Venkata G.R. Chada, 'Design and Synthesis of Hybrid Raman/Fluorescence Active Metallic Core-Shell Nanoparticle Probes'
IMB Mentor David Neivandt:
Joerg Fick, Sum Frequency Spectrometry

Graduate Students:
IMB Mentor Joerg Brewersdorf:
Glen Davenport, Master of Science in Teaching, Refractive Index Mismatch in 4Pi Microscopy
Bhupendra Nagpure, Master of Science in Teaching, Fluorescence Photoactivation Localization Microscopy
Andrew Doyle, Ph.D, Functional Genomics and Engineering, rotation on 4Pi microscope
IMB Mentor David Neivandt:
Andrew Doyle, Ph.D. Chemical Engineering and Functional Genomics, Non-classical membrane transport
Lei Li, Ph.D. Physics, SFS of cellulose surfaces
Sarah Sterling, Ph.D. Chemical Engineering and Functional Genomics, Non-classical membrane transport
IMB Mentor Lindsay Shopland:
Kathy Snow, Functional Genomics, Nuclear organization of chromosomal rearrangements in lymphoma
Valerie Johnson, Functional Genomic, Probing chromosome folding in inactived chromosomes
IMB Mentor Mike Mason:
Thanu Prabha Girirajan, M.S. (EE) Co-Advisor (Segee) 'Development of a Scanning Multi-Channel Time-Resolved Single Molecule Spectroscopic Imaging Microscope'
Mathias Uvieghara, M.S. (BLE) 'Enzyme Catalyzed Nanoparticle Signal Amplification for Rapid Detection' (enrolled Spring 2005, expected graduation Spring 2007), Chair.
Gary Craig, PhD. (BLE-IND) 'Pancreatic Cancer Detection using Engineered Metallic Nanoparticle Conjugates' (enrolled Spring 2005, expected graduation Spring 2009), Chair.
David Paul, M.S. (PHY): 'Raman Micro-spectroscopy of Nanoparticles in biological systems' (enrolled Spring 2005, expected graduation Summer 2007), Co-Chair.
Sarah Sterling, PhD. (CHE-GSBS) Co-Advisor (Neivandt): 'Sum-Frequency Spectroscopy of Model Bio-membrane systems'. Co-Chair.
Lei Li, PhD. (PHY) Co-Advisor (Neivandt) 'Computational modeling and investigation of thin films using Sum-Frequency Generation Spectroscopy'. Co-Chair.
Raymond Kennard PhD. (CHE) Co-Advisor (DeSisto) 'Single molecule methods for the characterization of mesoporous membranes'. Co-Chair.
Edward Algeyer PhD. (PHYS): 'Temporally and Chromatically modulated far-field backscatter imaging of nanoparticle bioconjugates in soft cancer tissue'.
IMB Mentor Igor Prudovsky:
Andrew Doyle, PhD Membrane biology
Sarah Sterling, PhD Membrane biology
IMB Mentor Anja Nohe:
Teresa Egeler (PhD student, Functional Genomics) and Kira Young (Master Student). Fall 2006 Tutor for the course from MMCRI: Special Topics in Cell Biology.
Betty Ingraham (PhD student, Individualized PhD, Primary Advisor, Chair of Committee). Fall 2005 - summer 2006 (independent study) Fall 2006 - present PhD thesis VitaminD receptor and cancer.
Lindsay Horton (Research Assistant). Fall 2004 - present. Isolation of Bone Marrow Stromal cells, BMP and IGF signaling.
Matthew King (Biological Engineering, Ms Student, Primary Advisor, Chair of Committee). Fall 2006 - present. Nanoparticle Toxicity.
Sarah Burke (Biochemistry, Microbiology and Molecular Biology , Co-advisor with Robert Gunderson,, Masters Committee). Fall 2006 - present. Palmitylation of G-proteins

Kira Young (Biological Engineering, MS Student, Functional Genomics IGERT, Primary Advisor, Chair of Committee). Fall 2004 - present. Mutations of BMP receptor Ia lacking CK2 binding sites.
Adam Johnson (Biochemistry, Microbiology and Molecular Biology, MS Student, Advisor Greg Mayer, Masters Committee and direct supervision at the confocal microscope). Fall 2004 - present. Toxicology of Nanoparticles.
Beth Bragdon (PhD student, Primary Advisor, Chair of Committee). Spring 2006 - present. IGF-1 signaling.
IMB Mentor Wolfgang Eck:
Gary Craig, Nanoparticle synthesis
Janice Duy, Nanoparticle synthesis
IMB Mentor Sam Hess:
Michael Mlodzianoski,Fluorescence Imaging and Physical Shape Analysis of Giant Unilamellar Vesicles
Mudalige Siyath Gunewardene, Quantification of Fluorescence Photoactivation Quantum Yield in Green Fluorescent Proteins
Travis Gould, Fluorescence Imaging and Spectroscopy of Single Molecules and Membrane Protein Distributions
Jennifer Rochira Quantification of Interactions between Apoptosis-Inducing
Andrew Paradis, Monte-Carlo Numerical Simulation of Membrane Heterogeneity
IMB Mentor Rob Burgess:
Tobias Wolfram, Ph.D student University of Heidelberg 'Material science approach to cell matrix interaction'
IMB Mentor Barbara Knowles:
Karen Francher, PhD student in Functional Genomics 'Gene expression during mammary carcinogenesis'

Undergraduate Students:
IMB Mentor Igor Prudovsky:
Christian Mc Intire, Biology, Non-classical protein release
IMB Mentor Mike Mason:
Adrian Hutchinson (Visiting, Physics NCSU, Summer '05), Co-Neivandt, Summer '05.
Johnny Tse (CHE 499-CHE/'06), Co-Neivandt, Fall '05, Spring 06.
Dale Veilluex (Non-Thesis, CHE/'06), Co-Neivandt, Spring '06.
Lucas Ellis (Visiting, Summer '06), Co-Neivandt, Summer '06.
Aruna Sigdel (BS BMB/'10), Spring '07.
Sushil Khadka (BS BLE/'10), Spring '07.
Adam Pongan (BS CHE/'10), Spring '07.
Chris Kerrigan (BS PHY/'08), Fall '06, Spring '07.
Laurel Grosjean (BS CHE/'07), Co-Neivandt, Spring '07.
IMB Mentor Anja Nohe:
Linda Ngyen (Undergraduate Student, Biological Engineering, experience without credit): Spring 2007 - present. DNA purification.
Valerie Dahlgreen (Undergraduate Student, Biology, experience without credit). Fall 2006. DNA purification, cloning.
James Cook (Undergraduate Student, Chemical Engineering, experience without credit). Fall 2004 - summer 2006 DNA preparation and cloning.
Megan Deering (Undergraduate Student, Biological Engineering, experience without credit). Fall 2005 - present DNA purification, confocal microscopy.
Joshua Verrill (Undergraduate, Biochemistry, Microbiology and Molecular Biology, Senior Research Project): Fall 2005 - fall 2006 Purification of BMP-2.
Shayamala Thinakaran (Medical Student, Ross University, Elective). Fall 2006 - Spring 2007 IGF signaling.
IMB Mentor Lindasy Shopland:
Jennifer Zhan (undergraduate summer student)
IMB Mentor Anne Peaston:
Zinaida Deideic (undergraduate student from College of the Atlantic) 'Genetically encoded fluorescently marked mammary stem cells'

