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On the size and shape dependence of the solubility of nano-particles in solutions

G. Kaptay*

Bay Zoltan Applied Research Nonprofit Ltd, Department of Nanomaterials, University of Miskolc, Department of Nanotechnology, Egyetemvaros, 606, E/7, Miskolc 3515, Hungary

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ABSTRACT

The general equation is derived for the equilibrium of a small solid particle and a large solution, being consistent with the thermodynamics of Gibbs. This equation can be solved in a closed form for solubility if an ideal (or an infinitely diluted) solution is considered, if the interfacial energy is independent of the composition of the solution and if all physical parameters (other than the solubility itself) are taken size independent. The solubility of the particles is found to increase with increasing its specific surface area, i.e. if non-spherical particles are applied. This simplified solution further simplifies if the shape of the solid is supposed to be spherical. This latter equation, however, is found to be in contradiction with the Ostwald–Freundlich equation, widely used in chemistry, biology and materials science to describe the size dependence of solubility of a spherical crystal. The reason for its incorrectness is shown to be due to the incorrect application of the Laplace equation. It is found that the solubility increases with decreasing the size of the dissolving phase not due to the increased curvature of the phase (Kelvin and Freundlich), but rather due to the increased specific surface area of the phase (Gibbs, Ostwald). Equations are also derived for the case, when the size effect of the interfacial energy is taken into account, and when the crystal is surrounded by several planes of different interfacial energies. The role of wettability is discussed on the size dependence of solubility.

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1. Introduction

Probably the first paper on the size dependence of solubility of solid particles in liquid solutions is due to Ostwald (1900). His derivation is based on the thermodynamics of Gibbs (1875–1878) and is applicable to the solubility of a spherical solid particle in a large liquid solution:

$$x_{A(\beta)} = x_{A(\beta)}^0 \cdot \exp \left(\frac{3 \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}^0}{R \cdot T \cdot r_{\alpha}} \right) \quad (1a)$$

where $x_{A(\beta)}$ is the solubility of component A (mole fraction) in the form of a spherical, pure phase α of radius r_{α} (m) in a given solution β at temperature T (K) and at a fixed pressure p (Pa), $x_{A(\beta)}^0$ is the same of an infinitely large phase α , $\sigma_{\alpha/\beta}^0$ is the interfacial energy (J/m²) between the two phases (supposed to be size independent), $V_{A(\alpha)}^0$ is the molar volume (m³/mol) of the pure phase A(α), and $R = 8.3145$ J/(mol K), the universal gas constant. Using the analogy of

the Kelvin equation (under the name Thomson, 1871), the Ostwald equation was quite soon corrected by Freundlich (1909) as:

$$x_{A(\beta)} = x_{A(\beta)}^0 \cdot \exp \left(\frac{2 \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}^0}{R \cdot T \cdot r_{\alpha}} \right) \quad (1b)$$

Since then, Eq. (1b) has become widely accepted and is called today as the Ostwald–Freundlich equation. According to Google Scholar, more than 400 papers refer to this equation under this name. Its usage accelerated during the recent years, as follows from Fig. 1. Except the year of 1999, the yearly number of papers mentioning the Ostwald–Freundlich equation was below 10 before 2005, while it started to increase in an unexpected way during the last 5 years. Although the equation is used time to time in chemistry (Wu and Nancollas, 1998; McCoy, 2001; Cherginets et al., 2002, 2010; Godec et al., 2009; Bouzid et al., 2011; Deflorian et al., 2011), physics (Letellier et al., 2007; Shchekin and Rusanov, 2008), materials science (Znaidi, 2010; Chiang and Sankaran, 2012), environmental sciences (Mudunkotuwa and Grassian, 2011; Bian et al., 2011) and nano-sciences (Ravichandran, 2010; Picher et al., 2011; Dodd and Saunders, 2011), the boom of its usage is due to its application in pharmaceutical nanotechnology (Müller et al., 2001; Nagy et al., 2012; Liu et al., 2012). Only in the 2010–2011 issues of this journal 9 papers are published citing the Ostwald–Freundlich equation (Cerdeira et al., 2010; Deng et al., 2010; Pardeike and Müller, 2010; Keck, 2010; Gao et al., 2011; Jiang et al., 2011; Kawabata et al., 2011; Pardeike et al., 2011).

* Tel.: +36 30 4150002; fax: +36 46 362916.

