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 database[1-3]. Before calculating binding free energy, the International System of Units (SI) is introduced (see Table 1). Most laboratory and literature use mol/dm^3, 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^{0} mol/m^3
micromolar	μM	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 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 (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).