**Electrostatics Calculations – A Quick overview**

1. General
   1. Gunner - pKa
      1. Klein
         1. Protein dielectric through pKa
      2. Nielson, Garcia-Moreno
         1. Blind pKa prediction
         2. Constant pH “generally achieved a closer match” than continuum methods.
         3. Empirical methods had the best result *after* tuning and are the least transferable result
   2. Warshel & Levitt
      1. PDLD
   3. Ren/Ponder
      1. Polarizable force fields
   4. Boxer/Fafarman
      1. Small molecule simulations
   5. Cerutti/Baker/McCammon
      1. PB – Reaction Field Method
      2. Bridging explicit solvent models and implicit solvent models
   6. Bredenberg, J. H.; Russo, C.; Fenley, M. O. Salt-Mediated Electrostatics in the Associsation of TATA Binding Proteins to DNA: A Combined Molecular Mechanics/Poisson-Boltzman Study. Biophys. J. 2008, 94, 4634−4645.
   7. Honig
   8. PB
   9. GB
2. Water
   1. Layfield
      1. Importance of nearest-water to polarization
   2. Fennel
      1. Implicit model distinguishing between bulk and hydration water
   3. Cho & Corcelli
      1. Solvatochromatic models
   4. Baker/McCammon
      1. First and second solvation shell matter
      2. Same paper as before

**Electrostatics Calculations – The Webb Group**

1. Sampling!
   1. “Accounting for the heterogeneous response of proteins is generally considered the chief difficulty in modeling pKa values in proteins”[1](#_ENREF_1) – I would argue that this statement can be generalized to being the chief difficulty in modeling *all* experimentally-measurable electrostatic properties in proteins.
   2. Multi-dimensional umbrella sampling
   3. REST?
2. APBS – Ensign, Ritchie, Walker
   1. Grid spacing
   2. Grid size
   3. “Reaction field method”
   4. Box position
3. AMOEBA
   1. The “protein dielectric” problem
   2. Need for clustering

**Electrostatics Calculations – Accounting for Water**

1. APBS
   1. H-bonding water
   2. 5 AA solvent sphere
   3. Sampling quality and restatement of the advantage of implicit solvent?
2. Amber03 explicit solvent
   1. Reaction Field Electrostatics
   2. Contributions to Electrostatic Fields
3. AMOEBA explicit solvent

**Electrostatics Calculations – Future Directions**

1. Nielsen, J. E.; Gunner, M. R.; Garcia-Moreno, E. B., The pK(a) Cooperative: A collaborative effort to advance structure-based calculations of pK(a) values and electrostatic effects in proteins. *Proteins-Structure Function and Bioinformatics* **2011,** *79* (12), 3249-3259.