• Supplement •

Detailed Description of Model Geometry, Equations and Parameters

for

Predicting Oxygen Tension along the Ureter

Bolus Model

Justification for Some of the Model Geometric Dimensions

Rabbit Model: The bolus volume based on the baseline length and bolus diameter is around 0.008 ml. This translates to a daily urine production of about 87 ml (i.e. 43.5 ml/ureter), assuming a bolus frequency of 3.8 boluses/min (27). This compares to a reported 24-hour urine volume of an adult rabbit ranging between 70 – 125 ml, for rabbits weighing 3.5 kg (14, 22, 23).

The reported histological ureter wall thickness (excluding the adventitia layer) for adult New Zealand white rabbits weighing 2.3 – 3.5 kg, after correcting for tissue estimated shrinkage of around 30% during fixation (18), ranged between 0.23 – 0.32 mm (10, 28, 35). Assuming a ureteral tissue density of about 1 g/cm^3 (17), it follows from the reported ureter length and thicknesses that the weight of a ureter would range between 0.02 – 0.04 g, depending on the body weight. This estimate is considerably less than a single rabbit ureter weight of ~0.31 g as reported by Batra et al (2), which may be due to the inclusion of additional tissue in Batra et al's measurements. Our model simulates ureteral activity in rabbits weighing 3.4 kg, so we have set the total wall thickness to 0.32 mm and the ureter weight to 0.04 g/ureter. We observe this closely matches the measurements reported in Ref (28), which were for New Zealand white rabbits with a similar body weight (3.5 kg).

Human Model: For a bolus volume of around 0.2 ml and bolus frequency of 3.0 boluses/min, the estimated urine flow is then approximately 0.6 ml/min/ureter (i.e. a total of about 1700 ml/day). This compares well to normal urine production rate in humans (0.55 to 1.67 ml/min; or 800 to 2400 ml/day (25)).

Governing Equations

Equations for the Darcy flow porous medium module: The conservation of fluid mass in a porous medium can be generally expressed as:

$$\frac{\partial}{\partial t}(\rho\epsilon_p) + \nabla \cdot (\rho \mathbf{v_d}) = S_i \quad [1]$$

where ρ (kg/m^3) is taken to be the (intrinsic) density of fluid (in this case, blood which is assumed to have constant density), ϵ_p (unit-less) is the porosity of the medium, t (s) is time, $\mathbf{v_d}$ (m/s) is the Darcy velocity of the fluid (blood) flow, and S_i (kg·m^{-3}·s^{-1}) is the fluid (blood) source/sink in domain *i*.

The true flow velocity ($\mathbf{v_t}$) and $\mathbf{v_d}$ have the following relationship:

$$\mathbf{v_d} = \epsilon_p \mathbf{v_t} \quad [2]$$

In the case of the tissue surrounding the bolus, $\mathbf{v_d}$ is (effectively) equal to $\mathbf{v_t}$, or in this case, the true velocity of the bolus ($\mathbf{v_{bolus}}$), because we are assuming the whole tissue is moving along the bolus due to the shift in the frame of reference from the tissue to the bolus. Accordingly, we set the ϵ_p equal to one. The source/sink term S_i is zero because there is no fluid loss/gain.

Therefore, for the axial pseudo-flow, equation [1] becomes:

$$\frac{\partial}{\partial t}(\rho) + \nabla \cdot (\rho \mathbf{v_{bolus}}) = 0 \quad [3]$$

Blood supplying the ureter wall tissues was modeled as a radial blood flow, with arterial blood directed inward and venous blood directed outward. For the radial blood flow, equation [1] becomes:

$$\frac{\partial}{\partial t}(\rho\epsilon_p) + \nabla \cdot (\rho \mathbf{v_d}) = \pm S_{TEL} \pm S_{SM} \quad [4]$$

where $\pm S_{TEL}$ is a flow sink/source in the TEL domain, and $\pm S_{SM}$ is a flow sink/source in the SM domain. Since the arterial blood flow transitions to venous blood flow (i.e. arteries lose blood to the veins), the terms S_{TEL} and S_{SM} are negative (sink) in the arterial flow module and positive (source) in the venous flow module. The term ϵ_p in equation [4] is the porosity of the vasculature in the ureteral tissue. The arterial blood slows as the arterial vessels divide and turn into capillaries in the tissue, and then later merge and turn into veins. Our model only has two compartments, arteries and veins, so capillary porosity is divided equally between the two. Note the porosity of the vasculature in the ureteral tissue in equation [4] is different to the porosity of the whole tissue for axial pseudo-flow in equation [3], which is set to one.

