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Simulation of Physiological Function of the Kidney in Filtering Blood Sodium Parameter by Micro and Nano Technologies: A Review

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Abstract- The main function of the kidney is filtration of the plasma, removal and excretion of unwanted substances from the filtrate in the urine and restoration of needed substances from the filtrate in the blood. These operations are essential since they maintain the volume of intracellular and extracellular fluids and ions should be maintained in a low range. If kidney cannot do their regular job, several ions and fluid will be accumulated in the extracellular. Forms of dialysis, despite successful improvement in quality of lives of the individuals, have several limitations. This may be due to unphysiologic nature of dialysis treatment. As regards sodium is the main osmole in the extracellular fluid (ECF) that disposal or retention of this element mainly determines the volume of extracellular fluid and the ECF volume should be maintained on an acceptable level in the body in order to maintain tissue perfusion. Therefore, a variety of methods include: nanotechnology, microfluidic, bioreactors, and the systems based on optical tweezers for treatment of renal failure are presented in this review that they are developed according to: removing and reabsorbing sodium of the blood, wearable or cultivable, their function is the same as kidneys, and etc.

Keywords- *extracellular fluid (ECF), intracellular fluid (ICF), Na^+، nanotechnology, optical tweezers, renal replacement therapy*

I. INTRODUCTION

The main function of the kidney is filtration of the plasma, removal and excretion of unwanted substances from the filtrate in the urine at variable rates based on needs of the body and restoration of needed substances from the filtrate in the blood [1, 2]. The rates at which different substances are excreted in the urine represent the sum of three renal processes, shown in Fig. 1: (1) glomerular filtration, (2) reabsorption of substances from the renal tubules into the blood, and (3) secretion of substances from the blood into the renal tubules. These operations are essential since they maintain the balance between water and all other electrolytes of the body. In other words, the volume of intracellular and extracellular fluids and ions should be maintained in a low range [2, 4]. This regulatory function of the kidneys maintains the stable environment of the cells necessary for them to perform their various activities. These actions can be divided into two main functions as below [1, 3]:

1. Excretion of metabolic waste products and other toxins.
2. Maintaining a constant composition of fluids within the body and regulating electrolyte concentrations.

The four main electrolytes of the plasma are Na+, K+, Cl-, Co3H- and other plasma-forming materials including urea, glucose, weak acids, which are non-degradable. Sodium is the main osmole of the extracellular fluid; In other words, sodium is the most important determinant of ion osmolality of body fluids. Na+ and Cl- ions are the dominant anions in the extracellular fluid. Therefore, these anions determine the ECF volume. Thus, disposal or storage of these anions (Na+- Cl-) is the main factor, which determines the ECF volume [1, 5]. As a result, sodium balance disorders may cause disorders in ECF volume. ECF volume should be maintained on an acceptable level in the body in order to maintain tissue perfusion because plasma volume is directly proportional to ECF volume. The balance between sodium intake and output should be maintained in the body, because most diseases with the ECF expansion (and edema or hypertension) or the ECF volume depletion achieve disorder of sodium balance [4, 6].

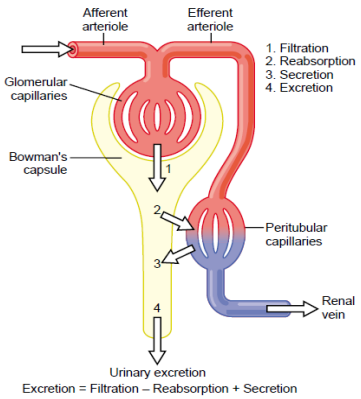


Figure 1. Basic kidney processes that determine the composition of the urine [3].

The term "dialysis" was first coined by Thomas Graham, a professor of chemistry in Glasgow, Scotland, in 1861. He was able to separate urea from urine using a vegetable parchment coated with albumin. In 1913, Abel, Rowntree and Turner invented a vivi-diffusion device for use in experimental animals. Subsequently, the first human dialysis was performed by George Haas in Germany in 1924, though the treatment time was only 15 min. The first device used successfully in humans was invented by W. J. Kolff and H. Berk in the Netherlands in 1943. It consisted of a cellophane tube (30 m × 2.5 mm) wound helically around a cylinder that rotated slowly while immersed in a dialysate bath of 70–100 l [7]. Hemofiltration was first described in the late 1970s as a means of removing extracellular fluid from patients with edema refractory to diuretics [8]. Waste removal is mainly done based on diffusion method in hemodialysis and convection method in hemofiltration and hemodiafiltration. The blood is passed through porous membranes by pump [7, 9, 10, 11, 12, 13, 14, 15]. Dialysis forms, despite success in improving quality of lives of the individuals, have many limitations that lead to various diseases, and increased rate of death among people. This may be due to unphysiologic nature of dialysis treatment. In this context, efforts have been made to improve the efficiency of dialysis. Therefore, an ideal form of renal replacement therapy (RRT) would mimic the functions of natural kidneys. In previous years, it seemed impossible to achieve these goals. However, advances in the science of nanotechnology, microfluidic, etc. made it possible to achieve these goals in the near future [16, 17, 18, 19]. Various methods are proposed including nanotechnology [20-23, 24], microfluidic [25, 26, 27], bioreactors with kidney living cells [28-32, 33, 34, 35, 36, 37, 38, 39, 40, 41], miniaturized sorbent systems [42, 43]. In summary, the combination of nephrology with new technologies has improved RRT. Extensive work has been done recently in this area. A review of methods and existing technologies for treatment of renal failure [13] that they are developed according to remove and reabsorb sodium of the blood according to the patient's needs, wearable or cultivable, inexpensive, reliable, and their function is the same as kidneys are presented and explained further in this paper.

