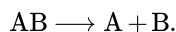


## 8.4: Reaction Coordinates

It is frequently the case that the progress of some chemical, mechanical, or thermodynamics process can be followed by following the evolution of a small subset of generalized coordinates in a system. When generalized coordinates are used in this manner, they are typically referred to as *reaction coordinates*, *collective variables*, or *order parameters*, often depending on the context and type of system. Whenever referring to these coordinates, we will refer to them as *reaction coordinates*, although the reader should be aware that the other two designations are also used in the literature.

As an example of a useful reaction coordinate, consider a simple gas-phase diatomic dissociation process



If  $\mathbf{r}_A$  and  $\mathbf{r}_B$  denote the Cartesian coordinates of atom A and B, then a useful generalized coordinate for following the progress of the dissociation is simply the distance  $r = |\mathbf{r}_B - \mathbf{r}_A|$ . A complete set of generalized coordinates that contains  $r$  as one of the coordinates is the set that contains the center of mass

$$\mathbf{R} = \frac{m_A \mathbf{r}_A + m_B \mathbf{r}_B}{m_A + m_B},$$

the magnitude of the relative coordinate

$$r = |\mathbf{r}_B - \mathbf{r}_A|$$

and the two angles  $\phi = \tan^{-1}(y/x)$  and  $\theta = \tan^{-1}(\sqrt{x^2 + y^2}/z)$ , where  $x$ ,  $y$  and  $z$  are the components of the relative coordinate

$$\mathbf{r} = \mathbf{r}_B - \mathbf{r}_A.$$

Of course, in the gas-phase, where the potential between A and B likely only depends on the distance between A and B,  $r$  is really the *only* interesting coordinate. However, if the reaction were to take place in solution, then other coordinate such as  $\theta$  and  $\phi$  become more relevant as specific orientations might change the mechanism or thermodynamic picture of the process, depending on the complexity of the solvent, and averaging over these degrees of freedom to produce a free energy profile  $A(r)$  in  $r$  alone will wash out some of this information.

As another example, consider a gas-phase proton transfer reaction



Here, although the distance  $|\mathbf{r}_H - \mathbf{r}_A|$  can be used to monitor the progress of the proton away from A and the distance  $|\mathbf{r}_H - \mathbf{r}_B|$  can be used to monitor the progress of the proton toward B, neither distance alone is sufficient for following the progress of the reaction. However, the difference

$$\delta = |\mathbf{r}_H - \mathbf{r}_B| - |\mathbf{r}_H - \mathbf{r}_A|$$

can be used to follow the progress of the proton transfer from A to B and, therefore, is a potentially useful reaction coordinate. A complete set of generalized coordinates involving  $\delta$  can be constructed as follows. If  $\mathbf{r}_A$ ,  $\mathbf{r}_B$  and  $\mathbf{r}_H$  denote the Cartesian coordinates of the three atoms, then first introduce the center-of-mass

$$\mathbf{R} = \frac{m_A \mathbf{r}_A + m_B \mathbf{r}_B + m_H \mathbf{r}_H}{m_A + m_B + m_H}$$

the relative coordinate between A and B,  $\mathbf{r} = \mathbf{r}_B - \mathbf{r}_A$ , and a third relative coordinate  $s$  between H and the center-of-mass of A and B,

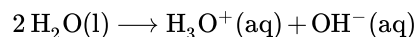
$$\mathbf{s} = \mathbf{r}_H - \frac{m_A \mathbf{r}_A + m_B \mathbf{r}_B}{m_A + m_B}.$$

Finally,  $\mathbf{r}$  is transformed into spherical polar coordinates,  $(r, \theta, \phi)$ , and from  $\mathbf{r}$  and  $s$ , three more coordinates are formed:

$$\sigma = \left| \mathbf{s} + \frac{m_B}{m_A + m_B} \mathbf{r} \right| + \left| \mathbf{s} - \frac{m_A}{m_A + m_B} \mathbf{r} \right| \quad \delta = \left| \mathbf{s} + \frac{m_B}{m_A + m_B} \mathbf{r} \right| - \left| \mathbf{s} - \frac{m_A}{m_A + m_B} \mathbf{r} \right|$$

and the angle  $\alpha$ , which measures the "tilt" of the plane containing the three atoms from the vertical. The coordinates  $(\sigma, \delta, \alpha)$  are known as **confocal elliptic coordinates**. These coordinates could also be used if the reaction takes place in solution. As expected, the generalized coordinates are functions of the original Cartesian coordinates. The alanine-dipeptide example above also employs the Ramachandran angles  $\phi$  and  $\psi$  as reaction coordinates, and these can also be expressed as part of a set of generalized coordinates that are functions of the original Cartesian coordinates of a system.

While reaction coordinates or collective variables are potentially very useful constructs, they must be used with care, particularly when enhanced sampling methods are applied to them. Enhanced sampling of a poorly chosen reaction coordinate can bias the system in unnatural ways, leading to erroneous predictions of free energy barriers and associated mechanisms. A dramatic example of this is the autodissociation of liquid water following the classic reaction



the ostensibly only requires transferring a proton from one water molecule to another. If this notion of the reaction is pursued, then a seemingly sensible reaction coordinate would simply be the distance between the oxygen and the transferring proton or the number of hydrogens covalently bonded to the oxygen. These reaction coordinates, as it turns out, are inadequate for describing the true nature of the reaction and, therefore, fail to yield reasonable free energies (and hence, values of the autoionization constant  $K_w$ ). Chandler and coworkers showed that the dissociation reaction can only be considered to have occurred when the  $\text{H}_3\text{O}^+$  and  $\text{OH}^-$  ions are sufficiently far apart that no contiguous or direct path of hydrogen-bonding in the liquid can allow the proton to transfer back to the water or its origin. In order to describe such a process correctly, a very different type of reaction coordinate would clearly be needed.

Keeping in mind such caveats about the use of reaction coordinates, we now proceed to describe a number of popular methods designed to enhance sampling along pre-selected reaction coordinates. All of these methods are designed to generate, either directly or indirectly, the probability distribution function  $P(q_1, \dots, q_n)$  of a subset of  $n$  reaction coordinates of interest in a system. If these reaction coordinates are obtained from a transformation of the Cartesian coordinates  $q_\alpha = f_\alpha(\mathbf{r}_1, \dots, \mathbf{r}_N)$ ,  $\alpha = 1, \dots, n$ , then the probability density that these  $n$  coordinates will have values  $q_\alpha = s_\alpha$  in the canonical ensemble is

$$P(s_1, \dots, s_n) = \frac{C_N}{Q(N, V, T)} \int d^N \mathbf{p} d^N \mathbf{r} e^{-\beta H(\mathbf{p}, \mathbf{r})} \Phi_{\alpha=1}^n \delta(f_\alpha(\mathbf{r}_1, \dots, \mathbf{r}_N) - s_\alpha)$$

where the  $\delta$ -functions are introduced to fix the reaction coordinates at values  $q_1, \dots, q_n$  at  $s_1, \dots, s_n$ . Once  $P(s_1, \dots, s_n)$  is known, the **free energy hypersurface** in these coordinates is given by

$$A(s_1, \dots, s_n) = -kT \ln P(s_1, \dots, s_n)$$

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