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A 2D model of axial symmetry for proximal tubule of an average human nephron: indicative results of diffusion, convection and absorption processes

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Abstract. A simplified model of a proximal convoluted tubule of an average human nephron is presented. The model considers the 2D axisymmetric flow of the luminal solution exchanging matter with the tubule walls and the peritubular fluid by means of 0D models for the epithelial cells. The tubule radius is considered to vary along the conduit due to the trans-epithelial pressure difference. The fate of more than ten typical solutes is tracked down by the model. The Navier-Stokes and Reaction-Diffusion-Advection equations (considering the electro-neutrality principle) are solved in the lumen, giving a detailed picture of the velocity, pressure and concentration fields, along with trans-membrane fluxes and tubule deformation, via coupling with the 0D model for the tubule wall. The calculations are carried out numerically by means of the finite element method. The results obtained show good agreement with those published by other authors using models that ignore the diffusive transport and disregard a detailed calculation of velocity, pressure and concentrations. This work should be seen as a first approach towards the development of a more comprehensive model of the filtration process taking place in the kidneys, which ultimately helps in devising a device that can mimic/complement the renal function.

1. Introduction

In the human organism almost all the cells are surrounded by extracellular fluid called internal environment. Survival of tissues depends on maintaining electrolyte composition, osmotic balance and volume of the liquid within very narrow ranges. In the excretory system, the kidneys are the main organs responsible in formation of the urine for its further excretion. In this process, the kidney filters the blood plasma forming a plasmatic ultrafiltrate, a solution without cellular components or proteins. Then, the kidneys reabsorb substances from the ultrafiltrate, some of which must remain in the internal environment, and secretes others that must be eliminated from it. Urine, is the result of the renal filtering, reabsorption and secretion processes and, once produced, it is excreted through a series of ducts that direct it towards the bladder where it will be stored until the next urination. Within the
kidney, these processes are performed in basic functional units of micrometer scales called nephrons. There are about one million nephrons per kidney in a healthy adult.

A nephron is essentially composed by a filtering component, called glomerulus, and a tubule in whose walls reabsorption and secretion of substances occurs. The luminal fluid that continues its path inside the tubule is then excreted. The urine is therefore formed by mixing the tubular liquid from all nephrons that are performing their functions. The tubule of a nephron is usually divided into segments: proximal convoluted tubule, descending limb of loop of Henle, thick and thin segments of ascending limb of loop of Henle, a short segment that contains a special group of cells called the macula densa, the distal convoluted tubule, and then, there is a collecting duct. Among the main electrolytes exchanged into the tubular walls include the cations sodium, potassium, hydrogen and the anions chloride and bicarbonate. Other substances without net charge are also exchanged like urea, creatinine and glucose. There are substances such as pesticides, pharmaceuticals and food additives, which after being ultrafiltered don’t interact with tubular walls and simply circulate through the tubules to be excreted, [1].

There are studies that models and analyzes the behavior of the nephron and surrounding structures involving many physiological details through constitutive equations for the exchange surfaces and constitutive equations of the substances involved as in [2], [3] or [4]. However, in those works it’s not take into account the bi and three-dimensional characteristic of diffusive phenomena in the tubular lumen, because it’s not their objective. A detailed understanding of the diffusive mass transport phenomenon and its effect on the spatial distribution of concentrations is essential for physically explain the approach of dissolved substances to the tubular walls.