The flow source/sink term S_i is expressed as a constant in each of the domains, so:

$$S_i = \frac{f_{Q,i} \cdot Q_{UBF} \cdot \rho}{Vol_i} \quad [5]$$

where $f_{Q,i}$ (unitless) is the fraction of ureteral blood that flows in domain *i*, Q_{UBF} (m^3/s) is the total volumetric rate of the ureteral blood flow (UBF), and Vol_i (m^3) is the volume of domain *i*.

Equations for the oxygen transport module: The conservation of oxygen through advective and diffusive transport in the capillaries can be generally expressed as:

$$\frac{\partial \epsilon_p C_T}{\partial t} = -\nabla \cdot \mathbf{J} - R_i \quad [6]$$

where ϵ_p (unitless) is the porosity of the capillaries in the ureteral tissue, C_T (mol/m^3) is the total concentration of oxygen (in the whole blood), t (s) is time, and R_i ($mol \cdot m^{-3} \cdot s^{-1}$) is an oxygen sink term in domain *i*. The term **J** ($mol \cdot m^{-2} \cdot s^{-1}$) is the oxygen flux, which is defined as:

$$\mathbf{J} = -\epsilon_p D \nabla c_f + \epsilon_p \mathbf{v_t} C_T \quad [7]$$

where D (m^2/s) is the oxygen diffusion coefficient and c_f (mol/m^3) is the free oxygen concentration (i.e. the concentration of oxygen dissolved in the interstitial fluid and cell fluid). Substituting equation [7] in equation [6] and assuming ϵ_p and $\mathbf{v_t}$ are constant leads to:

$$\epsilon_p \frac{\partial C_T^X}{\partial t} = \nabla \cdot \left(D_{eff} \nabla c_f^X\right) - \nabla \cdot \left(\mathbf{v_d^X} C_T^X\right) - R_i^X \quad [8]$$

The term D_{eff} (m^2/s) is the 'effective' diffusion coefficient $\left(D_{eff} = \epsilon_p D\right)$. The superscript X refers to either blood vessels with arterial blood flow (i.e. blood flowing into the tissue) (X→A) or blood vessels with venous blood flow (i.e. blood flowing out of the tissue) (X→V). Upon expanding equation [9] becomes:

$$\epsilon_p \frac{\partial C_T^X}{\partial t} = \nabla \cdot \left(D_{eff} \nabla c_f^X\right) - \mathbf{v_d^X} \cdot \nabla C_T^X - C_T^X\left(\nabla \cdot \mathbf{v_d^X}\right) \pm C_T^A\left(\nabla \cdot \mathbf{v_d^A}\right) - R_i^X \quad [9]$$

The term C_T can be converted to an equivalent free concentration c_f by solving the following conventional Hill equation:

$$C_T = c_f\left(1 + 4H\frac{c_f^{(n-1)}}{(K_H\sigma)^n + c_f{}^n}\right) = c_f F_H \qquad [10]$$

where H (mol/m^3) is the concentration of hemoglobin in whole blood, *n* is a Hill coefficient, K_H (mmHg) is a Hill function parameter for hemoglobin, and σ (mol·m^{-3}·mmHg^{-1}) is the solubility coefficient of oxygen in blood. For convenience, we have replaced the bracketed term with a single variable, 'F_H'.

