Multiscale Biomedical Imaging Tools and Databases

Stephen TC Wong
Center for Bioinformatics, Harvard Center for Neurodegeneration and Repair, Harvard Medical School and Department of Radiology, Brigham and Women's Hospital, HMS

Biological systems and organisms possess structure at all degrees of magnification, from molecular to whole organism and even population levels. Imaging has contributed to understanding biology using modalities that typically operate at a single resolution or within a relatively narrow range. To delineate the current status and predict where future discoveries might be made or human disease might be progressed using a combination of imaging modalities, there is a need to create an interdisciplinary-center of multiscale imaging within IIC to define the issues and opportunities as well as to develop innovative tools and databases for imaging modalities across spatial and temporal scales.

The array of biomedical imaging modalities is staggering. Medical imaging modalities include Magnetic Resonance Imaging (MRI), X-ray Computed Tomography (x-ray CT), Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), X-ray, Ultrasound, Electrical Impedance Tomography (EIT), Electrical Source Imaging (ESI), Magnetic Source Imaging (MSI), and Laser Optical Imaging. For microscopic animal imaging modalities include Magnetic Resonance Microscopy (MRM), micro-CT, micro-PET, micro-SPECT, ultrasound biomicroscopy (UBM). At the cellular and subcellular levels, we have laser scanning confocal microscopy with multiphoton excitation capability, fluorescence microscopy, wide-field microscopy, laser capture microdissection microscopy, optical coherence tomography (OCT), bioluminescence imaging, time lapse imaging (TLI), electronic microscopy (EM), and atomic force microscopy (AFM). Each can contribute a piece from a complex puzzle. Synergies among modalities are limited however, and multimodality imaging has been developed only in a few specific areas, e.g., PET-CT.

The utility of multiscale imaging is as expansive as its scope, for basic science; mapping protein-protein interactions; visualizing molecular dynamics within cells; understanding disease mechanisms; neurobiology; to drug trials and clinical diagnosis & staging for selecting, tailoring and monitoring therapy. Multiscale imaging is defined by its technology and range of applications, encompassing trans-species studies using multiple modalities that overcome limitations of any single modality. The principal focus is cellular and tissue environments which are manifested as whole organism effects that may extend to populations. The structure-functional relationship is investigated in the presence of biological complexity and heterogeneity. Gene and protein expression are reflected in the imaging phenotype and linkage of corresponding changes at the molecular level to phenotypic and physiologic states.

Given that imaging systems are available, the rate-limiting factor of the utility of multiscale imaging is in the post-processing tools for registration and segmentation, visualization, establishment of image databases, content based retrieval, image analysis, data sharing and integration (with gene/protein expression data, pharmacodynamic, and other biological databases) across modalities and scales are needed. Extended software tools and databases capable of relating individual images with populations (e.g., brain atlases) and comparing populations with spatial and temporal statistics are potential areas for fruitful development of innovative computing technology.

We envision the development of multiscale imaging tools and databases requiring close interaction with an interdisciplinary team of collaborators from Visualization Institute (VI), Database & Algorithms (D&A), and Hardware Innovation (real time multiscale imaging often demands computing powers beyond current means) of IIC. The team would compose of experts in medical imaging, microscopy imaging, visualization, image analysis, database, data modeling, algorithms, interoperability, hardware-software co-design, systems and software engineering, as well as the users of multiscale imaging systems who are researchers across Harvard University and Harvard Medical School, such as biologists, chemists, neuroscientists, biomedical engineers, industry, and clinicians. The research and development of the multiscale imaging software tools will be based on open source, multi-platform framework and with documentation and process models. We will also cultivate an open source community to disseminate the results of this IIC work and will organize educational programs in multiscale imaging for students and researchers.