The simulation techniques, Molecular Dynamics and Monte Carlo, as they are constructed, are only capable of calculating quantities expressible as averages of mechanical quantities $A = A(\{\mathbf{r}\}, \{\mathbf{p}\})$. Unfortunately, entropy, and consequently all the quantities that contain it, cannot be expressed in this way. In fact, from a statistical mechanics point of view, entropy is a measure of the accessible phase space to the system. To measure it, it is therefore necessary to visit the entire phase space Γ: the simulation can only stop if the system returns after a number n of steps within a predefined volume ω that surrounds the starting point, and only at this point can one give an estimate of the accessible volume as $\approx n\omega$ (in the microcanonical ensemble; similarly for others). But the number n, the *recurrence time*, is astronomically large even for systems of modest size, a few tens or hundreds of atoms, and increases rapidly with the number of degrees of freedom. This approach is therefore unfeasible.

It is therefore necessary to adopt more refined strategies. One of these consists in observing that mechanical quantities are often the derivatives of appropriate ones free energies or thermodynamic potentials. For example, pressure can be expressed as $P = -\partial A/\partial \Omega|_T$, where $A(N, \Omega, T)$ is the Helmholtz free energy $A = E - TS$. Let us therefore imagine that the system is described by a Hamiltonian $H_\lambda = K(\mathbf{p}) + V(\mathbf{r}; \lambda)$, where λ is any parameter that varies from 0 to 1. The partition function $Z = Z_p Z_q = \int d^{3N}p \ e^{-\beta K} \int d^{3N}q \ e^{-\beta V}$ will therefore be a function of λ, more precisely it will be the configurational part Z_q. But $A = -\frac{1}{\beta} lnZ$, a function of λ, therefore we can derive it:

$$\frac{\partial A}{\partial \lambda} = -\frac{1}{\beta}\frac{1}{Z_q}\frac{\partial Z_q}{\partial \lambda}$$

(the independence of Z_p from λ has been exploited). The derivative of Z_q gives

$$\frac{\partial Z_q}{\partial \lambda} = \int d^{3N}q \frac{\partial e^{-\beta V}}{\partial \lambda} = -\beta \int d^{3N}q \ e^{-\beta V}\frac{\partial V}{\partial \lambda} = -\beta Z_q \left\langle \frac{\partial V}{\partial \lambda} \right\rangle$$

and from the fundamental theorem of integral calculus we derive an expression for the difference in free energy between the states $\lambda = 1$ and $\lambda = 0$:

$$\Delta A = A(\lambda = 1) - A(\lambda = 0) = \int_0^1 d\lambda \frac{\partial A}{\partial \lambda} = \int_0^1 d\lambda \left\langle \frac{\partial V}{\partial \lambda} \right\rangle.$$

Let's discuss a few things:

1. The average value of $\frac{\partial V}{\partial \lambda}$ must be calculated at different values of λ. Each calculation is a different simulation, with its own thermalization. In practice, we will use values of λ corresponding to the points required by a suitably chosen numerical integration algorithm, for example the points of the various Gauss formulas. Note that these points will almost always be internal points of the segment $[0, 1]$.

2. Even when $\frac{\partial V}{\partial \lambda}$ is independent of λ, which as we will see is a frequent case, its average value is a function of λ because the dynamics of the system depends on it via V.

3. No hypotheses were made on λ, nor on the dependence of $V(\lambda)$, except for the differentiability of the quantities involved. In particular, the "intermediate" systems with $0 < \lambda < 1$ need not necessarily exist or be realizable in nature.

4. Given this freedom in the choice of $V(\lambda)$, it can be exploited to make the integrand $\left\langle \frac{\partial V}{\partial \lambda} \right\rangle$ as smooth as possible, thus facilitating numerical integration, which will require as few points as possible, therefore fewer simulations possible.

5. However, it will be very difficult to obtain an easily integrable function if the initial and final states, $\lambda = 1$ and $\lambda = 0$, correspond to different thermodynamic phases, given that at the transition any thermodynamic function is no longer regular.

