Hyperquad Definitions and Explanations

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Association and dissociation constants. In organic chemistry and biochemistry it is customary to use pK_avalues for acid *dissociation* equilibria. For a monobasic acid with formula AH, the acid *dissociation* constant, K_{diss}, is defined by

$$AH \rightleftharpoons A^- + H^+;\ K_{diss} = [A^-][H^+]/[AH];\ pK_a = -\log_{10}K_{diss} = \log_{10}(1/K_{diss})$$

On the other hand stability constants for metal complexes, and binding constants for host-guest complexes are generally expressed as *association* constants. It is therefore necessary, in computer programs, to use *association* constants for all equilibria. The *association* constant, K_{ass}, for the monobasic acid is defined by

$$A^- + H^+ \rightleftharpoons AH;\ K_{ass} = [AH]/[A^-][H^+]$$

It follows that $K_{ass}= 1 / K_{diss}$ and that log K_{ass} = pK_a. Since association constants are to be used, the subscript *ass* is generally omitted. For a dibasic acid the first dissociation constant is for the dissociation of the acid, AH_2.

$$AH_2 \rightleftharpoons AH^- + H^+;\ K_{diss,1} = [AH^-][H^+]/[AH_2]$$

but the first association constant K_1 is for the equilibrium $A^- + H^+ \leftrightharpoons AH$. It follows that

$$\log K_1 = pK_{a2} \text{ and } \log K_2 = pK_{a1}$$

In general the order of the stepwise association constants is the reverse of the order of the stepwise dissociation constants.

Burette is the name given to a device for adding a reagent to a mixture in a titration. It may be a real burette but it may also be a syringe or a electrolytic generator. The burette

may contain any of the reagents. The concentrations are to be given in moles dm^{-3}. Any reagent which is not present in the burette is given a concentration of zero.

Each (titre) reading of the burette is subject to experimental error. In Hyperquad this error is assumed to have a constant value, independently of the actual burette reading. This quantity can be measured experimentally, by weighing four or five aliquots of water delivered by the burette. The standard deviation of the volumes, calculated from the weights and density at the given temperature, is an estimate of the error.

The **competition method** is used where a stability constant is too large to be measured directly. By this one understands that the degree of formation of the species is close to 100% under all reasonable experimental conditions. To illustrate the competition method, suppose that the species in question is a metal-ligand complex of formula ML (such as a metal EDTA complex) whose stability constant, β_1, is defined by (1) and that the same metal forms a similar, but weaker, complex with another ligand, L', as in (2).

$$[ML] = \beta_1[M][L] \quad (1)$$

$$[ML'] = \beta_2[M][L'] \quad (2)$$

Now, the equilibrium constant, K, for the competition reaction

ML' + L $\rightleftharpoons$ ML + L' is given by (3).

$$[ML][L'] = K[ML'][L] \quad (3)$$

$$\beta_1[M][L][L'] = K\,\beta_2[M][L'][L]$$

It follows that the equilibrium constant for the competition reaction is given by $K = \beta_1/\beta_2$. Therefore if β_2 can be measured directly log β_1 can be derived from the expression (4)

$$\log \beta_1 = \log K + \log \beta_2 \quad (4)$$

In practice, one may determine either log β_1 or Log K from experimental data, using a previously determined value for log β_2.The other constant from the expression (4), if required. The important thing is that K has a value such that there is a significant equilibrium between ML and ML'.

A **correlation coefficient** relates the errors on two quantities. Even when experimental measurements are uncorrelated, that is, when the measurements are completely independent of each other, the errors on the parameters refined by the least-squares method are correlated. This is important when calculating stepwise constants from cumulative constants. For example, the variance on a stepwise constant, K_2, given by

$$\log K_2 = \log \beta_{12} - \log \beta_{11}$$

is equal to

$$\sigma^2 = \sigma_1^{\,2} + \sigma_2^{\,2} + 2\,\sigma_1\,\sigma_2\,\rho_{12}$$

where σ_1 is the standard deviation on log β_{12} , σ_2 is the standard deviation on log β_{11} and ρ_{12} is the correlation coefficient. Correlation coefficient is related to Covariance by

$$\text{Covariance}_{12} = \sigma_1 \sigma_2 \rho_{12}$$

A coulometric titration is so-called originally to apply to a titration in which the alkali is generated by electrolysis and is measured by means of a coulometer. Coulombometric is an alternative name.

