Online Supplement

Questioning the renoprotective role of L-type calcium channel blockers in chronic kidney disease using physiological modeling

Kyle H. Moore and John S. Clemmer

Department of Physiology and Biophysics, Center for Computational Medicine
University of Mississippi Medical Center
Jackson, MS 39216

Running head: Chronic kidney disease and calcium channel blockade

Address correspondence to:
John S. Clemmer, PhD
Department of Physiology and Biophysics
University of Mississippi Medical Center
2500 North State Street
Jackson, Mississippi 39216-4505
Phone: (601) 984-1816
Email: jclemmer@umc.edu

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Supplementary Figure 1. Equations and model parameters for heart function and blood pressure

Left Heart

$ESP = SBP$

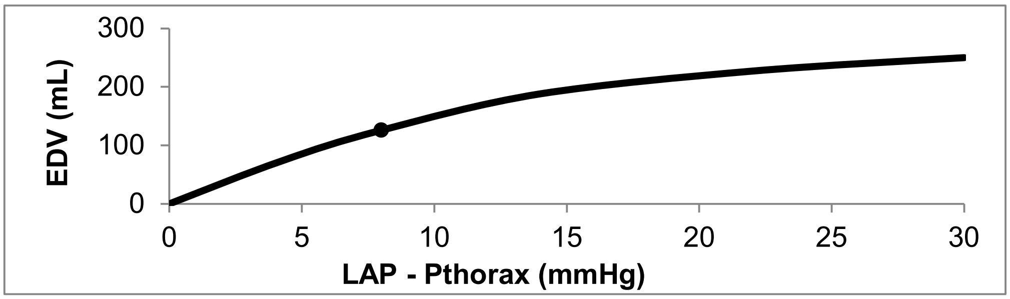
$EDP = LAP$

$SV = EDV - ESV$

$SBP = emax * (ESV - V\varphi) + Pthorax$

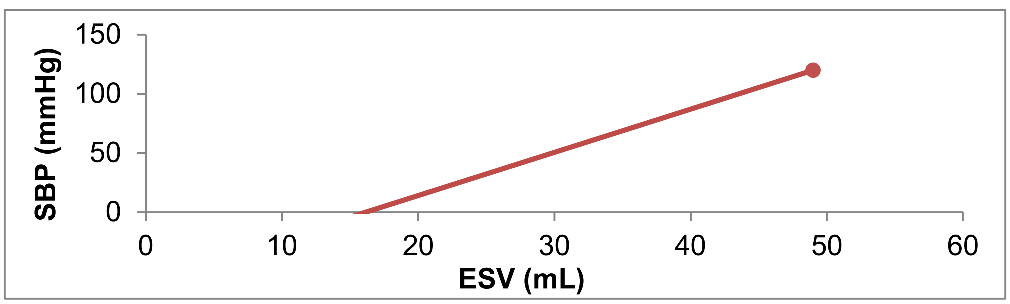
Diastole

if $TMP < 9.6$	$EDV = TMP / PVSlope$
if $TMP > 9.6$	$EDV = 144 + (TMP - 9.6)^{1/2} / K$
if $EDV < 144$	$TMP = EDV * PVSlope$
if $EDV > 144$	$TMP = 9.6 + (EDV - 144)^{2}$



Systole

if $Passive < 9.6$	$ESV = Passive / PVSlope$
if $Passive > 9.6$	$ESV = 144 + ((Passive - 9.6)/K)^{1/2}$
if $ESV < 144$	$Passive = PVSlope * ESV$
if $ESV > 144$	$Passive = 9.6 * K(ESV - 144)^{2}$



$emax = 3.5$ mmHg/mL

$V\varphi = 15$ mL

$PVSlope = 0.067$ mmHg/mL

$K = 0.01$

Supplementary Figure 2. Equations and model parameters for renal vascular function and GFR

