CHAPTER-3

Scaled particle theory

Outline of the scaled particle theory (SPT)

A typical cell represents a volume of $2 \times 10^{12}$ cm$^3$ and in this volume different types of proteins, nucleic acids, carbohydrates and other diverse molecules are present; they constitute about 30 percent of cellular weight (see table 4, 5 in chapter 2). The water present in cell interior forms about 70% of the cell weight (Darnell et al. 1986). The cell at best can be considered to represent a bounded structure where molecular crowding will be very large, in comparison to the concept of ideal solutions following the rules of thermodynamic. Very high concentration of macromolecules inside the cell will have its effect on the thermodynamic parameters of any molecule. In other words the volume occupied by any specific molecule will ensure the exclusion of any other molecule from the volume it occupy. Larger the volume occupied by the molecules more volume will be excluded from the next molecule. The calculations of thermodynamic activity for the non-ideal solutions has provided a way to understand these effects on the kinetics of reactions. The effect of increased concentration will cause a significant alteration in the activity of participating reactants. Approximate methods like virial coefficients (Hirshfelder et al., 1954) can be used to calculate the changes in the chemical potential of the given collection of molecule for non-ideal solutions. However, more exact and analytical
methods are needed to picture the effects of molecular crowding in terms of being able to
calculate the chemical potential $\mu_i$ of a species $i$ in a mixture of other diverse molecules.
The Scaled particle theory developed by Reiss, Frisch and Lebowitz in 1959, allows us to
calculate the chemical potential of the target molecule in a fluid conceptually made of
hard particles. The concept is novel and it provides an exact solution. Briefly, the salient
aspects of this theory are described below.

The theory uses a coupling parameter which measures the breadth of molecule and
its potential field rather than its amplitude. A molecule is coupled formally to a fluid by
letting it "grow" until it achieves the scale of its neighbour. The fluid is represented by
hard sphere. The hard spheres are spherically symmetric molecules which may exert
attractive forces upon one another, but they possess hard core of diameter $a$. No real fluid
exactly satisfies this requirement, but at low enough temperatures the repulsive part of
the intermolecular potential rises so steeply and its increment for a small fractional
change in intermolecular distance will be many times $kT$ (where $k$ is the Boltzmann
constant and $T$ is the temperature). To treat real solutions the value of $a$ will depend upon
the temperature. Smaller values of $a$ will be more suitable at higher temperatures.

The fluid is considered to consist $N$ molecules contained within a volume $V$ such that
the concentration or density is $\rho = N/V$. Within this fluid consider a spherical region of
radius $r$, denote $P_0(r)$ the probability that no other molecule has its center within the said spherical region (as shown in the schematic drawing in figure 11). It can be assumed that a spherical cavity would be created within the original fluid of $N$ molecules with diameters, $a$, if a hard molecule of diameter $b$ was inserted into the fluid such that the dimensions of this cavity changes $r = (a+b)/2$. The idea is to be able to calculate function $P_0(r)$. The probability $P(r+dr)$ represents that the centers of all other molecules are excluded from the augmented spherical cell of radius $r+dr$. The probability that the spherical shell of thickness $dr$ and volume $4\pi r^2 \cdot \rho \cdot G(r) \cdot dr$, where $G(r)$ is so defined that the product $\rho \cdot G(r)$ measures the concentration of molecular centers just
outside the spherical exclusion region. Thus \( G(r) \) measures the conditional probability that the center of a molecule will be found within the spherical shell at radius \( r \) when the region enclosed by the shell is known to be free of any other molecular centers. The chance that the spherical shell is itself free of centers will be

\[
1 - 4.\pi.r^2.\rho.G(r).dr. \tag{1}
\]

For the volume of radius \( r+dr \) to be devoid of centers of other molecules, it is necessary that the volume of radius \( r \), and the shell of thickness \( dr \), be simultaneously free of centers. Thus the probability \( P_0(r+dr) \) that the volume of radius \( r+dr \) is empty is given as a product of \( P_0(r) \) and the quantity in equation (1) as shown in equation (2).

\[
P_0(r+dr) = P_0(r)[1 - 4.\pi.r^2.\rho.G(r).dr] = P_0 + (\delta P_0/\delta r).dr \tag{2}
\]

or

\[
\delta(\ln P_0)/\delta r = - 4.\pi.r^2.\rho.G(r)
\]

Integration of last expression is given as equation (3)

\[
P_0(r) = \exp[-\int_0^r 4.\pi.\lambda^2.\rho.G(\lambda).c(\lambda)] \tag{3}
\]

The condition in equation (4) is satisfied.

\[
P_0(0) = 1 \tag{4}
\]

It is possible to express \( P_0(r) \), the probability, in terms of \( G(r) \).

