

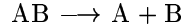
## I. REACTION COORDINATES

Often simple chemical processes can be described in terms of a one-dimensional coordinate, which is *not* one of the Cartesian coordinates in a system but a *generalized coordinate*,  $q$ . Such a coordinate is, in general, a function of the Cartesian coordinates:

$$q = q(\mathbf{r}_1, \dots, \mathbf{r}_N)$$

In some cases, a set of reaction coordinates is required.

**Examples 1:** Dissociation reactions. Consider a dissociation reaction of the form



A reaction coordinate for such a process is the distance  $r$  between the two atoms in the diatomic. If  $\mathbf{r}_1$  and  $\mathbf{r}_2$  are the Cartesian positions of atoms  $A$  and atom  $B$ , respectively, then

$$r = |\mathbf{r}_1 - \mathbf{r}_2|$$

What set of generalized coordinates contains  $r$  explicitly? Let us transform to center-of-mass and relative coordinate:

$$\mathbf{R} = \frac{m_A \mathbf{r}_1 + m_B \mathbf{r}_2}{m_A + m_B}$$

$$\mathbf{r} = \mathbf{r}_1 - \mathbf{r}_2$$

Then, let  $\mathbf{r} = (x, y, z)$  be transformed to spherical polar coordinates

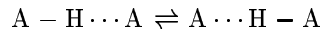
$$(x, y, z) \longrightarrow (r, \theta, \phi)$$

$$x = r \sin \theta \cos \phi$$

$$y = r \sin \theta \sin \phi$$

$$z = r \cos \theta$$

**Example 2:** Proton transfer reactions. Consider proton transfer through a hydrogen bond according to:



which is illustrated schematically in the cartoon below:

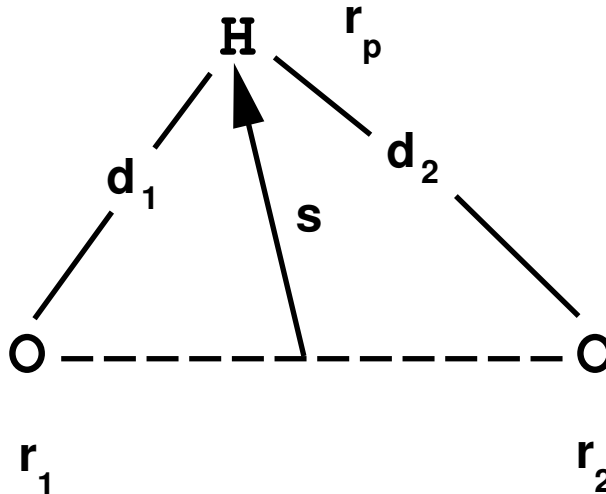


FIG. 1.

The two heavy atoms are assumed to be of the same type (e.g. oxygen atoms). A reaction coordinate describing this process is the difference in the two distances  $d_1$  and  $d_2$ :

$$\delta = d_1 - d_2 = |\mathbf{r}_p - \mathbf{r}_1| - |\mathbf{r}_p - \mathbf{r}_2|$$

What generalized coordinate system contains  $\delta$  explicitly?

To see what coordinate system this is, consider transforming to center of mass and two relative coordinates as follows:

$$\begin{aligned}\mathbf{R} &= \frac{m_{\text{O}}(\mathbf{r}_1 + \mathbf{r}_2) + m_{\text{H}}\mathbf{r}_p}{2m_{\text{O}} + m_{\text{H}}} \\ \mathbf{r} &= \mathbf{r}_1 - \mathbf{r}_2 \\ \mathbf{s} &= \mathbf{r}_p - \frac{1}{2}(\mathbf{r}_1 + \mathbf{r}_2)\end{aligned}$$

Now the six degrees of freedom ( $r_x, r_y, r_z, s_x, s_y, s_z$ ) are transformed to 6 new degrees of freedom, which are the spherical polar coordinates of  $\mathbf{r}$  and the confocal elliptic coordinates for the position of the proton:

$$\begin{aligned}r &= \sqrt{r_x^2 + r_y^2 + r_z^2} \\ \theta &= \tan^{-1} \frac{\sqrt{r_x^2 + r_y^2}}{r_z} \\ \phi &= \tan^{-1} \frac{r_y}{r_x} \\ \mu &= d_1 + d_2 = |\mathbf{s} + \frac{1}{2}\mathbf{r}| + |\mathbf{s} - \frac{1}{2}\mathbf{r}| \\ \nu &= d_1 - d_2 = |\mathbf{s} + \frac{1}{2}\mathbf{r}| - |\mathbf{s} - \frac{1}{2}\mathbf{r}| \\ \alpha &= \text{tilt angle of plane containing three atoms}\end{aligned}$$

Then, the coordinate  $\nu$  is the reaction coordinate  $\delta$ .

