■ SUPPLEMENT ■

Complete Model Equations and Parameters

for

Sex-Specific Computational Models for Blood Pressure Regulation in the Rat

Cardiovascular Function

$$P_{mf} = (\frac{1}{SF_V} \times 7.436 \times V_b - 30.18) \times \epsilon_{aum} \quad ^* \tag{S1}$$

$$P_{ra} = \max\left\{0.2787e^{SF_R \times 0.2281\Phi_{co}} - 0.9119, 0\right\} \quad ^* \tag{S2}$$

$$P_{ma} = \Phi_{co} \times R_{tp} \quad ^* \tag{S3}$$

$$\Phi_{vr} = \frac{P_{mf} - P_{ra}}{R_{vr}} \quad ^* \tag{S4}$$

$$\Phi_{co} = \Phi_{vr} \quad ^* \tag{S5}$$

$$\frac{dvas}{dt} = vas_f - vas_d \quad ^* \tag{S6}$$

$$vas_f = \frac{11.312 \times e^{-\Phi_{co} \times (SF_R \times 0.4714)}}{100000} \quad ^* \tag{S7}$$

$$vas_d = vas \times K_{vd} \quad ^* \tag{S8}$$

$$R_a = R_{ba} \times \epsilon_{aum} \quad ^* \tag{S9}$$

$$R_{ba} = SF_R \times K_{bar}/vas \quad ^* \tag{S10}$$

$$R_{vr} = (SF_R \times 8R_{bv} + R_a)/31 \quad ^* \tag{S11}$$

$$R_{tp} = R_a + R_{bv} \quad ^* \tag{S12}$$

$$\varepsilon_{aum} = \frac{4}{5}(a_{chemo} + a_{baro}) \quad ^* \tag{S13}$$

$$a_{chemo} = \frac{1}{4}a_{auto} \quad ^* \tag{S14}$$

$$\frac{da_{baro}}{dt} = \frac{3}{4}\left\{\frac{da_{auto}}{dt} - 0.0000667(a_{baro} - 1)\right\} \quad ^* \tag{S15}$$

$$a_{auto} = 3.0042e^{-0.0107P_{ma}} \quad ^* \tag{S16}$$

Renal Hemodynamics

$$\Phi_{rb} = \frac{P_{ma}}{R_r} \quad ^* \tag{S17}$$

$$\Phi_{gfilt} = P_f \times C_{gcf} \quad ^* \tag{S18}$$

$$P_f = P_{gh} - (P_B + P_{go}) \quad ^* \tag{S19}$$

$$P_{gh} = P_{ma} - \Phi_{rb} \times R_{AA} \quad ^* \tag{S20}$$

$$R_r = R_{AA} + R_{EA} \quad ^* \tag{S21}$$

$$R_{AA} = R_{aa-ss} \times \beta_{rsna} \times \Sigma_{tgf} \times \Sigma_{myo} \times \Psi_{AT1R-AA} \times \Psi_{AT2R-AA} \quad ^{*\star\dagger} \tag{S22}$$

$$R_{EA} = R_{ea-ss} \times \Psi_{AT1R-EA} \times \Psi_{AT2R-EA} \quad ^{*\star\dagger} \tag{S23}$$

$$\beta_{rsna} = \frac{2}{1 + e^{-3.16(rsna-1)}} \quad *\ddagger \tag{S24}$$

$$\Sigma_{tgf} = \begin{cases} 0.3408 + \dfrac{3.449}{3.88 + e^{(\Phi_{md-sod} - SF_S \times 3.890)/(SF_S \times -0.9617)}} & \text{in males} \\ 0.3408 + \dfrac{3.449}{3.88 + e^{(\Phi_{md-sod} - SF_S \times 6.589)/(SF_S \times -0.9617)}} & \text{in females} \end{cases} \quad * \tag{S25}$$

$$\Sigma_{myo} = 0.75 + \frac{1.2}{1 + 3.8e^{-0.6(P_{gh} - 63.8)}} \quad \ddagger \tag{S26}$$

$$\Psi_{AT1R-AA} = 0.8 + 0.2092 \times \frac{[AT1R]}{[AT1R]_{eq}} - 0.0092 \div \frac{[AT1R]}{[AT1R]_{eq}} \quad \dagger \tag{S27}$$

$$\Psi_{AT1R-EA} = 0.925 + 0.0835 \frac{[AT1R]}{[AT1R]_{eq}} - 0.0085 \div \frac{[AT1R]}{[AT1R]_{eq}} \quad \dagger \tag{S28}$$

$$\Psi_{AT2R-AA} = \begin{cases} 0.75 + 0.25e^{-0.15\left(\frac{[AT2R]}{[AT2R]_{eq}} - 1\right)} & \text{in females} \\ 1 & \text{in males} \end{cases} \quad \star\ddagger \tag{S29}$$

$$\Psi_{AT2R-EA} = \begin{cases} 0.8 + 0.2e^{-0.15\left(\frac{[AT2R]}{[AT2R]_{eq}} - 1\right)} & \text{in females} \\ 1 & \text{in males} \end{cases} \quad \star\ddagger \tag{S30}$$

<u>Renal Function</u>

$$\Phi_{filsod} = \Phi_{gfilt} \times C_{sod} \quad * \tag{S31}$$

$$\Phi_{pt-sodreab} = \Phi_{filsod} \times \eta_{pt-sodreab} \quad * \tag{S32}$$

$$\Phi_{md-sod} = \Phi_{filsod} - \Phi_{pt-sodreab} \quad * \tag{S33}$$

$$\Phi_{dt-sodreab} = \Phi_{md-sod} \times \eta_{dt-sodreab} \quad * \tag{S34}$$

$$\Phi_{dt-sod} = \Phi_{md-sod} - \Phi_{dt-sodreab} \quad * \tag{S35}$$

$$\Phi_{cd-sodreab} = \Phi_{dt-sod} \times \eta_{cd-sodreab} \quad * \tag{S36}$$

$$\Phi_{u-sod} = \Phi_{dt-sod} - \Phi_{cd-sodreab} \quad * \tag{S37}$$

$$\eta_{pt-sodreab} = \eta^{eq}_{pt-sodreab} \times \gamma_{filsod} \times \gamma_{AT1R} \times \gamma_{rsna} \quad * \tag{S38}$$