In the Hyperquad suite the term can be applied to any titration in which the solution volume remains constant as opposed to a titration in which the volume changes which is a “volumetric” titration.

A **conditional constant** is a concentration quotient which applies only when the concentration of one or more reactants or products is fixed at a particular constant value.

For example, when the equilibria: M + H_nL ⇌ ML + *n*H are studied at fixed pH a conditional (or effective) constant can be defined by (1),

$$[ML] = K_{eff}\,[M][H_nL] \qquad (1)$$

where *n* may be non-integral and H_nL may represent an equilibrium mixture of protonated ligand species, HL, H_2L *etc.* The concept of a conditional constant was introduced by G. Schwartzenbach, Die Complexometrische Titration, Enke, Stuttgart, 1956 in connection with EDTA complexes which show a maximum effective constant at a particular pH. This is useful in defining the pH at which EDTA is most efficient as a complexing agent. The concept was further developed by A. Ringbom, Complexation in Analytical Chemistry, Interscience 1963. Conditional constants are not equilibrium constants or stability constants and are valid only for the experimental conditions used. Calculation of conditional constants from known stability constants and a set of given conditions is illustrated in detail in the document conditional constants.doc

A concentration quotient will also be a conditional constant when the experimental method has not differentiated between the chemical forms of the complex (*e.g*. ML, MHL, $MH_{-2}L$) or ligand (L, HL, H_nL) in the reaction, both of which will be a function of pH:

e.g. for the binding of a metal to a protein at pH 7.4, M + ligand ⇌ complex:

$$[ML]+[MHL]+ \ldots = K_{eff}\,([M]\{[L]+[HL]+ \ldots [H_nL]\})$$

A very detailed set of recommendations for the use of conditional constants in biochemistry may be found at http://www.chem.qmw.ac.uk/iubmb/thermod/ "IUBMB-IUPAC JOINT COMMISSION ON BIOCHEMICAL NOMENCLATURE (JCBN) Recommendations for nomenclature and tables in biochemical thermodynamics".

Published stability constants are conditional in the sense that they refer to a particular temperature an, in most cases, to a particular strength of a particular ionic medium.

Cumulative and stepwise constants A cumulative or overall constant, given the symbol β, is the equilibrium constant for the formation of a complex from reagents. For example, the cumulative constant for the formation of AH_2 is given by

$A^{2-} + 2H^+ \rightleftharpoons AH_2$: $[AH_2] = \beta_{12}[A^{2-}][H^+]^2$

The stepwise constant, K, for the formation of the same complex from A^{2-} and H^+ in two steps is given by

$A^{2-} + H^+ \rightleftharpoons AH^-$: $K_1 = [AH^-]/[A^{2-}][H^+]$
$AH^- + H^+ \rightleftharpoons AH_2$: $K_2 = [AH_2]/[AH^-][H^+]$

Therefore $\beta_{12} = K_1K_2$ and $\log \beta_{12} = \log K_1 + \log K_2$. For the dibasic acid $\log \beta_2 = pK_1 + pK_2$

A cumulative constant can always be expressed as the product of stepwise constants. Each stability constant should be defined by reference to an equilibrium expression, as in the examples above.

Electroneutrality is an essential condition of any chemical system. Some elementary methods of calculation of species' concentrations use a condition of electroneutrality. In most computer programs electroneutrality is guaranteed by imposing the conditions of mass-balance. This means that the electrical charge that any species might carry does not need to be specified. However, charges should be specified when the species are written down.

Equilibrium constants are defined, in Hyperquad, as *concentration quotients*, that is, it is assumed that the quotient of activity factors is constant.

For a generalized equilibrium

$$pA + q\,B \ldots \rightleftharpoons A_pB_q\ldots \quad (1)$$

the concentration of the species $A_pB_q\ldots$ can be expressed in terms of the equilibrium constant, $\beta_{pq\ldots}$, the concentrations of the reagents A, B, ..., denoted by [A], [B]..and the stoichiometric coefficients, p,q, ... as follows:

$$[A_pB_q\ldots] = \beta_{pq}\ldots[A]^p[B]^q\ldots$$

The concentration of the product on the right-hand side of the equilibrium expression (1) is expressed as a product of the equilibrium constant and the free concentrations of the reagents. This follows from the definition of the equilibrium constant as an association constant.

$$\beta_{pq..} = \frac{[A_pB_q..]}{[A]^p[B]^q..}$$

Notes

1. Any electrical charges on the reagents and species are omitted in generalized expressions, but should be included when referring to specific reactions.
2. It is common practice to talk about the logarithm of an equilibrium constant as though it were a value, not its logarithm. This is harmless in verbal exchanges, but should be avoided in written documents.

