Dynamic Characteristics of an Artificial Implantable Electronic Kidney

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Abstract

The dynamic characteristics of an artificial implantable kidney that mimics the operation of real kidney is being studied. Three velocities of blood (slow, moderate. and fast) were tried through the cell and results were inferred after repeating each experiment a few times. The cell is a dialysate-free miniature size compartment with two plate electrodes covering two sides of the passage and two special semi-permeable membranes engulfing the electrodes without touching them. Each membrane is separated by a few millimetres from the adjacent electrode, and the two membranes themselves are at distance from each other. An electric field is applied between the electrode plates which will force the blood ions to migrate across a membrane towards the proper electrode. In this study, deterioration of the separation of ions was proportional to blood velocity. One possible way for compensation has been promising.

Keywords: Implantable, Kidney, Electronic, Artificial, Organ, Filtration University.

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1. INTRODUCTION:

This article aims to introduce an innovated design of an artificial electronic kidney instrument that enjoys a promising degree of efficiency, performance and is characterized by:

- Biocompatible, miniature size, so that it could be implanted inside human body.
- Independent from using dialysate.
- Integrated auto blood filtration treatment systems.

The blood clearance and dialysis processes in the current artificial kidney depend on the diffusion of blood constitutes across a semi-permeable membrane to a prepared solution (called dialysate). Blood flows in these filters on one side of the semi-permeable membranes in a direction opposing to the flow direction of dialysis solution (dialysate) on the other side of the separating membrane that prevents any mixing[1, 2, 3].

Figure 1 shows this arrangement where the dialysate must be prepared to have specific ionic concentrations, so it can make a ***concentration gradient*** (required for simple diffusive solute transport process) that enables blood constitutes to diffuse across the membrane to the dialysate. This is, also, the principal process for removing end-products of nitrogen metabolism (urea, creatinine, uric acid).[4]

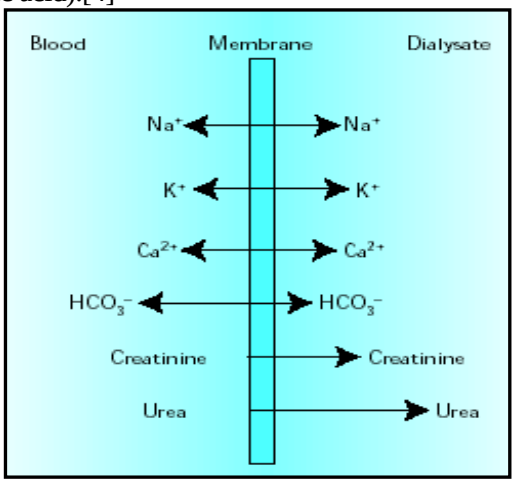

Figure 1: Membrane fluxes in dialysis. [2]

1.1: Double layer capacitance:

This double layer capacitance phenomenon which resulted from the contacting between the charge and the electrode surface is to be taken into consideration in the design.

In the proposed design, the incoming blood will be subjected to a proper Electric Field generated between a two plates capacitor engulfing the blood stream.

The stimulated ions of the solution will gather on the plate's surface to compensate (or neutralize) plate's charge, this will form an interfacial region similar to that of parallel plates capacitor, this phenomena is called "**Double Layer Capacitance (C_d)**". [4, 5]

When only electrostatic interaction operates, the surface's array of ions is cushioned on the electrode by a layer of solvent. The line drawn from the centre of such ions at this distance is considered as the known "**Outer Helmholtz Plane**" (**OHP**). The remaining charges will constitute another layer called "**Diffuse layer**". The ions in this layer will be arranged randomly. The disorder of the arrangement will increase as the distance from the electrode increased, where electrostatic force becomes weaker due to the thermal motion. The thickness of the diffuse layer depends on the total ionic concentration in the solution. Double Layer Capacitance $\mathbf{C_d}$ is generally function of electrostatic potential (Φ), that will increase if the applied voltage increases, and when this potential is varied, the results could be obtained using an average of C_d.[6]

