A STEVE SHARATE

MG

A Multicompartment Model of Respiratory, Renal, and Anatomical Contributions to the Regulation of Body pH Levels

INTRODUCTION: Life is compatible with only a small range of blood pH values, which the body sustains magically through the combined action of respiratory rate, renal filtration, and blood buffer regulatory mechanisms, all interrelated. This model attempts to simulate the interplay.

The enzymatic machinery that allows us to live operate efficiently only within the pH range of 7.35-7.45, termed "normal" physiological pH, and so it is imperative that the body maintains pH within this range. The systems employed by the body culminate into an enormous *buffering capacity*, which is the ability of a system to withstand changes in net proton flow with minimal pH fluctuation.

BACKGROUND:

pH In The Body - The area of concern is the pH of the blood, because it is representative of the body's state of affairs as a whole, as it serves as the common exchange route between individual cells and the external environment to which excess wastes are vented and from which needed nutrients are obtained. The pH of a solution is defined as the inverse logarithm (in base 10) of the concentration of hydronium ions (moles per liter):

$$pH = -\log_{10}[H^+]$$

A change of 1 pH unit reflects an alteration in free proton concentration by a factor of ten.

The body's pH has the potential to change for a number of reasons. The first reason is that many metabolic processes in the body are inherently acidic: insufficient oxygen supply to the muscles during physical activity results in the formation of lactic acid as a metabolite, keto-acids are formed as a result of low glucose availability (starvation), and other examples are readily available. Overall, metabolic processes contribute about 50-90mEq/day of fixed acid. The second reason a blood pH may change is due to pathology. Excessive vomiting causes an enormous loss of gastric hydrochloric acid, which can elevate pH to dangerous levels. The kidney must keep watch over the body's pH and adjust its excretion/reabsorption behavior accordingly. When it fails to due this job, the risks are obvious. Also, consumption of acidic foods is unavoidable, and if left unaccounted for, this factor alone could be fatal. Finally, respiratory behavior is directly tied to blood pH, discussed in the following section.

Buffers and Their Importance in the Human Body

Acids can be defined as a molecular species capable of contributing a free proton to aqueous solution, and *bases* are those that can accept free protons. A brief review:

AH <-> A- + H+

A proton donating species (AH) dissociates in aqueous solution into its *conjugate base* (can accept protons) and a proton, the extent of which depends on a property of the acid called its **pKa**. This is the pH at which half of the acid species is in its proton donating form, and half exists dissociated.

pKa = pH when [A-]/[AH] = 1

This has an important consequence. **Buffers** are acidic species capable of attenuating the pH changes associated with proton infusion/loss in a system by either accepting excess protons (the dissociated form acting as a base) or by donating protons (as an acid) to the system, thus acting to compensate for [H+] change. Imagine the case of pure water, who's pH is 7 (chemically neutral) by definition: adding an amount of protons to such a system translates *directly* to an increase in free protons in solution ([H+] is synonymous with [H3O+].) Buffers have the capacity to exchange protons with the aqueous environment. Of course, if a proton flux into/out of a system is sufficiently large, all of the pertinent buffer species will eventually be used up and its presence will become insignificant.

Different buffering substances act optimally under different conditions. But one thing remains true. Buffers are most effective in a solution who's pH is close to the buffer's pKa. This is because, at pH close to the pKa, there are the largest relative amounts of both forms of the buffer exist to either donate or receive protons as needed.

One can calculate the pH of a buffered solution based on the concentrations of the two forms of the buffer. This is the **Hendersen-Hesslebach(?) Equation:**

pH = pKa_Buffer + log([A-]/[AH])

This is the nature of chemical buffer capacity. What buffers exist in the human body to guard against abrupt pH changes? The major buffering is done through the **carbonic acid system**.

HCO3- + H+ <-> H2CO3

Carbonic is an extremely strong acid with a pKa of about 2.5. Since buffers act optimally at pH's near their pKa's, it is unobvious why something with such an absurdly low pKa should have anything at all to do physiological buffering. Part of the answer is that the above equation is only part of the picture. Carbonic acid also dehydrates, existing in equilibrium with water and carbon dioxide.

HCO3- + H+ <-> H2CO3 <-> H2O + CO2
Carbonic Anhydrase

The enzyme carbonic anhydrase catalyzes in vivo CO2 and H2O conversion to carbonic acid, and vice versa, and is exceedingly important in the whole regulation process. The pKa of this expanded system has a value of 6.1, much closer to physiological pH, but still not close enough to be an obvious buffer.

In the erythrocyte membrane, carbon dioxide waste from active cells is converted quickly and easily into carbonic acid by the enzyme and dissociates into a proton and bicarbonate ion. About 67% of the carbon dioxide in the human body is carried via bicarbonate, with the accompanying amount of free protons. Thus the level of CO2 in the blood has an acidic effect on blood pH.

The acidic effect is accounted for, however, in the pulmonary cappilary bed, where bicarbonate and proton meet again to form carbonic acid, are converted to CO2 and H2O by carbonic anhydrase, and the CO2 is vented through diffusion into the lung and exhalation by animal. Therefore protons are constantly being removed from the blood as carbon dioxide is exhaled, being fixed into benign H2O.
The final factor making the carbonic acid/bicarbonate system the buffer of choice is the volatile nature of carbon dioxide.
Since CO2 is easily, constantly, and quickly removed from the bloodstream, so exists the mechanism to decrease body pH.

A final addition to the system comes in the form of chemosensory changes in respiration rate. High CO2 levels signal the brain to increase breathing rate and volume in the hopes of expelling more CO2, faster. This taken into account, the buffering capacity of the system is increased further.

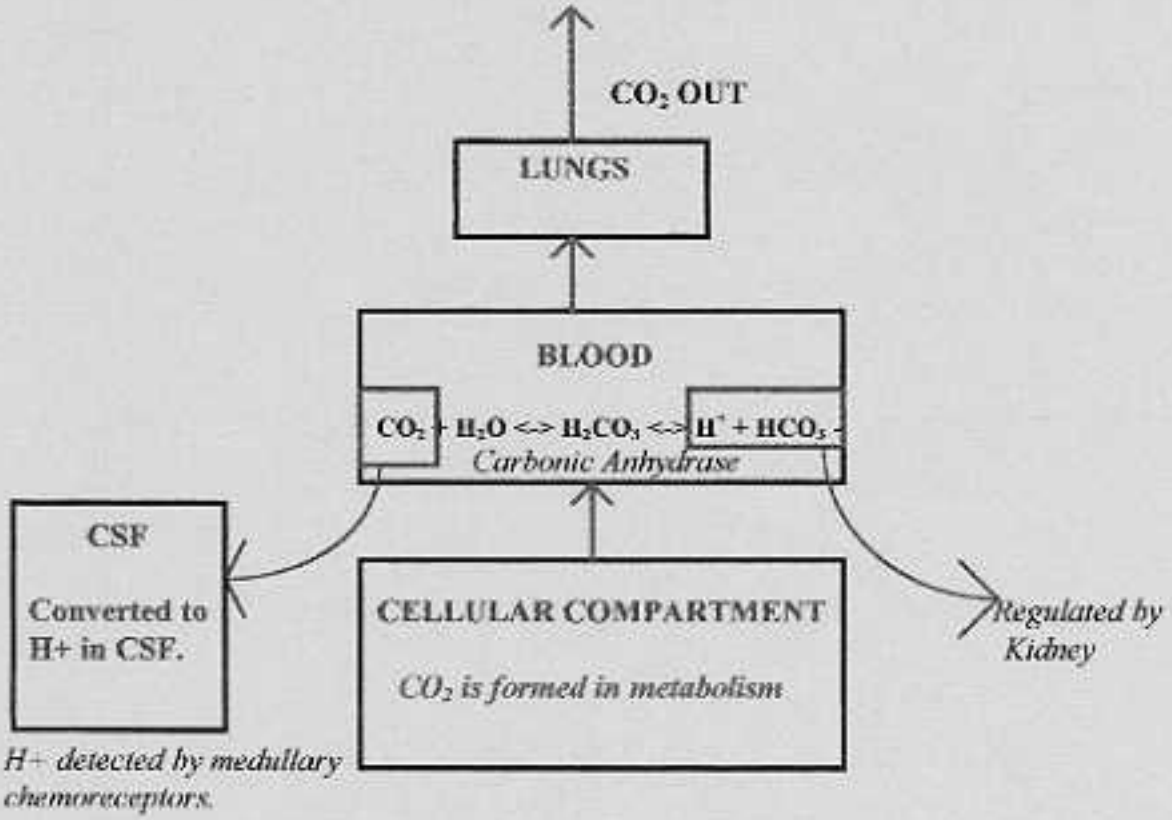
Other Buffering Systems in the Body: Other species exist within the blood that act as buffers, such as hemoglobin and phosphoric acid, but the bicarbonate is by far the most important and efficient.

To illustrate the point, consider the experiment in which a dog is transfused with 161 mEq of hydrocloric acid. The plasma pH went from 7.4 to 7.10. *Had the dog no buffers, the pH would have fallen to 1.84, low enough to melt steel and certainly incompatible with life!*

The Role of CO2
As stated, CO2 exists as a vehicle for transfer of acid (via carbonic anhydrase and bicarbonate) out of the body by the breathing process. It is also a standard bi-product of cell metabolism and is desireable to the body only in small quantites.

The main importance of CO2 to the body is that of a chemical indicator of respiratory needs.

FIGURE 1 - *The basic life of a CO2 molecule in the body. It is excreted by cells as a product of metabolism, and enters the bloodstream where it quickly attains equilibrium with protons and bicarbonate via carbonic anhydrase. CO2 readily diffuses across the blood-brain barrier into the CSF and stimulates breathing centers by lowering pH. Protons have a more difficult time diffusing.*



The Role of O2

Oxygen plays a role in regulating respiration as well and its levels are detected by via *peripheral chemoreceptors* located in the aorta and the carotid arteries. However, the effects of pO2 aren't expressed by the body until pCO2 is raised beyond a certain threshold level. For the purposes of this model, the regulatory effects of oxygen are ignored and carbon dioxide dominates.

Respiration

Respiration is the means by which gas exchange occurs between an organism and its environment. An organism seeks to discard carbon dioxide and obtain oxygen, the biproduct of and fuel for cellular energetics, respectively.

Diffusion of the gasses occurs across the lungs alveolar tissue. Expanding and contracting the lung space (breathing) ventilates the alveolar space and provides fresh air for transfer. The rate at which this needs to be done (breathing rate) and the size of each breath (tidal volume) are both variables which are subject to the respiratory regulation mechanisms of the body.

Inspiration is an active process requiring expendature of energy to move the diaphragm, and is signaled by the phrenic nerve. Expiration is normally passive, being due to the elastic recoil of the respiratory machinery: lung tissue, thoracic cage, and muscles.