II. DESIGN A BIOARTIFICIAL NEPHRON ON A CHIP

Each kidney in the human contains about 1 million nephrons, and each nephron contains (1) the glomerulus, (2) along tubule [2, 3]. There is an arrangement of basic tubular segments along the nephron whose physiologic function lies in excreting waste products from the blood. The structure of a nephron in the kidney is shown in Fig. 2 [44]. A bio artificial device is designed based on MEMS technology to mimic the operation of a nephron, which is compatible with both human anatomy and physiology. This device is named the human nephron filter (HNF).

This device is composed of two [22] or three [21] basic parts separately, as a nephron:

1) The glomerulus: the blood first flows into the glomerulus, and then it flows into nephron. In glomerulus, the blood is filtrated by an active mechanical filter by which large cells and proteins are kept.

2) The proximal tubule: the blood and filtrated material flow into proximal tubules from glomerulus. Then, plenty of fluids and solutions are actively reabsorbed.

3) The loop of Henle and associated collecting ducts: in the end, the blood and filtrated material flow into loop of Henle and associated collecting ducts. In this part of nephron, active pumps, osmosis and diffusion are combined to perform reabsorption and finally, the waste products are removed.

This system is efficient and effective in removing large amounts of urea without losing large amount of fluid. Proximal tubule cells are added to the filter in this device in order to perform reabsorption and metabolic activities [21]. In fact, the dialysis process with the glomerulus action is designed to mimic the actual function of the kidneys. Then, artificial kidney with capabilities to perform operations relevant to glomerulus and tubules is designed [21, 22]. In fact, the glomerulus and tubules parts of the kidney are modeled in this system. Diagram of urinary system that contains glomerulus and tubules parts is shown in Fig. 2 and the diagram of this system is presented in Fig. 4, which can be compared with the views of the nephrons of the kidney.

The paths in which blood passes all three parts, mentioned above, are shown separately in Fig. 3. The black arrows represent passive transport while white arrows show cell-mediated active transport. As it is observed in the Fig. 3, only passive transport between the blood and the filtrated material in a direct way is conducted in section G. In section T, both passive and active transports (with help of the cells) in HNF device with 3 parts and just passive transport in this device with 2 parts, between the blood and the filter in a direct way are conducted. In section L, both passive and active transport between the blood and the filtrated material through extracellular interface fluid is conducted [21]. In this system, dialysis fluid or external pumping system is not required. In other words, similar to nephrons in the human kidney, the human blood is filtrated in G section. Then, reabsorption operation between the blood and the filtrated material is conducted in the following paths. This artificial device that replicates this 2 or 3 step can potentially be synchronized with efficiency of the nephron and offers a compact wearable device [21, 22]. A variety of cell types with various functions is found in the nephron. In order to mimic the function of nephron, several cells are used in HNF device with 3 parts [21].

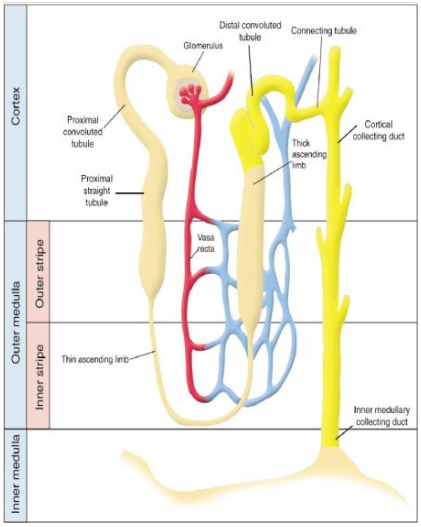


Figure 2. Diagram of the urinary system [44].

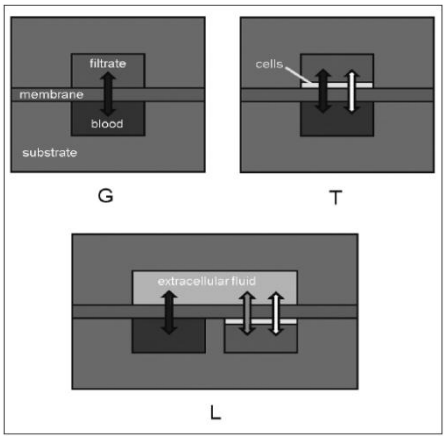
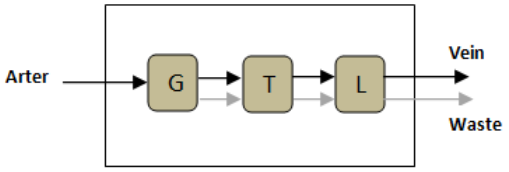
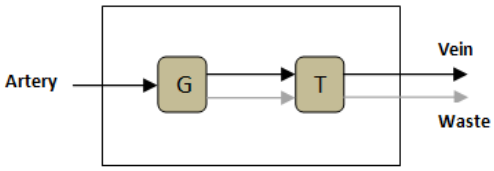


Figure 3. Schematic cross-sections of the 3 functional units [21].



