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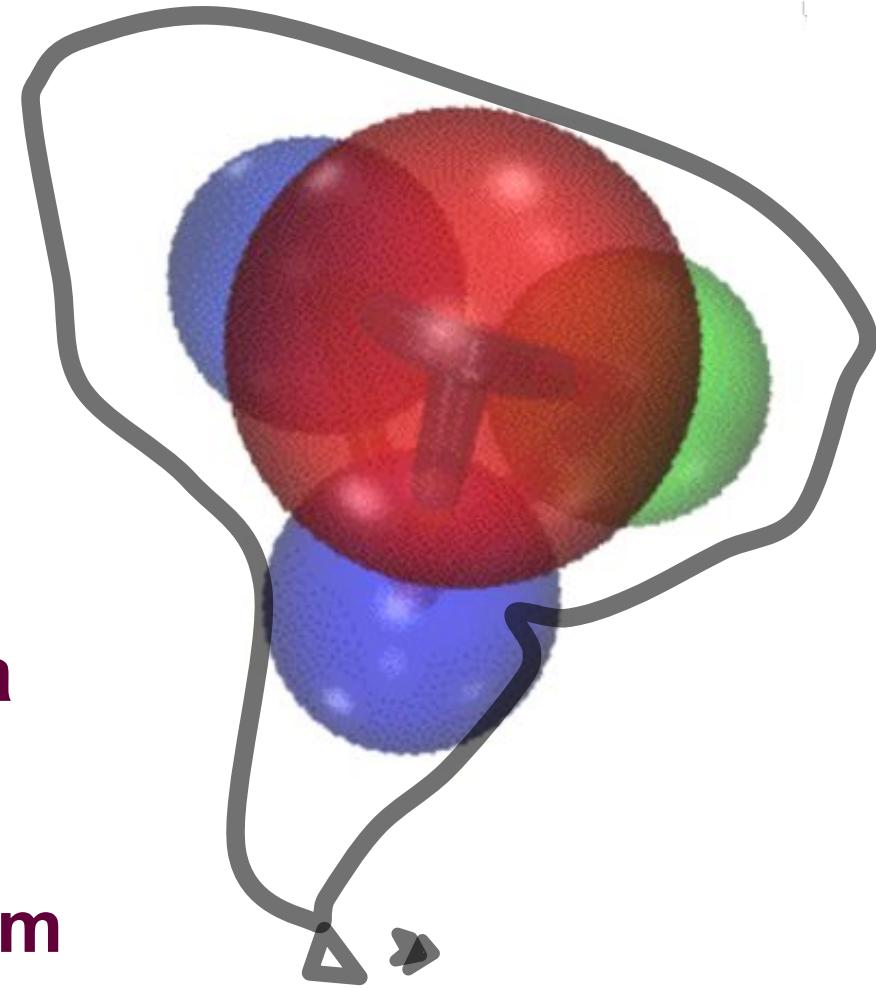
Potenciales simplificados para simulaciones biomoleculares

SIRAHFF

(Southamerican Initiative for
Rapid and Accurate Force Field)

Primer ejemplo de
desarrollo en Sud America

www.sirahff.com





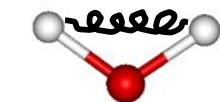
Force Field for Molecular simulations

$$\begin{aligned}
 U = & \sum_{bonds} \frac{1}{2} k_r (r - r_0)^2 \\
 + & \sum_{angles} \frac{1}{2} k_\theta (\theta - \theta_0)^2 \\
 + & \sum_{torsions} \frac{V_n}{2} [1 + \cos(n\phi - \delta)] \\
 + & \sum_{elec} \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} \\
 + & \sum_{LJ} \left[\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^6} \right]
 \end{aligned}$$

