

# Rat nephron model review

Chanoknun Sintavanuruk

March 7, 2022

2022-03-07

Rat nephron

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# Compartments

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- 1 nephrons
- 2 medullary vasculature
- 3 medullary interstitium

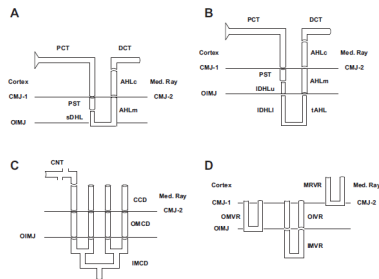


Figure 1: model compartments [Weinstein, 2017]<sup>1</sup>

<sup>1</sup>Alan M. Weinstein. A mathematical model of the rat kidney: K<sup>+</sup>-induced natriuresis.

*American Journal of Physiology-Renal Physiology*, 312(6):F925–F950, June 2017.  
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Compartments



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The model has 3 compartments: nephrons, medullary vasculature and medullary interstitium.

Nephrons and blood vessels are divided into multiple segments. In terms of spatial dimension, each segment has only length with the direction either going up or down the medulla.

The interstitial compartment is divided into 8 different homogeneous sub-compartments; each represents different depth and contains some segments of blood vessels and nephrons.

# Tubular segments of nephrons (1/2)

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- 1 unbranched segments
    - 1 Superficial (SF) nephrons
    - 2 Juxtamedullary (JM) nephrons
  - 2 distal nephron ensembles:  
collecting ducts
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Tubular segments of nephrons (1/2)

■ unbranched segments  
  ■ Superficial (SF) nephrons  
  ■ Juxtamedullary (JM) nephrons  
■ distal nephron ensembles:  
  collecting ducts

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The nephron compartment is composed of many distinct tubular segments which can be grouped into unbranched segments and the distal nephron ensembles or the collecting ducts.

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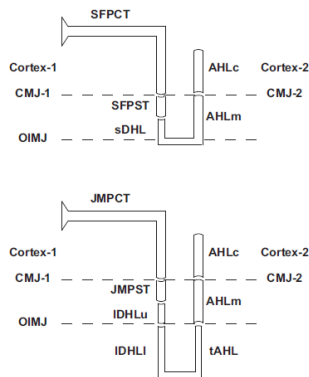


Figure 2: Unbranched tubules  
[Weinstein, 2015]<sup>1</sup>

<sup>1</sup> Alan M. Weinstein. A mathematical model of rat proximal tubule and loop of henle. *American Journal of Physiology-Renal Physiology*, 308(10):F1076–F1097, May 2015.  
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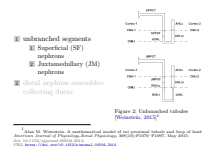
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Tubular segments of nephrons (1/2)

Tubular segments of nephrons (1/2)



The unbranched segments are connected in series in mainly two different ways resulting the superficial or SF and juxtamedullary or JM nephron.

These nephrons have distal segments that are identical, which are the thick ascending limbs, or AHL, in the outer medulla and the cortex. Meanwhile, the proximal convoluted tubule, or PCT, and straight tubule, or PST, of these two differ in the glomerular filtration rate, which determines the initial flow and pressure at the PCT, and ion permeabilities — which are mostly higher in the JM nephron.

For the segments in the middle, the SF nephron has only one segment of the descending Henle's limb, or DHL, at the outer medulla; while in JM nephron, DHL descends into the inner medulla in 5 different depths and comes back up via thin ascending Henle's limb, or tAHL.

