Mimicking Proximal Tubule Cell functioning for Artificial Kidney Applications

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ABSTRACT

The importance for artificial organs development is ever increasing, especially for artificial kidney is needed by a vast number of people suffering from kidney failure. This paper presents a novel Bio-reactor technique by using the size dependent reabsorption of the proximal convoluted tubule. The modelling, simulation and analysis are carried-out to optimize the flow in the proposed structure. The analytical formulae developed are considered and a model has been built in FEM tool. The total volumetric flow through straight channels is 0.63×10^{-16} which comparatively less than slant channels 0.72×10^{-16} The obtained simulated results have good correlation with analytical analysis. Finally, the shape of main tubule has been analysed with two different shapes straight and Diagonal. The straight tubule is considered for its ease of practical realization and acceptable flow velocity.

Keywords: Kidney-on-Chip, Microfluidics, Fluid Shear Stress, Re-absorption, Nephron and Proximal Convoluted Tubule.

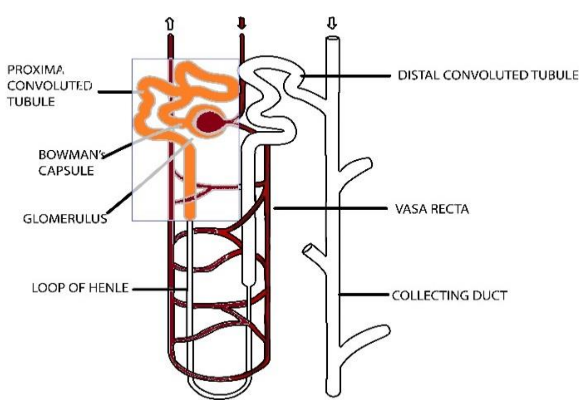
1 INTRODUCTION

Human Kidney is the organ which gets 20-25% of cardiac output. Kidneys filters the blood, maintains homeostasis, blood pressure and balances the solutes in the blood (1). The drug decomposition and supply to the body parts is also done by kidney. But, kidneys are more prone to get affected by external and internal factors. Kidney is mostly gets damaged by diet and acidic attack. As the pH and glucose levels in the blood increases, there is more chance to get damaged. Further ore, Heredity kills the kidneys inherently. In the world one in five man and one in four women have kidney disease (2). This makes the kidney disease as the one of the most life-threatening diseases (3). The stages of kidney diseases include Chronic kidney disease (CKD), Acute kidney injury (AKI) and End stage renal disease (ESRD). ESRD is observed when the nephrons functioning is less than 15 % of total nephron count. Dialysis is the first replacement for kidney, in fact it is first artificial organ produced. Since then it is being used with little technical changes. Dialysis has different types Intermittent hemodialysis (IHD), Peritoneal dialysis (PD), Continuous renal replacement therapies (CRRT). The cost of dialysis per one treatment may cost around 480 US dollars. The expense of this service two time a week is not affordable. However, dialysis is a painful process and reluctant to patient. The frequent insertion and removal of needles may welcome some other unintended diseases. The other way to treat kidney failure is transplantation. Transplantation gives much comfort to the patient, where a healthy kidney from a human is dissected and arranged in parallel functioning of the failed kidney. Again, transplantation is heavily costlier, and availability of donor kidneys is limited. There is much requirement for artificial kidney that is highly available, less costly and implantable. The drugs that are tested through 2D will not work effectively on humans [4]. All these problems makes researchers and engineers to look forward into a better technology which may reduce the CKD deaths all over the world. Organ-on-chip is the bio-engineering technology where the functions of human organ can be replicated on a small-chip and thus providing a better replacement for drugs and painful surgeries which leads to a better human life. One of the major sub-part is Kidney-on-chip (KOC), the novel concept in the present for future generations. The drug reactions, flow of solute substances functionalities are mimicking on the KOC which requires a clear understanding of microfluidics the advancement in fluid mechanics. Microfluidics gives a clear idea of fluid interactions at micro level in the micro channels [5, 6]. The effects that are neglected in macro level should be taken into account in microfluidics are fluid shear stress, viscosity, friction, fluid resistance [7]. The advancements in IC fabrication technology leads to a study of an inter-disciplinary subject Micro Electronic Mechanical Systems (MEMS) provides the idea in fabrication of the mechanical structures on chip that mimics the kidney functioning. In this paper, we have designed a significant part in Kidney-on-Chip by regenerating the proximal convoluted tubule. Re-absorption of solutes in the lumen fluid passing through nephron tubules is vital for providing proper kidney function.