Experimental error Errors on experimental measurements are of two kinds, random errors and systematic errors.

- Random errors are illustrated by the fact that repeated measurements of the same quantity are never quite the same. The standard deviation on a set of repeated measurements is a indicator of the *precision* of the measurements.
- A systematic error is the difference between the mean of a set of repeated measurements and the "true" value. This difference is an indicator of the *accuracy* of the measurements.

Random error is usually a property of the measuring device and the system in which the measurements are made. For example, a pH meter may show two or three digits after the decimal point, meaning that the precision is 0.01 or 0.001 pH units respectively. Random variation in temperature can add a further amount of random error.

Systematic error can be reduced by calibration against internationally accepted standards. An example of a systematic error is the drift, with time, of a pH reading. To reduce this error the electrode can be calibrated both before and after the experimental measurements. Otherwise systematic errors can only be reduced by good experimental practice.

Regarding stability constant determinations, the aim should be to reduce systematic errors to the same level as the unavoidable random errors; the accuracy should be commensurate with the precision.

Free concentrations are the concentrations of the reagents, however they may be defined.

See also mass balance.

The **ionic product of water (K_w)** refers to the self-ionization equilibrium of water

$$H_2O \rightleftharpoons H^+ + OH^-;\ [H_2O] = K_W\ [H^+][OH^-]$$

The equilibrium constant is specified as the formation constant for the species hydroxide (OH^-), a species whose stoichiometric coefficients are all zero except for the one referring to the proton, which will be -1.

$$[OH^-] = K_W [H^+]^{-1}$$

The value of this constant is around 10^{-14} and depends on ionic strength and on temperature. $Log_{10} K_W$ is about -14. pK_W is minus the logarithm of K_W and has a value around 14.

The method of **least squares** is a method used to calculate the parameters of a function which relates a calculated value to an observed value. For example, the calculated pH of a solution depends on the experimental conditions, which are known, and the stability constants of the species in equilibrium, which are the parameters. The difference between the values of observed and calculated quantities is known as a residual.

$$r_i = y_i^{observed} - y_i^{calculated}$$

The method of least-squares finds the parameter values that minimize a sum of squared residuals, U.

$$U = \Sigma_i r_i^2$$

The justification for using the method of least-squares in stability constant calculations is two-fold.

1. The values of the parameters obtained are those values that have the minimum variance, that is, the smallest calculated error. This property of the method is independent of the nature of the experimental errors.
2. If the experimental errors are distributed normally, the least-squares result is also a the maximum likelihood result. In general the distribution of experimental errors is not known, but may well be close to a normal distribution.

Mass-balance in the context of equilibria is a statement of the law of conservation of mass. The total, or analytical, concentration of each reagent must be a constant. Since the concentrations of the species change as the position of equilibrium changes, each reagent has an equation of mass-balance. For example,

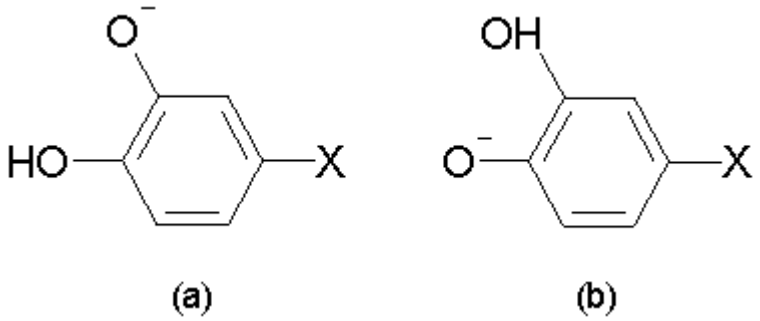
$$T_A = [A] + \Sigma\, p\, c_{pqr} = [A] + \Sigma\, p\, \beta_{pqr} [A]^p[B]^q[H]^r$$
$$T_B = [B] + \Sigma\, q\, c_{pqr} = [B] + \Sigma\, q\, \beta_{pqr} [A]^p[B]^q[H]^r$$
$$T_H = [H] + \Sigma\, r\, c_{pqr} = [H] + \Sigma\, r\, \beta_{pqr} [A]^p[B]^q[H]^r$$

Where T_A is the total concentration of the reagent A and [A] is the free concentration of the reagent. c_{pqr} is the concentration of the species $A_pB_qH_r$.