E-mail address: kaptay@hotmail.com

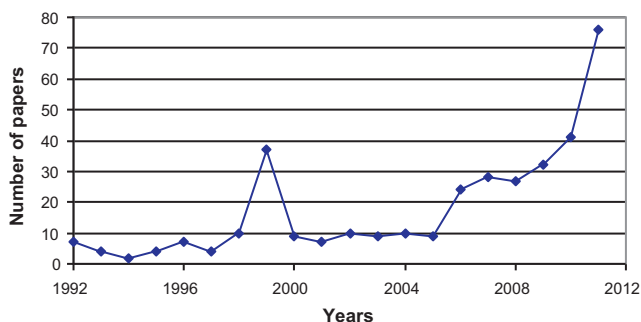


Fig. 1. The number of papers published yearly during the last 20 years, containing the expression “Ostwald–Freundlich” (according to Google Scholar, searched on 26 December, 2011).

One can see that Eqs. (1a) and (1b) differ from each other only by a numerical coefficient. However, behind this small qualitative difference, a quantitative difference between different approaches are hidden, as recently shown by Kaptay (2012a) for the vapor pressure of small droplets. In this paper the equation for the size and shape dependence of the solubility of small solid particles is described, based on the thermodynamics of Gibbs. In this context, the validity of Eqs. (1a) and (1b) will be discussed.

2. Derivation of the general equation

Let us consider component A in the form of a pure, solid phase α of any size and shape in an infinitely large solution β of any nature and number of components (including component A), at fixed temperature and pressure. The task is to derive a general equation to describe the solubility of A in β . Thus, we search for an equation for the equilibrium mole fraction of component A in solution β ($x_{A(\beta)}$), which keeps equilibrium with the solid phase A(α) of the given size and shape at given temperature and pressure.

The size and shape of the pure solid phase α is described by its volume V_α (m^3) and by its total surface area A_α (m^2). In the first approximation we consider that the interfacial energy is identical along the total interfacial area of the phase (for the correction, see below). Thus, the specific surface area of this phase α ($A_{S,\alpha}$, $1/\text{m}$), is defined as:

$$A_{S,\alpha} \equiv \frac{A_\alpha}{V_\alpha} \quad (2)$$

According to Gibbs (1875–1878), the condition of equilibrium between phases α and β is the equality of their partial Gibbs energies. In our particular case, the standard Gibbs energy of pure phase A(α) (denoted as $G_{A(\alpha),S}^\circ$, J/mol, where subscript “S” refers to the given specific surface area $A_{S,\alpha}$) and the partial Gibbs energy of component A in the solution phase β ($G_{A(\beta)}$, J/mol) should equal:

$$G_{A(\alpha),S}^\circ = G_{A(\beta)} \quad (3)$$

According to the theory of solutions (Lewis, 1907; Kaptay, 2004, 2012b; Lukas et al., 2007), the partial Gibbs energy of component A in solution β can be written as:

$$G_{A(\beta)} = G_{A(\beta)}^\circ + R \cdot T \cdot \ln x_{A(\beta)} + \Delta G_{A(\beta)}^E \quad (4)$$

where $G_{A(\beta)}^\circ$ is the standard Gibbs energy of component A in the pure phase β (J/mol) (being the function of only T and p), $\Delta G_{A(\beta)}^E$ is the partial excess Gibbs energy of component A in solution β (J/mol), being a difficult function of $x_{A(\beta)}$, T and p . The (molar) standard Gibbs energy of pure phase A(α) of the given specific

surface area can be written as (for the derivation of this equation, see Appendix A):

$$G_{A(\alpha),S}^\circ = G_{A(\alpha)}^\circ + A_{S,\alpha} \cdot V_{A(\alpha)}^\circ \cdot \sigma_{\alpha/\beta}^\circ \quad (5)$$

where $G_{A(\alpha)}^\circ$ is the standard Gibbs energy of component A in the pure phase α (J/mol) (being the function of only T and p). Substituting Eqs. (4) and (5) into Eq. (3):

$$G_{A(\alpha)}^\circ + A_{S,\alpha} \cdot V_{A(\alpha)}^\circ \cdot \sigma_{\alpha/\beta}^\circ = G_{A(\beta)}^\circ + R \cdot T \cdot \ln x_{A(\beta)} + \Delta G_{A(\beta)}^E \quad (6)$$

The requested solubility ($x_{A(\alpha)}$) is found by solving Eq. (6). This solution has a mathematically closed form only in simplified cases.

3. A simplified solution to Eq. (6)

Now, let us suppose that solution β is an ideal solution, at least, from the point of view of component A.¹ Thus, its excess partial Gibbs energy will be zero, by definition. Also, let us suppose that the interfacial energy $\sigma_{\alpha/\beta}^\circ$ is independent on the composition of phase β , i.e. can be taken as a constant parameter. Then, the solubility (i.e. the equilibrium mole fraction) of component A in phase β can be expressed from Eq. (6) as:

$$x_{A(\beta)} = \exp \left(\frac{G_{A(\alpha)}^\circ - G_{A(\beta)}^\circ + A_{S,\alpha} \cdot V_{A(\alpha)}^\circ \cdot \sigma_{\alpha/\beta}^\circ}{R \cdot T} \right) \quad (7)$$