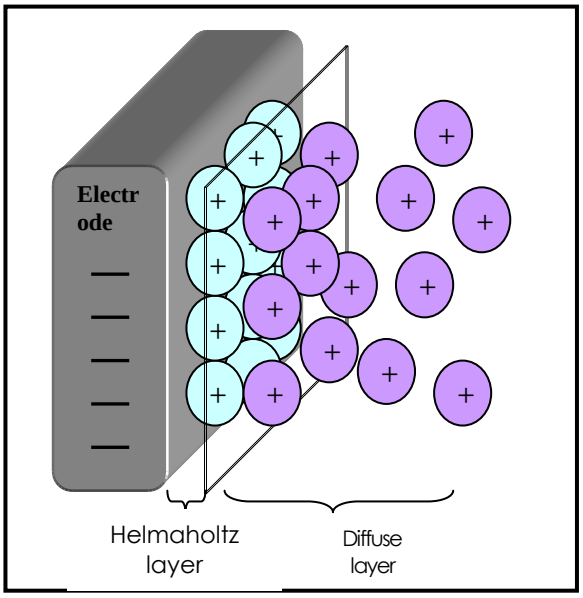

Figure 2: Helmholtz model of double layer. [6]

The distribution of ions in the Helmholtz model solution of the double layer considers the potential variation across the Helmholtz layer region to be linear as shown in Figure 3.

As the distance from electrode surface increases, and at any point within the diffuse layer, the solution ions distribution will decay exponentially and the potential variation over this non liner region is described by the following equation:

$$\phi = \frac{\sigma}{\varepsilon_o \epsilon_r K} \cdot e^{K(a-x)} \quad \dots(1)$$

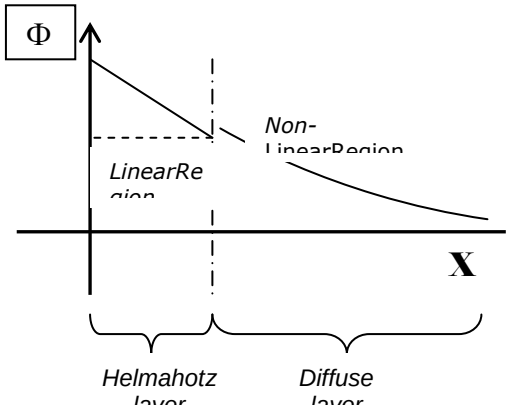

***Figure 3*: Potential profile through the solution side of the double layer.[6]**

Where:

σ: Charge Density at the elctrode surface ($x = 0$), a: Distance that defines the position of OHP, K: Thickness of the Diffuse Layer Capacitance C_D

So far, we can understand that the Helmholtz capacitance(C_H)and the diffuse layer capacitance(C_D)are the two components mainly responsible for determining the overall solution double layer capacitance *(*C_d*)*. If (C_H) and (C_D)are connected in series, then (C_d) can be calculated [7]:

$$C_d = \frac{C_H \, . \, C_D}{C_H + C_D} \quad \dots(2)$$

There are many models derived for describing the behaviour of $\mathbf{C_d}$ with the solution bulk concentration. These models are Helmholtz model, Gouy and Chapman model, Stern, and Grahame model.

The most conceivable form that approximates this behaviour to reality is the Stern and Grahame model. These models involve a diffuse layer of charges in the solution where the electrostatic forces are most able to overcome the thermal process.

In these models, it is also considered that the double layer capacitance is formed by a compact layer of ions next to the electrode followed by a diffuse layer extending into bulk solution. [6]

The overall ionic current is composed of diffusion current and migration current that obey the general Nernst_ Plank equation.

1.2:Electrical Migration and Transport Phenomena

When an electric field is applied to two capacitors plates, the blood ions constituent will reacts with the applied energy under what is known ions migration in which a current will charge the generated double layer capacitors (C_d) engulfing the blood stream and whose electrical equivalent model is depicted in Figure 4:

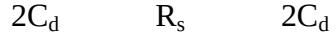

Figure 4: Electrical Equivalent Circuit for the solution.

