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Molecular thermodynamic model for equilibria in solution IV. Macroscopic partition functions

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Abstract

The molecular ensembles statistically distributed according to internal specific characteristics and distinguished for the different exchanges with the surroundings are represented on the macroscopic scale by appropriate partition functions. The partition function for *osmotic non-reacting* ensemble is a function of concentration or activity of the ligand and is suited to the definition of thermodynamic potential μ. The partition function for *thermal non-reacting* ensemble shows the dependence upon the temperature and that for *thermo-osmotic non-reacting* ensemble shows the dependence upon both concentration and temperature.

The *reaction* partition function is suited to show the distribution of the different species over the different enthalpy levels of the *reacting* ensemble. The dispersion of the distributions are represented by second derivatives of the partition function.

The information contained in the entropy axis of the thermodynamic space for *reacting* ensembles concerning the induced dilution of the bound ligand and final dilution of the free ligand can be spanned to a formation function diagram where free energy of reaction can be graphically represented. © 1998 Elsevier Science B.V.

Keywords: Chemical equilibria; Statistical mechanics; Theory

1. Introduction

In preceding articles [1–3], a statistical thermodynamic model for solutions has been developed. The properties of molecular ensembles for solution statistically distributed according to specific characteristics are represented on the macroscopic scale by appropriate partition functions. The derivatives of these function which describe the experimentally determinable properties of actual thermodynamic systems are here presented and analyzed.

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2. Partition functions

Formally, the properties of each type of ensemble are expressed by the mathematical properties of their respective partition function.

2.1. Osmotic no-reaction partition function

The *osmotic non-reacting ensemble* $\mathrm{nre_o}$ is open to the exchange of matter but closed to the exchange of heat. The *osmotic no-reaction* partition function Γ_A is referred to 1 mol and is therefore a partial molar

quantity

$$\Gamma_A = \exp(-\mu_A/RT) = \exp(-h_A/RT)\exp(s_A/R) \quad (1)$$

where $s_A = s_A([A])$ is the entropy dependent upon the concentration [A]. The derivative of the logarithm of the *microcanonical* partition function ln Γ_A with respect to ln[A] is

$$\partial \ln \Gamma_A / \partial \ln[A] = \partial(-\mu_A/RT)/\partial \ln[A] \quad (2)$$

By recalling the relationship between entropy and dilution

$$ds_A = -R\, d \ln[A] \quad (3)$$

and by considering that the enthalpy factor is constant, one can write

$$\partial \ln \Gamma_A / \partial \ln[A] = \partial(s_A/R)/\partial \ln[A] = -1 \quad (4)$$

The Eq. (4) by comparison with the Eq. (2) yields

$$\partial(-\mu_A/RT)/\partial \ln[A] = -1 \quad (5)$$

which can be integrated

$$\mu_A = \mu_A^{\phi} + RT \ln[A] \quad (6)$$

This is the general equation defining the chemical potential under the ideal condition that the concentration [A] equals the activity of A. It can be recalled from the Eq. (3) that the Eq. (6) is proportional to a change of entropy (i.e. dilution).

There is no dispersion of the enthalpy around the mean value and consequently the isobaric heat capacity is null, $C_{p,A}=0$. The dispersion or variance of entropy, is not null var $s[A]=-1$ as shown by the second moment of the distribution of the Eq. (4).

2.2. Thermal no-reaction partition function

The *thermal non-reacting* ensemble nre_t is characterized by being open to the exchange of heat but not to the exchange of matter. The system is closed and contained in a vessel with diathermal walls. There is no change of species concentration because the system is *non-reacting*. The *thermal no-reaction* partition function ζ_i of the species i represents the distribution of different conformational, translational, rotational, and vibrational modifications of the species among the different sublevels j of the set i. The logarithm of the canonical partition function can be derived with respect to the temperature. The first derivative of $\ln\zeta_i$ is the enthalpy of the species