Laboratory Assistants:
IMB Mentor Joerg Brewersdorf:
Mark Lessard, Research Assistant II, 4Pi Microscopy
IMB Mentor Lindsay Shopland:
Katie Gassman, Chromatin organization at the nuclear periphery

In addition, numerous post-doctoral associates, graduates and undergraduates from IMB affiliated institutions have worked with IMB mentors at TJL during the 4 years of NSF funding, providing mechanisms for tech transfer to Maine from their home institutions. These students are listed below.

University of Heidelberg:
Florian Staier (Mentor: Grunze)
Tobias Wolfram (Mentor: Spatz/Burgess/Bewersdorf)
Ann Kathryn Marquerre (Mentor: Cremer)
Marcel Muller (Mentor: Grunze)
Martin Schmidt (Mentor: Grunze)
Johann von Hase (Mentor: Cremer)
Jevgenij Raskatov (Mentor: Grunze)
Susanne Fenz (Mentor: Cremer)
Tobias Schoen (Mentor: Spatz)
Ferdinand Belz (Mentor: Spatz)
Manual Juette (Mentor: Bewersdorf)
McGill University:
Sam Clarke (Mentor: Nadeau)
Daniel Bahcheli (Mentor: Nadeau)
Jamie Lynn Schafer (Mentor: Nadeau)

Outreach Activities:

4. OUTREACH ACTIVITIES:

Year One:

The IMB and its importance to the State has been a significant topic of discussion by the Maine Biomedical Research Coalition/University of Maine System, and there has been widespread agreement that it is a critical component to the growth of the biomedical research enterprise in the State of Maine. The Founding Director is scheduled to give a presentation on the IMB to the 'Research CafÚ' at UMaine, which is a lecture series designed for the intelligent layperson.

Maine EPSCoR sponsored MaineTech 2003 in May of that year as the state's EPSCoR Conference, which provided an opportunity for industry, non-profit, and educational research organizations to showcase their R&D, discover potential collaborations, collect information on grant programs and other funding options, and to talk to patent experts.

IMB continues to work with the University of Maine System (UMS) Chancellor for appropriations for university-based R&D. IMB progress is reported to the Maine Research Capacity Committee, a statewide steering committee of 17 individuals from Maine's education, research, and business communities and State Government. Changes in UMS hiring practices now allow IMB to offer competitive salaries, even in highly competitive fields, e.g., biomedical. UM has initiated a collaborative research and education program with MMCRI, Mount Desert Island Biological Laboratories, TJL, and the University of Southern Maine. UMaine is working to enhance public visibility of the state's research and graduate programs by hiring a research communications manager and continuing production of a new research magazine (UMaine Today).

Year Two:

The official opening of the space at TJL was held May 5, 2004 and was attended by officials from participating institutions, as well as representatives of our Congressional delegation. The opening received widespread media coverage, including all three local television stations and an article in the Bangor Daily News.

The IMB has developed a website at http://imbmaine.org to provide information to members, interested researchers, and the general public, and is also planning to develop a secure, inter-IMB website for the sharing of ideas, data, and papers. EPSCoR information, as well as the IMB, is featured on the UMaine website for the Office of the V.P. for Research at http://www.umaine.edu/research/admin.htm. Short publications describing the mission of the IMB have also been developed, and presentations have been given to various organizations such as the Bangor Rotary Club.

Planning is underway for the Maine Technology Forum on Capitol Hill in April 2005, which will feature 15 major research initiatives in the state of Maine and include the IMB member organizations. Planning also began for Maine EPSCoR to sponsor MaineTech 2005 in May of this year as the state's EPSCoR Conference, which provides an opportunity for industry, non-profit, and educational research organizations to showcase their R&D, discover potential collaborations, collect information on grant programs and other funding options, and to talk to patent

experts. Approximately 120 exhibitors will be present at this event.

Planning is also underway to develop additional strategies for outreach activities that will enhance participation in science learning and increase Maine high school and undergraduate student awareness of science and engineering career options. This will include a number of activities for high school science classes by IMB scientists, graduate students, and postdoctorates in the Bar Harbor and Orono areas. In addition, internship programs for high school students will continue to be offered at TJL during the summer for ten weeks, and throughout the academic year.

Several slide presentations have been prepared (in PowerPoint) for use in educating the science community and public about the IMB research, and a presentation was given to the Bangor Rotary Club. An exhibit of display posters has also been developed, as well as a general brochure about the IMB. UMaine's V.P. for Research office has developed a research video that will be utilized to educate high school youth, and the general public, about the importance of scientific research in the region. Periodic Research CafÚ presentations are also given at UMaine, which are open to the public.

Additional Year Three and Four Outreach Activities:

In addition to the activities mentioned previously in this report, the Maine NSF EPSCoR office sponsored the following:
1) Co-sponsored MaineTech 2005 in May,which provided an opportunity for industry, non-profit, and educational research organizations to showcase their R&D, discover potential collaborations, collect information on grant programs and other funding options, and to talk to patent experts. Approximately 100 exhibitors were present at this event, with 250 participants.
2) Maine NSF EPSCoR State Conference, September 2006, UMaine: 140 participants took part in presentations and sessions that included: Maine's R&D Background - Miles Theeman, Chair, Maine Science & Technology Advisory Committee; Maine EPSCoR - Vicki Nemeth, UMaine Director of Research Administration/Maine EPSCoR; Maine's Growing Opportunities in the Forest Bioproducts Research Arena - Del Raymond, Retired Weyerhaeuser Director of Strategic Energy Technologies & Past Chairman of AF&PA Agenda 2020; National Science Foundation EPSCoR - Dr. Sherry Farwell, Director NSF EPSCoR; Environmental Protection Agency EPSCoR Overview - Dr. Darrell Winner, Director EPA EPSCoR; National Institutes of Health, NIH IDeA Overview - Dr. Sidney McNairy Jr., Director NIH Division of Research Infrastructure; National Science Foundation Funding Opportunities in Environmental Sciences - Dr. Jake Weltzin, NSF Ecological Biology Cluster (BIO Directorate); Staying Afloat Among Sinking Science & Technology Funding Trends - Dr. Maria Vassileva, Research Competitiveness Program, American Association for the Advancement of Science (AAAS); Overview of the Forest Bioproducts Research Project: Maine's NSF EPSCor RII Award - Dr. Hemant Pendse, FBRI Managing Director, Chair Chem. & Bio. Eng, Umaine; Dr. Steve Shaler, FBRI Scientific Director/Assoc. Dir. AEWC, UMaine; Vicki Nemeth, UMaine Director of Research Administration/Maine EPSCoR; Dr. Robert Wagner, Director Cooperative Forestry Research Unit; Technology Transfer in Maine - Jake Ward, Exec. Director for Research & Economic Development, UMaine; Renee Kelly, Director of Economic Development Initiatives, UMaine; Deborah Neuman, Director, Target Technology Incubator, UMaine; NIH Grant Workshop presentation - Dr. Sidney McNairy Jr., Director NIH, Division of Research Infrastructure; Dr. Touradj Solouki, Assoc. Prof. Chemistry, UMaine; Dr. Clarissa Henry, Assist. Prof. Biological Sciences, UMaine; Dr. Gregory Mayer, Assist. Prof. Molecular & Environ. Toxicology, UMaine; Dr. Michael Mason, Assist. Prof. Chemical & Biological Eng., UMaine; Dr. Anja Nohe, Assist. Prof. Chemical & Biological Eng., UMaine; Laura Ward, Office of Research & Sponsored Programs, UMaine; Maine Space Grant Consortium/NASA EPSCoR -Dr. Terry Shehata, Executive Director, Maine Space Grant; plus individual consulting sessions with the federal agency representatives.
3) Technical Assistance workshops: a series of four workshops were developed to provide technical assistance for grant-writing during the spring 2007 semester. Over 50 people participated.
4) DEPSCoR workshop: was hosted at the University of Southern Maine in Portland on May 22, 2006, with presenter Christian Cupp of the Office of the Deputy Undersecretary of Defense for Laboratories and Basic Sciences. Approximately 40 researchers from throughout the state attended.

The Maine NSF EPSCoR Associate Project Director also presented several grant workshops throughout the year; continued hosting the University's web-based funding opportunities database to encourage increased proposals; expanded the Maine EPSCoR website (www.umaine.edu/epscor); attended NSF EPSCoR and other workshops and conferences and disseminated relevant information to the rest of the state; and consulted with researchers to enhance proposal submissions.

The Maine NSF EPSCoR office also supported the following:
1) Math and Science Future Teachers Club Spring Conference on March 24, 2007, which involved over 50 participants
2) The Expanding Your Horizons conference for 7th and 8th grade girls on March 15, 2007, which involved 600 girls in hands-on STEM activities.
3) The week-long Consider Engineering Program for 60 high school juniors in July 2006.

Journal Publications

Doyle AW, Fick J, Himmelhaus M, Eck W, Graziani I, Prudovsky I, Grunze M, Maciag T, Neivandt DJ., "Protein deformation of lipid hybrid bilayer membranes studied by sum frequency generation vibrational spectroscopy (SFS).", Langmuir, p. 8961-8, vol. 20, (2004). Published,

Chen W, Masterman K-A, Basta S, Dimopoulos N, Knowles BB, Bennin JR, Yewdell JW., "Cross-priming of CD8 + T cells to viral and tumor antigens is a robust phenomenon.", Europ J Immunol, p. 194-199, vol. 34, (2004). Published,

de Vries WN, Evsikov AV, Fancher K, Haac BE, Solter D, Kemler R, Knowles BB., "Development of mouse preimplantation embryos lacking maternal ?Ò-catenin and E-cadherin: insights into zygotic genome activation", Development, p. 4435-4445, vol. 131, (2004). Published,

Peaston AE, Evsikov AV, Graber J, de Vries WN, Solter D, Knowles BB, "Retrotransposons regulate host genes in mouse oocytes and preimplantation embryos.", Dev Cell, p. 597-606, vol. 7, (2004). Published,

Kemler, R, Hierholzer A, Kanzler B, Kuppig S, Hansen K, Taketo M, de Vries WN, Knowles BB, Solter D, "Stabilization of ?Ò-catenin in the mouse zygote leads to premature epithelial-mesenchymal transition in the epiblast.", Development, p. 4435-4445, vol. 131, (2004). Published,

Mikaelian I, Blades N, Churchill GC, Fancher K, Knowles BB, Eppig JT, Sundberg JP., "Classification of spontaneous and transgenic mammary neoplasms", Breast Can Res, p. 668-679, vol. 6, (2004). Published,

Mehlmann LM, Saeki Y, Tanaka S, Brennan TJ, Evsikov AV, Pendola F, Knowles BB, EppigJJ, Jaffe LA., "The Gs-linked receptor GPR3 maintains meiotic arrest in mammalian oocytes", Science, p. 1947-1950, vol. 306, (2004). Published,

Heister K, Johansson LSO, Grunze M, Zharnikov M. 2003., "A detailed analysis of the C 1s photoemission of n-alkanethiolate films on noble metal substrates", Surface Science, p. 36-46, vol. 529, (2003). Published,

Adlkofer K, Eck W, Grunze M, Tanaka M., "Surface Engineering of Gallium Arsenide with 4-Mercaptobiphenyl Monolayers.", J Phys Chem B, p. , vol. 107, (2003). Published,

Schwendel D, Hayashi T, Steitz R, Schreiber F, Dahint R, Pertsin AJ, Grunze M, "Interaction of water with self assembled monolayers: neutron reflectivity measurements of the water density in the interface region.", Langmuir, p. 2284-2293, vol. 19, (2003). Published,

Pertsin AJ, Grunze M., "Long ranged solvation forces in a fluid with short ranged interactions.", J Chem Phys, p. 8004-8009, vol. 118, (2003). Published,

Pertsin AJ, Grunze M, "Erratum: Long ranged solvation forces in a fluid with short ranged interactions.", J Chem Phys, p. 9322, vol. 118, (2003). Published,

Herrwerth S, Rosendahl T, Feng C, Fick J, Eck W, Himmelhaus M, Dahint R, Grunze M., "Covalent coupling of antibodies to self-assembled nonolayers of carboxy-functionalized poly(ethyleneglycol): protein resistance and specific binding of biomolecules.", Langmuir, p. 1880-1887, vol. 19, (2003). Published,

Kaltenpoth G, Himmelhaus M, Slansky L, Caruso F, Grunze M., "Conductive core-shell particles: an approach to self-assembled mesoscopic wires", Adv Mat, p. 1113-1118, vol. 15, (2003). Published,

Walter EC, Murray BJ, Favier F, Kaltenpoth G, Grunze M, Penner RM, "Noble and coinage metal nanowires by electrochemical step edge decoration.", J Phys Chem B, p. 11407-114, vol. 106, (2003). Published,