The overall current of the blood ions migration is described in the flowing equation:

$$i = \frac{E}{R_S} e^{\left(\frac{-t}{R_S C_d}\right)} \quad \ldots (3)$$

Where:

R_s : is the solution resistance,
E : is the applied voltage difference or potential step
C_d : is the generated double

This current is considered as a double layer charging current and it decays exponentially with time as shown in Figure 5. [7]

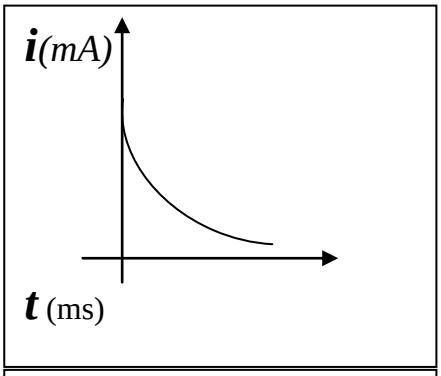

Figure 5: discharging current [7]

As a voltage step is applied to the plates, the ions that are affected by the electric field will accumulate on the plate's surface by charging process, this current will decay until it vanishes, and the remaining ions will be considered to be the ***filtrated ions***.

The equation of ions migration enables us to estimate the amount of double layer charges [7]. So by assuming that the amount of filtered ions per one double layer is equivalent to the amount of double layer capacitance charges (ignoring the amount of ions in the diffuse layer), then we can approximate the amount of filtrated ions.

$$Q_{ions} = E * C_d\left[1 - e^{(-t/R_S C_d}\right] \ldots (4)$$

For a voltage step function, the amount of double layer charges elevated exponentially until it could be considered to be constant as shown in Figure 6.

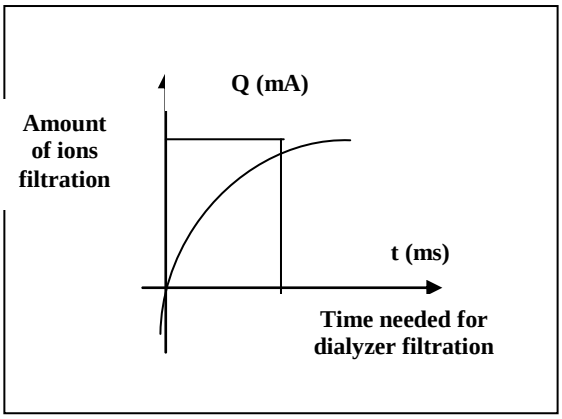

Figure 6: Charging the double layer capacitance. [7]

The overall ionic current is generated

1.3: Mass Transfer and Diffusion Phenomena:

The neutral molecules such as urea, certain, uric acids and all nitrogenous compounds will not be affected by the electrical field; because these molecules don't have any electrical dipole that may migrate like ions. These molecules will pass across a semi-permeable membrane due to simple diffusion.

Fick's Law of diffusion is the most general equation that describes the flux of substance and its concentration as a function of time and position. The flux of a substance (O) at a given location *x* and a time *t*, is written as $J_o(x, t)$. This expression describes the net mass transfer rate of O ($mol.s^{-1}.cm^{-2}$).

The ions in the region of high concentration will have the ability to move to the region of low concentration due to the forces of collision. The amount of material removed depends on the magnitude of the concentration gradient, the travelling distance of molecules, and on the area through which diffusion takes place.

$$\frac{\partial n}{\partial t} = -D.A\,\frac{\partial c(x,t)}{\partial x} \quad \ldots (5)$$

Where:

$\frac{\partial n}{\partial t}$: is the rate of movement of molecules per unit time
D : Fick's Diffusion Coefficient
A : is the Area of the boundary through which molecules move
∂c: Concentration gardient
∂x: distance through which molecules moves.

The Fick's diffusion coefficient could be expressed as the amount of solute cleared by a dialyzer depends on the flow rate of the solution delivered to the membrane. Figure7 shows some of waste blood product diffusion rate according to the flow rate.

Implantable Electronic Kidney considered the prospective solution for patients of renal failure for long term treatment. It has the ability to offer comfort and to save time and effort for the patients who are in dialysis.

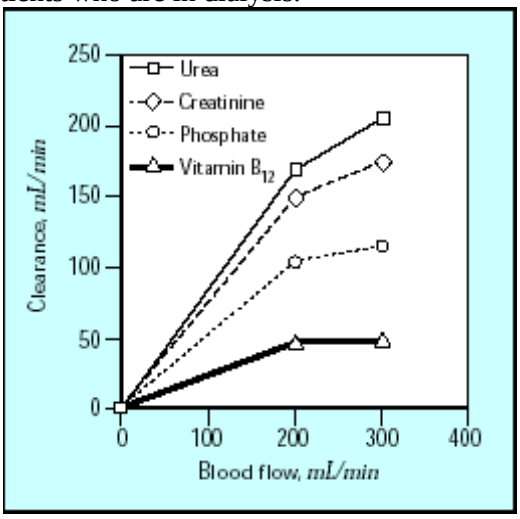

Figure 7: The Effect of flow rate on the diffusion. [11]

2.METHODS ANDCONSTRUCTION:

The basic design comprises three stages: inlet stage, inside apparatus stage, and outlet stage as Figure 8 shows.