2 PROPOSED STRUCTURE

The main basic building of kidney is Nephron. Nephron is a multifarious structure consisting of Efferent arteriole, afferent arteriole, Glomerulus, Bowman's capsule, Proximal Convoluted Tubule, Loop of Henle, Distal Convoluted Tubule and Collecting Duct as core components. Primarily, glomerulus is responsible for filtration and proximal tubule will diversify the solutes depending on size, shape, charge and fluid shear stress. The endothelial cells inside the tubule will collect the solutes that needs to be reabsorbed and transport back into the blood stream. The PCT having a length of 6 mm and width of 100 µm wounded in a cylindrical shape and surrounded by efferent arteriole helping the re-absorption throughout the length.

This paper proposes an artificial kidney functioning using size dependent absorption of solutes. The dimensions of the device are exactly designed by considering proximal tubule and specified in he further sections. The fluid shear stress inside the kidney which is responsible for functioning is also mimicked with same structure, its importance is determined. The structure has two blood carrying tubules connected with a main tubule as shown in figure1. The main tubule is placed in between the two blood tubules. Main tubule carries the lumen fluid. The re-absorption of solutes from main tubule to blood tubules is done by transporting channels etched between them. The intermediate channels size is selected based on the size of the solutes in the water. The geometry of the main channel has been considered as straight type and then simulated. The proposed design is a well-suited Bio-reactor for artificial kidney applications. The simulation of the structures allows easy modifications and more ease to analyse the structures for better performance. In case of the transporting channels two types of structures have been analysed; straight and slant type. The proposed structures are designed, simulated and analysed in a COMSOL software tool which results in the decent velocity values and fluid shear stress.



(a)

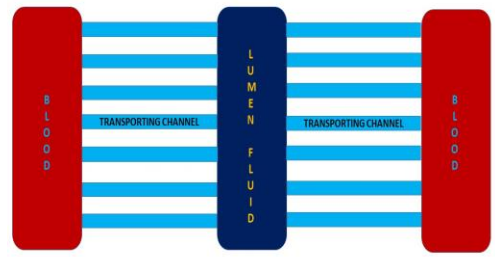


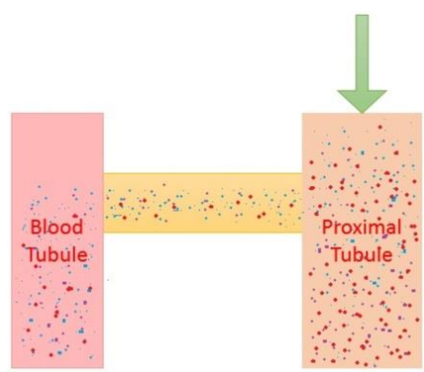
Figure 1: (a) The nephron structure highlighting the proximal convoluted tubule (b)Proposed structure showing main tubule carrying lumen fluid having blood carrying tubules on either side of main channel along with the transporting channels.

The main channel is 6 mm in length and 100µm width as well as transporting channels are 200 nm in length and 4 nm in width. 4 nm is selected which allows the solutes and proteins to pass through the channel smoothly. Selection of material for the fabrication is very prominent. Due to the biocompatibility and the most advanced fabrication methods, silicon is highly preferable. The other reason to choose silicon is the abundant availability in the Earth's Crust and also the very brittle in nature. The other semiconductor materials like germanium, arsenic and other compound semiconductors can also be used but the reliability and the performance is not feasible.

