



Respiratory Physiology

(Human 6.1 - Version Oct. 09, 2006)

Review- 1) Regulation of Resp. (Schmidt-Nielsen pg. 33-, 2) lecture notes on regulation and 3) the "sample scientific paper"

The computer modeling project for this week encompasses two main concepts in respiratory physiology. First, you will examine the well-characterized phenomenon of the response of the air ventilating mammalian respiratory system to **changing levels of pCO₂** in the arterial blood. Secondly, the functional importance of **dead space** in the vertebrate respiratory system will be explored.

I. REGULATION OF RESPIRATION - Role of Arterial Carbon Dioxide (PCO_{2A})

Introduction

The mammalian and avian respiratory systems are evolutionary very well-adapted to supply oxygen to support the rapid metabolism of these organisms. Surprisingly, the neural control centers for respiration are keyed *not* to the oxygen content or concentration of blood but rather to the *carbon dioxide* concentration (pCO₂) of the cerebrospinal fluid and blood. Through the *web-HUMAN* model, you may examine the sensitivity of respiratory system ventilatory responses to increasing content of CO₂ in the inspired air. The corresponding changes in acid-base balance and blood gas content may also be monitored.

Your objective is to design & run an experiment in which you achieve a range of arterial pCO₂'s [PCO_{2A}] and observe how ventilation varies as a function of pCO₂. In order to do this, you will need to generate a range of arterial PCO_{2A} values at, below & above the normal value (\approx 38 mmHg) and observe the corresponding changes in lung ventilation (**VENT**).

- To achieve above normal pCO₂'s you will raise the CO₂ fractional concentration in the air ventilated by the model (FCO_{2AT})* . Higher FCO_{2AT} levels naturally result in higher arterial PCO₂ values. [You can teach yourself the basics of FCO_{2AT} control by simply mousing Help Info on: FCO_{2AT} in the **Help** section].

- To achieve below normal pCO_{2A}'s, you will lower the CO₂ production rate (basal metabolic rate, BMRB) of the model. You must resort to lowering CO₂ production because normal FCO_{2AT} is already zero at baseline (i.e. atmospheric air normally has virtually no CO₂ in it) making it quite impossible to lower it any further. [You can teach yourself the basics of BMRB manipulation by simply mousing Help Info on: BMRB in the **Help** section].

* Note that while it may be possible to look up the value of dead space in the model, the objective here is to determine it graphically.

Procedure – Respiratory Regulation

A) Initialize <Run>, selecting Experiment #1, and run for 5 min. with 5 min. between printouts.

B) The variables to be monitored as time progresses are:

Ventilation, total (**VENT**)
Tidal volume (**TIDVOL**)
Respiration rate (**RESPRT**)
Arterial pCO₂ (**PCO2A**)
Arterial pO₂ (**PO2A**)
pH of the blood (**PH**)

Use the "View Output ..." section to set these up in columns 2-7.

Continue <Go> for 5 min. with 5 min. between printouts to verify your new tables settings and gather baseline data.

C) Increasing pCO₂ levels

Once you have established a baseline for these new table values (you now have the FCO2AT=0 value), Run Experiment: for 1 hour at 30 min. intervals *after* having him/her breathe 1% CO₂ by changing the parameter of fractional CO₂ (FCO2AT) in the atmosphere. **FCO2AT** may range in value from 0.0 (0% CO₂, the 'normal' value) to 1.0 (100% CO₂). Think about what value of FCO2AT you would assign to obtain a 1% CO₂ breathing mixture (Hopefully, you answered 0.01). Watch the changes in the above (tabular) physiological variables for one hour and record the values at the one hour time.

Repeat the procedure four more times, each at an increasing level of CO₂ (not to exceed 10-12%) each time recording results at 1 hr.. [Important: For each new FCO2AT start with a new subject that is, (<Start Over> each time. If you do not do this, you will be running a different experiment than you think you are! To retrieve most of your new View Output: settings, simply use your browser's back button.]

You now have 4-5 arterial pCO₂ values *above or at* the normal value and their corresponding lung ventilations. Record them. You will next generate pCO₂ values *below* normal.

D) Decreasing pCO₂ levels below normal

It is impossible to lower the atmospheric CO₂ below zero. Therefore, to achieve subnormal pCO₂ values we resort to a different tactic, lowering CO₂ production (i.e. lowering metabolism)

Design an experiment where the blood levels of CO₂ are lowered by decreasing the basic level of basal metabolism (**BMRB**) and therefore the CO₂ production rate. Obtain 3-4 sets of values for various lower levels of CO₂. Since your objective here is to lower pCO₂, 'eyeball' the PCO₂ values resulting from your decreases in BMRB for significance. Certainly, they should each be at least 1-2 mmHg or more pCO₂ below each preceding higher value. Record these values also.

The overall experimental objective is to achieve a total of 8 or more different levels of blood pCO₂ , 5 higher than normal, 3 noticeably lower, and to record the level of ventilation associated with each.