(a) HNF device with 3 parts



(b) HNF device with 2 parts

Figure 4. Schematic overview of HNF device.

A wide range of research and study has been reported controlling proximal tubule cells in relation to the existing bioartificial kidney devices; however, recent advances in application of Henle loop cells and collecting ducts are being developed. These include additional concepts similar to the role of circulating hormones such as antidiuretic hormone (ADH) released by the pituitary gland in modulating tubule permeability to water. It is important to design nephron functions as bioartificial nephron on a chip. This was done in HNF device with 3 parts [21].

A. Design of HNF device with 2 parts

This device consists of two membranes operating in series within one device cartridge. The design of this device is shown in Fig. 4(b). The first membrane is called the G membrane and is analogous to the glomerular membrane in the nephron. It mimics the functions of the glomerulus by using convective transport to generate plasma ultrafiltrate. This membrane is shown in Fig. 5. The second membrane is the T membrane, which mimics the function of the renal tubules. The T membrane is supported on a substrate and contains molecularly engineered pores that make it unique. The membrane contains approximately 1.6×10^{16} pores, 1 to 5 nm apart. The pores will come in different sizes and shapes, and eventually a pore library will be available to permit custom membranes to be produced, depending on patient needs. The T membrane is shown in Fig. 6. Molecularly engineered membranes (smart membrane) contain a predetermined number and size of pores that are atomically engineered and have specific interactions with solutes that provide selective transport characteristics to the membrane. The G membrane discriminates between solutes on the basis of molecular size. The ultrafiltrate formed after blood passes through the G membrane contains both desirable and undesirable solutes. The ultrafiltrate passes over the T membrane, which it is able to differentiate between both desirable and undesirable solutes because each of its pores is a designed discriminator and is made up of multiple unique pores. The pores were designed to reabsorb all of the desirable solutes and reject the undesirable ones. Modeling was done to assess the removal of some of key substances, including sodium, potassium, calcium, magnesium, phosphorus, and bicarbonate, under a variety of clinical conditions [16, 22].

B. Design of HNF device with 3 parts

The design of this device is shown in Fig. 7. This device consists of 3 main parts and 1 additional part, which include: G glomerulus, T tubule, L Henle loop, (these three parts model the function of nephron) and C interface (somehow this is the interface between three other parts, the blood and the filtrated stream). In our simplest conception, the HNF device is fabricated from 2 microfabricated layers, which are separated by a membrane [21].

Fig. 8 shows the model by which the fluid passes through these three sections. T and G sections are made from a combination of straight channels while the L section needs countercurrent loops. As it is shown in the Fig. 8, flow channels between the blood and the filtrated material are connected together in sections T and G while these loops are separated from each other in section L. The extracellular fluid flows into the space between these loops in section L. The looping geometry of L allows countercurrent transport. Section T requires renal proximal tubule cells, and section L requires a number of different cell types: cells of descending thin limb, ascending thin limb, thick ascending limb, cortical collecting duct, and medullary collecting duct [21]. Each cell type has distinct transport properties and characteristics. Characteristics of cells associated with each part of nephron cells for active transport and passive transport of sodium are presented in Table I.

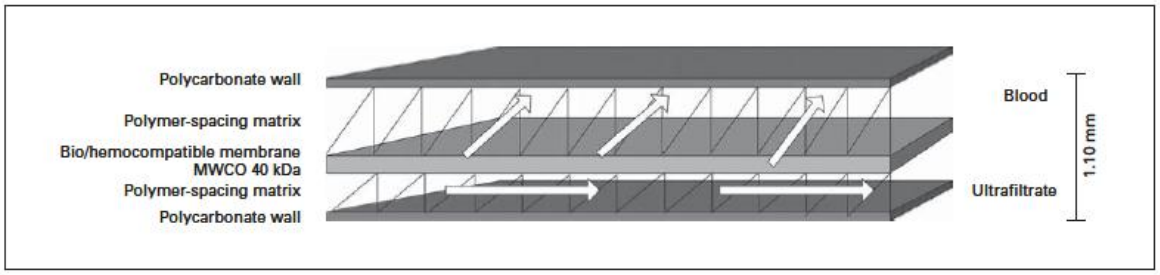


Figure 5. The G membrane

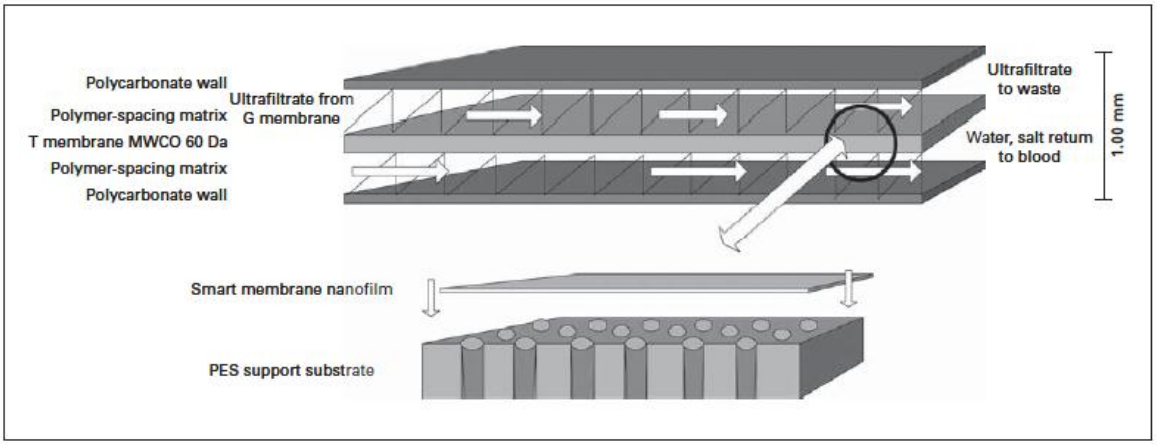


Figure 6. The T membrane [22]