$$\eta_{dt-sodreab} = \eta^{eq}_{dt-sodreab} \times \psi_{al} \quad * \tag{S39}$$

$$\eta_{cd-sodreab_0} = \eta^{eq}_{cd-sodreab} \times \lambda_{dt} \times \lambda_{anp} \times \lambda_{al} \quad *\dagger \tag{S40}$$

$$\gamma_{filsod} = \begin{cases} 0.8 + \dfrac{0.3}{1 + e^{[(\Phi_{filsod} - SF_S \times 113.7)/(SF_S \times 138)]}} & \text{in males} \\ 0.8 + \dfrac{0.3}{1 + e^{[(\Phi_{filsod} - SF_S \times 108.3)/(SF_S \times 138)]}} & \text{in females} \end{cases} \quad * \tag{S41}$$

$$\gamma_{AT1R} = 0.92 + \frac{0.136}{1 + e^{-1.7983(\frac{[AT1R]}{[AT1R]_{eq}} - 0.8017)}} \quad * \tag{S42}$$

$$\gamma_{rsna} = 0.72 + \frac{0.56}{1 + e^{(1-rsna)/2.18}} \quad * \tag{S43}$$

$$\psi_{al} = \frac{11.55}{1 + 0.1e^{-0.0081C_{al}}} - 10.5 \quad \ddagger \tag{S44}$$

$$\lambda_{dt} = \begin{cases} 0.8 + \dfrac{0.2750}{1 + e^{\frac{1}{SF_S} \times 2.314(\Phi_{dt-sod} - SF_S \times 2.224)}} & \text{in males} \\ 0.8 + \dfrac{0.2750}{1 + e^{\frac{1}{SF_S} \times 2.314(\Phi_{dt-sod} - SF_S \times 3.574)}} & \text{in females} \end{cases} \quad * \tag{S45}$$

$$\lambda_{anp} = -0.1 \times \hat{C}_{anp} + 1.1 \quad * \tag{S46}$$

$$\lambda_{al} = \frac{1}{C_{al}^{eq\,0.06}} C_{al}^{0.06} \quad \dagger \tag{S47}$$

$$\Phi_{pt-wreab} = \Phi_{gfilt} \times \eta_{pt-wreab} \quad ‡ \tag{S48}$$
$$\Phi_{md-u} = \Phi_{gfilt} - \Phi_{pt-wreab} \quad ‡ \tag{S49}$$
$$\Phi_{dt-wreab} = \Phi_{md-u} \times \eta_{dt-wreab} \quad ‡ \tag{S50}$$
$$\Phi_{dt-u} = \Phi_{md-u} - \Phi_{dt-wreab} \quad ‡ \tag{S51}$$
$$\Phi_{cd-wreab} = \Phi_{dt-u} \times \eta_{cd-wreab} \quad ‡ \tag{S52}$$
$$\Phi_{u} = \Phi_{dt-u} - \Phi_{cd-wreab} \quad ‡ \tag{S53}$$
$$\eta_{pt-wreab} = \eta^{eq}_{pt-wreab} \times \mu_{pt-sodreab} \quad ‡ \tag{S54}$$
$$\eta_{dt-wreab} = \eta^{eq}_{dt-wreab} \times \mu_{dt-sodreab} \quad ‡ \tag{S55}$$
$$\eta_{cd-wreab} = \eta^{eq}_{cd-wreab} \times \mu_{cd-sodreab} \times \mu_{adh} \quad ‡ \tag{S56}$$
$$\mu_{pt-sodreab} = 0.12 \tanh\left(10\left(\frac{\eta_{pt-sodreab}}{\eta^{eq}_{pt-sodreab}} - 1\right)\right) + 1 \quad ‡ \tag{S57}$$
$$\mu_{dt-sodreab} = 0.12 \tanh\left(10\left(\frac{\eta_{dt-sodreab}}{\eta^{eq}_{dt-sodreab}} - 1\right)\right) + 1 \quad ‡ \tag{S58}$$
$$\mu_{cd-sodreab} = 0.12 \tanh\left(10\left(\frac{\eta_{cd-sodreab}}{\eta^{eq}_{cd-sodreab}} - 1\right)\right) + 1 \quad ‡ \tag{S59}$$
$$\mu_{adh} = 1.0328 - 0.1938 e^{-0.4441 C_{adh}} \quad * \tag{S60}$$

Renin-Angiotensin-Aldosterone System

$$R_{sec} = N_{rs} \times \nu_{md-sod} \times \nu_{rsna} \times \nu_{AT1R} \quad * \tag{S61}$$
$$\frac{d[PRC]}{dt} = R_{sec} - \frac{\ln(2)}{h_{renin}}[PRC] \quad † \tag{S62}$$
$$PRA = [PRC] \times X_{PRC-PRA} \quad † \tag{S63}$$
$$\frac{d[AGT]}{dt} = k_{AGT} - PRA - \frac{\ln(2)}{h_{AGT}}[AGT] \quad † \tag{S64}$$
$$\frac{d[AngI]}{dt} = PRA - (c_{ACE} + c_{Chym} + c_{NEP})[AngI] - \frac{\ln(2)}{h_{AngI}}[AngI] \quad † \tag{S65}$$
$$\frac{d[AngII]}{dt} = (c_{ACE} + c_{Chym})[AngI] - (c_{ACE2} + c_{AII=AIV} + c_{AT1R} + c_{AT2R})[AngII] - \frac{\ln(2)}{h_{AngII}}[AngII] \quad † \tag{S66}$$
$$\frac{d[Ang(1\text{-}7)]}{dt} = c_{NEP}[AngI] + c_{ACE2}[AngII] - \frac{\ln(2)}{h_{Ang(1\text{-}7)}}[Ang(1\text{-}7)] \quad † \tag{S67}$$
$$\frac{d[AngIV]}{dt} = c_{AII=AIV}[AngII] - \frac{\ln(2)}{h_{AngIV}}[AngIV] \quad † \tag{S68}$$
$$\frac{d[AT1R]}{dt} = c_{AT1R}[AngII] - \frac{\ln(2)}{h_{AT1R}}[AT1R] \quad † \tag{S69}$$
$$\frac{d[AT2R]}{dt} = c_{AT2R}[AngII] - \frac{\ln(2)}{h_{AT2R}}[AT2R] \quad † \tag{S70}$$
$$\nu_{md-sod} = \begin{cases} 0.2262 + \dfrac{28.04}{11.56 + e^{(\Phi_{md-sod} - SF_S \times 1.658)/(SF_S \times 0.6056)}} & \text{in males} \\ 0.2262 + \dfrac{28.04}{11.56 + e^{(\Phi_{md-sod} - SF_S \times 4.358)/(SF_S \times 0.6056)}} & \text{in females} \end{cases} \quad * \tag{S71}$$

