11th World Congress on Computational Mechanics (WCCM XI)
5th European Conference on Computational Mechanics (ECCM V)
6th European Conference on Computational Fluid Dynamics (ECFD VI)
July 20–25, 2014, Barcelona, Spain

SPATIALLY RESOLVED SIMULATION OF GLUCOSE METABOLIZATION IN THE HUMAN LIVER

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Key words: *Hepatic Glucose Metabolism, Hepatic Sinuosid, Two-Scale Model, Advection-Reaction Simulation.*

Blood glucose concentrations in the human body are regulated in a narrow range between 3 and 9 mM despite large variations in systemic supply and demand. This is necessary on the one hand to provide constant supply for the brain for which glucose is essentially the exclusive nutrient [1] and on the other hand to avoid toxicity at high glucose concentrations. The liver plays central role in this regulation process, releasing stored or synthesized glucose as well as utilizing or storing it in case of low or high blood glucose levels, respectively. Various hormones influence this regulation process [2].

The contributions of the liver to the systemic glucose regulation mainly involve the processes of glucose utilization and production, glucose storage, freeing from glycogen, and glucose synthesis and degradation. A model for these processes was obtained here by reduction of a previous, detailed kinetic model of the hepatic glucose metabolism [2]. The reduced model considers the liver as one well-stirred compartment, permitting fast simulations due to a small number of variables. Investigating the influence of heterogeneity on the underlying processes, however, is not possible if well-stirredness is assumed. Heterogeneity can occur locally inside the hepatic lobuli, the functional units of the liver of approximately 1 mm size where the exchange between blood flowing through sinusoids and the surrounding liver cells takes place. It involves concentration gradients along the sinusoid as well as

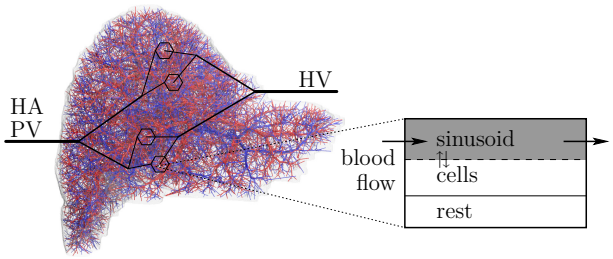

Figure 1: Conceptual overview of our two-scale liver model: Vascular trees supply and drain different parts of the liver. The glucose metabolization is described by considering representative sinusoids for each part. A realistic organ and vascular geometry (shown in the background) at the desired level of detail was obtained from MR image data of a human liver similarly as in [3].

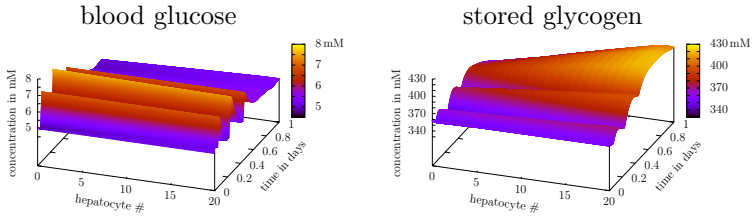

Figure 2: Using 24-hour blood glucose profiles from [4, Fig. 1], our model for a single sinusoid predicts an increasing amount of stored glycogen over time with a spatial gradient along the sinusoid.

different behavior of periportal and pericentral (at the beginning and end of the sinusoids, respectively) liver cells. Global heterogeneity can also be present, i.e. different larger regions in the liver may show different metabolization behavior, in particular if affected in a heterogeneous way by diseases.

We here present a spatially resolved model based on real organ and vascular geometry, in a similar fashion as in [3]. The liver is now viewed as consisting of a finite number of subvolumes, for each of which the metabolization behavior is modeled by a representative sinusoid. Along the sinusoid, we consider blood flow as well as exchange with the surrounding cells and metabolization/storage, both according to the reduced model above, leading to a 1D advection-reaction simulation. As in [3], the connection to the rest of the organism is given by the blood flow through the vascular structures, see Figure 1 for a conceptual sketch and Figure 2 for first results of a single-sinusoid simulation. This approach allows analyzing the effects of parameter variations both zonated along sinusoids and between different representative sinusoids. Thereby, effects of local and global alterations in structure or metabolism on the whole-organ metabolism can be analyzed.

Acknowledgments. This work was funded by the BMBF via the Virtual Liver Network (grant numbers 0315741 and 0315769). The authors thank Benjamin Knowles and Dipen Parekh for providing and processing the MR image data on which the vascular systems in Figure 1 are based.

REFERENCES

[1] J. E. Gerich. Control of glycaemia. *Bailliere Clin. Endoc.*, 7(3):551–586, 1993.

[2] M. König et al. Quantifying the contribution of the liver to glucose homeostasis: a detailed kinetic model of human hepatic glucose metabolism. *PLoS Comput. Biol.*, 8(6):e1002577, 2012.

[3] L. O. Schwen et al. Spatio-temporal simulation of first pass drug perfusion in the liver, 2013. In review.

[4] K. L. Stanhope et al. Twenty-four-hour endocrine and metabolic profiles following consumption of high-fructose corn syrup-, sucrose-, fructose-, and glucose-sweetened beverages with meals. *Am. J. Clin. Nutr.*, 87(5):1194–1203, 2008.