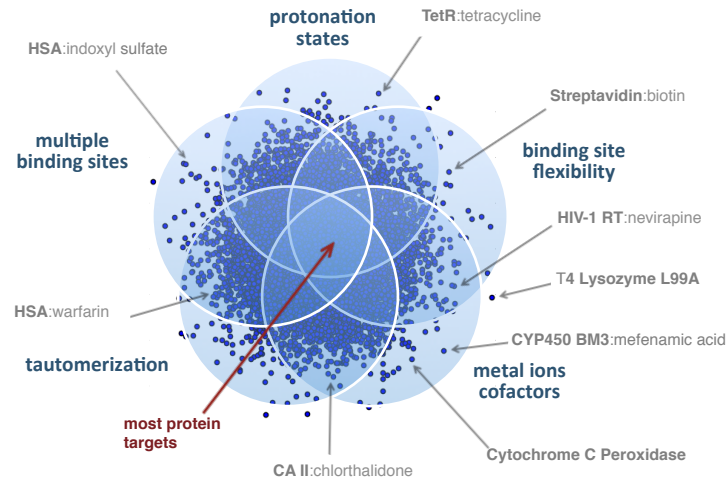


## A Challenges involved in predicting protein:ligand binding



B

### experimental tractability criteria

- Multiple protein crystal structures
- Known bacterial expression
- Availability of multiple purchasable known ligands
- Tractable experimental affinity measurements

### isolated challenge filters

- Ligand protonation state and tautomer effects
- Protein protonation state effects
- Protein conformational change upon binding
- Presence of PTMs affecting affinity
- Coordinated metals
- Ordered waters