In this paper a simplified model of the proximal convoluted tubule of an average human nephron with emphasis on the diffusion, convection, absorption and excretion of primary urine processes in the tubular lumen for a set of substances typically present in plasma ultrafiltrate is presented. For simplicity, a two-dimensional axisymmetric model is used to model the intratubular flow in combination with two dimensionless models to represent the epithelium of the tubular wall covered by a peritubular fluid whose characteristics are known. The tubular radius is considered variable along the length of the tubule with respect to the transepithelial pressure difference. This model considers the diffusive phenomena involved for a total of 15 intercellular and luminal solutes, 16 peritubular solutes and 18 intracellular solutes typically present in such compartments. In the luminal domain Navier-Stokes and Nernst-Planck equations are resolved considering the principle of electroneutrality to calculate pressure, velocity and concentration profiles, tubular transmembrane flows and deformation. In the remaining domains transepithelial and paracellular flows are resolved. The structures before, after or outside the proximal convoluted tubule are not considered. Calculations are performed using the finite element method. Agreement of calculated results with those of other authors to classic models that do not consider the diffusive fluxes and details of the concentration profiles, pressure and velocity, are observed. This last allows having a first approach to a comprehensive enough comparison model to aid in the design of microdevices aimed to complement and mimic the complex functions of the kidneys relating to the homeostasis maintenance of the internal environment.

2. Methodology

For modeling the proximal convoluted tubule of the nephron the advection-diffusion system of figure 1 is used, wherein can be seen an axis of axial symmetry. This geometry actually represents a surface that revolutionized generates two concentric cylinders, one hollow and the other filled with the same axis of symmetry as shown in figure 2. There are three distinct areas: Tubular lumen tubular, tubular renal epithelium and peritubular solution.
The compartments indicated interact through intercompartmental contact surfaces. The interface between luminal compartment and cell compartment is the apical cell membrane ($A_{LC}$), between the luminal compartment and intercellular space compartment is the tight junction surface ($A_{LI}$), between cell compartment and intercellular compartment is the lateral cell membrane or paracellular membrane ($A_{CI}$), between intercellular compartment and peritubular solution is the basement membrane ($A_{IP}$) and between cell compartment and peritubular solution is the basal cell membrane ($A_{CP}$). The characteristics for these exchange surfaces are adapted from [2] and are shown in table 1.

**Table 1.** Exchange areas between compartments.

| Exchange surface name (m.: membrane) | Symbol | Area in cm$^2$ cm$^{-2}$ of epithelium | Requires luminal domain integration |
|-------------------------------------|--------|----------------------------------------|-----------------------------------|
| Apical cell membrane                | $A_{LC}$ | 36                                     | Yes                               |
| Tight junction surface              | $A_{LI}$ | 0.001                                  | Yes                               |
| Paracellular membrane               | $A_{CI}$ | 36                                     | No                                |
| Basement membrane                   | $A_{IP}$ | $0.02 \times [1.0 - 0.01 \text{ mmHg}^{-1}(p_I - p_C)]$ | No                                |
| Basal cell membrane                 | $A_{CP}$ | 1                                      | No                                |
The last column of table 1 shows those areas which require integration schemes to properly interrelated amounts between compartments dimensionally different. Pressure in I compartment, $p_I$, is considered constant and equal to -23 mmHg. And pressure in C compartment, $p_C$, is considered equal to the intraluminal pressure, $p_L$.

Figure 3 shows a relation scheme between compartments with its exchange areas.

The luminal radius is $R = 10.6[1 + 0.03 \text{mmHg}^{-1}(p_L - p_P)] \mu m$ and the tubular length $L_0 = 12 \text{mm}$. The aspect ratio between length and radius within the tubular lumen is $L_0 R^{-1} \approx 800$. The volumes are $V_C$ for cellular compartment and $V_I$ for intercellular compartment. The values for these volumes were taken from [2] and are shown in table 2.

| Compartment name                  | Volume symbol | Value in $\text{cm}^3 \text{cm}^{-2}$ of epithelium |
|-----------------------------------|---------------|---------------------------------------------------|
| Cell compartment (C)              | $V_C$         | 1.00$x10^{-5}$                                    |
| Intercellular compartment (I)     | $V_I$         | $0.7x10^{-8} \times [1.0 - 0.1(p_L - p_C)]$        |

Due to the micro dimensions of the model, is established as a validity criterion to the continuous material hypothesis that the Knudsen number must be less than 0.01, according to [5]. In this system the Knudsen number is calculated as the ratio of the molecular mean free path ($\lambda$) of molecules that compose the circulating fluid and the radius ($R$), i.e. $Kn = \lambda R^{-1}$. If the molecular mean free path estimated value is about $\lambda \approx 0.7 \text{nm}$ then the Knudsen number is $Kn \approx 5x10^{-5}$ and fulfill the criterion because it's about 200 times less than 0.01.