# Tubular structure of DHL and tAHL



Figure 3: transepithelial fluxes of DHL and tAHL [Weinstein, 2015]<sup>1</sup>



Figure 4: epithelial cells and lateral interspaces [Weinstein and Krahn, 2010]<sup>2</sup>

<sup>1</sup> Alan M. Weinstein. A mathematical model of rat proximal tubule and loop of henle. *American Journal of Physiology-Renal Physiology*, 308(10):F1076–F1097, May 2015. doi: 10.1152/ajprenal.00504.2014. URL <https://doi.org/10.1152/ajprenal.00504.2014>

<sup>2</sup> Alan M. Weinstein and Thomas A. Krahn. A mathematical model of rat ascending henle limb. II. epithelial function. *American Journal of Physiology-Renal Physiology*, 298(3):F525–F542, March 2010. doi: 10.1152/ajprenal.00231.2009. URL <https://doi.org/10.1152/ajprenal.00231.2009>

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## Rat nephron Overview of structures

### Tubular structure of DHL and tAHL

These segments of DHL and tAHL in the middle, which are parts of the thin Henle's loop, do not have cellular structures and lateral interspaces. So transepithelial fluxes of ions and water are all passive.

The rest of the tubular segments including those of collecting ducts, however, have epithelial cells and lateral interspaces included which separate the luminal and the basement membranes.

Tubular structure of DHL and tAHL

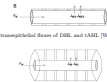


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# Tubular segments of nephrons (2/2)

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## 1 unbranched segments

- 1 Superficial (SF) nephrons
- 2 Juxtamedullary (JM) nephrons

## 2 distal nephron ensembles: collecting ducts

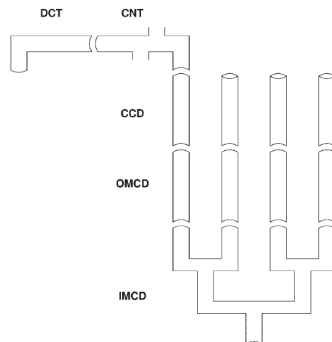


Figure 5: distal nephron [Weinstein, 2008]<sup>1</sup>

<sup>1</sup>Alan M. Weinstein. A mathematical model of distal nephron acidification: diuretic effects.

*American Journal of Physiology-Renal Physiology*, 295(5):F1353–F1364, November 2008.

doi: 10.1152/ajprenal.90356.2008.

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Tubular segments of nephrons (2/2)

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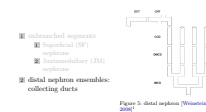


Figure 5: distal nephron [Weinstein, 2008]<sup>1</sup>

In distal nephron, the distal convoluted tubules, or DCT, come after the AHL. So there are total of 6 different profiles of DCT which receive flow from either 1 SF nephron or 5 JM nephrons. All of these flows into the connecting tubule, or CNT, in the way that each CNT are identical.

Similar branching can also be found at the inner medullary collecting ducts, or IMCD.



# Vasa recta

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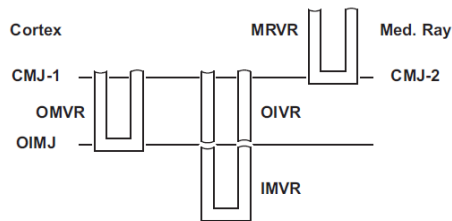


Figure 6: 7 distinct types of vasa recta [Weinstein, 2017]<sup>1</sup>

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Vasa recta

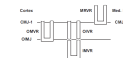


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In the vascular compartments, there are 5 different kinds of vasa recta: the short one, the long ones which reaches 5 different depths, and the medullary ray vasa recta, or MRVR, which is the blood vessels that surround the cortical AHL.

Similar to the thin Henle's loop, vasa recta are assumed to not have cellular and paracellular structures. Each types of vasa recta is composed of segments with 3 different profiles of solute permeability, first at outer medulla and MRVR, which is assumed to be the same as MRVR, second at the inner medulla vasa recta, or IMVR, at the descending direction; and this is different from the third profile of ascending IMVR.

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$$\text{AVR:DVR} = 2 : 1.$$

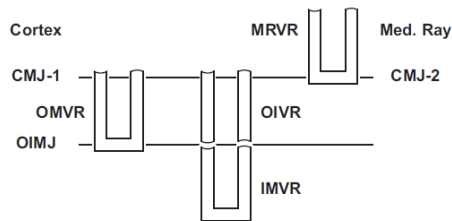


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It is also worth noting that, the branching of vasa recta is represented by the ratio between the number ascending vasa recta or AVR to the descending DVR; which was set to be 2 : 1.

