The Zwanzig Relation: In Practice

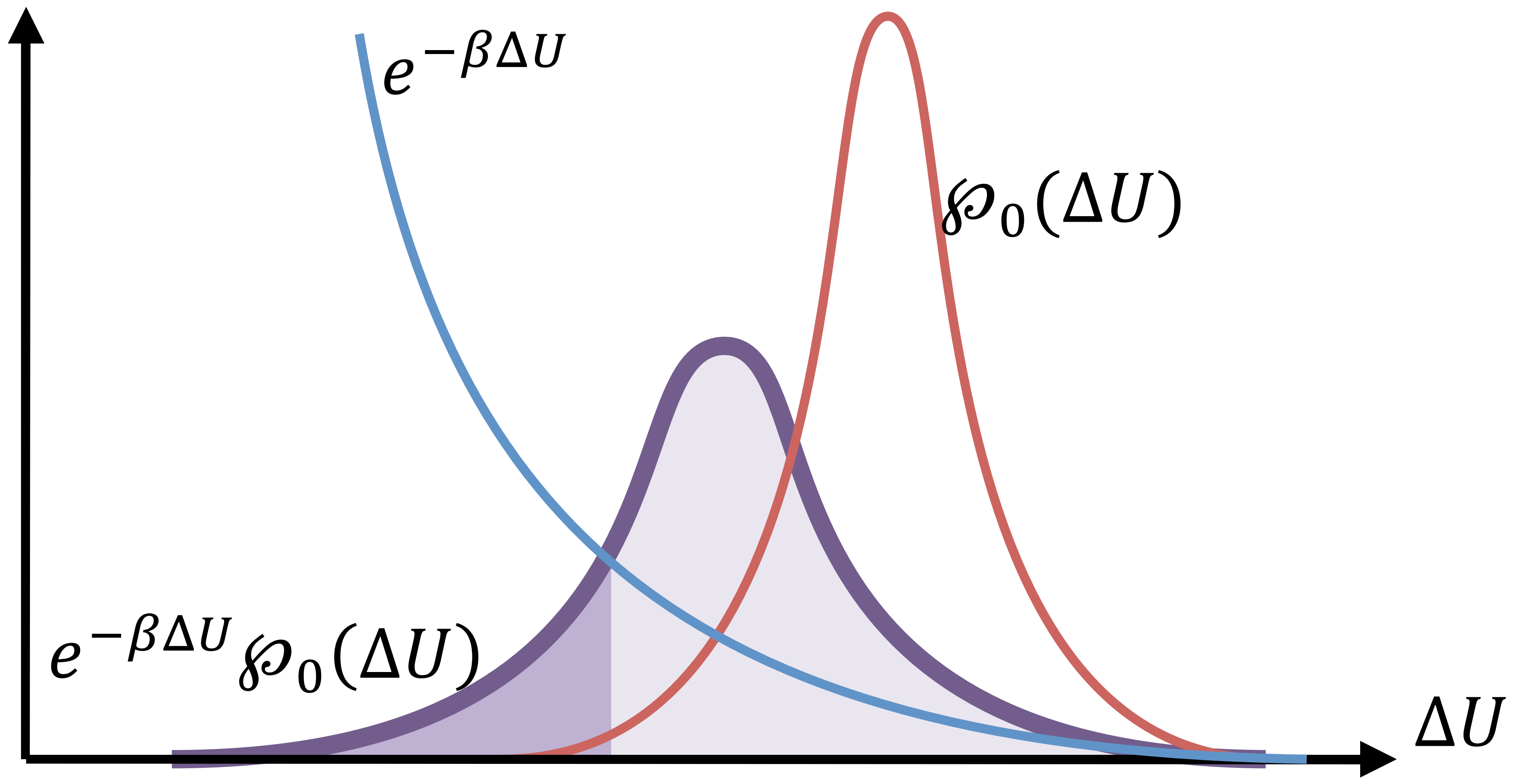
- Using the definition of $\rho_s(r^N)$, $\beta(A_1 - A_0) = -\ln \int \rho_0(r^N) e^{-\beta \Delta U(r^N)} dr^N$.
- The Zwanzig relation [2] is
  - $\beta(A_1 - A_0) = -\ln \left\langle e^{-\beta \Delta U} \right\rangle_0$ in a simpler notation.
  - $\beta(A_1 - A_0) = -\ln \left\langle e^{\beta \Delta U} \right\rangle_1$ 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

The Zwanzig Relation: Limitations

- In terms of an integral over the distribution of ΔU (instead of over $\rho_o(r^N)$) the Zwanzig relation is,

$$\beta(A_1 - A_0) = -\ln \int e^{-\beta \Delta U} \rho_0(\Delta U) d\Delta U.$$

- Sampling is from the red curve
- Accurate estimation requires the purple curve
- The calculation will not be accurate if U_0 and U_1 are very different!



(from [1])