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Multiscale Modelling of Red Blood Cell Production using Continuous and Hybrid Models

This presentation will be devoted to multiscale mathematical modelling of erythropoiesis, the process of production and regulation of red blood cells. It lies upon works recently published [1, 2, 3, 4], in collaboration with N. Bessononv (Institute of Mechanical Engineering Problems, St Petersburg, Russia), I. Demin (Novartis Pharma, Basel, Switzerland), O. Gandrillon (University Lyon 1, France), S. Genieys (INSA de Toulouse, France), P. Kurbatova (University Lyon 1), S. Fisher (INSA de Lyon, France), L. Pujo-Menjouet (University Lyon 1) and V. Volpert (University Lyon 1, France), within the INRIA Team Dracula (Lyon, France).

Erythropoiesis is a complex process, involving cells with different maturities, from very immature stem cells to circulating mature red blood cells. It is regulated both at the intracellular level and at the cell population scale. We propose two complementary approaches for a multiscale model of erythropoiesis [1, 2, 4], in which we describe together erythroid progenitor (immature red cells) dynamics and intracellular regulatory network that determines erythroid cell fate. The intracellular regulation model is based on several proteins inhibiting and activating one an other, under external actions of growth factors that influence their production. The levels of these proteins will decide of cell self-renewal, differentiation or death by apoptosis. Erythroid progenitors dynamics are either described with an individual-based model as discrete elements [1] or with structured models, either compartmental models (systems of ordinary differential equations) [2, 4] or partial differential equations [3]. In both cases, nonlinearities are considered in the models to account for cell fate regulation.

Analysis of the continuous models is performed and simulations are carried out to confront the models to experimental data of anemia (blood loss). The IBM is also confronted to experimental data, and this allows concluding on the roles of the different feedback controls and the relevance of such models, in order to provide more insights into the regulation of erythropoiesis.

References

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