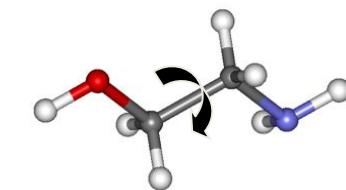
Bond stretching



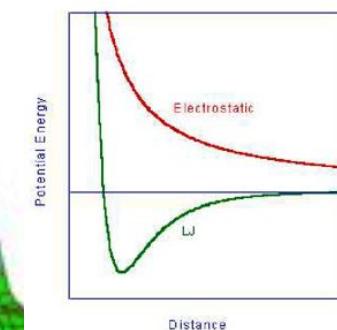
Angle bending



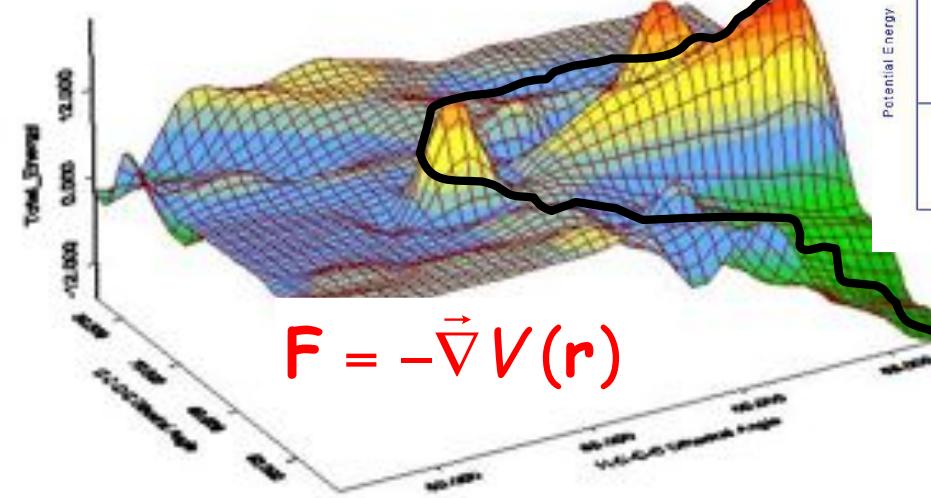
Dihedral angle torsion



Electrostatic interaction



Van der Waals interaction



Computational Scaling $\sim N \log (N)$



fs

Electronic excitations

100 fs - ps

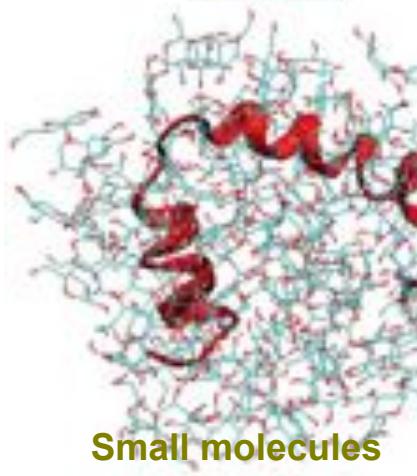
