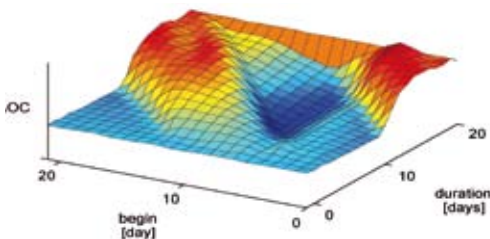


## KEYWORDS

- » Chronic Myeloid Leukemia (CML)
- » Imatinib
- » Simulation
- » Model-based Therapy Optimisation



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## MATHEMATICAL MODELING OF IMATINIB-TREATED CHRONIC MYELOID LEUKEMIA

Competition processes between normal and malignant cells can be observed in many hematopoietic disorders. The mechanisms underlying these processes are largely unknown. There is evidence that the competition is controlled by dynamic regulation processes at the level of hematopoietic stem cells which are influenced by cell-cell and cell-stroma interactions. As shown previously, clonal competition processes in animal systems can be explained using a mathematical stem cell model, based on the concept of within-tissue plasticity.

This model is applied and adapted to the human situation. It is used to describe and explain observed clonal competition processes between normal and malignant cells in patients with chronic myeloid leukemia (CML). A validated version of the model shall allow to simulate the development of the disease as well as different scenarios for treatment strategies. Using these simulation analyses we contribute to a deeper understanding of the malignant abnormalities of the leukemic cells. Furthermore, the theoretical results might be the basis for a model-based optimization of therapeutic strategies for CML patients.

One particular focus of the research group's model analysis is the treatment of CML with the tyrosine kinase inhibitor imatinib. Assuming selective effects of this drug on proliferative BCR-ABL1 positive (stem) cells, the model analysis predicts that the therapeutic benefit of imatinib might be improved by combination with proliferation stimulating treatment strategies.

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