# Databases contain protein binding

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| UID | @March 22, 2022 10:24 PM |
| Field | Datasets |
| To-Do | ☐ |

measurements of binding affinity:

***K*d, *K*i, IC50**

Ki refers to inhibition constant, while Kd means dissociation constant. Both terms are used to describe the binding affinity that a small molecule or macromolecule has for an enzyme or receptor.

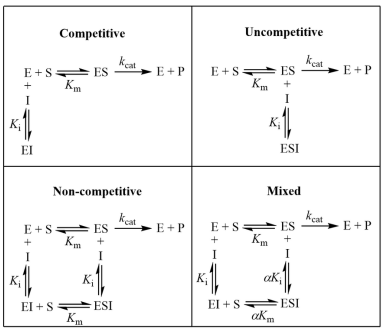
1. **Kd** is a more general, all-encompassing term. Kd measures the equilibrium between the ligand-protein complex and the dissociated components.

$$PL \rightleftharpoons P + L \quad (K_d)$$

$$K_d = \frac{[P][L]}{[PL]} = \frac{k_{-1}}{k_1}$$

*Where [P] is the free protein concentration, [L] is the free ligand concentration, [PL] is the protein-ligand complex, k-1 is the dissociation rate constant for the complex and k1 is the association rate constant.*

2. The **Ki** inhibition constant also represents a dissociation constant, but more narrowly for the binding of an inhibitor to an enzyme. That is, a ligand whose binding reduces the catalytic activity of the enzyme. The binding equilibrium described by the Ki value depends on the kinetic mechanism of inhibition. Common options include competitive, uncompetitive, non-competitive, and mixed inhibition. The equations are defined:




- In **competitive inhibition**, the inhibitor binds only to free enzyme (E), not to the enzyme-substrate complex (ES).
- In **uncompetitive inhibition**, the inhibitor binds only to the enzyme-substrate complex.
- In **non-competitive inhibition** is a special case of mixed inhibition where substrate binding has no effect on inhibitor binding (α = 1).

- **Mixed inhibition** involves inhibitor binding to both free enzyme and enzyme-substrate complex with different binding constants (Ki and αKi).

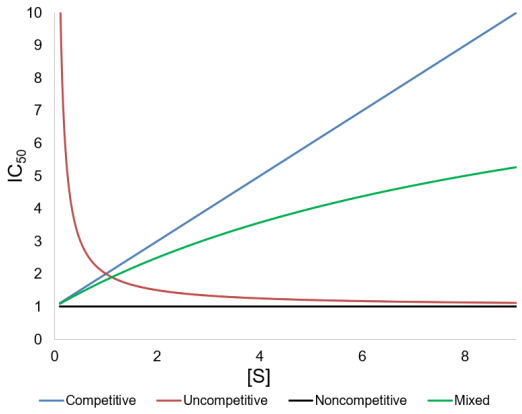
In competitive inhibition, Ki is like Kd.

3. **IC50** stands for inhibitory concentration 50%. That is, the concentration of inhibitor required to reduce the biological activity of interest to half of the uninhibited value. Because it does not directly measure a binding equilibrium, IC50 is less precise than Ki or Kd.

The relationship of IC50 and Ki:

| Mechanism | Initial velocity equation | $IC_{50}$ equation |
|---|---|---|
| Competitive | $\frac{V_{max}[S]}{K_m\left(1+\frac{[I]}{K_i}\right)+[S]}$ | $K_i\left(1+\frac{[S]}{K_m}\right)$ |
| Uncompetitive | $\frac{V_{max}[S]}{K_m+[S]\left(1+\frac{[I]}{K_i}\right)}$ | $K_i\left(1+\frac{K_m}{[S]}\right)$ |
| Non-competitive | $\frac{V_{max}[S]\Big/\left(1+\frac{[I]}{K_i}\right)}{K_m+[S]}$ | $K_i$ |
| Mixed | $\frac{V_{max}[S]}{K_m\left(1+\frac{[I]}{K_i}\right)+[S]\left(1+\frac{[I]}{\alpha K_i}\right)}$ | $K_i\frac{(K_m+[S])}{(K_m+\alpha[S])}$ |

Km is the Michaelis constant.




For a given value of Ki, the value of IC50 will still vary depending upon how tightly the substrate or labeled ligand binds the protein, and also upon its concentration. The higher the affinity of the substrate or labeled ligand and the higher its concentration, the more inhibitor will be needed to have an effect, and hence the higher IC50 will be -- even though Ki is unchanged. source

### Gibbs's energy $\Delta_G$

$\Delta G = \Delta H - T\Delta S = RTln(K_d) \Delta G = \Delta H - T\Delta S = RTln(K_d)$

and $K_d = 1/K_A = k_{off}/k_{on}$

ref

**Datasets with binding affinity**

| Name | websites | type | binding affinity type | updated |
|---|---|---|---|---|
| SKEMPI 2.0 | https://life.bsc.es/pid/skempi2 | all protein-protein | experimental | 2018 |
| BindingDB | https://www.bindingdb.org/bind/index.jsp | protein-ligand | experimental | 2022 |
| BioLip | https://zhanggroup.org/BioLiP/ | protein-ligand | experimental | 2022 |
| Binding MOAD | https://bindingmoad.org/ | protein-ligand | experimental | 2020 |
| PDBbind-CN | http://www.pdbbind.org.cn/ | all protein-ligand protein-protein | experimental | 2020 |
| Affinity Benchmark Version 2 | find on excel file | protein-protein | experimental | |
| AB-Bind | https://github.com/sarahsirin/AB-Bind-Database | | experimental | 2015 |
| AffinDB | | | | |
| PepBDB | http://huanglab.phys.hust.edu.cn/pepbdb/ | protein-small peptide | | |
| PepBank | http://pepbank.mgh.harvard.edu/ | protein-small peptide | | |
| PepBind | | protein-small peptide | | |
| PepX | | protein-small peptide | | |
| Propedia | | protein-small peptide | | |
| DBAASP | | protein-small peptide | | |
| Untitled | | | | |

**Other**

| Name | websites | updated | Property |
|---|---|---|---|
| PDBSite | https://www.rcsb.org/ | | protein binding site |
| LigASite | http://ligasite.org/ | 2012 | |
| sc-PDB | http://bioinfo-pharma.u-strasbg.fr/scPDB/ | 2017 | protein binding site |
| PDBLIG | | | molecular surfaces of proteins' functional sites |
| STRING | | | |