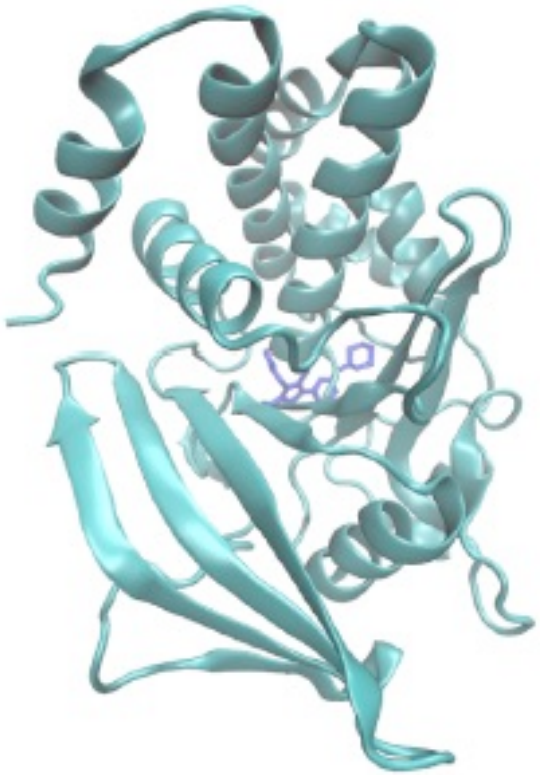


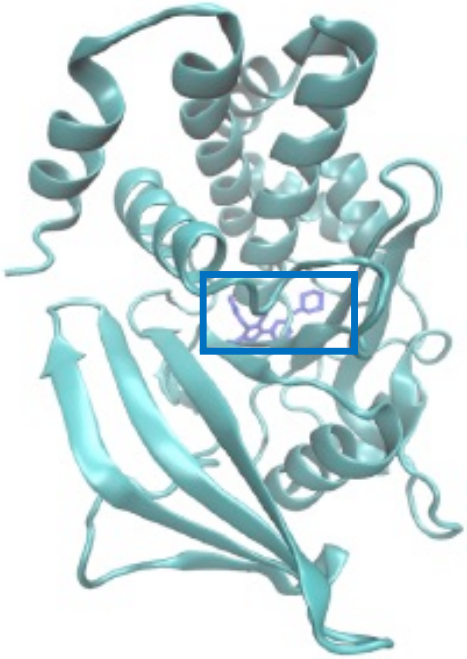
Computing Free Energy Using Quantum Annealing

Vaibhaw Kumar, Casey Tomlin, and JD Dulny

QUBITS 2019

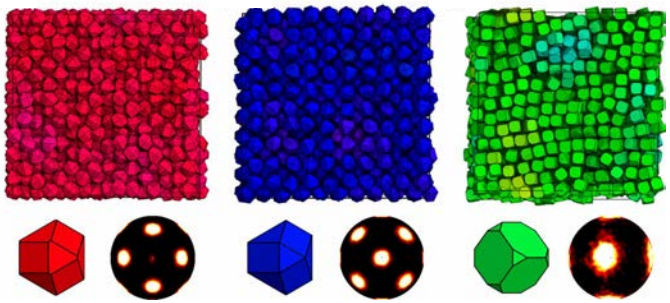
Free energy

Drug discovery



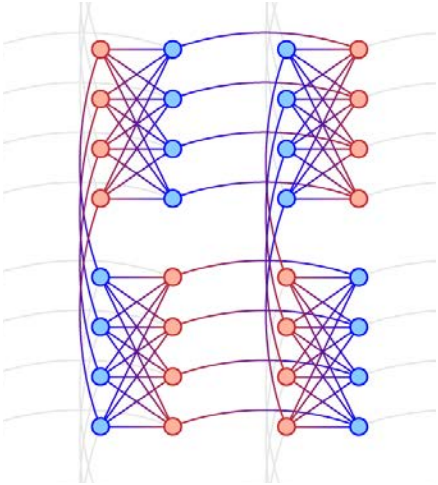
protein tyrosine phosphatase 1B (PTP1B); PDB: 2QBS,

