SIMULATING A VIRTUAL POPULATION'S SENSITIVITY TO SALT AND UNINEPHRECTOMY

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README File
HumMod Version 3.0.4
http://www.hummod.org

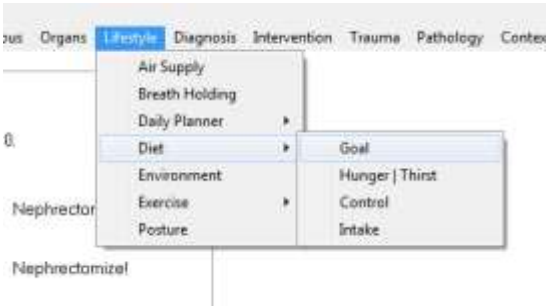
Overview

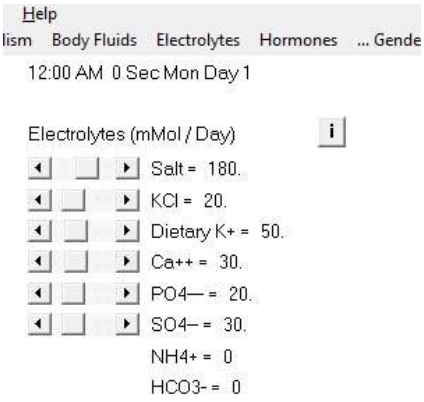
The model that was downloaded with this README file and related files are in a ZIP folder. To use HumMod, unzip it to the directory of your choice. HumMod can then be opened by running the executable file **HumMod.exe**.

HumMod is an integrated computer model of human physiology which allows the accurate simulation of the effects a person's changing environment can have on their physiology. It is developed and maintained by the University of Mississippi Medical Center, and is the successor to the QCP (Quantitative Circulatory Physiology) program.

Experimental Protocol

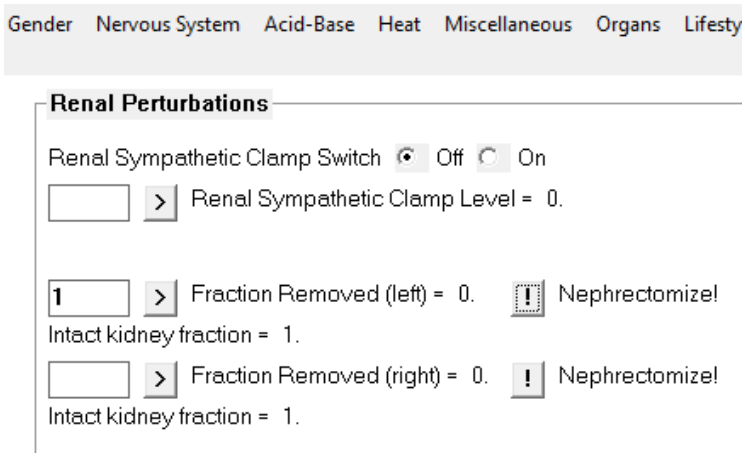
For this paper, patients (first normal, then with one kidney removed) were subjected to low, normal, and high salt intake (90, 180, and 720 mmol/day respectively) for 3 weeks at each salt level. First, run the model to reach steady state values for 2 weeks. Then, go to Lifestyle→Diet→Goal and change salt intake from normal (180) to a new level:





Restart the model, and simulate unilateral nephrectomy by running the model 2 weeks to get baseline, remove the left kidney, and then run the simulation again for 2 weeks to reach steady-state. Unilateral patients were subjected to the same salt loading protocol as before their kidney was removed.

To perform a unilateral nephrectomy, on the default page, enter 1 for a 100% removal of the left kidney, click the right arrow sign “>”, then click “Nephrectomize!”.