A homogeneous fluid occupy the tubular lumen, meaning that all functions are continuous in this domain. This fluid is considered to be circulating with a velocity profile governed by the Navier-Stokes equations (1) and continuity equation (2) for an incompressible fluid. The non-contact force effects are assumed to be null, [6].

\[
\frac{\rho}{\partial t} = -\nabla p - \mu \nabla \mathbf{v} \tag{1}
\]

\[
\nabla \cdot \mathbf{v} = 0 \tag{2}
\]

\[\lambda = (2^{0.5} \pi n a^2)^{-1} = (2^{0.5} \pi PM_{\text{water}} N_{\text{at}} a^2)^{-1} = (2^{0.5} 3.1415 55 140 \text{ mol m}^{-3} 6 \times 10^{23} (10^{-10} \text{m})^2)^{-1} \approx 0.7 \text{ nm}. \] This is an approximate calculation for liquid water because it's the most abundant species as solution's solvent. “a” is a molecular radio estimate for water molecule.
Figure 1 shows the approximately parabolic velocity profile that appears when these equations are solved being null the fluid absorption at the tubule luminal surface. Has to be consider here the radial symmetry of the geometry to correctly interpret the schema.

The used density is \( \rho = 1000 \text{ kg m}^{-3} \). The used viscosity for the circulating fluid is \( \mu = 1.2 \text{ cP} \equiv 1.2 \text{ mPa s} \). This value approaches the blood plasma viscosity according to [7]. To solve these equations a parabolic velocity profile is considered at the entrance and generates a rate about 0.5 nl s\(^{-1}\) entering the tubule. The exit pressure is assumed to be 8 mmHg and the solvent flow rate was calculated using expressions in which solute concentrations aside and another membrane is coupled to the transmembrane transport. The calculated Reynolds number is less than 1 in the luminal domain indicating a flow in laminar regime. This regime is considered valid for the entire fluid domain since the entry length \( L_e \) is approximately 0.124 \( \mu \text{m} \) which is less than the total length \( L_0 \) of the tubule by a factor of \( 9.6 \times 10^4 \) [6]. The assumptions assumed to solve the equations (1) and (2) permits them to be independent of the Nernst-Planck equations.

The circulating fluid is an aqueous solution of solutes listed in table 3 along with their relevant features for this model. Concentrations in the intercellular compartment \( I \), cell compartment \( C \) and the peritubular bath \( P \) are considered constant and are also shown in table 3.5

