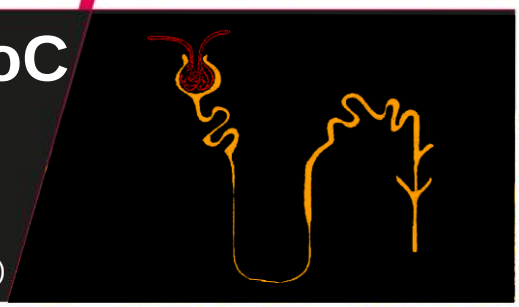
Technische Universiteit Eindhoven University of Technology

Fabricating fine structures in OoC by 2-photon laser ablation in hydrogels



Master Student Project Assignment For more information: s.lou@tue.nl (Sha Lou)

Introduction

- Organ-on-chip (OoC) is an ideal tool to study human disease [1] and has great potential in biomedical applications [2-4], because it has the capability of closely mimicking the 3D microenvironment as in the human body [5].
- Kidney disease is a major health issue worldwide [6], in the Netherlands alone, more than one in ten individuals has chronic kidney disease (Dutch Kidney Foundation 2016b) and this number is expected to increase in both the short and long term [7].
- A kidney-on-a-chip can mimic the structural, mechanical, transport, absorptive, and physiological properties of the human kidney [8]. Such in-vitro models would help to study kidney functionality, kidney disease and drugs screening. But it is difficult to create representative in-vitro kidney models mainly due to the difficulties of mimicking the fine structure of the nephron – the unit of the kidney (Fig.1.a) – which is a complex geometry of small tube-like kidney components, surrounded by vasculature.

Project

In this project, we are going to fabricate an artificial nephron that has the fine nephron structures and that will later form the basis of a functioning kidney on a chip. A simplified experimental design (Fig.1.b) mainly includes different tubular parts of the nephron with different tube diameter and curvatures (with names shown in the figure), as well as the nearby vasculature. We will use 2-photon laser ablation (2PLA) to write these structures in a hydrogel (that mimics the natural environment of the nephron).

2PLA has already been used in creating microfluidic networks with micrometer-sized cavities in hydrogels [9]. It potentially provides the possibilities of flexible geometry, fine features and easy change in diameter of the tubular nephron structure. Fig.2 sketches the fabrication procedure. One of the advantages of 2-photon excitation (compared to the more usual 1-photon excitation) is that the excitation is mostly limited to a small focal volume [10] (Fig.3) which is more suitable for fabricating fine structures such as in the nephron.

Techniques/skills you will learn:

- Hydrogel preparation/loading/curing/characterization
- µscale complex geometry design and fabrication by 2PLA
- Flow characterization in microsystems

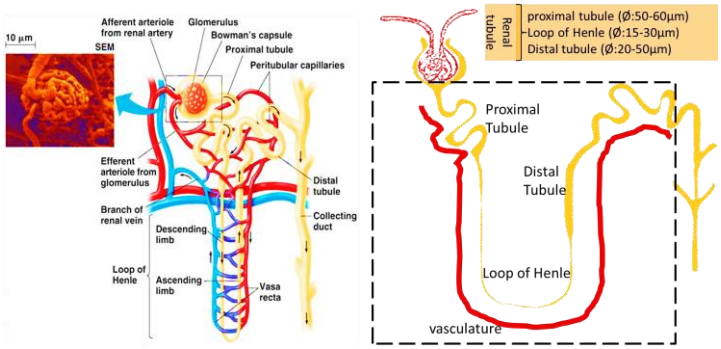


Fig. 1 The microscopic anatomy (a) and simplified experimental design of the nephron (b)

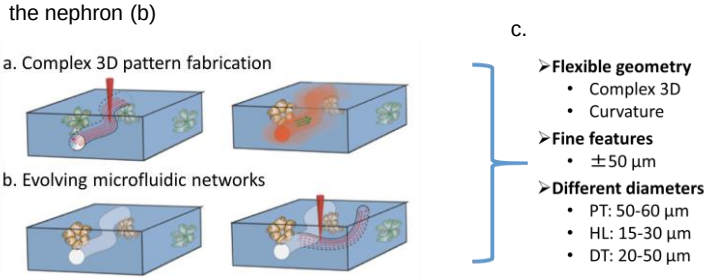


Fig. 2 The illustration (a, b) and advantages (c) of laser ablation in cell-laden hydrogel [9]

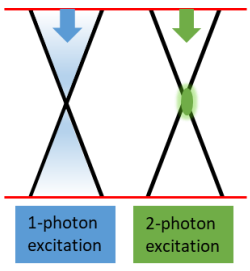


Fig. 3 Schematic comparison of the focal volum between 1-Photon and 2-Photon excitation (adapt from [10])

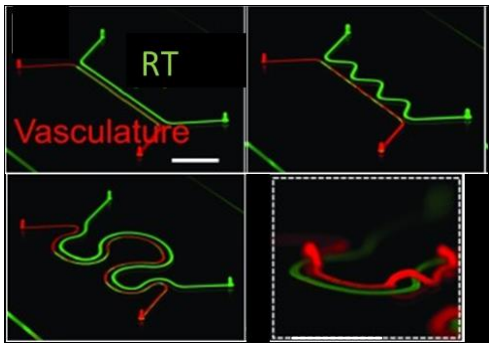


Fig. 4 Examples of simple and complex design of renal tubule (RT) and vasculature in the nephron [11]. Scale bar: 10 mm.

References

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We want to find out which laser exposure parameters (e.g. laser scanning speed and laser density per voxel) are optimal for fabricating the different fine nephron structures (Fig.4). We will also study which hydrogel materials are most suitable. Finally, we will find ways of connecting pumps to the written structures so that they can be tested for fluid flow behavior.

/ Interested? → **Prof. Jaap den Toonder (j.m.j.d.toonder@tue.nl), GEM-Z 3.130**