Let us express from Eq. (7) the solubility of a large phase, with negligible specific surface area (i.e. large size):

$$x_{A(\beta)}^\circ = \exp \left(\frac{G_{A(\alpha)}^\circ - G_{A(\beta)}^\circ}{R \cdot T} \right) \quad (8)$$

Substituting Eq. (8) into Eq. (7), the final equation for the solubility is obtained as:

$$x_{A(\beta)} = x_{A(\beta)}^\circ \cdot \exp \left(\frac{A_{S,\alpha} \cdot V_{A(\alpha)}^\circ \cdot \sigma_{\alpha/\beta}^\circ}{R \cdot T} \right) \quad (9)$$

Let us mention that Eq. (9) is valid only, if $G_{A(\alpha)}^\circ$, $V_{A(\alpha)}^\circ$ and $\sigma_{\alpha/\beta}^\circ$ are not size dependent. As follows from Eq. (9), the larger is the specific surface area of the particle, the larger is its solubility. Thus, the smaller is the particle, or the more its shape deviates from that of a sphere, the higher is its solubility.

For a spherical particle of radius r_α , the specific surface area equals: $A_{S,\alpha} = 3/r_\alpha$. Substituting this value into Eq. (9), the following particular expression is obtained:

$$x_{A(\beta)} = x_{A(\beta)}^\circ \cdot \exp \left(\frac{3 \cdot V_{A(\alpha)}^\circ \cdot \sigma_{\alpha/\beta}^\circ}{R \cdot T \cdot r_\alpha} \right) \quad (10)$$

Eq. (10) is obtained exactly under the same conditions as the Ostwald equation (1a) or as the Freundlich equation (1b). From the comparison of Eqs. (1a), (1b) and (10) one can see that our solution coincides with that of Ostwald. It is not surprising as both equations are derived using the thermodynamics of Gibbs.

Although the difference between Eqs. (1a), (10) and (1b) is only in a numerical coefficient 2 vs. 3, behind this quantitative difference a qualitative difference is hidden. The present author believes that the derivation of Eqs. (6), (9) and (10), presented in this paper, are free of contradictions. The reason why the Freundlich equation (and the Kelvin equation in its roots) contradicts the thermodynamics of Gibbs is explained in Appendix B. From the comparison of the present derivation with that, presented in Appendix B, the following qualitative difference follows:

¹ The same results of Eqs. (9), (10) and (13) are obtained, when solution β is real, but is infinitely diluted in component A (as in this case the solution is also quasi-ideal from the point of view of component A).

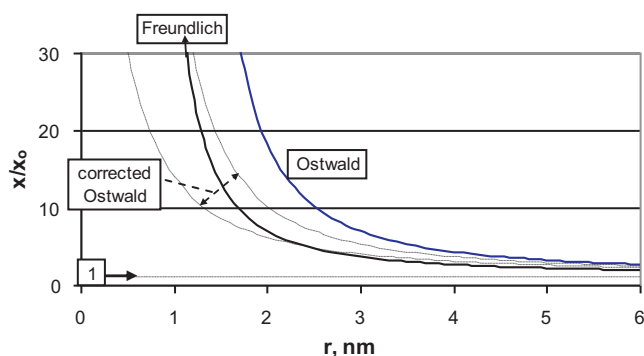


Fig. 2. Dependence of the ratio of the solubilities of small and large crystal as function of the size of the small crystal, in accordance to Eqs. (1a) and (10) (bold curve marked “Ostwald”), Eq. (1b) (bold curve marked “Freundlich”) and the Ostwald equation corrected by the Tolman equation: Eq. (13) (dotted thin curves marked “corrected Ostwald”). Parameters: $V_{A(\alpha)}^0 = 10^{-4} \text{ m}^3/\text{mol}$, $\sigma_{\alpha/\beta}^0 = 0.05 \text{ J/m}^2$, $T = 310 \text{ K}$, $d = 1.0 \text{ nm}$.

- i. In agreement with Gibbs and Ostwald, the size effect is due to a higher specific surface area of a smaller particle. This statement is in accordance with the thermodynamic of Gibbs, and the present author believes that it is a true statement.
- ii. In agreement with the derivation of Kelvin and Freundlich, the size effect is due to a higher curvature of a smaller particle. As shown in Appendix B, this statement is based on the incorrect usage of the Laplace equation, and thus this statement is incorrect itself.

The size dependence of the solubility in accordance to Ostwald and Freundlich is compared in Fig. 2. One can see that the Ostwald equation provides a much stronger size dependence compared to the Freundlich (Ostwald–Freundlich) equation. At this point one might note that the results calculated using the (incorrect) Ostwald–Freundlich (or Kelvin) equation appear to be closer to measurements (Adamson, 1990). The reason might be due to the secondary effect: the size dependence of the interfacial energy.