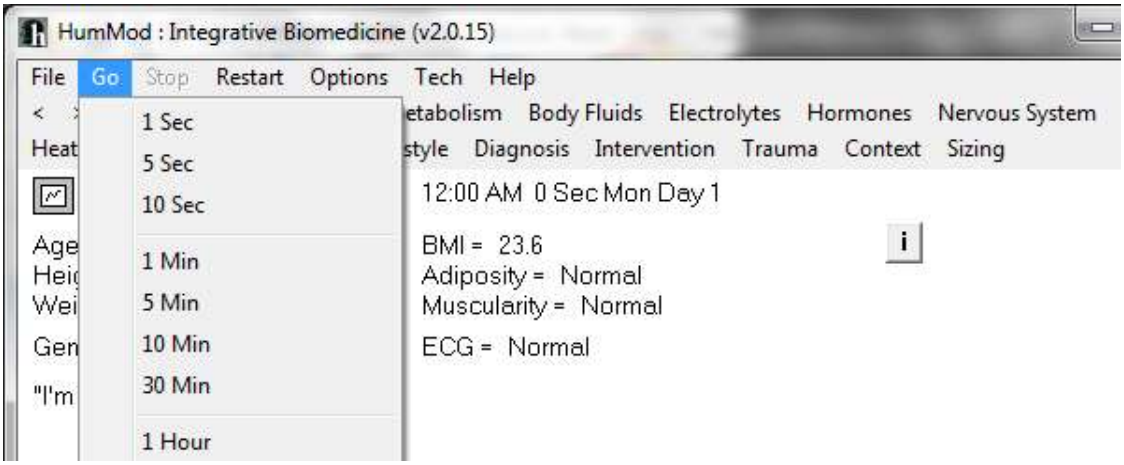


Detailed below are further instruction on the general commands, how to load initial conditions, and descriptions of the menu tabs.

General Use

When HumMod is first opened, it will be set to display the “Chart” results under the “Diagnosis” dropdown menu by default. The patient will also have the default characteristics of a 70.1 cm, 165 lb, 37-year-old man, existing in an uninteresting room temperature environment and following a fairly normal daily schedule. However, all of these parameters can be changed.

The most basic command in HumMod is the “Go” dropdown menu. Since solutions in HumMod are calculated as a function of time, time must be advanced in order to achieve results.

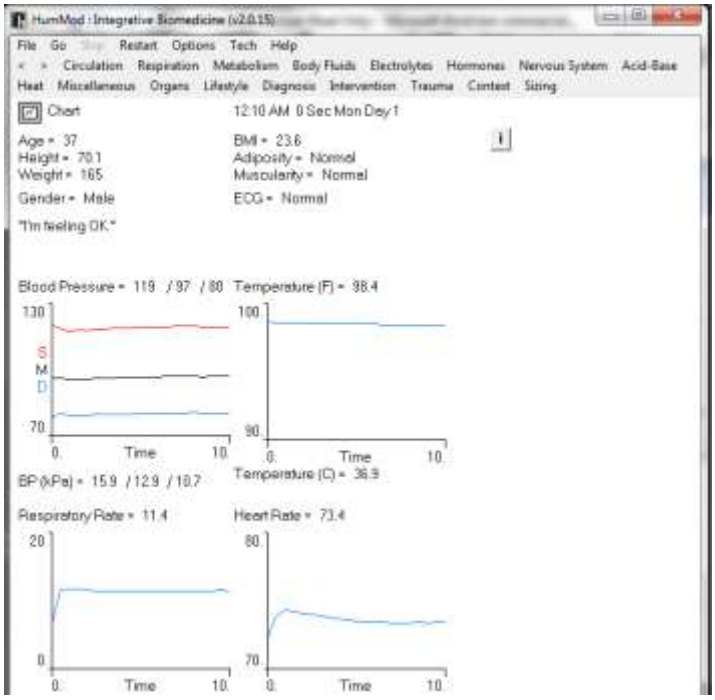


Advancing a patient under the default conditions for any period of time will yield predictable benchmark results. The “Stop” command can be used to pause the advancement of the simulation at any time if the user desires to examine a specific point or to change something before the simulation reaches its originally scheduled duration. The third command is “Restart”—this command immediately erases all data and sends the program back to its default parameters.

Running the model for 1 week will give steady-state values. Any variable changes before this represent the model settling. If the user wants to use the model many times with multiple experimental protocols, to save the user time, the model comes with a save/load feature.