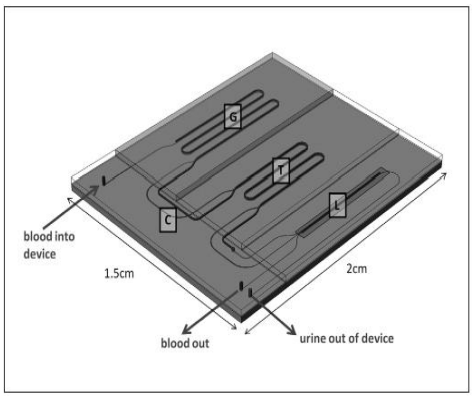


Figure 7. Overall view of complete device design [21]

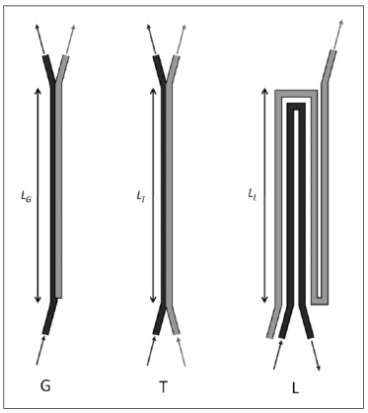


Figure 8. Schematics of overhead view of wafer for each component [21]

TABLE I. TRANSPORT PROPERTIES OF CELLS REQUIRED IN NEPHRON DEVICE (MORE + MARKS SIGNIFIES PERMEABILITY; NO + MARKS SIGNIFIES IMPERMEABILITY) [21]

location	Active NaCl transport	Passive permeabilities	
		NaCl	H_2O
Proximal tubule (T)	+++	+	+++
Descending thin limb (DTL)		+	+++
Ascending thin limb (ATL)		+++	
Thick ascending limb (TAL)	+++	+	
Cortical collecting duct (CCD)	+	+	
Medullary collecting duct (MCD)	+	+	+

III. APPLICATION OF LIVING MEMBRANES AND BIOARTIFICIAL KIDNEY

Although acute renal failure (ARF) and multiple organ dysfunction syndromes (MODS) are due to various causes, these diseases may be cause acute renal tubular epithelial cell injuries or acute tubular necrosis (ATN). Hemodialysis and Hemofiltration therapies can, clinically, replace glomerular filtration for treatmenting of ATN in removing uremic toxins in blood, rectifying fluid and electrolyte balance disorder. However, these methods cannot perform the biological functions of renal tubules [28]. The goal was to improve function of the kidney coupling the transport capability of living cells with a conventional hemofiltration device. In 1987, Aebischer and co-workers reported that selective transfer of the solution to dialysis membrane could be improved using renal epithelial cells, which were grown on these conventional dialysis membranes [45, 46]. In other words, the cell-aided solute transport concept was developed in the bioartifical kidney. Humes studied packaging of synthetic materials, biologic components and cellular components of specific tissues for replacing the physiologic function of diseased organs [29]. Humes, first introduced bioartificial renal tubule assist device (RAD) (The bioreactor unit seeded with proximal tubule-derived cells) in 1996 [28, 47, 48]. The development of portable, wearable or implantable artificial kidneys would be highly desirable and has been suggested by different authors during the past 20 years [33-38, 41, 49-54]. Fig. 9 shows flow diagram of a cultivatable bioartificial kidney system.

In Table II, Transport and metabolism functions of proximal tubular epithelial cells on artificial membranes are shown. Extensive studies were conducted on bioartifical kidney using renal tubular epithelial cells and porous synthetic membranes. Sodium reabsorption operation from confluent layers was studied as well. In this regard, the following steps were followed [28]:

1) Renal tubular epithelial cell lines were seeded onto the intraluminal surfaces of hollow fiber polysulfone membrane and growth of attached cells in intraluminal spaces was observed by transmission electron microscopy. The morphologies of attached cells were observed with scanning electron microscope, and the junctions of cells and polysulfone membrane were observed with atomic force microscope.

2) Then, Na^+ active transport and structural change in renal tubule cells after confluence and long culture have also been studied.

The cells types used for these experiments are as follows: pig, dog or rat renal organs are generally used for testing bioartifical kidney using renal epithelial cell lines [28, 29, 31].