Inserting equation [10] in equation [9] leads to:

$$\begin{aligned}\epsilon_p F_H\frac{\partial c_f^X}{\partial t} + \epsilon_p c_f\frac{\partial F_H}{\partial c_f^X}\frac{\partial c_f^X}{\partial t} \\ = \nabla\cdot\left(D_{eff}\nabla c_f^X\right) - \mathbf{v_d^X}\cdot F_H c_f^X - \mathbf{v_d^X}\cdot c_f^X\nabla F_H - c_f^X F_H\left(\nabla\cdot\mathbf{v_d^X}\right) \\ \pm c_f^A F_H\left(\nabla\cdot\mathbf{v_d^A}\right) - R_i^X\end{aligned} \qquad [11]$$

The term $-\mathbf{v_d^X}\cdot c_f^X\nabla F_H$ ensures there is oxygen mass conservation in the presence of a flow sink. An oxygen sink was incorporated into the model to represent the transition of oxygen from arterial blood flow to venous blood flow. The term $c_f^A F_H\left(\nabla\cdot\mathbf{v_d^A}\right)$ is a sink/source term associated with oxygen loss/gain due to arterial flow transitioning into venous flow after their 180 degree turn (a positive value represents a sink and a negative value represents a source).

The term ∇F_H in equation [11] can be rewritten as:

$$\nabla F_H = \frac{\partial F_H}{\partial c_f}\cdot\nabla c_f \qquad [12]$$

Such that equation [11] can be expressed as:

$$\begin{aligned}\epsilon_p\left(F_H + c_f^X\frac{\partial F_H}{\partial c_f}\right)\frac{\partial c_f^X}{\partial t} \\ = \nabla\cdot\left(D_{eff}\nabla c_f^X\right) - \mathbf{v_d^X}\cdot\left(F_H + c_f^X\frac{\partial F_H}{\partial c_f}\right)\nabla c_f^X - c_f^X F_H\left(\nabla\cdot\mathbf{v_d^X}\right) \\ \pm c_f^A F_H\left(\nabla\cdot\mathbf{v_d^A}\right) - R_i^X\end{aligned} \qquad [13]$$

Equation [13] is the general form of an oxygen transport equation applied in the arterial and venous oxygen transport modules. The terms $-c_f^X F_H\left(\nabla\cdot\mathbf{v_d^X}\right)$ and $c_f^A F_H\left(\nabla\cdot\mathbf{v_d^A}\right)$ in equation [13] cancel each other out exactly for the arterial oxygen transport module, but not for the venous

oxygen transport module. Note that if H equals zero, then F_H is equal to one and $\frac{\partial F_H}{\partial c_f}$ equals zero, so equation [13] reduces to the standard advection-diffusion equation.

The term $-R_i^X$ in equation [13] is an oxygen sink representing the loss of oxygen from the blood to the tissue, which can be written as:

$$R_i^A = \alpha_i\left(c_f^{cap} - c_f^{tissue}\right) \cdot f_A \quad [14]$$

$$R_i^V = \alpha_i\left(c_f^{cap} - c_f^{tissue}\right) \cdot (1 - f_A) \quad [15]$$

where α_i (1/s) is a constant representing the oxygen mass transfer coefficient between the capillaries and the ureteral tissue in domain *i*, c_f^{cap} (mol/m^3) is the weighted-average free oxygen concentration in the ureteral capillaries, c_f^{tissue} (mol/m^3) is the free oxygen concentration in the ureteral tissue, and f_A (unitless) is the fraction of oxygen lost to the tissue by the arterial blood (set to 0.1). The c_f^{cap} is set to ($0.1 \times c_f^A + 0.9 \times c_f^V$).

The oxygen transport in the ureteral tissue is governed by the standard advection-diffusion equation:

$$\frac{\partial c_f^T}{\partial t} = \nabla \cdot \left(D \nabla c_f^T\right) - \mathbf{v_d^T} \cdot \nabla c_f^T + R_i^T - R_i^{VO2} \quad [16]$$

where superscript T denotes ureteral wall tissue. The term $\mathbf{v_d^T}$ is the Darcy velocity of the tissue calculated from the pseudo-bolus flow module (i.e. $= \mathbf{v_{bolus}}$). The term R_i^T is an oxygen source term representing the oxygen supplied by the blood to the tissue, and is a sum of oxygen sinks described by equations [14] and [15]:

$$R_i^T = R_i^A + R_i^V = \alpha_i\left(c_f^{cap} - c_f^T\right) \quad [17]$$

The term R_i^{VO2} (mol·m^{-3}·s^{-1}) in equation [16] is the oxygen sink term representing the oxygen consumed by the ureteral tissue in domain *i*, and can be written as:

$$R_i^{VO2} = -\dot{V}O_{2,i} \cdot \left(\frac{c_f^T}{K_M + c_f^T}\right) \quad [18]$$