O?Brien TP, Bult CJ, Cremer C, Grunze M, Knowles B, Langowski J, McNally J, Pederson T, Politz JC, Pombo A, Schmahl G, Spatz JP, van Driel R., "Genome function and nuclear architecture: from gene expression to nanoscience.", Genome Res, p. 1029-1041, vol. 13, (2003). Published,

Herrwerth S, Eck W, Reinhardt S, Grunze M., "Factors that determine the protein resistance of oligoether self-assembled monolayers - internal hydrophilicity, terminal hydrophilicity and lateral packing density.", J Am Chem Soc, p. 9359-9366, vol. 125, (2003). Published,

Chan YM, Schweiss R, Werner C, Grunze M., "Electrokinetic characterization of oligo- and poly(ethylene glycol)-terminated self-assembled monolayers on gold and glass surfaces.", Langmuir, p. 7380-7385, vol. 19, (2003). Published,

Kreuzer HJ, Wang RLC, Grunze M, "Hydroxide ion adsorption on self assembled monolayers.", J Am Chem Soc, p. 8384-8389, vol. 125(27), (2003). Published,

Evsikov AV, de Vries WN, Peaston A, Fancher K, Chen F, Radford E, Latham K, Blake J, Bult C, Solter D, Knowles BB., "Systems biology of the 2-cell embryo.", Cytogenet. Genome Res, p. 240-250, vol. 105, (2004). Published,

Wang MC, Liao JD, Weng CC, Klauser R, Shaporenko A, Grunze M, Zharnikov M., "Modification of Aliphatic Monomolecular Films by Free Radical Dominant Plasma: The Effect of the Alkyl Chain Length and the Substrate", Langmuir, p. 9774-9780, vol. 19, (2003). Published,

Tzvetkov G, Zubavichus Y, Koller G, Schmidt T, Heske C, Umbach E, Grunze M, Ramsey MG, Netzer FP., "Growth of H2O layers on an ultra-thin Al2O3 film: from monomeric species to ice.", Surface Science, p. 131-140, vol. 543, (2003). Published,

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Zwahlen M, Herrwerth S, Eck W, Grunze M, Hähner G., "Conformational order in oligo(ethylene glycol)-terminated self-assembled monolayers on gold determined by soft X-ray absorption.", Langmuir, p. 9305-9310, vol. 19, (2003). Published,

Kaltenpoth G, Schnabel P, Menke E, Walter EC, Grunze M, Penner RM, "Multi-mode detection of hydrogen gas using palladium-covered silicon ?Ý-channels.", Anal Chem, p. 4756-4765, vol. 75, (2003). Published,

Himmelhaus M, Bastuck T, Tokumitsu S, Grunze M, Livadaru L and Kreuzer HJ., "Growth of a dense polymer brush layer from solution", Eur Phys Lett, p. 378-384, vol. 64(3), (2003). Published,

Kemler R, Hierholzer A, Kanzler B, Kuppig S, Hansen K, Taketo M, de Vries WN, Knowles BB, Solter D, "Stabilization of ?Ò-catenin in the mouse zygote leads to premature epithelial-mesenchymal transition in the epiblast.", Development, p. 5817-5824, vol. 131, (2004). Published,

Solter D, Hiragi T, Evsikov AV, Moyer J, DeVries WN, Peaston AE, Knowles BB, "Epigenetic mechanisms in early mammallian development", Cold Spring Harbor Symposium., p. 1-8, vol. 69, (2004). Published,

Zubavichus Y, Fuchs O, Weinhardt L, Heske C, Umbach E, Denlinger JD and Grunze M, "Soft X-ray induced decomposition of amino acids: a time-resolved XPS, mass-spectrometry, and NEXAFS study.", Radiation Res, p. 346-358, vol. 161(3), (2004). Published,

Zubavichus Y, Zharnikov M, Schaporenko A, Grunze M, "NEXAFS study of glycine and glycine-based oligopeptides", J Electron Spectroscopy, p. 25-33, vol. 134, (2004). Published,

Pertsin A and Grunze M., "Water-graphite interaction and the behavior of water near graphite surfaces.", J Phys Chem B, p. , vol. , ( ). Accepted,

Zubavichus Y, Yang Y, Zharnikov M, Fuchs O, Schmidt T, Heske C, Umbach E, Tzvetkov G, Netzer FP, Grunze M, "Local structure of amorphous ice as revealed by O K-edge EXAFS.", Chem Phys Chem, p. 509-514, vol. 5, (2004). Published,

Himmelhaus M, Buck M, Grunze M, "Kinetics of film formation of alkanethiols: Solvent-dependence of conformational transitions studied by IR-visible sum frequency generation (SFG).", PCCP, p. , vol. , ( ). Submitted,

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Web/Internet Site

URL(s):

www.imbmaine.org
www.umaine.edu/epscor

Description:

The IMB website is the main informational site for the Institute for Molecular Biophysics, which was formed through this award. It is used to inform the public, media, government, and other scientists, and also has a members-only section to keep collaborating members up to date on IMB activities.
The Maine EPSCoR website is hosted by the Maine NSF EPSCoR office at the University, and provides information for partners throughout the state.

Other Specific Products

Product Type:

Instruments or equipment developed

Product Description:

The following equipment was custom designed and built by IMB researchers: a 2? photon confocal microscope; a single photon time-correlated fluorescence Raman spectromicroscope; IR micro fluidic cell for synchrotron studies; SFG apparatus.

Sharing Information:

Uses of the instruments beyond our group is pending, as it has just recently been installed.

Product Type:

Data or databases

Product Description:

The Project Administrator has developed a searchable website and corresponding database that will host funding opportunities information that researchers throughout the state can utilize.

Sharing Information:

The database will be on the University of Maine's Office of Research and Sponsored Programs website, which is available to anyone in the state to utilize.

Product Type:

Audio or video products

Product Description:

Several slide presentations have been prepared (in PowerPoint) for use in educating the science community and public about the IMB research. An exhibit of display posters has also been developed, as well as a general brochure about the IMB. UMaine?s V.P. for Research office has developed a research video that will be utilized to educate high school youth, and the general public, about the importance of scientific research in the region.

Sharing Information:

The above will be used in educating the science community and public about the IMB research, and will be utilized to educate high school youth, and the general public, about the importance of scientific research in the region.

Contributions

Contributions within Discipline:

1. To the principal discipline(s) of the project:
Molecular biophysics has been identified as an interdisciplinary area that holds great promise for making major breakthroughs in biomedicine. Maine has many of the intellectual resources in
place to become nationally competitive in understanding the complex interrelationships among chemical composition, molecular structure, and function on a molecular and multi-cellular level.
A strategic recruitment of scientists in and collaborators has now positioned the IMB to make significant contributions to the international research arena.