Vibrations

μS

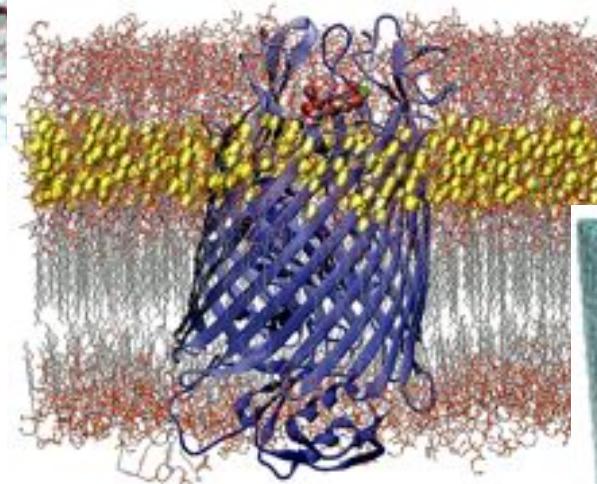
Rotations

ms

Conformational Transitions

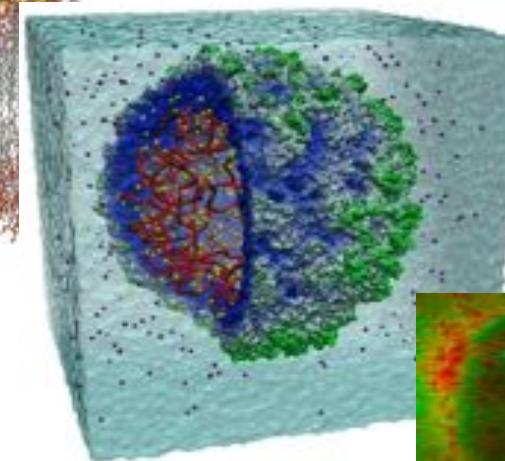


Small molecules
~ 1.000 atoms

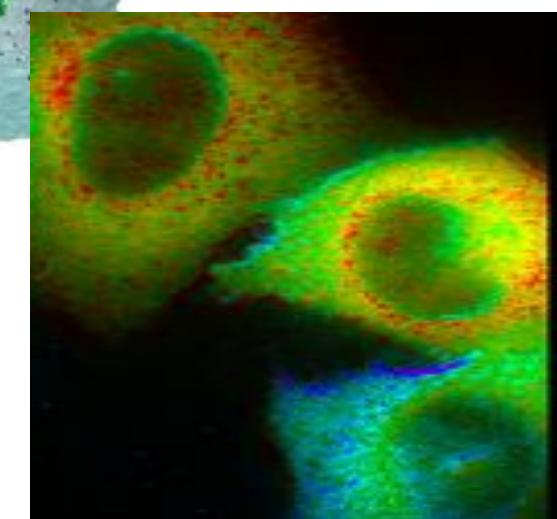


Macromolecular complexes
~ 50.000 to ~ 1.000.000 atoms

Virus
several millions of atoms



Bacteria/cells?
1 e+10 atoms