| Chemical species | Index \( i \) | Chemical formula | PM in g mol\(^{-1}\) | \( z_i^a \) | \( D_i^b \text{ m}^2 \text{s}^{-1} \) | Domain | \( c_e^c \text{ mmol l}^{-1} \) | \( c_i^d \text{ mmol l}^{-1} \) | \( c_P^e \text{ mmol l}^{-1} \) |
|------------------|------------|-----------------|-----------------|--------|-----------------|--------|-----------------|--------|-----------------|
| Hydron \( H^+ \) | 1 | 1.01 | +1 | 9.68 \times 10^{-9} | L, C, I, P | 4.69 \times 10^{-7} | 4.59 \times 10^{-7} | 4.95 \times 10^{-7} |
| Sodium \( Na^+ \) | 2 | 22.99 | +1 | 1.39 \times 10^{-9} | L, C, I, P | 19.60 | 140.30 | 140.0 |
| Potassium \( K^+ \) | 3 | 39.10 | +1 | 2.04 \times 10^{-9} | L, C, I, P | 138.1 | 4.66 | 4.90 |
| Ammonium \( NH_4^+ \) | 4 | 18.04 | +1 | 2.04 \times 10^{-9} | L, C, I, P | 0.23 | 0.18 | 0.20 |
| Chloride \( Cl^- \) | 5 | 35.45 | -1 | 2.11 \times 10^{-9} | L, C, I, P | 16.3 | 112.0 | 113.2 |
| Bicarbonate \( HCO_3^- \) | 6 | 61.02 | -1 | 1.23 \times 10^{-9} | L, C, I, P | 25.0 | 25.6 | 24.0 |
| Hydrogen phosphate \( HPO_4^{2-} \) | 7 | 95.98 | -2 | 7.94 \times 10^{-10} | L, C, I, P | 8.50 | 2.98 | 2.97 |
| Dihydrogen phosphate \( H_2PO_4^- \) | 8 | 96.99 | -1 | 9.16 \times 10^{-10} | L, C, I, P | 2.52 | 0.86 | 0.93 |
| Formate \( HCO_2^- \) | 9 | 45.02 | -1 | 1.51 \times 10^{-9} | L, C, I, P | 0.52 | 0.77 | 1.00 |
| Cellular anion \( \text{Imp}^- \) | 10 | - | -1 | - | C | 27.7 | - | - |
| Carbon dioxide \( CO_2 \) | 11 | 44.01 | 0 | 2.00 \times 10^{-9} | L, C, I, P | 1.49 | 1.49 | 1.50 |
| Urea \( CO(NH_2)_2 \) | 12 | 60.06 | 0 | 1.67 \times 10^{-9} | L, C, I, P | 4.96 | 4.91 | 5.00 |
| Carbonic acid \( H_2CO_3 \) | 13 | 62.02 | 0 | 1.40 \times 10^{-9} | L, C, I, P | 4.36 \times 10^{-7} | 4.36 \times 10^{-7} | 4.41 \times 10^{-7} |
| Ammonium \( NH_3 \) | 14 | 17.03 | 0 | 1.90 \times 10^{-9} | L, C, I, P | 3.48 \times 10^{-8} | 2.70 \times 10^{-8} | 2.82 \times 10^{-8} |
| Formic acid \( HCO_2H \) | 15 | 46.03 | 0 | 1.41 \times 10^{-9} | L, C, I, P | 0.91 \times 10^{-8} | 2.04 \times 10^{-8} | 2.85 \times 10^{-8} |
| Glucose \( C_6H_{12}O_6 \) | 16 | 180.2 | 0 | 9.40 \times 10^{-10} | L, C, I, P | 15.1 | 7.79 | 5.00 |
| Cellular acid \( \text{ImpH} \) | 17 | - | - | - | C | 41.1 | - | - |
| Protein | 18 | - | - | - | C, P | 68.9 | - | 2.00 |

5 The molecular weights given in this table have been estimated by http://es.webqc.org/mmcalc.php.
6 \( 1 \text{ e} \equiv 1.6 \times 10^{-19} \text{ C} \) and it's equivalent to the electric charge of an electron. Should not be confused \( z_i \) symbol for the number of electric charge of the solutes with the \( z \) symbol for longitudinal space coordinate the tubule.
Imp is assumed unreactive in this model so the amount of mass, considering the amounts involved in acid-base reactions, is constant within the cell space. The solute Prot allows modeling oncotic effects of protein confined at the C and P compartments. For these substances is not necessary to indicate diffusivities because they are inside dimensionless compartments.

The bidimensional model proposed for the luminal compartment has three edges and a symmetry axis as shown in figure 1. The left's contour (in green) represents a radial section of the surface through which fluid enters. The right's contour (in red) represents a radial cut surface where the fluid leaves the control volume (in light blue). The upper boundary (in orange) shows a longitudinal section of the inner tubular wall where it is assumed the possibility of a normal solvent flow, i.e. the solvent speeds are normal to this wall. The solvent’s intercompartmental flux density $N_{vOD}(z)$ is calculated according to equation (3). In exchanges C↔I, C↔P and I↔P the calculation is straightforward because conditions in compartments C, I and in peritubular fluid P are constants. Moreover, in exchanges L↔C and L↔I it is required a successive approximation scheme to the equilibrium solution because the solute and solvent streams are coupled. In equation (3) the first term represents the effect of the hydrostatic pressure, the second represents the oncotic pressure effect of proteins and the third the effect of dissolved solutes associated with its corresponding reflection coefficients. All terms are affected by the water permeability of the considered exchange surface.