		Input
Afferent Arteriole Conductance	**TGF Effect***	TGF Vascular Signal
	Sympathetic Effect*	α_1 Receptor Activity
	Myogenic Effect*	Interlobular Pressure
	ANP Effect	[ANP]
	CCB Effect	[CCB]
Baseline conductance (ml/min/mmHg/g) = 0.080883		
		Input
Efferent Arteriole Conductance	**Ang II Effect***	[Ang II]
	Sympathetic Effect*	Renal α Receptor Activity
	L/T CCB Effect	[L/T CCB]
Baseline conductance (ml/min/mmHg/g) = 0.06218		
		Input
GFR	**Colloid Osmotic Pressure**	Plasma Osmotic Pressure / (1 - FF)
	Bowman's Capsule Pressure	Pelvis Pressure + (SNGFR / PT conductance)
	Capillary Pressure	(RBF / Efferent Conductance) + Renal Venous Pressure
	GFR = Kf (P_C - P_{BC} - P_{osm})	

Tubuloglomerular feedback, TGF; atrial natiuretic peptide, ANP; filtration fraction, FF; single nephron glomerular filtration rate, SNGFR; proximal tubule, PT; filtration coefficient, Kf; capillary hydrostatic pressure, P_C; Bowman's Capsule hydrostatic pressure, P_{BC}; capillary colloid osmostic pressure, P_{osm}

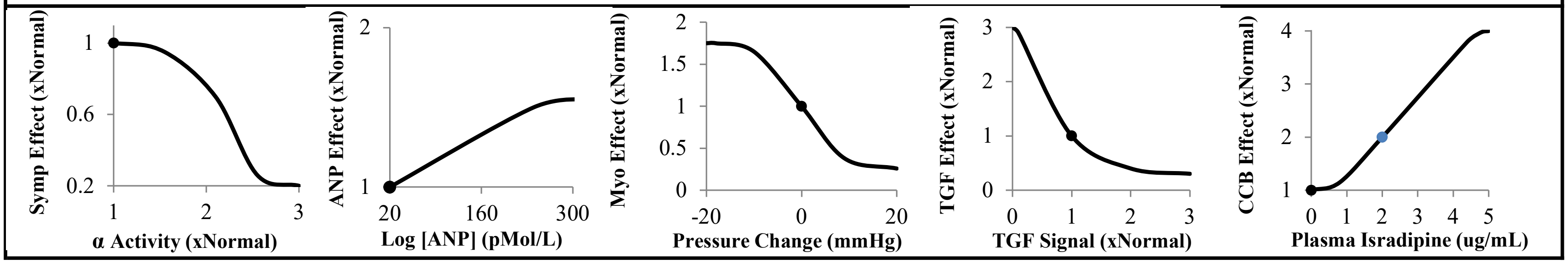
*Indicates a negative relationship

Supplementary Figure 3. Determinants of afferent arteriolar conductance in the model

Afferent Arteriolar Conductance

$$Conductance = Baseline \times Symp\ Effect \times ANP\ Effect \times Myogenic\ Effect \times TGF\ Effect \times CCB\ Effect$$

$$Baseline = 0.080883 \quad ml/min/mmHg/g$$



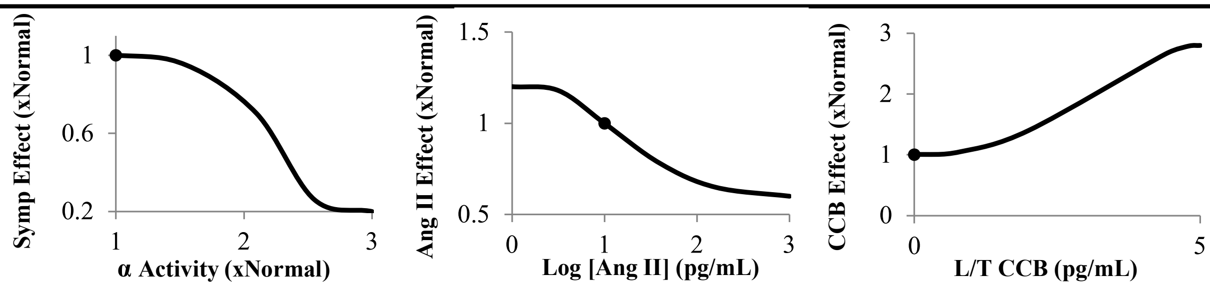
Angiotensin II, Ang II; atrial natriuretic peptide, ANP; Sympathetic, Symp; myogenic, myo; tubuloglomerular feedback, TGF; calcium channel blocker, CCB