ps

e-transfer reactions **Enzymatic reactions**

ns

Peptide folding

μS - s

Protein folding

μS

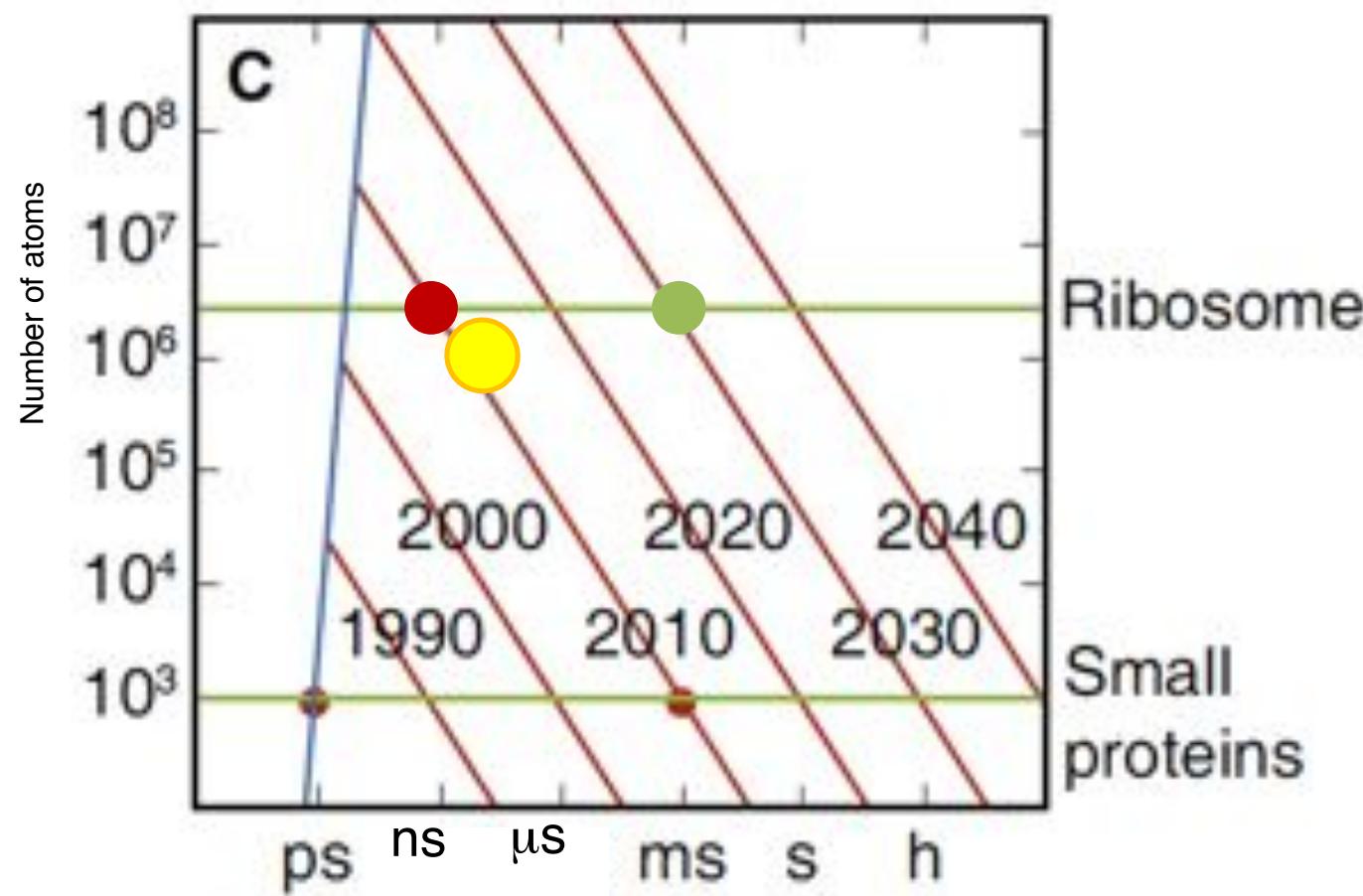
DNA melting

s - years

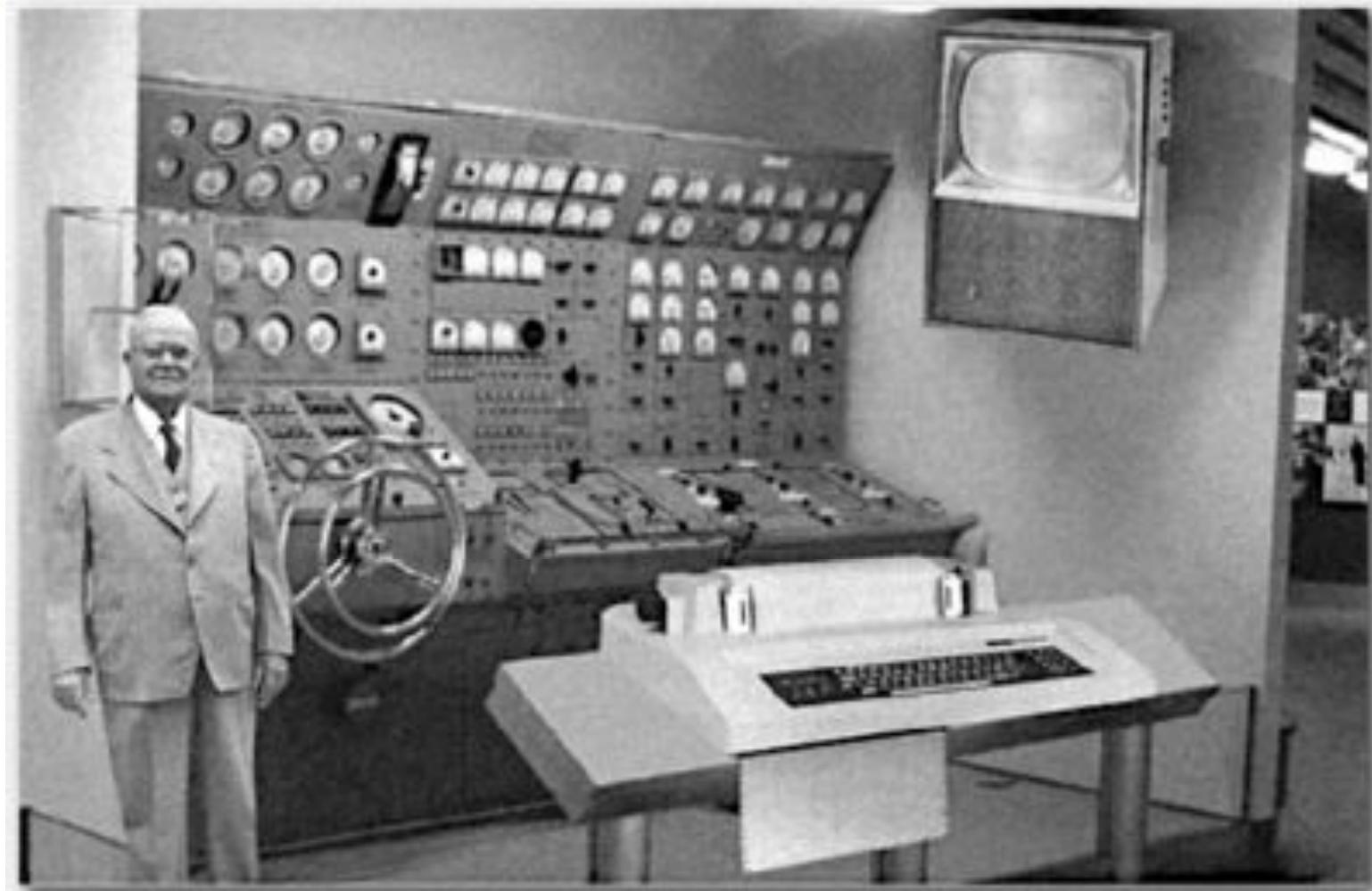
Life



Current Limitations of Molecular Simulations



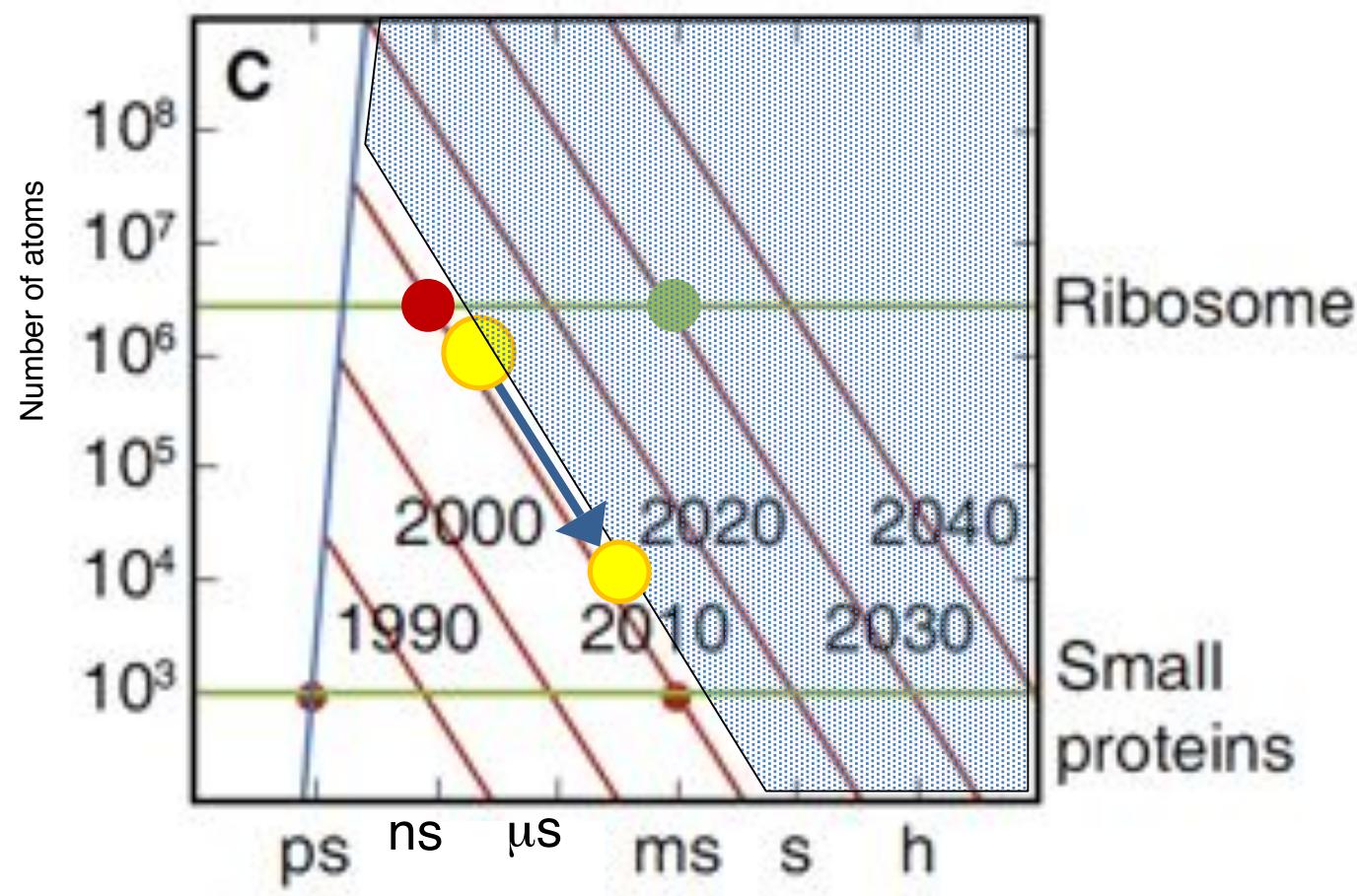
Curr. Biol. (2010) 21:R68.

