Engineering cellular microenvironments that more accurately reflect the in vivo situation is now recognized as being crucial for the improvement of the in vitro viability and in vivo-like function of cells or tissues. Microfluidic technologies have been increasingly applied since the late 1990’s for this purpose, with a growing number of examples of perfused cell and tissue cultures in microfluidic chambers and channels. The well-defined solution flows provided by microfluidics mean enhanced cell growth and function through improved nutrient delivery and waste removal. Additional benefits include the implementation of well-defined temporal and spatial (bio)chemical gradients, and mechanical signals that cells experience in their natural environment. Because the ability to culture cells and tissue under such controlled conditions leads to cellular function that is distinctly more organ-like, the microfluidic systems used are now referred to as “organs-on-a-chip”.

Reported organ-on-a-chip systems are as diverse as the biological models they have been designed to study. Most examples are based on cell culture models, which involve seeding cells into a chip with the eventual formation of a 2D or 3D tissue-like structure. The biological approach in these cases could be regarded as “bottom-up”. Less common are the “top-down” biological approaches, in which organotypic tissue samples are directly obtained from mammals or human subjects for further study. Regardless of biological model, there is an inherent need in these systems to monitor cell growth and behaviour under controlled conditions.

This presentation will focus on examples from our labs in which we have designed “top-down” and “bottom-up” organ-chips incorporating means to both monitor culture conditions and quantify cell behaviour. In a “top-down” example, a microfluidic device was designed for perfusion culture of precision-cut organ slices. Metabolic studies employing precision-cut liver slices and on-line HPLC analysis were successfully demonstrated with this device, as was a multi-organ slice experiment showing regulation of bile acid synthesis in the liver by the intestine. Our “bottom-up” example constitutes the culture and investigation of primary human endothelial cells in microfluidic devices. Here we present a new approach for real-time, non-invasive, label-free monitoring of cellular micromotion in endothelial cell cultures. Cells are cultivated in a microcuvette formed by etching through the silica and waveguiding layers of a solid-state device. Light (638 nm) is directly coupled into the cell monolayer from an integrated waveguide, and forward-scattered light is recorded as a measure for cellular micromotion. Motion behaviour could serve as a readout for changes in the cytoskeleton caused by various chemical and physical factors. Observation of cytoskeletal changes indicative of inflammatory status using this approach could therefore prove useful for the investigation of the role of endothelial cells in the onset of cardiovascular diseases.