FC map technical documentation

Documentation is provided here for FC map users who are interested in the technical details underlying the modelling framework used in the FC map.

Using the FC map as a modelling interface

We describe the bond graph approach to physiological modelling, show how it is used to create a simple model for the control of first blood volume and then blood pressure, and finally we show how the FC map is used both to display the model and to provide a user-interface to explore the model, to run simulations and to analyse the model predictions.

The bond graph modelling framework

Bond graphs provide a useful way of formulating and visualising a thermodynamically valid biophysical model because they ensure that mass, charge and energy are each conserved, and they clearly distinguish the mechanisms for (i) transmission of power (the product of flux v and potential u), (ii) energy storage (mechanically in a spring, electrically in a capacitor or chemically in a solute dissolved in a solvent), (iii) energy dissipation to heat (a mechanical damper, an electrical resistance or a chemical reaction), and (iv) energy transfer between mechanical, electrical or biochemical domains. Most importantly they distinguish between the conservation laws of physics and the empirically measured constitutive parameters that characterise particular materials. For example, a chemical species i is *stored* as a solute q_j^i (moles) in a solution at location j with a particular *solubility* that generates a chemical potential u_j^i (J.mol^{-1}). The diffusion of this solute through a dissipative medium from one location to another is a molar flux $v_j^i = \frac{dq_j^i}{dt}$ (mol.s^{-1}) that depends both on the difference in chemical potential between the two locations and on the *diffusivity* of that medium. The measured values for *solubility* and *diffusivity* are two distinct material constants, and both are quite separate from the equations representing mass and energy conservation.

We use the symbol q_j^i to denote the quantity in moles (mol) of a chemical species i at location j. Similarly, q_j^e represents electrical charge in Coulombs (C), and q_j^m represents distance in meters (m) or volume in m^3. Molar flux is denoted $v_j^i = \frac{dq_j^i}{dt}$ (mol.s^{-1}), where u_j^i (J.mol^{-1}) is the chemical potential generated by solute q_j^i, and $v_j^e = \frac{dq_j^e}{dt}$ (C.s^{-1}) is the electrical current associated with electrical potential u_j^e (J.C^{-1}). In mechanics $v_j^m = \frac{dq_j^m}{dt}$ is the velocity (m.s^{-1}) associated with a force u_j^m (J.m^{-1}), or the fluid flow (m^3.s^{-1}) associated with a pressure (J.m^{-3}), or the angular velocity (radians.s^{-1}) associated with a torque (J.radian^{-1}).

These units express the energy flux (J.s^{-1}) as the product of a potential in Joules per unit quantity (mol, C, m, m^3 or radian) that is driving the flow of that quantity in a way that is common to all physical systems. i.e. the product of potential u_j^i (J.mol^{-1}) and flux v_j^i (mol.s^{-1}), or potential u_j^e (J.C^{-1}) and flux v_j^e (C.s^{-1}), is always power (J.s^{-1}). Similarly, the product of mechanical potential (force, pressure, or torque) and mechanical flux (velocity, fluid flow, or angular velocity) is power. The product of heat flow, which is an entropy flux (entropy.s^{-1}), and thermal potential (J.entropy^{-1} or temperature in Kelvin K) is also power. It is therefore convenient to use the symbol q to represent any chemical, electrical, mechanical or heat quantity (with v and u being the flux and potential), with the superscript identifying the quantity and the subscript identifying the compartmental location.

Lines of power transmission called 'bonds' always have an associated flux v and potential u (see Figure 1). If these bonds meet, the sum of powers must be zero: $\sum u.v = 0$, to ensure power conservation. If they share a common potential u (called a '0:node'), power conservation $u\sum v = 0$ becomes just $\sum v = 0$ (for non-zero u), which is *mass conservation* if v is a molar flux or mechanical flow and *charge*

conservation if v is an electrical flux. Alternatively, if they share a common flux v (called a '1:node'), power conservation $v\sum u = 0$ becomes just $\sum u = 0$ (for non-zero v), which is *energy conservation*. For chemical reactions these correspond to mass conservation and stoichiometric relations, respectively. For electrical circuits they correspond to Kirchhoff's current law and voltage law, respectively. For mechanical systems they correspond to kinematic consistency and force or torque balance, respectively.

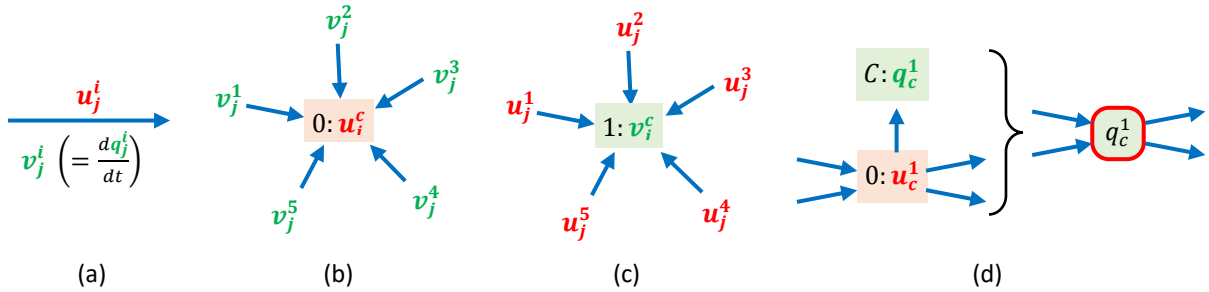


Figure 1. Key bond graph concepts: (a) a bond, which transmits energy, carries a flow v_j^i and a potential u_j^i; (b) a 0:node is a bond junction where the potential is the same for all bonds and therefore the sum of flows is zero (conservation of mass or charge); (c) a 1:node is a bond junction where the flow is the same for all bonds and therefore the sum of potentials is zero (conservation of energy); (d) a 0:node is usually associated with capacitive energy storage as well as flux balance (top) and can be more succinctly expressed by the red-bordered box where the potential u_c^1 is given by an empirically defined capacitive storage relationship $u_c^1 = f(q_c^1)$.

A model of blood pressure control

A schematic showing the mechanisms involved in the control of blood pressure is shown in Figure 2.

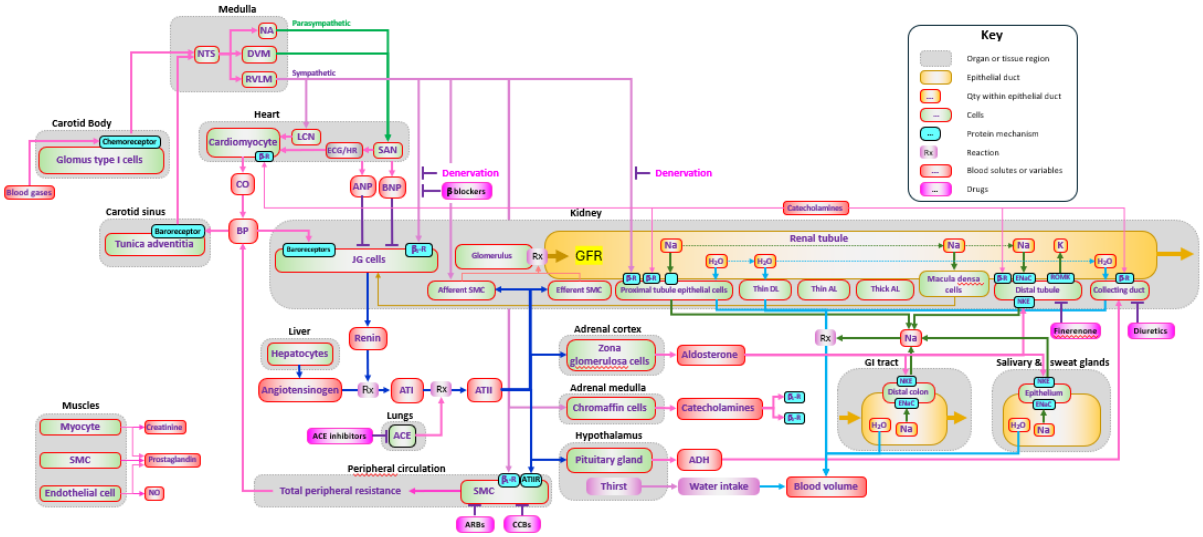


Figure 2. Schematic of the various mechanisms used in the control of blood pressure.