Novel Materials



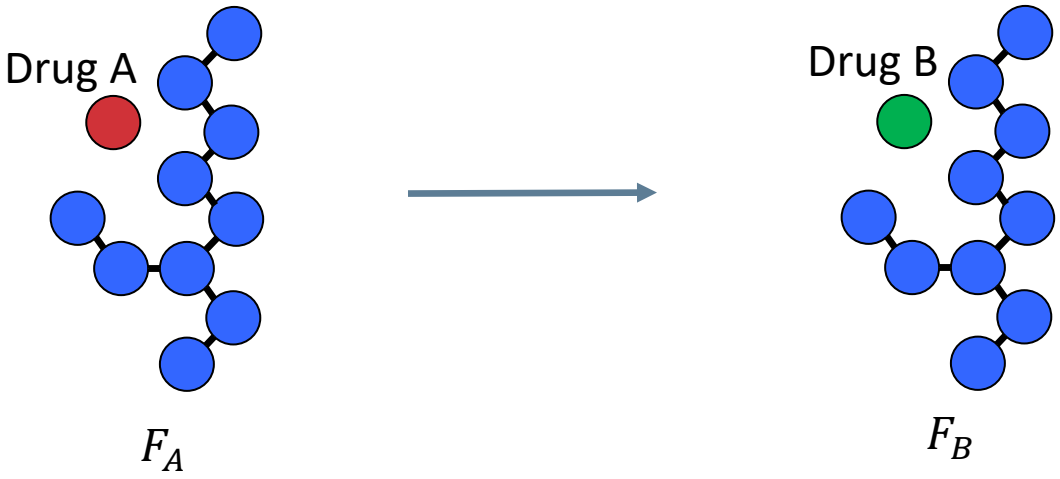
https://doi.org/10.1073/pnas.1621348114

Machine Learning



Free Energy of Binding

- Binding affinity is defined as free energy change associated with binding of a drug to a target protein



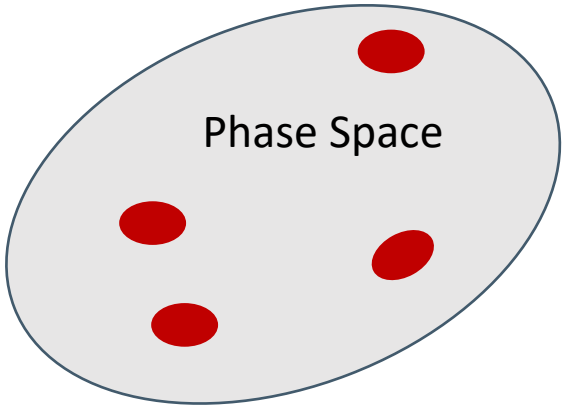
- $\Delta F = F_B - F_A$ indicates how potent drug B is compared to drug A

Free Energy Computation

- Expression for free energy

$$F = -kT ln\, Z$$

$$\boxed{Z = \sum_{x} e^{-E(x)/kT}}$$



- Computing partition function involves summing over all the states x a system can adopt
- Not possible to enumerate all the states
- Only few states contribute significantly to the sum

Free Energy as Ensemble Average

- Ratio of partition functions can be expressed as a Boltzmann average

$$\beta(\mathrm{F_B} - \mathrm{F_A}) = -\ln\left(\frac{Z_A}{Z_B}\right) = < M >_{Boltzmann\ average}$$

- This requires generation of samples according to Boltzmann distribution
- Different variants of MCMC is used for sampling
- Sampling from a rugged energy landscape is a challenge

Research questions

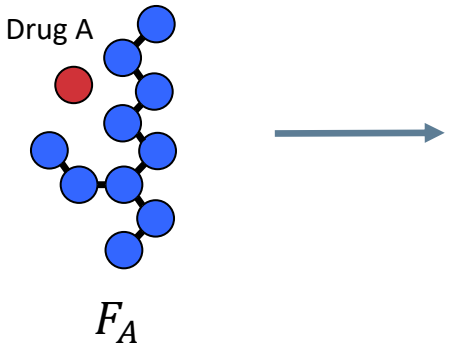
- ***Can we use the D-Wave for computing ensemble averages?***