When the analytical concentrations of all the reagents are known and values are set for the stability constants, solution of the mass-balance equations yields the free concentrations of the reagents and the concentrations of the species.

Micro- and macro- constants The equilibrium constants that refer to species by their stoichiometry alone are known as **macro-constants**. It may, however, be possible to write chemically distinct structural forms (isomers) for a given formula. The stability constants for

the formation a single isomer is called a **micro-constant**. For example, consider the protonation of a substituted catecholate ion. Two isomers may be formed.



The isomers show the remaining proton on the oxygen atom either *para* to the substituent X (a) or *meta* to X (b). In this case the K values for the formation of the two isomers are similar but not identical because the chemical environment of the two oxygen atoms is similar, but not identical. It follows that both isomers will be present in equilibrium together.

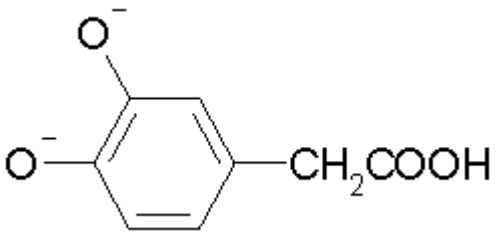
The equilibrium constants for the protonation reactions may be denoted as K^a and K^b. These are micro-constants. The macro-constant K is simply the sum of the micro-constants. This follows from the definitions. Writing LH_2 for the catechol,

$$[LH]^a = K^a[L][H]$$
$$[LH]^b = K^b[L][H] \qquad (1)$$
$$[LH] = [LH]^a + [LH]^b = (K^a + K^b)[L][H] = K[LH][H]$$

Micro-constants cannot be determined by methods which depend only on stoichiometry. Potentiometric methods therefore cannot yield micro-constants. To understand why this is so consider the ratio of concentrations $[LH]^a/[LH]^b$ in (1). Clearly this is equal to K^a/K^b, independent of concentration and pH. Therefore the ratio of concentrations of the two micro-species is a constant (equal to the quotient of stability constants) regardless of the total concentration of the macro-species. This will be true for all micro-species with the same stoichiometry.

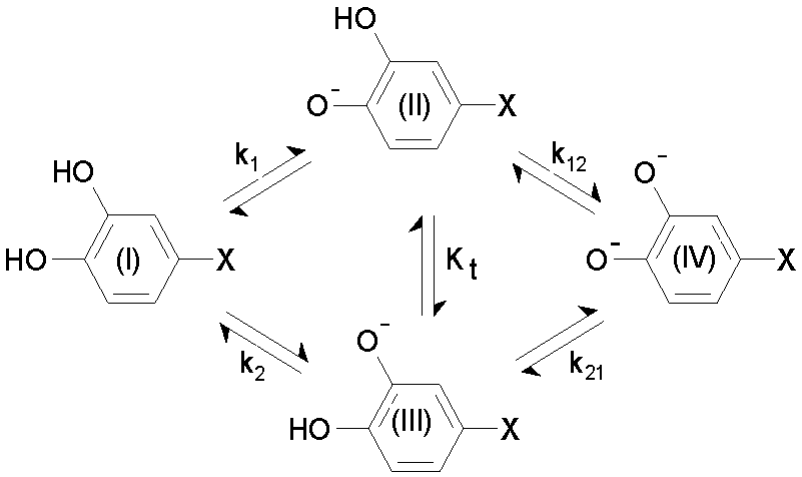
On the other hand spectroscopic methods can yield micro-constants if the corresponding species have distinct spectra, so that the concentrations of each micro-species can be determined separately.

