

## Components of Macromolecular Association Energies

Murcko A; Murcko MA. **Computational methods to predict binding free energy in ligand- receptor complexes.** Journal of Medicinal Chemistry, 1995 Dec 22, 38(26):4953-67.

- *Measuring affinities*
- *Additivity of free energy components? Factors that determine ligand affinities*
- *Perturbation methods, especially for small changes*
- *Solvation / Desolvation, Buried surface area, and free energy*

### **Hodgkin**

A. Figure 1.

Factors that affect binding?

Structure based drug design?

Jencks paper

Enthalpy and entropy

### **Crick**

B. Binding affinity?

Relationship between equilibrium and binding energy

Binding energy and interactions.

Standard state?

### **Khorana**

C. Measurement of Binding Affinity,  $K_d$

$IC_{50}$ ?  $K_d$ ,  $K_i$ , Units

Competitive v noncompetitive binding?

Reversible v irreversible binding?

### **Curie**

D. Thermodynamics of binding?

Factors 1-6

Master equation

Points 1-9

Particularly point 8?

### **Hodgkin**

E. Terms of the master equation

Solvent

Transfer experiments

Surface area based

ASPs

Electrostatics in water  
Water binding  
Conformation change  
Calculating interaction energies  
Dielectric constant  
Functional groups  
Water

### **Crick**

F. Molecular motion

### **Khorana**

G. Other important future aspects?

### **Curie**

H. Basic conclusions