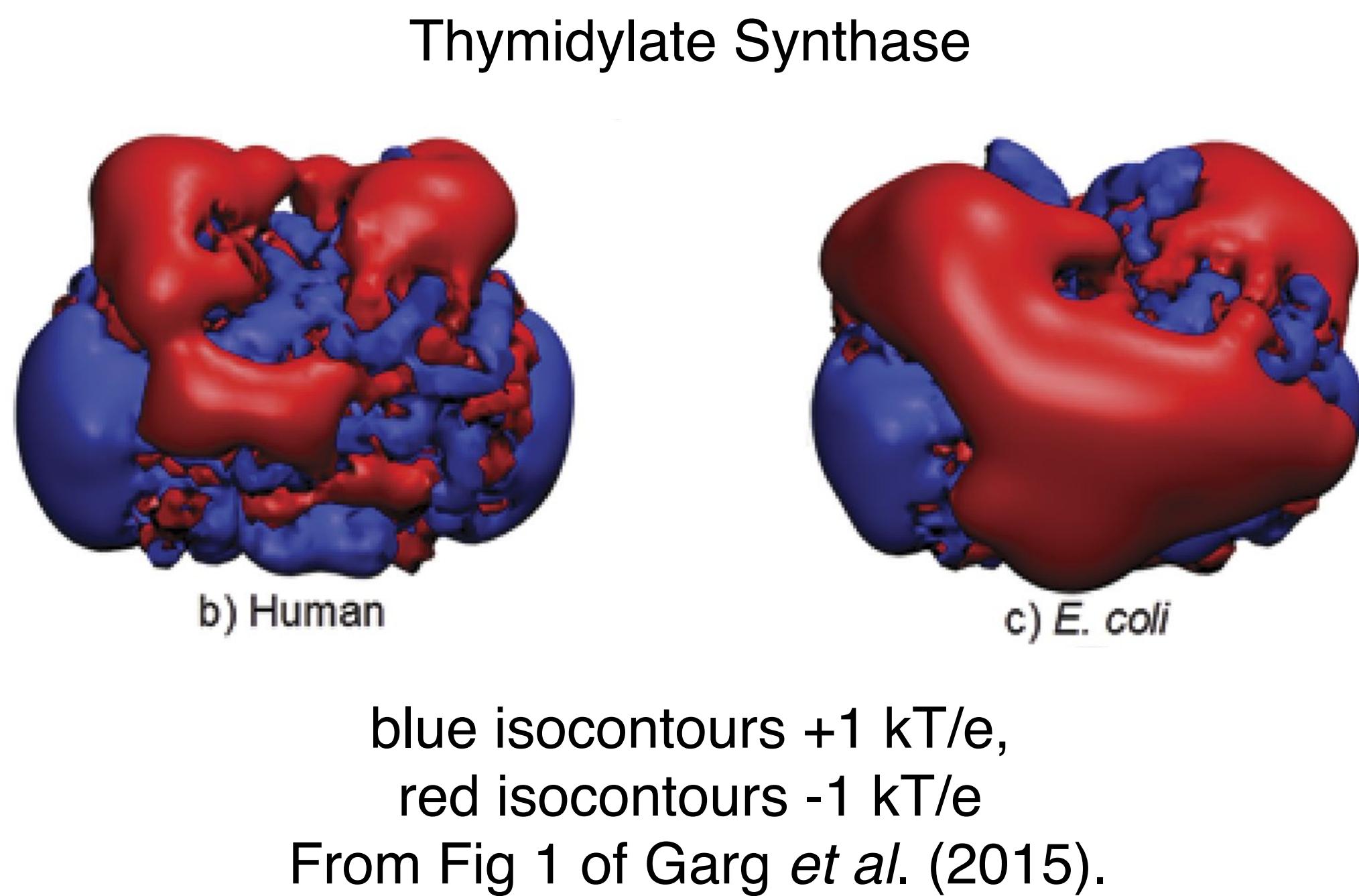


Biomolecular Electrostatics

- This mini-lecture and tour will be about electrostatics calculations
- At the end of this mini-lecture and tour, you should be able to
 - explain, in a general sense, the
 - importance of electrostatics in biological macromolecules
 - origin of the Poisson-Boltzmann equation
 - submit an electrostatics calculation to the APBS server

Roles of Biomolecular Electrostatics

- Electrostatics important in (at least)
 - protonation, influencing side chain pKa
 - binding for
 - steering, facilitating approach of species
 - complexation, as complementarity means lower potential energy
 - enzyme catalysis, as electric potential stabilizes transition state
 - solvation
 - Electrostatic potential usually conserved near functional sites