- Lewis lung cancer-porcine(LLC-PK1) cells
- Madin-Darby canine kidney (MDCK) cells
- Rat renal tubular epithelial cell lines (NRK-52E) cells

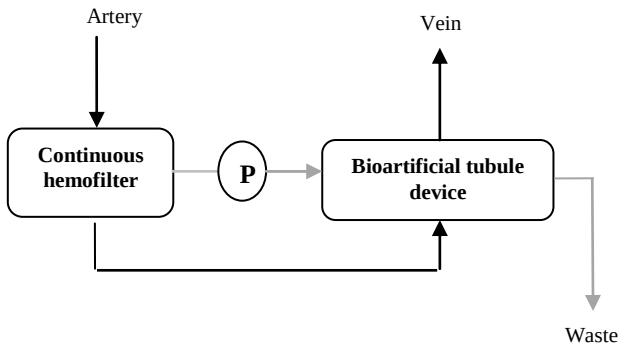


Figure 9. Flow diagram of a bioartificial kidney with two parts: (1) A device to replace blood ultrafiltration performed by renal glomeruli (2) A device to replace the transport regulatory function of the renal tubule

TABLE II. TRANSPORT AND METABOLISM FUNCTIONS OF PROXIMAL TUBULAR EPITHELIAL CELLS ON ARTIFICIAL MEMBRANES [30]

	Confirmed tubular function on artificial membranes
1	1,25-Dihydroxyvitamin D_3 production
2	Glutathione transport and metabolism
3	NH_3 production
4	Bicarbonate transport
5	Para-aminohippurate (PAH) secretion
6	Protein-linked pentosidine metabolism
7	Glucose reabsorption
8	Water transport
9	Sodium transport

A. Evaluation of sodium transport

To determine whether renal tubule epithelial cells can grow on permeable hollow fibers, establish electrochemical gradients, and express renal tubule transport functions [29]. Epithelial cells derived from the proximal tubules are most interesting for bioartificial kidneys development, because they perform a wide variety of functions, including reabsorption and secretion [32, 55-58]. In RAD construction, renal tubular epithelial cells were seeded onto hollow fiber polysulfone membrane in a bioreactor [28, 30, 32, 59].

1) Basic mechanism for active transport of sodium through the tubular epithelial cell:

In Fig. 10, reabsorption of filtered water and solutes from the tubular lumen across the tubular epithelial cells, through the renal interstitium, and back into the blood are shown [3, 4]. Solutes are transported through the cells (transcellular route) by passive diffusion or active transport, or between the cells (paracellular route) by diffusion. Basic mechanism transport of sodium is active transport through the tubular epithelial cells by the sodium-potassium pump. The sodium-potassium pump transports sodium from the interior of the cell across the basolateral membrane, creating a low intracellular sodium concentration and a negative intracellular electrical potential. The low intracellular sodium concentration and the negative electrical potential cause sodium ions to diffuse from the tubular lumen into the cell through the brush border [1, 3, 6, 60, 62].

2) Competition for survival and maintenance of monolayers and function of epithelial cells:

Although active transport of Na^+ by confluent layers of cells on the membrane was optimally performed at first, after a short time, the cell performance characteristics were not preserved in optimally transporting Na^+. The function associated with the cells was decreased with multilayer growth, necrosis, and the aberrant distribution of Na^+/K^+ ATPase [31].

The type of the membrane material and extracellular matrix (ECM) protein which coated the membrane appeared to be critical for the adhesion and functional differentiation of cells [62, 63, 39]. Therefore, there is a specific competition between survival and maintenance of complete and perfect monolayers and function of the epithelial cells. The purpose of this competition is completing cell coverage of the cartridge membranes. Consequently, it appropriately maintains a monolayer of epithelial cells for relevant solute transporter proteins [28-32, 59, 39, 38]. Exposure of renal epithelial cells to an atypical physicochemical environment, Lactate accumulation, Hypoxia, an aberrant ECM, and lack of heterotypic cell interactions, contribute to monolayer disruption [31]. Although, confluent layers of MDCK cells on polycarbonate (PC) membranes initially displayed active Na^+ transport, functional properties could not be maintained after 2 weeks. Also, reabsorption of water, glucose and sodium could be maintained up to 10 d when LLC-PK1 cells on polycarbonate (PC) membranes were used [31]. Cross-sectional of polysulfone hollow-fiber capillary, in which LLC-PK1 cells were grown on the membrane, is shown in Fig. 11. Culturing of renal epithelial cells under organotypic perfusion culture conditions might help to maintain differentiated renal epithelial cell characteristics [64, 65, 39].

Moreover, the production of such device requires application of processable polymers. Such circumstances may be possible using supramolecular, ureido-pyrimidinone (UPy) modified polymers electro-spun into fibrous membranes, as it is shown in Fig. 12. It is assumed that function of epithelial cells has been improved by electro-spun, supramolecular membranes. Many technologies have been used for the fabrication of membranes with the aim of tissue engineering. Examples of these techniques include: foaming, polymer casting, freeze-drying, salt leaching, sintering, electro-spinning. The results shown that fibrous supramolecular membranes have superior properties over conventional microporous membranes with respect to ability of primary tubular epithelial cells (PTEC) to form polarized monolayers on these membranes. This finding implies that application of these supramolecular membranes in a bioartificial kidney set-up might ameliorate its function [31].

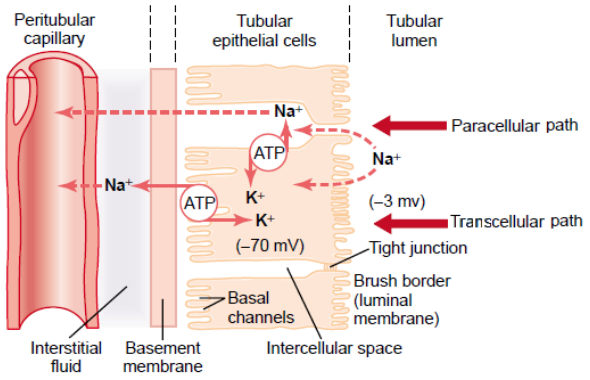


Figure 10. Basic mechanism for active transport of sodium through the tubular epithelial cell [3].

