

Computer modelling of haematopoiesis with applications to blood pathologies (CMBLOOD)

Intermediate report for the period January – December 2009

1. Main activities and results

WP1: Delay differential equations (DDEs). Various methods and algorithms for numerical solution of non-stiff and stiff ordinary differential equations (including DDEs) and software for their implementation can be found in the literature. Software package XPPAUT is freely available in internet and offers implementation of a set of classical solution methods and algorithms for DDEs. After installation and exploration of its characteristics, the package is modified and recompiled by G. Bencheva, to have the possibility to measure the computing time for the solution of the considered problem. Comparative analysis of the applicability of the XPPAUT algorithms for computer modelling of erythropoiesis (production and regulation of red blood cells) is made, and the results are published in [B3_09].

The dynamics of various white blood cells populations (T-, B- and NK-cells) is subject of observation after transplantation of haematopoietic stem cells, to track how fast the patient's immune system is recovered. Two leukopoiesis models are investigated – the first one is with a single delay and takes into account the influence of the growth factors, while the second one is with two delays and takes into account a period for intermediate differentiation of the blood cells (Fig. 1).

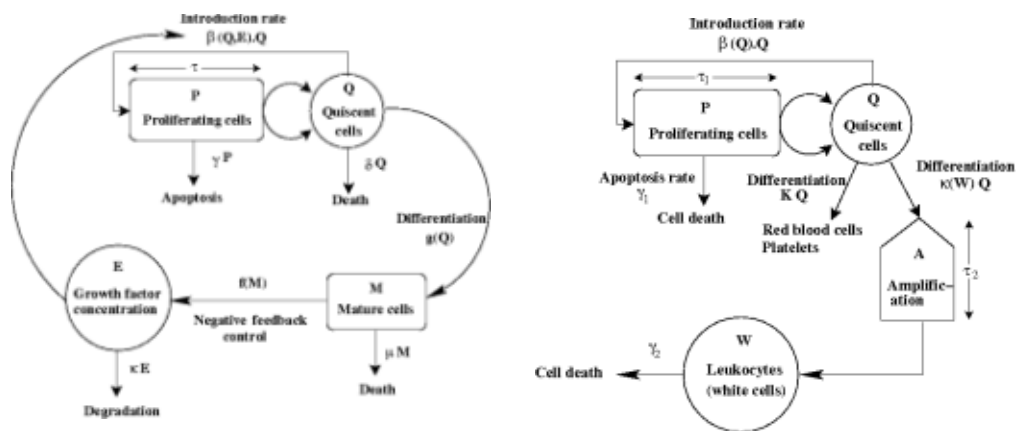


Fig. 1. Leukopoiesis models – relations among the parameters and unknowns

The parameters involved in the models, depend on the particular blood cell type and have to be properly tuned to make the computer model capable for personalized diagnostic and prognostic applications. As a first step in this direction, for both models it is done the following: a) systematization of the clinical data, provided by NHATHD; b) excerption of data from papers for the parameters which can not be measured; c) numerical experiments with various initial data (concrete patients) and values of the parameters. Comparative analysis of the results with each of the models is made and will be used as a starting point for sensitivity analysis and parameter estimation. G. Bencheva and P. Boyanova took part in the work to obtain the results on this package, some of the latter are published in [B1_09], [B2_09], and others are in preparation phase ([B4_09]).

WP2: Advection-diffusion-reaction equations (ADRE) for chemotactic cell motion. As in WP1, the first step in the investigations on this package is exploration and analysis of existing methods, algorithms and software tools for numerical solution of ADRE. The model for chemotactic motion of haematopoietic stem cells is not standard and includes ODEs and PDEs with nonlinearities in both system of differential equations and boundary conditions. Discretization methods as well as operator splitting techniques are investigated for systems of ADRE. Part of the opportunities given by the COMSOL package for computer modelling of physical processes and for solution of PDEs are studied and a set of preliminary numerical tests are performed with the investigated model. Results on the tasks in the current package are obtained by G. Bencheva and N. Kosturski, part of them are in preparation phase[B5_09].

2. *Publications, where the project DO 02-214/2008 is acknowledged*

a) published:

[B1_09] G. Bencheva, Towards Real-Time Data-Driven Computer Simulation of Blood Cells Production and Regulation, Proceedings of 3rd Annual meeting of BG SIAM'08, (2009), 15--18.

[B2_09] G. Bencheva, Development of parallel tools for biomedical simulations, Science and Supercomputing in Europe, report 2008, HPC-Europa++ 2008, (2009) pp. 467-474.

b) accepted:

[B3_09] G. Bencheva, Comparative Analysis of Solution Methods for Delay Differential Equations in Haematology, Large Scale Scientific Computing, Springer LNCS 5910

c) in preparation:

[B4_09] G. Bencheva, How does clinical data fit into two leukopoiesis models?

[B5_09] G. Bencheva, Towards computer modelling the therapy of leukaemia

3. *Presentations and talks*

- G. Bencheva, Comparative Analysis of Solution Methods for Delay Differential Equations in Haematology, 7th International Conference on Large Scale Scientific Computations, ([LSSC'09](#)), Sozopol, June 4-8, 2009
- G. Bencheva, Real-Time Data-Driven Computer Simulation of Blood Cells Production and Regulation, International Workshop on Advanced Numerical Methods and Applications, Technical University Gabrovo, Nov. 12, 2009.
- G. Bencheva, How does clinical data fit into two leukopoiesis models?, 4-th Annual meeting of the Bulgarian section of SIAM ([BGSIAM'09](#)), IMI-BAS, Sofia, Bulgaria, Dec. 21-22, 2009

4. *Others*

- Organizational and financial activities (G. Bencheva): a) organization of regular meetings of the team members as well as of working meetings with the colleagues from NHATHD; b) purchase of additional equipment for the working places of the PhD students.
- Development and support of a web page for the project (P. Boyanova, G. Bencheva)
- Additional activities on dissemination and popularization of obtained results in the framework of: a) Conference on Large Scale Scientific Computations, Sozopol, June 4-8, 2009 (organized by IPP-BAS); b) 4th annual meeting of the Bulgarian Section of SIAM, Sofia, December 21-22, 2009.