Reflections About Quantitative Acid-Base

This helpfile gives an introduction into the usage of the spreadsheet Schroeck_Peter_Stewart_standard_including_P.xls

(development state: 03-Aug-2009, Helmut Schröck)

The fundamental introduction into this area is given by the following book:

Peter A. Stewart: How to Understand Acid-Base.
 A Quantitative Acid-Base Primer for Biology and Medicine.
 New York: Elsevier/North Holland, 1981.

All chapters of this book are available for free from the following webpage (although without graphics):

http://www.acidbase.org/index.php?show=sb

A second edition of this book which includes the original pages from Peter Stewart's book and up to date follow ups and articles from many experts in this field is available in printed form from the same webpage.

The following introduction into applications of the Stewart model requires the knowledge of Stewarts book and a certain level of knowledge in chemistry.

Details to Tabelle1 of the spreadsheet file

pKa   : negative logarithm of the average dissociation constant for weak acids, mostly albumin. The total concentration of all weak acids (including albumin) had been lumped together in the Stewart model as Atot. The complete system is described as a single monoprotic weak acid with an average dissociation constant called Ka.

pKw   : Ionic product of water (negative logarithm hereof)

alpha : solubility coefficient for CO_2 in $Mol*l^{-1}*mmHg^{-1}$

pKc : pK-value from Henderson-Hasselbalch equation (CO_2/bicarbonate system)

pK3 : pK-value for the dissociation of HCO_3^-

limit : this is just a number to test whether electroneutrality is reached with sufficient accuracy. If the numerical result of the electroneutrality equation is smaller than **limit** the numerical approximation process is terminated and all the dependent variables are calculated and get printed into the results part of the same sheet.

hic, loc : the numerical approximation process requires the setting of an upper (hic) and a lower (loc) limit of values for the $[H^+]$ concentration; in other words: the search for the pH-value which solves the equations is limited to the range of pH=0 to pH=14

pKP1, pKP2, pKP3 : pK-values for 3 dissociation steps of phosphoric acid.

SID : strong ion difference, is usually calculated from:

$$SID = Na^+ + K^+ - Cl^- - lactate^-$$

The unit used is meq/l (milliequivalents per litre) because SID must be given as concentration of electrical charges.

Thus: 2 mmol Na^+ = 2 meq; 2 mmol Ca^{2+} = 4 meq !

pCO2 : CO_2 partial pressure, given in mmHg

Atot : Total concentration of weak acids, mainly albumin. The unit to be used is meq/l. The numerical value of Atot in the Stewart model gives the number of electrical charges maximally possible.

Ptot : total concentration of inorganic phosphate. The unit to be used is mmol/l. This is true molar concentration and you may think of it as numbers of atoms of phosphorus!

Yellow cells representing SID, PCO2, Atot, Ptot : this is the place where the **independent variables** are keyed in. You may try with your own numbers(see below). Zero is possible too. Negative numbers are useful only with the SID and gives you the possibility to simulate stomach fluids.

If the independent variables are given numerically, all the dependent variables are determined in a mathematical way and may be solved for. For convenience these are approximated numerically with the help of a computer program of course. In a physical sense there are no degrees of freedom left over for the dependent variables once the independent variables are given. The dependent variables may be changed only by changing one or more of the independent variables. This is the essential message of Peter Stewarts book.

Dependent variables are:

Hplus   : the concentration of hydrogen ions

OH-   : the concentration of hydroxide ions

pH, pOH   : the negative logarithms hereof

HCO3-   : the concentration of bicarbonate

CO3--   : the concentration of carbonate (not so important for medical acid-base)

total CO2 : A variable where bicarbonate, carbonate and physically dissolved CO_2 are
               lumped together. This is the moles of CO2 you will get if you add an excess
               of strong acid and do a vacuum extraction to remove all the CO2 out of the
               solution (as may be done with a Natelson microgasometer).

dissolved CO2 : physically dissolved CO_2, calculated from alpha x PCO_2

Prot-   : negative charges in weak acids, mostly albumin

HProt   : the nondissociated part of weak acids

(adding up Prot- and HProt gives Atot in the Stewart model)

H3PO4 : concentration of nondissociated phosphoric acid

H2PO4- HPO4-- PO4--- : concentrations of the remaining parts of the phosphoric acid system. In biological systems only H2PO4- und HPO4—are important and are present in the millimolar range.