Two values generally describe a respiratory state. The breathing rate (BR) is the number of breaths taken in a minutes time, and the tidal volume (TV) is the size of each breath measured in liters. The Respiratory Minute Volume can be calculated, and represents the amount of air "moved" in a minute's time:

$$\mathbf{RMV = (TV) \times (BR)}$$

However, there exists a portion of the lungs volume that is incapable of performing gaseous exchange. This is referred to as the conductive zone, or **dead space.** If one is interested in the amount of fresh air actually ventilating the alveolar, or gas-exchange, volume, one must account for the dead space air:

$$\mathbf{Alveolar\_Ventilation = [(TV - deadspace) \times (BR)]}$$

This equation implies that a breathing pattern of shallow, quick breaths is less efficient at ventilating the alveolar spaces than one of deeper, slower breaths. The consequences of this are explored in the experimentation section.

Diffusion of gasses across the alveolar wall is governed by the difference in pressure, between the lung and blood, of each gas. Gasses are usually spoken of in terms of their *partial pressures*, or the fraction of any total pressure (in the atmosphere, in solution in water, in the blood) due to the presence of that gas. It is measured in millimeters of mercury (mmHg), equal to the total pressure multiplied by the quantitative percentage of total gas that the gas of interest accounts for:

$$\mathbf{pGAS = pTOTAL \times [GAS/(Total\_Gas)]}$$

In must be remembered that this is an approximation, assuming that the gasses are "ideal."

So the difference in partial pressures across a diffusional barrier influences the rate of flow, along with what is called the *diffusion coefficient* of the gas for a given system.

Diffusion_Flow = dm/dt = D_Gas x (P1 - P2)

The diffusion coefficient contains temperature, molecular weight, barrier thickness, diffusional area, and *solubility* information. The solubility coefficient (S_Gas) of a gas tells how much gas (in mL or moles) will enter solution if the solvent system is exposed to a given partial pressure of that gas; it has units of mL/L/mmHg. Therefore:

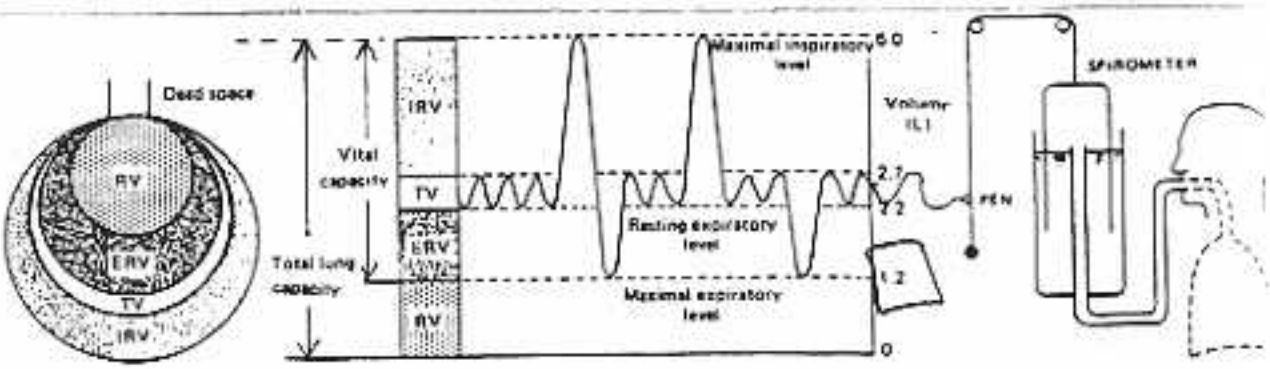
mL_Gas_in_Solution = S_Gas x (p_Gas_Outside_Solution)

S_CO2 (for blood) = .03 mmol/L/mmHg = .65 mL/L/mmHg
S_O2 (for blood) = 1.37 micromol/L/mmHg = .03 mL/L/mmHg

Sorry this is so boring. But I'm trying to be brief...

That being said, the diagram below illustrates respiratory process and outlines terminologies corresponding to different functional divisions of the respiratory volume.

FIGURE 2 - *Diagramatic view of different functional divisions of lung space.*



		Volume (L)		
		Men	Women	
Vital capacity	IRV	3.3	1.9	Inspiratory capacity
	TV	0.5	0.5	
	ERV	1.0	0.7	Functional residual capacity
	RV	1.2	1.1	
Total lung capacity		6.0	4.2	

Respiratory minute volume (rest): 6 L/min
Alveolar ventilation (rest): 4.2 L/min
Maximal voluntary ventilation (BTPS): 125–170 L/min
Timed vital capacity: 83% of total in 1 s; 97% in 3 s
Work of quiet breathing: 0.5 kg-m/min
Maximal work of breathing: 10 kg-m/breath

Figure 34–4. Lung volumes and some measurements related to the mechanics of breathing. The diagram at the upper right represents the excursions of a spirometer plotted against time. (Modified from Comroe JH Jr et al: *The Lung: Clinical Physiology and Pulmonary Function Tests*. 2nd ed. Year Book, 1962.)

Central (Medullary) Chemoreceptors

The levels of carbon dioxide in the body are monitored by *medullary chemoreceptors*, which sample the pH of the cerebrospinal fluid to indirectly measure CO2 levels. Thus the receptors are really looking at the concentration of hydronium ions. Respiratory response to increased pCO2 is brisk, but an infusion of acid (protons) into the bloodstream elicits a more sluggish response. This is because CO2, being a gas, diffuses readily through the blood-brain barrier and is converted to H^+ in the CSF by carbonic anhydrase, which is detected by the medullary receptors. Free acid, however, has a hard time crossing the blood-brain barrier (charged molecules generally do) and as a result fails to effect respiration quickly.

Cerebrospinal fluid generally has a lower concentration of bicarbonate ion and consequently a lower buffering capacity than blood. Therefore, a small change in pCO2 is able to substantially effect respiration. An acclimatization mechanism exists in the brain to compensate for long exposure to excess CO2: if the CSF remains at a low pH for too long, bicarbonate ion begins to be actively pumped across the blood brain barrier to buffer the pH and decrease respiratory sensitivity to high CO2.

The Role of the Kidney

Although the buffering capacity of the body can protect against abrupt changes in pH, normal physiological pH cannot be restored without restoring the levels of proton and bicarbonate to normal. In other words, eating a highly acidic meal will decrease body pH, and this cannot be resolved through exhalation of CO2 alone, because exhalation removes both a proton *and* a bicarbonate ion. As this happens, bicarbonate must be replaced, and it is, although the body would also benefit from an alternative means of acid removal.

The kidney functions in this capacity in two ways. First, it regulates the reabsorption of bicarbonate ion back into the bloodstream. When bicarbonate is in demand, very little is allowed to be excreted in the urine. When it is in excess, the kidney does not reabsorb it all and some is passed out of the body. A second mechanism of acid/base regulation by the kidney is the trapping of hydrogen ion by ammonia. If body pH is low, a lot of hydrogen ions are combined with ammonia in the urine and doomed to exit the body - the resulting ammonium ion is positively charged and will not be able to pass back into the bloodstream. In this process of hydrogen ion trapping, one fresh bicarbonate ion is created for each ammonium ion created, since the actual hydrogen ion comes from the carbonic anhydrase mechanism.

THE MODEL:
The building of this model was a pain in my ass. I can't wait to turn it in - I will then commence doing a little dance of glee.

See Attached Stella Diagram *(Figure 3)*

The unmodified base model contains 9 compartments (will change with improvements or alterations due to experimentation.)

The model is built in a modular format. The modules include **Respiratory Regulation, Breathing Engine, Lung Gas Dynamics, Blood Gas Dynamics, Renal Functions,** and **CSF Dynamics.**

Respiratory Regulation - Implements the equations that I derived empirically relating tidal volume and breathing rate to blood pH. I utilized Michaelis-Menten equations for sigmoidal curves in each case. **See Graphs** *(Figure 4)*
Breathing Engine - The portion of the model that serves as the "respiratory pacemaker" and is the actual part being "regulated upon" by everything else.
Lung Gas Dynamics - The inhalation and exhalation of gasses into the alveolar spaces. This module is connected to the next compartment via the respiratory diffusional barrier.
Blood Gas Dynamics - Once gas has diffused into the body (blood) compartment, it is free to equilibrate with stuff, move around, and react with other things in the blood. That is the function of this module - it handles the carbonic anhydrase mechanism, primarily.
Renal Functions - The blood module is connected to the kidney module via glomerular filtration. The kidney does kidney stuff, and in the model regulates hydrogen ion/bicarbonate throughput to the urine.
CSF Dynamics - The model has this module to allow for acclimatization to prolonged exposure to high pCO_2 and demonstration of the differing speeds by which hydrogen ion and gaseous CO_2 affect respiration.

There was a lot more I could of done, but the God of Computer Models frowned upon me and for the moment I'll have to wait until later to implement those other things.

<u>What the Model Doesn't Do</u>
Things I will add later:
- The entire blood volume is treated as homogeneous in its gas concentrations. My model does not differentiate between arterial and venous blood nor does it consider rates of perfusion of the respiratory capillary bed.
- O_2 does not contribute to respiratory regulation.
- The model is representative only of an average adult male and has less than moderate adaptability, for the time being, to variations in subject parameters. Especially for pathologies. Since the mathematical expressions for breathing regulation were derived empirically from studies of an average subject, I have no way of knowing how these

expressions will differ between asthmatic, emphysemic, healthy, and other types of individuals.
- The diffusion coefficients of the gasses involved can change with demand, via recruitment of new and distention of old open pulmonary capillaries. This is not represented in my model.
- The data used to derive the expressions was insufficient. I would like to find more thurough studies of respiratory regulation.
- Hemoglobin and its relationship to pH, blood buffering, etc., would be fun to do.
- Lot's of other things. Eventually I would like to model every aspect of the human being so thoroughly that my model comes to life.

The Normal Picture

In a resting state (devoid of ancillary physical activity) the following quantities are measured in the average adult male:

pCO2_Body (mmHG)	40	PCO2_Alveoli (mmHG)	40
pO2_Body (mmHG)	100	PO2_Body (mmHG)	100
[Bicarb]_Body (M/L)	.024	[H+] M/L, pH	10^(-7.4), 7.4
Max Lung Size (L)	6	Dead Space (L)	.150
Breaths Per Minute	12	Tidal Volume (L)	.5
Minute Vol. (L/min)	6	Alv. Vent. (L/min)	4.8
GFR (L/min)	.125		

Nonphysiological normals include:

pCO2_Atm (mmHg)	.03	pO2_Atm (mmHg)	150
D_CO2	450	D_O2 (who cares)	21
S_CO2 (mL/L/mmHg)	.65	S_O2 (mL/L/mmHg)	.03

See Normal_Graph, *(Figure 5)*

EXPERIMENTATION:

Experiment 1: I investigate the consequence of different atmospheric CO2 levels on resting breathing rate and tidal volume, assuming constant pO2. Increased atmospheric CO2 acts to increase body CO2 levels (and thusly pH) by disturbing the change in pressure term of the diffusion equation. Since I derived the equations that determine breathing rate and tidal volume empirically in the first place, this experiment serves to confirm (or demonstrate lack of) accuracy in the regulatory module of my model.

