Electrostatics surface potential and pKa prediction

Lars Skjærven
2010
Coulomb’s law:
The electric force acting on a point charge $q_2$ as the result of the presence of another charge $q_1$ is given by Coulomb’s law:

$$ \vec{F} = \frac{q_1 q_2}{4\pi\varepsilon_0 r^2} \hat{u} $$

$q_2$ “radiates”
Charged and polar amino acids
Charged and polar amino acids

Protein
Charged and polar amino acids

- Mix between charged amino acids
- Affect each other
- Total picture
Poisson-Boltzmann Equation

\[ \vec{\nabla} \cdot \left[ \epsilon(\vec{r}) \vec{\nabla} \Psi(\vec{r}) \right] = -4\pi \rho^f(\vec{r}) - 4\pi \sum_i c_i^\infty \, z_i q \lambda(\vec{r}) \cdot \exp \left[ \frac{-z_i q \Psi(\vec{r})}{k_B T} \right] \]

- Solve it!
- Joint electrostatic potential
Protein electrostatics

- Interaction between electric charges
- Some very important molecules are charged
- Electrostatic interaction are long range
- accelerate molecule association
Molecular recognition

- Highly relevant for biomolecules
  - Protein-protein
  - Protein-ligand
  - Folding and stability

- Evaluation of the electrostatic properties
micotubule
Ligand binding

A) WO2Fab-Aβ 2-8

B) PFA1Fab-Aβ 2-8

*
Next tutorial

• Learn how to calculate electrostatics potential
  • APBS
• Visualize it
  • PyMOL
pKa prediction

- measure of the proton affinity of a group
- lower the pKa, the more weakly the proton is held
**pKα prediction**

charged side chains at pH 7, pKα in water:
- Asp 4.5
- Lys 11.1
- His 6.8
- Glu 4.5
- Arg 12.5
- Cys 8.6

The protein environment is different from water, the pKα of certain aa might shift

**Prediction tool:** propKa: [http://propka.ki.ku.dk](http://propka.ki.ku.dk)
propKa

Please enter either:

- a PDB ID: [blank]
- upload a PDB file: [file selection]
- PDB file web address: [URL]

- Specify PDB chain IDs (separated by a comma ","),

- Include ligands: Enabling this will include ligands. Disabling will use PROPKA 1.0.

Or upload a "new_PDB" PROPKA 2.0 input file: [file selection]

[Submit]  [Clear Form]
Look for aa which pKa has shifted:
- from under 7 til above 7;
- and the other way around.

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<thead>
<tr>
<th>RESIDUE</th>
<th>pKa</th>
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charged side chains at pH 7, pKa in water:
- Asp 4.5
- Lys 11.1
- His 6.8
- Glu 4.5
- Arg 12.5
- Cys 8.6
Add charges and hydrogens

- PDB2PQR
- Run propKa
- Assign protonation
- Add hydrogens (at different pH)
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**REMARK**: 1 PQR file generated by PDB2PQR (Version 1.3.0)
**REMARK**: 1 FORCEFIELD USED: parse
**REMARK**: 1 NAMING SCHEME USED: parse
**REMARK**: 1 PKA calculated by propka and assigned using pH 7.00
**REMARK**: 6 Total charge on this protein: 3.0000 e
www.bioinfo.no
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