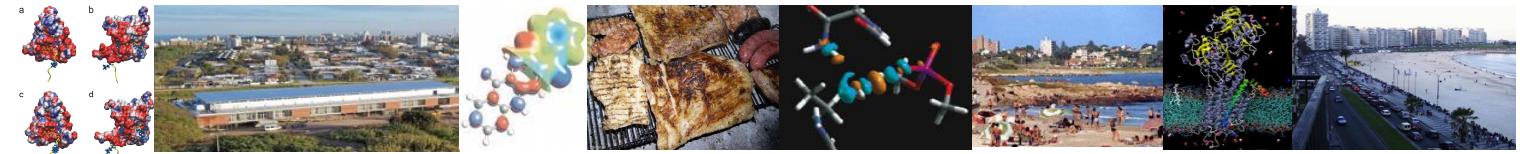


"Scientists from the RAND corporation have created this model
of how a home computer could look in the year 2001 ..."
(© Popular Mechanics 1954)



Current Limitations of Molecular Simulations



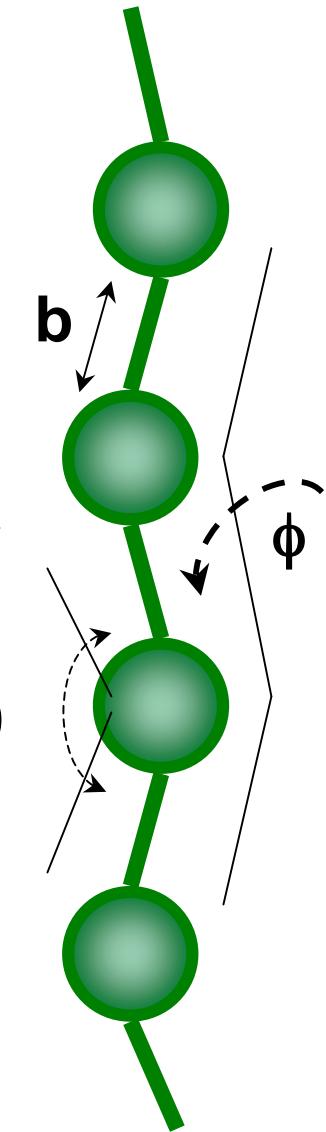
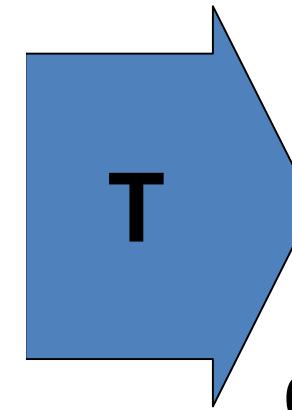
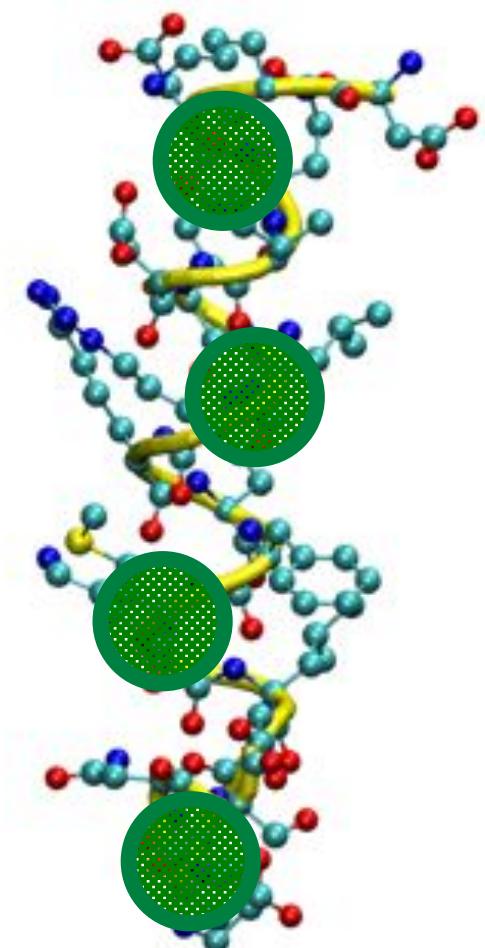