$$\nu_{rsna} = 1.822 - \frac{2.056}{1.358 + e^{(rsna-0.8662)}} \quad * \tag{S72}$$

$$\nu_{AT1R} = \left(\frac{[AT1R]}{[AT1R]_{eq}}\right)^{-0.95} \quad \dagger \tag{S73}$$

$$N_{als} = N_{als}^{eq} \times \xi_{k/sod} \times \xi_{map} \times \xi_{AT1R} \quad * \tag{S74}$$

$$\frac{dN_{al}}{dt} = \frac{1}{T_{al}}(N_{als} - N_{al}) \quad * \tag{S75}$$

$$C_{al} = 387N_{al} \quad * \tag{S76}$$

$$\xi_{k/sod} = \frac{5}{1 + e^{0.265(C_k/C_{sod}-23.7)}} \quad * \tag{S77}$$

$$\xi_{map} = \begin{cases} 70.1054e^{-(0.0425)\times P_{ma}} & \text{if } P_{ma} \leq 100 \\ 1 & \text{if } P_{ma} > 100 \end{cases} \quad * \tag{S78}$$

$$\xi_{AT1R} = 0.1 + \frac{2.9}{1 + e^{-2\left(\frac{[AT1R]}{[AT1R]_{eq}} - 1.399\right)}} \quad * \tag{S79}$$

<u>Miscellaneous</u>

$$rsna_0 = N_{rsna} \times \alpha_{map} \times \alpha_{rap} \quad *$$

$$rsna = \begin{cases} rsna_0^{\frac{1}{rsna_0}} & \text{in females} \\ rsna_0 & \text{in males} \end{cases} \quad \star \tag{S80}$$

$$\alpha_{map} = 0.5 + \frac{1}{1 + e^{(P_{ma}-103)/15}} \quad * \tag{S81}$$

$$\alpha_{rap} = 1 - 0.008P_{ra} \quad * \tag{S82}$$

$$\Phi_{win} = \frac{SF_U \times 0.002313}{1 + e^{-0.8(C_{adh}-4.340)}} \quad * \tag{S83}$$

$$\frac{dV_{ecf}}{dt} = \Phi_{win} - \Phi_u \quad * \tag{S84}$$

$$V_b = SF_V \times 4.548 + \frac{SF_V \times 2.431}{1 + e^{-(V_{ecf} - SF_V \times 18.11) \times (\frac{1}{SF_V} \times 0.4744)}} \quad * \tag{S85}$$

$$N_{adhs} = \begin{cases} [\max\{(C_{sod} - 140), 0\} + \max\{(\epsilon_{aum} - 1), 0\} - \delta_{ra}]/3 & \text{in males} \\ [\max\{(C_{sod} - 144), 0\} + \max\{(\epsilon_{aum} - 1), 0\} - \delta_{ra}]/3 & \text{in females} \end{cases} \quad * \tag{S86}$$

$$\frac{dN_{adh}}{dt} = \frac{1}{T_{adh}}(N_{adhs} - N_{adh}) \quad * \tag{S87}$$

$$C_{adh} = 4N_{adh} \quad * \tag{S88}$$

$$\frac{d\delta_{ra}}{dt} = 0.2\frac{dP_{ra}}{dt} - 0.0007\delta_{ra} \quad * \tag{S89}$$

$$\frac{dM_{sod}}{dt} = \Phi_{sodin} - \Phi_{u-sod} \quad * \tag{S90}$$

$$C_{sod} = \frac{M_{sod}}{V_{ecf}} \quad * \tag{S91}$$

$$\hat{C}_{anp} = 7.4052 - \frac{6.554}{1 + e^{(P_{ra}-3.762)/(1)}} \quad * \tag{S92}$$

Other

$$V_b = 0.06 \times W_b + 0.77 \quad ^{\circ} \tag{S93}$$

$$\text{Rat Value} = \text{Human Value} \times SF_{\alpha}, \quad ^{\ddagger} \tag{S94}$$
$$\alpha = \text{urine sodium flow, urine flow, volume, resistance}$$

Equation Reference Legend

* Ref. [1]
⋆ Ref. [2]
◦ Ref. [3]
† Ref. [4]
‡ This work

Reparametrization for the Rat

The human model formulated by Karaaslan et al. [1] is used as the basis for this work. The virtual rat is then created by reparametrizing the human model from the renal hemodynamic data reported in Ref. [5] and the renin-angiotensin system (RAS) hormone values reported in Ref. [6]. Model differences between humans and rats lie in blood flow, vascular resistance, urine flow, urine sodium flow, volume, and the RAS.

We assume that all pressures in the rat model are the same as the human model. Human mean arterial pressure, P_{ma}, is reported in Ref. [1], and rat renal blood flow, Φ_{rb}, is reported in Ref. [5], from which we determine the rat renal vascular resistance, R_r, from Eq. (*S17*). The rat to human ratio of R_r is then used to determine the human to rat resistance scaling factor, SF_R, which is used to scale all of the vascular resistances in the model from human to rat (e.g., basic arterial resistance, Eq. (*S10*)). Given the relationship,

$$\Delta \text{Pressure} = \text{Flow} \times \text{Resistance},$$

and from knowing the blood pressure and vascular resistance values, we calculate all rat blood flows in the model (e.g., venous return, Eq. (*S4*)). Moreover, the resistance scaling factor is used to reparametrize any equation where blood flow appears (e.g., vascular formation rate, Eq. (*S7*)).