See Experiment 1 Graph

Experiment 2: I investigate the efficacy of different breathing patterns in ventilating the alveolar space in the lungs. The graph is representative of a single desired alveolar ventilation (L/min) and the plotted black curve represents the combinations of tidal volume and breathing rate that satisfy the condition; in this case, alveolar ventilation equals 5 L/min. As breathing rate increases at the expense of tidal volume, one notices that the efficiency curve drops accordingly. Efficiency in this case is defined as the alveolar

ventilation (total volume of fresh air reaching alveolar spaces) devided by the respiratory minute volume (total air "moved" by lungs per minute), and is a fraction from 0 to 1. Clearly, the efficiency drops because of the existance of dead space in the lung area. For each breath taken, this dead space air must be displaced before used air can be expelled, or before fresh air can enter the alveolus. If one increases the rate of respiration, one increases the frequency that the dead space air must be dealt with. Slower, deeper breaths are more efficient (as defined) because a larger percent of the total air per breath is fresh air. Quick, shallow breaths give a small percentage of total air as fresh, with lots of energy wasted in moving dead space air around.

See Experiment 2 Graph

Experiment 3: I investigate the physiology of intravenous infusion of protons on the acid/base equilibrium and respiratory regulation of the body. Renal removal of protons is not considered here. 1E-9 protons per second are infused into the bloodstream of the subject. This is equivalent to 1 mL/sec of a solution at pH 3, which is highly acidic. Graph A and Graph A(zoom) shows the body's reaction to this acidic insult. Breathing rate and tidal volume quickly increase, as expected, to increase alveolar ventilation. This consequently lowers pCO2 in the body, which drives the carbonic anhydrase reaction towards CO2 formation and removal of H+. A new rate of CO2 removal from the body (and thus protons and bicarbonate via carbonic anhydrase) is quickly established by the respiratory response to equal and counteract the rate of proton infusion. Graph B shows these rates and illustrates how a level of CO2 removal from the body is reached so that proton removal via carbonic anhydrase equals proton infusion.

One will notice that the concentration of bicarbonate does not change substantially because of this insult, due to the fact that it is normally 250,000 times more abundant than the protons it seeks to remove. In this simulation, bicarbonate is not replaced, so it should eventually run out, and as it does, the infused protons will change the blood pH at a faster and faster rate due to decreased buffering capacity.

But that wouldn't happen for a long while.

Graph C repeats the experiment, this time with an infusion of 1 mL/sec of pH 2 solution. The subjects alveolar ventilation quickly shoots to its maximum and, given this bottleneck for the removal of CO2 from the body, the equilibrium of the carbonic anhydrase system shifts such that the new steady state pH is 6.5, and the subject is dead.

See Experiment 3 Graphs A, B, and C

Experiment 4: An illustration of alkalosis. At time 0, the subject has a bicarbonate concentration of .074 moles/L, about 3 times the physiologically normal level. As demonstrated by the graph, the body quickly takes measures to reduce pH of the blood, which peaks early on (at about 100 seconds) at 7.7. As expected, respiratory activity plummets such that the tidal volume and respiratory rate are at a minimum, and the

corresponding increase in pCO2_Body acts to slow the consumption of protons by the carbonic anhydrase system.

Unlike the previous experiment, the kidney will have a part in bicarbonate removal. The reaction to high bicarbonate levels in the blood is instantaneous, because the kidney does not have to specially prepare to pump the substance into the urine, as is the case with protons. Instead, excess bicarbonate is simply not reabsorbed into the body from the gromerular filtrate.

Fluid is filtered in the kidney at a rate determined by the GFR (Gromerular Filtration Rate) which has a normal value of .125 L/min. This filtrate has the same osmolarity and overall solute concentrations the blood plasma from which it was derived. The kidney generally acts quickly to "reabsorb" desired nutrients back into the bloodstream very soon after they are filtered from the plasma, and leaves less desirable materials alone, dooming them to excretion.

When bicarbonate levels in the filtrate are too high, the kidney cannot actively reabsorb the excess. The mechanisms of reabsorption become saturated and thusly some bicarbonate finds its way into the urine. This is the means of bicarbonate excretion by the kidneys in the case of acidosis.

Since the kidneys are constantly being filtered, excess bicarbonate in gromerular filtrate is detectable moments after I stick the needle into my ... patients... for infusion.

Refer to Graph A and A(zoom). One will notice that the concentration of bicarbonate drops a whole .012 mole/L during the course of the simulation, dramatic in contrast to Experiment 3 where a change in bicarbonate concentration was almost imperceptible. The pH begins to return to normal after only 100 seconds, and by the end of the simulation is close to 7.5.

Graph B shows us that the carbonic anhydrase/respiratory system reacts very quickly. At time 0 the rate of proton/bicarbonate consumption is (relatively) large but quickly gravitates towards zero as the rate of bicarbonate removal due to kidney excretion becomes the limiting factor.

The kidney plays the major role in returning levels of acid and base to their normal values in this simulation.

Graph C illustrates the same scenario with the renal bicarbonate excretion mechanism removed - this is very interesting. Initial reaction to the high bicarbonate level is very similar to the experiment including functional renal excretion - respiratory mechanisms are invoked, carbonic anhydrase quickly forces a new balance of species, and the pH quicky peaks at 7.7 before falling slowly to normal. However, at the end of this simulation, pH has only reached 7.6, a full point above the previous experiment. One also notices that the

concentration of bicarbonate has all but totally ignored the activities of carbonic anhydrase and remains basically static throughout the entirety of the simulation.

This highlights the utter importance of the kidney in re-establishing buffer capacity by performing net movement of protons and bicarbonate into and out of the body. But it is clear that the initial handling of a pH disturbance has almost nothing to do with the kidney. The first line of defense is the buffers.

See Experiment 4 Graphs A, B, and C

I don't like this part.

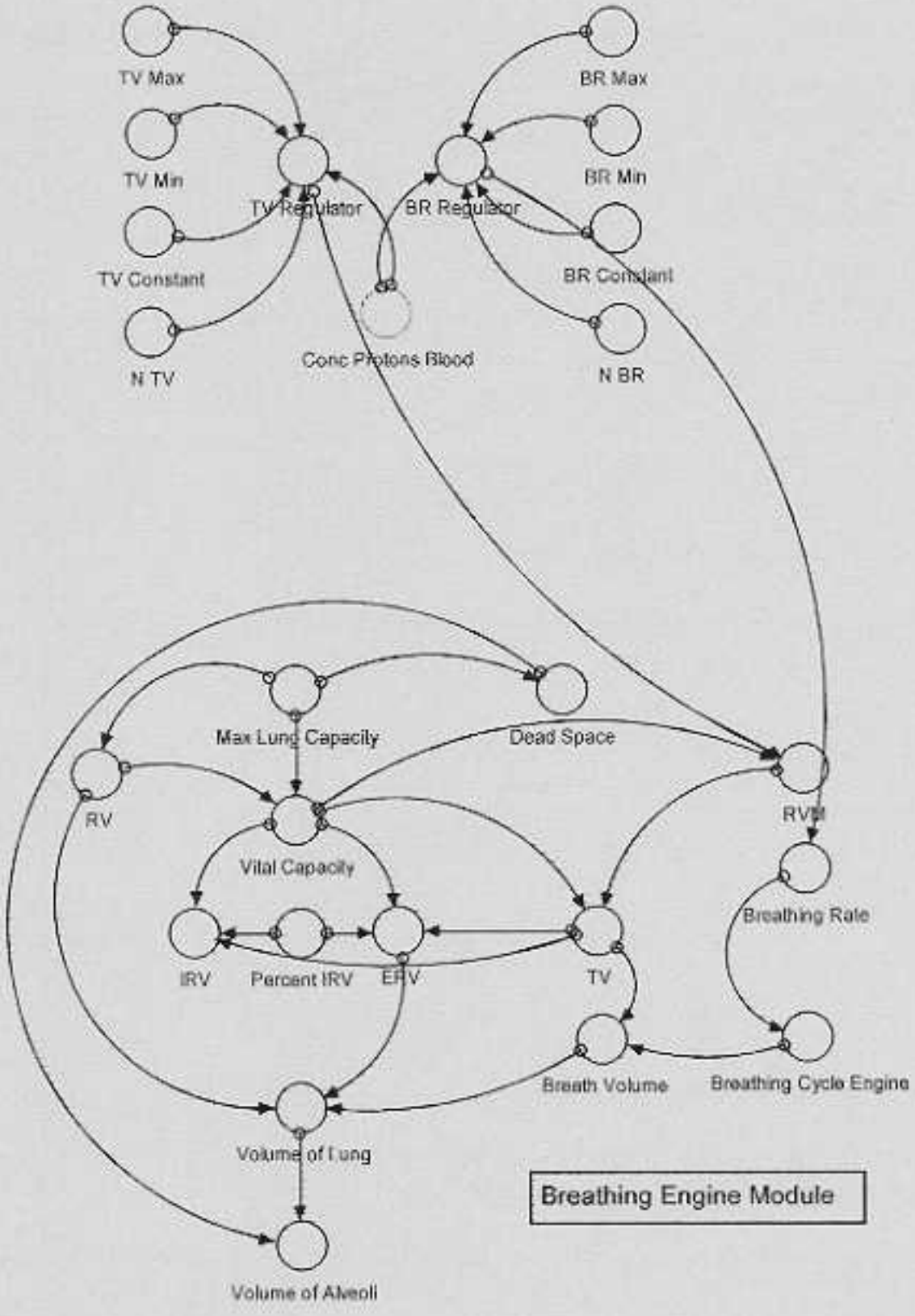
Experiment 4: This is the fun one. I *suffocate* my MCB136L T.A. in a closed area. After placing him in a box, I allow him to slowly suffocate under conditions of decreasing O2 and increasing CO2 in the atmosphere. I laugh maniacally to myself as his own metabolic processes doom him to death by asphyxiation! Ha!

CREDITS: Almost all information used in the development of this model was taken from MCB136 professor John Forte or his materials. God bless him.