Vasa recta

AVR:DVR = 2 : 1.

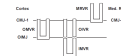


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## 8 sub-compartments

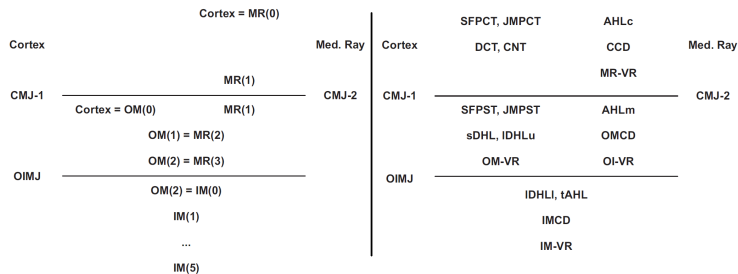


Figure 7: interstitial sub-compartments [Weinstein, 2017]<sup>1</sup>

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The third and last compartment is the medullary interstitium which is divided into 8 sub-compartments: 2 outer medulla, 5 inner medullae, and part of medullary ray that reaches the superficial layer. The cortical interstitium is not included and its solute concentrations and hydrostatic pressure are kept constant.

At the cortex, we have the PCT of SF and JM nephron, DCT, and CNT.

At the outer medulla junction, the cortex-medulla junction is separated into the part that continues from the cortex, which contains the PST, and from the medullary ray, which has the distal portion of medulla AHL. The two outer medulla sub-compartments then contain the short DHL, upper long DHL, and the outer medullary collecting duct and vasa recta.

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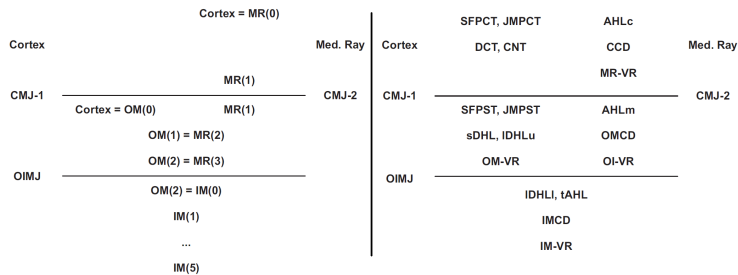


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The inner medulla has 5 levels of depth after the outer-inner medullary junction. These contain the rest of the thin Henle's loop, and the inner medullary collecting ducts and vasa recta.

Lastly, the medullary ray. This contains the AHL, cortical collecting ducts, or CCD, and the MRVR.

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- 1 lumen (M)
- 2 epithelial cell (I)
- 3 lateral interspace (E)

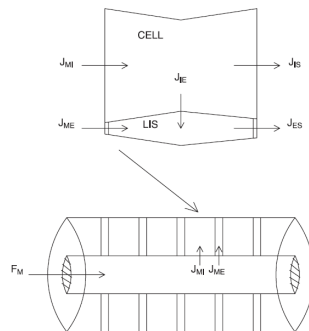


Figure 8: epithelial cells and LIS  
[Weinstein, 1998]<sup>1</sup>

<sup>1</sup>Alan M. Weinstein. A mathematical model of the inner medullary collecting duct of the rat: pathways for na and k transport.  
*American Journal of Physiology-Renal Physiology*, 274(5):F841–F855, May 1998.  
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└ Thick tubules (with cellular structures)

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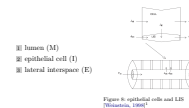


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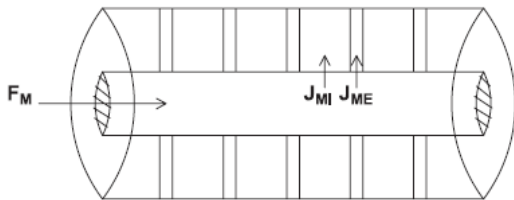
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# Thick tubules: lumen (M)

balance equations:

$$\frac{\partial A_M}{\partial t} = -\frac{\partial F_{vM}}{\partial x} - B_M (J_{vME} + J_{vMI}), \quad (2.1)$$

$$\frac{\partial}{\partial t} (A_M C_{M,i}) = -\frac{\partial F_{M,i}}{\partial x} - B_M (J_{ME,i} + J_{MI,i}) + s_{M,i}. \quad (2.2)$$