If the ratio of micro-constants is large then one species will predominate. This is illustrated in the case of 3,4-dihydroxyphenylacetic acid (X= $CH_2CO_2^-$) where the carboxylate group is completely deprotonated in the pH region where the phenolic proton is being lost. Therefore the micro-species



has negligible concentration in the alkaline region and can be ignored. The microconstants for this species were determined from ^{13}C NMR data by T. Ishimitsu, Y. Fujiwara and S. Hirose, *Talanta*, (1978) **26,** 74-78. (doi:10.1016/0039-9140(79)80160-5)

It was also assumed that the carboxyl group was not susceptible to protonation in the alkaline region. This being so, There are two micro-species in which one oxygen atom is protonated and the other is not. To describe this system fully 3 stability constants are needed. This is because there are relationships between the micro-constants and macro-constants which can easily be verified by reference to the scheme.



In this scheme the K's are *dissociation* constants.

$K_2=k_1+k_2$	$[LH]=[II]+[III]=(k_1+k_2)[LH_2][H]^{-1}$	
$1/K_3=1/k_{12}+1/k_{21}$	$[LH]=[II]+[III]=(1/k_{12}+1/k_{21})[L][H]$	
$K_2K_3=k_1k_{12}=k_2k_{21}$	$[L]=K_2K_3[LH_2][H]^{-2}$	(2)
$K_t=k_2/k_1=k_{12}/k_{21}$	$[II]=k_1[LH_2][H]^{-1}[III]=k_2[LH_2][H]^{-1}K_t=[III]/[II]$	

There are 4 independent equations and 7 stability constants, so determination of K_2, K_3 and any one micro-constant will suffice to determine all. In the DOPA system it was found that K_t was about 0.9 so that the two micro-species have almost equal concentrations.

A **normal distribution** is a statistics term. A normal distribution may be used to predict the probability that the value of a quantity, subject to random error, may have a certain magnitude. A normal distribution can be used to derive the confidence limits of a parameter found by the least-squares method. For example, there is a 95% probability that the value of a parameter lies within plus or minus two standard deviations from the calculated value. The difficulty with such predictions is that they rely on the assumption that the errors on the quantity concerned are distributed normally. The assumption may be reasonable, but very difficult to prove.

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pK_a, pK_b Although acid and base strengths have been traditionally expressed as pK values the definitions of these quantities are not consistent with the definitions of stability

constants for complex formation. In programs of general scope all equilibrium constants are defined as **overall** *association constants*. This means that for a polybasic acid such as phosphoric acid 3 equilibrium constants are defined as follows.

$PO_4^{3-} + H^+ \rightleftharpoons HPO_4^{2-} : [HPO_4^{2-}] = \beta_{11}[PO_4^{3-}][H^+]$
$PO_4^{3-} + 2H^+ \rightleftharpoons H_2PO_4^- : [H_2PO_4^-] = \beta_{12}[PO_4^{3-}][H^+]^2$
$PO_4^{3-} + 3H^+ \rightleftharpoons H_3PO_4 : [H_3PO_4] = \beta_{13}[PO_4^{3-}][H^+]^3$

A good general rule is always to write down the concentration expression with the concentration of the product(s) on the left-hand side. The stepwise equilibrium constants can easily be obtained from the cumulative constants by writing down the equilibrium and doing a little algebraic substitution. For example, for the stepwise equilibrium

$H_2PO_4^- + H^+ \rightleftharpoons H_3PO_4$
$[H_3PO_4] = K[H_2PO_4^-][H^+]$
$\beta_{13}[PO_4^{3-}][H^+]^3 = K\beta_{12}[PO_4^{3-}][H^+]^2[H^+]$

from which it follows that $K = \beta_{13}/\beta_{12}$ and, taking logarithms, $\log \beta_{13} = \log K + \log\beta_{12}$.

Now, pK_a is defined as the logarithm of a *stepwise* acid *dissociation constant.* For phosphoric acid this is written as

$[H_2PO_4^-][H^+] = K_a[H_3PO_4]$

It follows that pK_a is numerically equal to log K as defined above, which is convenient. The complications arise when considering the 2nd and 3rd acid dissociation constants. We may write

$\log \beta_{13} = pK_{a1} + \log\beta_{12}$
$\log \beta_{12} = pK_{a2} + \log\beta_{11}$
$\log \beta_{11} = pK_{a3}$

It follows that the **first** log *association constant* is equal to the **last** pK_a and that the **last** log *association constant* is equal to the sum of the pK's, $\log \beta_{13} = pK_{a1} + pK_{a2} + pK_{a3}$.