$$\partial \ln\zeta_i / \partial \ln(1/T) = -H_i/R \quad (7)$$

$$(1/T)\partial \ln\zeta_i / \partial \ln(1/T) = \partial \ln\zeta_i / \partial \ln T = -(1/T)H_i/R \quad (8)$$

and the second derivative is the non-null isobaric heat capacity, $C_{p,i}$

$$\partial^2 \ln\zeta_i / \partial \ln(1/T) \partial T = C_{p,i}/R \quad (9)$$

The first derivative of ln ζ_i with respect to ln$T$ is the entropy of the species i

$$\partial \ln\zeta_i / \partial \ln T = S_i/R \quad (10)$$

and the second derivative is again the isobaric heat capacity

$$\partial^2 \ln\zeta_i / \partial (\ln T)^2 = C_{p,i}/R \quad (11)$$

The isobaric heat capacity in *thermal non-reacting* ensembles is a measure of the dispersion (or variance) of both enthalpy and entropy. In fact

$$C_{p,i}/R = (1/R)^2(\langle (H_{i,j}/T)^2 \rangle - \langle (H_{i,j}/T) \rangle^2) \quad (12)$$

where the average is extended to all the energy sublevels j of the level i. The dispersion around the average enthalpy is due to the changes of population in the translational, rotational, and vibrational sublevels.

When the isobaric heat capacity is viewed as the derivative of entropy, it represents the distribution of the entropy around the average entropy of the species

$$C_{p,i}/R = (1/R)^2(\langle (S_{i,j})^2 \rangle - \langle (S_{i,j}) \rangle^2) \quad (13)$$

The dispersion around the average entropy is due to the changes in the translational, rotational, and vibrational degrees of freedom. The distinction between the dispersions of the Eqs. (12) and (13) is not possible by thermal measurements. The only change that can be observed experimentally is the ratio between the change of temperature ΔT and the heat added to or subtracted from the system.

2.3. Thermo-osmotic no-reaction partition function

The *thermo-osmotic non-reacting* ensemble $nre_{t,o}$ is open to exchange of both matter and heat. The system

is contained in a diathermal vessel with communication with the surroundings by means of a specific permeable membrane. Even one single component of a *reacting* ensemble can be considered as a *non-reacting* subensemble. The total differential of the *thermo-osmotic no-reaction* partition function can be calculated by recalling the definition of *thermal* ensemble which is independent from the concentration and the definition of *osmotic* ensemble which is isothermal and isoenthalpic. Therefore, the total differential for a component A is

$$\mathrm{d}\ln(\zeta_A \Gamma_A) = \mathrm{d}\ln\zeta_A + \mathrm{d}\ln\Gamma_A \tag{14}$$

The first term of the right-hand side (RHS) can be differentiated with respect to $\ln T$ thus obtaining, by recalling the Eqs. (10) and (11)

$$\mathrm{d}(s_A/R)_{[A]} = (C_{p,A}/R)\partial\ln T \tag{15}$$

The second term of the RHS of the Eq. (14) can be differentiated with respect to ln[A] thus obtaining, by recalling the Eq. (3)

$$\mathrm{d}(s_A/R)_T = -\mathrm{d}\ln[A] \tag{16}$$

We assume that the change of probability due to the change of temperature is equivalent to the change of probability due to a virtual change of concentration

$$\mathrm{d}(s_A/R)_T = \mathrm{d}(s_A/R)_{[A]} \tag{17}$$

and hence

$$C_{p,A}\mathrm{d}\ln T = -R\,\mathrm{d}\ln[A] \tag{18}$$

This is the mathematical expression of the thermal equivalent dilution [2]. It is equivalent to the adiabatic work for ideal gases [4].