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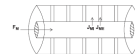
└ Thick tubules: lumen (M)

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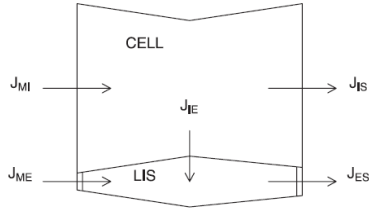


# Thick tubules: cells (I) & LIS (E)

balance equations for  $\alpha$  ( $\alpha$  represents I or E.):

$$\frac{\partial V_\alpha}{\partial t} = J_{vM\alpha} \mp J_{vIE} - J_{v\alpha S}, \tag{2.3}$$

$$\frac{\partial}{\partial t} (V_\alpha C_{\alpha,i}) = J_{M\alpha,i} \mp J_{IE,i} - J_{\alpha S,i} + s_{\alpha,i} \tag{2.4}$$



## Rat nephron └ Model formulation

└ Thick tubules: cells (I) & LIS (E)

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$$\frac{\partial}{\partial t} (V_\alpha C_{\alpha,i}) = J_{Id\alpha,i} \mp J_{IE,i} - J_{\alpha S,i} + s_{\alpha,i} \tag{2.4}$$

This block contains a smaller version of the schematic diagram described above, showing the 'CELL' and 'LIS' regions with their respective fluxes  $J_{MI}$ ,  $J_{ME}$ ,  $J_{IS}$ ,  $J_{ES}$ , and  $J_{IE}$ .



# Thin tubules

Only lumen:

$$\frac{\partial A_M}{\partial t} = -\frac{\partial F_{vM}}{\partial x} - B_M (J_{vMS} + J_{vMS}), \quad (2.5)$$

$$\frac{\partial}{\partial t} (A_M C_{M,i}) = -\frac{\partial F_{M,i}}{\partial x} - B_M (J_{MS,i} + J_{MS,i}) + s_{M,i}. \quad (2.6)$$

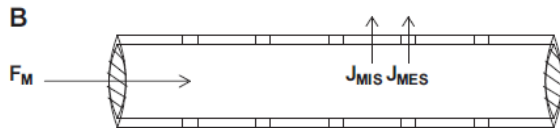


Figure 9: luminal flow & transepithelial fluxes [Weinstein, 2015]<sup>1</sup>

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Thin tubules  
Only lumen:  
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$$\frac{\partial}{\partial t} (A_M C_{M,i}) = -\frac{\partial F_{M,i}}{\partial x} - B_M (J_{MS,i} + J_{MS,i}) + s_{M,i}. \quad (2.6)$$

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# Blood vessels (C)

Only lumen [Weinstein, 2017]<sup>1</sup>:

$$\frac{\partial F_{vC}}{\partial x} = -B_C J_{vCS}, \quad (2.7)$$

$$\frac{\partial F_{C,i}}{\partial x} = -B_C J_{CS,i} + s_{C,i}. \quad (2.8)$$

<sup>1</sup>Alan M. Weinstein. A mathematical model of the rat kidney: K<sup>+</sup>-induced natriuresis.

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$$\frac{\partial F_{C,i}}{\partial x} = -B_C J_{CS,i} + s_{C,i}. \quad (2.8)$$

Relation between blood ( $F_{bC}$ ) and volume flow ( $F_{vC}$ ):

$$F_{vC} = F_{bC} (1 - \text{Hct}), \quad (2.9)$$

$$0 = \frac{\partial}{\partial x} (F_{bC} \cdot \text{Hct}). \quad (2.10)$$

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└ Blood vessels (C)

Blood vessels (C)