## II. FREE ENERGY PROFILES

For a reaction coordinate  $q$ , we can define a probability distribution function according to

$$\begin{aligned}P(\bar{q}) &= \langle \delta(q(\mathbf{r}_1, \dots, \mathbf{r}_N) - \bar{q}) \rangle \\ &= \frac{C_N}{Q} \int d^N \mathbf{p} d^N \mathbf{r} e^{-\beta H(\mathbf{p}, \mathbf{r})} \delta(q(\mathbf{r}_1, \dots, \mathbf{r}_N) - \bar{q})\end{aligned}$$

Then, we define the free energy profile,  $A(\bar{q})$ , to be

$$A(\bar{q}) = -kT \ln P(\bar{q})$$

Apart from the normalization of  $P(\bar{q})$  by the partition function,  $Q$ ,  $P(\bar{q})$ , itself is a kind of partition function corresponding to a fixed value of the reaction coordinate. Thus, defining the free energy profile in terms of the log of  $P(\bar{q})$  is analogous to defining the global free energy  $A = -kT \ln Q$ .

### A. Physical meaning of $A(\bar{q})$

Consider the free energy difference between two values of the reaction coordinate  $\bar{q}$  and  $\bar{q}_0$ , which can be written as

$$A(\bar{q}) - A(\bar{q}_0) = \int_{\bar{q}_0}^{\bar{q}} d\bar{q}' \frac{dA}{d\bar{q}'} = -kT \int_{\bar{q}_0}^{\bar{q}} d\bar{q}' \frac{1}{P(\bar{q}')} \frac{dP}{d\bar{q}'}$$

The integrand can be written as

$$\frac{1}{P(\bar{q}')} \frac{dP}{d\bar{q}'} = \frac{\frac{C_N}{Q} \int d^N \mathbf{p} d^N \mathbf{r} e^{-\beta H(\mathbf{p}, \mathbf{r})} \frac{\partial}{\partial \bar{q}'} \delta(q(\mathbf{r}_1, \dots, \mathbf{r}_N) - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle}$$

Now, we introduce a coordinate transformation from Cartesian coordinates to a set of generalized coordinates that contains  $q$ :

$$(\mathbf{r}_1, \dots, \mathbf{r}_N) \longrightarrow (u_1, \dots, u_n, q)$$

where  $n = 3N - 1$ . In addition, a corresponding transformation is made on the conjugate momenta according to:

$$(\mathbf{p}_1, \dots, \mathbf{p}_N) \longrightarrow (p_{u_1}, \dots, p_{u_n}, p_q)$$

so that, in the measure, no overall Jacobian appears:

$$d^N \mathbf{p} d^N \mathbf{r} = d^n p_u dp_q d^n u dq$$

Thus, we have

$$\frac{1}{P(\bar{q}')} \frac{dP}{d\bar{q}'} = \frac{\frac{C_N}{Q} \int d^n p_u dp_q d^n u dq e^{-\beta H(p_u, p_q, u, q)} \frac{\partial}{\partial \bar{q}'} \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle}$$

Next, the derivative with respect to  $\bar{q}'$  is changed to a derivative with respect to  $q$ :

$$\frac{1}{P(\bar{q}')} \frac{dP}{d\bar{q}'} = - \frac{\frac{C_N}{Q} \int d^n p_u dp_q d^n u dq e^{-\beta H(p_u, p_q, u, q)} \frac{\partial}{\partial q} \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle}$$

