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Mechanisms for liver size regulation

The liver is a multi-functional organ that participates in major physiological processes and that possesses a remarkable regeneration capacity. After loss of functional liver mass the liver regrows to its original, individual-dependent size. A transplanted liver adjusts its size to the host organism by increasing in size when small-for-size or decreasing in size when large-for-size. Yet, how does the liver "know" when it has achieved its correct size?

The mechanisms of organ size control are still not well understood. Intracellular signaling pathways that control cell size regulation, cell proliferation and apoptosis have already been studied in the literature. However, organ size control is the collective result of decentralized, individual cell decisions. It is proposed in several works that this collective behavior might be guided by nonlocal interactions mediated through morphogen gradients. Here, we pose the question, whether organ size control can also be accomplished by a mechanism solely based on local intercellular interactions.

Based on a careful review of currently debated mechanisms and recent experiments for organ size regulation we will develop and analyze several model prototypes. We will focus on an Interacting Cell System Model to study especially the implications of local intercellular interactions as well as the regulatory role of organ-intrinsic growth factors and organ-extrinsic growth regulators. The study is part of the Virtual Liver project funded by the German BMBF.