

Advanced Cell Cycle Analysis

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Dr. Jacobberger has been on the faculty of Case Western Reserve University since 1985. His general interests are analytical cytology and cancer. He has specialized in cytometry from his doctoral studies at the University of Rochester onwards, currently focusing on cell signaling and cell cycle processes viewed from a systems engineering orientation. Current research is centered in two enterprises—multivariate cell cycle analysis and modeling, and leukemia cell signaling—with a long-range goal of creating a cell-based analytical system that includes mathematical models of cell biochemistry.

Abstract

Multiparametric cytometry provides a unique view of cellular processes occurring in time. The reason is that cells within a population are not usually synchronized for any specific process. For any biochemical activity (e.g., synthesis of a protein) that changes periodically over time, a static measurement of a population of cells captures some of the cells at each point along the programmed kinetic "expression profile." For a single activity, the simplest description of an expression profile assigns cells to five states - basal, increasing, max, decreasing, and return to basal. The length of time spent in any one of these states creates the frequency with which cells populate clusters centered around the average expression of the state. Single-parameter cytometry of a population expressing this simple activity produces a measurement distribution that can be segmented into three clusters: low, dim, and high. Adding a second (offset) parameter resolves the dim cluster into cells that are in the increasing and decreasing states for both parameters.

In this lecture, these principles will be demonstrated using the cell cycle as a model system to explore this type of analysis. Laser scanning cytometry (LSC) is one of our principal approaches for cell cycle analysis. LSC provides quantitative expression measurements and morphological information. This is especially useful for measurement of mitotic stages, which will be illustrated in the afternoon workshop. LSC also brings sub-cellular localization to the analytical system, which becomes another analytical dimension, in terms of expression profiles.

The extraction of kinetic expression profiles from static cytometry data will be illustrated, and the application of this information to modeling cell biochemistry by systems of ordinary differential equations will be discussed.