Then, an integration by parts is performed, which yields

$$\begin{aligned} \frac{1}{P(\bar{q}')} \frac{dP}{d\bar{q}'} &= \frac{\frac{C_N}{Q} \int d^n p_u dp_q d^n u dq \left[ \frac{\partial}{\partial q} e^{-\beta H(p_u, p_q, u, q)} \right] \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle} \\ &= \frac{-\frac{\beta C_N}{Q} \int d^n p_u dp_q d^n u dq \frac{\partial H}{\partial q} e^{-\beta H(p_u, p_q, u, q)} \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle} \\ &= -\beta \frac{\langle \frac{\partial H}{\partial q} \delta(q - \bar{q}') \rangle}{\langle \delta(q - \bar{q}') \rangle} \\ &\equiv -\beta \langle \frac{\partial H}{\partial q} \rangle_{\bar{q}'}^{\text{cond}} \end{aligned}$$

where the final average is an ensemble average *conditional* upon the restriction that the reaction coordinate  $q$  is equal to  $\bar{q}'$ . Generally,

$$\langle \dots \rangle_{\bar{q}'}^{\text{cond}} = \frac{\langle (\dots) \delta(q - \bar{q}') \rangle}{\langle \delta(q - \bar{q}') \rangle}$$

Thus, the free energy difference becomes:

$$A(\bar{q}) - A(\bar{q}_0) = \int_{\bar{q}_0}^{\bar{q}} d\bar{q}' \langle \frac{\partial H}{\partial q} \rangle_{\bar{q}'}^{\text{cond}}$$

Note that the average in the above expression can also be performed with respect to Cartesian positions and momenta, in which case the derivative can be carried out via the chain rule. If

$$H = \sum_{i=1}^N \frac{\mathbf{p}_i^2}{2m_i} + U(\mathbf{r}_1, \dots, \mathbf{r}_N)$$

then

$$\begin{aligned}
\frac{\partial H}{\partial q} &= \sum_{i=1}^N \left[ \frac{\partial H}{\partial \mathbf{p}_i} \cdot \frac{\partial \mathbf{p}_i}{\partial q} + \frac{\partial H}{\partial \mathbf{r}_i} \cdot \frac{\partial \mathbf{r}_i}{\partial q} \right] \\
&= \sum_{i=1}^N \left[ \frac{\mathbf{p}_i}{m_i} \cdot \frac{\partial \mathbf{p}_i}{\partial q} + \frac{\partial U}{\partial \mathbf{r}_i} \cdot \frac{\partial \mathbf{r}_i}{\partial q} \right] \\
&= \sum_{i=1}^N \left[ \frac{\mathbf{p}_i}{m_i} \cdot \frac{\partial \mathbf{p}_i}{\partial q} - \mathbf{F}_i \cdot \frac{\partial \mathbf{r}_i}{\partial q} \right]
\end{aligned}$$

The quantity  $-\partial H/\partial q$  is the generalized force on the generalized coordinate  $q$ . Thus, let the conditional average of this force be  $\mathcal{F}_{\bar{q}'}$ . Then,

$$\mathcal{F}_{\bar{q}'} = -\left\langle \frac{\partial H}{\partial q} \right\rangle_{\bar{q}'}^{\text{cond}}$$

and

$$A(\bar{q}) - A(\bar{q}_0) = -\int_{\bar{q}_0}^{\bar{q}} d\bar{q}' \mathcal{F}_{\bar{q}'}$$

Thus, the free energy difference can be seen to be equal to the work performed against the averaged generalized force in bringing the system from  $\bar{q}_0$  to  $\bar{q}$ , irrespective of the values of the other degrees of freedom. Such an integration is called *thermodynamic integration*.

Another useful expression for the free energy derivative can be obtained by integrating out the momenta before performing a transformation. We begin with

$$\frac{1}{P(\bar{q}')} \frac{dP}{d\bar{q}'} = \frac{\frac{C_N}{Q} \int d^N \mathbf{p} d^N \mathbf{r} e^{-\beta H(\mathbf{p}, \mathbf{r})} \frac{\partial}{\partial \bar{q}'} \delta(q(\mathbf{r}_1, \dots, \mathbf{r}_N) - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle}$$

Now, noting that the  $\delta$ -function condition is independent of momenta, we can integrate out the Cartesian momenta to yield:

$$\frac{1}{P(\bar{q}')} \frac{dP}{d\bar{q}'} = \frac{\frac{C_N}{Q \lambda^{3N}} \int d^N \mathbf{r} e^{-\beta U(\mathbf{r}_1, \dots, \mathbf{r}_N)} \frac{\partial}{\partial \bar{q}'} \delta(q(\mathbf{r}_1, \dots, \mathbf{r}_N) - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle}$$

