NBIC- SIB PhD summer school 2010

Quantitative imaging and modeling of biological processes

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Speakers' Abstracts

nbic netherlands bioinformatics centre

SIB Swiss Institute of Bioinformatics

Speakers' Abstracts:

(in chronological order)

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Image-based Modelling and Simulation

The promise of computational biology to render hidden variables observable and controllable through in silico experiments largely depends on the availability of appropriate imaging and simulation methods. We present some of the challenges in using image data as a basis for modelling and simulation, and illustrate the benefits of novel algorithms in an example. This example considers fluorescence recovery after photo-bleaching experiments of protein diffusion in the endoplasmic reticulum. We show how a combination of imaging and simulation methods made it possible for the first time to accurately measure molecular diffusion constants from in vivo FRAP data.

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Optical Microscopy Image Segmentation, Cell & Organelle Tracking, Feature Computation, and Statistical Analysis

This session will describe the fundamentals of biological image analysis. We will start by reviewing the characteristics of multi-dimensional images acquired by modern optical microscopes. Then we will discuss the need for automated image-based measurements for hypothesis testing, computationally enabled discovery, drug screening, model-building in systems biology, assays, toxicology, histopathology, and tissue engineering applications. Then we will learn the tools required to produce these measurements, including image pre-processing, segmentation, tracking, intrinsic and associative feature extraction, cell classification, and analysis of multi-cellular units. Finally, we will learn about ways to validate automated image analysis results and assess their performance. Time permitting, we will conduct experiments with the FARSIGHT image analysis toolkit (www.farsight-toolkit.org).

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In Vivo Trafficking of mRNAs from Nucleus to Cytoplasm

The transcriptional process is positioned at the centre of the gene expression pathway. Emerging is a detailed picture of the atomic structure of the polymerase complex, the various protein players, the biochemical modifications involved and the intricate mechanistic properties of the molecules that control transcription and mRNA processing. The use of in vivo approaches for measuring intracellular dynamics now adds new levels of molecular dynamics and quantifiable kinetics to our view of gene expression. I will discuss live-cell quantitative imaging methods for: a) analyzing the kinetics of mammalian transcription, b) assaying the affects of co-transcriptional mRNA processing; c) tracking of single mRNA particles during mRNA transport and export events; and d) the tracking of the dynamics of cytoplasmic Processing Bodies (PBs) that function in mRNA decay and storage. Finally, I will describe new methodologies for following and quantifying of the kinetics of single-copy genes in living cell systems.

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3D-Imaging of Morphogenetic Parameters in Embryology

Gene expression profiling projects have provided us with increasing knowledge about overall gene activity levels in developing, healthy, and diseased tissue. For the functional interpretation of this wealth of information, the need to know in which part of the organ or tissue these genes are expressed becomes more and more pressing. Specific histological staining of proteins (with ICC) or mRNAs (with ISH) is therefore used to visualize these gene products, and thus the level of gene expression, in sections. Similarly, morphogenetic processes, like cell proliferation and apoptosis, can be visualized with histological procedures. In structurally complex organs the interpretation of the resulting sections is hampered by the loss of 3D morphology. However, the required level of detail and the limited penetration of staining agents in whole mount staining procedures dictates the use of serially sectioned biological material and makes the use of 3D computer reconstructions unavoidable. The 3D reconstruction protocol can be broken down into parallel qualitative (i.e. morphology) and quantitative (i.e. cell proliferation) methods. The qualitative method identifies the organ or tissue of interest, resulting in a surface reconstruction. The quantitative method relies on a specific staining method to identify individual nuclei. The number of nuclei is then systematically measured, providing local 3D information on i.e cell proliferation rate. Mapping of these local data onto the morphological surface reconstruction results in a reconstruction that not only conveys morphological information, but also quantitative morphogenetic data. Similarly local measurement can be applied on the staining intensity resulting from ICC and ISH staining and can thus be used to quantitatively reconstruct gene expression information in association with morphogenetic parameters.

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Using CellProfiler to Identify and Measure Objects in Images

Automated microscopes can generate tens of thousands of images per day. Automatic image analysis is less tedious then visual inspection; using software to analyze images is also more objective and quantitative. In this session, we will use the open-source software CellProfiler (http://www.cellprofiler.org/) as a vehicle to teach important concepts in image analysis. We will focus on concepts necessary for non-interactive, automated image analysis, as is required for large image sets from time-lapse or high-throughput screening experiments. The course will include instruction on how to set up and run an image analysis pipeline, how to tweak analysis parameters to optimize results, how to check data quality, and common pitfalls to avoid. We will also cover some downstream data analysis and exploration techniques as well as easy-to-use machine-learning tools for scoring complex phenotypes in images.

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In-vivo molecular Imaging in Small Animals: Applications and Data Processing Challenges.

With the rapid progress in molecular imaging technology, biomedical imaging is now covering a broad scale range, from the molecular level through the cellular level to the scale of the whole organism. Molecular processes such as gene expression can be visualized in live animals with optical, nuclear and MR imaging using targeted contrast agents, anatomical details with structural modalities (CT, MR, ultrasound), and functional information with e.g. specialized MR acquisitions. In pre-clinical research, all this complementary information greatly enhances knowledge discovery and treatment development. These lectures introduces a number of recently emerged small animal imaging modalities, and discusses data processing challenges emerging from these new modalities in the context of translational cancer research. Several application examples will be discussed ranging from evaluation of novel drugs to prevent metastatic disease to fluorescence-guided tumor and lymph node resection.

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Image-Based Neuro-Anatomy.

Advances in genomics, molecularly-encoded reagents, and electron and light microscopy, have brought us to the point where we can now contemplate building atlases of the brains of flies, and reconstruct modules, such as a cortical column, in mammalian brains. Such morphology" projects are a prerequisite to understanding how neural systems work. The informatics challenges of such projects are the rate limiting aspect.

We will survey the landscape of current efforts, identify the core image analysis challenges involved, and to the degree time permits, discuss methods for the problems of deformable registration, neural tracing, and shape comparison.

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Quantitative Imaging of Molecular Interactions and Conformation in Living Cells.

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