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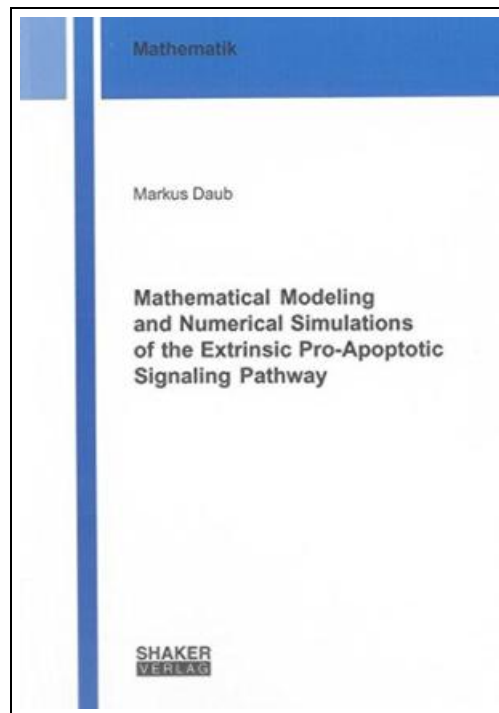
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Mathematical Modeling and Numerical Simulations of the Extrinsic Pro-Apoptotic Signaling Pathway

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Shaker Verlag Mrz 2013, 2013. Buch. Condition: Neu. Neuware - Apoptosis is a special form of programmed cell death and plays an important role in cancer research for instance. An essential part of the apoptotic process is the extrinsic signaling pathway, which is initiated at the cellular membrane by active ligand-receptor clusters. The activation of special proteins, so-called caspases, starts a caspase cascade, a reaction network of diverse caspase types, that finally results in the death of the cell. The extrinsic signaling pathway can simply be separated into two components: on the one hand, the formation of ligand-receptor clusters on the cellular membrane which act as stimulus of the signaling pathway, and on the other hand, the intracellular reaction network where diverse caspase types are involved in. In this thesis, mathematical models for these two processes are introduced and analyzed. According to the structure of the signaling pathway, the thesis is separated into two parts. 1) In the first part of the thesis, we introduce a spatially extended reaction-diffusion model for the reaction network with diverse caspase types. First, we show that the system has an unstable and two asymptotically stable, spatially homogeneous, stationary solutions. Moreover, we prove that the reaction-diffusion system admits a bounded invariant region that guarantees the boundedness of the solution for all time. After the analytic part of the first chapter, we proceed with a numerical analysis of the reaction-diffusion system. The numerical simulation shows that the diffusion rapidly balances the caspase concentration and that the behavior of the system is subsequently described by the reaction kinetics. We use this fact for the investigation of the long-time behavior of the reaction-diffusion system and split the simulation into two steps. With numerical simulations, we show that the system is switch-like concerning the initial condition with the outputs...

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