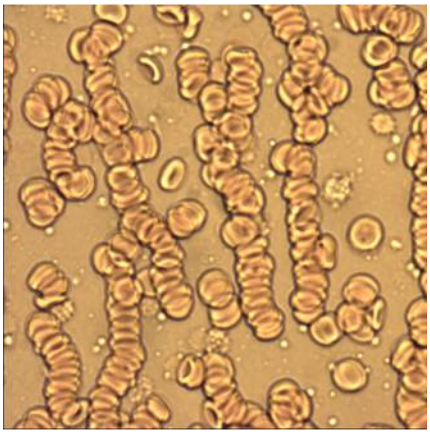
Xue-Feng Yuan - *A novel lab-on-a-chip platform for quantitative analysis of the microcirculation in health and disease*



An increasing amount of clinical evidence shows that the flow behaviour of blood is a major determinant of proper tissue perfusion and rheological abnormalities correlate strongly with various diseases. Increased whole blood viscosity and red blood cell (RBC) aggregation have been observed in patients with risk factors for cardiovascular disease such as hypercholesterolemia, hypertension, diabetes mellitus and cigarette smoking. The complications of diabetes are often seen in large and small blood vessels with patients developing premature mortality or morbidity from cerebrovascular and cardiovascular disease including atherosclerotic narrowing of medium-sized blood vessels leading to stroke and myocardial infarction. In addition, smaller blood vessels are often involved and there are abnormalities of structure and function leading to change in blood flow characteristics. The majority of patients develop the disease as a result of the increased prevalence of obesity leading to insulin resistance and ultimately overt Type-2 Diabetes mellitus. Plasma viscosity has been suggested as an early atherosclerotic risk factor for obese subjects. Increased fibrinogen levels, plasma viscosity and whole blood viscosity seem to be associated with insulin resistance and metabolic syndrome. In order to reveal the coherent relationships between haemodynamics and diseases, we consider the microvascular networks as a hierarchical system involving strongly correlated physiological processes at the different length and time scales. Haemodynamics in the microcirculation depends on the combined effects of the interaction and deformability of the cells, plasma viscosity, vascular wall compliance, vessel geometry, flow rate, physiological and biological factors. It calls for an integrated approach to facilitate a better understanding of the pathogenesis of cardiovascular diseases and the complexity of self-regulated biological system, hence to identify new surrogate makers in health and disease.

We have obtained significant results from studying the correlation between rheological properties of blood and the evolution of RBC structure in rheometric flows. A polymer aqueous solution has also been formulated as a blood analogue to mimic the shear-thinning behaviour of blood. Moreover we have developed a novel lab-on-a-chip platform to study the correlation between the ***onsite*** pressure drop, flow rate and cellular structural evolution, not only in straight channels but also in complex benchmark flow problems. The new platform enables us to precisely perform quantitative analysis of the microcirculation in the physiologically relevant flow regime, with a minimum amount of blood sample and a short period of time. It is also feasible to modify the internal surface and to integrate biosensors into the same lab-on-a-chip for *in-situ* biological analysis of blood. A model microvascular system with precisely defined geometry of micro-flow channels with a range of the hydraulic diameter from 500 to 5 micron can be easily etched on microfluidic chip. The haemorheological properties of whole blood in health and disease can be measured and correlated with the structural information including cellular deformation, aggregation and spatial distribution in the microvascular network. Constitutive models are under development for extracting the material functions of whole blood sample, including viscosity, modulus and relaxation time corresponding to physiological processes with various characteristic length and time scales in the microcirculation. We will identify the variation of the material functions of the cells and bloods in health and disease, and hence to search for manifestations of hypertension and diabetes, and gain insight on the relationships between individual cell properties, haemorheological properties of blood, haemodynamics and cardiovascular diseases. The integrated approach spanning from cellular characterisation to full haemodynamic characterisation is the first of its kind in quantitative analysis of the microcirculation with significant impact on healthcare and patient benefit. The lab-on-a-chip platform can be readily exploited not only in clinic applications as a high-throughput diagnostic kit but also in fundamental research as an in-vitro platform for quantitative study of haemodynamics in the microcirculation.