4. The role of the secondary and ternary size effects

Gibbs (1875–1878) also derived a general equation on the size dependence of surface tension. However, this subject received attention only after the work of Tolman (1949):

$$\sigma_{\alpha/\beta} = \frac{\sigma_{\alpha/\beta}^0}{1 + ((2 \cdot \delta)/r_\alpha)} \quad (11)$$

where $\sigma_{\alpha/\beta}$ is the size dependent interfacial energy (J/m^2) and δ is the distance (m) from the surface of tension to the dividing surface for which the superficial density of the particle vanishes. Its value can be estimated after (Tolman, 1949):

$$\delta = k_T \cdot d \quad (12)$$

where d is the intermolecular distances (m) in the α phase and $k_T \approx 0.25\text{--}0.60$, the Tolman coefficient. Although there are also some other approaches in the literature to describe the size effect of the interfacial energy (Buff, 1951; Jiang et al., 2001; Samsonov et al., 2004), Eqs. (11) and (12) will be substituted into Eq. (10) in this paper in the first approximation:

$$x_{A(\beta)} = x_{A(\beta)}^0 \cdot \exp \left[\frac{3 \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}^0}{R \cdot T \cdot (r_\alpha + k_T \cdot d)} \right] \quad (13)$$

The interval of possible values of the relative solubilities is shown in Fig. 2, together with Eqs. (1a) and (1b). Suppose, that experimental points fall into the interval calculated by the corrected Ostwald equation (13). As follows from Fig. 2, in this case

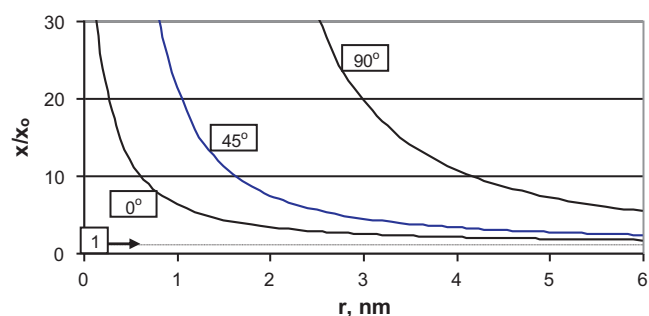


Fig. 3. Dependence of the ratio of the solubilities of small and large crystal as function of the size of the small crystal, in accordance to the corrected Ostwald equation (13) (figures on lines correspond to different contact angle values). Parameters: $V_{A(\alpha)}^0 = 10^{-4} \text{ m}^3/\text{mol}$, $\sigma_{\alpha/g}^0 = 0.10 \text{ J/m}^2$, $\sigma_{\beta/g}^0 = 0.07 \text{ J/m}^2$, $T = 310 \text{ K}$, $d = 1.0 \text{ nm}$.

the experimental points seems to confirm the validity of the Freundlich equation. However, as follows from the present paper, the experimental points actually confirm the validity of the Ostwald equation, corrected by the Tolman equation.

Let us also mention that a ternary effect is also expected. As follows from Eq. (7), the solubility depends also on the standard Gibbs energy of the crystal. On the other hand, molecular dynamic simulations of Chamaani et al. (2011) show that the cohesion energy weakens when the size of the nano-particle decreases, leading to the shift of $G_{A(\alpha)}^0$ towards more positive values. As follows from Eq. (7), this is a partial compensation effect to the size dependence of the surface energies. This ternary effect is not shown here explicitly, as it is believed to be within the uncertainty of the Tolman coefficient ($k_T \approx 0.25\text{--}0.60$).

5. The effect of wettability of the particle by the liquid

According to the equation of Young (1805), the interfacial energy depends on the contact angle as:

$$\sigma_{\alpha/\beta}^0 = \sigma_{\alpha/g}^0 - \sigma_{\beta/g}^0 \cdot \cos \Theta \quad (14)$$

where $\sigma_{\alpha/g}^0$ and $\sigma_{\beta/g}^0$ are interfacial energies of the corresponding phase against gas (J/m^2) and Θ is the contact angle of phase β on phase α in a gaseous environment (degrees). If the contact angle can be altered without changing other parameters, it will have an influence on the value of $\sigma_{\alpha/\beta}^0$, and thus, through Eq. (10), on the size dependence of the interfacial energy. The weaker is the adhesion, i.e. the poorer is the wettability (i.e. the larger is the contact angle), the stronger is the size dependence of the solubility, and vice versa (see Fig. 3).