Next, the coordinate transformation to generalized coordinates is performed:

$$(\mathbf{r}_1, \dots, \mathbf{r}_N) \longrightarrow (u_1, \dots, u_n, q)$$

associated with which there is a Jacobian given by

$$J(u_1, \dots, u_n, q) = \frac{\partial(\mathbf{r}_1, \dots, \mathbf{r}_N)}{\partial(u_1, \dots, u_n, q)}$$

Introducing the coordinate transformation, we obtain

$$\begin{aligned}
\frac{1}{P(\bar{q}')} \frac{dP}{d\bar{q}'} &= \frac{\frac{C_N}{Q \lambda^{3N}} \int d^n u dq J(u_1, \dots, u_n, q) e^{-\beta U} \frac{\partial}{\partial \bar{q}'} \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle} \\
&= -\frac{\frac{C_N}{Q \lambda^{3N}} \int d^n u dq J(u_1, \dots, u_n, q) e^{-\beta U} \frac{\partial}{\partial q} \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle} \\
&= \frac{\frac{C_N}{Q \lambda^{3N}} \int d^n u dq \left[ \frac{\partial}{\partial q} J(u_1, \dots, u_n, q) e^{-\beta U} \right] \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle} \\
&= \frac{\frac{C_N}{Q \lambda^{3N}} \int d^n u dq \left[ \frac{\partial}{\partial q} e^{-\beta(U - kT \ln J)} \right] \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle} \\
&= \frac{-\frac{\beta C_N}{Q \lambda^{3N}} \int d^n u dq \left( \frac{\partial U}{\partial q} - kT \frac{\partial \ln J}{\partial q} \right) e^{-\beta(U - kT \ln J)} \delta(q - \bar{q}')}{\langle \delta(q - \bar{q}') \rangle}
\end{aligned}$$

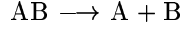
$$\begin{aligned}
&= \frac{-\beta C_N}{Q \lambda^{3N}} \int d^n u dq J(u_1, \dots, u_n, q) \left( \frac{\partial U}{\partial q} - kT \frac{\partial \ln J}{\partial q} \right) e^{-\beta U} \delta(q - \bar{q}') \\
&= \frac{\langle \delta(q - \bar{q}') \rangle}{\langle \delta(q - \bar{q}') \rangle} \\
&= -\beta \left\langle \left( \frac{\partial U}{\partial q} - kT \frac{\partial \ln J}{\partial q} \right) \right\rangle_{\bar{q}'}^{\text{cond}}
\end{aligned}$$

or

$$\frac{dA}{d\bar{q}'} = \left\langle \left( \frac{\partial U}{\partial q} - kT \frac{\partial \ln J}{\partial q} \right) \right\rangle_{\bar{q}'}^{\text{cond}}$$

### III. EXAMPLE OF A DISSOCIATION REACTION

Let us again look at the dissociation reaction



for which the reaction coordinate  $r = |\mathbf{r}_1 - \mathbf{r}_2|$  is appropriate. The transformation to center of mass and relative coordinate is:

$$\begin{aligned}
\mathbf{R} &= \frac{m_A \mathbf{r}_1 + m_B \mathbf{r}_2}{M} \\
\mathbf{r} &= \mathbf{r}_1 - \mathbf{r}_2
\end{aligned}$$

The inverse of this transformation is

$$\begin{aligned}
\mathbf{r}_1 &= \mathbf{R} + \frac{m_2}{M} \mathbf{r} \\
\mathbf{r}_2 &= \mathbf{R} - \frac{m_1}{M} \mathbf{r}
\end{aligned}$$

