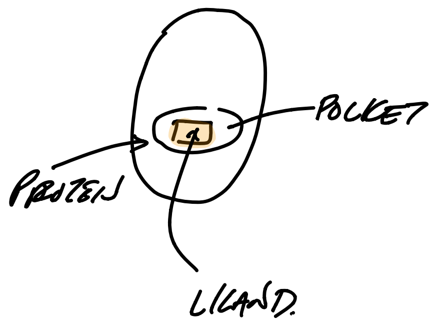
ELECTROSTATICS I: 10/26/19

IMAGINE WE HAVE A HYDROPHOBIC LIGAND IN A HYDROPHOBIC POCKET:



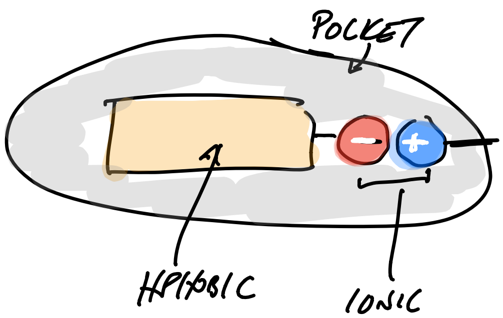
HOW DO WE CALCULATE ΔG_{BIND}?

1. $\Delta G(\Delta ASA)$: ASA OF POCKET AND LIGAND <u>UNBOUND</u> VS ASA OF COMPLEX.

2. FULL MD SIMULATION WITH ALL ATOMS.

GOING TO USE ASA FOR THIS TALK.

NOW ADD IONIC INTERACTION:



HOW DO WE CALCULATE ΔG_{BIND}?

$$\Delta G_{BIND} = \Delta G_{ASA} + \Delta G_{COULOMB}.$$

$$U_{COULOMB} = \frac{q_i \cdot q_j}{r_{ij} \cdot \varepsilon} \cdot \alpha$$

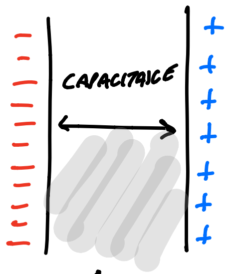
$\alpha = 1389$ Å·kJ/mol
r = DIST IN Å
q_x = CHARGE

DIELECTRIC CONSTANT (ε) MEASURES HOW GOOD ENVIRONMENT IS AT ATTENUATING ELECTROSTATIC INTERACTION.

ENERGY TO TAKE CHARGE FROM INFINITE DISTANCE TO DISTANCE "r". THIS IS BASICALLY A BINDING REACTION, SO

$$\Delta G_{COUL} = U_{COUL}$$

WHAT IS A DIELECTRIC CONSTANT, IF MEASURED EXPERIMENTALLY?



STICK IN MATERIAL

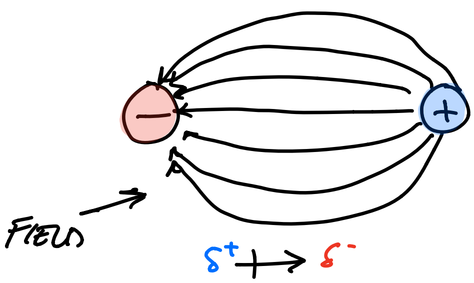
ATTENUATION OF CAPACITANCE → DIELECTRIC CONSTANT RELATIVE TO VACUUM.

$\varepsilon_{vacuum} = 1$

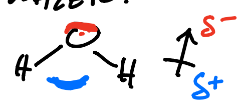
$\varepsilon_{oil} = 2$

$\varepsilon_{H_2O} = 78.5$

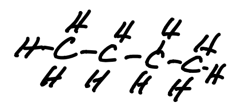
WHAT IS A DIELECTRIC CONSTANT MOLECULARLY?



WATER:



OIL:



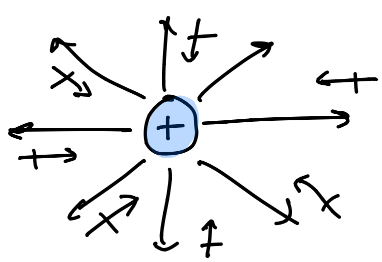
WATER ALIGNS WITH FIELD, ATTENUATING INTERACTION.

$\varepsilon_{H_2O} = 78.5$

IN OIL, <u>ELECTRONS</u> ALIGN WITH FIELD, MILDLY ATTENUATING INTERACTION.

$\varepsilon_{oil} = 2$

BUT WHAT ABOUT INDIVIDUAL IONS? DON'T THEY HAVE FIELDS TOO?



- IONS INTERACT WITH THEIR ENVIRONMENT.
- "BORN" ENERGY MEASURES ENERGY TO CARVE OUT ION IN A GIVEN ENVIRONMENT.

$$G_{Born} = \frac{q^2}{r_{ion}\cdot\varepsilon}\cdot\alpha$$

← ENERGY TO BRING BITS OF CHARGE ONTO SURFACE OF SPHERE OF RADIUS r_{ion}.

$$\Delta G_{BORN} = \frac{q^2}{r_{ion}} \alpha \left(\frac{1}{\varepsilon_{PROT}} - \frac{1}{\varepsilon_{H2O}} \right)$$

ENERGY TO BRING ION FROM WATER INTO PROTEIN WITH DIELECTRIC OF ε_{PROT}.

WHAT IS "RIGHT" VALUE OF ε_P?

- DEPENDS ON EXACT ENVIRONMENT.
- $\varepsilon_{PROT} \approx 4$ DEEP IN INTERIOR
- $\varepsilon_{PROT} \approx 15$ ON PROTEIN SURFACE.
- HARD PROBLEM: HOW TO ATTENUATE ELECTROSTATICS.

$$\Delta G_{BIND} = \Delta G_{ASA} + \Delta G_{COUL} + \Delta G_{BORN} + \cdots$$