Nevertheless, equation (3) prove useful as an intermediate result, and \( G(r) \) is used as the central function of SPT.

To determine \( G(r) \), \( P_0(r) \) is expressed in another way. If \( P_1(r) \), \( P_2(r) \), etc., represent
the probabilities that the centers of exactly one particle, exactly two particles, etc., lie in the spherical region of radius \( r \). Then following condition will hold.

\[
P_0 + P_1 + P_2 + P_3 + \ldots = 1
\]  
(5)

Since either no particles or some combination of them will have their centers in the region, the equation (5) can be rearranged to yield

\[
P_1 = 1 - (P_1 + 2P_2 + 3P_3 + \ldots) + (P_2 + 3P_3 + 6P_4 + \ldots) - (P_3 + 4P_4 + \ldots) + \ldots
\]  
(6)

The first sum in brackets, in equation (6), represents the average number of individual particles to be found in the region of radius \( r \), while the second sum is the average number of pairs, the third the average number of triplets, and so on. If the n-particle correlation function \( g^{(n)}(1,2,\ldots,n) \) is introduced where, the numbers in the brackets refer to the coordinates of position of the volume elements, \( d\tau_1, d\tau_2, \ldots, d\tau_n \) (cell of radius \( r \)), this can be expressed (Reiss et. al, 1965) as equation (6) in different form as

\[
P_0(r) = 1 + \sum_{n=0}^{\infty} \frac{(-1)^n P^n}{n!} \int g^{(n)}(\tau_1, \tau_2, \ldots, \tau_n) d\tau_1 d\tau_2 \ldots d\tau_n
\]  
(7)

for molecules with hard cores of diameter \( a \), \( g^{(n)} \) will be zero (for all values of \( n \geq n \), where \( n \) depends on \( r \)) when \( d\tau_1, d\tau_2, \ldots, d\tau_n \) will all lie within the cell of radius \( r \). If \( r \leq a/2 \), it is clear that only the center of one molecule at a time can lie within the cell, otherwise hard cores would be forced to overlap. Similarly, for
a/2 < r ≤ a/3 only two molecules may simultaneously occupy the cell. When r = a, twelve molecules can be accommodated. As a result of this exclusion feature the series in equation (7) contains a finite number of terms as long as r is finite. With r ≤ a/2 there is only room for one molecule in the cell and equation (7) becomes

\[ P_0(r) = 1 - \rho \int_0^r 4\pi \lambda^2 g(1) d\lambda = 1 - \frac{4}{\pi} r^3 \rho, \quad r ≤ a/2 \]  \hspace{1cm} (8)

since in fluid \( g^{(1)} \) is unity. Thus in this case, an exact expression for \( P_0(r) \) can be derived. Substituting equation (8) into equation (2) yields

\[ G(r) = \frac{1}{[1 - (4/3)\pi r^3 \rho]} \]  \hspace{1cm} (9)

so that an exact expression for \( G(r) \) can be had for \( r ≤ a/2 \).

In the region \( (a/2 < r ≤ a/3) \) two molecules can be accommodated and equation (7) takes the form of equation (10) by using equation (8).

\[ P_0 = 1 - (4/3)\pi r^3 \rho + \int (p^2 / 2) g^{(2)} d\tau_1 d\tau_2, \quad a/2 < r ≤ a/3 \]  \hspace{1cm} (10)

[cell of radius r]

