Mathematical models of hemaopoietic stem cell renewal and differentiation

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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 hematopoietic 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 diffferentiation 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 to address the role of asymmetric cell divisions and replicative senescence in tissue maintenance and regeneration. The models are formulated both in the discrete and continuous framework as multicompartment and structured populations models. The differences between the two approaches are investigated. Results of numerical simulations compared to clinical data lead to the conclusion that the regulation of the asymmetry of cell divisions is significantly more efficient that the regulation of the proliferation rates. Moreover, analysis of the model equations leads to a generalization of the concept of self-renewal potential, which might be helpful to define the stem cell compartment.