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 (e.g. training Vinardo score) 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 1). Most laboratory and literature use mol/dm³, which is the same as mol/L (also named "M"). For example:

 $mol/m^3 = 10^{-3} \ mol/dm^3 = 10^{-3} \ mol/L = 10^{-3} \ M = 1 \ mmol/L = 1 \ mM$.

Table 1. Molar concentration units

Name	Abbreviation	Concentration	Concentration (SI unit)
millimolar	mM	10 ⁻³ mol/L	10^0mol/m^3
micromolar	μΜ	10 ⁻⁶ mol/L	10^{-3} mol/m^3
nanomolar	nM	10 ⁻⁹ mol/L	10^{-6} mol/m^3
picomolar	pM	10 ⁻¹² mol/L	10^{-9} mol/m^3
femtomolar	fM	10 ⁻¹⁵ mol/L	10^{-12} mol/m^3
attomolar	aM	10 ⁻¹⁸ mol/L	10 ⁻¹⁵ mol/m ³
zeptomolar	zM	10 ⁻²¹ mol/L	10 ⁻¹⁸ mol/m ³
yoctomolar	yM	10 ⁻²⁴ mol/L (6 particles per 10 L)	10 ⁻²¹ mol/m ³

The "millimolar" and "micromolar" refer to mM and μ M (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 (https://doi.org/10.1093/bib/bbaa161) 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).