Contributions to Other Disciplines:

2. To other disciplines of science or engineering:
The interdisciplinary nature of molecular biophysics predicts new applications for the traditional areas of mathematics, physics, chemistry, engineering, computer sciences, biology, and genetics.
The healthy interplay between basic and applied research is very evident in the approach taken by the IMB. Moreover, combining the individual R&D strengths of TJL, MMCRI, and UMaine and establishing key collaborations elsewhere will lead to an internationally competitive program.

Contributions to Human Resource Development:

3. To the development of human resources:
The IMB is creating a nationally recognized interdisciplinary center for research and graduate education in molecular biophysics. It has begun this process by attracting worldwide interest and expertise as demonstrated by offers of association, and by providing opportunities for research and teaching for a full roster of researchers and collaborators. In addition, a significant portion of researchers and students are from traditionally underrepresented groups (female, minority), thereby improving their access to research and teaching careers. An increasing number of graduate students have expressed an interest in being associated with the IMB, and its members and collaborators have indicated a willingness to participate in graduate education. The IMB has been featured in many articles and presentations throughout the state, and has set an example that changed the character of graduate training in the state and internationally.

As detailed in our annual report, our hiring practices strongly encourage women and minorities to apply for positions that will be funded under this program, and any hiring is strictly overseen by an Equal Opportunity officer at the University.

The following is a summary of the personnel involved with the IMB since its creation in 2003 (baseline year):
PI/Co-PIs: 7 total, includes 3 women
Senior personnel hired: 7 total, includes 4 women
Collaborating Researchers: 35 total; includes 8 women and 4 minority (two Asian males, two Asian females)
Post-docs: 23 total; includes 6 women and 3 minority (one Asian male, two black males)
Graduate students: 26 total; includes 11 women and 4 minority (two black males, two Asian females)
Undergraduate students: 13 total; includes 2 women and 3 minority (two Asian males, one Asian female)
Administration/other: 13 total; includes 7 women and 2 minority (two Asian males)

TOTALS: 124 total; includes 41 women and 16 minority

The following details from the annual report indicate the status of the IMB's efforts to incorporate women and underrepresented minorities in positions involved in this program:

Year One:
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1) Founding Director: three men and one woman were considered for the position û a male (M. Grunze) was hired for a period of April 1, 2003 through August 31, 2004.
2) Lindsay Shopland, Ph.D. û IMB Research Assistant Professor, UMaine û hired December 1, 2003
3) Barbara Knowles, Ph.D. û IMB Co-Principal Investigator, TJL
4) Six faculty positions were offered to three males, three females (one Asian) û one male, one female accepted and were hired in Year 2 (see below); one female accepted adjunct status
5) Kate Merritt û IMB Executive Assistant û hired February 19, 2004
6) Jennifer Isherwood û NSF EPSCoR Program Administrator
7) Deirdre Mageean, Ph.D. û Assoc. V.P. for Research and Dean of Graduate School, UMaine û IMB oversight
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Year Two:

The following women and members of underrepresented groups were added to the roster of personnel involved in IMB activities:
1) Barbara Knowles, Ph.D. û hired as part-time IMB Co-Director August 2004
2) Anja Nohe, Ph.D. û IMB Assistant Professor of Chemical and Biological Engineering û hired July 1, 2004
3) Vicki Nemeth û Research Programs Administrator/UMaine & NSF EPSCoR Program Administrator û hired July 1, 2004
4) IMB Collaborating Researchers: Carol Kim, Ph.D., UMaine; Jay Nadeau, Ph. D., McGill University; Carol Bult, Ph.D., TJL.
5) Postdocs: Kim MacEwan, Ph.D., UMaine; Gopal Chada, Ph.D., UMaine.
6) Angela Hildreth û part-time clerical, UMaine û began August 2004
7) IMB graduate students: Thanu Girirajan û graduate student with IMB Researcher Michael Mason, UMaine; Kira Young û IMB graduate student with IMB Researcher Anja Nohe, UMaine
9) The following women are graduate students in the Functional Genomics program, and serve research rotations with IMB members: Karen Fancher, Jennifer Rochira, Kathleen Thornton, Sarah Vincent
10) Meigan Dean û IMB undergraduate student with IMB Researcher Anja Nohe, UMaine
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Year Three and Four:

The following women and members of underrepresented groups were added to the roster of personnel involved in IMB activities:
1) IMB Co-Director/Co-PI: Rosemary Smith, Ph.D., UM
2) IMB Collaborating Researchers: Ilka Pinz, Ph.D., MMCRI; Andre Khalil, Ph.D., UMaine; Shaoguang Li, Ph.D., UMaine; Patsy Nishina, Ph.D., TJL; Dorothy Croall, Ph.D., UMaine; Rosemary Smith, Ph.D., UMaine; Susan Ackerman, Ph.D., TJL.
3) IMB Postdocs: Anne Peaston, Ph.D., TJL; Mimi DeVries, Ph.D., TJL; Renee LeClair, Ph.D., TJL; Irene Graziani, Ph.D., TJL; Aleksandra Terzic, Ph.D., TJL; Manesa Gudheti, Ph.D., UMaine.
4)IMB graduate students: Beth Bragdon û graduate student with IMB Researcher Anja Nohe, Umaine; Tahir Durmus û graduate student with IMB Associate Member Volkhard Lindner, MMCRI; Claudia Batram û graduate student with IMB Adjunct member Christoph Cremer, UHeidelberg; Lei Li û graduate student with IMB Associate Member David Neivandt, UMaine; Sarah Sterling û graduate student with IMB Associate Member David Neivandt, UMaine; Jennifer Rochira û graduate student with IMB Associate Member Sam Hess, UMaine; Sabine

Rinck-Jahnke û graduate student with IMB Adjunct Joachim Spatz UHeidelberg; Mudalige Gunewardene û graduate student with IMB Associate Member Sam Hess, UMaine; Kathy Snow - graduate student with IMB member Lindsay Shopland; Valerie Johnson - graduate student with IMB member Lindsay Shopland; Karen Fancher - graduate student with IMB member Barbara Knowles.
4)IMB undergraduate students: Jennifer Dunham û undergraduate student with the Maine EPSCoR office; Johnny Tse û undergraduate student with IMB Researchers Michael Mason & David Neivant, UMaine; Bhupendra Nagpure û undergraduate student with IMB Associate Member Sam Hess, UMaine.
5)Other IMB; Doreen Kacer û Research Associate with IMB Associate Member Igor Prudovsky, MMCRI; Megan McOsker û Research Assistant with IMB Researcher Lindsay Shopland, TJL; Qiaozeng Wang û Research Assistant with IMB Associate member Volkhard Lindner, MMCRI; Raffaella Soldi û Research Fellow with IMB Associate Member Igor Prudovsky, MMCRI; Kathleen Carrier û Research Associate with IMB Associate Member Igor Prudovsky, MMCRI; Mathias Uvieghara û Research Technician with IMB Researcher Michael Mason, UMaine; Susan Mueller û temporary administrative assistant with the Maine EPSCoR office; Betty Ingraham - Research Technician with IMB Researcher Anja Nohe.