AA → CG Mapping:

$r_{(i)}$ (high detail)

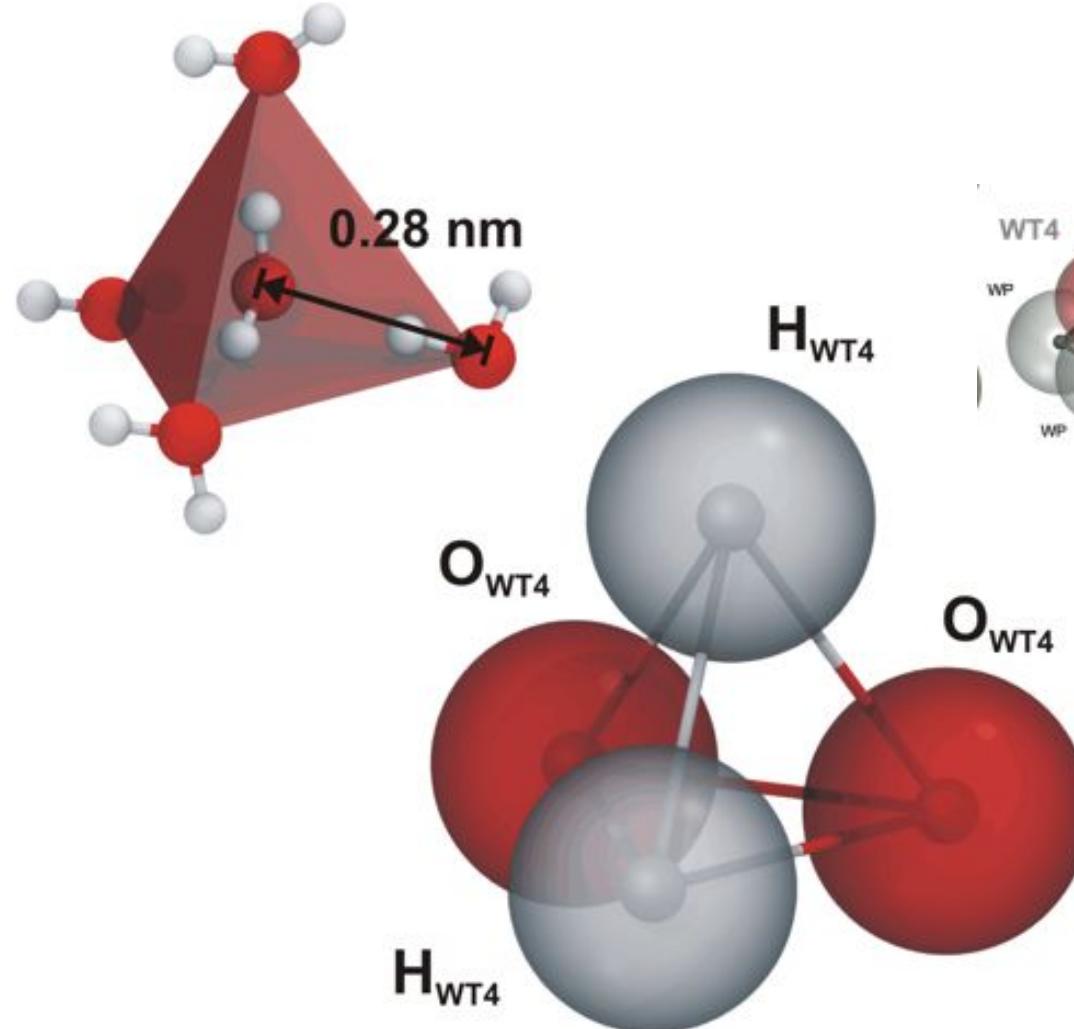
$R_{(j)}$ (low detail)