2.1:Inlet and Outlet stages:

The inlet and outlet stages both are important stages in the apparatus. Since these two stages must maintain the same velocity of the blood which enters the apparatus via the renal artery. The volume of the blood passing through the renal artery is almost (1L/min.)

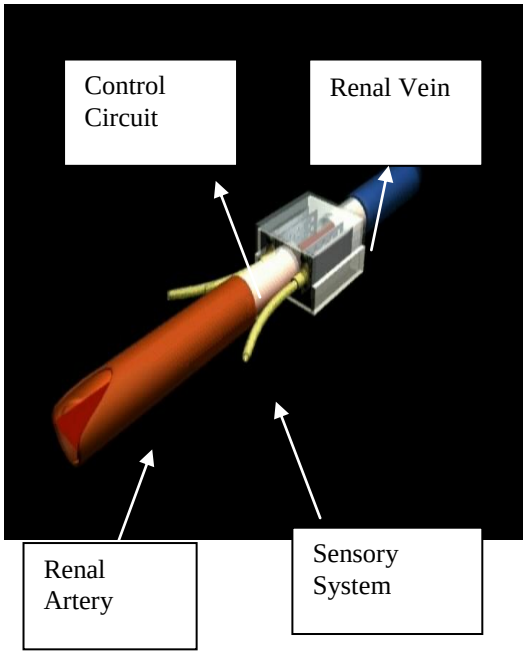

Figure 8: The Inlet and Outlet stages connecting the apparatus.

As the blood enters new section that is different in cross-section area, the blood will change its flowing state, and in this design it is expected to change its state from laminar into turbulent, and hence, a proper nozzle contacting between the renal artery and the inlet pipe in the apparatus. Same must be applied to the outlet.

2.2:The integrated sensory system:

As the blood leaves the renal blood, and starting to enter the apparatus, two sensory systems, proposed to be situated at the inlet of the apparatus pipe, will work simultaneously; to sense the states of the blood, see Figure 8, which are mainly changing in Osmolarity and changing in blood flow rate (i.e. blood pressure).

2.2.1 Osmolarity sensors:

The Osmolarity of the blood is defined as the concentration of ions in the blood. During hunger, thirst, hot environment, cold environment, meals contents, kind of drinks and many other factors, the blood Osmolarity will

change in different percentages. The most important ions are the sodium and chloride, so the sensors must be very sensitive to them.
This design is proposing to position chemical sensors at the inlet of the apparatus pipe to measure the concentration of the sodium and chloride as the main ions.

2.2.2 Flow rate Sensors.

Incoming blood from the renal artery pass through the flow rate sensor; in order to measure the flow rate.
The two sensors are working simultaneously in order to measure two values and, then, the control circuit will judge whether the reason behind increasing the renal pressure is the increment of the concentration of the ions, or the increment of the water intake.
Both the Flow rate sensor and Osmolarity sensor must have the following features:

- Small size and Long term work.
- Biocompatible and able to be implanted into human body.
- Inert so not to interact with ambient environments; especially the blood and its contents.

2.3 Control circuit.

The circuit will control the two main processes inside the apparatus according to the readings obtained from the sensors, and the state of the blood; high Osmolarity or high water intakes. In the first state, power supply is switched on to charge the capacitors enough voltage to separate the excess amount of undesired ions, while, in the second, the micro-pump is turned on with the proper amount of the pressure to remove excess amount of water from the blood.

2.4 Inside the Apparatus.

As the blood enters the apparatus, it will be separated into many identical units; each unit has two electrodes, and two specific membranes as shown in Figure 9. However, difficulties in implementation will be discussed later.