Contributions to Resources for Research and Education:

4. To the physical, institutional, or information resources that form the infrastructure for research and education:
The project has contributed to resources for research and education as specified in previous sections of this report. In particular, the UMaine bio-MEMS clean room is a 3,000 sq. ft. class 1000/100 facility equipped for fabrication of MEMS and microelectronics devices, and is the largest university-based facility of its kind in the Maine, New Hampshire, and Vermont region. The 4 Pi confocal scanning microscope, the second of its kind in the world, will give scientists in the state access to cutting edge technology that will greatly augment their ability to bring national funding to Maine.

Contributions Beyond Science and Engineering:

The IMB's research contributes significantly to the public welfare by providing world-class resources that allow researchers to work at the frontier of science, providing answers that directly affect society's overall health and well-being.

Conference Proceedings

Categories for which nothing is reported:

Any Conference

Maine NSF EPSCoR EPS-0132384
"Establishing Research Competitiveness in Biophysical Sciences in Maine"
Executive Summary of Final Report
University of Maine
for period of April 2003-March 2007

This project established the Institute for Molecular Biophysics (IMB) as an internationally recognized interdisciplinary research center for investigating the molecular processes that determine cell function and fate. The IMB integrates a robust, sustainable research program with education and outreach agendas to significantly enhance Maine's R&D infrastructure and human capital. As a collaboration between the University of Maine (UMaine) and two Maine non-profits, The Jackson Laboratory (TJL) and Maine Medical Center Research Institute (MMCRI), IMB leverages the significant strengths of these partners. It bolsters Maine's capacity and competitiveness in biomedical research with vibrant research programs in biological applications of ultra-high resolution microscopy, the development of novel probes for microscopy and *in vivo* imaging, biocomputing and bioengineering.

This project was completed on-budget for the period of April 2003 to March 2007, which included a one-year no-cost extension. Federal outlays of $6M have been completely expended as of March 31, 2007, and matched by $6M in additional funds by UMaine. Expenses included a subcontract of $1,727,704 to TJL for facilities renovations ($1,122,017), program support ($234,821) and supplies and materials ($115,150), and TJL provided an additional $727,366 in direct support of this project. MMCRI received a subcontract for $30,000 for capital equipment and provided an additional $34,767 in matching support. Both partner organizations have provided complete documentation, financial statements, and audits for these subcontracts. Both TJL and UMaine have committed to providing continuing support for the IMB over two years as it further transitions into a self-sustaining, independent research center.

The following pages summarize our efforts, commitments, and accomplishments over the lifetime of the award. Evidence of achievement is presented under the 3 main objectives that are being used to evaluate the success of the program. These objectives were revised from those in our original proposal to reflect a reduction in the anticipated award from $3 million/year to $2 million/year and are delineated in The Budget Impact/Change of Scope document submitted to NSF in January 2002.

In our EPSCoR award letter NSF requested that we specifically: 1) identify numbers of women & members of other under-represented groups in staff positions and as participants in the activities funded by the award and 2) indicate the results of efforts to increase such staffing and participation. We address these issues in the "Women and Underrepresented groups" section under objective 2.

Objective 1. Create an internationally recognized interdisciplinary center for biophysics research in Maine through an effective partnership between UMaine and Maine's non-profit research organizations. Categories of evidence include:

1) Strength of the Partnership: Since its inception, the IMB has increased its membership from a handful of researchers in Maine to over 30 scientists and engineers at seven research institutions, including TJL, UMaine, MMCRI, and several international partners which include the University of Heidelberg (UH) and The Max Planck Institute, McGill University, and the Ecole

Normale Superieure de Lyons. This group spans genetics/genomics, chemistry, physics, mathematics, electrical engineering and bioengineering and has spawned numerous unique and productive research collaborations (see 3). Through these exceptional partnerships, IMB has become a burgeoning international force in several research areas (see 2).

The senior management teams of TJL, UMaine and MMCRI have made significant investments of time and capital in the IMB. Rick Woychik, TJL's Director; The President of UMaine, Robert Kennedy, and Bob Friesel at MMCRI serve on the IMB's Institutional Policy Committee (IPC) and advise the co-Directors of IMB on financial and administrative matters. The IMB's co-Director, Barbara Knowles, is also Vice President of Education and External Collaborations at TJL, and Michael Eckert, UMaine's Vice President for Research, is the PI of this EPSCoR award. As mentioned earlier and below, both TJL and UMaine have, and continue to, support the IMB financially.

In March 2007, the IMB finalized the development of a long-term strategic plan and research vision, and scientists at each of the partner institutions committed to sustaining the IMB beyond the lifetime of the EPSCoR award. Several IMB members have significant research support; the IMB has developed a sustainability model and has submitted, or is in the process of submitting, several proposals (see 4). Over the lifetime of the IMB, TJL and UMaine have provided considerable financial backing, and have pledged 2 years of bridging support while IMB transitions from the EPSCoR award to other external funding sources.

2) Scientific Research: During the 4 years of NSF support, IMB has developed robust programs that occupy the cutting-edge of research in 1) biological applications of ultra-high resolution microscopy & spectroscopy 2) development of nanoprobes 3) biocomputing and 4) bioengineering.

Ultra-high resolution microscopy and spectroscopy— The application of ultra high-resolution microscopy to resolving nuclear and membrane structures within cells has started bearing fruit on a technical level, and we are using this technology to tackle a series of challenging biological questions. Our 4Pi confocal laser scanning microscope (CLSM), acquired with NSF and Keck funding, is the only 3D super-resolution microscope in the United States. We have developed techniques to image biological samples such as cell nuclei, mouse blastocysts and mouse brain and nerve cells that were previously believed to be unsuitable for 4Pi imaging. Research using the 4Pi to investigate the role of free and phosphorylated H2AX in DNA repair mechanisms and the structure of the presynaptic CaV2.2 channel-transmitter release site core complex has recently been published. Projects that will use the 4Pi CLSM to examine 3D chromatin structure, nuclear compartments and neural cell organization are currently in progress.

Last year, IMB scientists developed a revolutionary new microscopic technique, Fluorescence Photo-Activated Localization Microscopy (FPALM), which provides resolution at the 20 nm scale and can be used to image single molecules in living cells. We are currently working to apply these techniques to biological samples and to combine FPALM with the 4Pi to create a 3D version of FPALM. 3D FPALM would provide 30 nm resolution in all dimensions—a significant step toward the ultimate goal of single molecule localization. Researchers are also designing and developing a 3D participle-tracking microscope (3D PTM). This microscope will allow researchers to track the movement of single molecules (1 nm) in live cells in real time. 3D FPALM and 3D PTM are seminal breakthroughs in modern microscope development; more importantly, taken together they hold the promise of revolutionizing our view of sub-cellular *structure and function*.

