

Free Energy Calculations 🧊

The primary motivation for calculating free energy is to predict the phase behavior of a material, such as determining the melting point of a crystal.

Methods for Determining Melting Point

1. **"Heat-Until-Melts" Method:** This simple approach involves gradually heating a simulated crystal until it melts. However, it often overestimates the true melting temperature due to metastability.
2. **Coexistence Method:** A more accurate technique involves simulating a system with both solid and liquid phases in direct contact. By running simulations at different temperatures, one can find the temperature at which the two phases remain stable, which corresponds to the melting point.

The most stable phase of a system under specific conditions is the one with the minimum free energy.

- For a system at constant **N, V, T** (canonical ensemble), the **Helmholtz free energy ($F = E - TS$)** is minimal.
- For a system at constant **N, P, T** (isothermal-isobaric ensemble), the **Gibbs free energy ($G = E - TS + pV$)** is minimal.

A major challenge in simulations is that free energies cannot be "measured" directly as a simple average of some function over phase space. Instead, they are related to the volume of phase space accessible to the system, expressed through the partition function, Z . For example, the Helmholtz free energy is given by $F = -k_B T \ln Z$.

Thermodynamic Integration

To calculate free energy differences, we can use a method called **thermodynamic integration**. This involves defining a potential energy function, $V(\lambda)$, that smoothly transitions from an initial state I (at $\lambda = 0$) to a final state II (at $\lambda = 1$).

$$V(\lambda) = (1 - \lambda)V_I + \lambda V_{II}$$

By differentiating the free energy with respect to the coupling parameter λ , we arrive at the central formula for thermodynamic integration:

$$F(\lambda = 1) = F(\lambda = 0) + \int_0^1 \left\langle \frac{\partial V(\lambda)}{\partial \lambda} \right\rangle_{\lambda} d\lambda$$

Here, $\left\langle \frac{\partial V(\lambda)}{\partial \lambda} \right\rangle_{\lambda}$ is the ensemble average of the derivative of the potential, calculated in a simulation using the potential $V(\lambda)$.

Practical Implementation

1. **Evaluating the Integral:** The integral is typically evaluated numerically by running a series of simulations at different, fixed values of λ between 0 and 1. The results are then used to numerically integrate the function.
2. **Choosing a Reference State:** The calculation gives the difference in free energy. Therefore, the state at $\lambda = 0$, $F(\lambda = 0)$, must be a simple system whose free energy can be calculated analytically. Common reference systems include the **ideal gas** for liquids and the **Einstein crystal** or **harmonic crystal** for solids.

Constraints and Rare Events

Simulations can struggle with **rare events**, which are important processes (like chemical reactions or phase transitions) that are hindered by a large energy barrier, ΔE^\ddagger . If the thermal energy is much smaller than this barrier ($k_B T \ll \Delta E^\ddagger$), the event will almost never occur during a standard simulation. Special methods like thermodynamic integration or potential of mean force calculations can be used to overcome this.

For simulations of rigid molecules, it's often necessary to apply **constraints**, such as keeping bond lengths constant. This is handled using the **Lagrange multiplier method**, which introduces constraint forces into the equations of motion. These forces act to keep the system on a defined hypersurface in phase space where the constraint conditions are met.

The resulting equations of motion are:

$$m_k \ddot{r}_k = F_k + F_k^C$$

Where F_k is the physical force and F_k^C is the constraint force. Solving these equations for all constraints can be complex. Popular algorithms that provide approximate, self-consistent solutions include **SHAKE** (for the Verlet integrator) and **RATTLE** (for the velocity-Verlet integrator).