At this stage \( P_0 \) can be eliminated between equations (3) and (10). Some manipulation of the integral on the right side of equation (10) coupled with differentiation of both sides of the equation obtained by eliminating \( P_0 \) yields the following relations for the first and second derivatives of \( G \) with respect to \( r \) (for \( r ≥ a/2 \)) at \( r = a/2 \); and
\[ G'(a/2) = G'[(a/2) - \epsilon] \]  
\[ G''(a/2) = G''[(a/2) - \epsilon)] - \left[ 8. \pi. a. \rho. g(a) \right] / \left[ 1 - (\pi. a^3. \rho) / 6 \right] \]

where the argument \([(a/2) - \epsilon]\) indicates that the derivatives of \(G\) for \(r \leq a/2\) taken at \(r = a/2\). These derivatives can be obtained immediately from equation (9). From equation (11) it is clear that the first derivative of \(G\) is continuous at \(r = a/2\) while from equation (12) in which \(g(a)\) represents the radial distribution function between two molecules at hard core contact, i.e., \(r = a\), we see that the second derivative of \(G\) possesses a discontinuity at \(r = a/2\), proportional to \(g(a)\). It is evident that this discontinuity is related to the appearance of a new physical process at \(r = a/2\), namely the process in which the centers of two molecules are accommodated simultaneously in the spherical cell for the first time. The possibility of this new configuration activates an additional term in equation (7). The discontinuity is proportional to the probability of the new event, as is clear from its dependence on \(g(a)\).

Such discontinuities appear whenever it becomes possible to include three particles, there is a discontinuity proportional to the triplet correlation function \(g^{(3)}(a,a,a)\), as mentioned earlier in equation (6), in the fourth derivative of \(G\). At this point the first three derivatives are continuous. It appears as though the order increases by 2 at each succeeding singular point. Thus \(G(r)\) is nonanalytic but quite smooth for higher order derivatives. One might expect that \(G\) can be approximated rather closely by a
suitably chosen analytical function.

A known theorem of statistical mechanics (Tolman, 1938) states that the probability of observing some fluctuated configuration of a statistical system is given by the expression 

\[ P_0(r) = \exp\left(-\frac{W(r)}{kT}\right) \]  

(13)

where \( W(r) \) is the reversible work required to produce a spherical cavity of radius \( r \) in the fluid. Comparing this expression with equation (2) we get

\[ W(r) = kT \int \omega \pi \lambda^2 G(\lambda) d\lambda \]  

(14)

This expression in equation (14) can also be arrived at in another manner. Suppose the cavity is produced (as suggested earlier) by expanding a hard sphere immersed in the fluid. The diameter \( b \) of this hard sphere is specified by equation (1). Then the force exerted by the fluid on the surface of the sphere will be the kinetic force due to encounters with the surrounding molecules. The force per unit area will be \( kT \) times the local concentration, and for the entire spherical surface it is

\[ f(r) = 4\pi r^2 kT \rho G(r). \]  

(15)

Consequently, in expanding through the interval \( dr \) the sphere must perform the
work given by equation (16)

\[ dW = f(r)dr = 4\pi r^2 kT \rho G(r)dr \]  \hspace{1cm} (16)

Integration from \( r=0 \), we obtain equation (14).

Substituting equation (10) into equation (14) we have

\[ W(r) = -kT \ln [1 - (4/3) \pi r^3 \rho] , \]  \hspace{1cm} (17)

for \( r \leq a/2 \), an exact expression is available for \( W(r) \). In general, the ability to
arrive at these exact expressions for \( r \leq a/2 \) is a direct consequence of the limited
occupancy of the cell in this range. Only the center of one molecule can be
accommodated and molecular correlation need not be considered.

When we specialize our fluid to a hard spheres the equation of state can be
expressed \( \) (Fowler and Guggenheim, 1939; Hill, 1956) in the following form:

\[ \left( \frac{p}{kT} \right) = \rho + \frac{2}{3} \pi a^3 \rho^2 g(a,p,T). \]  \hspace{1cm} (18)

In general, \( g \) and \( G \) depend upon both temperature and density. It is instructive
to note that only the value of \( g \) at \( r = a \) appears in equation (18), where \( p \) is the
pressure. Thus, for the equation of state it appears wasteful to attempt evaluation of
the pair correlation function for all values of its arguments. This is one of the factors
which is central to the development of SPT.

\[ G(r) \] is most convenient central function of SPT. One of the reasons for this is the
fact that $g(r)$ and $G(r)$ are numerically identical for $r = a$, even though they differ for other values of $r$. Thus $G(a)$ might just appear in equation (18) as $g(a)$, and the pressure of the hard sphere fluid may be rigorously related to $G$. It proves possible to establish many exact conditions which constrain the form of $G(r, \rho)$, and, with the form of $G$ established in its dependence on $r$, it can be specialized to $a$, and its value used in equation (18). The quantity $\rho G(r)$ has been defined as the local concentration of molecular centers adjacent to a spherical cavity of radius $r$ from which all molecular centers have been excluded. It is also possible to regard the cavity as having been produced by the addition of a hard sphere of diameter $b$. This hard sphere may be regarded as (and is) a solute molecule.