The term $\dot{V}O_{2,i}$ (mol·m^{-3}·s^{-1}) is the rate of oxygen consumption per volume in the *i*th domain. The term $\frac{c_f^T}{K_M+c_f^T}$ represents the aerobic/anaerobic metabolism transition in the ureteral tissue. The constant K_M (mol/m^3) represents the oxygen concentration at which half the cellular energy production is derived from aerobic metabolism and half is derived from anaerobic metabolism.

The oxygen transport within the bolus is governed by the standard diffusion equation:

$$\frac{\partial c_f^B}{\partial t} = \nabla \cdot \left(D^B \nabla c_f^B\right) \quad [19]$$

where superscript B denotes the urine bolus.

Assuming the free and bound oxygen are always in equilibrium, the partial pressure of oxygen (PO_2) can be determined by converting c_f using Henry's Law:

$$c_f = \sigma PO_2 \quad [20]$$

Continuous Flow Model

The model parameters were calibrated against experimental data reported by Sgouralis et al (27). Assuming a bolus volume of 0.008 ml, the infusion rates employed in the experiment by Sgouralis et al implies a very high peristaltic frequency (13 - 125 boluses/min), which can be simplified to a continuous flow through an open tube. So we created what we refer to as the 'continuous flow model', or CF model to serve as a baseline model for modeling the experiment by Sgouralis et al (27).

Model Geometry

In the CF model, the ureter is a 2D axisymmetric pipe with a continuous stream of urine flowing through it. This setup closely matches the experimental setting described by Sgouralis et al (27). The CF model consists of a single domain representing the continuous stream of urine surrounded by two domains ('Transitional Epithelium and Lamina propria (TEL)' and 'Smooth Muscle (SM)' domains) representing the ureter wall. The ureteral wall volume and thickness in the CF model for each infusion rate is shown in Table S1. We assumed the wall volume and thickness are constant at its expanded state.

Table S1. List of major dimensions for the rabbit continuous model for four rates of urine flow (1, 0.5, 0.25, and 0.1 ml/min) based on experimental data in Ref (27)

	Value			
Parameter	**1 ml/min**	**0.5 ml/min**	**0.25 ml/min**	**0.1 ml/min**
Ureter length (cm)	11.5			
Urine Luminal Radius (μm)	402	368	338	301
TE Thickness (μm)	20.5	22.3	24.1	26.8
LP Thickness (μm)	22.2	23.8	25.6	28.1
SM Thickness (μm)	69.2	73.5	77.7	83.3
TEL (TE + LP) Volume (mm^3)	13.0			
SM Volume (mm^3)	24.0			
Total Ureter Wall Volume (mm^3)	37.0			
Total Transit Time (s)	3.5	5.9	9.9	19.7

Abbreviations: TE = transitional epithelium. LP = lamina propria. SM = smooth muscle.

Governing Equations

Equations for the Darcy flow porous medium module: The capillary blood flow in the CF model is modeled in the same way as in the bolus model using equations [4] and [5].

The continuous urine flow was modeled as Poiseuille flow with a parabolic velocity profile. According to Poiseuille's Law, the pressure gradient (Δp (Pa)) required to drive the flow (urine) through a circular pipe (ureter) is given by**:**

$$\Delta p = \frac{8\mu L Q_U}{\pi R^4} \qquad [21]$$

where μ (Pa·s) is the dynamic viscosity of water, L (mm) is the length of the ureter, Q_U (mm^3/s) is the volumetric rate of urine flow through the ureter, and R (mm) is the internal radius of the pipe. The velocity of urine flowing through the ureter as a function of the distance from the center of the ureter is:

$$v_U = \frac{1}{4\mu}\frac{\Delta p}{L}(R^2 - r^2) \quad [22]$$

where v_U (mm/s) is the velocity of urine at a certain distance from the center of the ureter, r (mm; r = 0 at the center). As a function of r, v_U forms a parabolic profile along the radial axis, with the maximum v_U at the center of ureter ($v_{U,max} = 2 \times \bar{v}_U$ at r = 0; $\bar{v}_U$ = mean urine velocity), and minimum v_U at ureter wall boundary ($v_{U,min} = 0$ at r = R). Once the pressure gradient and the velocity profile are known, the required permeability κ (m^2) to generate the equivalent Poiseuille flow in the Darcy flow module can then be calculated using:

$$\kappa(r) = \frac{\mu v_U}{\Delta p} = \frac{1}{4L}(R^2 - r^2) \quad [23]$$

Note κ is also a function of the radial distance (r) from the center of the ureter. In the model, κ is approximated by a quadratic equation in the form of $A \cdot r^2 + B \cdot r + C$.

Equations for the oxygen transport model: The CF model does not have an intermediate ureteral tissue module connecting the oxygen transport from the blood in the capillaries to the urine, so the oxygen in the CF model is directly transported from the arterial and venous capillary modules to the urine module. Hence, equation [13] for arterial and venous capillary oxygen transport in the bolus model becomes:

$$\begin{aligned} \epsilon_p \left(F_H + c_f^X \frac{\partial F_H}{\partial c_f}\right)\frac{\partial c_f^X}{\partial t} & \\ = \nabla \cdot \left(D_{CF}^X \nabla c_f\right) - \mathbf{v_d^X} \cdot \left(F_H + c_f^X \frac{\partial F_H}{\partial c_f}\right)\nabla c_f^X - c_f^X F_H\left(\nabla \cdot \mathbf{v_d^X}\right) & \\ \pm\, c_f^A F_H\left(\nabla \cdot \mathbf{v_d^A}\right) - R_i^{X,VO2} & \end{aligned} \quad [24]$$

where D_{CF}^X (m^2/s) is the oxygen diffusion coefficient applied specifically to the arterial and venous capillary modules in the CF model, and $R_i^{X,VO2}$ ($mol \cdot m^{-3} \cdot s^{-1}$) is the oxygen sink term representing the oxygen lost by either arterial blood flow or venous blood flow to the surrounding ureteral tissue. Note the CF model is intended to match the steady-state measurements reported in Ref (27) so the solutions in the CF model are also steady-state solutions.

The term $R_i^{X,VO2}$ in equation [24] is written as:

$$R_i^{X,VO2} = -\left(f_X \cdot \dot{V}O_{2,i}\right) \cdot \left(\frac{c_f^{cap}}{K_M + c_f^{cap}}\right) \quad [25]$$

where f_X (unitless) is the distribution of total oxygen consumption between the arterial oxygen transport module and the venous oxygen transport module, and c_f^{cap} (mol/m^3) is the weighted-average free oxygen concentration in the capillaries, which is set to ($0.1 \times c_f^A + 0.9 \times c_f^V$). For simplicity, we have assumed all of the oxygen consumption occurs in the venous module (i.e. f_A= 0 and f_V=1).

The oxygen transport in the urine domain is governed by the standard advection-diffusion equation:

$$\frac{\partial c_f^U}{\partial t} = \nabla \cdot \left(D \nabla c_f^U\right) - \mathbf{v_d^U} \cdot \nabla c_f^U \quad [26]$$

Boundary conditions: The boundary conditions applied to the CF model is almost identical to the bolus model with few exceptions. For the urine Darcy flow module, an inlet boundary condition ($\rho \mathbf{v_d} = \rho \mathbf{v_{urine}}$, where $\mathbf{v_{urine}}$ is the true velocity of the urine flow reported in Ref (27); the magnitude of $\mathbf{v_{urine}}$ is also equal to $\bar{v}_U$ of the parabolic velocity profile in equation [22]) is applied at the top boundary of the urine domain, and a pressure boundary condition (p = 0) is applied at the bottom boundary of the urine domain.

In the CF model, the Robin boundary condition is applied to the venous oxygen transport module instead:

$$\mathbf{n} \cdot \mathbf{J^X} = \pm h\left(c_f^{cap} - c_f^U\right) \quad [27]$$

where the superscript X could signify either the venous capillary module (V) or the urine module (U). Unlike the bolus model where the oxygen flux is driven by $\left(c_f^T - c_f^B\right)$, in the CF model, the oxygen flux is driven by the difference between the weighted-average capillary concentration (c_f^{cap}) and the urine concentration (c_f^U).