FIGURE 3a

Graph 1

Regulatory Mechanism Module



Breathing Engine Module

Medullary Chemoreceptor Module - pH Sensitivity of CSF

FIGURE 3b

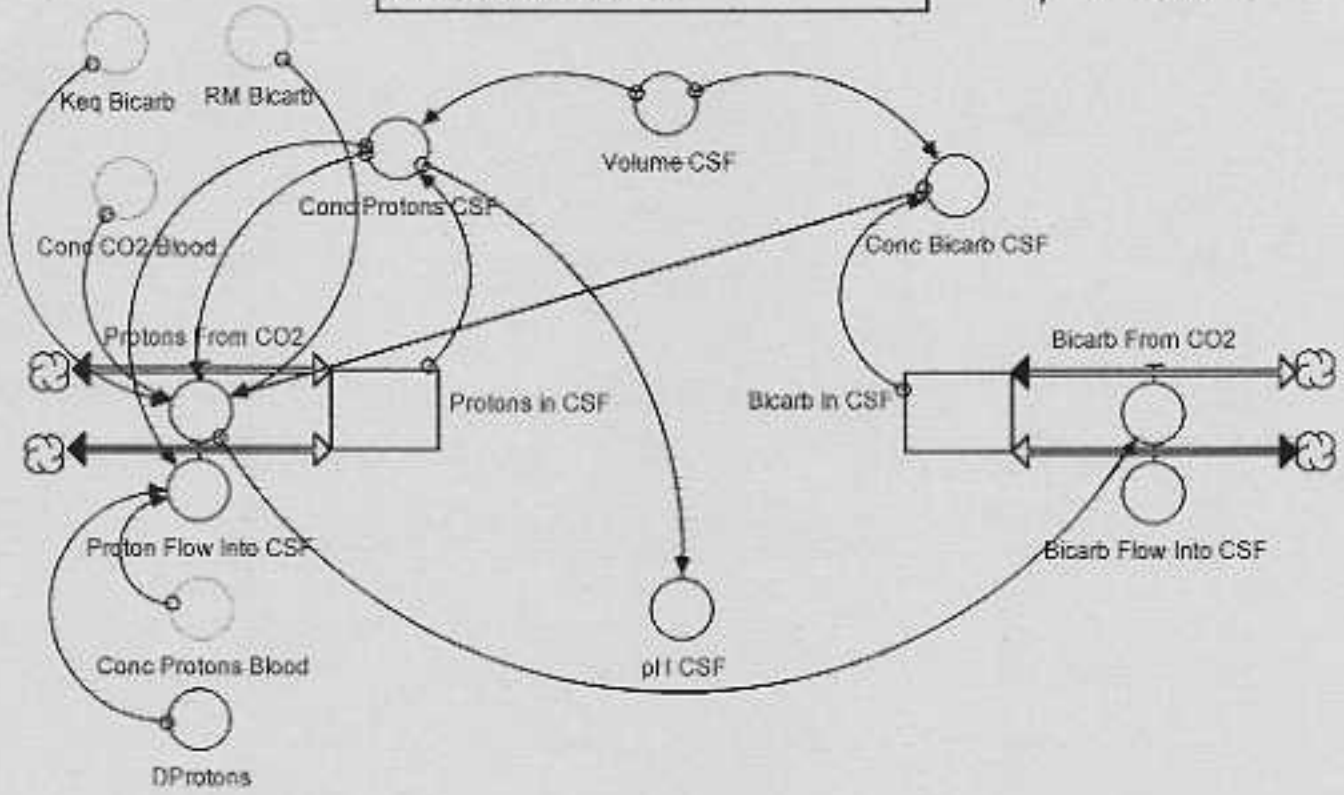
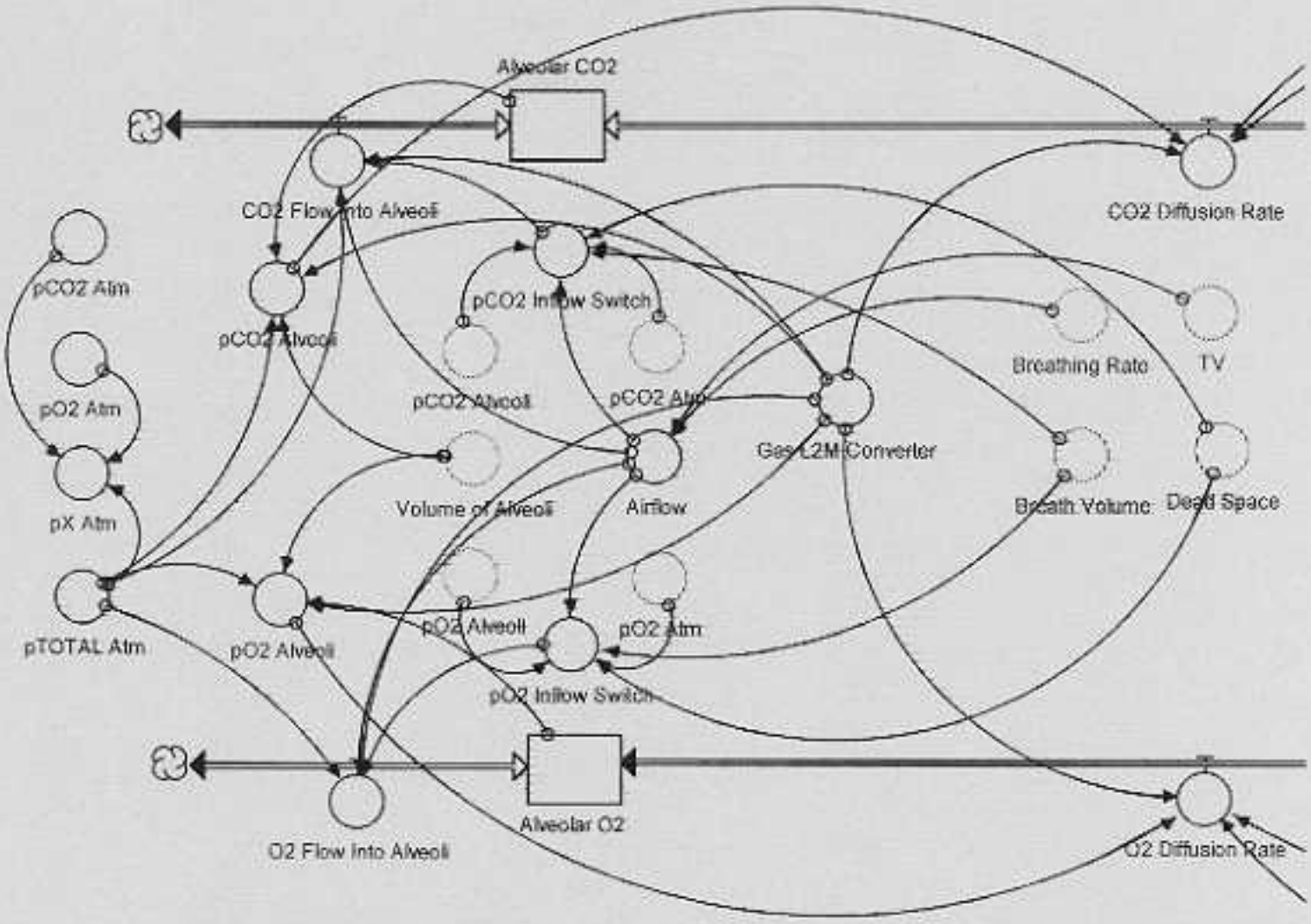