Next, the vector  $\mathbf{r} = (x, y, z)$  is transformed to spherical polar coordinates according to

$$\begin{aligned}
x &= r \sin \theta \cos \phi \\
y &= r \sin \theta \sin \phi \\
z &= r \cos \theta
\end{aligned}$$

and the derivative of the potential with respect to  $r$  can be easily worked out using the chain rule:

$$\begin{aligned}
\frac{\partial U}{\partial r} &= \frac{\partial U}{\partial \mathbf{r}} \cdot \frac{\partial \mathbf{r}}{\partial r} \\
\frac{\partial U}{\partial \mathbf{r}} &= \frac{\partial U}{\partial \mathbf{r}_1} \frac{m_2}{M} - \frac{\partial U}{\partial \mathbf{r}_2} \frac{m_1}{M} \\
&= -\frac{1}{M} [m_2 \mathbf{F}_1 - m_1 \mathbf{F}_2] \\
\frac{\partial \mathbf{r}}{\partial r} &= \left( \frac{x}{r}, \frac{y}{r}, \frac{z}{r} \right) \equiv \hat{\mathbf{n}} \equiv (\sin \theta \cos \phi, \sin \theta \sin \phi, \cos \theta) \\
\frac{\partial U}{\partial r} &= -\frac{1}{M} [m_2 \mathbf{F}_1 - m_1 \mathbf{F}_2] \cdot \hat{\mathbf{n}}
\end{aligned}$$

The Jacobian is clearly

$$J = r^2 \sin \theta$$

so that

$$\frac{\partial \ln J}{\partial r} = \frac{2}{r}$$

Thus, the free energy derivative is

$$\frac{dA}{d\bar{r}'} = \left\langle -\frac{1}{M} [m_2 \mathbf{F}_1 - m_1 \mathbf{F}_2] \cdot \hat{\mathbf{n}} - \frac{2kT}{|\mathbf{r}_1 - \mathbf{r}_2|} \right\rangle_{\bar{r}'^{\text{cond}}}$$

which is expressed completely in terms of Cartesian quantities and can be calculated straightforwardly.

Once  $dA/d\bar{r}'$  is known, it can be integrated to obtain the full free energy profile  $A(\bar{r}')$ . This is another use of thermodynamic integration.

It is always interesting to see what  $A(r)$  looks like compared to the bare potential. Suppose the dissociation reaction is governed by a pair potential describing the interaction of the dissociating molecule with a solvent:

$$U(\mathbf{r}_1, \dots, \mathbf{r}_N) = u_0(|\mathbf{r}_1 - \mathbf{r}_2|) + \sum_{j \neq 1,2} [\tilde{u}(|\mathbf{r}_1 - \mathbf{r}_j|) + \tilde{u}(|\mathbf{r}_2 - \mathbf{r}_j|)] + \sum_{i,j,i \neq j,i,j \neq 1,2} v(|\mathbf{r}_i - \mathbf{r}_j|)$$

The potential  $u_0(r)$  might look like:

