Digital Liver Twin - Data- and Model-Driven Multiscale Liver Modelling

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We use computational multiphase and multiscale continuum-biomechanical modelling of biological tissue to simulate the hepatic deformation-perfusion-function relationship and allow patient-specific prediction of liver surgery [1, 2]. Using coupled continuum-biomechanical PDE-ODE models based on the theory of porous media (TPM) [3, 4], we obtain a precise mathematical description and thus perform numerical simulation of function-perfusion processes in the human liver. For this purpose, we describe the functional liver units, the liver lobules, as a homogenized porous medium, while considering an anisotropic blood flow. By coupling the metabolic processes at the cellular level, a poroelastic multiphase and multiscale function-perfusion model is thereby obtained. Additionally, the multiscale liver model is integrated into a whole-body ODE-based physiological-based pharmacokinetics model that includes multiple organ compartments that account for detoxification, such as the lung or kidney. The coupling of the different scales is done using the coupling library preCICE [5]. Based on this framework as shown in figure 1, depending on the considered phases, solutes, and metabolic processes, we can not only describe tumor growth, but will also support clinical decision-making processes during the treatment of acute and chronic end-stage liver diseases in the future.

During the last decades, liver diseases such as non-alcoholic fatty liver disease (NAFLD) or advanced forms with acute and chronic end-stage liver disease like a liver tumor account for a significant proportion of Western civilization diseases (see also figure 2). In addition to chemotherapeutic treatment, tumors are treated by removing the tumor-bearing tissue (resection) or liver transplantation. Based on our model, we describe not only the residual liver function after resection, but also the resulting perfusion changes, as well as regeneration by regrowth of healthy tissue. However, also liver transplantation is a curative treatment option, which in turn is confronted with an increasing number of elderly multi-morbid potential recipients and donors as well as ischemia reperfusion injury (IRI) occuring during the non-perfused transportation time. According to the considered condition, in addition to the blood phase and healthy liver tissue phase, further solid phases such as necrotic, tumor, or fatty tissue are included all with their respective solutes.

To make patient-specific predictions for these cases, we enhance the model through the integration of experimental, clinical, and *in silico* data from cooperation partners [6]. This involves not only laboratory data to provide initial and boundary values for solutes and the ODE models, but also automated image analysis from the field of machine learning to read geometry of liver lobules and

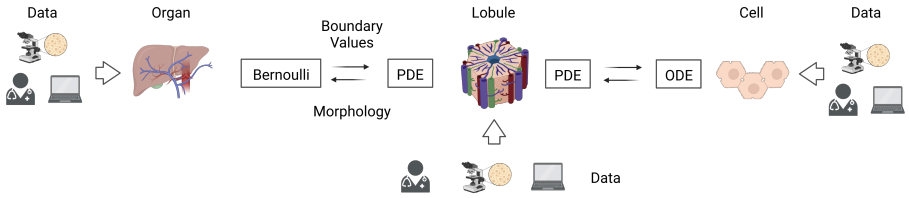

Figure 1: The underlying model consists of several scales, which are linked to form an ODE-PDE-ODE model, where each scale is supplied with patient-specific data. Image created with BioRender.com

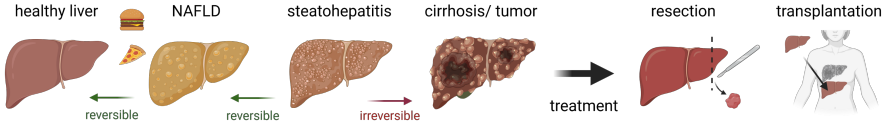

Figure 2: Stages of liver disease and treatment due to western lifestyle choices. Image created with BioRender.com

zoning patterns of steatosis from histopathological images. For object identification, we use Mask R-CNNs [7], for which training data were annotated by pathologists. Subsequently, liver lobules and the individual zonations can be constructed from the positions and classification of the identified portal fields, central veins, and hepatocytes. Further, we use physics-informed machine learning (cf. [8]) to allow near-real time predictions for clinical applications of the models.

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