Multiscale modeling of liver regeneration in 3D

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During the last years, modeling of different physiological and pathological aspects of the liver advanced significantly with the development of increasingly realistic models on molecular, cellular, tissue and whole organ scale. Nevertheless, model driven liver research is still hampered by a lack of techniques that allow robust integration of these different scales into unifying frameworks. We here present a novel multiscale spatio-temporal 3D model of liver tissue (Fig.1) that is based on *in-vivo 3D* imaging and that may serve as such unifying framework.

We use this model to study liver regeneration upon damage or tissue loss which depends on intracellular and tissue scale processes, which interplay with tissue mechanics. In order to capture all these processes at their respective scales, the presented multiscale modelling framework integrates sub-models at all relevant scales from intracellular signalling to body level. It thereby allows predictions on a wide range of possible regeneration scenarios and helps to identify on one hand particularly informative experiments permitting to distinguish between alternative mechanisms, on the other hand impossible scenarios that should not be pursued experimentally. In this way, the model predictions can guide the experimental strategy. The multiscale tissue model is able to simultaneously reproduce all experimental observations including the regeneration process kinetics on the tissue scale.

The presented study is an example for how the tight systems-biological integration of experimentation and modelling, both covering multiple scales, can facilitate understanding of complex multi-scale processes as liver regeneration.

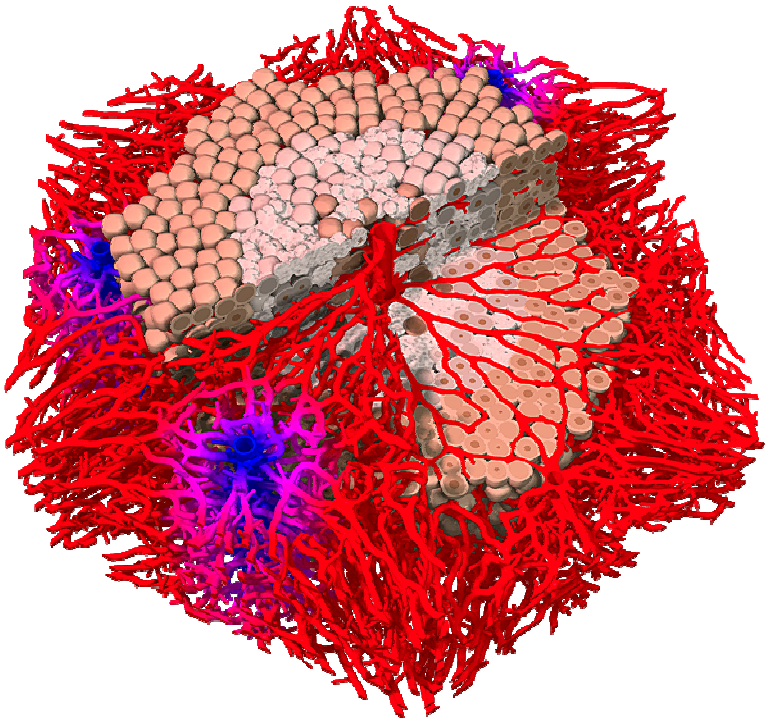

***Fig.1**: Visualisation of spatio-temporal model of a liver lobule*