Average blood pressure is primarily determined by the volume of fluid in the circulatory system since excess fluid is accommodated by the elastic distension of the blood vessels, which requires a higher pressure. This circulatory blood volume is primarily dependent on the osmotic pressure generated by sodium ions as the dominant blood solute. The osmotic pressure of sodium is used to absorb water from the GI tract and the salivary glands, and to reabsorb some of the water lost to the renal tubules in Bowman's capsule and to sweat glands (for temperature control). *Natriuresis*, the process of sodium excretion in the urine via the kidneys, is promoted by atrial and ventricular natriuretic peptides (ANP and BNP - in response to atrial and ventricular stretch), and by calcitonin (which regulates calcium and phosphate levels in the blood). Natriuresis is inhibited by aldosterone acting on the epithelial cells of the distal tubule where the final stage of sodium reabsorption is regulated (see below).

Central systemic arterial blood pressure is further controlled by three mechanisms: (i) *cardiac output*, which is dependent on heart rate, myocardial contractility and LV filling pressure (determined by both atrial pressure and the upstream impedance), (ii) *peripheral vascular resistance*, and (iii) *venous blood volume fraction* (i.e. shifting blood from the veins to the arteries by contracting the venous circulatory volume). Note that normally the venous system holds about 70% of blood volume, but contraction of smooth muscle cells (SMCs) in the walls of the large veins in the abdomen can shift up to 10% of blood volume from the venous system to the arterial system and thereby raise arterial pressure. Physical exercise also affects venous return since muscle activity helps propel venous blood towards the heart.

The signalling pathways used for controlling sodium levels in the blood, cardiac output, peripheral vascular resistance and venous blood volume fraction are the autonomic nervous system (sympathetic and parasympathetic activity) and the release of the circulating catecholamines epinephrine (adrenaline) and norepinephrine (noradrenaline).

Renin, released by the juxta-glomeruli cells of the kidney in response to baroreceptor and sympathetic stimulation, and tubular sodium levels (sensed by the macula densa cells), catalyses the conversion of angiotensinogen (released by hepatocytes in the liver) to AT-1 (angiotensin 1). AT-1 is converted to AT-2 by ACE (angiotensin converting enzyme) in the lung circulation.

AT-2 stimulates (i) SMC contraction in both the afferent and efferent arterioles before and after the glomerular capillaries, respectively, to control perfusion pressure in the glomeruli; (ii) the release of aldosterone from the zona glomerulosa cells of the adrenal cortex (thereby upregulating NKE expression in the epithelial cells of the distal tubules and the distal colon to increase sodium uptake into the blood); (iii) the release of epinephrine from the chromaffin cells of the adrenal medulla which acts on α_1- adrenoreceptors in endothelial cells to increase vascular tone; and (iv) the release of ADH (antidiuretic hormone) from the pituitary gland of the hypothalamus to increase the reabsorption of water from the collecting ducts in the kidney.

Water movement

The non-cellular liquid component of blood (plasma), making up about 55% of blood volume, contains water, proteins, salts, hormones, enzymes, vitamins, etc. The other 45%, called the haematocrit, is the percentage volume occupied by red blood cells (RBCs).

The movement of water between the blood and other tissue compartments, including the renal tubules that excrete excess water, is largely controlled by the concentration of sodium in those compartments, since movement of sodium creates the osmotic pressure for fluid movement. Note that, in comparison with the 140mM sodium concentration on blood, potassium (4.5 mM) and glucose (5-10 mM) provide a much smaller contribution to the osmotic pressure.

Using the bond graph framework, we start by identifying the volume $q_j^{H_2O}$ (L) of water and the amount of sodium $q_j^{Na^+}$ (mol) in various compartments (j=1..). We use two-letter subscripts as follows:

- *aa* ascending aorta
- *ac* arterial circulation
- *vc* venous circulation
- *gl* glomeruli of the kidney
- *pt* proximal tubule
- *gi* gastro-intestinal tract

The fluid potential (i.e. hydrostatic pressure) of water and the chemical potential of sodium in compartment j are $u_j^{H_2O}$ (J.L^{-1} or kPa) and $u_j^{Na^+}$ (J.mol^{-1}), respectively. The flow of water and sodium between compartments j_1 and j_2 are given by $v_{j_1-j_2}^{H_2O}$ (L.s^{-1}) and $v_{j_1-j_2}^{Na^+}$ (mol.s^{-1}), respectively. The concentration of sodium in compartment j is given by

$$c_j^{Na^+} = q_j^{Na^+}/q_j^{H_2O} \quad \text{(mol.L}^{-1}\text{ or mM)}$$

We now need constitutive relations that define the storage of water via the elasticity of compliant blood vessels, the storage of sodium in the various compartments, and constitutive relations that characterise the flows of water and sodium between compartments.

Elasticity of blood vessels

The constitutive relationship between the pressure and volume of water in an elastic vessel is given by the following J-shaped 'pole-zero' relation (see Figure 3):

$$u_j^{H_2O} = E_j . \frac{q_j^{H_2O} - \hat{q}_j^{H_2O}}{\left(\bar{q}_j^{H_2O} - q_j^{H_2O}\right)^2}$$

where

$u_j^{H_2O}$ is fluid pressure

$q_j^{H_2O}$ is fluid volume

$\hat{q}_j^{H_2O}$ is unstressed volume

$\bar{q}_j^{H_2O}$ is maximum volume

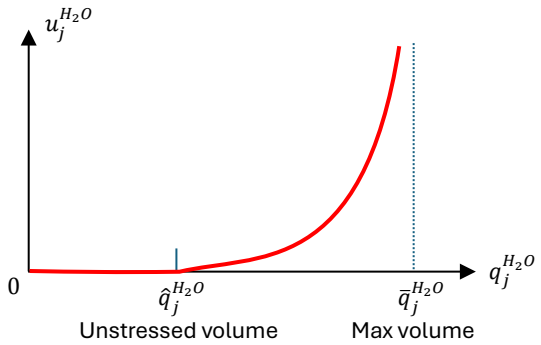


Figure 3. Pressure-volume relation for a fluid container. The parameter E_j scales the pressure at a given volume.

The elasticity parameter E_j, which incorporates the effects of both vessel wall compliance and smooth muscle contraction, needs to be a function of both sympathetic neural activity to the peripheral vessels (q_j^{symp}) and to the level of the hormone AT2 circulating in the blood (q_j^{AT2}).