Rat glomerular filtration rate, Φ_{gfilt}, is reported in Ref. [5], and human net filtration pressure, P_f, is reported in Ref. [1], from which we determine the rat glomerular capillary filtration coefficient, C_{gcf}, from Eq. (*S18*). Water and sodium transport parameters in the nephron are obtained from Refs. [7] and [1], respectively. From here we determine urine and urine sodium excretion, Φ_u and Φ_{u-sod}, respectively, through flow and transport along the nephron for water, Eqs. (*S48*) - (*S53*), and sodium, Eqs. (*S32*) - (*S37*). At steady state, water and sodium intake are equal to excretion. The rat to human ratios of Φ_u and Φ_{u-sod} are then used to determine the human to rat urine flow and urine sodium flow scaling factors, SF_U and SF_S, respectively. SF_U is used to reparametrize the equation for water intake, Eq. (*S83*). SF_S is used to reparametrize any equation where sodium flow appears (e.g., tubuloglomerular feedback signal, Eq. (*S25*)).

Rat body weight, W_b, is report in Ref. [5]. Blood volume, V_b, is a function of body weight. Using the relationship given in Ref. [3] (Eq. (*S93*)), we calculate rat V_b. The rat to human ratio of V_b is then used to determine the human to rat volume scaling factor, SF_V. SF_V is used to determine rat extracellular fluid volume, V_{ecf}, and to reparametrize the equation for V_b, Eq. (*S85*).

Rat baseline values for hormones in the RAS are obtained from Ref. [6]. These values are used to determine the rate constants in the RAS reaction cascade by solving the steady state system, Eqs. (*S62*) - (*S70*), as done in Ref. [6].

Baseline values of all model variables and parameters for male and female rats are given in Table S1.

References are given for where (model or experiment) a value is obtained from if it is either reported directly or determined indirectly through calculation. For instance, Φ_{rb} cites Ref. [5] because this value is reported therein. While C_{gcf} cites Refs. [1] and [5] because it is calculated from the P_f value reported in the former and from the Φ_{gfilt} value reported in the latter.

Table S1: Baseline values of all model variables and parameters for male (M) and female (F). ADH, antidiuretic hormone; ALD, aldosterone; ANP, atrial natriuretic peptide; CD, collecting duct; DT, distal tubule; MAP, mean arterial pressure; PT, proximal tubule; RSNA, renal sympathetic nerve activity.

Symbol	Description	Units	Baseline M Value	Baseline F Value	Ref.
	Cardiovascular Function				
P_{mf}	Mean filling pressure	$mmHg$	7.28	7.26	[1]
P_{ra}	Right atrial pressure	$mmHg$	0	0	[1]
P_{ma}	Mean arterial pressure	$mmHg$	103	103	[1]
Φ_{vr}	Venous return	$\frac{ml}{min}$	54.6	34.8	[1, 5]
Φ_{co}	Cardiac output	$\frac{ml}{min}$	54.6	34.8	[1, 5]
vas	Vascularity	–	1	1	[1]
vas_f	Vascularity formation rate	–	1×10^{-5}	1×10^{-5}	[1]
vas_d	Vascularity destruction rate	–	1×10^{-5}	1×10^{-5}	[1]
K_{vd}	Vascularity destruction coefficient	–	1×10^{-5}	1×10^{-5}	[1]
K_{bar}	Coefficient relating basic arterial resistance to vascularity	$\frac{mmHg}{ml/min}$	1.57	2.45	[1, 5]
R_a	Arterial resistance	$\frac{mmHg}{ml/min}$	1.57	2.45	[1, 5]
R_{ba}	Basic arterial resistance	$\frac{mmHg}{ml/min}$	1.57	2.45	[1, 5]
R_{vr}	Resistance to venous return	$\frac{mmHg}{ml/min}$	0.134	0.209	[1, 5]
R_{bv}	Basic venous resistance	$\frac{mmHg}{ml/min}$	0.321	0.503	[1, 5]
R_{tp}	Total peripheral resistance	$\frac{mmHg}{ml/min}$	1.89	2.96	[1, 5]
ε_{aum}	Autonomic multiplier effect	–	1	1	[1]
a_{chemo}	Chemoreceptor activity	–	0.25	0.25	[1]
a_{baro}	Baroreceptor activity	–	1	1	[1]
a_{auto}	Autonomous system activity	–	1	1	[1]
	Renal Hemodynamics				
Φ_{rb}	Renal blood flow	$\frac{ml}{min}$	13.1	8.35	[5]
Φ_{gfilt}	Glomerular filtration rate	$\frac{ml}{min}$	2.44	1.67	[5]
C_{gcf}	Glomerular capillary filtration coefficient	$\frac{ml/min}{mmHg}$	0.136	0.094	[1, 5]
P_f	Net filtration pressure	$mmHg$	17.9	17.7	[1]
P_{gh}	Glomerular hydrostatic pressure	$mmHg$	63.9	63.7	[1]
P_B	Bowman hydrostatic pressure	$mmHg$	18	18	[1]
P_{go}	Glomerular osmotic pressure	$mmHg$	28	28	[1]
R_r	Renal vascular resistance	$\frac{mmHg}{ml/min}$	7.87	12.3	[1, 5]
R_{AA}	Afferent arteriolar resistance	$\frac{mmHg}{ml/min}$	2.99	4.68	[1, 5]
R_{EA}	Efferent arteriolar resistance	$\frac{mmHg}{ml/min}$	4.88	7.64	[1, 5]
β_{rsna}	Effect of RSNA on afferent arteriolar resistance	–	1	1	[1]
Σ_{tgf}	Tubuloglomerular feedback signal	–	1	1	[1]
Σ_{myo}	Myogenic response	–	1	1	[8]
$\Psi_{AT1R-AA}$	Effect of AT1R-bound Ang II on afferent resistance	–	1	1	[9]
$\Psi_{AT1R-EA}$	Effect of AT1R-bound Ang II on efferent resistance	–	1	1	[9]
$\Psi_{AT2R-AA}$	Effect of AT2R-bound Ang II on afferent resistance	–	1	1	[6]
$\Psi_{AT2R-EA}$	Effect of AT2R-bound Ang II on efferent resistance	–	1	1	[6]
	Renal Function				
Φ_{filsod}	Filtered Na^+ load	$\frac{\mu eq}{min}$	349	244	[1, 5]
$\Phi_{pt-sodreab}$	Proximal tubule Na^+ reabsorption rate	$\frac{\mu eq}{min}$	279	122	[1]
Φ_{md-sod}	Macula densa Na^+ flow	$\frac{\mu eq}{min}$	69.8	122	[1]
$\Phi_{dt-sodreab}$	Distal tubule Na^+ reabsorption rate	$\frac{\mu eq}{min}$	34.9	61.1	[1]
Φ_{dt-sod}	Distal tubule Na^+ flow	$\frac{\mu eq}{min}$	34.9	61.1	[1]
$\Phi_{cd-sodreab}$	Collecting duct Na^+ reabsorption rate	$\frac{\mu eq}{min}$	32.4	58.6	[1]
Φ_{u-sod}	Urine Na^+ flow	$\frac{\mu eq}{min}$	2.44	2.44	[1, 5]
$\eta_{pt-sodreab}$	Fractional proximal tubule Na^+ reabsorption	–	0.80	0.50	[1]
$\eta_{dt-sodreab}$	Fractional distal tubule Na^+ reabsorption	–	0.50	0.50	[1]
$\eta_{cd-sodreab}$	Fractional collecting duct Na^+ reabsorption	–	0.93	0.96	[1]