$$N_{vOD}(z) = L_{pOD}.A_{OD}.\left[(p_O - p_D) + (\pi_D - \pi_O) + R_g.T \sum_{j=1}^{\text{NEQ}} \sigma_{OD,i}(c_{D,i} - c_{O,i})\right]$$

(3)

The tubular wall ability in absorption or secretion of solutes to and from the luminal compartment is considered normal thereto and its magnitude is governed by the transport equation (4), [2].

$$N_{OD,i}(z) = N_{vOD}.(1.0 - \sigma_{OD,i}).\xi_{OD,i}.\bar{h}_{OD,i}.\bar{A}_{OD}.c_{OD,i} \cdot \frac{c_{D,i} - c_{OD,i}}{1 - 1.e^{-\xi_{OD,i}}} + \sum_{j=1}^{\text{NEQ}} L_{OD,i,j}.A_{OD}.(\bar{\mu}_{O,j} - \bar{\mu}_{D,j}) + N_{act}.OD,i$$

(4)

Where: O is the origin compartment, D is the destination compartment, $N_{OD,i}(z)$ is the molar flux from O to D of the $i$-th specie and is given as a longitudinal coordinate $z$ function, $N_{vOD}$ is the density of solvent volumetric flow from O to D, $\sigma_{OD,i}$ is the reflection coefficient for the $i$-th solute in the plasmalemma, $\bar{h}_{OD,i}$ is the logarithmic average for concentration of solute $i$ over the exchange surface, $\bar{A}_{OD}$ is the area that separate both compartments, $c_{D,i}$ and $c_{O,i}$ are solute $i$ concentration in the O and the D side of the plasmalemma respectively, NEQ is the total number of chemical species, $L_{OD,i,j}$ is the coupled transport coefficient, $\bar{\mu}_{O,j}$ and $\bar{\mu}_{D,j}$ are the electrochemical potentials of the solute $j$ in the O and D compartments respectively, $N_{act}.OD,i$ is the active transport of the $i$ solute from the compartment O to compartment D.

In equation (3) the first term shows the effect of membrane reflection coefficient in determining the convective transport. The second term includes the Goldman ratio for determining transmembrane ion fluxes. The third term represents the coupled transport of species according to the model of linear nonequilibrium thermodynamic. The fourth term is an active transport of solutes. This equation and the above definitions also apply to the transports C↔I, I↔P and C↔P with the simplification that there are not dependent variables of $z$ coordinate. In these cases the average values of the parameters in compartment C, compartment I and the fluid P are used to calculate intercompartmental matter flow’s.

The hypothesis are: (a) the system is in steady state, (b) the electric potential gradient in the domain is zero, (c) the solution within the domain are considered dilute, (d) the temperature is constant, (f) the electroneutrality principle is met, (g) the chemical activity coefficient is one, (h) the density is constant, (i) can be assumed the hypothesis of material continuity (Knudsen number less than 0.01 according to [5]), (j) the dissociation of carbonic and dihydrogen phosphate acids at their respective resulting bases and hydron are instant. In addition, due to the hypothesis (c), it is also accepted that the contributions of speeds, shear stresses and other solutes forces are negligible compared to the
corresponding quantities in the solvent (water), and thus is considered valid the approximation of pseudobinary behavioral for dissolved chemical species.

The diluted solution hypothesis (c) is assumed because the mol percentage of all solutes in the solution is about 0.5%, while the mol percentage of water solvent in entire solution is 99.5%. With this concentration ratio it is reasonable to assume that molecules of each solute interacts most of the time with solvent molecules and, almost never with other solute molecules. Thus, for each solute can be considered a binary behavior between this one and the solvent. Because the solution is not strictly binary in the sense of having only two chemical species (one solute and one solvent), it is called solution with pseudobinary behavioral because for each solute can be thought a binary behavior between this and the solvent. This assumption greatly simplifies the equations used to describe the advective-diffusive behavior of substances.