Sodium potential

The constitutive relationship between the chemical potential and molar quantity of sodium is given by

$$u_j^{Na^+} = RTln\left(\bar{q}_j^{Na^+}\right),$$

where $\bar{q}_j^{Na^+} = K_j^{Na^+} . q_j^{Na^+}$ is dimensionless and $K_j^{Na^+}$ is the thermodynamic constant for sodium.

Osmotic pressure

Osmotic pressure in compartment j (for a dilute solution) is given by the van't Hoff equation (a version of the ideal gas law $p = \frac{n}{V}RT$):

$$u_j^{osmotic} = RTc_j^{Na^+}$$

With RT=25 kJ.mol^{-1} and $c_j^{Na^+}$=140 mM, $u_j^{osmotic}$=25x10^3 J.mol^{-1} x 140 mol.m^{-3} = 3500 kPa

Since blood hydrostatic pressure is only 100 kPa, it is clear that osmotic pressure is a huge driving force for fluid movement. Loss of this osmotic pressure can lead to dysentery and severe clinical conditions such as cholera.

For comparison, note that gravitational effects are as follows: Since 1 kg is 1 J.m^{-1}/m.s^{-2} = 1 J.s^2.m^{-2} (mass=force/acceleration) and water has a density of 1 g.cm^{-3} = 1 kg.L^{-1} = 1 J.s^2.m^{-2}.L^{-1} x 10^3 L.m^{-3} = 10^3 J.s^2.m^{-5}, the pressure difference from the gravitational (mass) effect of a height difference of $h = 1$ m is:

$$p = \rho g h = 10^3 \text{ J.s}^2\text{.m}^{-5} \times 9.81 \text{ m.s}^{-2} \times 1 \text{ m} \approx 10^4 \text{ J.m}^{-3} = 10 \text{ kPa}$$

i.e. when a person stands up, the pressure in their feet increases by about 10 kPa.

Exchange of sodium and water between compartments

Constitutive permeability relations are needed to characterise the flow of water and sodium between compartments. These expressions for flow take one of three general forms: (i) linear dependence on potential differences, such as a diffusive process where the flux is linearly dependent on the difference

in pressure (e.g. water flux driven by hydrostatic or osmotic gradients), (ii) saturating behaviour (e.g. the transmembrane flux of sodium via a membrane-bound SLC transporter), and (iii) the balance between a diffusive process and an opposing electrostatic potential (e.g. an ion channel).

Most of the water movement we wish to model is driven by differences in osmotic pressure between the vasculature and the epithelial ducts in the digestive system and kidney.

Sodium-potassium pump

Active transport of sodium depends primarily on the sodium-potassium ATPase exchange pump (NKE).

We assume the following sigmoid expression for the dependence of NKE flux on the concentrations of sodium and potassium in the gastrointestinal tract ($\bar{q}_{gi}^{Na^+}$, $\bar{q}_{gi}^{K^+}$) and the circulation ($\bar{q}_{vc}^{Na^+}$, $\bar{q}_{vc}^{K^+}$)

$$v_{gi}^{NKE} = k_{gi}^{NKE} \frac{\left(\bar{q}_{gi}^{Na^+}\right)^3 \cdot \left(\bar{q}_{vc}^{K^+}\right)^2 - \left(\bar{q}_{vc}^{Na^+}\right)^3 \cdot \left(\bar{q}_{gi}^{K^+}\right)^2 \cdot e^{2Fu_m^e/RT}}{\left\{1+\left(\bar{q}_{gi}^{Na^+}\right)^3\right\} \cdot \left\{1+\left(\bar{q}_{vc}^{Na^+}\right)^3\right\} \cdot \left\{1+\left(\bar{q}_{vc}^{K^+}\right)^2\right\} \cdot \left\{1+\left(\bar{q}_{gi}^{K^+}\right)^2\right\}}$$

Note that the NKE flux is zero when

$$\left(\bar{q}_{gi}^{Na^+}\right)^3 \cdot \left(\bar{q}_{vc}^{K^+}\right)^2 = \left(\bar{q}_{vc}^{Na^+}\right)^3 \cdot \left(\bar{q}_{gi}^{K^+}\right)^2 \cdot e^{2Fu_m^e/RT}$$

or

$$u_m^e = \frac{RT}{2F} ln \left[\left(\frac{c_{gi}^{Na^+}}{c_{vc}^{Na^+}} \right)^3 \cdot \left(\frac{c_{vc}^{K^+}}{c_{gi}^{K^+}} \right)^2 \right].$$

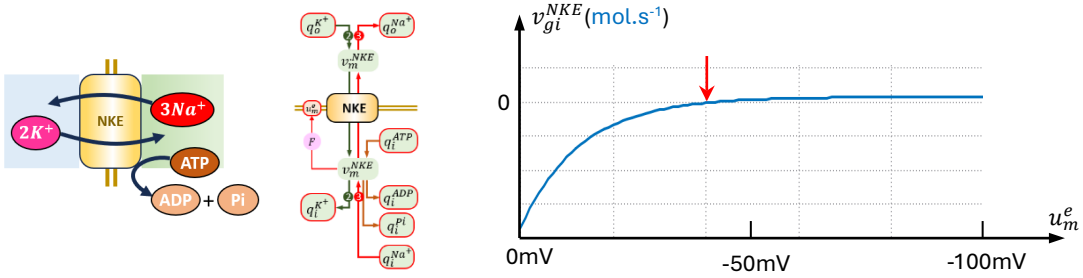
The NKE ATPase is located in the basolateral surface of gut epithelial cells (adjacent to capillaries). By lowering intracellular levels of sodium in these cells, the pump provides the drive to move sodium out of the GI tract.

With $c_{gi}^{Na^+}$=100 mM, $c_{cv}^{Na^+}$=140 mM, $c_{gi}^{K^+}$=15 mM and $c_{cv}^{K^+}$=5 mM, the membrane reversal potential is

$$u_m^e = \frac{25}{2} ln \left[\left(\frac{100}{140} \right)^3 \cdot \left(\frac{5}{15} \right)^2 \right] = -40 \text{ mV}$$

i.e. setting the membrane potential to -40mV will ensure that equilibrium is achieved when the sodium concentrations in the circulation and GI tract are respectively 140 mM and 100 mV.

Figure 1 shows a bond graph model of NKE and illustrates the behaviour of the pump as $\bar{q}_{gi}^{Na^+}$ is increased. Note that the ATP-consuming pump is moving sodium out of the GI tract and into the circulation against the sodium gradient.



(a) (b) (c)

Figure 4. The NKE pump. (a) NKE chemistry, (b) bond graph model, and (c) dependence of NKE flux on membrane potential, with zero flux shown by the red arrow at -40mV for the solute concentrations specified in the text.

Cardiac output

Cardiac output (L.s^{-1}), which is stroke volume (L.beat^{-1}) times heart rate (beats.s^{-1}), is a major determinant of the balance of blood volume between the venous and arterial compartments. The

volume of plasma (water) in the arterial circulation is the volume of blood q_{ac}^{blood} times the haematocrit (k_{ac}^{Hb}), or

$$q_{ac}^{blood} = q_{ac}^{H_2O} / k_{ac}^{Hb} \text{ (L)}.$$

The simplest way of characterising cardiac output is Starling's law,

$$v_{aa}^{H_2O} = k_{heart}^{H_2O} . u_{vc}^{H_2O},$$

in which cardiac output (the flow $v_{aa}^{H_2O}$ in the ascending aorta) is proportional to filling pressure $u_{vc}^{H_2O}$ and a parameter $k_{heart}^{H_2O}$ that depends on heart rate and the strength of myocyte contraction.