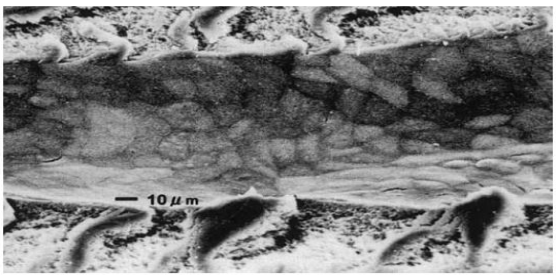


Figure 11. Cross-sectional finding of polysulfone hollow-fiber capillary, in which LLC-PK1 cells were grown confluently on the inner surface of the membrane [30].

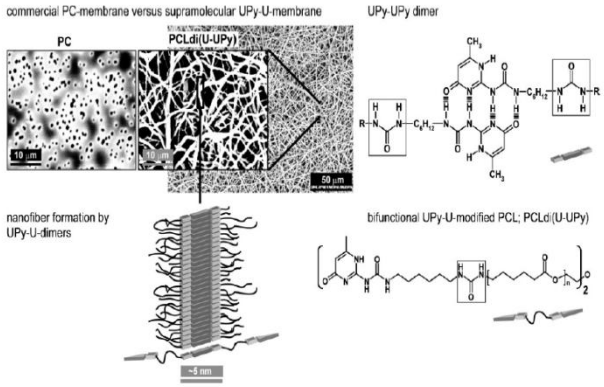


Figure 12. Membrane design: fibrous, supramolecular membranes and commercial microporous membranes. UPy-U-groups were used to end-functionalize short polycaprolactones in order to obtain supramolecular UPy-U-polymers (PCLdi(U-UPy)) [31]

B. Isolation and culture of PTEC

Studies implies the functional read-out of human primary tubular epithelial cells (PTEC) cultured on fibrous, supramolecular PCLdi(UUPy) membranes in comparison to PTEC cultured on microporous PC membranes. Their capability to form monolayers, biochemical performance and ability to maintain epithelial cell specific gene expression were investigated. In Fig. 13, it is shown that Toluidin blue staining is cultured from PTEC parts on PC and PCLdi membranes [31].

- Control: PTEC were precultured on membranes for the appropriate analyses.
- Static Culture: PTEC were cultured on membranes under static conditions, After 7 days of static culture, monolayers of PTEC were found on the electrospun PCLdi(U-UPy) membranes and In contrast, PTEC did not form monolayers on PC membranes but grew in densely packed multilayers (with regular medium replacements).
- Perfusion: PTEC were cultured on membranes in the perfusion system for 7 d. The integrity of the epithelial monolayer on the electro-spun meshes was improved by perfusion.

Furthermore, in Fig. 14, the difference cell-cell junctions of PTEC cultured on PC and PCLdi(U-UPy) under static culture conditions or perfusion by formation transmission electron microscopy (TEM) of the cells is shown. Thus, it is shown that culturing PTEC on fiber membranes and SupraMolecular maintain the characteristics of epithelial cells and epithelial phenotype to some extent. PTEC culture produced polarized monolayers on these membranes and the presence of these membranes can improve the function of bioartificial kidneys. Therefore, it is recommended that these PCLdi(U-Upy) membranes be used as a base material in adjusting the function of bioartificial kidney [31]. The authors demonstrated the electrophysiologic capacity of MDCK and LLC-PK1 cells attached to the membrane and active transport of glucose and sodium and water from these cells [30].

The PC membrane and PCLdi(U-UPy) fibers are indicated with *. Scale bars represent 10µm.

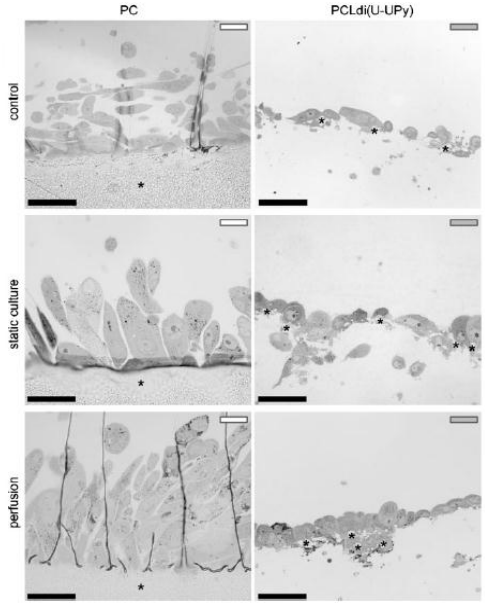


Figure 13. Toluidin blue staining of sections of PTEC cultured on the membranes. PTEC were precultured on the membranes until confluency was reached (control). Then they were cultured under static culture conditions or in the single chamber perfusion system for 7 d [31].

