Personalized Medicine

Optimization of EPO Dosing

Executive summary

The project concerns the use of optimal control methods for computation of EPO (Erythropoietin) doses in hemodialysis patients.

Challenge overview

Currently, EPO doses are often prescribed using empirical algorithms which are in general charts where doses can be looked up based on a current hemoglobin measurement. The aim is to stabilize hemoglobin levels within a narrow target window. This is a delicate objective, as patients' response to treatment varies highly and doses should be as small as possible to mitigate drug-related hazards. The Renal Research Institute (RRI) has developed a predictive model of erythropoiesis which takes EPO administration into account. This model possesses a number of personalized parameters and parameter estimation is done at the institute individually for each patient. A joint project was initiated to develop and implement a nonlinear model predictive control method for computation of the EPO doses based on the previously developed erythropoiesis model.

Implementation of the initiative

The collaboration between the University of Konstanz and the RRI started already in 2014 with several master theses on this topic. A research associate in the working group of Prof. Volkwein developed and implemented the control algorithm while the institute provided anonymized model parameters of several patients to test the algorithm with. The research associate visited the institute twice and regular video meetings were held between the project partners allowing a permanent dialogue.

The problem

The named model of erythropoiesis consists of five hyperbolic partial differential equations for the different cell stages a cell passes through when becoming an erythrocyte. Time delay in the sense that the cells remain about two weeks in the bone marrow before getting released into the bloodstream makes therapy difficult. The optimal control problem is formulated for an assumed continuous but piecewise constant EPO administration. I.e. the optimal administration rate over time is searched. The problem is nonlinear and numerically solved without linearization.

Results and achievements

We successfully found an optimization setting which works for the so far tested patient data sets. Here, the developed algorithm has been able to control the patients' number of erythrocytes very satisfactorily. The numerical tests have shown that the algorithm can handle the mentioned time delay as well as simulated bleedings. This can be seen in the figure below. On-going work is devoted to the restriction that EPO can only be administered during dialysis treatments and it remains to test the algorithm for all available data sets.

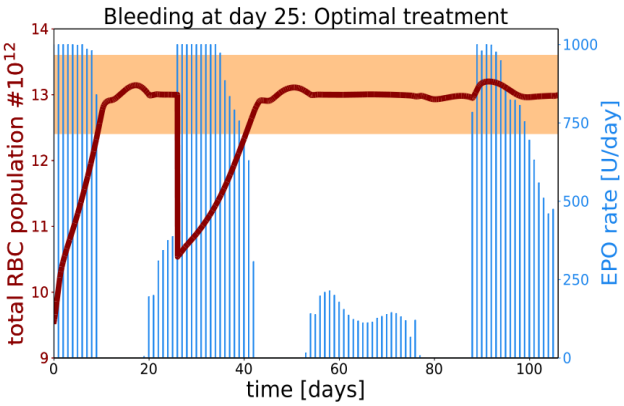

Figure: Optimally controlled erythrocytes population with corresponding EPO administration rate. The orange range is the target window for the RBC population.

Partners in the project

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