Only lumen [Weinstein, 2017]<sup>1</sup>:

$$\frac{\partial F_{vC}}{\partial x} = -B_C J_{vCS}, \quad (2.7)$$

$$\frac{\partial F_{C,i}}{\partial x} = -B_C J_{CS,i} + s_{C,i}. \quad (2.8)$$

Relation between blood ( $F_{bC}$ ) and volume flow ( $F_{vC}$ ):

$$F_{vC} = F_{bC} (1 - \text{Hct}), \quad (2.9)$$

$$0 = \frac{\partial}{\partial x} (F_{bC} \cdot \text{Hct}). \quad (2.10)$$

<sup>1</sup>Alan M. Weinstein. A mathematical model of the rat kidney: K<sup>+</sup>-induced natriuresis.  
*American Journal of Physiology-Renal Physiology*, 312(6):F925–F950, June 2017.  
doi: 10.1152/ajprenal.00536.2016.  
URL <https://doi.org/10.1152/ajprenal.00536.2016>

# Solute ( $J_{\alpha\beta,i}$ ) and water fluxes ( $J_{v\alpha\beta}$ )

Water fluxes [Weinstein, 1983]<sup>1</sup>:

$$J_{v\alpha\beta} = L_{v\alpha\beta} A_{\alpha\beta} \left( P_{\alpha} - P_{\beta} + \pi_{\beta} - \pi_{\alpha} + RT \sum_i \sigma_{\alpha\beta,i} (C_{\beta,i} - C_{\alpha,i}) \right) \quad (2.11)$$

Solute fluxes:

$$J_{\alpha\beta,i} = (1 - \sigma_{\alpha\beta,i}) J_{v\alpha\beta} \bar{C}_{\alpha\beta,i} + z_i h_{\alpha\beta,i} A_{\alpha\beta} \phi_{\alpha\beta} \left( \frac{C_{\alpha,i} - C_{\beta,i} e^{-z_i \phi_{\alpha\beta}}}{1 - e^{-z_i \phi_{\alpha\beta}}} \right) + A_{\alpha\beta} \sum_j L_{\alpha\beta;i,j} \mu_{\alpha\beta,j} + J_{\alpha\beta,i}^{\text{act}} \quad (2.12)$$

<sup>1</sup>A.M. Weinstein. Nonequilibrium thermodynamic model of the rat proximal tubule epithelium. *Biophysical Journal*, 44(2):153–170, November 1983. doi: 10.1016/s0006-3495(83)84287-8.

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## Rat nephron └ Model formulation

└ Solute ( $J_{\alpha\beta,i}$ ) and water fluxes ( $J_{v\alpha\beta}$ )

Solute ( $J_{\alpha\beta,i}$ ) and water fluxes ( $J_{v\alpha\beta}$ )

Water fluxes [Weinstein, 1983]<sup>1</sup>:

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# Hydrostatic pressure (M & C)

## Poiseuille's flow equations:

- tubules [Weinstein, 1998]<sup>1</sup>:

$$\frac{\partial P_M}{\partial x} + \frac{8\pi\eta}{A_M^2} \cdot F_{vM} = 0, \quad (2.13)$$

- vessels [Weinstein, 2017]<sup>2</sup>:

$$\frac{\partial P_C}{\partial x} + \frac{8\pi\eta_C}{A_C^2} \cdot F_{bC} = 0. \quad (2.14)$$

<sup>1</sup>Alan M. Weinstein. A mathematical model of the inner medullary collecting duct of the rat: pathways for na and k transport. *American Journal of Physiology-Renal Physiology*, 274(5):F841–F855, May 1998. doi: 10.1152/ajprenal.1998.274.5.f841. URL <https://doi.org/10.1152/ajprenal.1998.274.5.f841>

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Hydrostatic pressure (M & C)

Poiseuille's flow equations:

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# Tubular compliance

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Thick tubules of nephron are compliant [Weinstein, 2015, Weinstein et al., 2007]<sup>1</sup>:

$$R_M = R_{M0} \left( 1 + \frac{1}{2} \tanh(\nu_M(P_M - P_S)) \right) \quad (2.15)$$

