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Introduction

The mission of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) is to improve health by leading the development of biomedical technologies and accelerating their application. The NIBIB encourages the integration of the physical sciences and the life sciences to advance human health by improving quality of life and reducing the burden of disease.

The NIBIB's Intramural Research Program (IRP), based in Bethesda, Maryland, has expertise that spans technologies ranging in scale from near-atomic resolution to intact organisms.

Current Research

• *Molecular Imaging Probe Development*

Developing molecular imaging probes for *in vivo* imaging of biochemical processes, including: positron emission tomography, optical imaging (fluorescence and Raman), magnetic resonance imaging, as well as contrast enhanced ultrasound, photoacoustic, and multimodal imaging. Molecular imaging in combination with anatomic and functional imaging can improve understanding of disease, enable early detection, and enhance monitoring of therapeutic responses and drug discovery and development. Methods include chemical synthesis, protein engineering, bioconjugation, radiolabeling, chemical analysis, preclinical studies, and clinical translation using various *in vitro* and *in vivo* techniques.

• *Nano Theranostics*

Rational design of water-soluble, biocompatible nanoparticles for combined imaging and therapy. Nanoparticles (<100nm) synthesized from materials such as polymers, metals, ceramics, and lipids permit simultaneous diagnostic imaging, drug delivery, and monitoring of therapeutic responses. Methods include synthesis, physiochemical characterization, surface modification and bioconjugation, and pharmacokinetic and pharmacodynamic evaluation in rodents for translation to clinical application.

• *Cardiovascular Imaging*

Developing patient-based methods for detection and quantitative characterization of subclinical cardiovascular disease of the myocardium and blood vessels in both early phase clinical trials as well as in multi-

center studies. Areas of study include genetically determined disease and acquired cardiovascular disease as a result of common risk factors. Methods include advanced magnetic resonance techniques, cardiovascular computed tomography, and molecular probes.

• *High-Resolution Optical Imaging*

Developing super-resolution optical imaging techniques, such as photoactivated localization microscopy, and applying them to the study of cells and tissues by combining wide-field optical sectioning techniques with existing approaches that utilize defocus or astigmatism for enhanced axial resolution. Developing fast optical sectioning techniques, such as selective plane illumination microscopy and multiphoton temporal focusing, that enable high-speed volumetric imaging of cells and embryos.

• *Biophotonics*

Developing probes and techniques for use in diffraction limited and subdiffraction limited fluorescence imaging of cells and tissues. Major emphasis is placed on developing new and improving existing genetically encoded fluorescent proteins for use as markers and sensors. Methods and technologies include confocal, TIRF, and widefield microscopies, single molecule imaging, fluorescence spectroscopy, and protein engineering.

• *Supramolecular Structure and Function*

Determining the organization and composition of supramolecular assemblies and small organelles in a cellular context and relating structure to function at the subcellular and molecular level. Methods include quantitative, high-resolution electron microscopy, scanning transmission electron microscopy, electron tomography, electron spectroscopy, nanoscale spectroscopic imaging, and novel labeling techniques.

• *Dynamics of Macromolecular Assembly*

Developing biophysical methods to characterize macromolecules and their reversible interactions, including elucidating the relationship between protein structure and function and the assembly of multi-protein complexes and molecular machines. Methods include analytical ultracentrifugation, surface plasmon resonance biosensing, photon correlation spectroscopy, isothermal titration and differential scanning microcalorimetry, and circular dichroism.

• *Complex Biological Systems*

Developing novel instrumentation and mathematical models for improved understanding of complex biological systems at the nanoscale. Methods include high-resolution atomic force microscopy under physiological conditions with sensitive force measurements and mathematical modeling, optical and laser technologies, fluorescence and optical spectroscopy, and applications of novel reporter molecules.

• *Immunochemical Nanoscale Analysis and Diagnostics*

Developing new technologies, including real-time, minimally invasive, microdialysis techniques and “lab on a chip” microfluidic immunoassays for the identification of biomolecules. Methods include microfabrication, laser-induced fluorescence detection, measurement of analytes at subfemtogram levels, mass spectrometry, time-resolved fluorescence, chromatographic analysis of protein expression, and secretion from single cells.

• *Non-invasive Optical Imaging*

Developing real-time, non-invasive methods to evaluate and monitor tissues and organs, with applications to cancer diagnosis, obesity, sickle cell disease, and monitoring the viability of kidneys destined for transplantation. Methods include optical subsurface imaging of fluorophores, functional laser speckle imaging, laser Doppler flowmetry, and sensitive infrared imaging of thermal gradients in tissues.

• *Remote Monitoring*

Developing wireless detectors for such variables as microvascular status, motor activity, and circadian rhythm.

Training Opportunities

The NIBIB's IRP offers training opportunities at several educational levels:

• *Imaging Sciences Training Program –*

A joint NIBIB/NIH Clinical Center program for MDs and PhDs seeking research careers in clinical, translational, and basic imaging research

www.cc.nih.gov/drd/training/index.html

• *Research Associateship Program –*

A joint NIH/NIST program for postdocs

www.training.nih.gov/postdoctoral/nist.asp

• *Biomedical Engineering Summer Internship Program –*

For college students completing their junior year in a bioengineering program.

www.nibib.nih.gov/Training/UndergradGrad/besip/home