"Statistical Inference about Cell Population Dynamics Using Flow Cytometry Data"

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ABSTRACT

Flow cytometry has become a standard tool in biomedical studies, with applications ranging from identification of abnormal cell populations, to fluorescence-activated cell sorting, or analysis of cell proliferation and differentiation. In recent years, statisticians have become more involved in addressing methodological issues associated with the use of this experimental technique.

This talk will consider the problem of gaining some quantitative insight into the processes of cell division, differentiation and death using flow cytometry data. Our work in this area stems from several ongoing projects that investigate such problems as the dynamics of activated lymphocytes, the development of the spinal cord during embryonic stages, or the progression of leukemia. Our ultimate objective is to quantify how treatments, toxicant exposures, or abnormal developmental conditions may modulate or alter the growth of cell populations. The statistical approach that we propose couples a regression mixture model with an age-dependent branching stochastic process. Two composite likelihood estimators are constructed for parameters estimation. The first estimator, which is akin to currently used estimators, is shown to be inefficient under conditions that appear reasonable in practice. The second estimator is proven to achieve root-n consistency. Simulation studies corroborate this finding by showing clear superiority of the second estimator. A penalized version of the estimator that takes direct advantage of known specific features of the data is also proposed. Finally, an application to the proliferation of T lymphocytes will be presented, and an extension of this work to study the regulation of gene expression will also be discussed.