However, in this first model of blood volume control, cardiac output has to be set as an input variable because the factors (primarily sodium) that control blood volume do not control cardiac output.

A simple model of blood volume control by sodium

Figure 4 shows a very simple model of the movement of water and sodium.

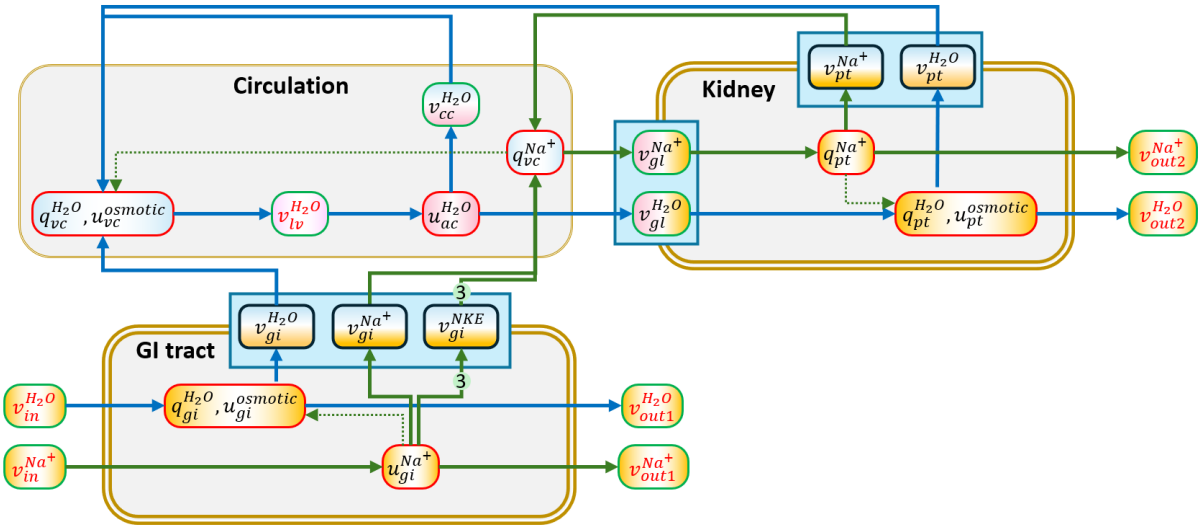


Figure 4. A simple model of the control of blood volume by sodium. The three compartments (GI tract, kidney, and circulation system) are shown with grey backgrounds. The blue-background rectangular boxes indicate the 6-layer FTUs (Functional Tissue Units) that encompass exchange of substances (in this case just water and sodium) between the epithelial compartments and blood. The 0:nodes and 1:nodes provide the link to protein mechanisms in subcellular compartments. The variables shown in red are specified boundary conditions.

There are four major compartments: (i) a circulation system including a specified left ventricular cardiac output $v_{lv}^{H_2O}$ (with arterial blood pressure $u_{ac}^{H_2O}$ determined by the arterial compliance) and a return circulation from the arterial circulation (flow $v_{ac}^{H_2O}$) to the venous circulation via the capillary compartment (flow $v_{cc}^{H_2O}$); (ii) a gastrointestinal compartment that takes in water ($v_{in}^{H_2O}$) and sodium ($v_{in}^{Na^+}$) at the mouth, generates an osmotic pressure $u_{gi}^{osmotic}$ and expels the waste water ($v_{out1}^{H_2O}$) and sodium ($v_{out1}^{Na^+}$); (iii) a kidney compartment that receives water flow ($v_{gl}^{H_2O}$) and sodium flux ($v_{gl}^{Na^+}$) at the glomeruli to generate osmotic pressure ($u_{pt}^{osmotic}$) and tubular sodium ($q_{pt}^{Na^+}$) in the proximal tubule, and to expel water ($v_{out2}^{H_2O}$) and sodium ($v_{out2}^{Na^+}$) in the urine.

Water and sodium are absorbed into the circulation ($v_{gi}^{H_2O}$ and $v_{gi}^{Na^+}$, respectively) from the GI tract and reabsorbed ($v_{gi}^{H_2O}$ and $v_{pt}^{Na^+}$, respectively) into the venous circulation from the proximal tubule. Sodium is also pumped by NKE ATPase against its concentration gradient from the digestive tract to the circulation. Note that 3 sodium ions are swapped for 2 potassium ions (not shown) for each ATP consumed. The transmembrane transport of water is via osmotic pressure differences set by the sodium concentrations.

The 0:node mass balance equations for the model are:

$$\frac{dq_{gi}^{H_2O}}{dt} = v_{in}^{H_2O} - v_{gi}^{H_2O} - v_{out1}^{H_2O}$$

$$\frac{dq_{pt}^{H_2O}}{dt} = v_{gl}^{H_2O} - v_{pt}^{H_2O} - v_{out2}^{H_2O}$$

$$\frac{dq_{vc}^{H_2O}}{dt} = v_{cc}^{H_2O} + v_{gi}^{H_2O} + v_{pt}^{H_2O} - v_{lv}^{H_2O}$$

$$\frac{dq_{ac}^{H_2O}}{dt} = v_{lv}^{H_2O} - v_{cc}^{H_2O} - v_{gl}^{H_2O}$$

$$\frac{dq_{gi}^{Na^+}}{dt} = v_{in}^{Na^+} - v_{gi}^{Na^+} - 3v_{gi}^{NKE} - v_{out1}^{Na^+}$$

$$\frac{dq_{pt}^{Na^+}}{dt} = v_{gl}^{Na^+} - v_{pt}^{Na^+} - v_{out2}^{Na^+}$$
$$\frac{dq_{vc}^{Na^+}}{dt} = v_{gi}^{Na^+} + 3v_{gi}^{NKE} + v_{pt}^{Na^+} - v_{gl}^{Na^+}$$

(the variables specified as boundary conditions are shown in red).

