Mathematical Modeling of Human Lymphocyte Proliferation with CFSE Data

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Abstract

CFSE analysis of proliferating cell populations is a tool of growing popularity for the study of cell division and division-linked changes in cell behavior. Partial differential equation (PDE) models are presented to describe lymphocyte dynamics in a CFSE proliferation assay. Previously unknown physical mechanisms accounting for the exact degree of dye dilution by division are explained in the context of cellular auto fluorescence. The rate at which label decays/diffuses out of the cell is also quantified using a Gompertz decay process. A new class of division-dependent compartmental models allows one to separate proliferation and death rates from intracellular label dynamics. By fitting the new models to the commonly used histogram representation of the data, it is shown that these improvements result in models with a strong physical basis which are still fully capable of replicating the behavior observed in *in vitro* data. Some mathematical aspects of the corresponding inverse problems are discussed. The new models provide quantitative techniques that are useful for the comparison of CFSE proliferation assay data across different data sets and experimental conditions.