Supplementary Figure 4. Determinants of efferent arteriolar conductance in the model

Efferent Arteriolar Conductance

$$Conductance = Baseline \times Symp\ Effect \times Ang\ II\ Effect \times LT\ CCB\ Effect$$

$$Baseline = 0.06218 \quad ml/min/mmHg/g$$

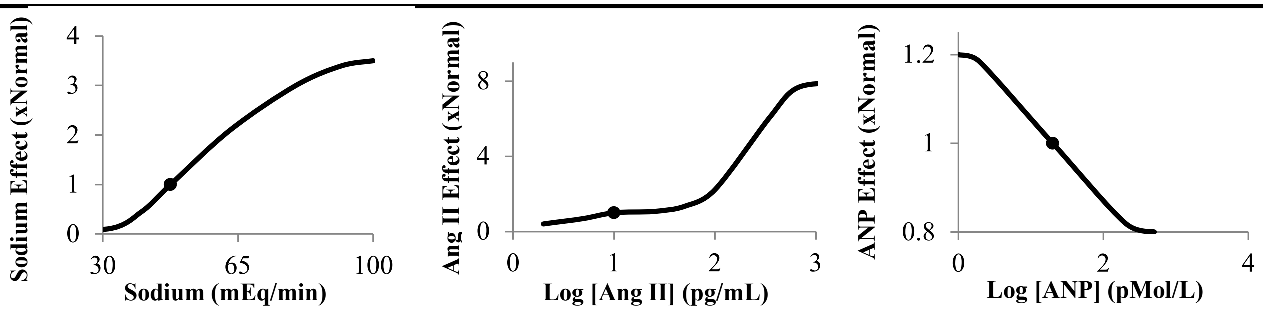


Sympathetic, Symp; angiotensin II, Ang II; calcium channel blocker, CCB

Supplementary Figure 5. Determinants of tubuloglomerular feedback

TGF Signal

$$Signal = \boldsymbol{Sodium\ Effect} \times \boldsymbol{Ang\ II\ Effect} \times \boldsymbol{ANP\ Effect}$$



Angiotensin II, Ang II; atrial natriuretic peptide, ANP

Supplementary Figure 6. Body compartment volumes

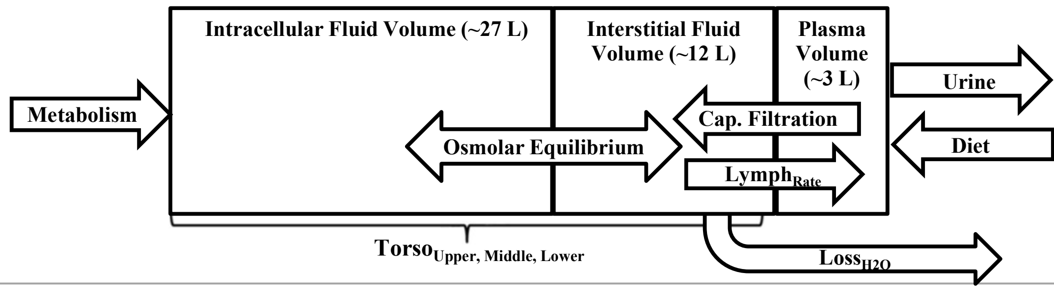
Total Body Water

$$TBW = Tissue_{H2O} + Plasma_{Vol} + RBC_{H2O}$$

$$Tissue_{H2O} = Torso_{Upper} + Torso_{Middle} + Torso_{Lower}$$

$$\frac{dTorso_{Upper,\ Middle,\ Lower}}{dt} = Intracellular + Interstitial = CapillaryFiltration + Metabolism_{H2O} - Lymph_{Rate} - Loss_{H2O}$$