2.4. Reaction partition function

The *thermal reacting* ensemble re_t is open to the exchange of heat and closed to the exchange of matter. Even in this case, however, there is redistribution of populations among the different levels. The process of redistribution can be accompanied by heat effects which are compensated by dilution effects if the process is conducted isothermally. If the *thermal reacting* ensemble re_t is open to the exchange of matter but not to the exchange of heat the system undergoes a reaction transformation which is accompanied by redistribution of matter and by internal heat effects which can produce a change of the temperature. If the *reacting* ensemble is open to the exchange of both matter and heat the transformation produces changes in the distribution of the species which are accounted for by the partition function. Again, an isothermal process is suited to evaluate the whole transformation in terms of total entropy change. The *reaction* partition function, Z_M is suited to the representation of the concentration distributions among the i levels either because of a change of concentration or of temperature

$$Z_M = \sum_{i=0}^{i=t} \beta_i [A]^i \tag{19}$$

where M is the reacting receptor, [A] is the concentration of the reacting ligand, and β_i is the cumulative formation constant for the species MA_i

$$\beta_i = [MA_i][M]^{-1}[A]^{-i} \tag{20}$$

The *reaction* partition function is the product of the probability enthalpy factor $\exp(-\Delta H_F/RT)$ times the probability entropy factor, $\exp(\Delta S_F/R)$ for the formation of the species present in solution at a certain stage of the reaction. The product is the joined probability of the state, $\exp(-\Delta G_F/RT)$

$$\begin{aligned} Z_M &= \exp(-\Delta G_F/RT) \\ &= \exp(-\Delta H_F/RT)\exp(\Delta S_F/R) \end{aligned} \tag{21}$$

The enthalpy ΔH_F is actually a weighted average enthalpy depending on the advancement of the reaction

$$-\Delta H_F = -\overline{n}\Delta H_0 \tag{22}$$

where $\overline{n}$ is the average number of ligand A bound per mole of receptor M or Bjerrum formation function and ΔH_0 the specific site enthalpy for binding one ligand A to one site of the receptor M. The same weighted average holds for the entropy ΔS_F and for the free energy ΔG_F. Note that the weighted average conforms with average binding energy (BE) of Ben-Naim [5] for generalized molecular distribution functions (GMDF).

Z_M gives the probability of finding in solution and species MA_i, where free M is assumed as the reference state. When the receptor M represents more classes of binding sites, the partition function can be factorized into class partition functions. Cooperativity effects among sites of the same class can be accounted for

by introducing appropriate cooperativity functions in the partition function [6,7].

Alternatively the sate of the solution can be described by a dissociation partition function, Z_M^D which gives the probability of finding in the solution any species MA_i, when the completely saturated complex, MA_t is assumed as the reference state. The coefficients of this polynomial are dissociation constants, β_i^{-1}

$$Z_M^D = \sum_{i=0}^{i=t} (\beta_{t-i}[A])^{t-i} \tag{23}$$

The ratio of the two partition functions $Z_M/Z_M^D = F_M^C$ gives the ratio between the probability of formation and the probability of dissociation at some chosen value of ln[A]. The ratio F_M^C is another partition function, the saturation function

$$F_M^C = \beta_t([A])^t \tag{24}$$

At standard unit concentration, one obtains the standard saturation function, $F_M^{C\phi}$. The saturation function can be factorized into stepwise formation constants

$$F_M^C = (K_1[A])(K_2[A]) \ldots (K_i[A]) \ldots (K_t[A]) \tag{25}$$

In standard unit concentration, [A]=1, the standard saturation function, $F_M^{C\phi}$ is the product of the stepwise formation constants K_i.

Note that in a one-site receptor, the saturation function is identical with the site affinity constant, k times the concentration of the ligand

$$F_M^C = k[A] \tag{26}$$

In some cases, the distribution of the solute species can be described by the total partition function Ξ_M=[M]Z_M.

Depending on the problem at hand, the different *reaction* partition functions can be employed to describe the properties of the system. In particular, we recall the principle that the equilibrium constant itself is a type of partition function [3] to which the same properties can be assigned as the *reaction* partition function.