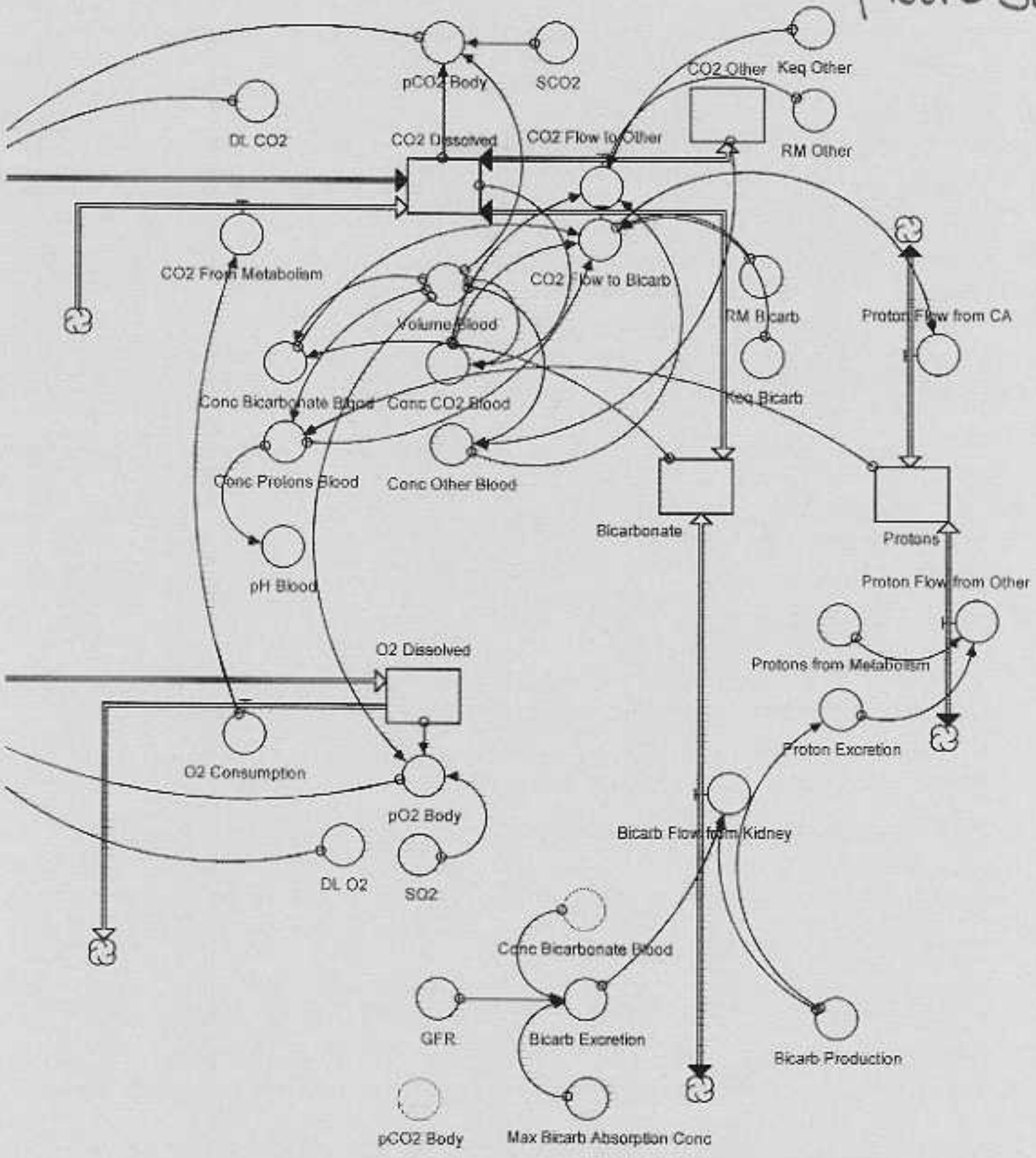
FIGURE 3c

Gas Behavior Module - Lung Compartment



Gas Behavior Module - Body Compartment

FIGURE 3d



Renal Acid/Base Regulation

FIGURE 4 GRAPHS OF EMPIRICALLY DERIVED EXPRESSIONS FOR BREATHING BEHAVIOR VS. pH

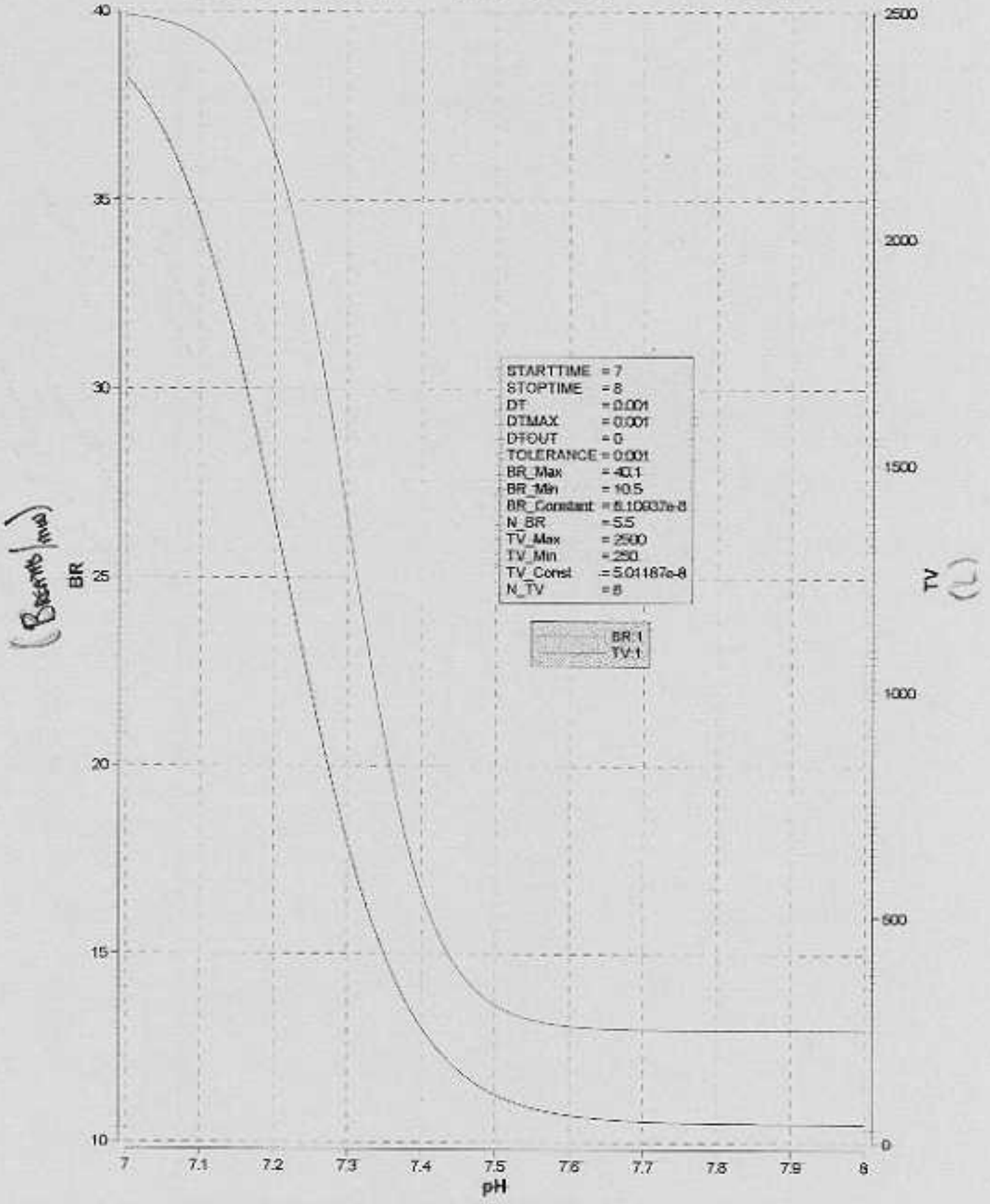
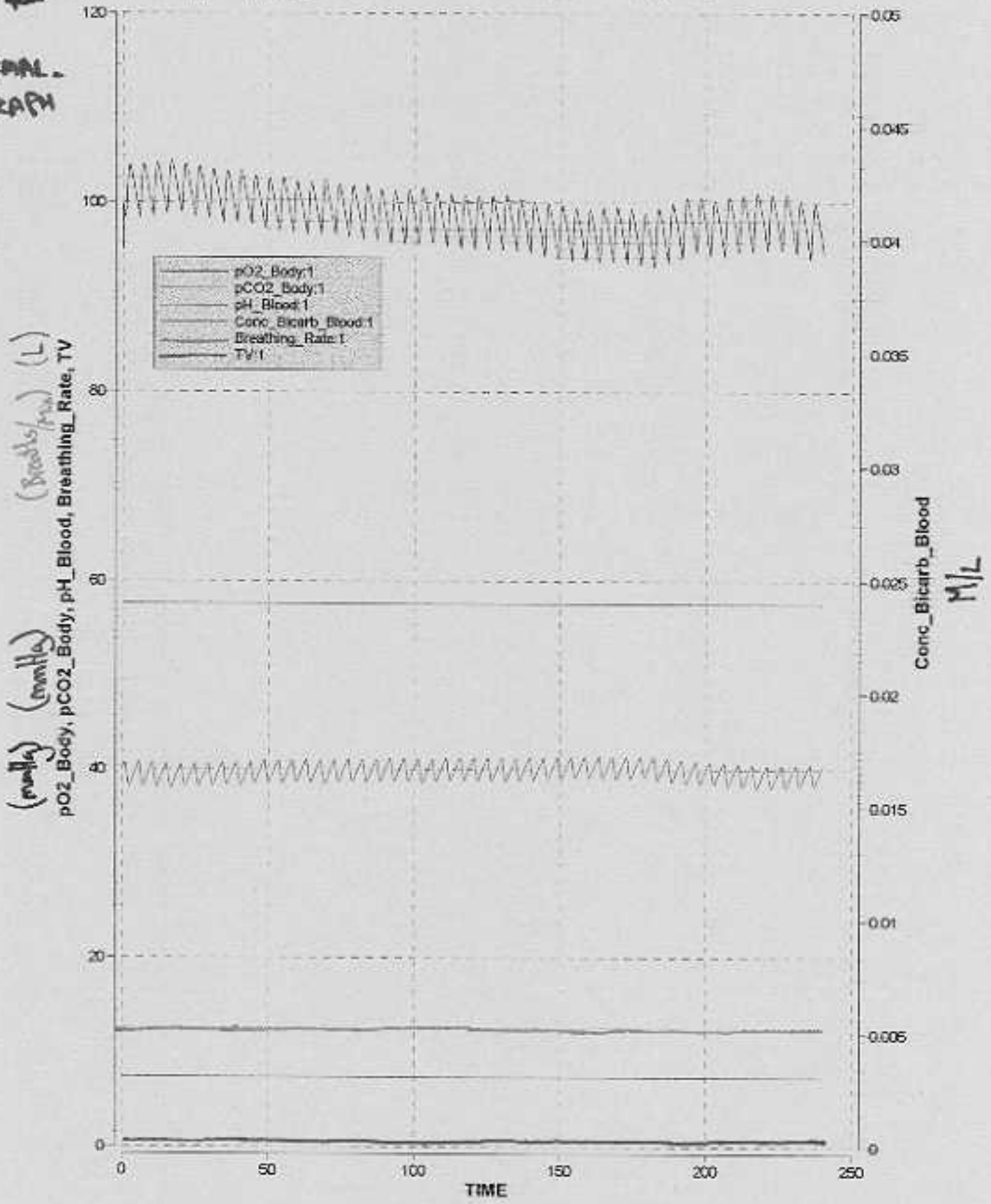


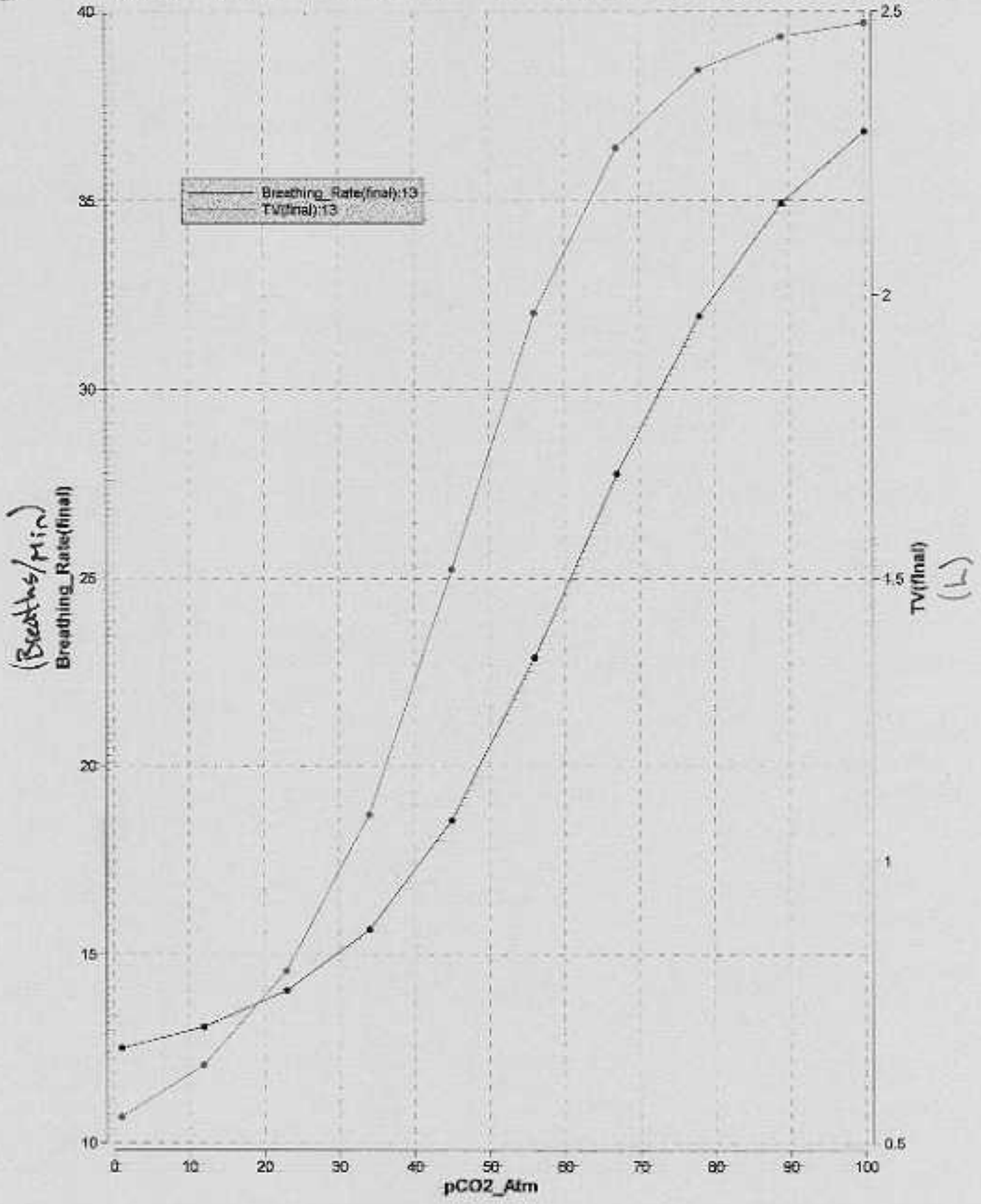
FIGURE 5

• EXPECTED NORMS FOR RESPIRATORY VARIABLES IN AVERAGE ADULT MAN AT REST.