$$R_{(j)} = T \cdot r_{(i)}$$



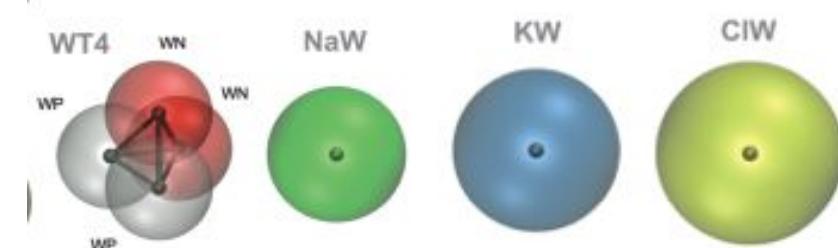


Water: ~85 % of the problem



Another CG Model for Aqueous Solution: Wat Four?
Darre et al JCTC 2010

Hydrated ions Na^+ , K^+ , Cl^-
(Ion + 1st hydration shell)

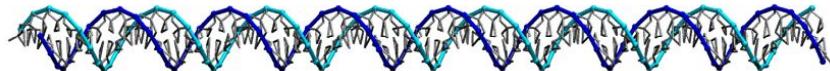


- 11 “real” waters = 1 WT4
- Permittivity (110)
(not dielectric constant!)
- Debye length ✓
- Bjerrum length ✓
- Osmotic Pressure ✓

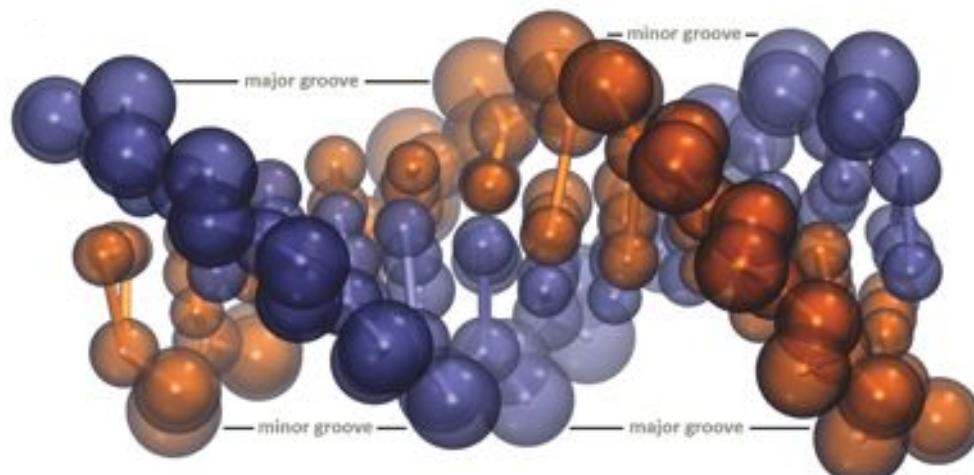
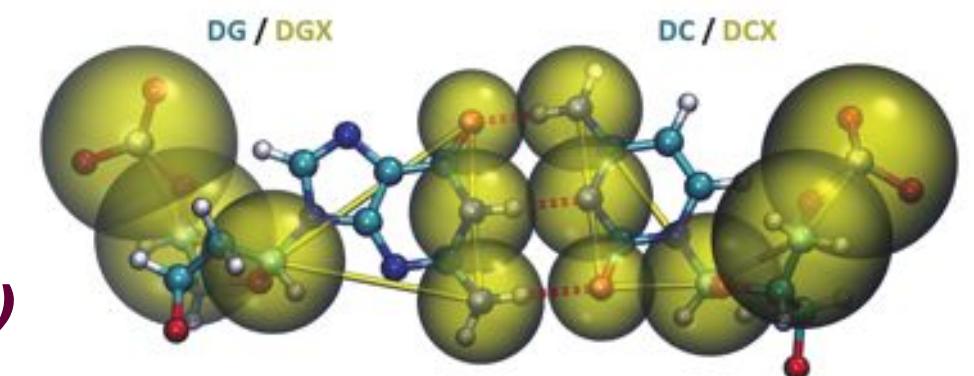
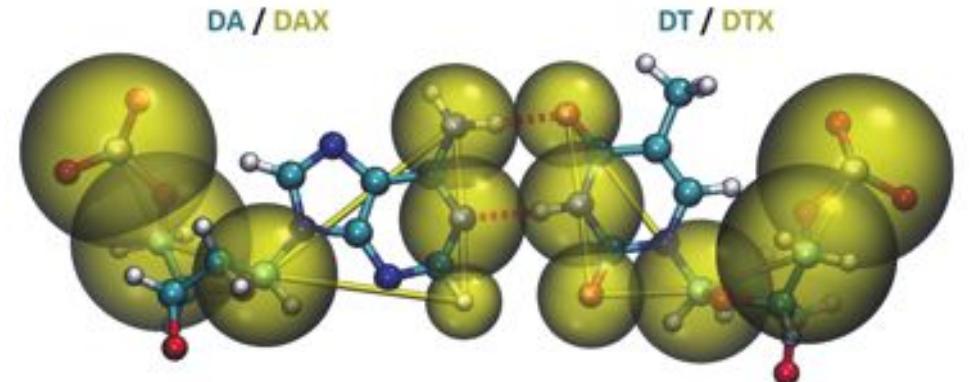