γ_{filsod}	Effect of the filtered Na^+ load on fractional PT Na^+ reabsorption	–	1	1	[1]
γ_{AT1R}	Effect of AT2R-bound Ang II on fractional PT Na^+ reabsorption	–	1	1	[1]
γ_{rsna}	Effect of RSNA on fractional PT Na^+ reabsorption	–	1	1	[1]
ψ_{al}	Effect of ALD on fractional DT Na^+ reabsorption	–	1	1	[8]
λ_{dt}	Effect of DT Na^+ outflow on fractional CD Na^+ reabsorption	–	1	1	[1]
λ_{anp}	Effect of ANP on fractional CD Na^+ reabsorption	–	1	1	[1]
λ_{al}	Effect of ALD on fractional CD Na^+ reabsorption	–	1	1	[4]
$\Phi_{pt-wreab}$	Proximal tubule water reabsorption rate	$\frac{ml}{min}$	2.09	0.833	[8]
Φ_{md-u}	Macula densa ultrafiltrate flow	$\frac{ml}{min}$	0.341	0.833	[8]
$\Phi_{dt-wreab}$	Distal tubule water reabsorption rate	$\frac{ml}{min}$	0.205	0.500	[8]
Φ_{dt-u}	Distal tubule ultrafiltrate flow	$\frac{ml}{min}$	0.136	0.333	[8]
$\Phi_{cd-wreab}$	Collecting duct water reabsorption rate	$\frac{ml}{min}$	0.106	0.303	[8]
Φ_u	Urine flow	$\frac{ml}{min}$	0.0300	0.0300	[1, 5]
$\eta_{pt-wreab}$	Fractional proximal tubule water reabsorption	–	0.86	0.50	[7]
$\eta_{dt-wreab}$	Fractional distal tubule water reabsorption	–	0.60	0.60	[7]
$\eta_{cd-wreab}$	Fractional collecting duct water reabsorption	–	0.78	0.91	[7]
$\mu_{pt-sodreab}$	Effect of osmotic gradient in PT	–	1	1	[8]
$\mu_{dt-sodreab}$	Effect of osmotic gradient in DT	–	1	1	[8]
$\mu_{cd-sodreab}$	Effect of osmotic gradient in CD	–	1	1	[8]
μ_{adh}	Effect of ADH on CD fractional water reabsorption	–	1	1	[1]
	Renin-Angiotensin-Aldosterone System				
R_{sec}	Normalized renin secretion rate	–	1	1	[1]
$[PRC]$	Plasma renin concentration	$\frac{fmol}{ml}$	17.3	17.3	[6]
PRA	Plasma renin activity	$\frac{fmol}{ml \cdot min}$	136	114	[6]
$[AGT]$	Angiotensinogen concentration	$\frac{fmol}{ml}$	5.76×10^5	5.76×10^5	[6]
$[AngI]$	Angiotensin I concentration	$\frac{fmol}{ml}$	90	75	[6]
$[AngII]$	Angiotensin II concentration	$\frac{fmol}{ml}$	6.0	6.0	[6]
$[Ang(1\text{-}7)]$	Angiotensin (1-7) concentration	$\frac{fmol}{ml}$	50	25	[6]
$[AngIV]$	Angiotensin IV concentration	$\frac{fmol}{ml}$	1.29	1.29	[6]
$[AT1R]$	AT1R-bound Angiotensin II concentration	$\frac{fmol}{ml}$	20	20	[6]
$[AT2R]$	AT2R-bound Angiotensin II concentration	$\frac{fmol}{ml}$	6.8	6.8	[6]
$X_{PRC\text{-}PRA}$	Ratio of PRA to [PRC]	$\frac{1}{min}$	7.83	6.60	[6]
k_{AGT}	AGT production rate	$\frac{fmol}{ml \cdot min}$	801	780	[6]
c_{ACE}	Reaction rate of Ang converting enzyme	$\frac{1}{min}$	0.0968	0.116	[2]
c_{Chym}	Reaction rate of chymase	$\frac{1}{min}$	0.0108	0.0128	[6]
c_{NEP}	Reaction rate of neutral endopeptidase	$\frac{1}{min}$	0.0127	0.00767	[6]
c_{ACE2}	Reaction rate of Ang converting enzyme 2	$\frac{1}{min}$	2.67×10^{-3}	4.33×10^{-4}	[6]
$c_{AII=AIV}$	Reaction rate of conversion of Ang II to Ang IV	$\frac{1}{min}$	0.298	0.298	[6]
c_{AT1R}	Reaction rate of binding of Ang II to AT1R	$\frac{1}{min}$	0.197	0.197	[6]
c_{AT2R}	Reaction rate of binding of Ang II to AT2R	$\frac{1}{min}$	0.0657	0.0657	[6]
h_{renin}	Half life of renin	min	12	12	[6]
h_{AGT}	Half life of AGT	min	600	600	[6]
h_{AngI}	Half life of Ang I	min	0.5	0.5	[6]
h_{AngII}	Half life of Ang II	min	0.66	0.66	[6]
$h_{Ang(1-7)}$	Half life of Ang (1-7)	min	30	30	[6]
h_{AngIV}	Half life of Ang IV	min	0.5	0.5	[6]
h_{AT1R}	Half life of AT1R-bound Ang II	min	12	12	[6]
h_{AT2R}	Half life of AT2R-bound Ang II	min	12	12	[6]
ν_{md-sod}	Effect of macula densa Na^+ flow on renin secretion rate	–	1	1	[1]
ν_{rsna}	Effect of RSNA on renin secretion rate	–	1	1	[1]
ν_{AT1R}	Effect of AT1R-bound Ang II on renin secretion rate	–	1	1	[4]
N_{als}	Normalized ALD secretion rate	–	1	1	[1]
N_{al}	Normalized ALD concentration	–	1	1	[1]
C_{al}	Aldosterone concentration	$\frac{ng}{l}$	387	387	[10]
T_{al}	Time constant for ALD hormone secretion	min	60	60	[1]
$\xi_{k/sod}$	Effect of K to Na^+ concentration ratio on ALD secretion rate	–	1	1	[1]
ξ_{map}	Effect of MAP on ALD secretion rate	–	1	1	[1]