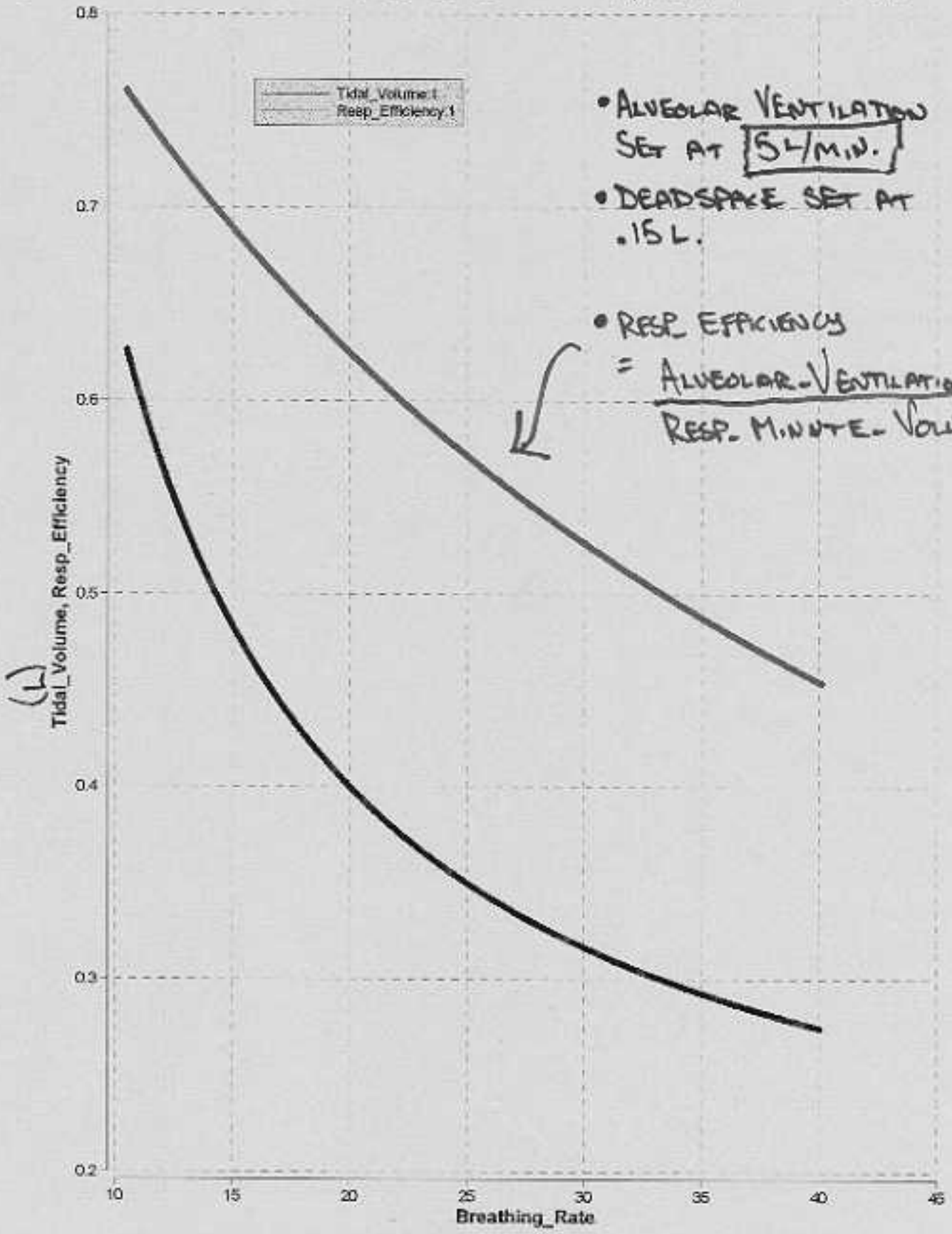
NORMAL GRAPH



EXPERIMENT #1 STEADY STATE VALUES OF BREATHING RATE AND TIDAL VOLUME AT VARYING ATMOSPHERIC pCO_2



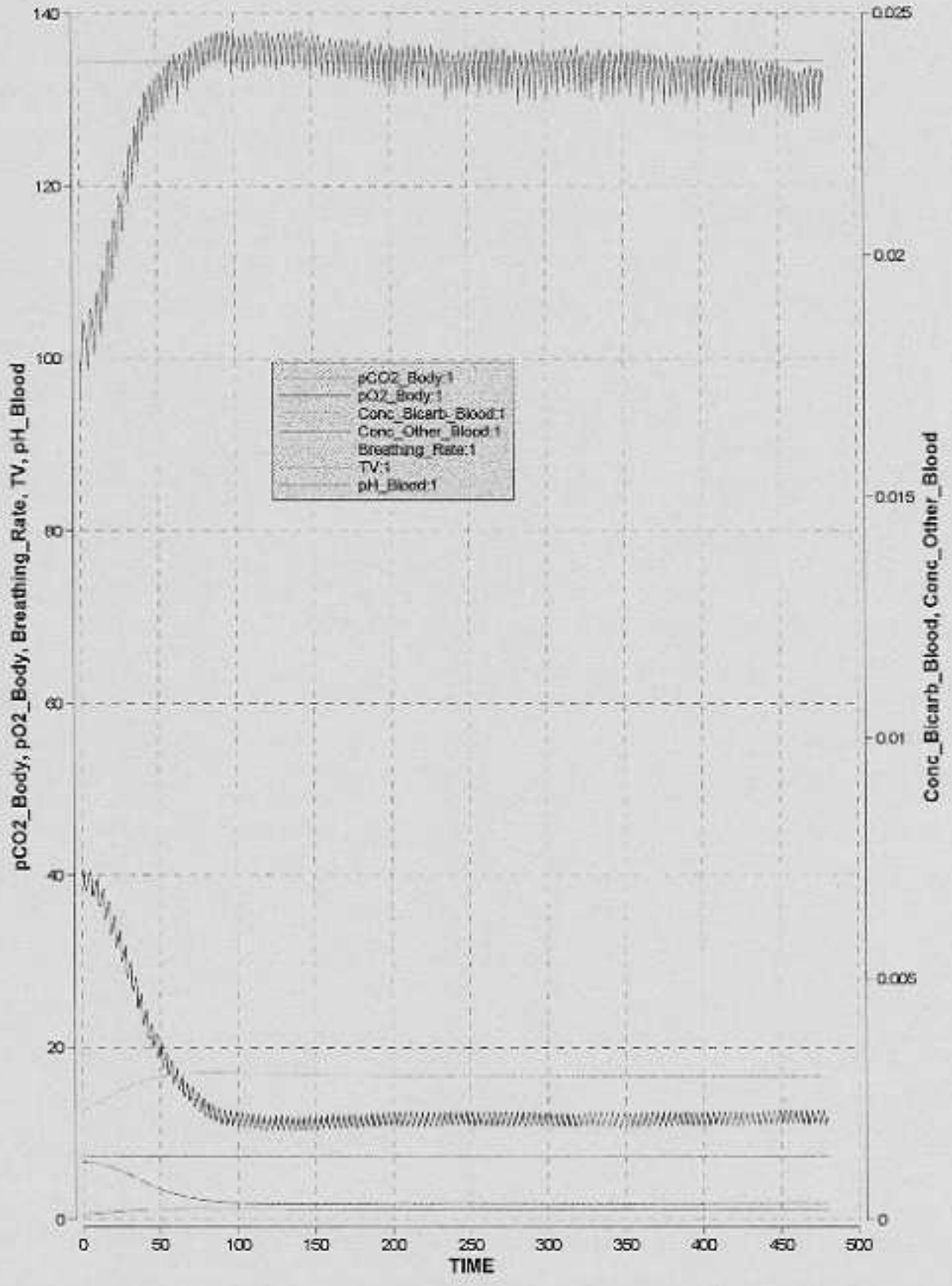
EXPERIMENT #2 AT ANY SET ALVEOLAR VENTILATION; BR & TV SATISFY CONDITION ALV_VENT = 5 L/MIN



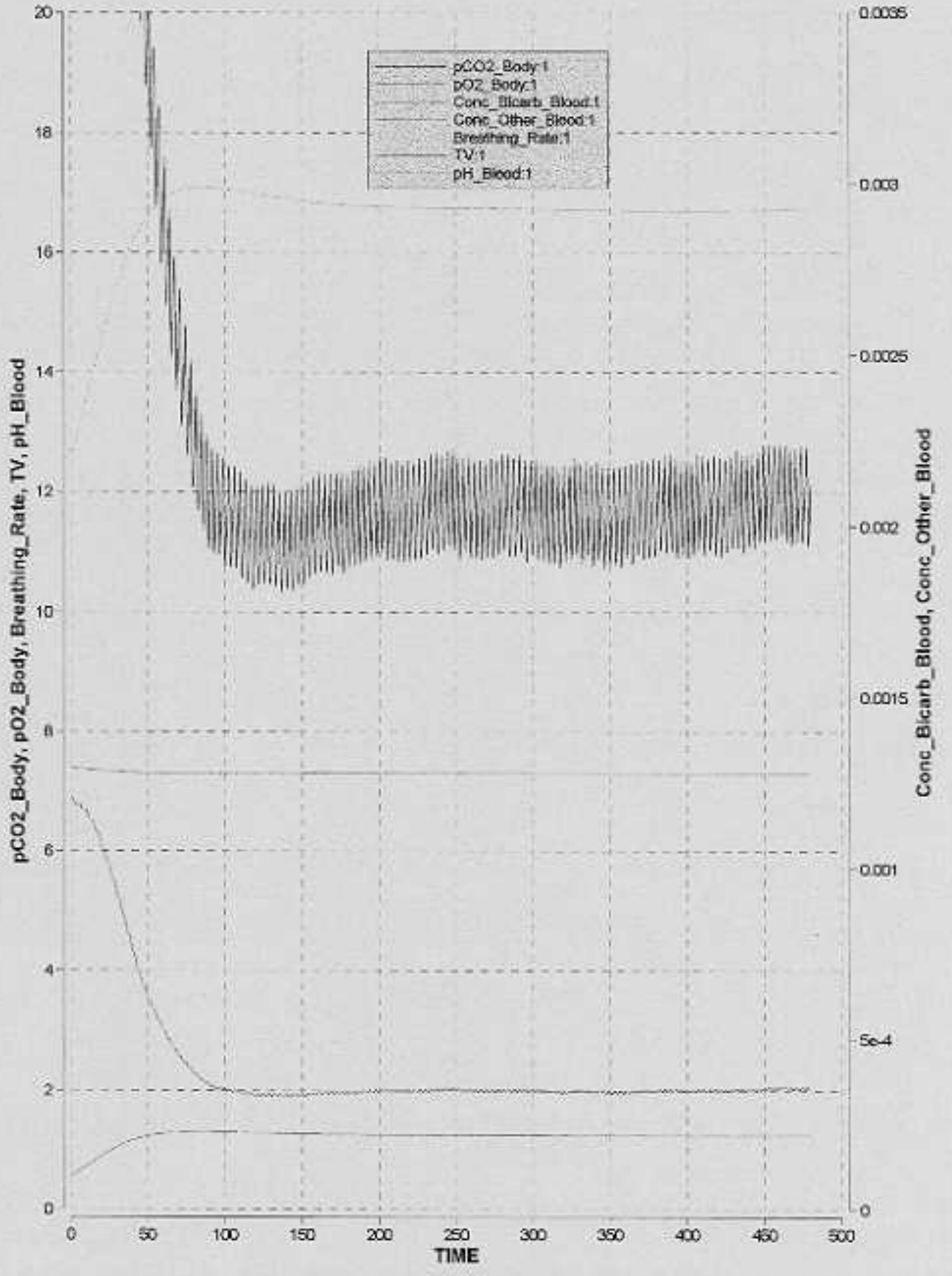
- ALVEOLAR VENTILATION SET AT 5 L/MIN.
- DEADSPACE SET AT .15 L.
- RESP. EFFICIENCY = $\frac{\text{ALVEOLAR\_VENTILATION}}{\text{RESP\_MINUTE\_VOLUME}}$

