Comparative Vertebrate Physiology 2005
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Introduction to *web*-HUMAN 6

(This introduction is designed to be used while also interactively running the *web*-HUMAN program)

Note: This write-up is divided into two portions. The *first* is a *general description* of what *web*-HUMAN is and will either be covered in class or be assigned to read at your leisure. The *second* is a nuts and bolts step-by-step *set of procedures* that teach you basic *web*-HUMAN skills. It is the latter that forms the core of this session.

I. General Introduction to *web*-HUMAN

What is *web*-HUMAN?

HUMAN is a mathematical model that simulates the integrated systems physiology of the human organism in both health and disease. This version was written/released in 1978-1984 by Tom Coleman at the University of Mississippi Medical Center and has since been maintained, modified and put into web format at Skidmore College. The model is comprehensive, encompassing 6 major core systems (cardiovascular, respiratory, renal, fluid balance, acid-base balance and thermoregulatory) and aspects of 3 other systems (nervous, endocrine and muscle metabolism). With each iteration of the model, approximately 137 user accessible physiological variables are computed and updated. In running a simulation, the user may manipulate one or more parameters from a list of 67 alterable physiological, environmental and clinical factors. The value of such an integrated comprehensive systems physiology model is defined and discussed further below.

The version you are now working in, *web*-HUMAN 6.0, provides a web 'front end' to the model that allows users to

- access the model via the web (http://www.skidmore.edu/academics/human).
- input values and variables desired for their experiments via a familiar web interface.
- view outputs in a web format.
- access on-line help and many sample simulation labs.

How will we use *web*-HUMAN in this course?

Several of our laboratory sessions will involve running experiments using the *web*-HUMAN model to generate data. In this way we will *simulate* actual experiments (traditionally done on animals and/or too complex to perform in lab) that illustrate how mammalian systems respond to various stresses and perturbations imposed on them. For example, on the basis of your lecture/text derived knowledge of respiratory physiology you might be asked to predict how the human respiratory system would respond when a normal human subject moves to a mountain top (high altitude). You can then test your predictions by running the *web*-HUMAN model under conditions of simulated high altitude (i.e. low barometric pressure). The model will generate data not only about the responses of the breathing apparatus (respiration rate and depth) but also alterations in blood gases, acid-base balance, renal and cardiovascular changes, etc.

After a short bit of practice with this computer simulation, you will begin to appreciate the *interrelated functions* of whole animal physiology. Furthermore, you will work with *quantitative data* and become familiar with the *normal ranges* of standard physiological measurements. With experience, students will develop a knowledge of what constitutes normal (and abnormal) values for several physiological variables and clinical readings.

What are some key features of the program one needs to know in order to run *web*-HUMAN?

Inputs- In order to manipulate the program and understand its output, one needs to be familiar with the abbreviated names (code) for the variables and parameters and the units of measurement associated with each. Since there are more than 150 *variables* (i.e. physiological phenomena that vary in response to conditions) and *parameters* (i.e. factors of the physiological, environmental or clinical situation that the experimenter can manipulate), one cannot memorize them all! One can get information about the variables and parameters in three ways: 1) as a *printed list* that we sometimes provide in classes, 2) as *a searchable list* linked to the main *web*-HUMAN page, or 3) called up one by one (if you know or can recognize the abbreviation) by clicking the program command "View Variable".

Outputs- There are four ways of retrieving output from a *web*-HUMAN simulation run. The most information is gained by tracking as many as six variables in time through the tabular output of the program. Prior to computing a simulation, the experimenter selects which variables are to be displayed in the View Output table, determines the total length of time over which the simulation will be run, and decides the frequency of sampling of the variables within the total time frame. As the model is computed, a table of values is generated that shows the time course of the physiological responses.

At the end of any simulation run, one can retrieve the "current" value of any variable or parameter at that particular point in time by using the "View Variable" command. Similarly at the end of a simulation run, the current values for a group of related variables can be displayed using the Obtain ..Help, Extra Data or Charts: option.

Finally, in version 6.0 or higher, users can graph the data by having picked the graph option instead of text in the View Output section. For example, one can display a chart of blood gases as measured at the stopping time point. Users have the opportunity to graph the response pattern of any of 1 to 6 variables in any of four Graph Styles (see screen, lower right).

II. Practice in using *web*-HUMAN

Practice using *web*-HUMAN
Call up *web*-HUMAN by going to http://www.skidmore.edu/academics/human and click on <**Run**>.

