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Stochastic journeys of cell progenies through compartments and the role of self-renewal, symmetric and asymmetric division

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Abstract-

Division and differentiation events by which cell populations with specific functions are generated often take place as part of a developmental programme, which can be represented by a sequence of compartments. A compartment is the set of cells with common characteristics; sharing, for instance, a spatial location or a phenotype. Differentiation events are transitions from one compartment to the next. Cells may also die or divide. We consider three different types of division events: (i) where both daughter cells inherit the mother’s phenotype (self-renewal), (ii) where only one of the daughters changes phenotype (asymmetric division), and (iii) where both daughters change phenotype (symmetric division). The self-renewal probability in each compartment determines whether the progeny of a single cell, moving through the sequence of compartments, is finite or grows without bound. We analyse the progeny stochastic dynamics with probability generating functions. In the case of self-renewal, by following one of the daughters after any division event, we may construct lifelines containing only one cell at any time. We analyse the number of divisions along such lines, and the compartment where lines terminate with a death event. Analysis and numerical simulations are applied to a five-compartment model of the gradual differentiation of hematopoietic stem cells and to a model of thymocyte development: from pre-double positive to single positive (SP) cells with a bifurcation to either SP4 or SP8 in the last compartment of the sequence.

Index Terms- mathematical modeling, theoretical immunology, stochastic processes

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