From this point of view $W(r)$ in equation (14) is the reversible work which must be expended in adding a solute molecule to a fixed point in a pure solvent. Furthermore $\rho G(r)$ measures the concentration of solvent molecules in contact with the solute, so that if $g_{ab}^{(2)}(R)$ is the pair correlation function between a solvent and a solute molecule whose centers are separated by the distance $R$,

$$G(r) = g_{ab}^{(2)}[R = r = (a+b)/2]$$

The fact that $W(r)$ is the reversible work which must be expended in adding a solute molecule in terms of $W$, and therefore in terms of $G$ (Reiss, 1965). The proper expression for chemical potential can be written as
\[ \mu_b = k.T.\ln(\Lambda_b, \rho_b) + k.T.\int_0^{(a+b)/2} 4.\pi.\lambda^2.G(\lambda).d\lambda \]

where \( \Lambda_b \) is the translational partition function \( \rho_b \) is the concentration of solute, \( \mu_b \) is the chemical potential of particle having radius \( b \) and

\[
(\Lambda_b)^{\frac{3}{2}} = \frac{(h^3)}{(2.\pi.m_b.k.T)^{3/2}}
\]  

(21)

where \( h \) is Plank's constant and \( m_b \) is the mass of the solute molecule. In equation (20) it is assumed that the solution is so dilute with respect to "solute" that solute molecules do not interact with one another. For the special case of equation (20) the origin of the term "scaled particle" is clearly revealed, since the molecule can be added by scaling up from an initial radius of \( -a/2 \) to a final radius \( b/2 \), and the reversible work can be computed during this process. The fact that the initial radius is negative and the requirement \( r=0 \) so that the solute be completely absent. If one wishes, one may interpret the negative radius as corresponding to a situation involving a point molecule having the ability to penetrate a solvent molecule to the depth \( a/2 \). Such a point molecule permits the assembly of solvent molecules to assume all configuration which were accessible before the addition of the solute. In this circumstances the solute brings nothing with it except its free energy of mixing. In any event, the added solute is a formal device and the interpretation of the negative radius should cause no difficulty.

The addition of a point molecule which cannot penetrate the cores of the solvent
molecules requires the expenditure of a considerable amount of work. Such a molecule has $b=0$ so that according to the relation $r = (a+b)/2$ it is equivalent to a cavity of radius $r=a/2$; thus, $W(a/2)$ can be computed by using equation (17) and we have a simpler expression given by equation (22)

$$\mu_b = kT \ln \left( \frac{\Lambda_b^3}{V} \right) - kT \ln \left( 1 - \frac{a^3 \rho}{6} \right)$$  \hspace{1cm} (22)

This result is the exact result for evaluating the chemical potential of particles having different dimensions in a solution.

The scaled particle theory was further modified by Gibbons (1969, 1970) where he extended the SPT approach for particles of arbitrary shapes, non-spherical particles and mixture of particles of different shapes. The concept of excluded volume was introduced to establish a link with the physical dimensions of the particles and configurational entropy. The work done to add a particle $j$ to a system of $N$ particles in a volume $V$ where for the particle $j$'s center is excluded by particle $i$ can be given as:

$$\beta \omega(R_j) = -\ln \left[ 1 - \sum_{i=1}^{m} (X_{ij}N_i) / V \right]$$  \hspace{1cm} (23)

$\omega(R_j)$ term can take the range of values of $R_j$. Approximating the first three terms of the
Taylor's series for $R_j = 0$ and a term $V_{ij}$ is added where, $V_i$ represents the volume occupied by the particle $j$. The expression takes the form of equation (24)

$$\omega(R_j) = \omega(0) + R_j \omega'(0) + R_j^2/2. \omega''(0) + V_{ij}. \tag{24}$$

The $\omega(R_j)$ is a continuous function for both positive and negative values of $R_j$, the leading term in $\omega(R_j)$ must be $V_{ij}$ for $R_j > 0$.