6. A correction due to different surface planes

In the derivation of Eqs. (6), (9), (10) and (13), we supposed that the interfacial energy along the α/β interface is identical. However, for crystals covered by different crystal planes hkl , the situation is more complex. In this case, Eq. (A1) should be modified as:

$$G_{A(\alpha),S,abs}^0 = G_{A(\alpha),abs}^0 + \sum_{hkl} A_{\alpha(hkl)} \cdot \sigma_{\alpha(hkl)/\beta}^0 \quad (15)$$

where $A_{\alpha(hkl)}$ is the partial surface area (m^2) of phase α , covered by plane hkl and $\sigma_{\alpha(hkl)/\beta}^0$ is the interfacial energy (J/m^2) between the hkl plane of phase α and phase β . To the analogy of Eq. (2), the specific surface area of the plane hkl of phase α is defined as:

$$A_{S,\alpha(hkl)} \equiv \frac{A_{\alpha(hkl)}}{V_\alpha} \quad (16)$$

Then, instead of Eqs. (A6) and (5) the following equation is obtained:

$$G_{A(\alpha),S}^0 = G_{A(\alpha)}^0 + V_{A(\alpha)}^0 \cdot \sum_{hkl} A_{S,\alpha(hkl)} \cdot \sigma_{\alpha(hkl)/\beta}^0 \quad (17)$$

Then, instead of Eqs. (6) and (9), the following equations are obtained, if the above derivation is repeated using Eq. (17) instead of Eq. (5):

i. for the most general case:

$$G_{A(\alpha)}^0 + V_{A(\alpha)}^0 \cdot \sum_{hkl} A_{S,\alpha(hkl)} \cdot \sigma_{\alpha(hkl)/\beta}^0 = G_{A(\beta)}^0 + R \cdot T \cdot \ln x_{A(\beta)} + \Delta G_{A(\beta)}^E \quad (18)$$

ii. for the case of an ideal (or infinitely diluted) solution:

$$x_{A(\beta)} = x_{A(\beta)}^0 \cdot \exp \left(\frac{V_{A(\alpha)}^0 \cdot \sum_{hkl} A_{S,\alpha(hkl)} \cdot \sigma_{\alpha(hkl)/\beta}^0}{R \cdot T} \right) \quad (19)$$

7. Conclusions

1. The general equation is derived for the equilibrium of a small solid pure phase and a large solution, being consistent with the thermodynamics of Gibbs (see Eq. (6)). However, this general equation can be solved only in a numerical way to find solubility.
2. The general equation (6) can be solved in a closed form for solubility if an ideal (or an infinitely diluted) solution is considered for component A, and if the interfacial energy is independent of the composition of the solution (see Eq. (9)). As follows from Eq. (9), the solubility increases for the same volume of the crystal as its specific surface area increases (i.e. if its shape deviates more from sphericity).
3. If all physical parameters (other than the solubility itself) are taken as size independent parameters, then Eq. (9) further simplifies if the shape of the solid is supposed to be spherical (see Eq. (10)). This equation, however, is found to be in contradiction with the Ostwald–Freundlich equation (=the extended Kelvin equation), widely used in chemistry, biology and materials science to describe the size dependence of solubility. The reason for the incorrectness of the Kelvin equation is due to the incorrect application of the Laplace equation (see Appendix B).
4. It is found that the solubility increases with decreasing the size not due to the increased curvature of the phase (Kelvin and Freundlich), but rather due to the increased specific surface area of the phase (Gibbs and Ostwald).
5. When the size dependence of the interfacial energy is taken into account, the corrected Ostwald equation (13) is obtained. Numerical values obtained from the corrected Ostwald equation might seem to be more similar to the predictions of the Ostwald–Freundlich equation than to that of the Ostwald equation. This coincidence might explain the long lifetime of the principally incorrect Ostwald–Freundlich equation.
6. It is shown that the size dependence of solubility can be enhanced if the particle to be dissolved has a poorer wettability by the liquid solution.
7. Eqs. (6) and (9) are modified for the case, when the crystal is surrounded by several planes of different interfacial energies (see Eqs. (18) and (19)).

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Appendix A. Derivation of Eq. (5)

According to Gibbs (1875–1878), the absolute value of the standard Gibbs energy of pure phase A(α) of the given surface area A_α in solution β ($G_{A(\alpha),S,abs}^0$, J) can be written as:

$$G_{A(\alpha),S,abs}^0 = G_{A(\alpha),abs}^0 + A_\alpha \cdot \sigma_{\alpha/\beta}^0 \quad (A1)$$

where $G_{A(\alpha),abs}^0$ is the absolute value of the bulk standard Gibbs energy of A(α) (J). Let us define the molar standard Gibbs energies by dividing the absolute standard Gibbs energies by the amount of material in phase α (n_α):

$$G_{A(\alpha),S}^0 = \frac{G_{A(\alpha),S,abs}^0}{n_\alpha} \quad (A2)$$

$$G_{A(\alpha)}^0 = \frac{G_{A(\alpha),abs}^0}{n_\alpha} \quad (A3)$$

Now, let us divide Eq. (A1) by the amount of material in phase α (n_α). Then, taking into account Eqs. (A2) and (A3), the following equation is obtained:

$$G_{A(\alpha),S}^0 = G_{A(\alpha)}^0 + \frac{A_\alpha}{n_\alpha} \cdot \sigma_{\alpha/\beta}^0 \quad (A4)$$