Let's see some examples. Suppose we want to calculate the free energy of an anharmonic crystal with interaction V_A. A suitable reference system consists of a crystal, of the same structure, in which the atoms are considered as independent harmonic oscillators (*Einstein crystal*). The corresponding potential is

$$V_H = \sum_I^N m_I \omega^2 (\mathbf{r}_I - \xi_I)^2$$

where the ξ_I are the equilibrium positions of the atoms in the crystal target of the calculation and ω a frequency representative of the frequencies of the system, typically the optical phonons, if present, or the acoustic phonons at about half of the Brillouin zone. A parameterization could therefore be

$$V_\lambda = \lambda V_A + (1-\lambda)V_H, \qquad \frac{\partial V}{\partial \lambda} = V_A - V_H.$$

We therefore see that $\frac{\partial V}{\partial \lambda}$ is independent of λ even if, as mentioned, its average in general will not be. This calculation, given the similarity of the extreme states, promises to be easily feasible. However, care must be taken as it is not just the harmonic system it is not ergodic, which is of little importance since no calculations are actually performed on it, but systems with small λ are weakly anharmonic, and since the Fermi-Pasta-Ulam calculations we know how little ergodic the latter are. One will therefore need to pay particular attention to the correct thermalization of the system and, if necessary, use a massive chain of Nosè-Hoover thermostats.

A more complicated case consists in the calculation of the free energies of formation of lattice defects. If we consider a vacancy, for example, and for simplicity we imagine the volume to be kept fixed, the concentration of vacancies will be given by $c = e^{-\beta A}$, where A is the Helmholtz free energy of formation of an isolated vacancy. In general other contributions should also be taken into account, but here we have considered the simplest case. If A_C^N is the free energy of a perfect crystal of N atoms and A_V^{N-1} that of a crystal of $N-1$ plus a vacancy, we have for the free energy of formation

$$A^N \triangleq (N-1)\left[\frac{1}{N-1}A_V^{N-1} - \frac{1}{N}A_C^N\right] = A_V^{N-1} - A_C^N + \frac{1}{N}A_C^N.$$

In our simulations, however, the number of atoms will necessarily, being an integer, remain N in all systems regardless of λ. We therefore proceed not to eliminate an atom from the cell, but to decouple it from the others in this way, hypothesizing for simplicity only two-body potentials and labeling the atom to decouple with $I = 1$:

$$V_\lambda = \sum_{J>I, I>1} v_{IJ} + (1-\lambda)\sum_{J>1} v_{1J}, \qquad \frac{\partial V}{\partial \lambda} = -\sum_{J>1} v_{1J}.$$

The system with $\lambda = 1$ therefore corresponds to the defective crystal plus a decoupled atom (only kinetic energy), the one with $\lambda = 0$ corresponds to the perfect crystal. Thermodynamic integration would then give

$$\int_0^1 d\lambda \left\langle -\sum_{J>1} v_{1J} \right\rangle = A_V^{N-1} + \varphi_1 - A_C^N$$

where φ_1 is the free energy of an atom not interacting with the others, which is obviously known. One finally obtains

$$A^N = \int_0^1 d\lambda \left\langle -\sum_{J>1} v_{1J} \right\rangle + \frac{1}{N} A_C^N - \varphi_1.$$

This scheme, however, presents a serious problem. In simulations at $\lambda \sim 1$ the interatomic potential goes to 0, therefore the atom being decoupled can get very close to the others, as the repulsive core is greatly weakened. During these approaches however $\frac{\partial V}{\partial \lambda} = -\sum_{J>1} v_{1J}$, which *does not* depend on λ, preserves said core in full, therefore $\langle \sum_J v_{1,J} \rangle \to \infty$ when $\lambda \to 1$, making the integration very complicated. This is an example of a case where the systems are not similar enough. To make them more similar, we proceed as for the case of the anharmonic crystal, adding a potential $V_h = m_1 \omega^2 (\mathbf{r}_1 - \xi)^2$ on the decoupling atom, which will therefore oscillate in a similar way to the others. Its free energy at $\lambda = 1$ therefore is no longer φ_1 but that of a harmonic oscillator, ϕ_h, which is also known, so we are still able to calculate A:

$$A^N = \int_0^1 d\lambda \left\langle -\sum_{J>1} v_{1J} \right\rangle + \frac{1}{N} A_C^N - \phi_h$$

as long as the decoupling atom thermalizes, i.e. that the system is ergodic. Even in this case it can be remedied, if necessary, by using a Nosè-Hoover chain on atom 1.