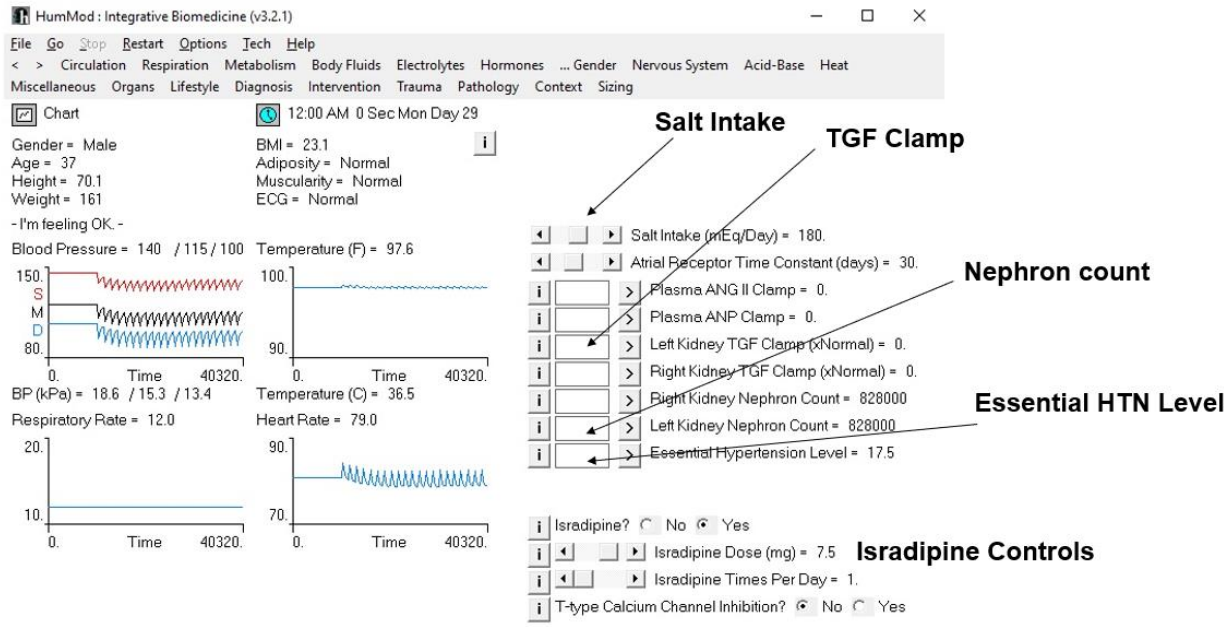
Experimental Protocols

To run simulations, either Essential HTN or CKD or normal, please load initial condition files (.ICS files) labeled “Essential HTN.ICS, CKD.ICS, or Normal.ICS to load conditions described below. (Go to “File” then “Load Initial Conditions”.)

All simulations were run 1 year although 3 months of baseline are shown for clarity. Running the model is performed under the menu “Go” and then selecting a simulation time (from 1 second to 90 days). Six simulations were performed with or without 3 years of CCB therapy (labeled “Isradipine?”):

1. **Essential HTN**. Control simulation based off of a 17.5 “Essential Hypertension Level” and 900,000 nephron count in each kidney. This was run for 2 weeks. Nephron count was set to 828,000 in each kidney with “Delay” set to 2190 days to account for the natural decrease in renal mass over time. The simulation was then run to 1 year for steady-state values). “Isradipine?” was left on “No” and simulation was run for 6.5 hours and then for 3 years and served as Essential HTN control.
2. **Essential HTN+CCB**. Simulation was setup similar to control. “Isradipine?” was turned to “Yes”, Isradipine Dose (mg) was set to 7.5 and Isradipine Times Per Day was left at 1. Simulation was run for 6.5 hours and then for 3 years.
3. **Essential HTN+CCB-TGF**. Simulation was setup similar to Essential HTN+CCB simulation but with “Left Kidney TGF Clamp (xNormal)” and “Right Kidney TGF Clamp (xNormal)” clamped at 0.81, which was the baseline TGF level in this model. Isradipine was turned on as described above and simulation was run for 6.5 hours and then for 3 years. “0.81” can be typed in the box and then the “>” button to activate the clamp.
4. **CKD**. Control simulation based on low renal mass and increased salt intake. Salt intake was set to 293 mmol/day and Right and Left Kidney Nephron Count variables were set to 350,000. Erythropoietin levels were set to 15 mU/mL to account for chronic effects of renal disease. This was run for 2 weeks. Nephron count was then set to 278,000 with a 2190 day delay for similar nephron decline as the other models. This was run for 1 year for steady-state values. “Isradipine?” was left on “No” and simulation was run for 6.5 hours and then for 3 years and served as CKD control.
5. **CKD+CCB**. Simulation was setup similar to control. “Isradipine?” was turned to “Yes”, “Isradipine Dose (mg)” was set to 7.5 and “Isradipine Times Per Day” was left at 1. Simulation was run for 6.5 hours and then for 3 years.
6. **CKD+T/L CCB**. Simulation was setup similar to the CKD+CCB simulation but with “T-type Calcium Channel Inhibition” set to “Yes”. Isradipine was turned on as described above and simulation was run for 6.5 hours and then for 3 years.


HumMod : Integrative Biomedicine (v3.2.1)
File Go Stop Restart Options Tech Help
< > Circulation Respiration Metabolism Body Fluids Electrolytes Hormones ... Gender Nervous System Acid-Base Heat
Miscellaneous Organs Lifestyle Diagnosis Intervention Trauma Pathology Context Sizing
Chart
12:00 AM 0 Sec Mon Day 29
Gender = Male
Age = 37
Height = 70.1
Weight = 161
BMI = 23.1
Adiposity = Normal
Muscularity = Normal
ECG = Normal
- I'm feeling OK. -
Blood Pressure = 140 / 115 / 100
Temperature (F) = 97.6
150.
S
M
D
80.
100.
90.
0.
Time
40320.
BP (kPa) = 18.6 / 15.3 / 13.4
Temperature (C) = 36.5
Respiratory Rate = 12.0
Heart Rate = 79.0
20.
10.
90.
70.
Salt Intake
TGF Clamp
Nephron count
Essential HTN Level
Salt Intake (mEq/Day) = 180.
Atrial Receptor Time Constant (days) = 30.
Plasma ANG II Clamp = 0.
Plasma ANP Clamp = 0.
Left Kidney TGF Clamp (xNormal) = 0.
Right Kidney TGF Clamp (xNormal) = 0.
Right Kidney Nephron Count = 828000
Left Kidney Nephron Count = 828000
Essential Hypertension Level = 17.5
Isradipine? No Yes
Isradipine Dose (mg) = 7.5
Isradipine Controls
Isradipine Times Per Day = 1.
T-type Calcium Channel Inhibition? No Yes