The amount of material in phase α can be defined as the ratio of its volume (m^3) to its molar volume (m^3/mol):

$$n_\alpha \equiv \frac{V_\alpha}{V_{A(\alpha)}^0} \quad (A5)$$

Let us substitute Eq. (A5) into Eq. (A4) and take into account Eq. (2), the definition of the specific surface area of phase α . Then, the final equation is obtained for the (molar) standard Gibbs energy of pure phase A(α) of the given specific surface area:

$$G_{A(\alpha),S}^0 = G_{A(\alpha)}^0 + A_{S,\alpha} \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}^0 \quad (A6)$$

Eq. (A6) is used in the main text of this paper as Eq. (5).

Appendix B. The derivation of Eq. (1b) and the proof of its incorrectness

Let us consider a small solid, spherical phase α of radius r_α , composed of only component A, being in equilibrium with an infinitely large ideal solution phase β , with an equilibrium mole fraction $x_{A(\beta)}$. Then, substituting Eq. (4) with $\Delta G_{A(\beta)}^E = 0$ into Eq. (3), the following condition of equilibrium is obtained:

$$G_{A(\alpha),r}^0 = G_{A(\beta)}^0 + R \cdot T \cdot \ln x_{A(\beta)} \quad (B1)$$

where $G_{A(\alpha),r}^0$ is a standard Gibbs energy of phase α of pure component A and radius r_α . This Gibbs energy is composed of three terms, written for an arbitrary outside pressure p :

$$G_{A(\alpha),r}^0 = U_{A(\alpha)}^0 + p \cdot V_{A(\alpha)}^0 - T \cdot S_{A(\alpha)}^0 \quad (B2)$$

where $U_{A(\alpha)}^0$ and $S_{A(\alpha)}^0$ are the standard inner energy and entropy of phase A(α), in the first approximation taken as independent of the size of phase A(α). Let us consider the system under the standard outside pressure p^0 . Then, inside the small spherical phase α the pressure equals:

$$p = p^0 + \frac{2 \cdot \sigma_{\alpha/\beta}^0}{r_\alpha} \quad (B3)$$

The second term of Eq. (B3) is the pressure difference, due to de Laplace (1806). This pressure arises due to the curvature of phase α . Let us substitute Eq. (B3) into Eq. (B2):

$$G_{A(\alpha),r}^0 = U_{A(\alpha)}^0 + p^0 \cdot V_{A(\alpha)}^0 - T \cdot S_{A(\alpha)}^0 + \frac{2 \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}}{r_{\alpha}} \quad (\text{B4})$$

At infinitely small curvature, i.e. at infinitely large size of phase α , Eq. (B4) transforms into the standard Gibbs energy of a large phase α at $p = p^0$:

$$G_{A(\alpha)}^0 = U_{A(\alpha)}^0 + p^0 \cdot V_{A(\alpha)}^0 - T \cdot S_{A(\alpha)}^0 \quad (\text{B5})$$

Substituting Eq. (B5) into Eq. (B4):

$$G_{A(\alpha),r}^0 = G_{A(\alpha)}^0 + \frac{2 \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}}{r_{\alpha}} \quad (\text{B6})$$

Now, let us substitute Eq. (B6) into Eq. (B1):

$$G_{A(\alpha)}^0 + \frac{2 \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}}{r_{\alpha}} = G_{A(\beta)}^0 + R \cdot T \cdot \ln x_{A(\beta)} \quad (\text{B7})$$

The equilibrium mole fraction can be expressed from Eq. (B7) as:

$$x_{A(\beta)} = x_{A(\beta)}^0 \cdot \exp \left(\frac{2 \cdot \sigma_{\alpha/\beta} \cdot V_{A(\alpha)}^0}{R \cdot T \cdot r_{\alpha}} \right) \quad (\text{B8})$$

Eq. (B8) is the result of this derivation, as it appears in textbooks, whenever the Freundlich version of the Ostwald equation is derived. One can see that Eq. (B8) is identical with Eq. (1b).

Although the above derivation is mathematically correct, it is incorrect physically. Indeed, the inner Laplace pressure described by Eq. (B3) is not identical with the outside pressure p of Eq. (B2). Therefore, Eq. (B3) should not be substituted into Eq. (B2) and then Eq. (B8) cannot be derived. Thus, the Freundlich equation is incorrect, as the Laplace equation should not be substituted into the equation for the Gibbs energy. Actually, just an opposite is the case: the Laplace equation can be derived from the general equation of Gibbs, Eq. (A1), as shown by Kaptay (2005, 2012c).