- GRAPH SHOWS THAT HIGH BREATHING RATE & LOW TIDAL VOLUME IS NOT EFFICIENT IN ACHEIVING A DESIRED ALVEOLAR VENTILATION DUE TO DEADSPACE.

EXPERIMENT #3A INFUSION OF 1 mL/sec pH 3 MATERIAL



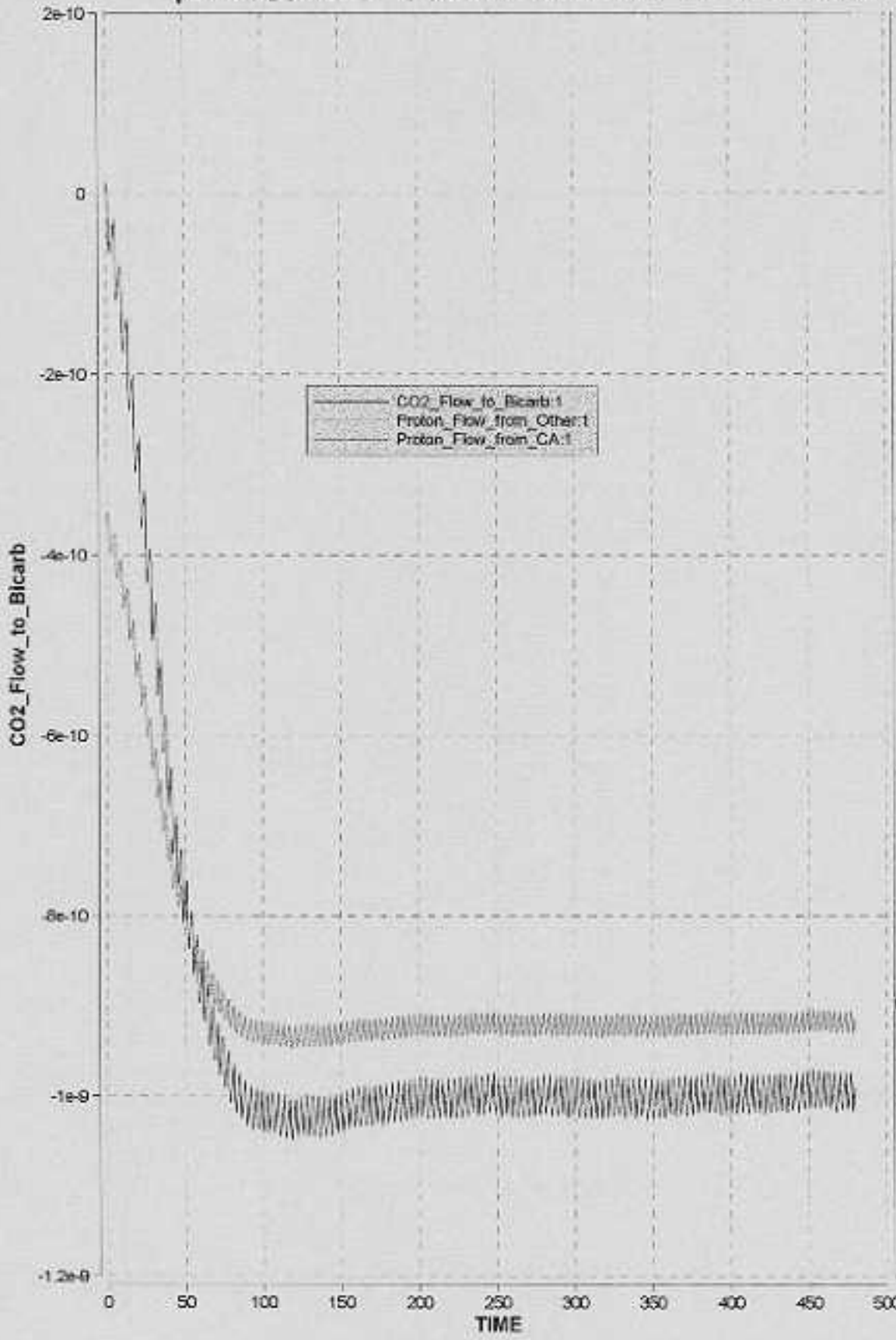
EXPERIMENT #3A (800ml) INFUSION OF 1 mL/sec pH 3 SOLUTION



EXPERIMENT #3B

INFUSION OF 1mL/sec pH 3 SOLUTION

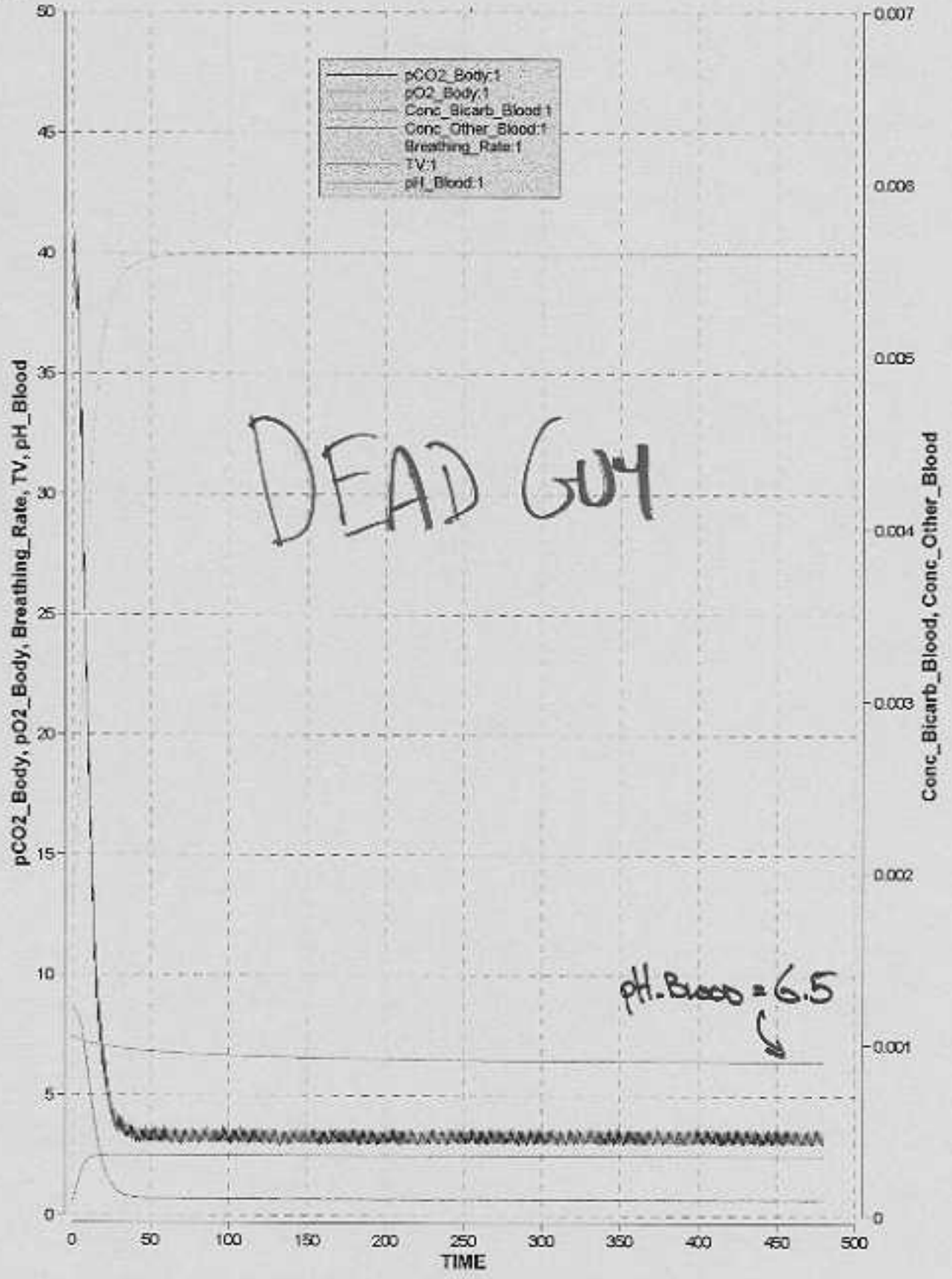
*FOCUSES ON FLOW CHANGES IN RESPONSE TO ↑ H+