For phosphoric acid the pK values are $pK_1 = 2.15$, $pK_2 = 7.2$ and $pK_3 = 12.37$. It follows that $\log \beta_{11} = 12.37$, $\log \beta_{12} = 19.57$, $\log \beta_{13} = 21.72$.

Note, however, that pK is a very useful concept. In particular, the pH at half neutralization is numerically equal to the corresponding pK. For an acid this means that the pH for half neutralization of the first proton is given by pK_1 and for the second by pK_2, etc. For phosphoric acid this means that at pH 2.15 the solution will contain 50% H_3PO_4 and 50% $H_2PO_4^-$ and at pH 7.2 the solution will contain 50% $H_2PO_4^-$ and 50% HPO_4^{2-}. The third proton will only be removed in strongly alkaline solutions.

A second complication arises because of the way pK_a is defined for bases, which is in effect the *dissociation constant* of the conjugate acid.

$[B][H] = K_a[B]$ (charges omitted)

Therefore this pK_a is numerically equal to log *association constant*.

Here is an example to show how to use pK values. An aromatic amine, RNH_2, is quoted as having an acid $pK_a = 10$, and a base $pK_a = 4$. The chemical interpretation of this data is that the proton is difficult to remove from the amine and will be 50% removed only at the high pH of 10. On the other hand the amine is a moderate base and below pH 4 the base will be more than half protonated. To use these data, define the reagent, L, to be the most deprotonated form, RH^- and use the two protonation constants log $\beta_{11} = 10$ and log $\beta_{12} = 14$.

Incidentally, a simple extension of the half neutralization rule is that the reaction is 10% complete 1 pH unit below pK (90% complete 1 pH unit above pK) and 1% complete 2 pH units below pK. This means that in a titration there will be an end-point starting at about pH = pK +2. The height of the pH jump at an end point is at most about 4 pH units less than the difference between successive pK values.

The **proton** occupies a special position in relation to equilibria in aqueous solution. The proton is a reagent and occurs as such in the case of protonated species. It is also in equilibrium with the hydroxide ion because of the self-dissociation of water. The term is synonymous with **hydrogen ion**.

Note. The proton does not exist as such in aqueous solution. It reacts with water to form the hydronium ion, H_3O^+, which in turn is associated with other water molecules through hydrogen bonding. When water is in vast excess, as is the case for dilute solutions, the concentration of water molecules associated with the hydrogen ion is constant. Because of this, their concentrations can be ignored in equilibrium expressions and the concentration of protons is denoted as $[H^+]$ or sometimes, $[H^+]_{aq}$.

The **hydroxide ion**, OH^-, is a species whose concentration, in aqueous solution, is related to the concentration of hydrogen ions through the self-ionization of water.

The equilibrium constants for species containing the hydroxide ion are expressed in terms of the hydrogen ion concentration. For example, the first step in metal ion hydrolysis can be expressed, omitting electrical charges and water molecules coordinated to the metal, as

$$M + OH \rightleftharpoons M(OH); K = [M(OH)] / [M][OH]$$

However, in aqueous solution the concentration of hydroxide ions is not independent of the hydrogen ion concentration. Rather, the two concentrations are related by the equilibrium

$$K_w = [H^+][OH^-]: [OH^-] = K_w[H]^{-1}$$

Substituting the expression for hydroxide ion concentration into the hydrolysis constant

$$K = [M(OH)] / [M]K_w[H]^{-1}$$

Upon rearrangement this expression becomes

$$K^* = K K_w = [M(OH)] / [M][H]^{-1}$$

Thus, the concentration of the hydrolyzed species is expressed as follow

$$[M(OH)] = \beta^*_{0,-1}[M][H]^{-1}$$

Hydrolysis constants are usually reported in the β^* form and this leads to them appearing to have strange values. For example, if log K = 4 and log K_W = -14, log β^* = 4 -14 = -10. In general when the hydrolysis product contains n hydroxide groups log β^* = log β + n log K_W

$$[M(OH)_n] = \beta^*_{0,-n}[M][H]^{-n}$$

The term **pX** is used as an extension of the term pH. It is defined as minus the logarithm of the concentration of X

$$pH = -\log[H^+] = \log (1/[H^+])$$
$$pX = -\log[X] = \log (1/[X])$$

A **random variable** in chemistry is something whose value cannot be predicted. Most commonly experimental error has a component which varies randomly. If systematic error is ignored, the value of a measured quantity can be expressed as the sum of the true value and a random error value.