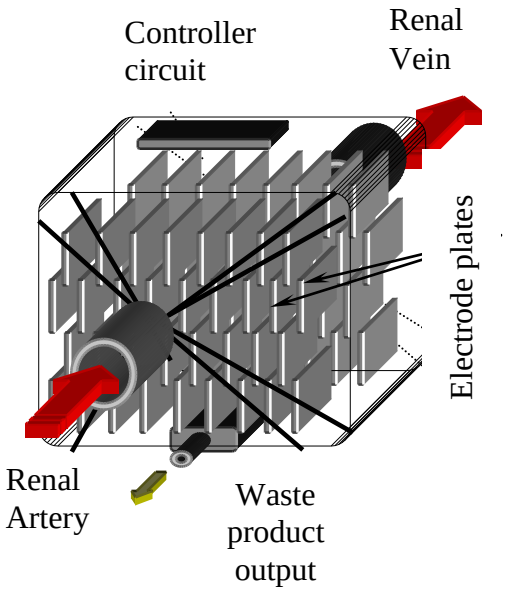

Figure 9: The overall system design

2.5: The electric field in parallel plate

The electric filed lines are pseudo lines leaving the positive plates and entering the negative one; they are almost parallel in the region between the two plates, and curved in the both ends. For a one plate, the number of charges on its surface measured by the quantity σ which refers to surface charge density [7].
When two parallel plates are charged with a specific amount of DC voltage, and if the two plates are conductors, the excess charge on one plate attracts the excess charge on the other plate, and all the excess charge moves onto the inner face of the plates. With twice as much charge on each inner face, the new surface charge density (or as it called σ) on each inner surface is twice[7].

2.5 Membranes.

The membrane must meet requirements to achieve the desired functions:

- Allowing the passage of the ions (mainly Na+, K+, and Cl-) which will be separated from the blood stream to electrodes. The Membrane Pores Diameter MPD must be larger than the diameter of the ions (specially Na+, K+ ,and Cl-)

- Allowing water molecules to pass from blood stream to the space between the membrane and the electrode according to the diffusion or suction principles. The MPD should be larger than those of water molecules diameter to admit diffusion or suction processes to be carried out.
- Blocking the red blood cells (RBC's) from being attracted to the electrode. The pores diameter of the membrane smaller than the diameter of the red blood cells to block theirs passage.
- Blocking other blood contents such as protein and creatinine from passing to the charged electrodes.
- MPD RBC's/ other blood contents>MPD membrane
- MPD membrane> MPD ions/ water.

The used membrane was filter membrane with the following value MPD membrane pores: 0.45 μm

The values of the diameters for the ions are as follow:

- Diameter of Na^+ ions =0.19nm,
- Diameter of Cl^- ions =0.365nm,
- Diameter of K^+ ions =0.266nm.
- Diameter of RBC= 6-7 μm.

The instrument is capable of regulating the amount of water excretion by controlling a required range of suction pressure (micro-pump) relative to the incoming blood pressure to enhance the generated osmotic pressure across the membrane. The nitrogenous waste products were removed by simple diffusion enhanced with an applied ultra-filtration pressure. [7]

In this technique, the blood ions filtrations are performed by making a blood streams (considered to be a dielectric material) to flow between two charged capacitor plates, that create a proper electric field across the blood path, which, in turn, enforces the blood ions (such as Na^+, Cl^- , Mg^+, K^+ ...etc) to move (migrate) towards the suitable electrode according to polarity, penetrating the pores the semi-permeable membranes and then accumulating on the charged plate surfaces as Figure 10 shows.

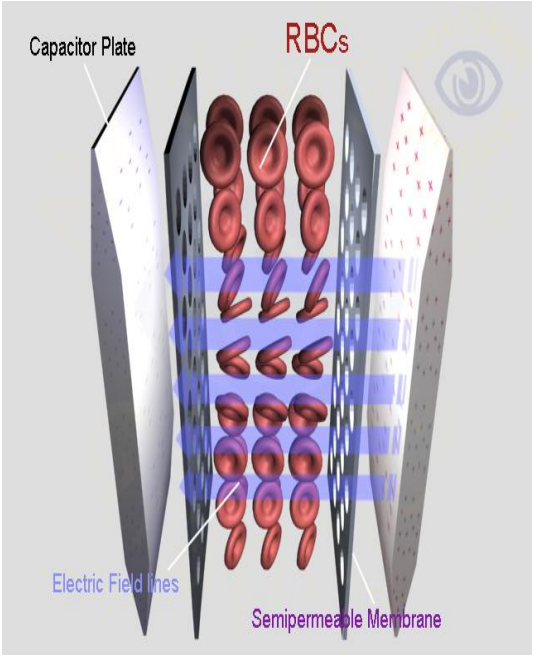

Figure 10.One cell shows the capacitor plates and membranes and the direction of the electric field.