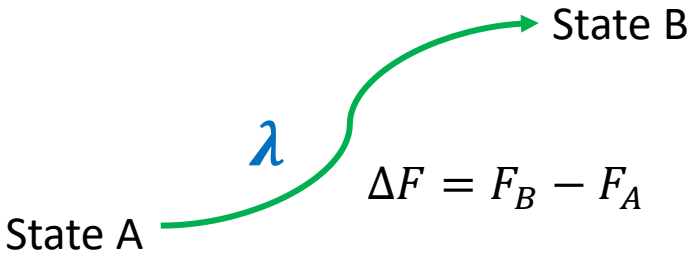
- ***Does it offer any advantages over classical techniques?***

Thermodynamic Integration

- Free energy difference between states A and B can be computed along a path of transformation

$$H(\lambda) = (1-\lambda)H_A + \lambda H_B$$

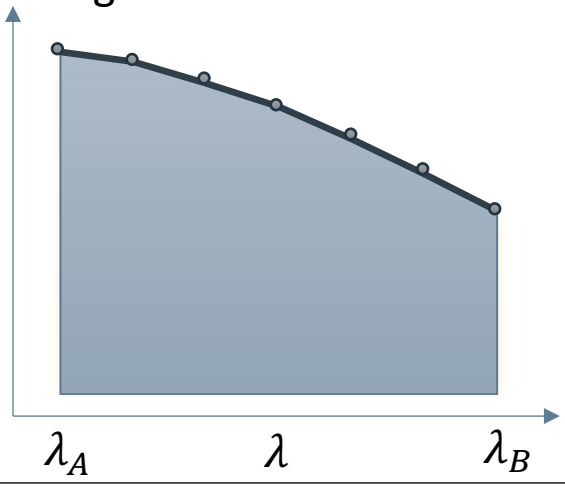




- Free energy difference computed from ensemble average

$$\Delta F = \int_A^B \left\langle \frac{\partial H}{\partial \lambda} \right\rangle \, d\lambda$$

$$\left\langle \frac{\partial H}{\partial \lambda} \right\rangle$$

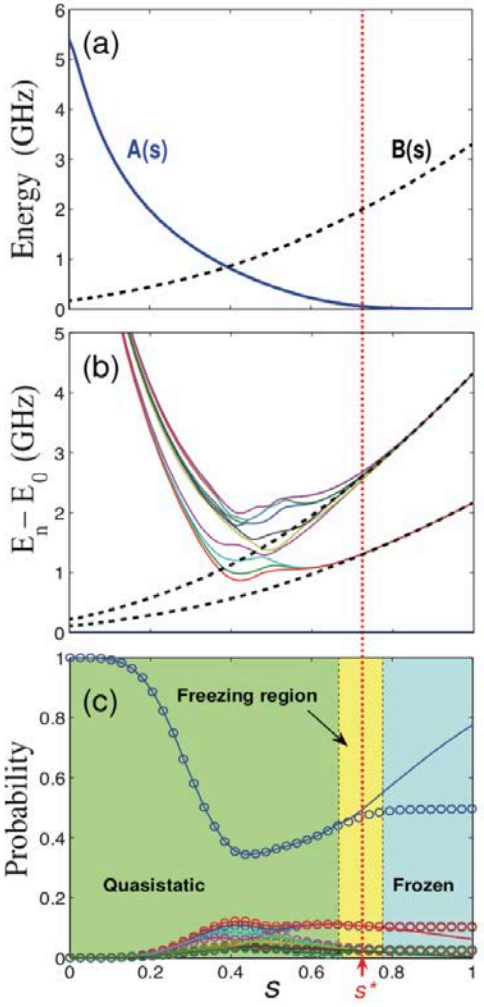


Boltzmann Sampling

- $H(s) = A(s)H_d + B(s)H_p$

where $H_d = -\sum_i \sigma_i^x$ is the driver(mixing) Hamiltonian and
$H_p = \sum_{ij} J_{ij}\sigma_i^z\sigma_j^z + \sum_i h_i\sigma_i^z$ is the problem Hamiltonian

- Towards the end of anneal, when transverse field diminishes, dynamics slows down and system essentially freezes
- It is conjectured that at the "freeze-out" point, device returns Boltzmann distributed samples at an instance-dependent inverse-temperature β_{eff} different from the hardware temperature
- If "freeze-out" point is earlier in the anneal, such promises cannot be made