$$y = y^{true} + \varepsilon$$

Because the value of the error cannot be predicted the true value can never be known exactly. The mean or average value, $\bar{y}$, of a set of *n* replicate measurements, is an estimate of the true value.

$$\bar{y} = \frac{\sum_{i=1,n} y_i}{n}$$

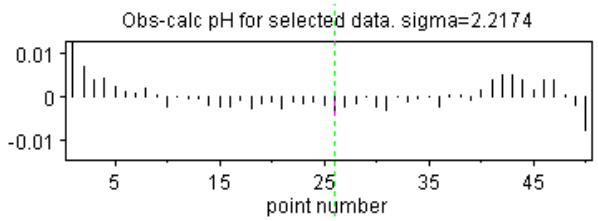
and approaches the true value asymptotically as *n* increases to infinity.

A **Reagent** is defined in conjunction with the stoichiometric coefficients in such a way that the species and equilibrium constants are consistent. It is usual to define the reagents in such a way that the equilibrium constants refer to the association of reagents (not dissociation). For example, with acetic acid the reagent, A, would normally be defined as acetate so that the concentration of the species, acetic acid, is given by

$$[\text{acetic acid}]=[AH]=K[A]][H].$$

Residual A residual is the difference between the value of an observed quantity and the value of the corresponding calculated quantity. A least-squares calculation is used to find the minimum value of the weighted sum of squared residuals. There is a connection between a residual and the corresponding experimental error but they are not the same thing. Least-squares theory shows that residuals calculated at the minimum are, on average, smaller than random experimental errors.

Theory also shows that least-squares residuals are correlated, that is, they show systematic trends. Experimental errors, on the other hand, should show only random variation.



This plot of residuals is as nearly ideal as possible. A systematic trend is visible, overlaid with the effects of random errors in the observations, of the same order of magnitude.

Sigma (σ) is measure of overall goodness of fit, derived from the sum of squared residuals, *r*,

$$\sigma = \sqrt{\frac{\sum_i w_i r_i^2}{m - n}}$$

where *m* is the number of data points and *n* is the number of parameters. Theory predicts that, when the weights, *w*, have been correctly assigned, σ has an *expectation value* of one.

That said, σ is a single statistic and as such tells nothing about the various equilibria that may co-exist. It is a relic of the days before computer graphics made it possible to examine the fit in detail. In fact a residual plot is much more informative as it shows the residuals point by point. If the residuals are scattered randomly the correctly-weighted σ value will be close to one.

A **Solubility product** is defined as the product of the concentrations of reagents present in a saturated solution (each raised to the power of the stoichiometric coefficient. Thus, the solubility product, K_{sp}, of a sparingly soluble species A_pB_q is defined by the relation

$K_{sp} = [A]^p[B]^q$.. (charges omitted)

For example, the solubility product for beryllium hydroxide, $Be(OH)_2$ can be specified as

$$K_{sp} = [Be][OH]^2$$

It is normal practice to replace [OH] by $K_w[H]^{-1}$. In that case the concentration of beryllium hydroxide in solution is given by

$$K^*_{sp} = (K_w)^2[Be][H]^{-2}$$

The species is specified by the stoichiometric coefficients 0,-2 and has a solubility product (expressed in terms of hydrogen ion concentration) numerically equal to $K_{sp}/(K_w)^2$.

A **Species** in the present context is a compound containing more than one of the reagents For example, in a system with two reagents, a base, L, and the proton, H, there may be species such as LH, LH_2, LH_3. Hydrolyzed species usually have formulae such as MLH^{-1}, but, because of the way the equilibrium constants are defined (see proton), the calculated concentration of such a species is the same as the concentration of the species ML(OH).

Standard deviation is a statistic associated with a random variable. It is an estimate of the error on the variable. If a series of *n* replicate measurements is made, such as repeated weighing of a chemical sample, the mean and standard deviations are calculated by means of the following formulae.

$$\text{Mean: } \bar{y} = \frac{\sum_{i=1,n} y_i}{n}$$

$$\text{Standard deviation: } \sigma = \sqrt{\frac{\sum_{i=1,n} \left(y_i - \bar{y}\right)^2}{n-1}}$$

This shows that the standard deviation is a kind of average of the differences between the measured quantities and the mean of those quantities.