The 1:node flux equations are

$$v_{gi}^{H_2O} = k_{gi}^{H_2O}.\left(u_{vc}^{osmotic} - u_{gi}^{osmotic}\right)$$
$$v_{pt}^{H_2O} = k_{pt}^{H_2O}.\left(u_{vc}^{osmotic} - u_{pt}^{osmotic}\right)$$
$$v_{gl}^{H_2O} = k_{gl}^{H_2O}.\left(u_{ac}^{H_2O} - u_{pt}^{H_2O}\right)$$
$$v_{cc}^{H_2O} = k_{cc}^{H_2O}.\left(u_{ac}^{H_2O} - u_{vc}^{H_2O}\right)$$
$$v_{gi}^{Na^+} = k_{gi}^{Na^+}.\left(\bar{q}_{gi}^{Na^+} - \bar{q}_{vc}^{Na^+}\right) = k_{gi}^{Na^+}.K^{Na^+}.\left(q_{gi}^{Na^+} - q_{vc}^{Na^+}\right)$$
$$v_{gl}^{Na^+} = k_{gl}^{Na^+}.\left(\bar{q}_{vc}^{Na^+} - \bar{q}_{pt}^{Na^+}\right) = k_{gl}^{Na^+}.K^{Na^+}.\left(q_{vc}^{Na^+} - q_{pt}^{Na^+}\right)$$
$$v_{pt}^{Na^+} = k_{pt}^{Na^+}.\left(\bar{q}_{pt}^{Na^+} - \bar{q}_{vc}^{Na^+}\right) = k_{pt}^{Na^+}.K^{Na^+}.\left(q_{pt}^{Na^+} - q_{vc}^{Na^+}\right)$$
$$v_{gi}^{NKE} = k_{gi}^{NKE}\frac{\left(\bar{q}_{gi}^{Na^+}\right)^3.\left(\bar{q}_{vc}^{K^+}\right)^2 - \left(\bar{q}_{vc}^{Na^+}\right)^3.\left(\bar{q}_{gi}^{K^+}\right)^2.e^{2Fu_m^e/RT}}{\left\{1+\left(\bar{q}_{gi}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{K^+}\right)^2\right\}.\left\{1+\left(\bar{q}_{gi}^{K^+}\right)^2\right\}}$$

where the osmotic pressures are generated via concentrations by

$$c_{gi}^{Na^+} = \frac{q_{gi}^{Na^+}}{q_{gi}^{H_2O}}\ (\text{mol.L}^{-1});\quad u_{gi}^{osmotic} = RT.c_{gi}^{Na^+} = RT.\frac{q_{gi}^{Na^+}}{q_{gi}^{H_2O}}\quad (\text{J.L}^{-1})$$
$$c_{pt}^{Na^+} = \frac{q_{pt}^{Na^+}}{q_{pt}^{H_2O}}\ (\text{mol.L}^{-1});\quad u_{pt}^{osmotic} = RT.c_{pt}^{Na^+} = RT.\frac{q_{pt}^{Na^+}}{q_{pt}^{H_2O}}\quad (\text{J.L}^{-1})$$
$$c_{vc}^{Na^+} = \frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}}\ (\text{mol.L}^{-1});\quad u_{vc}^{osmotic} = RT.c_{vc}^{Na^+} = RT.\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}}\quad (\text{J.L}^{-1})$$

The hydrostatic pressures generated by the elastic stiffness of the compliant water containers (arteries, veins & kidney tubules) are based on the pole-zero law described above:

$$u_{vc}^{H_2O} = E_{vc}.\frac{q_{vc}^{H_2O} - \hat{q}_{vc}^{H_2O}}{\left(\bar{q}_{vc}^{H_2O} - q_{vc}^{H_2O}\right)^2}\quad (\text{kPa})$$
$$u_{ac}^{H_2O} = E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2}\quad (\text{kPa})$$
$$u_{pt}^{H_2O} = E_{pt}.\frac{q_{pt}^{H_2O} - \hat{q}_{pt}^{H_2O}}{\left(\bar{q}_{pt}^{H_2O} - q_{pt}^{H_2O}\right)^2}\quad (\text{kPa})$$

where E_{vc}, E_{ac} & E_{pt} have units of joules (so that the pressures $u_{vc}^{H_2O}, u_{ac}^{H_2O}$ & $u_{pt}^{H_2O}$ have units kPa).

Substituting the potentials into the fluxes gives

$$v_{gi}^{H_2O} = RT.k_{gi}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{gi}^{Na^+}}{q_{gi}^{H_2O}}\right)$$
$$v_{pt}^{H_2O} = RT.k_{pt}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{pt}^{Na^+}}{q_{pt}^{H_2O}}\right)$$
$$v_{gl}^{H_2O} = k_{gl}^{H_2O}.\left(u_{ac}^{H_2O} - u_{pt}^{H_2O}\right) = k_{gl}^{H_2O}.\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2} - E_{pt}.\frac{q_{pt}^{H_2O} - \hat{q}_{pt}^{H_2O}}{\left(\bar{q}_{pt}^{H_2O} - q_{pt}^{H_2O}\right)^2}\right\}$$
$$v_{cc}^{H_2O} = k_{cc}^{H_2O}.\left(u_{ac}^{H_2O} - u_{vc}^{H_2O}\right) = k_{cc}^{H_2O}.\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2} - E_{vc}.\frac{q_{vc}^{H_2O} - \hat{q}_{vc}^{H_2O}}{\left(\bar{q}_{vc}^{H_2O} - q_{vc}^{H_2O}\right)^2}\right\}$$
$$v_{gi}^{Na^+} = k_{gi}^{Na^+}.\left(\bar{q}_{gi}^{Na^+} - \bar{q}_{vc}^{Na^+}\right) = k_{gi}^{Na^+}.K^{Na^+}.\left\{q_{gi}^{Na^+} - q_{vc}^{Na^+}\right\}$$

$$v_{pt}^{Na^+} = k_{pt}^{Na^+}.\left(\bar{q}_{pt}^{Na^+} - \bar{q}_{vc}^{Na^+}\right) = k_{pt}^{Na^+}.K^{Na^+}.\left\{q_{pt}^{Na^+} - q_{vc}^{Na^+}\right\}$$

$$v_{gl}^{Na^+} = k_{gl}^{Na^+}.\left(\bar{q}_{vc}^{Na^+} - \bar{q}_{pt}^{Na^+}\right) = k_{gl}^{Na^+}.K^{Na^+}.\left\{q_{vc}^{Na^+} - q_{pt}^{Na^+}\right\}$$

$$v_{gi}^{NKE} = k_{gi}^{NKE}.\frac{\left(\bar{q}_{gi}^{Na^+}\right)^3.\left(\bar{q}_{vc}^{K^+}\right)^2 - \left(\bar{q}_{vc}^{Na^+}\right)^3.\left(\bar{q}_{gi}^{K^+}\right)^2.e^{2Fu_m^e/RT}}{\left\{1+\left(\bar{q}_{gi}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{K^+}\right)^2\right\}.\left\{1+\left(\bar{q}_{gi}^{K^+}\right)^2\right\}}$$

Substituting these fluxes into the mass balance equations gives:

$$\frac{dq_{gi}^{H_2O}}{dt} = v_{in}^{H_2O} - RT.k_{gi}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{gi}^{Na^+}}{q_{gi}^{H_2O}}\right) - v_{out1}^{H_2O}$$

$$\frac{dq_{pt}^{H_2O}}{dt} = k_{gl}^{H_2O}.\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2} - E_{pt}.\frac{q_{pt}^{H_2O} - \hat{q}_{pt}^{H_2O}}{\left(\bar{q}_{pt}^{H_2O} - q_{pt}^{H_2O}\right)^2}\right\} - RT.k_{pt}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{pt}^{Na^+}}{q_{pt}^{H_2O}}\right) - v_{out2}^{H_2O}$$

$$\frac{dq_{vc}^{H_2O}}{dt} = k_{cc}^{H_2O}.\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2} - E_{vc}.\frac{q_{vc}^{H_2O} - \hat{q}_{vc}^{H_2O}}{\left(\bar{q}_{vc}^{H_2O} - q_{vc}^{H_2O}\right)^2}\right\} + RT.k_{gi}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{gi}^{Na^+}}{q_{gi}^{H_2O}}\right) + RT.k_{pt}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{pt}^{Na^+}}{q_{pt}^{H_2O}}\right) - v_{lv}^{H_2O}$$