Parameter Selection

UBF: To the best of our knowledge, there are only two available reports of studies in which UBF was experimentally quantified. One dataset on anesthetized Sprague-Dawley rats using a radiotracer is described by Mooney et al (24), who reported a mean UBF of 108 ml/min/100 g tissue. Another dataset is on female rabbits described by Batra and colleagues using radioactive

microspheres (2, 3). They reported the blood perfusion to the ureter relative to the cardiac output is about 0.006 (2). This translates to about 2.1 ml/min (for paired ureters weighing a total of 0.65 g) or 323 ml/min/100 g tissue, for an anesthetized rabbit (weighing 2.8 kg) (2), with an average cardiac output of 125 ml/min/kg body weight (BW) (reduced by 20% using a barbiturate anesthesia relative to *in vivo* cardiac output of 150 ml/min/kg BW (8)).

For comparison to other 'peristaltic tissues', the blood flow in canine small intestine is reported to be about 47 ml/min/100 g tissue (6), and in rat small intestine ranges between 53 – 75 ml/min/100 g tissue (29). We recognize that the UBF in female rabbits, as reported by Batra et al (2) is significantly higher than the blood flow reported in other tissues and species. Given this, we have chosen a compromise baseline UBF of 100 ml/min/100 g tissue for our model.

$\dot{V}O_2$**:** The $\dot{V}O_2$ was estimated indirectly using UBF together with a measurement of ureteral tissue PO_2. According to the results of a ureteral oxygenation study by Weld et al (33), the PO_2 in the transected ureteral wall in pigs with an arterial PO_2 of 400 mmHg was about 52 mmHg at the ureteropelvic junction and about 44 mmHg at the ureterovesical junction. From these data we calculated what the ratio of $\dot{V}O_2$ to UBF would be for a given condition based on the Bohr curve (i.e. $UBF \cdot (C_T^A - C_T^V) = \dot{V}O_2$). Assuming the arterial PO_2 is around 400 mmHg (anesthetized state), the ureteral capillary PO_2 is around 52 mmHg and venous PO_2 is around 47 mmHg, we then estimate the ratio of $\frac{\dot{V}O_2}{UBF}$ to be approximately 2.1 mol/m^3 (or 2.1 × 10^{-6} mol/ml of tissue) for a rabbit with a hematocrit of 0.40 (19). Based on this data and reasoning, we chose the $\frac{\dot{V}O_2}{UBF}$ ratio of 2.1 mol/m^3 as our baseline value. Then, the total $\dot{V}O_2$ based on the estimated $\frac{\dot{V}O_2}{UBF}$ ratio of 2.1 mol/m^3 and the baseline UBF of 0.04 ml/min is about 1.3 × 10^{-9} mol/s, or 0.04 mol·m^{-3}·s^{-1}.

Andersson et al (1) and Hypolite et al (16) report the $\dot{V}O_2$ per volume in the bladder mucosa (i.e. TEL layer) could be up to 60% greater than in the SM. Therefore, we have distributed the $\dot{V}O_2$ per volume as 40% in the SM and 60% in the TEL, or 50% greater $\dot{V}O_2$ in the TEL than in the SM. Thus, the $\dot{V}O_{2,SM}$ of the rabbit ureter is 0.03 mol·m^{-3}·s^{-1} (or 7.15 × 10^{-10} mol/s for a single whole ureter), and the $\dot{V}O_{2,TEL}$ is 0.045 mol·m^{-3}·s^{-1} (or 5.84 × 10^{-10} mol/s).