-1e-9 | PROTON REMOVAL DUE TO C.A EQUALS INFUSION

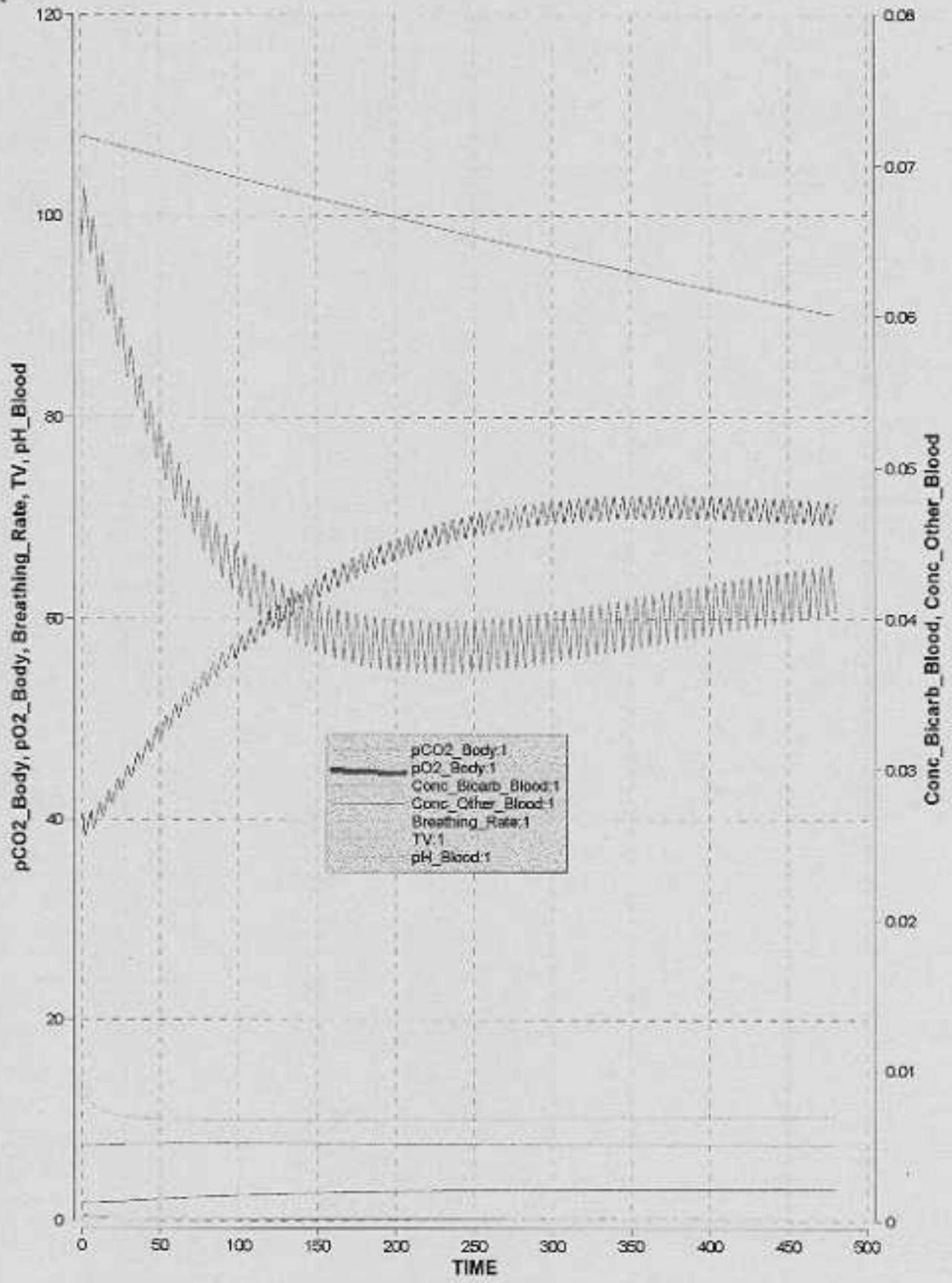
EXPERIMENT #3C

1 mL/sec pH 2 solution

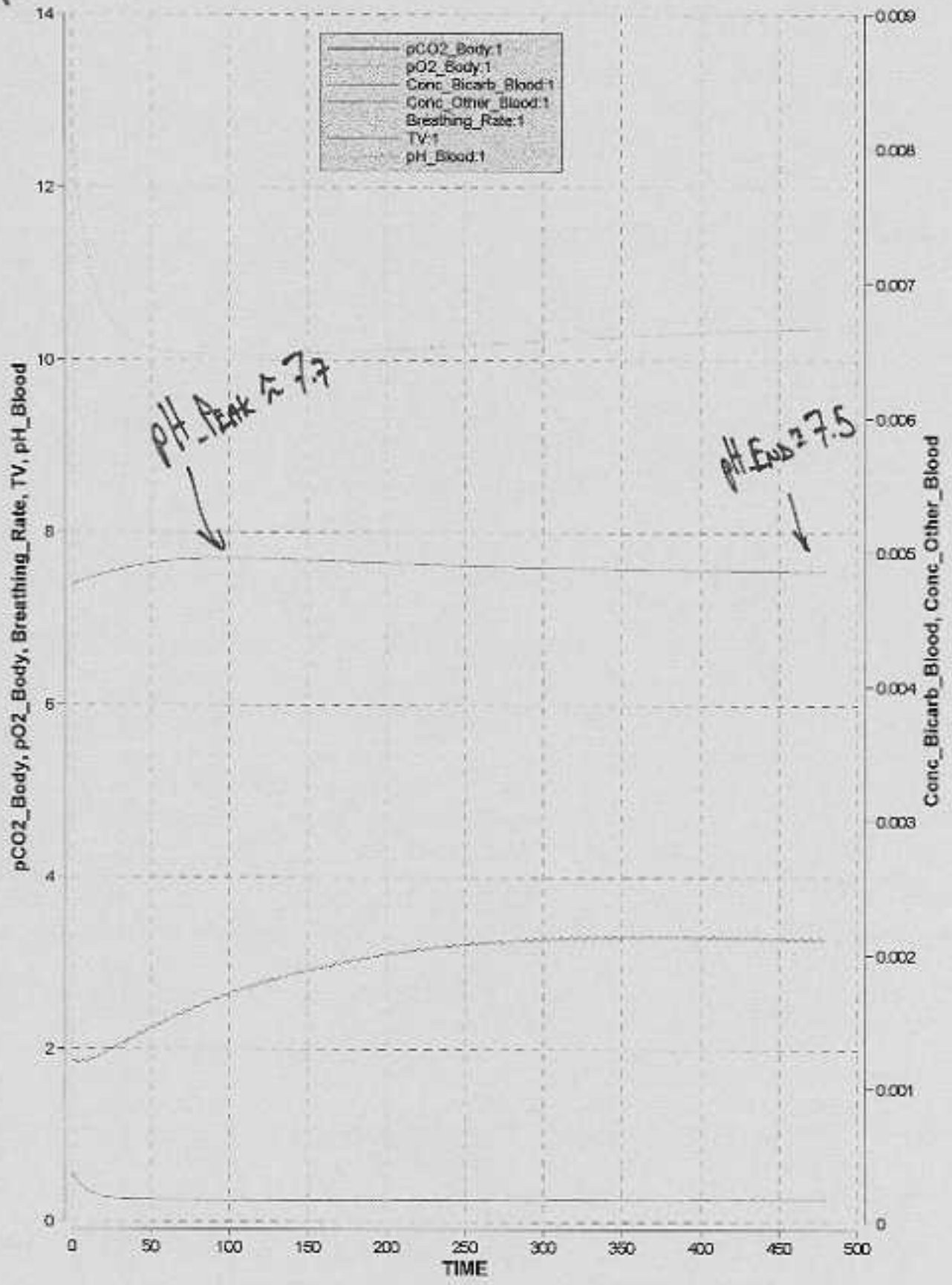


EXPERIMENT #4A

BODY'S REACTION TO .072M BICARBONATE



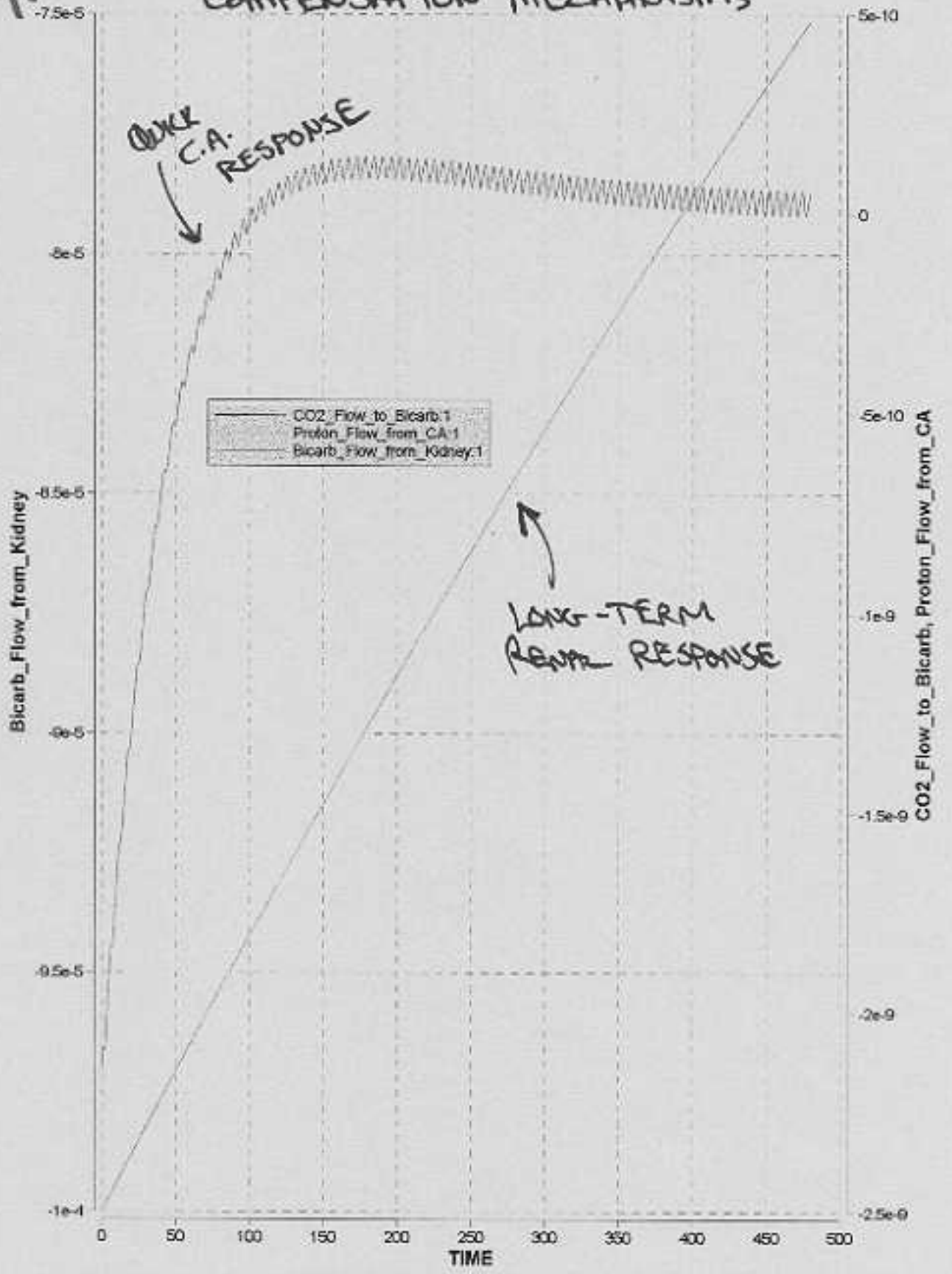
EXPERIMENT #4A(ZOOM) BODYS REACTION TO .072 M BICARBONATE



EXPERIMENT #4B

• .072 M BICARBONATE

• COMPARISON OF RATES OF COMPENSATION MECHANISMS



EXPERIMENT #4C Body's Reaction to .072M Bicarbonate WITHOUT RENAL BICARB EXCRETION