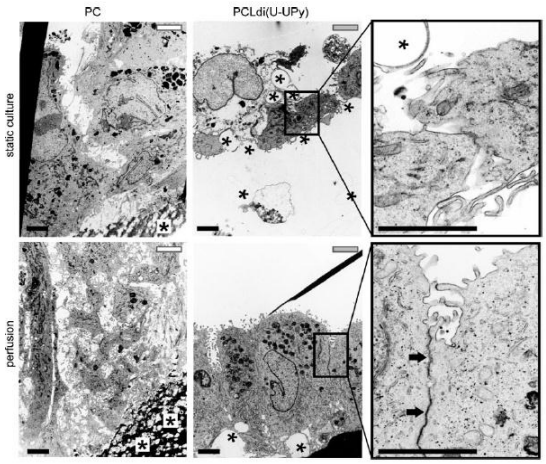


Figure 14. Visualization of cell-cell junctions of PTEC cultured on PC and PCLdi(U-UPy) membranes by TEM. PTEC were precultured on these materials until confluency was reached [31]

IV. Design Based on Optical Tweezers by Microfluidics Technology Tweezers

A cell can be moved without physical contact using special properties of laser. Artus Ashkin first introduced laser clamps at Bell laboratories in 1986 [66]. Then, optical trapping was used as an important tool with broad applications in biology, physics, engineering, medicine [67-73, 74, 75, 76], etc.

A. Optical Tweezers

The basic rules of this tool can be expressed in the form of laws of Newton. As light carries momentum, light direction change means that there is a force in relation to this change (a force change the light direction). Thus, if a laser beam shines light on a particle, the light refracts when it enters that particle. The involved force in changing the direction of light affects the particle and the particle will be pushed towards more intense part of the laser. Laser beam has Gaussian-shape. Thus, the most intense part of the light beam is focused at the center. The particle moves to the part where the light is focused and it is confined in three dimensions. This does not require high energy level (a few mV); however, it needs large-magnitude gradient and the light is focused to a spot whose diameter is about a few microns. Two forces are posed to the particle due to Gaussian shape of the beam. Ultimately, the pure force guides the particle to the beam [74, 75].

B. Design of blood cleaner based on optical tweezers

The new design of a blood cleaner on-chip using Optical Wave Guide as PANDA ring resonator is offered. By controlling certain parameters, the optical vortices (gradient optical fields/wells) can be generated and used to form the trapping tools in the same way as optical tweezers [25]. In operation, trapping force was made by combining gradient field and scattering photons using intensive optical vortices (gradient optical fields/wells) generated in PANDA resonator rings. This feature can be used for blood waste trapping and dynamical moves inside the blood cleaner on-chip system (bioartificial kidney) with help of Wavelength router. Finally, the blood quality test is performed before transferring it to the destination. The schematic of an artificial kidney manipulation on-chip system is shown in Fig. 15. Dynamic optical tweezers or vortices are developed in [25, 70, 71, 74] using dark soliton, bright soliton, and pulse gaussian, which can be used to trap the required microscopic volume; and they are reproduced in form of a multiplexer, along with two nanoring resonators. Using the proposed system, blood waste and unwanted substances can be trapped and transferred to the artificial kidney. The required trapping tool sizes can be generated and formed for the specific blood waste molecules, where finally the clean blood can be obtained and sent to the destination via the through port. However, in practice, several sensors are required [25].

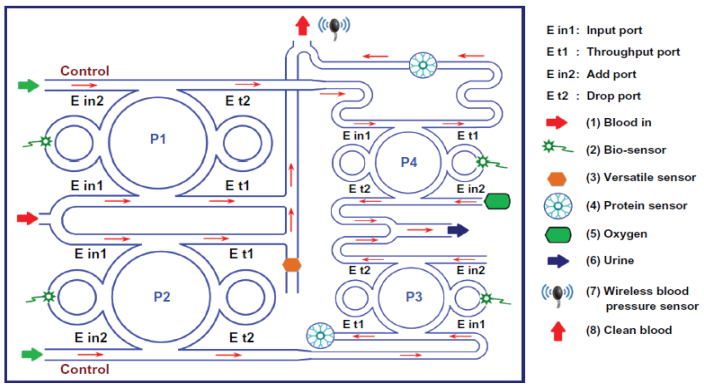


Figure 15. The schematic of an artificial kidney manipulation on-chip system [25]

C. Device description

The PANDA ring resonator systems by incorporating a wavelength router with using optical trapping and transportation technique are used in the blood cleaner on-chip. In this device, as shown in Fig. 16, blood flows into the input port of PANDA resonating rings. Therefore, system 1 of PANDA resonating rings (P1)، function the same way as system 2 of PANDA resonating rings (P2). The whole blood volume can be trapped and delivered in liquid-core waveguide. When blood flows into the waveguide channel, blood concentrate detector measures the blood viscosity. Blood protein reabsorption is one of the important processes in dialysis; therefore, several sensors to detect the protein components of blood are used before the proteins are transferred to the urine. In addition, oxygen can be fed to the system via the added port (control) to the system in order to increase the quality of blood [25].