Amin et. al, https://arxiv.org/pdf/1503.04216.pdf

Boltzmann Sampling

- D-Wave samples from an unknown device temperature β_{eff} different from the physical temperature
- Close examination of the samples must be done to ensure that samples are indeed Boltzmann distributed
- A cheap post-processing which incurs small overhead sounds promising
- In situations where post-processing succeeds, one doesn't need to obtain β_{eff}
- Post-processing brings samples close to the target distribution
- Such an approach can be more efficient when distribution exhibits well-separated modes

Global warming: Temperature estimation in annealers, Raymond et. al

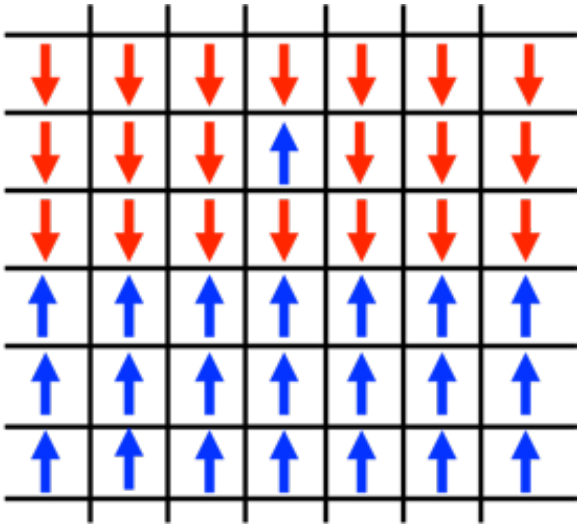
Simulation details

- We ran our simulations on USRA 2000Q D-Wave machine
- Post-processing was switched on
- $\beta = 4.0$ was set as the post-processing temperature for all the runs
- D-Wave heuristic solver was used to find the embedding for all models except the Chimera graph based model
- Spin-reversal transforms were used
- Exact values and classical sampling techniques were used for comparisons