The *reaction* partition function can be derived with respect to $(1/T)$ and/or ln[A] corresponding to exchange of heat or matter. The derivative of lnZ_M with respect to the reciprocal temperature is the average enthalpy of the reaction

$$\partial \ln Z_M / \partial \ln(1/T) = \langle -\Delta H_F/R \rangle = -\Delta H_F/R \tag{27}$$

The enthalpy of the reaction, $-\Delta H^{\phi}$ can be found from the derivative of ln$k$ against $1/T$ (van't Hoff equation)

$$\partial \ln k / \partial \ln(1/T) = -\Delta H^{\phi} \tag{28}$$

The equilibrium constant is determined by isothermal experiments at different temperatures.

The derivative of lnZ_M with respect to dilution of the ligand is the mean number of ligand bound per molecule of receptor or Bjerrum formation function and at the same time is the change of entropy due to the dilution of the ligand.

$$\partial \ln Z_M / \partial \ln[A] = \overline{n} = \Delta S/R \tag{29}$$

The second derivative of lnZ_M with respect to temperature is the heat capacity change $\Delta C_p/R$

$$\partial^2 \ln Z_M / \partial \ln(1/T) \partial T = \Delta C_p/R \tag{30}$$

and is found from the change of the slope in the plot of ln$k$ against $1/T$ provided that Z_M is the true and only partition function describing the behaviour of the system.

The second mixed derivative of lnZ_M with respect to temperature and dilution of the ligand is an apparent isobaric heat capacity $\Delta C_{p,app}/R$. The second mixed derivative for a 1 : 1 complex, on the assumption that $\Delta C_{p,app}/R \gg \Delta C_p/R$ is related to the molar fraction by

$$\begin{aligned} \partial^2 \ln Z_M / \partial(\ln[A]) \partial(\ln T) &= -\partial\alpha/\partial(\ln T) \\ &= \Delta C_{p,app}/R = -(-\Delta H/RT + C_{p,A}/R) \end{aligned} \tag{31}$$

which comes out to be negative for exothermic and positive for endothermal reactions. The apparent isobaric heat capacity is found in DSC experiments where the temperature is changing. The equilibrium is displaced even if the system is closed to the addition of substance from outside. It can also be obtained from values of equilibrium constant at different temperatures, if the ligand A is the solvent and the system can be considered as a convolution of two ensembles [8,9]. In this case, the reaction is completely displaced toward the maximum coordination number and the

value comes out to be multiplied by the number of ligand (solvent), n_w involved in the reaction.

In case of multiple complexation reaction, the apparent isobaric heat capacity is calculated by considering that the molar fraction is a particular value of $\overline{n}$. The first derivative with respect to ln$T$ is $\overline{n}$ which can be further derived with respect to ln[A]

$$\Delta C_{p,app}/R = \partial^2 \ln Z_M/(\partial \ln[A]\partial \ln T) = -\sum_{i=1}^{i=t} \alpha_i (i-\overline{n})(1/i)((-\Delta H_i/RT + iC_{p,A}/R) \quad (32)$$

where the enthalpy $-\Delta H_i$ is the enthalpy change for the cumulative formation constant β_i of the complex $M+iA=MA_i$.

3. Chemical potential

The reacting ensemble is suited to define the chemical potential, μ of the ligand. Consider a solution where receptor M and ligand A bind to form complexes M_pA_q with $0 \le p, q \le t_p, t_q$. The chemical potential of the ligand A is defined as

$$\partial\{(\Delta G_A/RT)/\partial \overline{n}_M^A\}_{[M],T,P} = \mu_A/RT \quad (33)$$

where $\overline{n}_M^A$ is the mean number of ligand A bound to M. The free energy, $-\Delta G_A/RT = \ln Z_M$ is related to $\overline{n}_M^A$ also by the relation (Fig. 1)

$$\partial\{(-\Delta G_A/RT)/\partial \ln[A]\} = \overline{n}_M^A \quad (34)$$

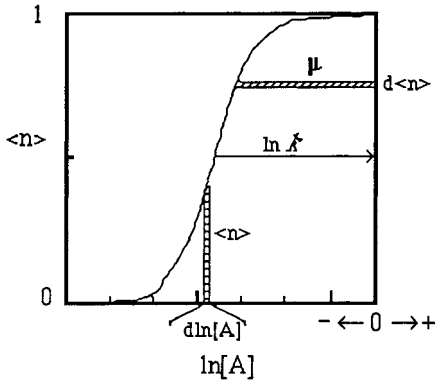

Fig. 1. Bjerrum plane.