$$\frac{dq_{ac}^{H_2O}}{dt} = v_{lv}^{H_2O} - k_{cc}^{H_2O}.\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2} - E_{vc}.\frac{q_{vc}^{H_2O} - \hat{q}_{vc}^{H_2O}}{\left(\bar{q}_{vc}^{H_2O} - q_{vc}^{H_2O}\right)^2}\right\} - k_{gl}^{H_2O}.\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2} - E_{pt}.\frac{q_{pt}^{H_2O} - \hat{q}_{pt}^{H_2O}}{\left(\bar{q}_{pt}^{H_2O} - q_{pt}^{H_2O}\right)^2}\right\}$$

$$\frac{dq_{gi}^{Na^+}}{dt} = v_{in}^{Na^+} - k_{gi}^{Na^+}.K^{Na^+}.\left(q_{gi}^{Na^+} - q_{vc}^{Na^+}\right) - 3k_{gi}^{NKE}.\frac{\left(\bar{q}_{gi}^{Na^+}\right)^3.\left(\bar{q}_{vc}^{K^+}\right)^2 - \left(\bar{q}_{vc}^{Na^+}\right)^3.\left(\bar{q}_{gi}^{K^+}\right)^2.e^{2Fu_m^e/RT}}{\left\{1+\left(\bar{q}_{gi}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{K^+}\right)^2\right\}.\left\{1+\left(\bar{q}_{gi}^{K^+}\right)^2\right\}} - v_{out1}^{Na^+}$$

$$\frac{dq_{pt}^{Na^+}}{dt} = k_{gl}^{Na^+}.K^{Na^+}.\left(q_{vc}^{Na^+} - q_{pt}^{Na^+}\right) - k_{pt}^{Na^+}.K^{Na^+}.\left\{q_{pt}^{Na^+} - q_{vc}^{Na^+}\right\} - v_{out2}^{Na^+}$$

$$\frac{dq_{vc}^{Na^+}}{dt} = k_{gi}^{Na^+}.K^{Na^+}.\left(q_{gi}^{Na^+} - q_{vc}^{Na^+}\right) + k_{pt}^{Na^+}.K^{Na^+}.\left(q_{pt}^{Na^+} - q_{vc}^{Na^+}\right) - k_{gl}^{Na^+}.K^{Na^+}.\left(q_{vc}^{Na^+} - q_{pt}^{Na^+}\right)$$
$$+3k_{gi}^{NKE}\frac{\left(\bar{q}_{gi}^{Na^+}\right)^3.\left(\bar{q}_{vc}^{K^+}\right)^2 - \left(\bar{q}_{vc}^{Na^+}\right)^3.\left(\bar{q}_{gi}^{K^+}\right)^2.e^{2Fu_m^e/RT}}{\left\{1+\left(\bar{q}_{gi}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{K^+}\right)^2\right\}.\left\{1+\left(\bar{q}_{gi}^{K^+}\right)^2\right\}}$$

These equations can be simplified as shown below:

$$\frac{dq_{gi}^{H_2O}}{dt} = v_{in}^{H_2O} - RT.k_{gi}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{gi}^{Na^+}}{q_{gi}^{H_2O}}\right) - v_{out1}^{H_2O}$$

$$\frac{dq_{pt}^{H_2O}}{dt} = k_{gl}^{H_2O}.\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2} - E_{pt}.\frac{q_{pt}^{H_2O} - \hat{q}_{pt}^{H_2O}}{\left(\bar{q}_{pt}^{H_2O} - q_{pt}^{H_2O}\right)^2}\right\} - RT.k_{pt}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{pt}^{Na^+}}{q_{pt}^{H_2O}}\right) - v_{out2}^{H_2O}$$

$$\frac{dq_{vc}^{H_2O}}{dt} = k_{cc}^{H_2O}.\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2} - E_{vc}.\frac{q_{vc}^{H_2O} - \hat{q}_{vc}^{H_2O}}{\left(\bar{q}_{vc}^{H_2O} - q_{vc}^{H_2O}\right)^2}\right\} + RT.k_{gi}^{H_2O}.\left\{\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{gi}^{Na^+}}{q_{gi}^{H_2O}}\right\} + RT.k_{pt}^{H_2O}.\left(\frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} - \frac{q_{pt}^{Na^+}}{q_{pt}^{H_2O}}\right) - v_{lv}^{H_2O}$$

$$\frac{dq_{ac}^{H_2O}}{dt} = v_{lv}^{H_2O} + k_{cc}^{H_2O}.\left\{E_{vc}.\frac{q_{vc}^{H_2O} - \hat{q}_{vc}^{H_2O}}{\left(\bar{q}_{vc}^{H_2O} - q_{vc}^{H_2O}\right)^2}\right\} - \left(k_{gl}^{H_2O} + k_{cc}^{H_2O}\right).\left\{E_{ac}.\frac{q_{ac}^{H_2O} - \hat{q}_{ac}^{H_2O}}{\left(\bar{q}_{ac}^{H_2O} - q_{ac}^{H_2O}\right)^2}\right\} + k_{gl}^{H_2O}.E_{pt}.\frac{q_{pt}^{H_2O} - \hat{q}_{pt}^{H_2O}}{\left(\bar{q}_{pt}^{H_2O} - q_{pt}^{H_2O}\right)^2}$$

$$\frac{dq_{gi}^{Na^+}}{dt} = v_{in}^{Na^+} - k_{gi}^{Na^+}.K^{Na^+}.\left(q_{gi}^{Na^+} - q_{vc}^{Na^+}\right) - 3k_{gi}^{NKE}.\frac{\left(\bar{q}_{gi}^{Na^+}\right)^3.\left(\bar{q}_{vc}^{K^+}\right)^2 - \left(\bar{q}_{vc}^{Na^+}\right)^3.\left(\bar{q}_{gi}^{K^+}\right)^2.e^{2Fu_m^e/RT}}{\left\{1+\left(\bar{q}_{gi}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{K^+}\right)^2\right\}.\left\{1+\left(\bar{q}_{gi}^{K^+}\right)^2\right\}} - v_{out1}^{Na^+}$$

$$\frac{dq_{pt}^{Na^+}}{dt} = K^{Na^+}\left(k_{gl}^{Na^+} + k_{pt}^{Na^+}\right).\left(q_{vc}^{Na^+} - q_{pt}^{Na^+}\right) - v_{out2}^{Na^+}$$

$$\frac{dq_{vc}^{Na^+}}{dt} = K^{Na^+}\left\{k_{gi}^{Na^+}.q_{gi}^{Na^+} + \left(k_{pt}^{Na^+} + k_{gl}^{Na^+}\right).q_{pt}^{Na^+} - \left(k_{gi}^{Na^+} + k_{pt}^{Na^+} + k_{gl}^{Na^+}\right).q_{vc}^{Na^+}\right\} + 3k_{gi}^{NKE}.\frac{\left(\bar{q}_{gi}^{Na^+}\right)^3.\left(\bar{q}_{vc}^{K^+}\right)^2 - \left(\bar{q}_{vc}^{Na^+}\right)^3.\left(\bar{q}_{gi}^{K^+}\right)^2.e^{2Fu_m^e/RT}}{\left\{1+\left(\bar{q}_{gi}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{Na^+}\right)^3\right\}.\left\{1+\left(\bar{q}_{vc}^{K^+}\right)^2\right\}.\left\{1+\left(\bar{q}_{gi}^{K^+}\right)^2\right\}}$$

These 7 ODEs are solved for the 4 water volumes and 3 sodium ion molar quantities. Boundary conditions are shown here in red. Parameters are related to water permeability (purple), vessel elastance (brown) and sodium transport (green).

