

Convergence of Microscopy and Imaging Bioinformatics

Bahram Parvin

Lawrence Berkeley National Laboratory

Berkeley, CA 94720

vision.lbl.gov

Advanced methods in microscopy continue to generate large amounts of data due to improved automation, development of new probes, and advanced instrumentation. Although management and quantitative representation of this data continues to be a significant problem, new requirements for standardization, data exchange, and coupling microscopy data with other data modalities have emerged. In this talk, we will first present our approach for managing experimental variables, multidimensional images, and introduce novel techniques for quantitative image analysis. Second, we will review our plan for data sharing and integration of different data modalities.

Presently, our infrastructure supports three different applications: (1) classical microscopy problems for protein identification, localization, and activation, (2) optimization and screening synthetic oligos for imaging mRNA, and (3) the development of optimized assays based on physiological responses. Although these applications have different end points, they share a set of common threads. The main challenges are large amounts of generated data from different microscopy modes, design and implementation of complex schema and accessing disparate ontologies, and the development of advanced visual routines for quantitative analysis. Our infrastructure integrates two systems: novel instrumentation, known as Visual Servoing Optical Microscopy (VSOM), and an imaging bioinformatics system, known as BioSig.

Visual Servoing Optical Microscopy (VSOM) protocols and instrumentation accomplish real-time interaction with living cells by repeatedly performing the following steps: (1) perturbation or stimulation of cells (immobilized on a surface in a perfusion chamber) via computer-controlled syringes; (2) analysis of the resultant physiological responses of individual cells and organelles; and (3) adjustment infusion of reagents based on currently observed cell responses and previously archived cell responses. The bioinformatics framework is designed to make the richly annotated cellular responses of previous VSOM experiments available during this process. In this context, the decision to put the instrument in a specific state can be as a function of stored cellular responses, or the currently computed response based on thresholding or event specification. The close-loop servo control enables accelerated development of new assays.

BioSig's imaging bioinformatics framework provides the basis for data management and analysis of samples, which have been imaged across multiple channels of information. The framework enables comparison and visualization at experimental level (meta data), image level, and feature level for each cell in the tissue. The system has been used for both fixed specimen and VSOM assays. It provides detailed annotation for sample preparation, type of sample, images, and multiscale quantitative representation of images. The system is currently being revised for compatibility with Open Microscopy Environment. In addition, controlled vocabulary and standard ontologies are being used to facilitate data exchange among multiple researchers. Finally, the database and its API are being specified through Web services to facilitate database integration with other Web-based resources.