In stability constant calculations, the standard deviations of the parameters (stability constants) are calculated by error propagation from the estimated errors on the observations.

Stoichiometric coefficients specify the number of mols of a reagent in 1 mol of a species. They are the subscripts in empirical chemical formulas For example. In

$$1\ Ni + 3\ L + 1\ H \rightleftharpoons NiL_3H$$

the stoichiometric coefficients are 1 for the reagent Ni, 3 for the reagent L, and one for the reagent H. By convention stoichiometric coefficients of one and not shown in a chemical formula. The equilibrium constant for this reaction is defined as

$$[NiL_3H] = \beta_{131}[Ni][L]^3[H]$$

The stoichiometric coefficients are optionally shown as subscripts on β.

Total mmoles is a quantity of reagent. If the reagent is weighed out then

$$\text{Total mmoles} = \frac{\text{mass /mg}}{\text{molecular weight /g}}$$

If a solution is added then

$$\text{Total mmoles} = \text{concentration /mol l}^{-1} \times \text{volume /ml}$$

Total mmoles H^+ is the amount of acid/ millimoles of hydrogen ions (protons) added to the titration vessel initially. It consist of the amount of mineral acid plus any protons that are added with a reagent.

For example, consider the case where the protonation constants for a dibasic acid, LH_2,are being sought and suppose that 2 cm^3 of 0.101 M HCl and 2.1 mmoles of LH_2 were added to the titration vessel. In this case the total amount of H^+ added will be

$$2\times0.101 + 2\times2.1 = 4.402 \text{ mmoles}$$

Similarly, if a base is added to the titration vessel as an acid salt, $BH_n^+Cl_n^-$, n mmoles of hydrogen ion will be added with every mmole of the acid salt.

If an acidic solution is added the total mmoles added will be equal to the volume/ ml times the acid concentration /mol dm^{-1}.

Variance is the square of standard deviation, in effect, the square of an error. It is usually denoted by σ^2. Variance is additive whereas error is not. Examples of simple error propagation formulae are shown in the following table.,

Function	Variance
$f = aA$	$\sigma_f^2 = a^2\sigma_A^2$
$f = aA \pm bB$	$\sigma_f^2 = a^2\sigma_A^2 + b^2\sigma_B^2 \pm 2ab\,\mathrm{COV}_{AB}$
$f = AB$	$\left(\frac{\sigma_f}{f}\right)^2 = \left(\frac{\sigma_A}{A}\right)^2 + \left(\frac{\sigma_B}{B}\right)^2 + 2\frac{\sigma_A\sigma_B}{AB}\rho_{AB}$
$f = \frac{A}{B}$	$\left(\frac{\sigma_f}{f}\right)^2 = \left(\frac{\sigma_A}{A}\right)^2 + \left(\frac{\sigma_B}{B}\right)^2 - 2\frac{\sigma_A\sigma_B}{AB}\rho_{AB}$

Note that error propagation formula for sums and products may contain a covariance term, shown as COV, or the corresponding correlation coefficient, ρ. This is important when calculating the error on a stepwise constant from the errors on overall constants.

Wikipedia Articles in the series “Concepts in chemical equilibria” are generally reliable as I have either authored them or been a major contributor. (except “Chemical equilibrium”.)
http://en.wikipedia.org/wiki/Equilibrium_chemistry
Is a good starting point.

Weights Ideally each weight should be equal to the reciprocal of the variance of a measurement. This assumes that the errors on the measurements are independent of each other. Unfortunately that may not be true for certain kinds of UV-vis spectra, but let that pass. The calculation of the weights requires estimates of the experimental errors.

With potentiometric data two errors must be estimated, σ_E, the error on an electrode reading and σ_V, the error on a titre reading. These estimates are used to calculate the weights from the following expression

$$w = \frac{1}{\sigma_E^{\,2} + \text{slope}^2 \sigma_V^{\,2}}$$

The *slope* of the titration curve, is calculated by numerical differentiation of the data. This expression implies that points near an end-point, where the titration curve rises steeply, are given less weight than points in a buffer region.

With spectrophotometric and NMR data weights are inversely proportional to the variance on the measured quantity.