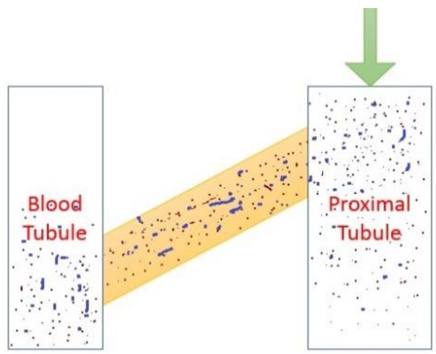
3 RESULTS

3.1 Transporting Channels:

The inlet flow velocity is given as 10^{-4} nl/min and the outlet velocities are recoded from the simulation results. These results provides the reabsorption performance in the tubules which is one of the important functions in nephron. It assumes that all the channels are uniform without slippery boundary conditions. Flow of solute particles from main tubule to blood tubule is demonstrated in figure2.



(a)



(b)

Figure 2: Solute moment (a) Straight Channel (b) Slant Channel

Straight Channel:

In case of Straight Channel, Theoretically calculated the total flow velocity through the channels is 9.5×10^{-5} m/s. The fluid starting at the aperture seems to have less flow and when it reaches the boundary at the channel the flow turns turbulent and flows quickly into channel.

From the simulated results as shown in figurre3, average flow velocity is concentrated in the channels is 8.27×10^{-5} m/s and the rest is excreted out as urine.

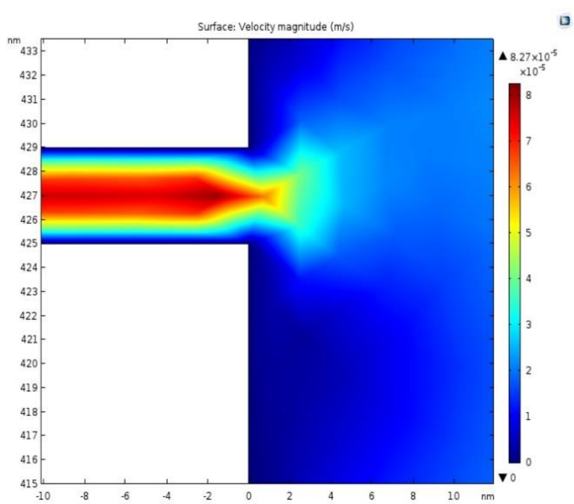


Figure 3: Exploded view of simulated results in Straight Channel case along with main tubule.

Slant Channel:

In case of Slant Channel, The flow velocity obtained through the modelling is 10.4×10^{-5} m/s. According to the simulation as shown in figure 4, the average flow velocity is attained at 8.82×10^{-5} m/s.

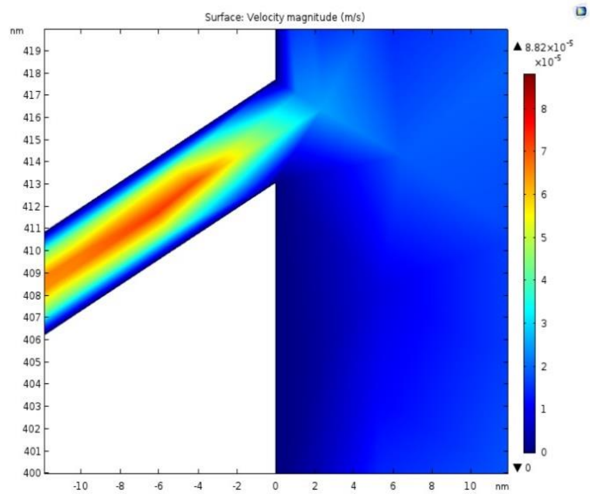


Figure 4: Exploded view of simulated results in Slant Channel case along with main tubule.