The subjection of blood to that electric field will stimulate blood cations and anions to flow as a bio-ionic current, fluxing through the main blood stream to the electrodes, and hence, showing it to be responsible for the required main blood ions filtration. This technique controls the various blood osmolarities (an indication of the amount of ions and particles in the blood), by an auto-regulating system that regulates the voltage difference on the capacitor plates and hence control the value of the ionic current and the amount of blood ions filtration.

It is supposed that, as Figure 11 shows, if many such units working simultaneously, it is expected to filtrate a reasonable amount of blood ions during a small interval of time. The figure shows the alternating presence of electrodes in these structured layers. The ultimate design strives to use the largest possible area for the electrodes and the membranes so as to provide a wide area for the ions to gather, while maintaining the smallest distance between each two facing electrodes in which case, small voltages are sufficient.

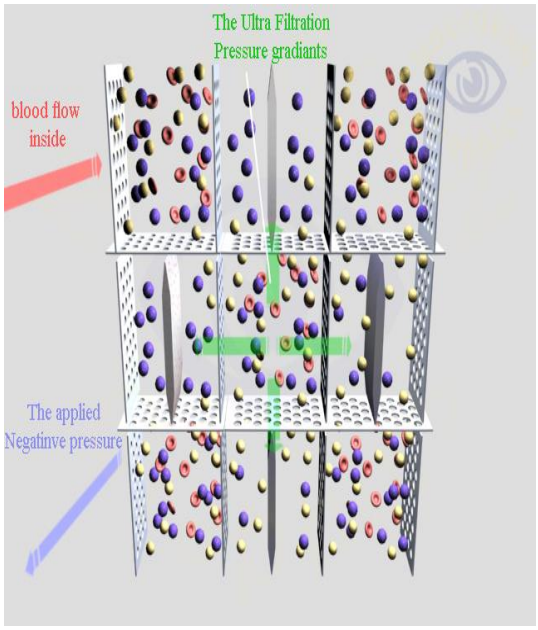

Figure 11. Multi-cell unit in parallel highlights the applied negative pressure, and the blood flow inside the unit.

The transport of ions and masses toward the electrodes and the accumulation on its surfaces depends on the following points:

A. The applied electric field flux

The voltage difference applied to capacitor plates can be controlled to determine the required range of the proper electric field flux on the blood, and hence controlling the amount of blood ions filtration. This regulation of the DC voltage on the electrodes depends on the feedback information that we get from an integrated system of sensors measuring blood Osmolarity, blood pressure, and the renal flow rate. The measured data is fed to a programmed micro-controller system, responsible for setting the value of the required DC voltage on the electrodes.

B. Renal Blood Pressure vs. Applied Negative Pressure:

The renal blood pressure is exploited in this system to enhance simple diffusion for mass transfer from the blood. This pressure will apply forces on the membranes that will enable some of blood constitutes such a blood ions, the nitrogenous end products and water molecules to diffuse from the blood side across the membrane to the electrodes' side. These end products are pumped out to retain the required balance between water and ions and hence keep the concentration at normal and acceptable levels.

This mass flow rate (blood constitutes and water molecules) crossing the membrane depends on the measured value of the renal blood pressure.

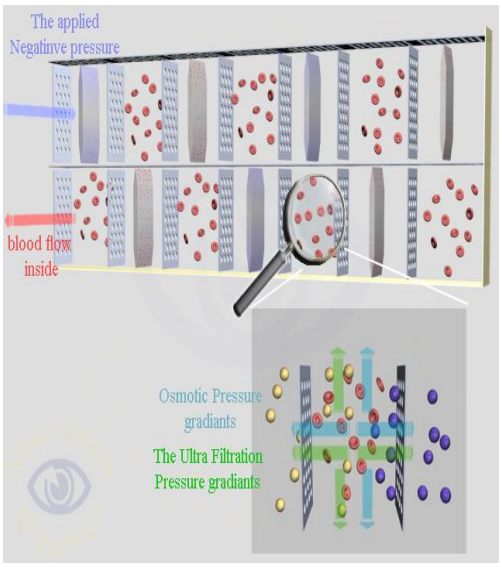

Figure12: Illustrates the pressure gradients across the membranes relative to the whole structure.