1. Finding Values for Variables (and familiarization with *web*-HUMAN variable names)

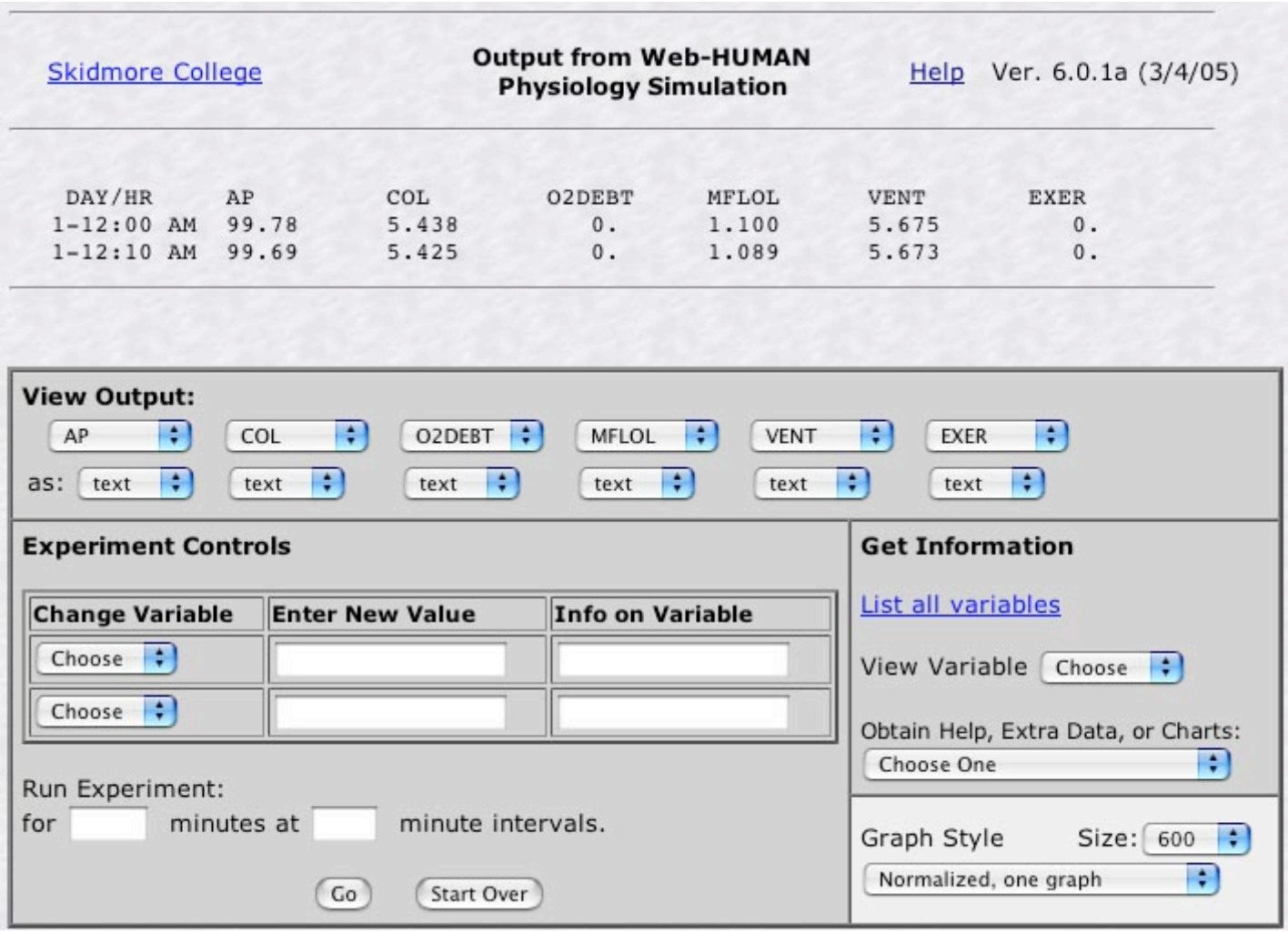
A. **Use the printed lists*** to find the normal values for the following variables:

Note- We will **NOT** be using printed lists in this class but you may wish to use this option at some time in the future.
* Users can at any time print out their own variables list hard copy by clicking on the List all variables option (see below) and printing the list.

B. **On-line variables list access** –
- Load *web*-Human if you have not already done so. (http://www.skidmore.edu/academics/human).

- The default values for the "Run the Model" commands are "OK as is" for this step, so simply click the <**Run**> button.

From the <List all variables> option on the main *web*-HUMAN page control panel access the *web*-HUMAN Variables and Parameters list. You can then use the Explorer, Safari or Firefox Edit menu's "Find... " feature (CMD-F) to search for key words or parts of words that occur in the lists. Multiple Finds can be achieved by selecting "Find Again.." (CMD-G).



Let's go through the four below *as a group*.

Code	Variable or Parameter	Normal Value	Units
BV	Blood Volume	_____	_____
HCT	Hematocrit	_____	_____
IFV	Interstitial Fluid Volume	_____	_____
ARVOL	Artificial Respirator, Tidal Volume	_____	_____

Try each of these *on your own* and then *stop* for group discussion.