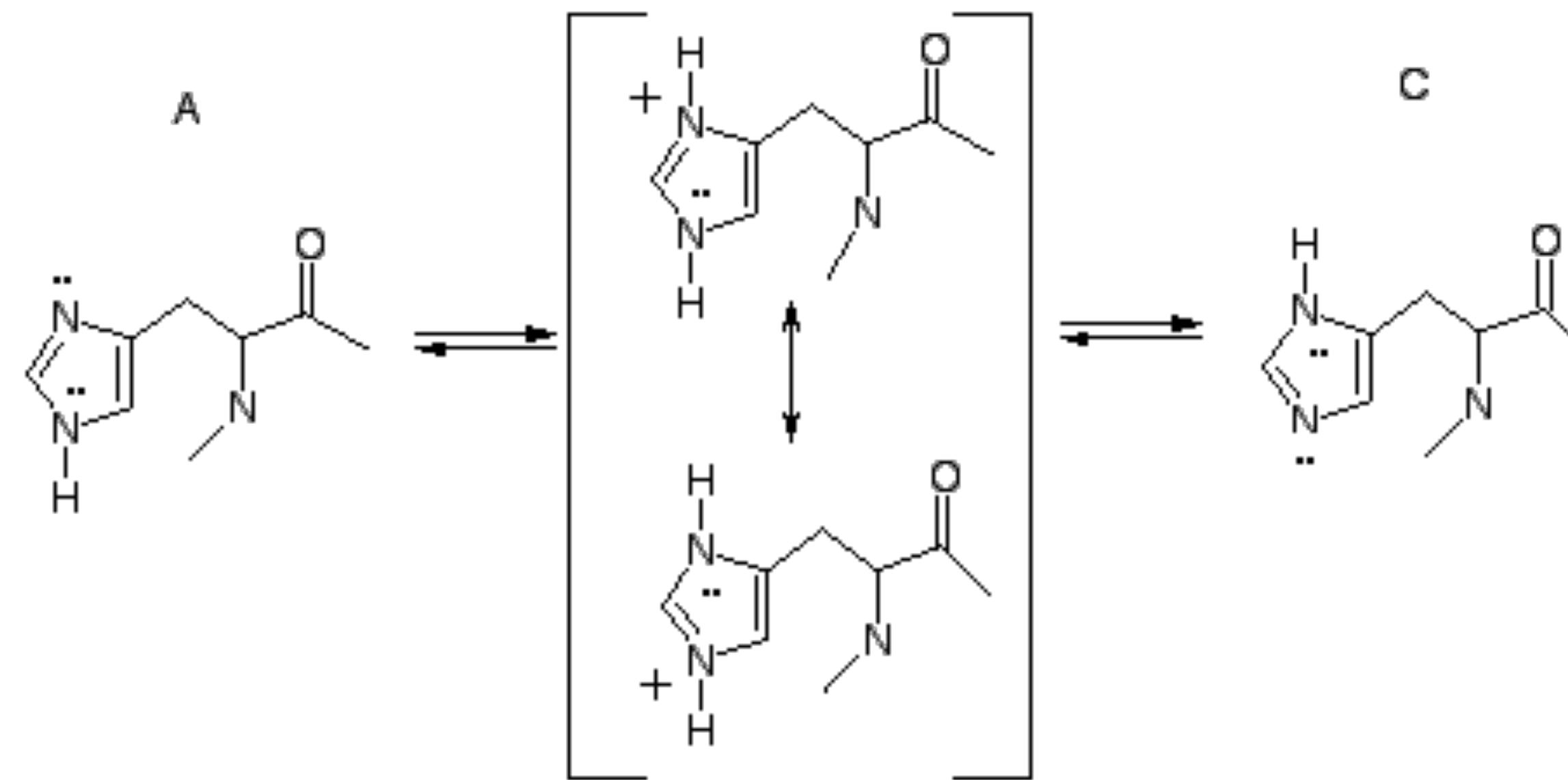


Protein Protonation

- Which structure determination technique(s) identify the position of hydrogen atoms?
 - A. X-ray crystallography
 - B. X-ray crystallography, at very high resolution
 - C. Nuclear magnetic resonance
 - D. Cryo-electron microscopy
 - E. All of the above
 - F. None of the above

Histidine

B



<https://spdbv.unil.ch/TheMolecularLevel/Goodies/Get2NoHistidine.html>

- As the side chain has a $\text{pK}_a \sim 7.0$, imidazolium ion (B) and imidazole (A or C) are all present in physiological conditions
- Which state(s) are stabilized by a negative electrostatic potential?
- What can stabilize a specific form of imidazole?

Electrostatics is important in solvation

- It is an *implicit solvent* model that does not account for specific water positions
- Solvent is assumed to modify the dielectric constant

- Coulomb's law is $F = \frac{1}{4\pi\epsilon} \frac{Q_1 Q_2}{r^2}$.