For hard spheres, the excluded volumes can be expressed as:

$$X_{ij} = 4.\pi/3.(R_j + R_i)^3 \tag{25}$$

Hayashida and Kihara (1950a,b) have solved the general case and showed that for any convex body:

$$X_{ij} = V_i + V_j + R_iS_j + R_jS_i \tag{26}$$

where $S_i$ and $V_i$ are the surface area and volume of particle $i$ respectively and $R_i$ is the radius, averaged over all orientations, of particle $i$. The volume, surface area and average radius can be rewritten in terms of the characteristic radius or length for a particle as:

$$V = c_i R_i^3,$$

$$S = b_i R_i^2,$$

$$\bar{R} = a_i R_i \tag{27}$$
The values of $a_1$, $b_1$, and $c_1$ for several shapes have been tabulated by Ishihar and Hayashida (1950a and 1950b) and Kihara (1953a, 1953b) however, these values for some shapes were subsequently corrected by Minton (1981) and Chatelier and Minton (1987). If the expressions from equation (26) and (27) are substituted into (25) and the differentiations carried out with respect to $R_i$ we get equation (28)

$$
\beta \omega(R_i) = -\ln(1-Y) + a_i R_i B / (1-Y) + b_i R_i^2 A / (1-Y) + 0.5 a_i^2 R_i^2 B^2 / (1-Y)^2 + \beta \nu_{ip} 
$$

where,

$$
d = \sum_{i=1}^{m} d_i 
$$

$$
A = \sum_{i=1}^{m} a_i R_i d_i 
$$

$$
B = \sum_{i=1}^{m} S_i d_i 
$$

$$
Y = \sum_{i=1}^{m} V_i d_i 
$$

$$
C = \sum_{i=1}^{m} a_i^2 R_i^2 d_i 
$$

To obtain the chemical potential from this expression one has to add the ideal gas contribution:

$$
[\beta \mu_i = \beta \omega(R_i) + \ln[d_i h^3 / 2 \pi m_i k T]^{3/2}] 
$$

(29)
The equation of state can then be obtained from (29) and the thermodynamic equation

\[
\frac{\Delta p}{\Delta d_i} = \sum_i d_i \frac{\Delta \mu_i}{\Delta d_i}
\]  

(30)

For carrying out the analysis for a system of particles with the same shape one equation derived by Gibbons (1969) takes the simplified form of equation (31)

\[
\beta p = d/(1-Y) + \frac{1}{3}(B^2C)/(1-Y)^3 + A.B/(1-Y)^2
\]  

(31)

To check that the above equation is correct the values of \( a_i, b_i \) and \( c_i \) for a system of hard spheres were substituted into equation (31) and it was found that the Scaled Particle Theory or Percus Yevick theory (Percus and Yevick, 1960) for condensed systems equation for mixtures is recovered (31). For one component system in equation (31) \( j = 1 \) and equation takes the form

\[
(\beta p \div d_i) = 1/(1-V_1.d_i) + (1/3)\bar{R}_i^2.S_1^2.d_i^2 / (1-V_1.d_i)^3 + \bar{R}_i.S_1.d_i / (1-V_1.d_i)
\]  

(32)

If the values of \( a_i, b_i, \) and \( c_i \), for a sphere are substituted into this equation, the PY equation is recovered. This approach has been used to derive the virial coefficients for
different shapes and the comparison was found to be in good agreement. The values used in the present work for a, b and c for relevant shapes are tabulated in table 8.

Table 8: Values of parameters, a, b and c for different shapes of equivalent particles (Gibbons, 1970; Chatelier and Minton, 1987)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sphere</th>
<th>Cube</th>
<th>Right circular cylinder ($L=$ length/diameter)</th>
<th>Regular Tetrahedron</th>
<th>Oblate Ellipsoid ($\epsilon^2=0.75$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>1</td>
<td>0.75</td>
<td>$0.25(\pi+2L)$</td>
<td>$\approx 0.4561$</td>
<td>$0.25 + \pi\sqrt{27}$</td>
</tr>
<tr>
<td>b</td>
<td>$4\pi$</td>
<td>6</td>
<td>$\pi(4L+2)$</td>
<td>$\sqrt{3}$</td>
<td>$2.76\pi$</td>
</tr>
<tr>
<td>c</td>
<td>$4\pi/3$</td>
<td>1</td>
<td>$2\pi L$</td>
<td>$\sqrt{2}/12$</td>
<td>$2\pi/3$</td>
</tr>
</tbody>
</table>