Compliant lateral interspaces:

$$A_{ES} = A_{ES0} (1 + \nu_{AE}(P_M - P_S)), \quad (2.16)$$

$$V_E = V_{E0} (1 + \nu_{VE}(P_M - P_S)). \quad (2.17)$$

<sup>1</sup>Alan M. Weinstein, Sheldon Weinbaum, Yi Duan, Zhaopeng Du, QingShang Yan, and Tong Wang. Flow-dependent transport in a mathematical model of rat proximal tubule. *American Journal of Physiology-Renal Physiology*, 292(4):F1164–F1181, April 2007. doi: 10.1152/ajprenal.00392.2006. URL <https://doi.org/10.1152/ajprenal.00392.2006>

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Tubular compliance

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# Flow-dependent transport of PCT

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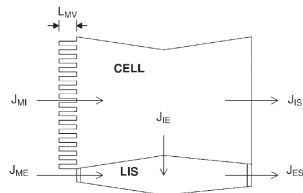
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PCT transporter density parameters (Par) depend on torque of microvilous ( $T_M$ )[Weinstein et al., 2007]<sup>1</sup>:

$$\text{Par} = \text{Par}_0 \left( 1 + T_s \left( \frac{T_M}{T_{M0}} \right) \right) \quad (2.18)$$

$$T_M = \frac{8\eta l F_{vM}}{R_M^2} \left( 1 + \frac{l + \delta}{R_M} + \frac{l^2}{2R_M^2} \right) \quad (2.19)$$



<sup>1</sup> Alan M. Weinstein, Sheldon Weinbaum, Yi Duan, Zhaopeng Du, QingShang Yan, and

Tong Wang. Flow-dependent transport in a mathematical model of rat proximal tubule. *American Journal of Physiology-Renal Physiology*, 292(4):F1164–F1181, April 2007.  
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# Solute generation ( $s_{\alpha,i}$ ) in M & C

Acid-base ( $\text{H}^+ + \text{B} \rightleftharpoons \text{HB}$ ) [Weinstein, 2017]<sup>1</sup>:

$$s_{\alpha,\text{B}} + s_{\alpha,\text{HB}} = 0 \quad (2.20)$$

$$C_{\text{M},\text{H}^+} = K_1 \frac{C_{\text{M},\text{HB}_1}}{C_{\text{M},\text{B}_1^-}} = K_2 \frac{C_{\text{M},\text{HB}_2}}{C_{\text{M},\text{B}_2^-}} = \dots \quad (2.21)$$

$$\sum_i z_i s_{\text{M},i} = 0, \quad \sum_i z_i C_{\text{M},i} = 0 \quad (2.22)$$

<sup>1</sup> Alan M. Weinstein. A mathematical model of the rat kidney:  $\text{K}^+$ -induced natriuresis.

*American Journal of Physiology-Renal Physiology*, 312(6):F925–F950, June 2017.

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└ Solute generation ( $s_{\alpha,i}$ ) in M & C

Solute generation ( $s_{\alpha,i}$ ) in M & C

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$$\sum_i z_i s_{\text{M},i} = 0, \quad \sum_i z_i C_{\text{M},i} = 0 \quad (2.22)$$

$\text{CO}_2$ : ( $\text{H}^+ + \text{HCO}_3^- \rightleftharpoons \text{H}_2\text{CO}_3^- \xrightleftharpoons[k_-]{k_+} \text{H}_2\text{O} + \text{CO}_2$ ):

$$s_{\alpha,\text{HCO}_3} + s_{\alpha,\text{H}_2\text{CO}_3} + s_{\alpha,\text{CO}_2} = 0 \quad (2.23)$$

$$s_{\text{I},\text{HCO}_3} + s_{\text{I},\text{H}_2\text{CO}_3} + s_{\text{I},\text{CO}_2} = M_{\text{I},\text{CO}_2} \quad (2.24)$$

<sup>1</sup> Alan M. Weinstein. A mathematical model of the rat kidney:  $\text{K}^+$ -induced natriuresis.

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Solute generation ( $s_{\alpha,i}$ ) in M & C

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# Hemoglobin buffering species

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