In this system a negative pressure difference across the membranes is to be applied in order to increase water excretion efficiency from the blood stream side through the membrane to the vicinity of the electrodes.

A micro-pump is responsible for controlling the additional negative pressure (the ultra-filtration pressure) that will enhance water and end-products excretion out from this instrument. The micro-pump will regulate the amount of water excretion by scaling up or down a required range of ultra-filtration pressure, so that varying the net pressure across the membranes, and hence controlling the excretion amounts of water and blood constituents as Figure 13 shows.

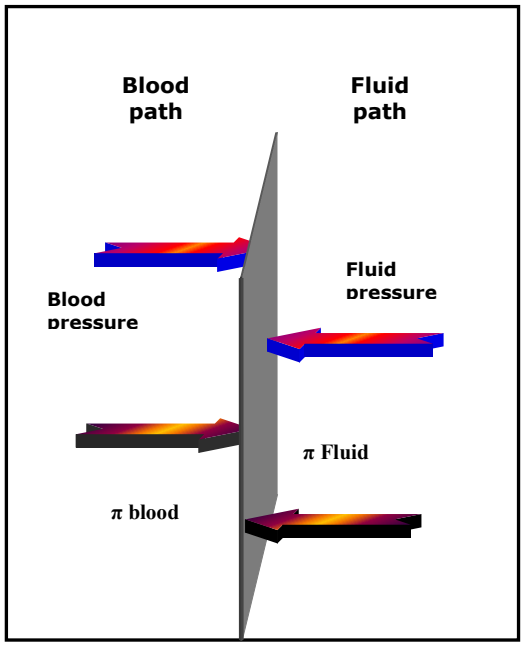

Figure13: Shows the expected forces which will enforce blood fluids to flow across the membranes.

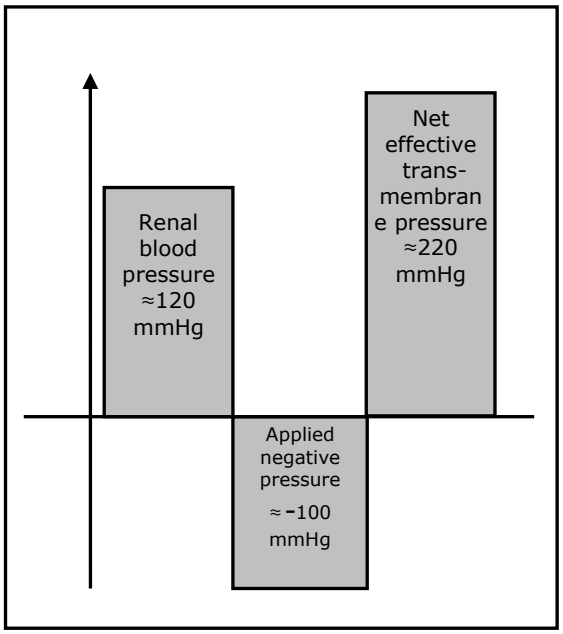

Fig. 14Graphical representation of the values of the pressures used in the unit.

Knowing the mean renal blood pressure and the applied required negative pressure, the overall blood-fluids *filtration rates (**J**)* could be evaluated using the following equation:

$$J = S.L_p\left[\Delta P - R.T\sum_i \sigma_i .\Delta C_i\right] \ldots (6)$$

where:

L_p: *represents the flow resistance of the membrane*

T: *Temperature,* R: *Gas Constant*

S: *is the Membrane Surface Area*

C: *is the Ion Concentration*

The first term in the above equation (ΔP) represents the net effective ultra-filtration pressure; while, on the other hand, the second term comes from Osmosis pressure gradient generated from the ionic migration current. Practical values used are shown in Figure 14.

It is also been considered to add more than one stage of the same structure arranged successively. Thus, applying negative pressure as well as the suction of waste from the area between the membrane and electrode is much easier. Furthermore, the problem accompanied with original parallel structure of units is overcome. Three such units were implemented as is shown in Figure 15.