$$Plasma_{Vol} = GI\ Absorption + Lymph_{Rate} - Urine - CapillaryFiltration$$



Tissue H_2O calculated for each torso region:

$$Gain_{H2O} = CapillaryFiltration + Metabolism$$

$$Loss_{H2O} = Sweat + Skin_{ins} + Lymph_{Rate}\ \textit{(+ Lung for Torso}_{Middle}\textit{)}$$

$$CapillaryFiltration = Perm \times [P_{capillary} + COP_{interstitial} - P_{interstitial} - COP_{capillary}]$$

$$Lymph_{Rate} = K \times [P_{interstitial} \times Effect]$$

$Perm_{Upper}$ = 1.16075 ml/mmHg/min

$Perm_{Middle}$ = 2.5374 ml/mmHg/min

$Perm_{Lower}$ = 1.7006 ml/mmHg/min

K_{Upper} = 4.43

K_{Middle} = 8.73

K_{Lower} = 4.6

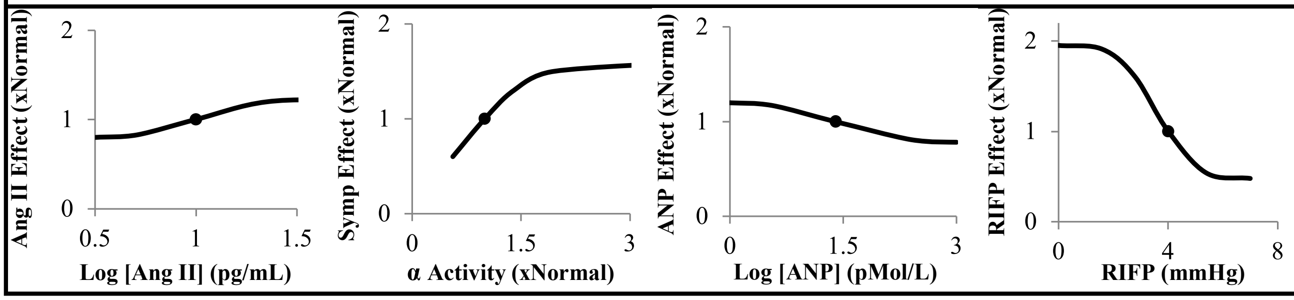
Supplementary Figure 7. Determinants of proximal tubular sodium reabsorption

Proximal Tubule Sodium Reabsorption

$$Reabsorption = PTNa\ Inflow \times Baseline^{Effects^{-1}}$$

$$Baseline = 58\%$$

$$Effects = \mathbf{Ang\ II\ Effect} \times \mathbf{Symp\ Effect} \times \mathbf{ANP\ Effect} \times \mathbf{RIFP\ Effect}$$



Proximal tubular sodium, PTNa; angiotensin II, Ang II; sympathetic, symp; atrial natriuretic peptide, ANP; renal interstitial fluid pressure, RIFP

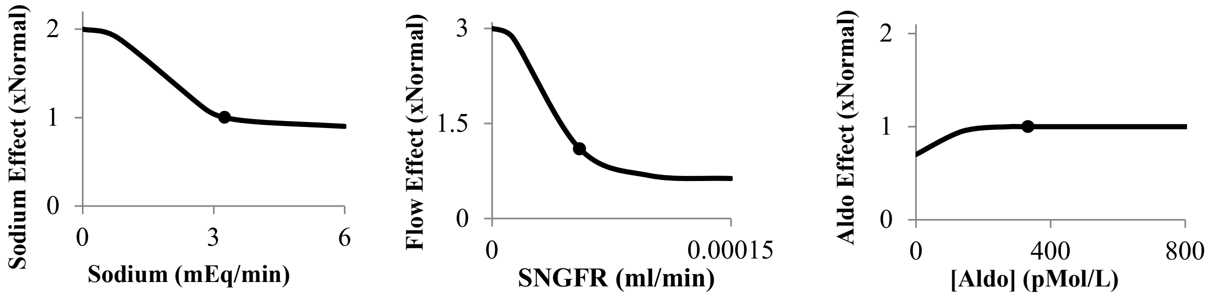
Supplementary Figure 8. Determinants of loop of henle sodium reabsorption