Code	Variable or Parameter	Normal Value	Units
_____	Blood Lactate	_____	_____
_____	Ambient Temperature	_____	_____
_____	Pulmonary Membrane Surface Area	_____	_____
_____	Muscle Oxygen Debt	_____	_____

C. **Using the model's <View Variable> option**- Use the *web*-HUMAN program itself to find the values necessary to complete the table below.

To look up the variables and their normal values, pull down the menu next to "View Variable - Choose" section and scroll through to choose a variable. Then at the bottom left of the screen click "Go". When the data are returned, you will find the most recently updated information (i.e. your requested variable) at the bottom of the "**Output from Web-HUMAN Physiology Simulation**" section.

Code	Variable or Parameter	Normal Value	Units
PH	_____	_____	_____
MFLOL	_____	_____	_____
SWETC	_____	_____	_____
VENT	_____	_____	_____

2. Changing Table Column Headers

The most common method of tracking *web*-HUMAN output is to place the variables of interest in columns in a table. This allows one to follow their progress through time. The section below gives you practice in this task.

A. Begin a new simulation by clicking on "**Start Over**" to return to the initial *Web*-HUMAN page.

B. Select Experiment number 2, for 30 minutes, print every 5 minutes and then **Run** the model.

C. In the "**View Output:**" section, pull down the menu for any table location .

D. Use the scrollable menus (e.g. AP, COL) to set the column headings as indicated *below*. Look up the missing information by any one of the methods practicedpreviously.

Column	Code	Variable or Parameter	Units
2	RESPRT	_____	_____
3	_____	Tidal Volume	_____
4	_____	Arterial Oxygen Content	ml/ml
5	PCO2A	Arterial CO2 tension	_____
6	_____	Blood PH	pH units
7	CO	_____	ml/min

F. Now click "**Go**" to enter your changes to the table. The resulting output will inform you of the current values for these variables. Notice that these tables have been chosen to read out values appropriate for a respiratory experiment.

3. Run a High Altitude Experiment

A. Once you have set up the table (as above) to record variables related to respiratory function, one is well poised to conduct an experiment revealing the responses and stresses created by altitude ascent. What is the basic stress encountered when one moves to a high altitude? What are the physiological responses to this and succeeding perturbations? What are the variables that trigger these responses?

B. Test your predictions by continuing to run the *web*-HUMAN program. As you already have your table set up in View Output: , the next step is to alter the environmental conditions to simulate high altitude.

- First, click on one of the menus in the section entitled "**Change Variable - Choose**".
- Then, scroll to the variable BAROP (barometric pressure). The default value appears in the Info box on the right.

- Enter a numerical value for barometric pressure that is one-half the normal pressure at sea level. Do not enter units, only the numerical value
- Click "**Go**" to put this change into effect. You will see an Output from web-HUMAN that verifies your change.

C. Run the experiment (Run Experiment option) for 480 minutes at 30 minute intervals (enter these numbers into the boxes) and click "**Go**".

D. Review the results and answer the following questions. (You will find the textbook index item Altitude to be useful in educating yourself somewhat more on high altitude)

Over the eight hours at high altitude, how did your subject's breathing pattern change? How rapid was the onset of these changes in breathing pattern? What was the magnitude of these changes?

Though your subject is working harder to ventilate his lungs, is he maintaining a normal level of oxygen in the arterial blood? Characterize the time course and magnitude of changes in his blood oxygenation.

Has the heart function been affected? If so, what factor(s) may have caused the change?

E. Observe the CO2 and PH responses graphically*.
=> Turn off your browser's pop-up window blocker as *web*-HUMAN generates graphs in a new (i.e. pop-up) window. Pop-up control- (Safari – under Safari menu / IE – under the Tools menu) .

To set up for graphing:
- use the browser *Back button* to return to the previous screen (where you input time [480 min.] to run and hit Go).

- in the **View Output:** section notice that for any variable you can choose **as: text** or **as: graph**.
- for PCO2A (column 5) and for PH (column 6) pick **as: graph** with your mouse.

- notice (lower right) the default Graph Style is normalized, one graph. (one graph = plots all variables on a single graph, normalized = plots the change i.e. the current value of the variable relative to the initial value)

- to run your experiment and create the graphic output mouse click the "**Go**" button.

What effect does the hyperventilation have on your subject's blood carbon dioxide? Why does this happen?

The amount of CO_2 in the blood is a crucial factor in determining the pH of the blood. Based on the results of your experiment, is dissolved CO_2 an acid or a base? Explain.

* (It is always a good idea to Close graph windows after using them as they take up extra memory)

F. If you wish to also graph your high altitude data in Excel click Help and follow the instructions under the link "Graphing *web*-HUMAN data in Excel."

web-HUMAN has many other capabilities not covered today that you will use later in the course. Of these the most important is that you can Save/Retrieve/Share with others your experiments. Step-by-step instructions on this and a similar altitude experiment can be accessed by simply clicking on Help.