Models studied

- 1D Ising spin model

- 2D Ising square-lattice spin model

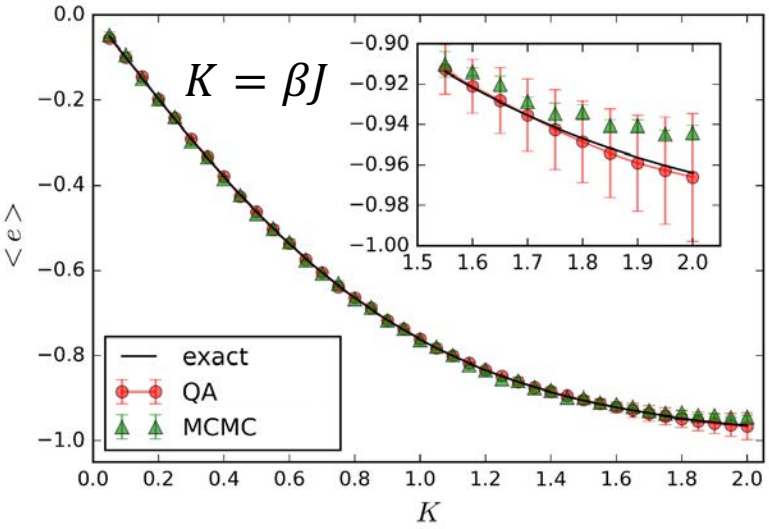


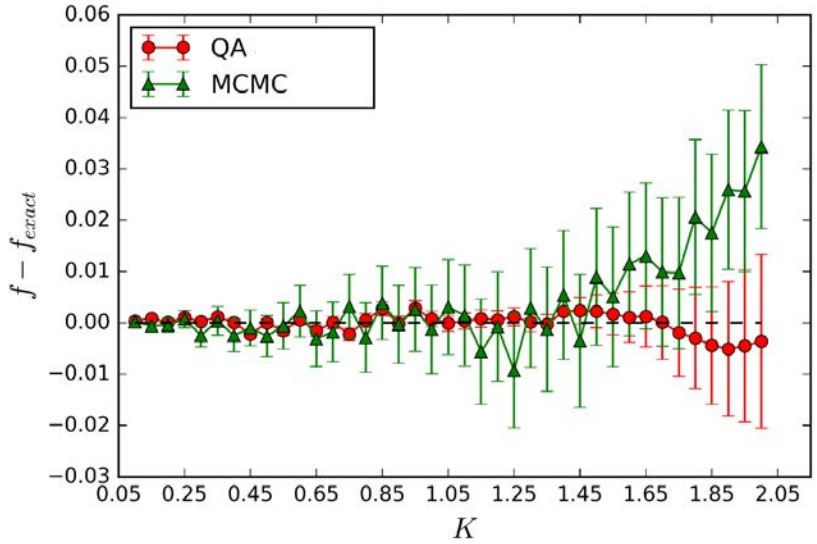
1D Ising model

- Integration path along a path where interaction strength J changes

$$E(x) = \sum_{i,j} J_{ij} x_i x_j$$

- Integrand is simply the energy in this case. $N = 48$ spins



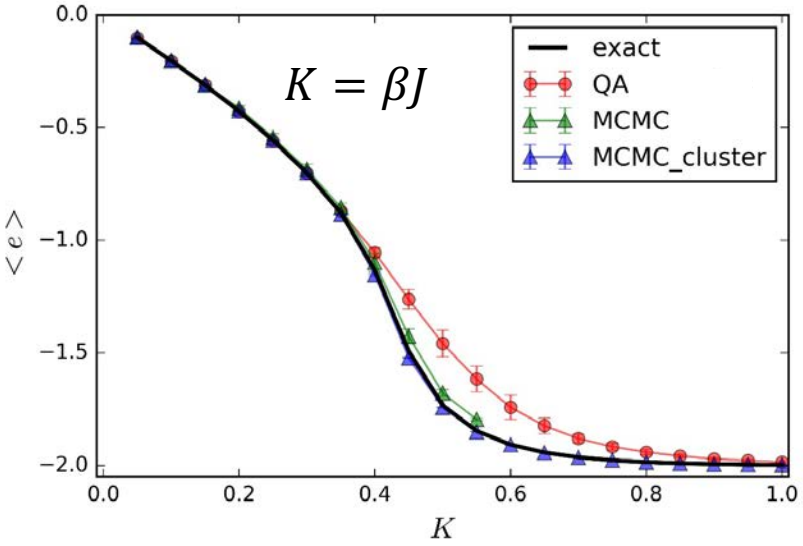


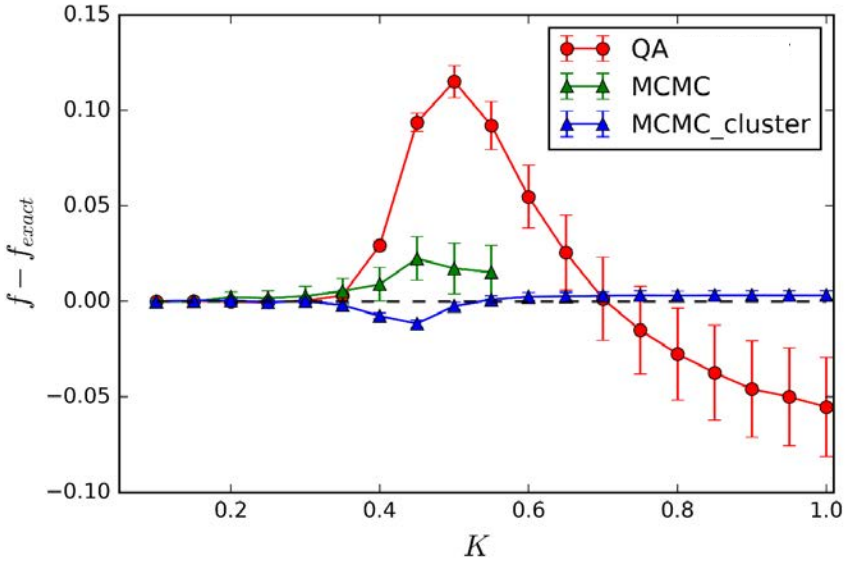
Note: Post-processing temperature was set to $\beta = 4.0$