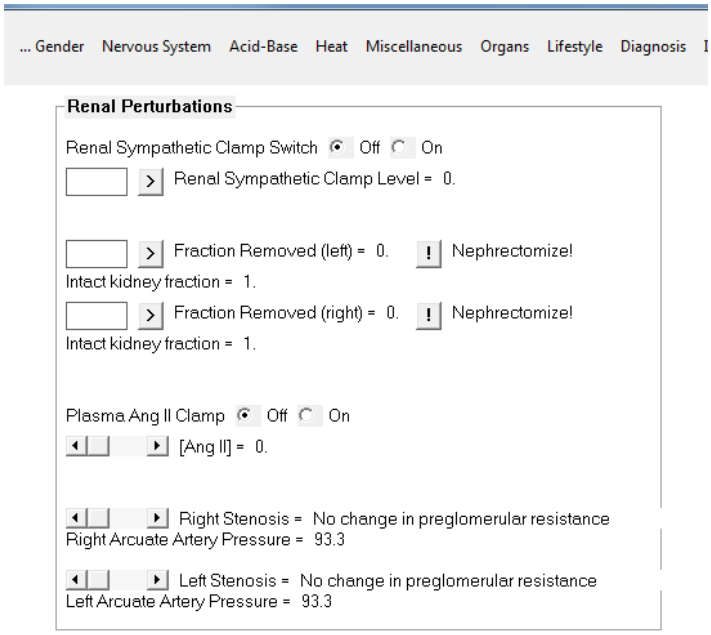
Basic Operation

Chart



Any advancement of time will yield results in ~8000 variables that run the program. For example, just opening the program and immediately advancing it some period of time will give you values for blood pressure, body temperature, respiratory rate, and heart rate. The figure to the left is the default Chart display which is opened up every time HumMod launches. Conditions are changed either through the use of radio buttons (used for options that are toggled on/off) or sliders (used to set variables which have many possible quantitative settings). Another important feature of HumMod's user interface are the information boxes contained in many of the displays. Clicking on these boxes will yield a dialog box yielding information, usually either the normal values in a human being for the variables in question, the units they are measured in, conversion factors for several units, or combinations of these three.

Renal Perturbations



Also on the Chart page are several renal perturbations that the user can perform. For the current study, the nephrectomy controls are displayed here (and described above). Another experiment available includes clamping renal sympathetic nerve activity (for example, to simulate sympathetically-mediated hypertension or renal denervation during high or low renal nerve activity, respectively.) Other experiments include clamping plasma angiotensin II levels or creating a renal artery stenosis.

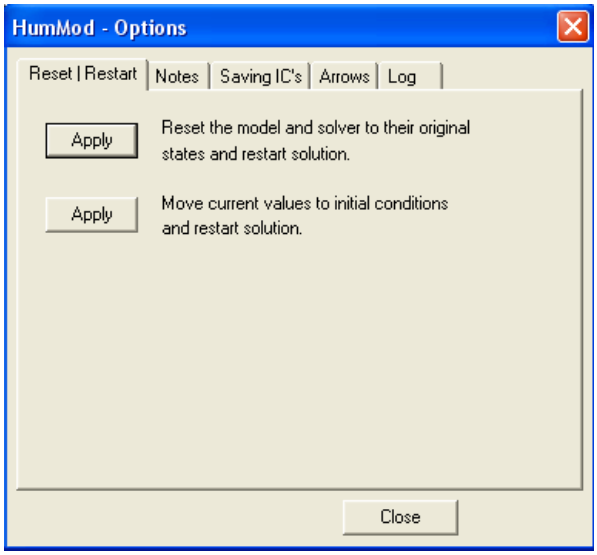
Please keep in mind that any experiment or perturbation performed by the user should be executed after the model has settled. For any experiment, run the model for at least 1 week or load a previously saved initial condition file (see next section).

