Complexity Miniproject Proposal – 2012 Summer

Developing the basis for a model of capillary blood vessels in humans

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Research question: The main scientific question is how the arterial blood flow can be reduced or impeded by changes to the capillary structure or the number of capillaries. Even under normal conditions, only a subset of the vessels within a given capillary bed are open, such that the flow fluctuates around an value between the *maximum availability* and the *resting availability* of the capillaries. In otherwise healthy adults the number of capillaries can evolve during the course of only a few months. For example during a healthy pregnancy the number of capillaries of the mother increases significantly, whilst in pregnant women with pre-eclampsia (high blood pressure, protein in the urine and low blood albumin) the capillary density decreases by around 25%.

Why is it interesting? The regulation of blood flow in capillaries is critical for good health as the capillaries deliver nutrition to the cells, remove waste products and control the biological activity of the endothelial cells layer. Several serious cardiovascular disorders are associated with changes in the capillary microcirculation. These include high blood pressure and angina.

The key aim of the miniproject is to provide the basis for a model for how blood flow in capillaries changes when it is coupled to a full capillary network.

The main objectives of the miniproject are:

1. to select the most suitable image frames from an extensive current database of video recordings available of the microscopic flow of cells through the capillary blood vessels in patients with a range of cardiovascular conditions as well as in healthy control subjects;
2. to extract the relevant features of capillaries suitable for applying to a model which could be applied to the development of a companion diagnostic for monitoring human health and disease, like resting and maximum perfusion, possible capillary shapes and anomalies;
3. to identify biological factors most relevant to describing capillary behaviour in health and disease, including upstream haemodynamics, bioactivity of endothelial cells that line capillaries, and the fluid and particulate composition and biochemical function of perfusing blood.

Background to be assimilated: Principles of the technique of capillary videomicroscopy; of topological descriptions of 3-D tubular structures; of the impact of abnormal fluid dynamics on shear stress.

Techniques required: Image capture using software in Prof Singer's group applied to an existing image resource from patients with cardiovascular disease; literature synthesis on biological variables relevant to structural and functional abnormalities in the capillary microcirculation; use of fluid dynamic and engineering principles to describe observed primary aspects of structural and flow characteristics of biological tube networks.

A list of prospective deliverables:

- A pilot database of capillary images from cardiovascular patients and controls;
- a description of key morphological variables to describe capillary anatomy in health and disease;
- a description of key local, upstream and systemic biological variables from which a refined model could be developed to describe functional consequences of abnormalities of capillary networks for human disease.

Who should benefit from this research? Cardiovascular researchers and clinicians interested in new biomarkers of disease and new druggable targets. Patients in whom cardiovascular risk is not explained by classical risk factors such as high blood pressure, smoking and raised cholesterol.

Avenues for a follow-up PhD project: This work could lead to PhD research on cardiovascular patients where these observations are compared to numerical simulations of the implications of abnormal capillary microcirculation. This would be developed as clinically relevant parameters to refine assessment of cardiovascular risk. Specific research studies would include evaluating application of these capillary parameters to monitoring response to pharmacological therapies for people at increased risk of cardiovascular disease.