2D Ising square lattice

$N = 12\text{x}12$

$K^* = 0.4407$

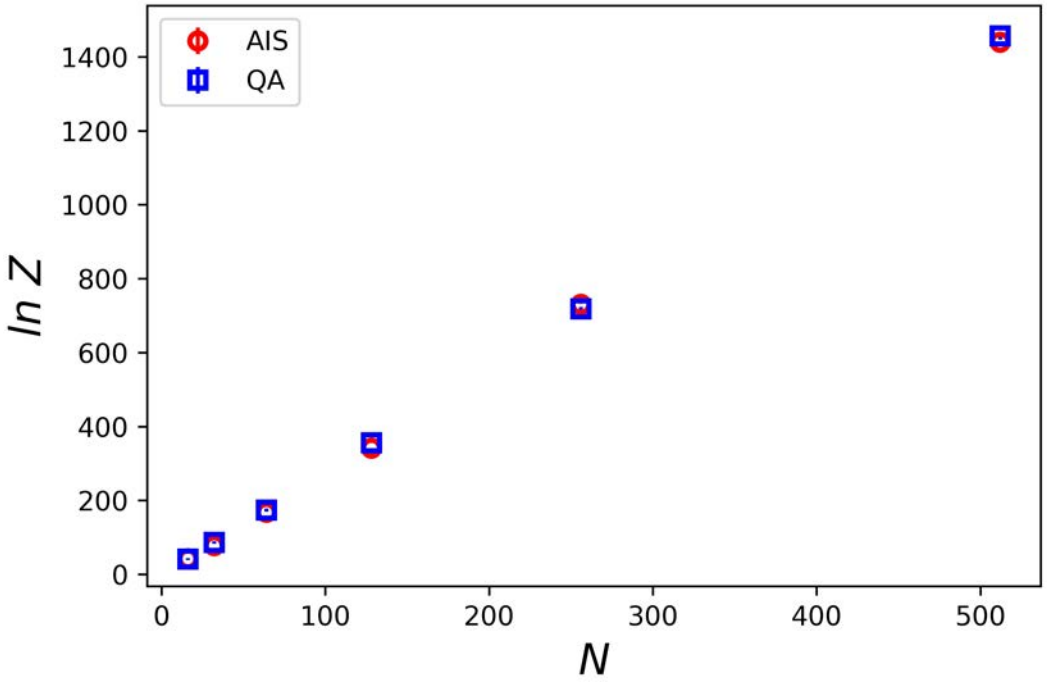


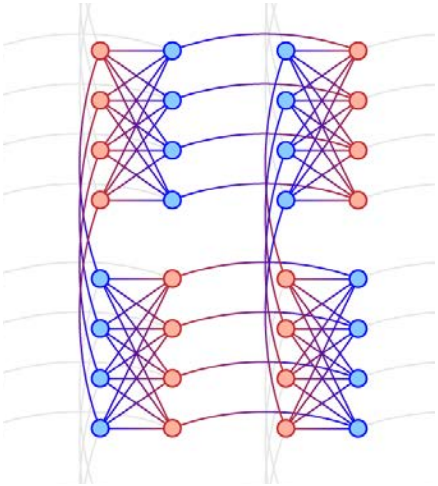


Boltzmann Machines

- Reference graph is a “bias-only” model
- Calculations done on graph size $2N$
- Annealed Importance Sampling (AIS) was used for comparisons

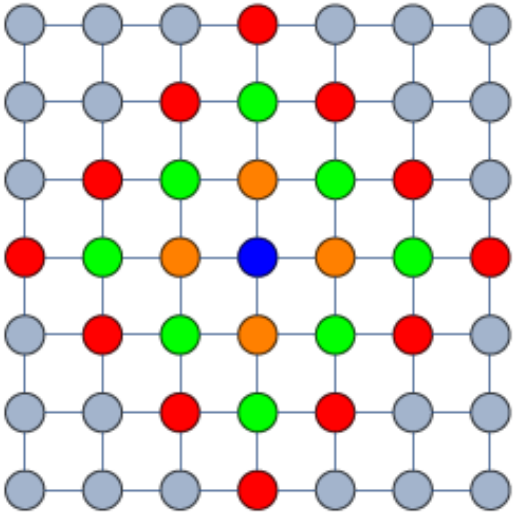
$$H = (1-\lambda)H_{ref} + \lambda H_{target}$$