References

- Adamson, A.W., 1990. *Physical Chemistry of Surfaces*. John Wiley and Sons Inc., NY.
- Bian, S.W., Mudunkotuwa, I.A., Rupasinghe, T., Grassian, V.H., 2011. Aggregation and dissolution of 4 nm ZnO nanoparticles in aqueous environments: influence of pH, ionic strength, size, and adsorption of humic acid. *Langmuir* 27, 6059–6068.
- Bouzid, M., Mercury, L., Lassini, L., Matray, J.-M., Azaroual, M., 2011. In-pore tensile stress by drying-induced capillary bridges inside porous materials. *J. Colloid Interface Sci.* 355, 494–502.
- Buff, F.P., 1951. The spherical interface. I. Thermodynamics. *J. Chem. Phys.* 19, 1591–1594.
- Cerdeira, A.M., Mazzotti, M., Gander, B., 2010. Miconazole nanosuspensions: influence of formulation variables on particle size reduction and physical stability. *Int. J. Pharm.* 396, 210–218.
- Chamaani, A., Marzbanrad, E., Rahimpour, M.R., Yaghmaee, M.S., Aghaei, A., Kamachali, R.D., Benhamian, Y., 2011. Thermodynamics and molecular dynamic investigation of a possible new critical size for surface and inner cohesive energy of Al nanoparticles. *J. Nanopart. Res.* 13, 6059–6067.
- Cherginets, V.L., Deineka, T.G., Demirska, O.V., Rebrova, T.P., 2002. Potentiometric investigation of oxide solubilities in molten KCl–NaCl eutectic. The effect of surface area of solid particles on the solubilities. *J. Electroanal. Chem.* 531, 171–178.
- Cherginets, V.L., Rebrova, T.P., Datsko, Y.N., Deineka, T.G., Kisil, E.P., Kosinov, N.N., Voronkina, E.E., 2010. Processes of europium oxide dissolution in molten alkali metal iodides. *J. Chem. Eng. Data* 55, 5696–5700.
- Chiang, W.H., Sankaran, R.M., 2012. The influence of bimetallic catalyst composition on single-walled carbon nanotube yield. *Carbon* 50, 1044–1050.
- de Laplace, P.S., 1806. *Mechanique Celeste*, Supplement to Book 10.
- Deflorian, F., Fedel, M., Rossi, S., Kamarchik, P., 2011. Evaluation of mechanically treated cerium (IV) oxides as corrosion inhibitors for galvanized steel. *Electrochim. Acta* 56, 7833–7844.
- Deng, J., Huang, L., Liu, F., 2010. Understanding the structure and stability of paclitaxel nanocrystals. *Int. J. Pharm.* 390, 242–249.
- Dodd, A., Saunders, M., 2011. Synthesis of rare earth hydroxide nanorods by room temperature reaction of oxide precursors with water. *J. Nanopart. Res.* 13, 2633–2639.
- Freundlich, H., 1909. *Kolloidchemie*. Akademischer Verlag, Leipzig (English translation: 1923, E.P. Dutton Co Publ., New York).
- Gao, L., Liu, G., Wang, X., Liu, F., Xu, Y., 2011. Preparation of a chemically stable quercetin formulation using nanosuspension technology. *Int. J. Pharm.* 404, 231–237.
- Gibbs, J.W., 1875–1878. On the equilibrium of heterogeneous substances. *Trans. Conn. Acad. Arts Sci.* 3, 108–248 and 343–524.
- Godec, M., Gaberscek, J., Jamnik, A., 2009. Comment on the article: “A new understanding of the relationship between solubility and particle size”, by W. Wu and G.H. Nancollas. *J. Solution Chem.* 38, 135–146.
- Jiang, Q., Zhao, D.S., Zhao, M., 2001. Size-dependent interface energy and related interface stress. *Acta Mater.* 49, 3143–3147.
- Jiang, W., Kim, S., Zhang, X., Lionberger, R.A., Davit, B.M., Conner, D.P., Yu, L.X., 2011. The role of predictive biopharmaceutical modeling and simulation in drug development and regulatory evaluation. *Int. J. Pharm.* 418, 151–160.
- Kaptay, G., 2004. A new equation for the temperature dependence of the excess Gibbs energy of solution phases. *Calphad* 28, 115–124.
- Kaptay, G., 2005. Classification and general derivation of interfacial forces, acting on phases, situated in the bulk, or at the interface of other phases. *J. Mater. Sci.* 40, 2125–2131.
- Kaptay, G., 2012a. The Gibbs equation versus the Kelvin and the Gibbs–Thomson equations to describe nucleation and equilibrium of nano-materials. *J. Nanosci. Nanotechnol.*, <http://dx.doi.org/10.1166/jnn.2011.5774>.