from which the total free energy can be obtained by integration

$$-\Delta G_A/RT = \int d\{-\Delta G_A/RT) = \int \overline{n}_M^A d \ln[A] \quad (35)$$

The RHS of the Eq. (34) can be integrated by parts, thus yielding

$$-\Delta G_A/RT = [\overline{n}_M^A \ln[A]]_1^{[A]} - \int_{[A]}^{0} \ln[A] d\overline{n}_M^A \quad (36)$$

which transforms the integral of the Eq. (35) into a function of the differential $d\overline{n}_M^A$. The differential of the Eq. (36) is

$$\partial\{(-\Delta G_A/RT)/\partial \overline{n}_M^A\} = \ln[A] \quad (37)$$

By comparison with the Eq. (33) we can write

$$\partial\{(\Delta G_A/RT)/\partial \overline{n}_M^A\}_{[M],T,P} = \mu_A/RT = \ln[A] \quad (38)$$

This equality defines also the differential of the chemical potential of the ligand A

$$d\mu_A/RT = d \ln[A] \quad (39)$$

For complexes M_pA_q sufficiently strong that $Z_M \approx k \gg 1$, the Eq. (36) gives the standard free energy, $\Delta G_A^\phi/RT$. In fact, if [A]=1, the first term on the RHS vanishes and the second term, integrated between the limits [A]=0 and [A]=1, yields

$$-\Delta G_A^\phi/RT = \ln k \quad (40)$$

In weak complexes or multiple complexes M_pA_q, the saturation function $F_M = \ln \beta_t [A]^t$ (cfr. Eq. (5)) must be used. In the presence of excess A, the only complex present is M_pA_t and on the other hand, if $\langle -\Delta H_A \rangle/RT \to 0$, the *reacting* ensemble tends to the *microcanonical* ensemble. Under these conditions, the limit is

$$\lim_{\langle \Delta H_A \rangle \to 0} \partial\{(\Delta G_A/RT)/\partial \overline{n}_M^A\}_{[M],T,P} = G_{A,t}/RT = \mu_A/RT \quad (42)$$

which holds for *non-reacting microcanonical* ensemble.

The chemical potential of M can be defined in a similar way by reference to the partition function Z_A

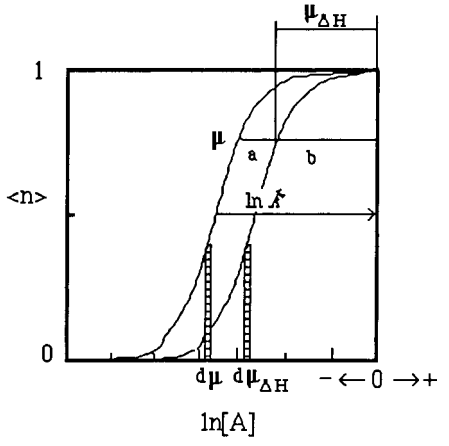

Fig. 2. Definition of chemical potential from *reaction* partition function.

where A is considered the receptor and M the ligand. The formation function $\overline{n}_{\mathrm{A}}^{\mathrm{M}}$ giving the mean number of M bound to A is employed. Alternatively, in polynuclear complexes $\mathrm{M}_p\mathrm{A}_q$ with $p>1$, the chemical potential μ_{M} of M can be calculated from Z_{M} by $\overline{n}_{\mathrm{M}}^{\mathrm{M}}$, which is the average number of M bound to M.