The outputs shown when solving this model on the portal are arterial blood pressure ($u_{ac}^{H_2O}$), blood sodium concentration ($q_{vc}^{Na^+}$), arterial blood volume ($q_{ac}^{H_2O}$), and venous blood volume ($q_{vc}^{H_2O}$). The

parameters shown on the portal for controlling the model are cardiac output ($v_{lv}^{H_2O}$), venous elastance (E_{vc}), and the rate constant for the sodium transporter in the proximal tubule ($kK_{pt}^{Na^+} = k_{pt}^{Na^+}.K^{Na^+}$).

Note that all water quantities are in litres (L) and the flow in L.s^{-1}, while all sodium amounts are in moles (mol) and the fluxes in mol.s^{-1}. All pressures are in kPa.

Initial values for the volume of water and molar quantity of sodium are given in Table 1.

Parameter	Name	Value	Units	Note
$q_{ac}^{H_2O}$	Volume of water in the arteries	2	L	
$q_{vc}^{H_2O}$	Volume of water in the veins	4	L	
$q_{gi}^{H_2O}$	Volume of water in the GI tract	1	L	
$q_{pt}^{H_2O}$	Volume of water in the proximal tubule	0.1	L	
$q_{vc}^{Na^+}$	Amount of sodium in the blood	0.84	mol	$c_{vc}^{Na^+} = \frac{0.84}{6} = 140$ mM
$q_{gi}^{Na^+}$	Amount of sodium in the GI tract	0.1	mol	$c_{gi}^{Na^+} = \frac{0.1}{1} = 100$ mM
$q_{pt}^{Na^+}$	Amount of sodium in the proximal tubule	0.01	mol	$c_{pt}^{Na^+} = \frac{0.01}{0.1} = 100$ mM
$q_{vc}^{K^+}$	Amount of potassium in the blood	0.03	mol	$c_{vc}^{K^+} = \frac{0.03}{6} = 5$ mM
$q_{gi}^{K^+}$	Amount of potassium in the GI tract	0.015	mol	$c_{gi}^{K^+} = \frac{0.015}{1} = 15$ mM

Table 1. Initial values for the simple blood volume control model.

The recommended daily intake of water is 2.1 L for men and 2.6 L for men. With 8.64e4 s.day^{-1} and assuming an intake of 2.4 L.day^{-1}, $v_{in}^{H_2O}$ averages $\frac{2.4}{8.64}$ =28e-6 L.s^{-1}.

The daily intake of sodium is about 2.3 g, which with a molecular mass of 23 g.mol^{-1} is 0.1 mol.day^{-1} or 1.16e-6 mol.s^{-1}.

Boundary conditions are given in Table 2.

Parameter	Name	Value	Units	Note
$v_{in}^{H_2O}$	Water flow from drinking	28e-6	L	2.4 L.day^{-1}
$v_{out1}^{H_2O}$	Water flow excreted in faeces	0	L	
$v_{out2}^{H_2O}$	Water flow excreted in urine	28e-6	L	2.4 L.day^{-1}
$v_{in}^{Na^+}$	Input sodium flux at the mouth	1.16e-6	mol.s^{-1}	0.1 mol.day^{-1}
$v_{out1}^{Na^+}$	Excreted sodium flux in faeces	0	mol.s^{-1}	
$v_{out2}^{Na^+}$	Excreted sodium flux in urine	1.16e-6	mol.s^{-1}	0.1 mol.day^{-1}

Table 2. Boundary conditions for the simple blood volume control model.

Parameter values are given in Table 3. The parameters shown in bold are adjustable in the FC interface.

Parameter	Name	Value	Units
$k_{gi}^{H_2O}$	Membrane permeability	1	L.s^{-1}.kPa^{-1}
$k_{gl}^{H_2O}$	Membrane permeability	1	L.s^{-1}.kPa^{-1}
$k_{pt}^{H_2O}$	Membrane permeability	0	L.s^{-1}.kPa^{-1}
$k_{cc}^{H_2O}$	Vascular conductance	1	L.s^{-1}.kPa^{-1}
$v_{lv}^{H_2O}$	**Cardiac output**	0	L.s^{-1}

E_{ac}	Vascular stiffness (arteries)	1	kPa.L
$\hat{q}_{ac}^{H_2O}$	Unstressed volume (arteries)	2	L
$\bar{q}_{ac}^{H_2O}$	Limiting volume (arteries)	3	L
E_{vc}	**Vascular stiffness** (veins)	1	kPa.L
$\hat{q}_{vc}^{H_2O}$	Unstressed volume (veins)	4	L
$\bar{q}_{vc}^{H_2O}$	Limiting volume (veins)	5	L
$k_{gi}^{Na^+}.K^{Na^+}$	Sodium transporter flux rate (GI tract)	1	s^{-1}
$k_{pt}^{Na^+}.K^{Na^+}$	**Sodium transporter flux rate** (proximal tubule)	1	s^{-1}
$k_{gl}^{Na^+}.K^{Na^+}$	Sodium transporter flux rate (glomerulus)	1	s^{-1}

Table 3. Parameter values for the simple blood volume control model.

Steady state solution

Assuming $v_{out1}^{H_2O} = 0$, $v_{out1}^{Na^+} = 0$, $v_{out2}^{H_2O} = v_{in}^{H_2O}$, and $v_{out2}^{Na^+} = v_{in}^{Na^+}$, and setting derivatives to zero,

$$\frac{dq_{gi}^{H_2O}}{dt} = v_{in}^{H_2O} - v_{gi}^{H_2O} = 0 \qquad \text{or } v_{gi}^{H_2O} = v_{in}^{H_2O} \tag{1}$$

$$\frac{dq_{pt}^{H_2O}}{dt} = v_{gl}^{H_2O} - v_{pt}^{H_2O} - v_{in}^{H_2O} = 0 \qquad \text{or } v_{gl}^{H_2O} = v_{pt}^{H_2O} + v_{in}^{H_2O} \tag{2}$$

$$\frac{dq_{vc}^{H_2O}}{dt} = v_{cc}^{H_2O} + v_{gi}^{H_2O} + v_{pt}^{H_2O} - v_{lv}^{H_2O} = 0 \qquad \text{or } v_{cc}^{H_2O} + v_{gi}^{H_2O} + v_{pt}^{H_2O} = v_{lv}^{H_2O} \tag{3}$$

$$\frac{dq_{ac}^{H_2O}}{dt} = v_{lv}^{H_2O} - v_{cc}^{H_2O} - v_{gl}^{H_2O} = 0 \qquad \text{or } v_{cc}^{H_2O} + v_{gl}^{H_2O} = v_{lv}^{H_2O} \tag{4}$$

$$\frac{dq_{gi}^{Na^+}}{dt} = v_{in}^{Na^+} - v_{gi}^{Na^+} = 0 \qquad \text{or } v_{gi}^{Na^+} = v_{in}^{Na^+} \tag{5}$$

$$\frac{dq_{pt}^{Na^+}}{dt} = v_{gl}^{Na^+} - v_{pt}^{Na^+} - v_{in}^{Na^+} = 0 \qquad \text{or } v_{gl}^{Na^+} = v_{pt}^{Na^+} + v_{in}^{Na^+} \tag{6}$$

$$\frac{dq_{vc}^{Na^+}}{dt} = v_{gi}^{Na^+} + v_{pt}^{Na^+} - v_{gl}^{Na^+} = 0 \qquad \text{or } v_{gl}^{Na^+} = v_{pt}^{Na^+} + v_{gi}^{Na^+} \tag{7}$$