Z : All negative charges of the phosphate system summed up.
Thus Z = H2PO4- + 2 x HPO4-- + 3 x PO4---

dissalpha : the degree of dissociation, alpha, for weak acids. According to textbooks of chemistry. alpha=Prot-/(Prot- + HProt). Do not mix up with the solubility coefficient for CO_2.

Relative Alkalinity : [OH-]/[H+]; the ratio indicates how many more ions of hydroxide than hydrogen ions are present. It seems, this parameter is regulated constant in the blood plasma of all members of the animal kingdom (at a value of about 16), not the pH!

The spreadsheet program itself, what is it for?

The program contained within the spreadsheet is a mathematical representation of the properties of dilute solutions of acids and bases in water. The single equations are derived and explained in detail in Peter Stewarts book (except the phosphate system). You may simulate the state of equilibrium of many different kinds of solutions without having to make experiments. This is so, because for setting up the system of equations, generally accepted laws of chemistry have been considered exclusively and nothing else, no fudge factors to accommodate the calculated results to actual measurements.

The generally accepted laws of chemistry are:

1. Law of conservation of mass

Example: the mass of sodium ions in a given solution does not change, except sodium ions are added to or removed. The same holds true for the ions of potassium, chloride, calcium, magnesium, sulfate and total phosphate. For weak electrolytes you have to be careful, the law of conservation of mass is valid too, thus the number of atoms stays constant. But there may be a change in appearance because of the law of mass action. If you add 1 mmol of HCl to 1 litre of blood plasma, the cloride concentration will increase by 1 mmol, but hydrogen ion concentration will never change by 1 mmol.

2. Strong electrolytes are considered as being in the completely dissociated state

3. Validity of the law of mass action for weak electrolytes

4. Rule of Electroneutrality.

In a given piece of solution there are equal numbers of positive and negative charges. (We do not consider separation of charges in biological membranes and generation of membrane potentials here. In fact this does not apply to the chemical behaviour of pieces of solution.)

With sufficient knowledge in chemistry from your side, you may "ask" questions to the program and get answers in numerical form. In that way you may satisfy your curiosity in this special scientific area, undoubtedly somewhat difficult to understand.

Some numerical examples:

Fire up the spreadsheet file.

Allow macros to be executed.

Tabelle1 should be seen:

1)Enter the following numbers (all zeros) into the cells as indicated. Make sure all 4 numbers are accepted by the spreadsheet by hitting the Enter key.

SID = 0   PCO2 = 0 Atot = 0 Ptot = 0

Click the „Calculate" Button with the mouse.

Numbers in the dependent variables section should change now. Otherwise the macros are not activated yet. (Go to Extras...Options...Security...Macro Security and change the security level to average. Click OK and restart Excel again. Allow execution of macros when you are asked during startup)

The solution does not contain any solutes, thus with all independent variables set to zero, we do have pure water.

The pH is calculated to be 6.8. This is the pH of pure water at 37°C. The valid pKw = 13.6 for this temperature.

Change the pKw to 14.0 (don't forget the enter key) and calculate again. This time pH = 7.0 and temperature is 25°C (as is assumed in most chemistry textbooks, but is not so helpful in medical science).

Please set pKw back to 13.6.

Please notice that the relative alkalinity was 1.0 in pure water irrespective of the temperature used.

2) Please enter the following numbers and click calculate:

SID = 24   PCO2 = 0 Atot = 0 Ptot = 0

This is a solution of 24 mM sodium hydroxide in water. The pH is about 12. Very dangerous to your skin and your eyes.

Now we gas the solution with a mixture of 5.6% CO_2 in oxygen.

Please enter:

SID = 24   PCO$_2$ = 40 Atot = 0 Ptot = 0

The pH decreases to 7.4 and the solution is not dangerous any longer. The bicarbonate concentration suddenly is 23.4 mM although we did not add any "bicarbonate"! This is so because the laws of chemistry tell us that the following equilibrium reaction is taking place

automatically:

$$CO_2 + OH^- = HCO_3^-$$
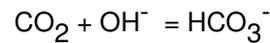
The equilibrium is shifted to the right side of the equation completely. Therefore: if you have bicarbonate inside a solution it must not have been added itself but it may be generated in a chemical reaction in the presence of CO_2.

