Mathematical Models of Stem Cells Renewal and Differentiation

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Abstract: In higher organisms, a steady supply of somatic cells is accomplished by proliferation of various types of stem cells, which retained the capability for almost indefinite self-renewal. According to need, driven by hormonal signals from the organism, some stem cells commit to differentiation and maturation in the direction of more specialized cell lineages. A well-know example is provided by haemopietic stem cells, which give rise to several lineages including precursors of erythrocytes (red cells), lymphocytes (white cells) and megakaryocytes (platelets), among other. One established method of modeling of such hierarchical cell systems is to use a discrete collection of ordinary differential equations, each of which describes a well-defined differentiation stage. In such framework, a range of mathematical results have been obtained (such as stability and oscillation criteria), some of which are applicable to modeling of the underlying biological systems. However, there are indications that the differentiation process is less rigid and that it involves transitions which are continuous, along with discrete ones. We propose new mathematical models of stem cells renewal and differentiation. The models of continuous differentiation are based on branching processes with continuous type space, elements of which represent the range of differentiation stages. Distributions of branching processes with continuous types can be described using stochastic point processes and probability generating functionals. We demonstrate that using this approach, one obtains the transport-type equations as equations for expected values of the process. We illustrate our approach with examples based on experimental observations of mesenchymal and hematopoietic stem cell systems. The models are applied to address the role of asymmetric cell divisions and replicative senescence in tissue maintenance and regeneration.

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