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 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).