To calculate the concentration profiles in the luminal domain is used the convection-diffusion equation associated with the fundamental principle of stoichiometry (5) assuming the electroneutrality hypothesis (6) in the domain. The total surface current density flow (7) is assumed to be null for all surface exchanges. Convective flow of substances is established in $x = L_0$ and concentrations are fixed on the surface of fluid entry to the tubular lumen, at $z = 0$. In the axis of symmetry it is assumed that the concentration gradients are zero in the radial direction $r$, see (8).

$$\nabla \cdot \mathbf{N}_I = R_i \quad \text{with} \quad \mathbf{N}_I = -D_i \nabla c_i + c_i \mathbf{v} \quad \text{and} \quad \sum_{i=1}^{\text{NEQ}} R_i P \mathbf{M}_i = 0$$ (5)

$$\sum_{i=1}^{\text{NEQ}} z_i c_i = 0 \quad \text{in luminal domain } L$$ (6)

$$j = \sum_{i=1}^{\text{NEQ}} z_i (-D_i \nabla c_i)$$ (7)

$$\frac{\partial c_i}{\partial r} \bigg|_{r=0} = 0 \quad \text{for } i = 1.. \text{NEQ}$$ (8)

The buffer reactions pairs carbonic acid-bicarbonate and hydrogen phosphate-dihydrogen phosphate are considered. It is assumed that the dissociation of acids is instantaneous and always in chemical balance in the whole domain in accordance with constants $pK_{HCO_3^-} = 6.1$ and $pK_{HPO_4^{2-}} = 6.8$. The reaction rate of hydration and dehydration of carbon dioxide is considered finite, and for that reason are provided the first-order reaction constants, $k_h$ and $k_d$, that allow to calculate the reaction rates $R_{CO_2}$ and $R_{H_2CO_3}$.

$$CO_2 + H_2O \xleftrightarrow{k_h} H_2CO_3 \xleftrightarrow{k_d} HCO_3^- + H^+$$ (6)

Solving this diffusive-advective-reactive system means to find the concentration distributions for all chemical species dissolved in the luminal domain $\Omega_L$ and finding the amount of solute and solvent that flows through all intercompartmental membranes, including the surface of tight junctions linking apical cell membranes in the wall of the tubular lumen. The $\Omega_L$ domain with the domain $\Omega_C$ (cellular compartment) and $\Omega_I$ (intercellular compartment) constitute the domain $\Omega$ given by its union.

The remaining parameters used to obtain the results are in table 4.

| Table 4. Additional parameters and modeling equations. |
|-----------------------------------------------|
| Solute | $c_{\text{inlet}}$ | $\sigma_{LL,I}$ | Solute | $c_{\text{inlet}}$ | $\sigma_{LL,I}$ | Solute | $c_{\text{inlet}}$ | $\sigma_{LL,I}$ |
|--------|-----------------|---------------|--------|-----------------|---------------|--------|-----------------|---------------|
| H$^+$  | 4.94x10$^{-3}$  | 0.20          | H$^+$  | 2.970           | 0.90          | H$^+$  | 1.51            | 0.90          |
| Na$^+$ | 140             | 0.75          | Na$^+$ | 0.926           | 0.90          | Na$^+$ | 2.86x10$^{-3}$  | 0.30          |
| K$^+$  | 4.90            | 0.60          | K$^+$  | 1.000           | 0.30          | K$^+$  | 2.84x10$^{-4}$  | 0.70          |

$^7$ Los datos de la tabla 4 se tomaron de [2] a excepción de los coeficientes de reflexión unitarios en nota $a$ y la constante $pK_{HCO_3^-}$ que en el citado documento vale 3.57 y no concuerda con los datos bibliográficos.
\( \text{NH}_4^+ \) 0.20 0.60  
\( \text{Cl}^- \) 113 0.30  
\( \text{CO}_2 \) 1.200 0.90  
\( \text{C}_{\text{S}_2}\text{O}_6 \) 5.00 1.00  
\( \text{HCO}_3^- \) 24.2 0.90  
\( \text{CO} \) 5.000 0.70  