ξ_{AT1R}	Effect of AT1R-bound Ang II on ALD secretion rate	$-$	1	1	[1]
	Miscellaneous				
$rsna$	Renal sympathetic nerve activity	$-$	1	1	[1]
α_{map}	Effect of MAP on RSNA	$-$	1	1	[1]
α_{rap}	Effect of right atrial pressure on RSNA	$-$	1	1	[1]
Φ_{win}	Water intake	$\frac{ml}{min}$	0.0300	0.0300	[1, 5]
Φ_{sodin}	Na^+ intake	$\frac{\mu eq}{min}$	2.44	2.44	[1, 5]
W_b	Body weight	g	238	194	[5]
V_{ecf}	Extracellular fluid volume	ml	46	38	[1]
V_b	Blood volume	ml	15	12	[3, 5]
T_{adh}	Time constant for ADH secretion	min	6	6	[1]
N_{adhs}	Normalized ADH secretion rate	$-$	1	1	[1]
N_{adh}	Normalized ADH concentration	$-$	1	1	[1]
C_{adh}	Antidiuretic hormone concentration	$\frac{\mu units}{ml}$	4	4	[1]
δ_{ra}	Effect of right atrial pressure on ADH secretion rate	$-$	0	0	[1]
M_{sod}	Total amount of Na^+	μeq	6560	5527	[1, 5]
C_{sod}	Plasma Na^+ concentration	$\frac{\mu eq}{ml}$	143	147	[1]
$\hat{C}_{anp}$	Normalized atrial natriuretic peptide concentration	$-$	1	1	[1]
C_K	Plasma K concentration	$\frac{\mu eq}{ml}$	5	5	[1]
	Scaling Factors				
SF_S	Human to rat urine sodium flow scaling factor	$\frac{\mu eq}{meq}$	19.4	19.4	[1, 5]
SF_U	Human to rat urine flow scaling factor	$\frac{ml}{l}$	30.0	30.0	[1, 5]
SF_V	Human to rat volume scaling factor	$\frac{ml}{l}$	3.01	2.48	[1, 5]
SF_R	Human to rat resistance scaling factor	$\frac{l}{ml}$	0.0945	0.148	[1, 5]

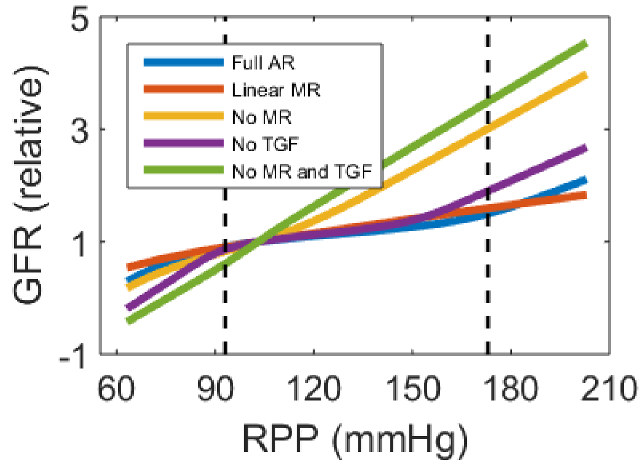

Figure S1: Renal autoregulation. Following the same experimental protocol as in Ref. [9], renal perfusion pressure is perturbed from its baseline value of 103 mmHg within a wide range. Male GFR is plotted as relative change from baseline value for full autoregulation, no myogenic response, no TGF, and no myogenic response and TGF. Dashed vertical lines are at the end points of the autoregulatory range of 90-170 mmHg. Female GFR curves are the same.