- Kaptay, G., 2012b. On the tendency of solutions to tend toward ideal solutions at high temperatures. *Metall. Mater. Trans. A* 43A, 531–543.
- Kaptay, G., 2012c. Interfacial forces in dispersion science and technology. *J. Disper. Sci. Technol.* 33, 130–140.
- Kawabata, Y., Wada, K., Nakatani, M., Yamada, S., Onoue, S., 2011. Formulation design for poorly water-soluble drugs based on biopharmaceutics classification system: basic approaches and practical applications. *Int. J. Pharm.* 420, 1–10.
- Keck, C.M., 2010. Particle size analysis of nanocrystals: improved analysis method. *Int. J. Pharm.* 390, 3–12.
- Letellier, P., Mayaffre, A., Turmine, M., 2007. Solubility of nanoparticles: nonextensive thermodynamic approach. *J. Phys. Condens. Matter* 19, 436229 (9 pp.).
- Lewis, G.N., 1907. Outlines of a new system of thermodynamic chemistry. *Proc. Am. Acad. Arts Sci.* 43, 259–293.
- Liu, G., Zhang, D., Jiao, Y., Zheng, D., Liu, Y., Duan, C., Jia, L., Zhang, Q., Lou, H., 2012. Comparison of different methods for preparation of a stable risedronate D formulation via nano-technology. *Int. J. Pharm.* 422, 516–522.
- Lukas, H.L., Fries, S.G., Sundman, B., 2007. *Computational Thermodynamics. The Calphad Method*. Cambridge University Press, Cambridge, UK.
- McCoy, J., 2001. A new population balance model for crystal size distribution: reversible, size-dependent growth and dissolution. *J. Colloid Interface Sci.* 240, 139–149.
- Mudunkotuwa, I.A., Grassian, V.H., 2011. The devil is in the details (or the surface): impact of surface structure and surface energetics on understanding the behavior of nanomaterials in the environment. *J. Environ. Monit.* 13, 1135–1144.
- Müller, R.H., Jacobs, C., Kayser, O., 2001. Nanosuspensions as particulate drug formulation in therapy. Rationale for development and what we can expect for the future. *Adv. Drug Deliv. Rev.* 47, 3–19.
- Nagy, Z.K., Balogh, A., Vajna, B., Farkas, A., Patyi, G., Kramarics, A., Marosi, G., 2012. Comparison of electrospun and extruded soluplus®-based solid dosage forms of improved dissolution. *J. Pharm. Sci.* 101, 322–332.
- Ostwald, W., 1900. Über die vermeintliche Isomerie des roten und gelben Quecksilberoxyds und die Oberflächenspannung fester Körper. *Z. Phys. Chem.* 34, 495–503.
- Pardeike, J., Müller, R.H., 2010. Nanosuspensions: a promising formulation for the new phospholipase A₂ inhibitor PX-18. *Int. J. Pharm.* 391, 322–329.
- Pardeike, J., Strohmeier, D.M., Schrödl, N., Voura, C., Gruber, M., Khinast, J.G., Zimmer, A., 2011. Nanosuspensions as advanced printing ink for accurate dosing of poorly soluble drugs in personalized medicines. *Int. J. Pharm.* 420, 93–100.
- Picher, M., Anglaret, E., Arenal, R., Jourdain, V., 2011. Processes controlling the diameter distribution of single-walled carbon nanotubes during catalytic chemical vapor deposition. *ACS Nano* 5, 2118–2125.
- Ravichandran, R., 2010. Physico-chemical evaluation of gymnemic acids nanocrystals. *Int. J. Nanoparticles* 3, 280–296.
- Samsonov, V.M., Sdobnyakov, N.Y., Bazulev, A.N., 2004. Size dependence of the surface tension and the problem of Gibbs thermodynamics extension to nanosystems. *Colloid Surf. A* 239, 13–17.
- Shchekin, K., Rusanov, A.I., 2008. Generalization of the Gibbs–Kelvin–Köhler and Ostwald–Freundlich equations for a liquid film on a soluble nanoparticle. *J. Chem. Phys.* 129, 154116.
- Thomson, W., 1871. On the equilibrium of vapour at a curved surface of liquid. *Phil. Mag.* 42, 448–452.
- Tolman, R.C., 1949. The effect of droplet size on surface tension. *J. Chem. Phys.* 17, 333–337.
- Wu, W., Nancollas, H., 1998. A new understanding of the relationship between solubility and particle size. *J. Solution Chem.* 27, 521–531.
- Young, T., 1805. An essay on the cohesion of fluids. *Phil. Trans.*, 65–87.
- Znaidi, L., 2010. Sol–gel-deposited ZnO thin films: a review. *Mater. Sci. Eng. B* 174, 18–30.