Equilibrium equations in buffers, with \( \ln K_a \)

\[
\begin{align*}
\text{Chemical equilibrium for pair HCO}_3^- - \text{H}_2\text{CO}_3: & \quad pK_{\text{HCO}_3^-} = 6.1 \\
& \quad [\text{H}^+] = K_{\text{HCO}_3^-}[\text{H}_2\text{CO}_3][\text{HCO}_3^-]^{-1} \\
\text{Chemical equilibrium for pair HPO}_4^{2-} - \text{H}_2\text{PO}_4^2-: & \quad pK_{\text{HPO}_4^{2-}} = 6.8 \\
& \quad [\text{H}^+] = K_{\text{HPO}_4^{2-}}[\text{H}_2\text{PO}_4^-][\text{HPO}_4^{2-}]^{-1} \\
\end{align*}
\]

Oncotic pressure \( (\pi_D) \):

\[ \pi_D = RT[\text{Prot}]_D, \text{ with } R = 8.314 \text{ Pa m}^3 \text{ mol}^{-1} \text{ K}^{-1}. \]

Electrochemical potential \( (\mu_{D,i}) \):

\[ \mu_{D,i} = RT \ln c_{i,d} + z_iF \]

Equation for active \( \text{Na}^+ \) transport:

\[ J_{\text{Cl}-\text{Na}^+}^{\text{act}} = 10.8 \left( \frac{[\text{Na}^{+}]_c}{[\text{Na}^{+}]_c + K_{\text{Na}^+}} \right)^2 \left( \frac{[\text{K}^+]_l + [\text{NH}_4^+]_l}{[\text{K}^+]_l + [\text{NH}_4^+]_l + K_{\text{K}^+}} \right)^2 \]

\[ K_{\text{Na}^+} = 0.2 \times 10^{-3} \left( 1 + \frac{[\text{K}^+]_c}{8.33 \times 10^{-3}} \right) \]

\[ K_{\text{K}^+} = 0.1 \times 10^{-3} \left( 1 + \frac{[\text{Na}^{+}]_l}{18.5 \times 10^{-3}} \right) \]

\( ^a \) The reflection coefficients \( \sigma_{c,i}, \sigma_{c,i}, \sigma_{p,i} \) and \( \sigma_{p,i} \) are taken as unit.

\( ^b \) The subscript \( D \) can take values \( C \) and \( P \).

The above equations are solved using a numerical scheme based on the finite element method implemented in the commercial software COMSOL Multiphysics®. The results are shown below corresponding to a mesh of 1640 triangular elements with quadratic basis and form functions in all cases, and cubic functions to describe the velocity field.

3. Results

The inner tubular radius is shown in figure 4. The integral over the revolution surface that it generates is \( A_{\text{pti}} = 0.831 \text{ mm}^2 \), which is considered as internal tubular wall area. Taking an epithelium thickness of 8 \( \mu \text{m} \) microns, then the epithelial area is calculated from this radius \( R \) showed in the graph. Epithelial area is \( A_{\text{ep}} = 1.43 \text{ mm}^2 \).

![Figure 4](image)

Figure 4. Deformed tubular radius \( R \), in violet color, and undeformed tubular radius \( R \), in dotted lines.

The tubular lumen pressure and the transepithelial density of volumetric flow is shown in figures 5 and 6. The resulting pressure drop in the proximal tube is about \( \Delta P = P_{\text{in}} - P_{\text{out}} = 5.5 \text{ mmHg} \), being reasonable compared to a typical filtration pressure of 20 mmHg, [1]. The tubular wall, reabsorbs approximately 80% of the solvent flow at the inlet agreeing with [2].
Membrane flows obtained can be seen in table 5. Intercompartmental compensation flows is observed. About 46% of solvent water passes through the tight junctions. In [2] the water reabsorption in tight junctions is around 57%.