Now change the PCO_2 from 40 to 80 mmHg and click calculate.

The pH drops to 7.1 and the $[HCO_3^-]$ stays constant at 23.9 mM. Therefore: For all practical cases, with varying PCO2, the bicarbonate stays constant as long as the CO2/bicarbonate is the only buffering system present in the solution.

3) Please enter the following numbers and click calculate:

SID = 41   PCO$_2$ = 40 Atot = 20 Ptot = 0

This is isolated human blood plasma (without erythrocytes). Atot is set to a maximal value of 20 meq/l. Atot represents the total concentration of weak acids (mainly albumin). In the Stewart model weak acids including albumin are represented as a system with one monoprotic weak acid. The chemical equilibrium reads:
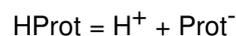
$$HProt = H^+ + Prot^-$$

with a dissociation constant of Ka=2.25E-7 or pKa = 6.648

To include this into the Stewart model the law of mass action and the law of conservation of mass has to be formulated:

$$[H+] \times [Prot-] = Ka \times [HProt]$$
and
$$Atot = [HProt] + [Prot-]$$

The presence of another buffer system influences the CO2/bicarbonate buffer system.

Change the **pCO2 from 40 to 80 mmHg** and click calculate.

The pH does not drop as much as in case 2). The bicarbonate does not stay constant any longer but increases while Prot- decreases. The total buffer base concentration stays constant. This is so because we kept the SID constant.
Physiology textbooks say that a solution is buffered more effectively against changes in pH caused by changes in PCO2 if there is a second buffer system present besides the CO2/bicarbonate system.

4) Please enter:

SID = 41   PCO$_2$ = 40 Atot = 20 Ptot = 0

And click calculate.

Please change **Atot from 20 to 10** and calculate again.

This time we simulated some kind of damage to the liver. Plasma protein synthesis rate is decreased and thus plasma protein concentration is decreased. When calculating the pH with the Stewart model we get an increase in pH. This kind of acid-base derangement was first predicted theoretically by the Stewart model, later verified as really existing in patients (1986) and named hypoproteinemic alkalosis.

5)Please enter and calculate:

SID = 43   PCO$_2$ = 40 Atot = 20 Ptot = 1,12

This is isolated human blood plasma. The total inorganic phosphate (Ptot) is considered as a separate independent variable. It is easy to extend the Stewart model and add more chemical compounds with its equations.

Please change **Ptot from 1.12 to 5 mM** and calculate.

The pH drops considerably. This was the mathematical simulation of one aspect of chronic renal

failure with accumulation of inorganic phosphate in the blood plasma of the patient. There is a considerable influence of Ptot on the pH of blood plasma.

6) Please enter and calculate:

SID = 41   PCO$_2$ = 40 Atot = 20 Ptot = 0

Shortly after finishing an exercise with heavy muscular work a venous blood sample is drawn and plasma lactate concentration determined to be 11 mM. It is your task to calculate an approximate pH of the arterial blood plasma under the assumption that arterial PCO2 was normal and did not change after exercise.

Solving: Because regular plasma lactate concentration in the resting human is about 1 mM there must have been an increase in lactate of about 10 mM.

SID must therefore be 41 - 10 **= 31** meq/l.

Please enter and calculate (all other independent variables staying unchanged):

SID = 31

Now, with a significant decrease of the SID, we did simulate a metabolic acidosis. With the help of a numerical approximation we got an idea about how much the pH of arterial blood plasma approximately had been dropped from normal in this individual case.

If a respiratory compensation would take place we could consider its influence on the pH of blood plasma.

Please change **pCO2 from 40 to 25 mmHg and calculate.**

The decrease in pH caused by metabolic acidosis is almost completely compensated for. In addition, please notice that bicarbonate further decreased during the respiratory compensation!

The excel spreadsheet

schroeck_peter_stewart_standard_including_P.xls

together with the file

Schroeck_Peter_Stewart_Helpfile_3.rtf

may be distributed freely and without charge.

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Exclusion of liability:

As to the program code which is contained within the Excel spreadsheet file named Schroeck_Peter_Stewart_standard_inculding_P.xls and the numerical results obtained hereof, I do not take any responsibility for the accuracy of the calculated results or for drawing conclusions out of the calculated results.

03-Aug-2009, Mannheim, Germany