3.2 Main Channel:

The above analysis provides interesting results about the optimization of the channel that is connecting the main tubule and Blood carrying tubules. Now there is a need to consider the effect of main tubule which carries the lumen fluid. For this reason we have considered the main tubules with straight shape. Lumen fluid while passing through the PCT will experience a force due to the walls (obstruction by the PCT walls to the flow of the lumen fluid).The importance of this assumption is, we can estimate effects that are being posed by the PCT walls artificially. Accordingly, the structures can be made to allow more compact operation of the Artificial Kidney.

The structure simulated with straight main tubule is shown in the Figure 5. The inlet is supplied with 1 ml/min of flow, it is observed that the flow through the transporting channels is mostly uniform. The velocity if the lumen fluid entering the blood tubules is 0.06 m/s.

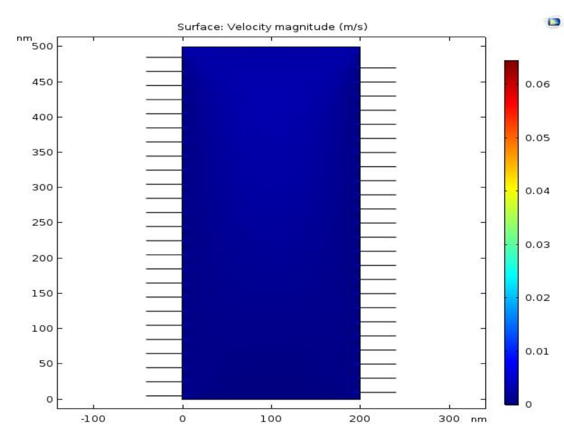


Figure 5: Main channel simulation results.

Fluid shear stress is an important phenomenon, where there is a chance to find out the amount stress the walls are experiencing the fluid is being flown. At the same time we can estimate reabsorption rate, as the kidney reabsorption rate also depends on the FSS. This FSS effects on the cell morphology, ion transport and endocytosis. It is tough to quantify the shear stress experienced by every channel. Figure 6 shows the fluid shear stress responses.

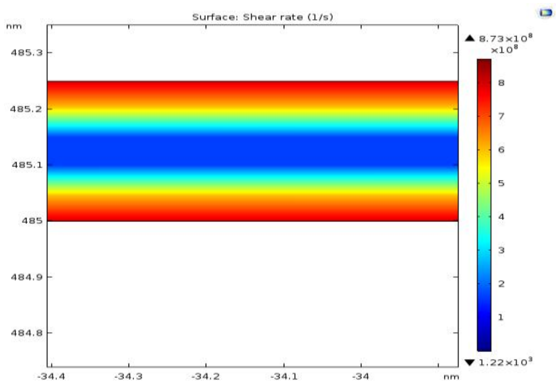


Figure 6: Fluid Shear stress response of the transporting channels.

4 CONCLUSION

This paper presents bio-reactor with different structural changes that regenerate the function of Proximal Convoluted Tubule in Kidney. A main tubule that carries lumen fluid is surrounded by two blood tubules, both the tubules are connected to maintubule by transporting channels. The transporting channels support the reabsorption of required solutes and proteins. The structure is subjected to different structural changes and simulated using COMSOL Multiphysics. The results that are obtained from the simulation for different structure are 0.63×10^{-16} for straight channel and 0.72×10^{-16} for slant channel. It is concluded that slants channel exhibits slightly larger flow velocity than the straight channel. In addition to that the main tubule shape been changed to diagonal and straight, where diagonal tubule is providing high flow velocity. Owing to the difficulties of practical implementation of the diagonal tubule, the straight tubule are considered and optimized by increasing the number of channels. The advancements in the microfluidics fabrication technology makes easier to fabricate the proposed structure at low cost. The proposed structure has characteristics to be as Bio-Reactor in Kidney-on-Chip applications.

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