The diagram of Fig. 2 is actually an entropy plane because both the axes represent entropic quantities, namely $\overline{n}_{\mathrm{M}}^{\mathrm{A}}$ represent the induced dilution of the ligand and $-\ln[\mathrm{A}]$ represents the final dilution of the free ligand. This entropy plane ($\overline{n}_{\mathrm{M}}^{\mathrm{A}}$, ln[A]) spans the whole information projected and contained in the abscissa axis of the thermodynamic space. This abscissa expresses (i) the intrinsic entropy change, $\Delta S/R$, (ii) the projected equivalent enthalpy change, $\Delta S_H/R=-\Delta H/RT$, (iii) the projected free energy or total entropy change, $\Delta S_{\mathrm{tot}}/R=-\Delta G/RT$, and (iv) the dilution of the free ligand, $-\ln[\mathrm{A}]$.

On these grounds, the entropy plane is suited to show how the enthalpy and the entropy change can also be assigned a chemical potential, $\mu_{\Delta H}/RT$ and $\mu_{\Delta S}/RT$, respectively. The whole area below the curve equals the standard free energy change $-\Delta G_{\mathrm{A}}^{\phi}/RT$ of the Eq. (40), obtained by integration of the Eq. (35)

$$-\Delta G_{\mathrm{A}}^{\phi}/RT = a + b \tag{43}$$

where $a = \Delta S_{\mathrm{A}}^{\phi}/RT$ and $b = -\Delta H_{\mathrm{A}}^{\phi}/RT$. Either the total area ($a+b$) or the partial area a or b can be obtained by integration of the respective potentials

$$\partial\{(\Delta G_{\mathrm{A}}/RT)\partial\overline{n}_{\mathrm{M}}^{\mathrm{A}}\}_{[\mathrm{M}],T,P} = \mu_{\mathrm{A}}/RT \tag{44}$$

$$\partial\{(\Delta H_{\mathrm{A}}/RT)\partial\overline{n}_{\mathrm{M}}^{\mathrm{A}}\}_{[\mathrm{M}],T,P,S} = \mu_{\mathrm{A},\Delta H}/RT \tag{45}$$

$$\partial\{(\Delta S_{\mathrm{A}}/RT)\partial\overline{n}_{\mathrm{M}}^{\mathrm{A}}\}_{[\mathrm{M}],T,P,H} = \mu_{\mathrm{A},\Delta S}/RT \tag{46}$$

Note that the potentials of the Eqs. (44) and (45) are different although their differentials are equal

$$\mathrm{d}\mu_{\mathrm{A}} = (\mathrm{d}\mu_{\mathrm{A},\Delta H})_S = (\mathrm{d}\mu_{\mathrm{A},\Delta S})_H = RT\,\mathrm{d}\ln[\mathrm{A}] \tag{47}$$

4. Conclusion

The statistical model for solutions which is based on the principle that the systems can be either *non-reacting* or *reacting* depending upon the non-existence or existence, respectively of well-separated enthalpy levels, is described at the macroscopic level by means of molar partition functions. The derivatives of the *no-reaction* and *reaction* partition functions with respect to the variables concentration and temperature correspond to the experimental observables. Therefore, the partition functions are fundamental tools for the mathematical representation and molecular interpretation of the experimental thermodynamic data.

5. List of symbols

μ_{A}^{ϕ}	standard chemical potential
$\mathrm{nre}_{\mathrm{o}}$	*osmotic non-reacting* ensemble
ζ_i	thermal canonical partition function
$\langle H_{i,j}\rangle$	average enthalpy
j	index of sublevel
i	index of level or species
ΔH_0	specific site enthalpy
$Z_{\mathrm{M}}^{\mathrm{D}}$	dissociation partition function
$F_{\mathrm{M}}^{\mathrm{C}}$	saturation function (formation/dissociation)
$F_{\mathrm{M}}^{\mathrm{C}\phi}$	standard saturation function
K_i	stepwise formation constant
Ξ_{M}	total partition function
n_{w}	number of water molecules
$\mathrm{M}_p\mathrm{A}_q$	complex
$\mu_{\Delta H}$	enthalpy chemical potential

$\mu_{\Delta S}$	entropy chemical potential
R	gas constant
T	absolute temperature

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