### Table 5. Total membrane’s flows for solute and solvent.

| Solvent volume flow in nl s\(^{-1}\) cm\(^{-2}\) of epithelium | \(LI\) | \(LC\) | \(CL\) | \(CP\) | \(IP\) |
|------------------------------------------------------------|-------|-------|-------|-------|-------|
| \(\frac{1}{A_{sp} A_{pt}} \int N_{vOD} dA\)                | 40.5  | 46.5  | 46.6  | -0.112| 87.1  |

| Solute flows in pmol s\(^{-1}\) cm\(^{-2}\) of epithelium | \(LI\) | \(LC\) | \(LI\) | \(LC\) |
|-----------------------------------------------------------|-------|-------|-------|-------|
| \(H^+\)                                                   | 6.72x\(10^{-4}\) | -0.154 | 312.0 | 3523  |
| \(K^+\)                                                   | 134.0 | 0.000 | \(NH_4^+\) | 5.750 | 0.000 |
| \(Cl^-\)                                                  | 3094  | 0.000 | \(HCO_3^-\) | 663.0 | 0.000 |
| \(HPO_4^{2-}\)                                            | 81.30 | 0.000 | \(H_2PO_4^-\) | 34.30 | 0.000 |
| \(HCO_3^-\)                                               | 27.40 | 0.000 | \(CO_2\) | 28.50 | 0.000 |
| \(CO(NH_2)_2\)                                            | 137.0 | 0.000 | \(H_2CO_3\) | 0.0283 | 0.000 |
| \(NH_3\)                                                  | 0.0785 | 0.000 | \(H_2CO_3\) | 1.700 | 0.000 |
| \(C_6H_12O_6\)                                            | 0.000 | 136.0 | | | |

**Figure 7.** Glucose concentration in tubular domain in mmol/l. The concentration is 5 in red zones and is 0 in blue zones. Compare with blue curve in figure 8.

Are shown the glucose concentration distribution in domain in figure 7 and the concentration variations on the inner tubular wall for some important solutes in figure 8, where the values are represented as fractions of the inlet concentrations. In figure 8, concentrations are taken on the tubular wall and for bicarbonate, potassium and ammonium concentrations there are differences regarding [2].
At entry, pH is 7.31 and at exit is about 7. The osmolarity remains constant. Essentially perfect compensation charges is observed throughout the luminal domain.

4. Discussion
The 2D model shows in greater detail the concentration, pressure and velocity distributions in the tubular lumen respect to one-dimensional classical models. Morphological differences are observed for concentration distributions regarding those given by other authors, who use radial average values. These morphological differences are attributed to: concentrations are constant in the compartments 0D, reflection coefficients are assumed to be identical in all exchange surfaces, except in tight junctions, all the instantaneous chemical equilibrium equations present in existing models are not included yet, the membrane potential that influences the transmembrane solute flows is not applied yet in this model.

On the other hand, the model retains the essential characteristics of pre-existing models, in relation to terms present in equations. At the same time incorporates additional spatial dimensions at the lumen compartment, in apical cell surface and in tight junctions, and incorporates the simulation of the diffusion effects. This makes more direct the comparison of concentration distributions with those that take place in artificial assistance devices.

5. Conclusions
In this paper a simplified model of a proximal convoluted tubule of an average human nephron, considering the radial coordinate and diffusive fluxes in the tubular domain, is presented. The Navier-Stokes and Nernst-Planck equations were resolved in a tubular domain of variable radius coupled to transepithelial pressure, and assuming the condition of electroneutrality. Accordance with data provided by other authors was found for integral values of intercompartmental flow profiles, solvent's volumetric flow, pressure, pH, luminal osmolarity and distribution of the most abundant solutes in the tubular lumen, namely, sodium, chloride and bicarbonate.

It is projected incorporating the remaining phenomena, mentioned in the discussion section, to the bidimensional model in order to obtain greater consistency in the integral values in relation to those provided by one-dimensional models currently available for proximal convoluted tubule.

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