ϵ_p**:** To our best knowledge, there are no reported measurements of capillary porosity in the ureter in the literature. So, we estimated the capillary porosity in the ureteral tissue using the relationship between the ϵ_p, $\mathbf{v_{UBF}}$ (true velocity of the ureteral blood flow) and $\mathbf{v_d}$ in equation

[3] $\left(\epsilon_p = \frac{\mathbf{v_d}}{\mathbf{v_{UBF}}}\right)$. According to several authors, the reported average capillary blood velocity measured in renal tissues was around 0.93 mm/s and the equivalent red blood cell (RBC) velocity is around 1.1 mm/s (4, 11, 15, 21, 37). We assumed the capillary blood and RBC velocity in the ureteral tissue is similar to that measured in the renal tissue. For simplicity, we have set the true capillary blood velocity to 1 mm/s. So $\epsilon_p = \mathbf{v_d}/(1\ \mathrm{mm/s})$ in the model**.** From simulation, for baseline UBF of 0.04 ml/min for rabbit ureter, the baseline ϵ_p at the external boundary of the SM domain is found to be around 0.002. Note the ϵ_p in the model is not constant (i.e. it varies with depth of the ureter wall). At the inner wall of epithelium, we applied an outflow velocity condition so that there is a non-zero $\mathbf{v_d}$ and so a non-zero ϵ_p. This outflow becomes an inflow for the venous flow module, so the mass balance is maintained (i.e. $\mathbf{v_d}$ at arterial outflow boundary = $\mathbf{v_d}$ at venous inflow boundary). We assumed the outflow for arterial blood flow and inflow for the venous blood flow at the inner wall is a small fraction (5%) of the total UBF and the resulting $\mathbf{v_d}$ is about 1.33×10^{-4} mm/s ($\frac{\mathrm{UBF}\times 0.05}{\mathrm{SA}}$; SA = surface area of ureter). The ϵ_p at the inner wall is found to be 1.33×10^{-4}.

Diffusion coefficient: The baseline physiological diffusion coefficient (D) for oxygen was set to 2.8×10^{-9} m^2/s in accordance with Refs (12, 13). The effective diffusion coefficient for oxygen (D_{eff}) is thus equal to $(2.8 \times 10^{-9} \times \epsilon_p)$ m^2/s. A non-physiological 'diffusion coefficient' was employed for the fluid of the bolus model (D^B), so there was only a very small radial oxygen concentration gradient (to account for oxygen mixing associated with fluid circulation within a travelling bolus, which is not included in the model). That is, to ensure the oxygen is 'well-mixed' by dispersion in the bolus, D^B was set to 100 times larger than the baseline D (i.e. 2.8×10^{-7} m^2/s). A non-physiological diffusion coefficient was also employed for the arterial modules in the CF model (D_{CF}^A), which was set to 1000 times smaller than the baseline D (i.e. 2.8×10^{-12} m^2/s). This was necessary because the ureteral wall domains are long and thin, and a combination of a concentration boundary at the external boundary of the SM domain and a large D_{CF}^A would otherwise result in a very large diffusive flux that is non-physiological. This ensures that advective oxygen transport is flux limiting, as it is physiologically (i.e. the diffusive oxygen flux is less than 1% of the total oxygen flux). On the other hand, D_{CF}^V is set to the real oxygen diffusion coefficient to model a free boundary condition for oxygen (i.e. one with zero diffusive flux). There is also no concentration boundary condition applied in the venous oxygen transport, so no artificial oxygen diffusion will arise there.

Bolus velocity: The baseline urine bolus velocity ($\mathbf{v_{bolus}}$) in rabbits was interpolated from urine velocities reported in other species, namely, rats (30), dogs (5, 31, 34), pigs (26, 32, 36) and humans (5, 7, 9, 20, 36), normalized by the body weight. The normalized urine velocities were about 43.9 $mm \cdot s^{-1} \cdot kg^{-1}$ for rats, 2.0 $mm \cdot s^{-1} \cdot kg^{-1}$ for dogs, 0.42 $mm \cdot s^{-1} \cdot kg^{-1}$ for pigs and 0.34 $mm \cdot s^{-1} \cdot kg^{-1}$ for humans, which fitted to an inverse power equation of $12.1 \times (\text{body weight})^{-0.82}$. From these data, we interpolated that the normalized urine velocity for rabbits weighing 3.5 kg to be about 4.33 $mm \cdot s^{-1} \cdot kg^{-1}$, with an absolute $\mathbf{v_{bolus}}$ of about 15.2 mm/s. Hence, we have set the baseline $\mathbf{v_{bolus}}$ to 15.2 mm/s, and transit time to 7.6 s for the rabbit bolus model.

Reference

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