Virtual Blood Flow
A new computer technique can realistically simulate how medicine affects the liver

Bremen, March 19, 2014 What happens when chemicals flow through the blood stream into the liver and react with the organ? What if parts of the liver are damaged and medicine cannot be properly metabolized? A new computer simulation can now answer questions such as these in greater detail. Experts at the Fraunhofer Institute for Medical Image Computing MEVIS in Bremen were primary partners in developing a program to simulate realistic blood streams and metabolic processes. Their results are now being published in the *PLOS Computational Biology* scientific journal.

The liver performs many tasks in the body. It removes toxic matter from the blood, produces important proteins, and stores vitamins. Each hour, around 90 liters of blood flow through the human liver. To provide a detailed simulation of how blood flows through and reacts with the liver, researchers start with a high-resolution 3D image of the organ. For the publication in *PLOS Computational Biology*, the experts used an image of a mouse liver produced with a CT scanner.

Based on this image data, they reconstructed the exact structure of the fine branches of the vessel system. The liver was then split into 50,000 small blocks, in contrast to most of today's pharmacokinetic simulations, which simply treat the liver as a single 'black box'. "Even a mouse liver is made up of millions of cells," explains MEVIS researcher Ole Schwen. "To keep computation time in check, we combine the procedure for the thousands of cells in each block." To make sure the results are realistic, the experts rely on a large database of medical research that describes the metabolic characteristics of liver cells.

The results of the simulation show that blood flow and metabolic reactions can be tracked in detail on the computer screen. In one instance, a virtual contrast agent is injected. The computer monitor can be used to observe how quickly the contrast agent reaches the various sections of the liver and how it gradually decays. However, the procedure, developed as part of the Virtual Liver Network with the Department for Experimental Molecular Imaging at the RWTH Aachen University and Bayer Technology Services in Leverkusen, can do even more. Simulation can also be performed to show areas of the liver with steatosis, a widespread illness also known as fatty liver disease. After the simulation has begun, the steatotic sections of the liver can be observed to absorb lipophilic contrast agents more effectively than healthy tissue. The metabolic reactions of other medications can also be simulated for both healthy livers and those that are diseased or damaged, for instance, by a paracetamol overdose.

"Currently available computer models only consider the liver as a whole," explains project leader Tobias Preusser. "Our technique is the first to simulate what actually happens inside the organ." It has the potential to become a useful research tool for the pharmaceutical industry. How does a new medication affect a patient suffering from steatosis or other liver diseases? Questions such as these can be answered with this new software simulation. Animal testing could be reduced as well. In the future, the technique could also be used in clinical practice. This could allow clinicians to estimate whether a specific liver medication should be applied for a specific patient.

Before this occurs, MEVIS experts are looking to develop their software further. The current publication in the *PLOS Computational Biology* journal is based on the CT scan of a mouse liver. "In principle, it is also possible to apply the simulation to a human liver" says Ole Schwen. "In addition, we are currently

comparing our simulation with the results of experiments in order to determine whether this new technique can produce quantitatively correct results."

The Fraunhofer Institute for Medical Image Computing MEVIS
Embedded in a worldwide network of clinical and academic partners, Fraunhofer MEVIS develops real-world software solutions for image-supported early detection, diagnosis, and therapy. Strong focus is placed on cancer as well as diseases of the circulatory system, brain, breast, liver, and lung. The goal is to detect diseases earlier and more reliably, tailor treatments to each individual, and make therapeutic success more measurable. In addition, the institute develops software systems for industrial partners to undertake image-based studies to determine the effectiveness of medicine and contrast agents. To reach its goals, Fraunhofer MEVIS works closely with medical technology and pharmaceutical companies, providing solutions for the entire chain of development from applied research to certified medical products.
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The Virtual Liver Network
The Virtual Liver Network is composed of 70 work groups at 41 clinics and research institutes who aim to improve knowledge of liver function. The goal of the interdisciplinary project is to create a computer model that can simulate the liver and its processes as accurately as possible. All relevant scales are researched – from molecules and cells up to the complete liver. The model will be evaluated using laboratory experiments and clinical data. This should allow for well-grounded prognoses and create the basis for the development of new therapy and diagnosis procedures. The BMBF is funding the Virtual Liver Network with 43 million Euro for five years, beginning in April 2010. Fraunhofer MEVIS receives a yearly sum of €380,000.
www.virtual-liver.de