Loop of Henle Sodium Reabsorption

$$Reabsorption = Loop\ Inflow \times Baseline^{\ Effects^{-1}}$$

$$Baseline = 75\%$$

$$Effects = \boldsymbol{Sodium\ Effect} \times \boldsymbol{Flow\ Effect} \times \boldsymbol{Aldo\ Effect}$$



Single nephron glomerular filtration rate, SNGFR; aldosterone, Aldo

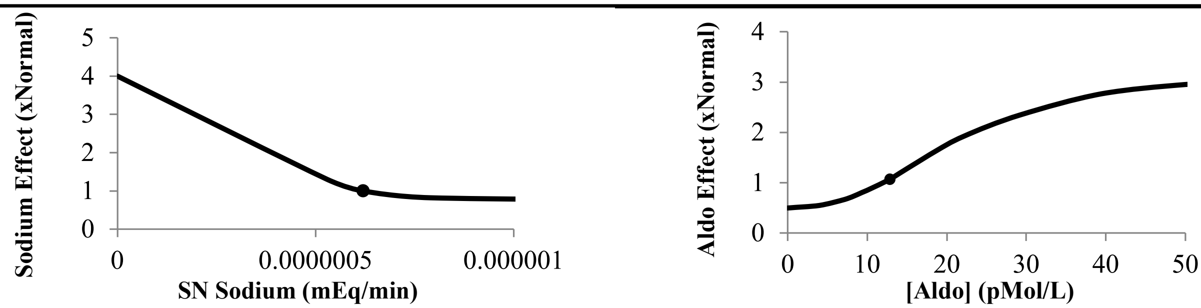
Supplementary Figure 9. Determinants of distal tubular sodium reabsorption

Distal Tubule Sodium Reabsorption

$Reabsorption = Loop\ Inflow \times Baseline^{\ Effects^{-1}}$

$Baseline = 75\%$

$Effects = \boldsymbol{Sodium\ Effect} \times \boldsymbol{Aldo\ Effect}$



Single nephron, SN; aldosterone, Aldo

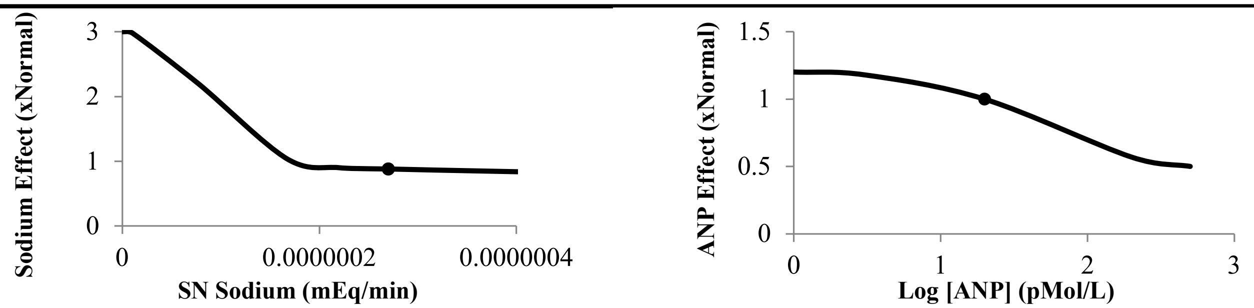
Supplementary Figure 10. Determinants of collecting duct sodium reabsorption

Collecting Duct Sodium Reabsorption

$Reabsorption = Loop\ Inflow \times Baseline^{\ Effects^{-1}}$

$Baseline = 75\%$

$Effects = \boldsymbol{Sodium\ Effect} \times \boldsymbol{ANP\ Effect}$



Single nephron, SN; aldosterone, Aldo