In [25], sodium is filtered in (~0.4 nm) size. This System is integrated into a single chip, which is equivalent to one Bowman's capsule consisting of the glomerulus. It requires a special environment in which multiple sensors are needed to be integrated into the systems that include: bio-sensor, blood sensor, versatile sensor, protein sensor, and blood pressure sensor. Waveguides were made in different sizes and different Indexes. Various waveguides with 1nm ، $5-8\,\mu m$ sizes respectively were made for the blood cells and proteins, Fig. 17 shows schematic diagram of these blood waveguides. The whole blood cells enter the system through Ein via liquid-core1 (input port), and the required trapping molecules can be trapped and filtered by liquid-core 2. Liquid core 2 is used for the trapped proteins, in which the protein molecule size is 1 nm, which is smaller than the RBC (red blood cells), and therefore, RBCs cannot be transported via liquid-core2. Thus, only unwanted substances are trapped and transported via Liquid-Core2. Finally unwanted substances are tapped and filtered via the drop ports. After the blood waste substances are filtered by the glomerulus, they are filtrated via the proximal tubule [3]. The dynamics tweezers can be in forms of bright solitons, gaussian pulses and dark solitons for trapping the blood waste. In [25], to form the optical trapping tools, a bright soliton with center wavelength at 1.50 μm, peak power 4 W, pulse 35fs is input into the system via the input port. The parameters that ensure more reliable construction of this device

are radii of resonating rings. The results relevant to optical trapping generated by PANDA ring with various wave lengths are shown in the Fig. 18, the bright soliton is used as the control signal for the results obtained. By using the appropriate dark soliton input power, the required trapping tool sizes can be controlled and obtained [25, 70, 71, 74, 75]. In operation, blood concentration has no significant effect on optical trapping ability, because the blood refractive index changes slightly, although it may affect the filtration speed. Dark soliton inputs for trapping operation while bright soliton receives the trapped molecules as the control port signal. This system can be performed as a hemofiltration device, which its depth is equal to 90 μm, its width is equal to 200 μm, and its length is equal to 300 μm [25].

V. CONCLUSION

In this paper, a variety of methods and existing technologies for treatment of renal failure are presented. These methods are developed according to following criteria. They are developed to remove and reabsorb sodium of the blood according to the patient's needs. They are wearable, or cultivable, inexpensive and reliable. Their function is the same as kidneys. The methods presented in this article include: nanotechnology, microfluidic, bioreactors with living renal cells and the systems designed based on optical tweezers with help of microfluidic technology.

In this article, three important devices are presented: 1) A bioartificial device based on nano technology for replicating the function of a single nephron. It has 2 or 3 distinct sections, replicating the function of the glomerulus, the proximal tubule, and the loop of Henle. The proposed device can be built using existing microfabrication technologies and populated with various renal cell types. 2) A bioartificial kidney is developed by using tubular epithelial cells and artificial membranes. For this device, it is necessary to select appropriate tubular and epithelial cells, which will be based on physiological similarities with human kidney function. 3) A PANDA ring resonator system that blood waste molecules can be trapped, filtered, and transported from the artificial blood cleaner (kidney), which can be performed on-chip using an optical waveguide. In operation, the trapping force is formed by the combination between the gradient field and scattering photons by using the intense optical vortices generated within the PANDA ring resonator. There is still a need for new technologies, which can support all functions of the kidney and can be used by public people simply, so that they save more number of people who are at risk of renal failure.

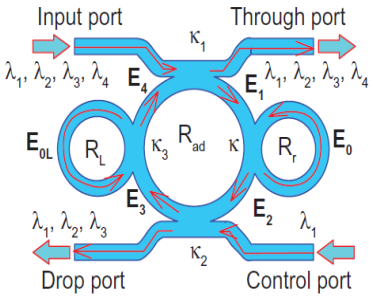


Figure 16. Schematic diagram of a PANDA ring resonator proposed in [25, 70, 71]

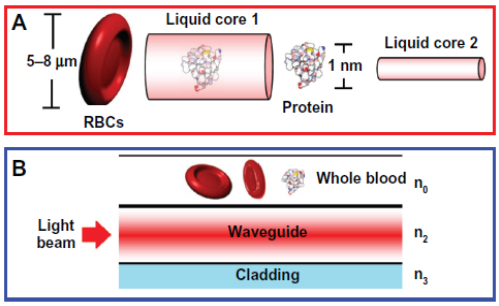


Figure 17. Schematic diagram of A) blood waveguide, B) blood waveguide structure [25]

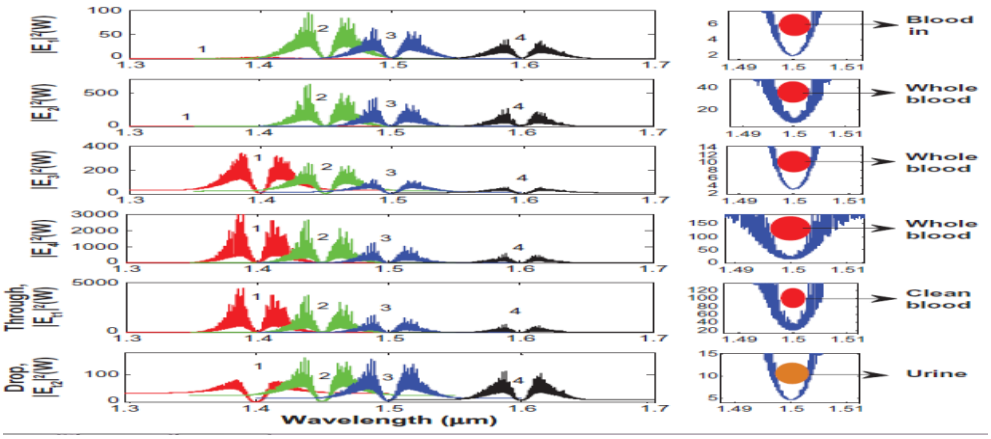


Figure 18. The optical tweezers with different A) sizes and wavelengths [25]

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