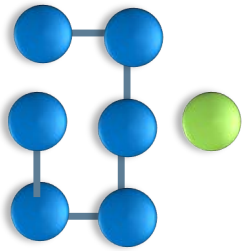




Protein-ligand Model

- We use diamond encoding to model the protein-ligand Hamiltonian in the QUBO form
- An improved encoding scheme was devised that uses fewer variables compared to the original implementation
- Self-avoiding walk of the chain is modeled using penalty terms in the Hamiltonian
- We study a six amino acid protein with a ligand fixed at a lattice position. Ligand has the same interaction with all the acids.

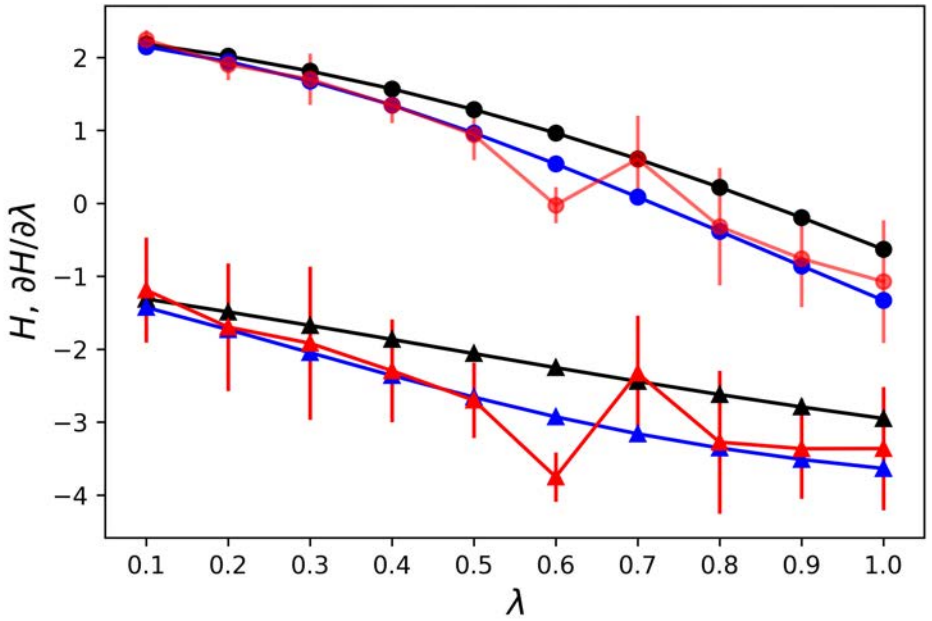




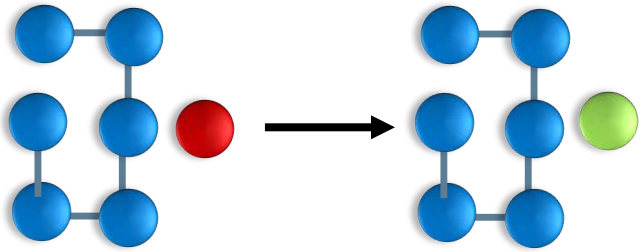
Construction of Energy Functions for Lattice Heteropolymer Models: A Case Study in Constraint Satisfaction Programming and Adiabatic Quantum Optimization, Babbush et. al

Protein-ligand Binding Free Energy

- Along the integration path, interaction strength of the drug with the protein is gradually increased
- ~37 binary variables in the Hamiltonian
- Embedding uses relatively long qubit chains
- The current precision limit on the device leads to under-specification of the Hamiltonian



$$\beta\Delta F_{exact} = -2.43$$
$$\beta\Delta F_{calc} = -2.36 \pm 0.48$$



Conclusions

- We examined the feasibility of using Quantum annealing based sampling for free energy calculations
- Our results indicate comparable accuracy compared to the classical samplers
- We would like to investigate cases where QA can possibly show considerable improvements over a purely classical scheme

OUR COLLABORATORS AND PARTNERS

Thank You