Saving and Loading

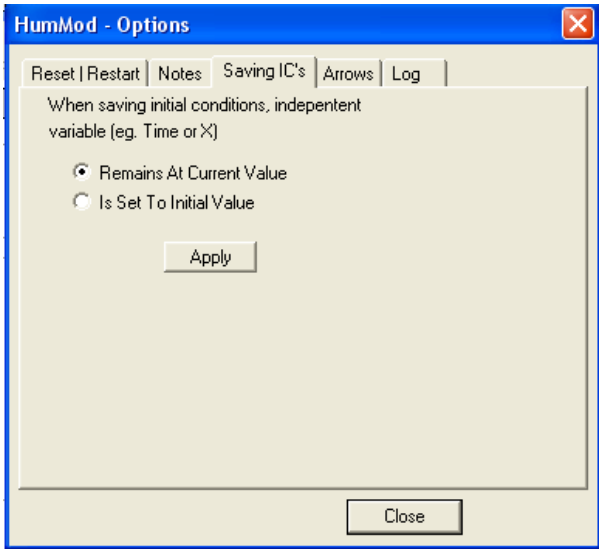
Saving a particular time point in the model can be done using an .ICS file. Initial conditions files can be loaded or saved using the ".ICS" file extension.
Before saving an initial condition file, the model must run to the desired time point, move the current values to initial conditions (under Options→Reset / Restart). If desired, the time point can be set to initial value (under Options→Saving IC's). *(See Below)*

These actions only have to be performed once. Afterwards, saving is done by File→Save Initial Conditions; and loading is done by File→Load Initial Conditions.
A sample ICS file, "2 Weeks", has been provided to establish a 2 week simulation (steady-state).

Options Window



The options window contains a couple of different subsets. The first tab is "Reset/Restart." There are two buttons under this category. Picking the first option will duplicate the action of the "Restart" button and clear all data while returning values to their default settings. Clicking the second button will reset the solution to time zero and initial conditions but keep environmental and physiological factors at the values they have been changed to.



The user also has the option to save initial conditions with a time of "0". This affects the time displayed at the top of the model.

Again, these actions only have to be performed **once** after you first download the model. Afterwards, saving is done by File→Save Initial Conditions; and loading is done by File→Load Initial Conditions.

Menu Tabs

This section is to familiarize you with what is generally found in the tabs of HumMod version 2.0.15. Keep in mind this is a general list, if you are looking for a specific variable you can look under the “Tech” tab and click on “Variables”.

Circulation:

The circulation tab holds the values for variables involved in the circulatory system. For instance, blood flow, blood pressure, and aspects affecting both the right and left heart pumping can be found in this tab.

Respiration:

Respiration holds the variables involved in the respiratory system. This can involve drive, total ventilation, and gas exchange.

Metabolism:

Metabolism shows the uptake, loss, use, mass, and concentration of several important molecules such as glucose, ketoacids, and urea.

Body Fluids:

Body Fluids tracks the volume, distribution, and several other factors of water, blood, and osmoles.

Electrolytes:

Tracks mass, concentration, use, uptake and gain of important electrolytes in the body.

Hormones:

Show the secretion synthesis and use of important hormones in the body. It can be hormones such as EPO or can be set to gender hormones such as estradiol.

Nervous System:

This tab shows the firing rate and sensitivity of the receptors in the body's nervous system. Also involves chemicals that affect the nervous system such as epinephrine.

Acid-Base:

This tab shows the pH and concentrations of hydrogen, pCO2, and SID in the blood.

Heat:

Heat shows the storage, transfer, and the loss of energy in the body. This also involves the temperature of sections of your body.

Miscellaneous:

This tab shows information on carbon monoxide, cell protein, Orthostasis, Pharmacokinetics, and the torso (upper, middle, and lower).

Organs:

This tab shows the structure, function, nerves, metabolism, and several other factors specifically for the organ you picked in the list.

Lifestyle:

Lifestyle allows you to set important parameters in the patient's life. These parameters include diet, posture, gas inflow, environment, and several others.

Diagnosis:

Diagnosis allows you to view overall information for the patient such as their chart or even an autopsy.

Intervention:

Intervention allows you to give treatments to patients to see how it affects patients with certain traumas.

Trauma:

Trauma allows you to set parameters that specifically place a patient under certain types of trauma such as hemorrhage, or myocardial infarction.

Pathology:

Under the pathology menu, the user has the ability to make the model have inadequate circulating insulin (Type 1 Diabetes) or insulin resistance (Type 2 Diabetes) as well as have Adrenal Insufficiency.

Context:

Context gives you (and lets the user set) specifics about a patient such as gender, fat, muscularity, height, and other parameters.

Sizing:

Keeps track of mass, volume and percent of organs, blood, and extracellular H_20.