- The permittivity ϵ is related to the permittivity of free space ϵ_0 by the dielectric constant κ , $\epsilon = \kappa\epsilon_0$.
 - ~80 for water
 - ~1 for the protein interior
- The electrostatic component of the solvation energy is modeled as the difference between the energy in water and in vacuum

Modeling Electrostatics

- In biological macromolecules, the electrostatic potential is usually calculated based on the Poisson-Boltzmann equation
 - The Poisson equation $\nabla \cdot \epsilon(r) \nabla \phi(r) + 4\pi\rho(r) = 0$ describes the potential $\phi(r)$ due to a given charge density $\rho(r)$ and dielectric $\epsilon(r)$. Atoms in the biomolecule are assumed to have a fixed charge.
 - The Poisson-Boltzmann equation assumes that (infinitely small) ions surround a biomolecule in accordance with the Boltzmann distribution
 - The PB equation is a partial differential equation that is solved numerically
 - The equation is often linearized to be more numerically stable

Review Questions

- Discuss some of the ways in which electrostatics is important for the function of biological macromolecules
- An equation often used to model the electrostatics of biological macromolecules is the Poisson-Boltzmann equation. Why does the equation have this name?
- How can the Poisson-Boltzmann equation be used to calculate the electrostatic component of the solvation free energy?

The PDB2PQR-APBS web server

<https://server.poissonboltzmann.org/pdb2pqr>

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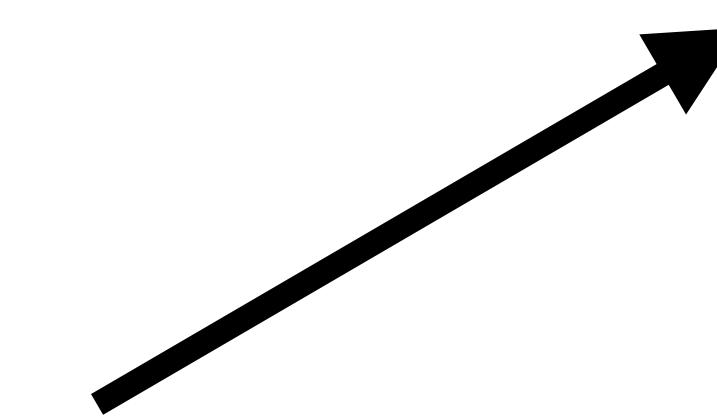
Home

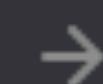
APBS

Welcome to the new home for running the APBS-PDB2PQR software suite

Please [register](#) to ensure continued support for this software.

Getting Started:

[PDB2PQR](#)[APBS](#)



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3 APBS Configuration

PDB Selection

* PDB Source

PDB ID

Upload a PDB file

* Please upload a PDB file

Select File

bestmodel_aligned.pdb

For continued support of this server, please register your use of this software:

Register Here

pKa Options

pH: 7.0

 No pKa calculation Use PROPKA to assign protonation states at provided pH



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pH: 7.0

- No pKa calculation
- Use PROPKA to assign protonation states at provided pH

Forcefield Options

Please choose a forcefield to use

AMBER

CHARMM

PEOEPB

PARSE

SWANSON

TYL06

User-defined Forcefield

CLI

ning scheme to use

--ff=AMBER

AMBER

CHARMM

PARSE

PEOEPB

SWANSON

TYL06

Additional Options

- Ensure that new atoms are not rebuilt too close to existing atoms
- Optimize the hydrogen bonding network
- Assign charges to the ligand specified in a MOL2 file
- Create an APBS input file
- Add/keep chain IDs in the PQR file
- Insert whitespaces between atom name and residue name, between x and y, and between y and z
- Make the protein's N-terminus neutral (requires PARSE forcefield)
- Make the protein's C-terminus neutral (requires PARSE forcefield)
- Remove the waters from the output file

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Data Retention

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To return to your results after leaving, [save this page.](#)

Job ID:

k5f10lg2t7_20220306

Job Type:

PDB2PQR

Time Elapsed:

00:00:13

Next:

[Use results with APBS >](#)

Submitted

Pending Job Start

Running

Complete

PDB2PQR Input Files

bestmodel_aligned.pdb

375.95 KB | [Download](#)**PDB2PQR Output Files**

pdb2pqr-metrics.json

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k5f10lg2t7.pqr

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PDB2PQR Configuration

PDB2PQR Job Status

APBS Configuration

4 APBS Job Status



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Job ID:

k5f10lg2t7_20220306

Job Type:

APBS

Time Elapsed:

00:00:33

Next:

View in 3Dmol >

Submitted

Pending Job Start

Running

Complete

APBS Input Files

k5f10lg2t7.pqr

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336 Bytes | [Download](#)

APBS Output Files

io.mc

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apbs.stderr.txt

0 Bytes | [Download](#)

apbs.stdout.txt

6.07 KB | [Download](#)

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References

- Garg, D.; Skouloubris, S.; Briffotaux, J.; Myllykallio, H.; Wade, R. C. Conservation and Role of Electrostatics in Thymidylate Synthase. *Sci Rep* 2015, 5 (1), 17356. <https://doi.org/10.1038/srep17356>, adapted under the CC BY 4.0 license.