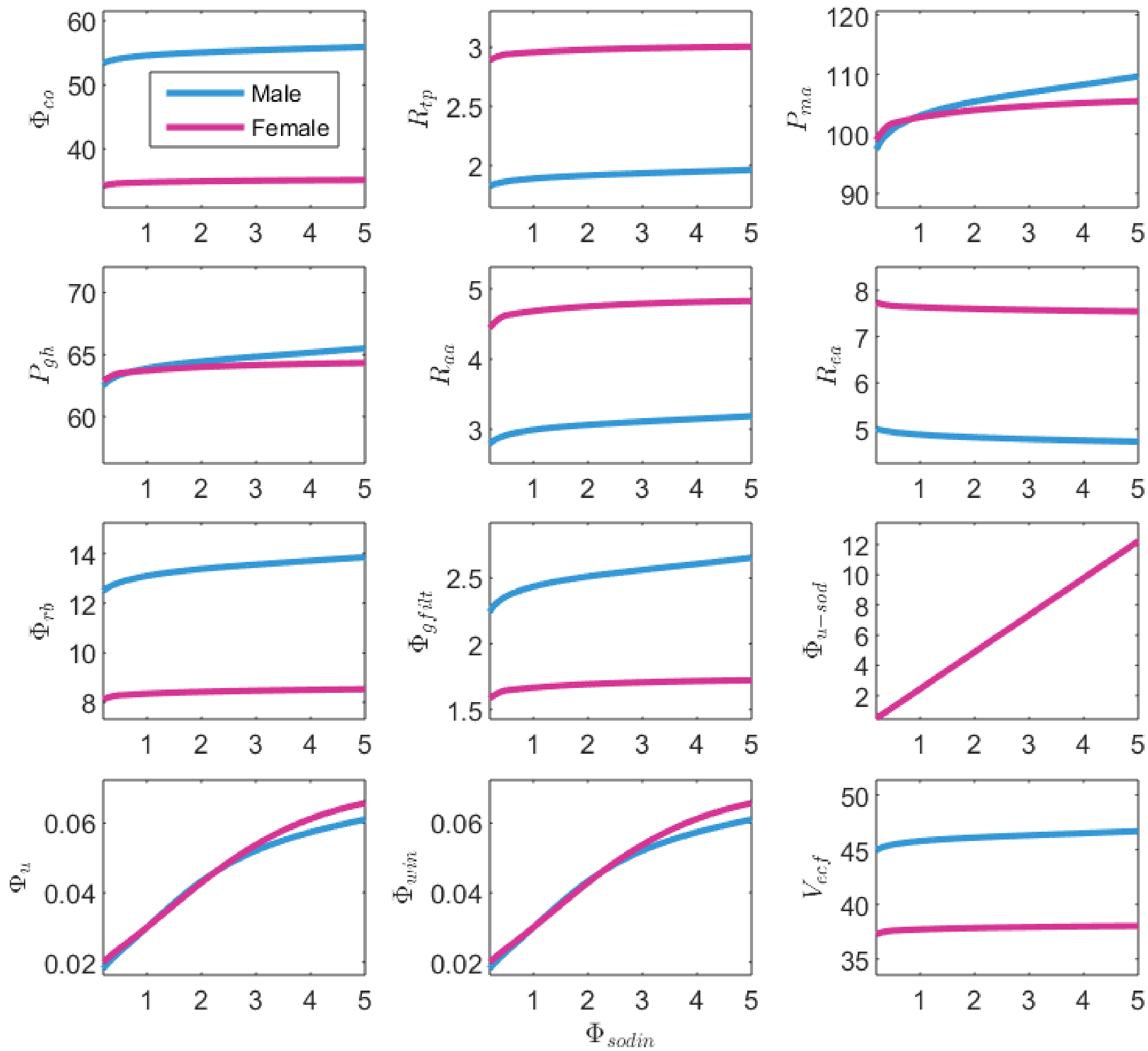

Figure S2: Response of several cardiovascular and renal variables to varying sodium intake.

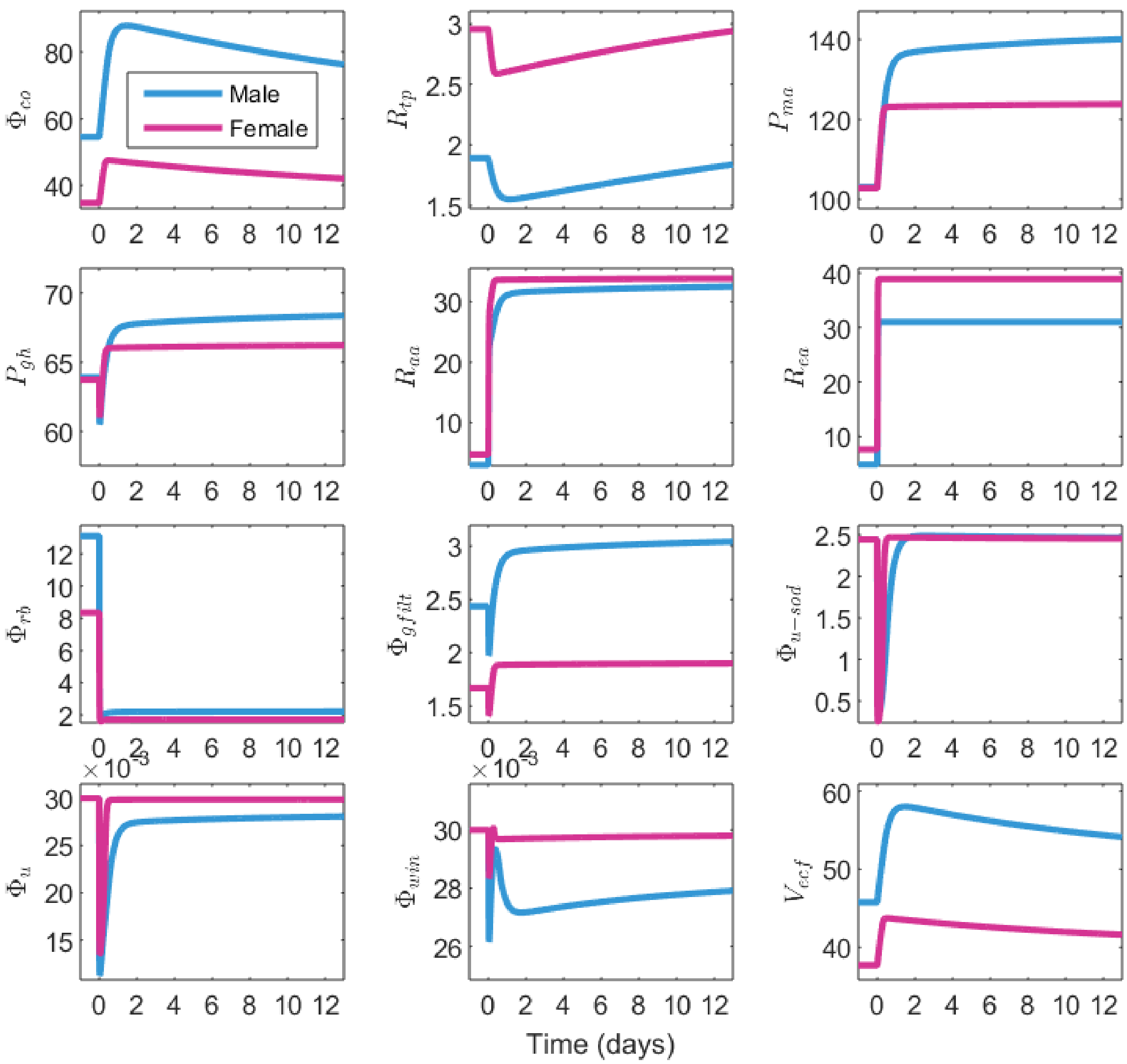

Figure S3: Response of several cardiovascular and renal variables to Ang II infusion.

