(adapted from Spring 2002 Comparative Vertebrate Physiology - Skidmore College - by Loretta Parsons & Roy Meyers)

Introduction to *web*-HUMAN

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

What is *web*-HUMAN?

HUMAN is a FORTRAN mathematical model that simulates the integrated 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. 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 themodel, 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 version you are now working in, *web*-HUMAN 4.0, 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 the values and variables for their experiments via the familiar web interface.
- view outputs in a web format.
- access via the web on-line help and many sample simulated labs.

How will we use *web*-HUMAN in this workshop (and in your courses)?

Our workshop 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 human systems respond to various stresses and perturbations imposed on them. For example, from their knowledge of respiratory physiology you might ask students to predict how the human respiratory system would respond when a normal human subject moves to a mountain top (high altitude). They can test their 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, your students will begin to appreciate the *interrelated functions* of whole animal physiology. Furthermore, they 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 200 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 *web*-HUMAN web 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 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 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 ..extra data or charts feature. For example, one can display a chart of blood gases as measured at the stopping time point. Finally, Version 4.0 also offers the opportunity to graph the response pattern of any two of the variables.

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 workshop but you may wish to use this option with your classes depending on their ability to "not misplace" their lists from class to class.

* 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. (The address for the *web*-Human Front End page is 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 HUMAN output page control panel access the *web*-HUMAN Variables and Parameters list. You can use then use the Netscape or Explorer "Find on Page" feature (CMD-F) to search for key words or parts of words that occur in the lists.

Lets 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 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 section.

Code	Variable or Parameter	Normal Value	Units
PH	______________________	__________	________
MFLOL	______________________	__________	________
SWETC	______________________	__________	________
VENT	______________________	__________	________

2. Changing Table Column Headers

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 "**Change Table Columns**" section, pull down the menu for any table location (2-7).

D. Column 1 is always reserved for time (i.e. Day/Hour).

E. Use the scrollable "**Change Table Columns**" menus to set the column headings as indicated below. Look up the missing information by any one of the methods practiced above.

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.

3. Run a High Altitude Experiment

A. Once students have set up the table (as above) to record variables related to respiratory function, they are 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 their/your predictions by continuing to run the *Web*-HUMAN program. As you already have your Tables set up, 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.
- Click "**Go**" to put this change into effect.

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.

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*.
Use the "Graph the latest data" option (lower right), picking column 5 (the CO2 data) and column 6 (PH) and click on "**do it**".

What effects 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)

Note: The student version of this introductory exercise is available on the opening *web*-HUMAN screen at the link "About HUMAN - an introduction."