From (1), (2),

$$v_{gl}^{H_2O} - v_{pt}^{H_2O} = v_{gi}^{H_2O} = v_{in}^{H_2O}, \tag{8}$$

and from (3) & (4),

$$v_{cc}^{H_2O} = v_{lv}^{H_2O} - v_{in}^{H_2O}. \tag{9}$$

From (5), (6) & (7),

$$v_{gl}^{Na^+} - v_{pt}^{Na^+} = v_{gi}^{Na^+} = v_{in}^{Na^+}. \tag{10}$$

The steady state requires the difference in water flow $v_{gl}^{H_2O} - v_{pt}^{H_2O}$ to match the input flow $v_{in}^{H_2O}$, and the difference in sodium flux $v_{gl}^{Na^+} - v_{pt}^{Na^+}$ to match the input flux $v_{in}^{Na^+}$, but the actual values of $v_{gl}^{H_2O}$, $v_{pt}^{H_2O}$, $v_{gl}^{Na^+}$ & $v_{pt}^{Na^+}$ will be determined by solving the differential equations subject to specified initial conditions.

Solutions

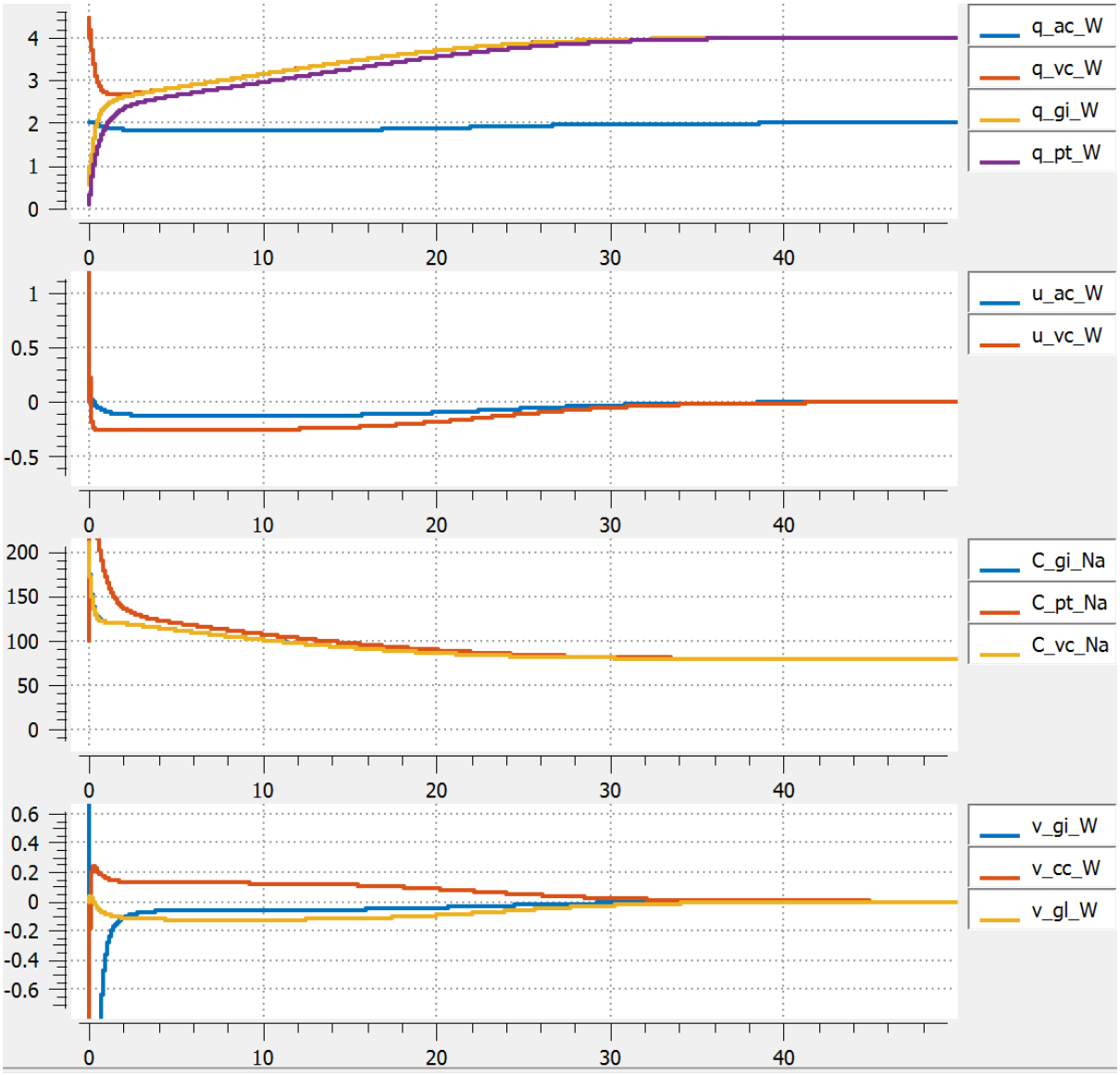
In the following sections we analyse the solutions from the blood volume control model.

Solution 1

Set the initial values given in Table 1 and boundary conditions that are consistent with achieving a steady state solution. i.e.

$v_{out1}^{H_2O} = 0$, $v_{out1}^{Na^+} = 0$, $v_{out2}^{H_2O} = v_{in}^{H_2O} = 0$, and $v_{out2}^{Na^+} = v_{in}^{Na^+} = 0$.

In this first example we set the cardiac output to $v_{lv}^{H_2O} = 0$.



The solution reaches steady state after about 40s with

$q_{ac}^{H_2O} = 2L$, and $q_{vc}^{H_2O} = q_{gi}^{H_2O} = q_{pt}^{H_2O} = 4L$

$C_{gi}^{Na^+} = C_{pt}^{Na^+} = C_{vc}^{Na^+} = 79.2mM$, consistent with $\frac{q_{gi}^{Na^+}}{q_{gi}^{H_2O}} = \frac{q_{pt}^{Na^+}}{q_{pt}^{H_2O}} = \frac{q_{vc}^{Na^+}}{q_{vc}^{H_2O}} = \frac{0.317}{4} = 0.0792\ mol.L^{-1}$

Changing the boundary sodium fluxes ($v_{out2}^{Na^+} = v_{in}^{Na^+} = 1.16e-6$) gives the same steady state results.

Solution 2

As above with $v_{out2}^{Na^+} = v_{in}^{Na^+}$ = 1.16e-6 (mol.s^{-1}) and now with $v_{out2}^{H_2O} = v_{in}^{H_2O}$ = 28e-6 (L.s^{-1})