The Zwanzig Relation: Derivation

- From before, $\beta(A_1 - A_0) = -\ln\left(\frac{Q_0}{Q_1}\right)$.
- Substituting in partition functions, $\beta(A_1 - A_0) = -\ln\left(\frac{\int e^{-\beta U_1(r^N)} dr^N}{\int e^{-\beta U_0(r^N)} dr^N}\right)$.
- Multiplying by one, $\beta(A_1 - A_0) = -\ln\left(\frac{\int e^{-\beta U_1(r^N) + \beta U_0(r^N) - \beta U_0(r^N)} dr^N}{\int e^{-\beta U_0(r^N)} dr^N}\right)$.
- Defining the potential energy difference $\Delta U(r^N) = U_1(r^N) - U_0(r^N)$,

$$\beta(A_1 - A_0) = -\ln\left(\frac{\int e^{-\beta \Delta U(r^N)} e^{-\beta U_0(r^N)} dr^N}{\int e^{-\beta U_0(r^N)} dr^N}\right)$$

The Zwanzig Relation: In Practice

- Using the definition of $\rho_s(r^N)$, $\beta(A_1 - A_0) = -\ln \int \rho_0(r^N) e^{-\beta \Delta U(r^N)} dr^N$.
- The Zwanzig relation [2] is
  - $\beta(A_1 - A_0) = -\ln \left\langle e^{-\beta \Delta U} \right\rangle_0$ in a simpler notation.
  - $\beta(A_1 - A_0) = -\ln \left\langle e^{\beta \Delta U} \right\rangle_1$ can be derived with similar steps
- This shows us that
  - The free energy difference can be computed based on an average over configurations taken from one of the states of interest
  - We can generate these configurations with MC or MD
  - The free energy comes from evaluating the energies of these configurations in both potentials U_0 and U_1, and taking an appropriate average of the energy difference