It is, of course, necessary to enable the voltages applied to each pair of electrodes of every successive stage to be separately controlled. This is thought to yield better results since it allows for several patterns of voltage variations depending on the concentration of ions and water in the flowing blood. This particularly useful for the dynamic work of the implantable kidney since blood does not remain in one area long enough to be completely stripped of all extra unwanted liquid and charged ions. So, a dynamic complex control scheme of voltages applied to each successive unit is to be further studied later.

3. EXPERIMENT and RESULTS

A one-cell model (5x5x5 cm) was built. The inert electrodes were placed 2 cm apart, the membranes were spaced at 1 cm from each other leaving a distance of 0.5 cm from the adjacent electrode.

Despite all the problems facing the construction of this model, positive results were achieved.

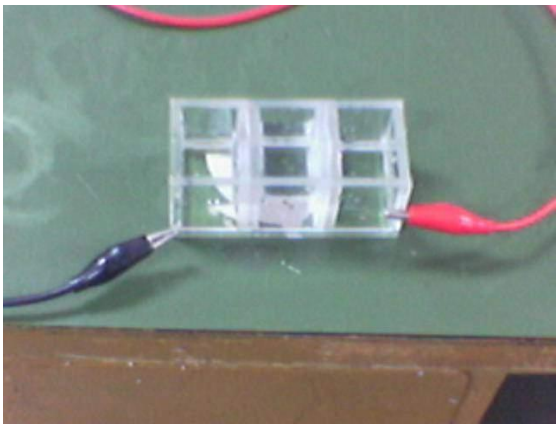

Figure15.experimental setup for one cell 5x5x5 cm with two electrodes and membranes on the sides

Preliminary results from a one cell static experiments (no flow of blood) showed a 20% separation of ions from the main stream [8]. Despite of the difficulties encountered during model construction and performing the experiments using the one-cell compartment, the obtained results show a reasonable reduction of the time required for the patient to attend hospital sessions.

To test the dynamic characteristics of the designed cell, three speeds of blood flow were tried so to see the behaviour under different physiological states (resting, normal activity, and hyperactivity). Measurements were repeated several times. Blood from the area enclosed between electrode and membrane were removed and tested in the lab to see ion concentration. The procedure was repeated several times, averaged and standard deviation calculated as shown in Figure 16. Results have shown deterioration of separation as blood flow increases.

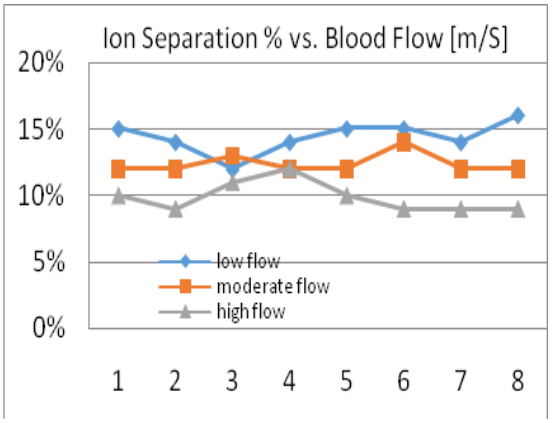

Figure16: Variation in ion separation percentage as blood flow is varied to match physical activities.

This makes sense because blood does not have sufficient time between the electrodes to be attracted and the membrane contributes more to this deterioration.

These results lead to the necessity of having several such cell units in succession to compensate for this deterioration and to make this system worthwhile. Building more one unit was costly due the high prices of electrodes and membrane. A special arrangement has been devised to simulate this situation with only the existing cell alone. The excessive liquid rich in waste and extra ions was pumped out from the area between electrode and membrane, while the remaining blood were fed back to input of the same cell through a one and a half meter tube. This cycling of blood was repeated several time and samples taken every five minute to tested.

This configuration, however crude might be, has given good indication of the feasibility of improvement when building several units in succession. Further research into this is needed to cover all aspects of the design and tackle all possible problem arising.

4- Conclusions:

The basic theoretical calculation shows that this is a feasible path of research and preliminary practical results from a crude experimental model with only one cell has shown good potential. Compact, multi-cell industrial model that depicts the theoretical designed model will, hopefully, achieve much better results and

ultimately make patient visits to kidney dialysis centres less often.

The flow of blood was considered to be laminar going through the unit and coming out of it. However, net filtration should be monitored and precisely measured when turbulent flow is present and see what effects this makes on the above results. Modifications on the mathematical model must be incorporated to account for turbulent flow.

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