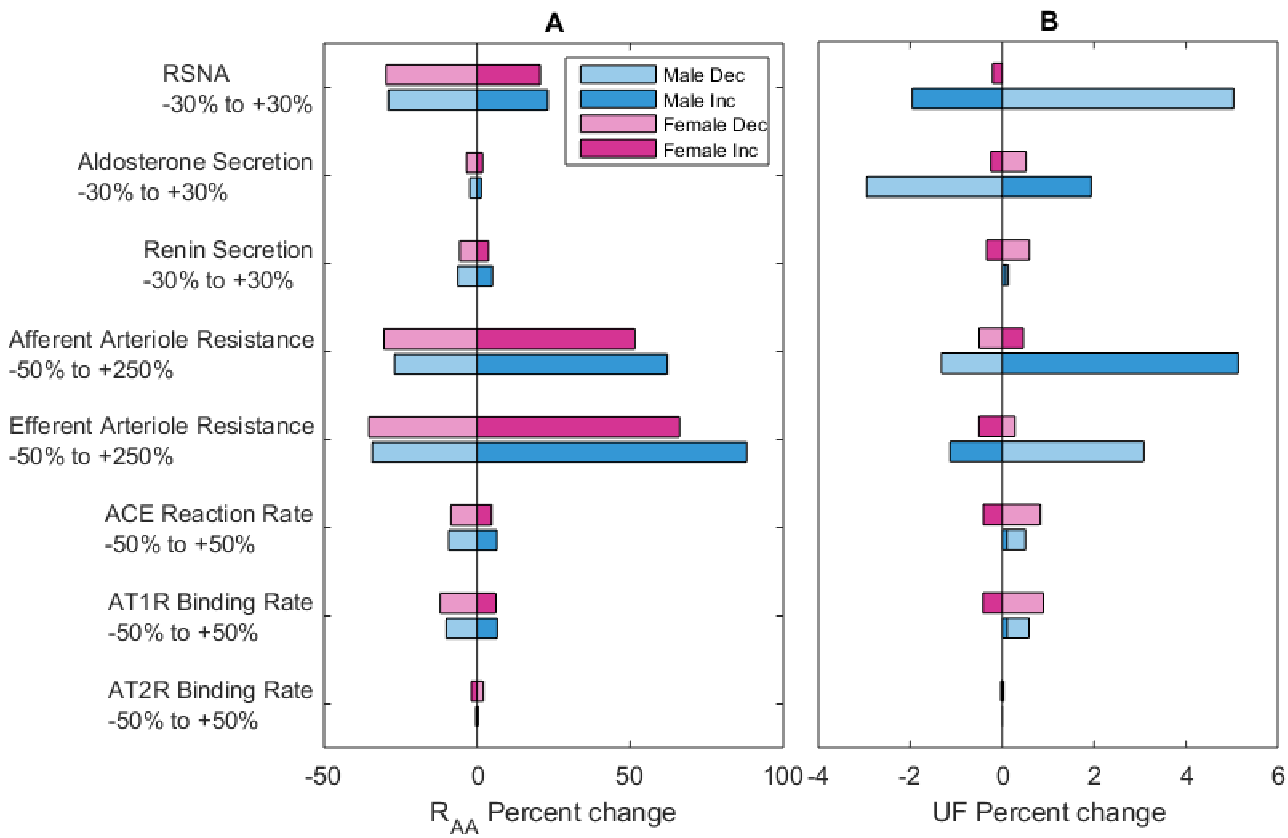

Figure S4: Sensitivity analysis. Percent change in afferent arteriolar resistance and urine flow due to various perturbations.

References

1. Karaaslan, F., Denizhan, Y., Kayserilioglu, A. & Gulcur, H. O. Long-Term Mathematical Model Involving Renal Sympathetic Nerve Activity, Arterial Pressure, and Sodium Excretion. *Annals of Biomedical Engineering* **33,** 1607–1630. ISSN: 0090-6964, 1573-9686. `http://link.springer.com/10.1007/s10439-005-5976-4` (2019) (Nov. 2005).
2. Leete, J. & Layton, A. T. Sex-specific long-term blood pressure regulation: Modeling and analysis. *Computers in Biology and Medicine* **104,** 139–148. ISSN: 00104825. `https://linkinghub.elsevier.com/retrieve/pii/S0010482518303408` (2019) (Jan. 2019).
3. Lee, H. B. & Blaufox, M. D. Blood Volume in the Rat. *Journal of Nuclear Medicine* **26,** 72–76. ISSN: 0161-5505, 2159-662X. `http://jnm.snmjournals.org/content/26/1/72` (2019) (Jan. 1, 1985).
4. Hallow, K. M. *et al.* A model-based approach to investigating the pathophysiological mechanisms of hypertension and response to antihypertensive therapies: extending the Guyton model. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* **306,** R647–R662. ISSN: 0363-6119, 1522-1490. `http://www.physiology.org/doi/10.1152/ajpregu.00039.2013` (2019) (May 2014).
5. Munger, K. & Baylis, C. Sex differences in renal hemodynamics in rats. *American Journal of Physiology-Renal Physiology* **254,** F223–F231. ISSN: 1931-857X. `https://physiology.org/doi/abs/10.1152/ajprenal.1988.254.2.F223` (2019) (Feb. 1, 1988).
6. Leete, J., Gurley, S. & Layton, A. T. Modeling sex differences in the renin angiotensin system and the efficacy of antihypertensive therapies. *Computers & Chemical Engineering* **112,** 253–264. ISSN: 00981354. `https://linkinghub.elsevier.com/retrieve/pii/S0098135418300723` (2019) (Apr. 2018).
7. Layton, A. T., Laghmani, K., Vallon, V. & Edwards, A. Solute transport and oxygen consumption along the nephrons: effects of Na+ transport inhibitors. *American Journal of Physiology-Renal Physiology* **311,** F1217–F1229. ISSN: 1931-857X. `https://www.physiology.org/doi/full/10.1152/ajprenal.00294.2016` (2019) (Oct. 5, 2016).
8. Ahmed, S. & Layton, A. *This work.*
9. Hilliard Lucinda M. *et al.* Gender Differences in Pressure-Natriuresis and Renal Autoregulation. *Hypertension* **57,** 275–282. `https://www.ahajournals.org/doi/full/10.1161/HYPERTENSIONAHA.110.166827` (2019) (Feb. 1, 2011).
10. Pendergrass, K. D. *et al.* Sex differences in circulating and renal angiotensins of hypertensive mRen().Lewis but not normotensive Lewis rats. *American Journal of Physiology-Heart and Circulatory Physiology* **295,** H10–H20. ISSN: 0363-6135. `https://www.physiology.org/doi/full/10.1152/ajpheart.01277.2007` (2019) (July 1, 2008).