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Model Order Reduction (MOR) of Function-Perfusion-Growth Simulation in the Human Fatty Liver via Artificial Neural Network (ANN)

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Numerical modeling of biological systems has become an important assistance for understanding and predicting hepatic diseases like non-alcoholic fatty liver disease (NAFLD) or the detoxification of drugs and toxines by the liver. We developed a model for the simulation of hepatic function-perfusion processes using a multiscale and multiphase approach. Here, the liver lobules are described using a homogenization approach with a coupled set of partial differential equations (PDE) based on the Theory of Porous Media (TPM) to describe the coupled blood transport and tissue deformation. For the description of metabolic processes on cellular scale ordinary differential equations (ODE) are used. For many practical and clinical applications, e.g. optimization procedures or uncertainty quantification, a fast but reliable computation is required. Thus, we use a non-linear model order reduction (MOR) based on an artificial neural network (ANN) for the prediction of simulation results. The practicability of this approach is shown in a comparison between the high fidelity numerical simulation of a NAFLD and the predicted results by the ANN.

1 Mathematical Model

Hepatic tissue has a complex hierarchical structure, with different processes taking place in each functional unit, see Figure 1. The organ with the macroscopic blood perfusion can be divided into liver lobules with a complex biological structure and an anisotropic blood flow, that is described with a Darcy approach. The liver lobules contain the liver cells, called hepatocytes, which are responsible for the metabolic processes. Small capillaries, called sinusoids, run along the hepatocytes and supply them with blood as well as nutrients and other substances. To simulate those scale-depending processes, we developed a numerical model using a multicomponent, poro elastic multiphasic and mutiscale function-perfusion approach based on the Theory of Porous Media (TPM, see EHLERS [1] and DE BOER [2]) including the processes on the lobule scale and the cell scale, cf. RICKEN ET AL. [3–7].

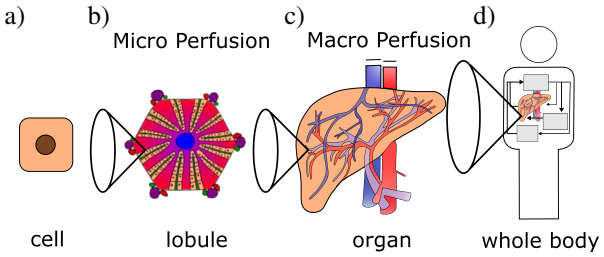

Fig. 1: Different scales of the human liver. a) Metabolic processes on the cell scale, b) anisotropic blood flow on the lobule scale, c) macroscopic vascular on the organ scale, d) interaction between different organs in the whole body

1.1 Lobule Scale

The lobule scale with its complex biological structure is described with a homogenization approach using the TPM. According to RICKEN ET AL. [8] the total body φ consists of κ different phases $\varphi^{\boldsymbol{\alpha}}$, including $(\nu-1)$ miscible substances $\varphi^{\alpha\beta}$

$$\varphi = \sum_{\boldsymbol{\alpha}=\mathbf{1}}^{\boldsymbol{\kappa}} \varphi^{\boldsymbol{\alpha}} := \sum_{\alpha=1}^{\kappa} [\sum_{\beta=1}^{\nu-1} (\varphi^{\alpha\beta}) + \varphi^{\alpha}]. \tag{1}$$

The presented model contains four phases, namely the solid liver tissue $\varphi^{\mathbf{S}}$, the fatty liver tissue with the ability of growth $\varphi^{\mathbf{T}}$, a phase representing necrotic hepatocytes $\varphi^{\mathbf{N}}$ and a fluid phase describing the blood $\varphi^{\mathbf{F}}$. Additionally, we include miscible substances converted via hepatic processes that can either be stored in the liver tissue or transported through the liver via the blood flow.

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1.2 Cell Scale

The hepatic metabolic processes, depending on local availability of nutrients or substances, take place in the hepatocytes resulting in either bioconversion or storage. Our model takes into account the glucose homeostasis, the development of NAFLD due to the accumulation of fat as well as the detoxification of paracetamol using ODEs. The fat metabolism is implemented using an approach by SCHLEICHER ET AL. [9].

1.3 Model-order reduction (MOR)

Since the numerical simulations are computationally demanding, we employ a MOR using an ANN that we trained on the simulation data to reduce computational time. For this, we generate samples with a random distribution of the material parameters responsible for a hepatic fat accumulation. These data are used for training, testing and validation of the ANN, which afterwards is capable of calculating the required results without expensive numerical simulation. The used network is build with 3 inputs, 2 hidden layers of 30 neurons each and 85 outputs.

2 Results

Figure 2 a) shows the numerical results of the fat accumulation in the hexagonal liver lobule with a zonated fat distribution from the pericentral zone to the periportal outer region. Figure 2 b) illustrates the results by the ANN, calculated with the same input parameters as chosen in the numerical simulation.

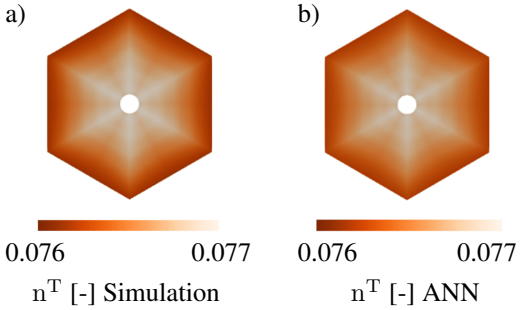

Fig. 2: Comparison of the fat volume fraction calculated using a) the numerical simulation and b) the ANN

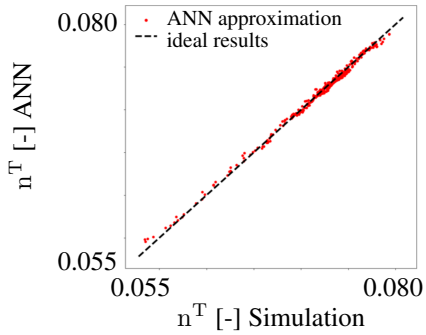

Fig. 3: Relation between simulated and predicted results

It becomes clear that the ANN predicts sufficiently the zonated spatial distribution of the fat fraction analogously to the simulation. The range of the fat volume fraction is comparable to the numerical results and the relative error is ≤ 1.2 %. The accuracy of the approximation can also be seen in Figure 3 where the ANN prediction results at one point in the pericentral zone are depicted. The discrepancy between the simulation data and the predicted outcome via ANN is extremely low and the approximation corresponds to the ideal results at all levels of fat accumulation, while the largest derivation occurs during a minor development of NAFLD. Since we provide more parameter samples that lead to a higher fat accumulation and use them to train the ANN, the accuracy of the predicted results becomes better in areas with more testing samples.

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