II. DEAD SPACE DETERMINATION

Introduction

The lack of unidirectional respiratory medium flow in non-avian air ventilators creates the existence of an anatomical dead space. The anatomical dead space of an air ventilator is a fixed volume not normally under physiological control. However, the relative *importance* of dead space is adjustable by appropriate respiratory maneuvers. The use by panting animals of their dead space to reduce a potentially harmful respiratory alkalosis is a good example of such a maneuver. In general, for any given level of lung ventilation, the fraction of the tidal volume attributed to dead space will affect the resulting level of alveolar ventilation, and therefore the efficiency (in terms of gas exchange) of that ventilation. [You should, of course, refresh your knowledge and be able to distinguish between total ventilation and alveolar ventilation.]

Your objective here is to observe the effects of a constant "unknown" dead space on resulting alveolar ventilation by respiring the model at a variety of tidal volume-frequency combinations. You are then asked to calculate the functional dead space based on the data you collect.

Procedure

The HUMAN model allows you to control tidal volume and frequency by putting the subject on an artificial respirator. You must first <Run> a new subject i.e. <Start Over> and select the following variables (in View Output:) for your tables:

Ventilation, total	(VENT)	
Tidal volume	(TIDVOL)	<-These are the actual resulting tidal volume and resp.
Respiration rate	(RESPRT)	<-rate regardless of whether under control or 'natural'
Arterial pCO ₂	(PCO2A)	
Arterial pO ₂	(PO2A)	
Alveolar ventilation	(AVENT)	

Controlling respiration with the artificial ventilator

HUMAN contains the ability to simulate the function of various organs/systems artificially (an artificial ventilator, heart, kidney, etc.). In each case there are two logical steps

1) Your 'throw' a switch (set from 0 to 1) to tell HUMAN *you* are taking over the job of running that organ.

2) *You* then have the responsibility, on your own, to set the level of those (parameters) properly (or the model will usually die ... no heart, no respiration, etc.).

In this particular case today you need to 1) set the respirator switch to ON & 2) control VENT (rate & frequency) on our own. [Note that you can teach yourself the basics of respirator manipulation by simply mousing Tips: Artificial Respirator in the **Help** section].

a) Turn the artificial respirator switch on [**ARTRES**=1 turns it on, **ARTRES**=0 turns it off, its' default is 0]

b) Run the experiment for 0 min. at 0 min. intervals to verify having successfully turned on the respirator and

c) set the respirator rate (**ARRT**) and respirator volume (**ARVOL**) at levels (approximately) equal to the subject's normal levels (what were RESVRT & TIDVOL before you turned the respirator on?).

d) Run the simulation for one min. with one min. between printouts and record values at that time.

Note that the resulting physiological variables (RESVRT, TIDVOL) should now be completely under the control of the values you set on the ventilator (ARVOL, ARRT). Be aware that it is a very common error to set the respirator rate and volume but forget to turn the respiration on (**ARTRES=1**). Also beware running the model for long time periods as some of your ventilator settings are potentially fatal.

e) Repeat the procedure with a new subject three times, each time **raising respirator tidal volume** and lowering the rate to achieve a total lung ventilation (VENT= rate x volume) equal to your control run above. For example, if your VENT started at 6.00 L/M (i.e.. 12*500) then raising the tidal volume to 1000 & dropping the rate to 6 will achieve the same VENT (6.0 L/M). You can retrieve the above View Output: tables settings by simply using the *back button* on your browser to restore the screen at which your ventilator is already turned on but volumes and frequencies have not yet been set.

Then repeat the procedure with three **lowered tidal volumes** and appropriate calculated respiratory rates. Record all your values.

The objective is to achieve 6 runs in addition to the control run, all with the same level of lung ventilation (VENT) but differing resulting alveolar ventilation.

The assignment [short write-ups are worth 1/3 of full papers]

Pick either choice 1 or 2 below and turn your work in before leaving lab.

1) Ventilation-pCO₂ relationship- From your data (part I), plot ventilation as a function of arterial blood pCO₂. *Briefly*(!!) summarize the nature of the relationship you obtained in HUMAN and compare it to the classical relationship (Neilson ACTA Physiol. Scand. 1952, 24:293-313) (see figure in the sample paper).

2) Dead space determination* - The objective is to determine *graphically* the functional dead space from the data you have collected. The simplest way is to plot a graph of AVENT vs. TIDVOL. From the graph, very briefly answer the following two questions: a) what is the value of the functional dead space? b) What was your reasoning?

2a) A more elegant way to attack the analysis is to ask at what tidal volume does the dead space *ventilation* become equal to the total ventilation? To do this you will need to calculate & add to a data table you construct the dead space ventilation for each volume-frequency pair. Then proceed to answer the two questions above (a & b).

* Note that while it may be possible to look up the value of dead space in the model, the objective here is to determine it graphically.

Reminders: Please type all text sections. All labs due before you leave today.