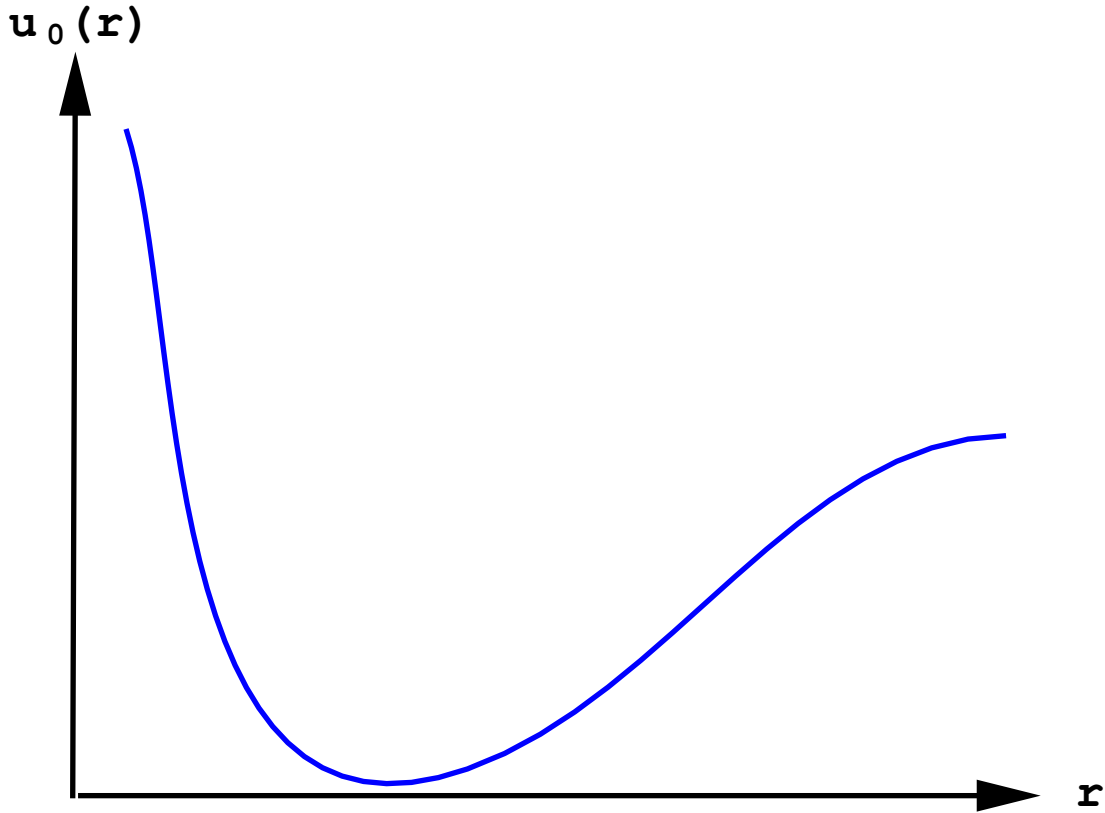


FIG. 2.

If, at a given temperature  $T$ , the solvent assists in the dissociation process, then we might expect  $A(r)$  to have a lower dissociation threshold and perhaps a slightly longer effective minimum bond length:

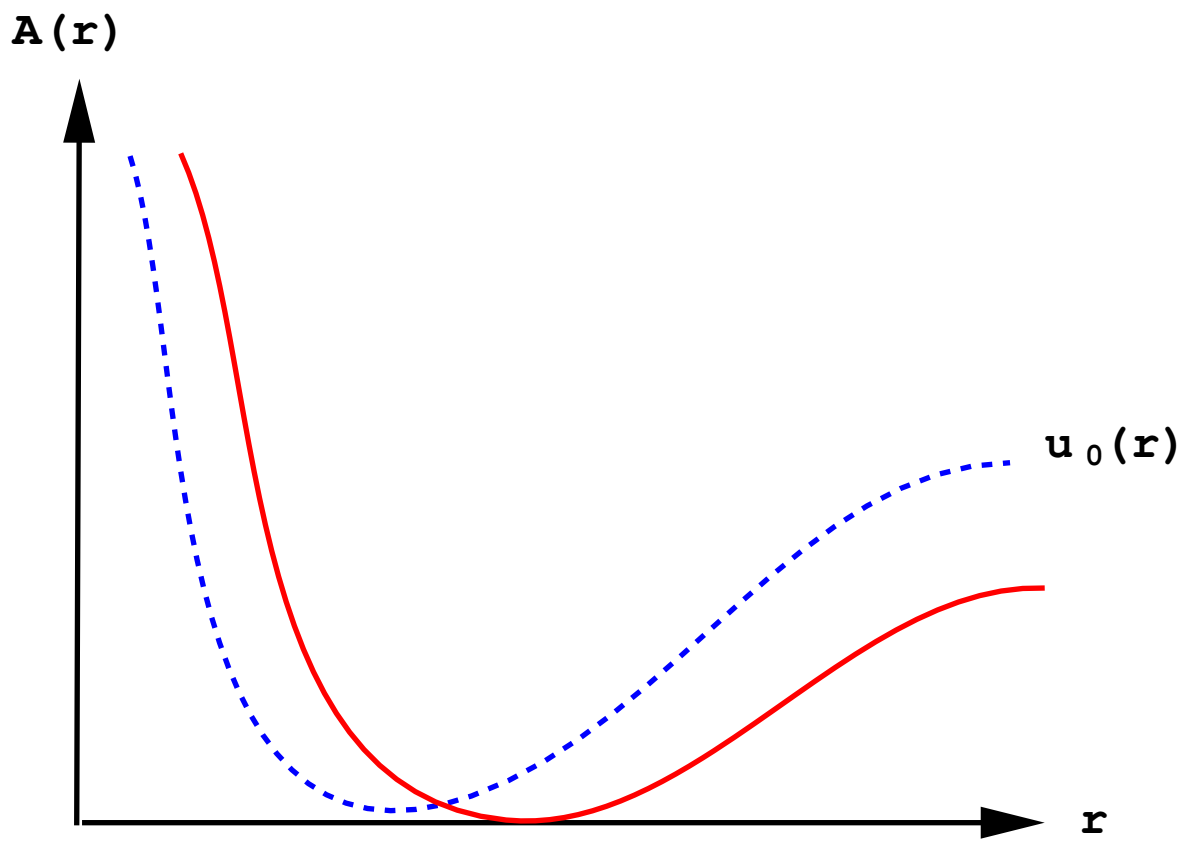


FIG. 3.