IMB researchers have developed sum frequency spectroscopy for biological applications. This technique probes chemical processes at surfaces and provides unique structural, directional, and functional information about biological processes in membranes. It is critical technique for improving our understanding of membrane structure and cross-membrane transport mechanisms.

IMB researchers are also expanding the biological applications of Raman spectroscopy, which can locate biological structures with 20 nm resolution. Prior to our work, use of Raman spectroscopy in examining complex cellular processes was limited because only two fluorescent labels could be imaged simultaneously. IMB researchers have shattered this barrier by developing techniques which allow for the simultaneous labeling and measurement of up to ten species with 20nm resolution. This work has transformed the utility of Raman spectroscopy in identifying and tracking biological structures and biochemical interactions and has the potential to localize components of molecular machines.

IMB houses this unique set of microscopic and spectroscopic techniques for biological imaging, an array of complementary, one-of-a-kind instruments. In addition, IMB has assembled the expertise and fostered the interdisciplinary collaborations necessary to exploit these technologies to tackle fundamental biological questions. Thus, IMB is a powerful resource that provides our researchers, and scientists worldwide, new windows into the world of gene expression, nuclear structure and membrane function. New research opportunities—pathways to examine functioning neurons and neural networks, tracking single proteins, and elucidate the connection between epigenetic changes and gene expression depend on the emerging research synergies and techniques developed by IMB technologists, biologists and chemists.

Nanoprobe Development—This cutting-edge program in functional materials complements our advances in biological imaging and spectroscopy. IMB scientists have been working with gold nanoparticles and Raman fluorescent probes. They are developing new methods to synthesize these probes and fine-tuning their characteristics including, brightness, bleaching, blinking, and toxicity. Our scientists are also working on ways to direct these probes to specific sites within cells using unique sol-gel coatings and antibody conjugation techniques. These gold and Raman probes are also at the center of a breakthrough in developing contrast agents for CT scanning. In addition, our researchers have devised a way to get quantum dots to enter the nucleus of living cells, which was previously considered impossible. This technique has huge implications for nuclear imaging and chromatin structure elucidation. The contrast agents and nuclear staining technique are the subjects of preliminary patents as are several other developments by IMB researchers (see 6).

Biocomputing—Biocomputing and sequence analysis is a critical aspect of the IMB research portfolio. The methods provide key links between microscopic and spectroscopic images and biochemical and structural data that allows the images to be correctly interpreted and integrated into solutions to biological questions. Our researchers are combining sequence-specific analysis of DNA with an understanding of 3D chromatin nanostructure by using advanced image analysis and biocomputing techniques. IMB researchers have demonstrated the direct association between genome features in the primary sequence and a higher-order organization in the interphase nucleus. They also have made new discoveries by using image analysis techniques to investigate the proximity of translocation break points in the interphase nucleus. Affiliated IMB researchers have developed wavelet transform techniques to evaluate the structural nature of DNA across different scales. These approaches are particularly useful for detecting possible long-range correlations among structural features of the genome that may

also correlate to chromatin conformation, in particular, the positioning and dynamics of nucleosomes.

Bioengineering—This is our newest research focus. It has literally exploded within the last year through key collaborations between IMB technologists, bioengineers, neurobiologists and geneticists. IMB scientists are currently devising and applying remote sensing of physiological parameters within mice or within cages of mice. A pilot program for these devices is ongoing in TJL's animal facilities. In addition, IMB scientists have created a microchamber to determine the factors involved in nerve growth and synaptogenesis *in vivo*; the prototype chamber is currently being tested. IMB collaborators are also working on nanopatterned surfaces, which may provide a method to understand cell migrations during development.

3) Collaborations: A major strength of the IMB is its ability to foster and support numerous interdisciplinary collaborations among IMB members, between IMB members and scientists at the 7 participating institutions and between IMB members and researchers at external institutions. In 4 years, IMB members have established numerous productive research collaborations which involve multi-centered exchanges of ideas, researchers and students and enhance scientific, education and technology development activities. They have produced significant, sustainable research partnerships resulting in scientific publications, new patents and intellectual property, successful applications for external funding and unique educational opportunities for graduate, undergraduate and high school students.

4) Grant Proposals Submitted: In the 4 years of NSF funding, IMB members submitted over 50 grant proposals in support of IMB related projects. Of those, 23 have been funded for more than $ 6 million. Notably, the IMB received an NSF MRI award and a $ 1.2 million grant from the Keck Foundation that supported the acquisition of a 4Pi microscope and a multiphoton confocal microscope. Researchers at UMaine recently received another NSF MRI to acquire and develop ultra-high resolution spectroscopic instruments. Our international partners have received nearly 6 million Euros from the European Union and Deutsche Forschungsgemeinschaft (DFG) to support IMB research and collaborations. The IMB is implementing a long-term sustainability plan. As part of this plan, over 14 additional proposals are pending or in preparation, including an NIH/NCI Bioengineering Research Partnership proposal for November 2007.

5) Presentations, Colloquia & Conferences: IMB researchers gave more than 50 technical presentations at regional, national and international scientific conferences. The IMB has organized and held a series of Colloquia and Conferences, hosted by TJL. Since 2003, IMB has hosted four 1.5-day colloquia and four 3-day international conferences, focusing on cutting-edge IMB research areas. An average of 38 IMB investigators attended each colloquium while over 100 scientists attended each conference. These meetings attract both young investigators and established researchers, showcase cutting-edge scientific developments, stimulate formal and informal scientific discussions and foster new collaborations. IMB members also hold weekly meetings to strengthen IMB collaborations. These meetings are videocast across four sites: TJL, UMaine, MMCRI and UH, and all interested scientific staff and students are invited to attend. At each meeting, one research group presents their current findings to the group, followed by questions and a general discussion. Funding opportunities, the status of current grant proposals, and possible collaborations are also discussed. In addition, the NSF EPSCoR office also sponsored the statewide activities and events as.

6) Publications & Patents: In the 4 years of NSF funding, IMB researchers published 92 articles in peer-reviewed journals and completed 5 book chapters. Well-respected, high profile international journals in fields ranging from chemistry to genomics and cell biology to optics and physics are represented. In addition, IMB researchers developed 6 novel technologies or ideas that resulted in patents and /or intellectual property rights.

