**Tutorial of binding free energy based on the value of Kd, Ki, pKd or pKi by MolAICal**

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**1. Introduction**

Sometimes, it needs to calculate the binding free energy according to the Ki, Kd, pKd or pKi values from PDBBind database1-3. Before calculating binding free energy, the International System of Units (SI) is introduced (see Table 4.4.5.1). Most laboratory and literature use mol/dm3, which is the same as mol/L (also named “M”). For example:

mol/m3 = 10−3 mol/dm3 = 10−3 mol/L = 10−3 M = 1 mmol/L = 1 mM.

**Table 4.4.5.1** Molar concentration units

|  |  |  |  |
| --- | --- | --- | --- |
| **Name** | **Abbreviation** | **Concentration** | **Concentration (SI unit)** |
| millimolar | mM | 10−3 mol/L | 100 mol/m3 |
| micromolar | μM | 10−6 mol/L | 10−3 mol/m3 |
| nanomolar | nM | 10−9 mol/L | 10−6 mol/m3 |
| picomolar | pM | 10−12 mol/L | 10−9 mol/m3 |
| femtomolar | fM | 10−15 mol/L | 10−12 mol/m3 |
| attomolar | aM | 10−18 mol/L | 10−15 mol/m3 |
| zeptomolar | zM | 10−21 mol/L | 10−18 mol/m3 |
| yoctomolar | yM | 10−24 mol/L  (6 particles per 10 L) | 10−21 mol/m3 |

The "millimolar" and "micromolar" refer to mM and μM (10−3 mol/L and 10−6 mol/L), respectively. About the detail relative information of molar concentration units, please see the website: <https://en.wikipedia.org/wiki/Molar_concentration>

In this tutorial, the MolAICal provides an easy way to calculate binding free energy if the value of Ki, Kd, pKd or pKi is given.

**2. Materials**

**2.1. Software requirement**

1) MolAICal: <https://molaical.github.io>

**2.2. Example files**

1) All the necessary tutorial files are downloaded from:

<https://github.com/MolAICal/tutorials/tree/master/010-pkdEnergy>

**3. Procedure**

Go to the directory “010-pkdEnergy”:

#> cd tutorial\010-pkdEnergy

Open file “INDEX\_refined\_data.2018” which is extracted from PDBBind database, the 4th column represents pKd or pKi, while the 5th column represents Ki and Kd.

1) Calculate binding free energy from pkd (pkd = -logKd or pki = -logKi), use default temperature:

298.15 K

molaical.exe -tool pkdpki -i 11.92 -t pkx

2) Calculate binding free energy from pkd (pkd = -logKd or pki = -logKi), use appointed temperature.

molaical.exe -tool pkdpki -i 11.92 -t pkx -k 300

3) Calculate from Kd or Ki with concentration. Default is M (mol/L)

molaical.exe -tool pkdpki -i 1.2 -t molar

4) Calculate from Kd or Ki with pm unit

molaical.exe -tool pkdpki -i 1.2 -t molar -u pm

For more detail about binding free energy, please see the manual of MolAICal.

**References**

1 Wang, R., Fang, X., Lu, Y. & Wang, S. The PDBbind database: collection of binding affinities for protein-ligand complexes with known three-dimensional structures. *J Med Chem* **47**, 2977-2980 (2004).

2 Kim, R. & Skolnick, J. Assessment of programs for ligand binding affinity prediction. *J Comput Chem* **29**, 1316-1331 (2008).

3 Karney, C. F., Ferrara, J. E. & Brunner, S. Method for computing protein binding affinity. *J Comput Chem* **26**, 243-251 (2005).