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Mathematical modelling of liver metabolism — do we need a multi-scale approach?

The liver is the central metabolic organ of the human organism authoritatively involved in the detoxification of xenobiotics (drugs), the homeostasis of numerous blood compounds and production of anti-inflammatory agents. Most of these metabolic functions are accomplished by hepatocytes comprising about two thirds of liver cells. Therefore, mathematical modelling of liver metabolism hitherto has widely focused on the single hepatocytes. However, hepatocytes arranged along the same supporting vessel have different access to oxygen, nutrients and hormones in the blood and therefore differ in their functional capacities. Irregularities of the vascular tree and regional partial occlusions of blood vessels (e.g. caused by swollen cells due to lipid accumulation) may entail that within the organ normoxic and partly ischemic regions coexist. Furthermore, the molecular processes underlying complex physiological liver functions proceed at different time scales: Seconds for the hormonal initiation of glycogen degradation, some weeks for liver regeneration after partial hepatectomy and several months or even years for the development of a non-alcoholic fatty liver. Finally, the metabolic state of hepatocytes is affected by cellular contacts with each other and signals received from other hepatic cells, e.g. endothelial cells or macrophages. These are aspects that necessitate to study the metabolism of the liver on the basis of a multi-scale model that covers different spatial and temporal scales. This talk outlines the basic structure of such a liver model and presents some first results.