Objective 2: Enhance human resources in the biophysical sciences by hiring exceptional researchers and developing current and future scientists. Categories of evidence include:

1) Scientists hired and supported: NSF funds allowed IMB to create a critical mass of exceptional researchers necessary to the success of the program. This project provided direct support to hire 3 tenure track faculty at UMaine in the fields of chemistry, mathematics, physics and bioengineering. In addition, two scientists in cell biology and nanoprobe development who worked primarily at TJL were supported, and have subsequently been retained by TJL and UH, respectively and continue to participate in the IMB collaboration. In addition, three research scientists and two graduate students working at TJL with IMB faculty were supported during years 2 and 3 of NSF funding. One of these scientists has also been hired by TJL to establish a research program in biological applications of super-resolution microscopy, centered around the 4Pi microscope. Thus, NSF funding provided the catalyst to launch several young investigators' research programs and scientific careers. In addition, NSF funding allowed UMaine and TJL to attract high-quality scientists to the IMB program; scientists who will continue their careers in Maine and the IMB consortium.

2) Non-science jobs created & supported: This project provided direct salary support for 6 staff at UMaine including project administrators and clerical staff. In addition, the grant provided administrative support for the founding director and co-directors to pay for their release from other duties. The directors were instrumental in mentoring younger faculty, encouraging and helping individual researchers on their grant proposals, creating key collaborations with international institutions, developing the strategic plan, garnering support from institutional stakeholders, planning, writing and submitting collaborative proposals for IMB funding.

3) Education programs & students supported: The research and education of 61 post-doctoral, graduate and undergraduate students was directly supported by NSF funds. In addition, IMB scientists mentored over 23 post-doctoral associates and 20 graduate students in the Functional Genomics Program (supported by NSF IGERT DGE-0221625). At TJL, over 30 undergraduate and high school students participated each year in the Summer Research Program supported with NSF REU (DBI-0453189) and HHMI funds; many of these students interned in IMB research laboratories. IMB scientists participated in teaching courses for the Functional Genomics Ph.D program and special videocast classes on key IMB topics such as bioinformatics, interdisciplinary studies and bioengineering.

4) Involvement of women and underrepresented groups: Maine is a small, rural state of 1,250,000 people, and one of the least diverse states in the nation with minorities representing only 3% of the population. Despite this challenge, the IMB is committed to expanding the participation of women and underrepresented groups in STEM careers.

The following is a summary of the personnel involved with the IMB since its creation in 2003 (baseline year):
PI/Co-PIs: 7 total, includes 3 women
Senior personnel hired: 7 total, includes 4 women

Collaborating Researchers: 35 total; includes 8 women and 4 minority (two Asian males, two Asian females)
Post-docs: 23 total; includes 6 women and 3 minority (one Asian male, two black males)
Graduate students: 26 total; includes 11 women and 4 minority (two black males, two Asian females)
Undergraduate students: 13 total; includes 2 women and 3 minority (two Asian males, one Asian female)
Administration/other: 13 total; includes 7 women and 2 minority (two Asian males)

TOTALS: 124 total; includes 41 women and 16 minority

Women represent 30% of the scientists participating in the IMB and 42% of the graduate students. This represents a strong advantage in having sufficient female mentors who are able to mentor the future women scientists in the program. All of the collaborating institutions continue to actively seek minority applicants for faculty and staff positions. The Functional Genomics Graduate Program (supported by NSF IGERT) has made considerable efforts to increase the participation of female and minority students, including Native Americans. In addition, TJL is committed to serving a broad spectrum of underrepresented students through its REU and HHMI summer research programs. Minorities in TJL's internship programs in 2006 totaled 37 percent, which represents a doubling of minority participation since 2003, while the enrollment of women remains high, and has averaged over 60 percent during that time period.

Objective 3: Improve the state's physical infrastructure in biophysical science. Categories of evidence include:

1) Facilities, renovation or expansion: NSF funding of the IMB program has played a key role in creating a robust physical infrastructure for biophysical research in Maine. At TJL, a Biophysical Sciences Suite encompassing over 2300 n.s.f. of research and laboratory space as well as 3 investigator offices (360 n.s.f.) was created. This renovation includes wet laboratories for cell biology, chemistry and nanoprobe development as well as an Advanced Microscopy Facility that is specially designed with vibration dampening, climate control and room-darkening controls to accommodate high-resolution microscopy equipment, such as the 4Pi Confocal Laser Scanning Microscope (see 2). At UMaine a fully equipment 4,000 sq. ft, class 100/10 micro/nano fabrication facility was created. These state-of-the-art facilities have helped IMB to attract and support new faculty, to acquire equipment, and to support visiting investigators—key factors in establishing and expanding IMB's unique research capabilities (see Objective 1 and 3 below).

2) Acquisition & Development of new equipment: Given the technical nature of IMB's research aims, instrument acquisition and development have been key components of our program and an important aspect of improving Maine research infrastructure. Using EPSCoR funds, support from other external sources as well as institutional dollars, IMB researchers in Maine have assembled a collection of major laboratory instrumentation with critical and unique research capabilities. These instruments are available to all IMB members, scientists at partner institutions and external collaborators through exchanges of data, students and researchers and as much as possible, by remote access. Maine researchers have access to one-of-a-kind instruments located at our international partner institutions. At TJL, new IMB equipment includes a microaxial tomography, a multiphoton confocal microscope (acquired with Keck funding) and the only 4 Pi CLSM in the United States (acquired with NSF and Keck Funding). TJL researchers also collaborated on the development and construction of a glucose-monitoring device. UMaine has a Field Emission Scanning Electron Microscope/Focused Ion Beam (FESEM/FIB) with cryogenetic stage (one of two in the US), a unique Sum Frequency

Spectrometer, a direct-write laser machining system, an FPALM confocal microscope, and a hybrid Scanning Fluorescence and Sum-Frequency Spectroscopy Imaging Microscope. At MMCRI, a 442 laser was purchased for a confocal fluorescence microscope system.

3) New research capabilities: The facilities and equipment described above have created a wealth of new research opportunities and capabilities unavailable anywhere else in the world. The researcher-built microaxial tomograph can image the nucleus of whole cells without distortion and has been used to examine genome architecture in the nuclei of mouse embryos. IMB researchers are the first scientists to apply 4Pi microscopy to complex biological samples. Our work has revolutionized scientists understanding of 3D subcellular structures and established light microscopy as a key visualization resource in fundamental biological research (see objective 1). The glucose-monitoring device allows for the non-invasive measurement of glucose levels in mice and rats and has been instrumental in forwarding several investigations on Type 1 and Type 2 diabetes. The FESEM/FIB allows unprecedented 3D imaging of biological samples at 2nm-5nm resolution. Additionally, the FESEM/FIB is equipped to provide 3D elemental mapping of biological structures. This instrument will provide significant advances in biological understanding at the molecular level. A unique Sum Frequency Spectrometry (built by IMB members) has supplied fundamental information about the structure and mechanism inherent in biological membranes. A confocal Raman Spectrometry built at UMaine provides multi spectral imaging at the 20nm scale and has been used to study the cytotoxic effect of gold nanoparticles in the lung.