If, on the other hand, at a given temperature,  $T$ , the solvent hinders dissociation, by causing the molecule to bury itself in a cavity, for example, then we might expect  $A(r)$  to appear as follows:

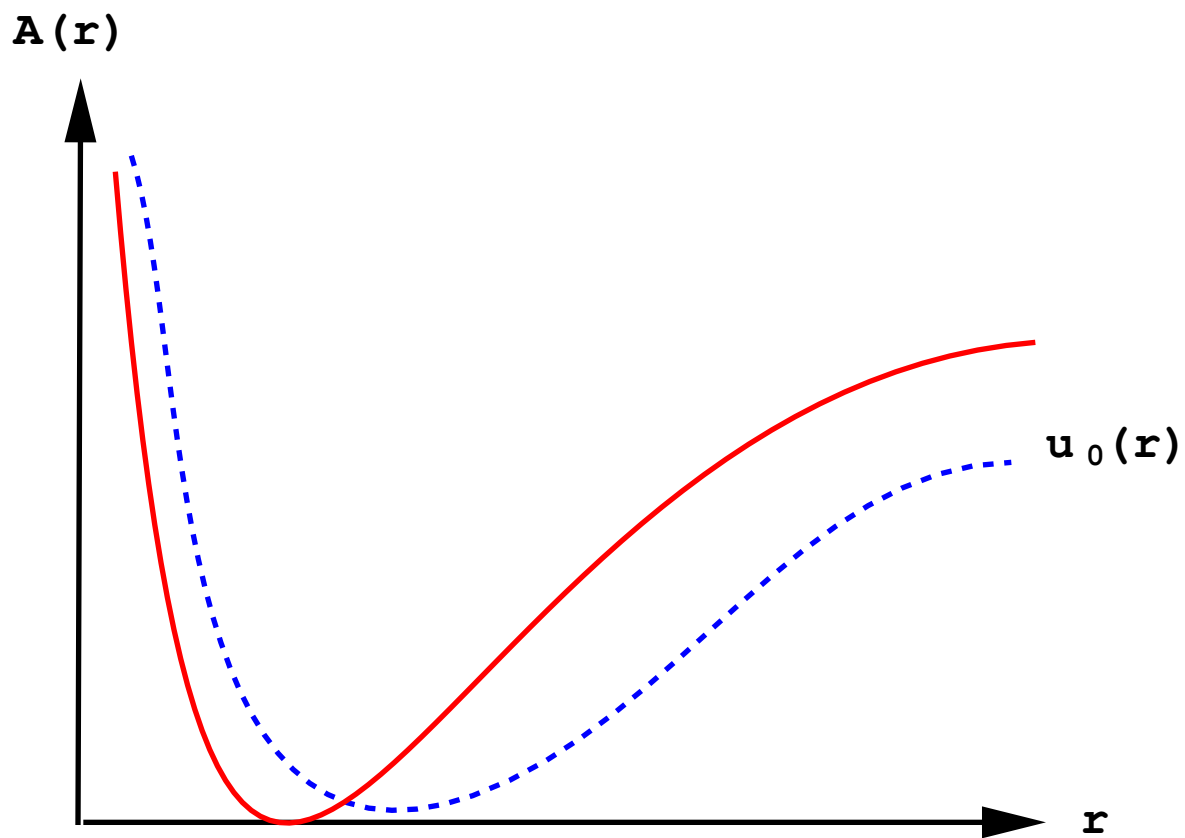


FIG. 4.

with a higher dissociation threshold energy and slightly shorter effective minimum bond length. Such curves will, of course, be temperature dependent and depend on the specific nature of the interactions with the solvent.