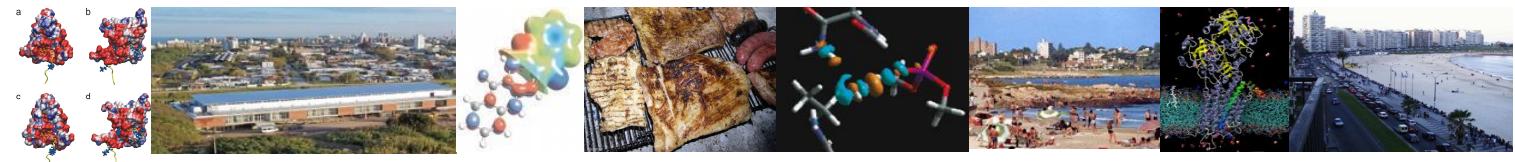
CG Model for DNA

- ***6 Beads per Nucleotide***
- ***Implicit Solvation via Generalized Born Model***
- ***OR Explicit solvation using our CG model for water (WT4)***
- ***Fully Backmappable***

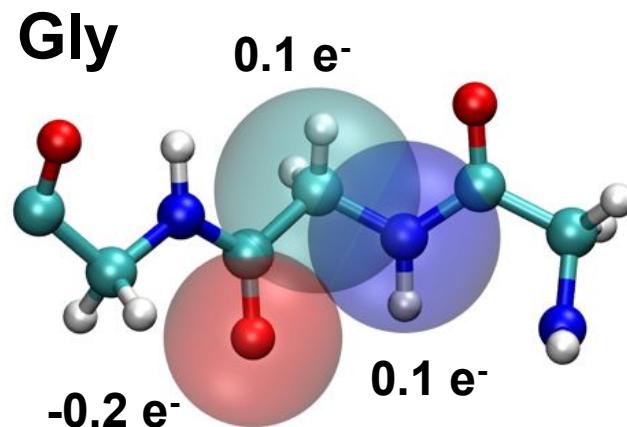


• Dans et al. JCTC, 2010
• Zeida et al. PRE, 2012





SIRAH Force Field for Proteins



Nearly atomistic backbone (vdW)

- Right packing (helices, β strands, etc)
- Easy to backmap
- Compatible with atomistics (not yet ready!)

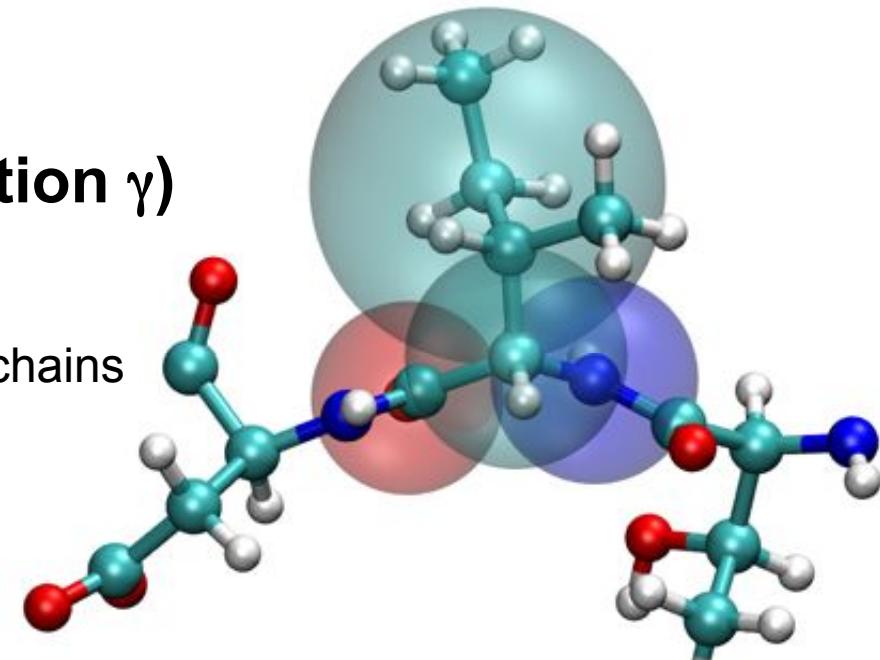
Partial charges on each bead

- HBond-like interactions
- Helix macrodipole

Leu (neutral CG bead at position γ)

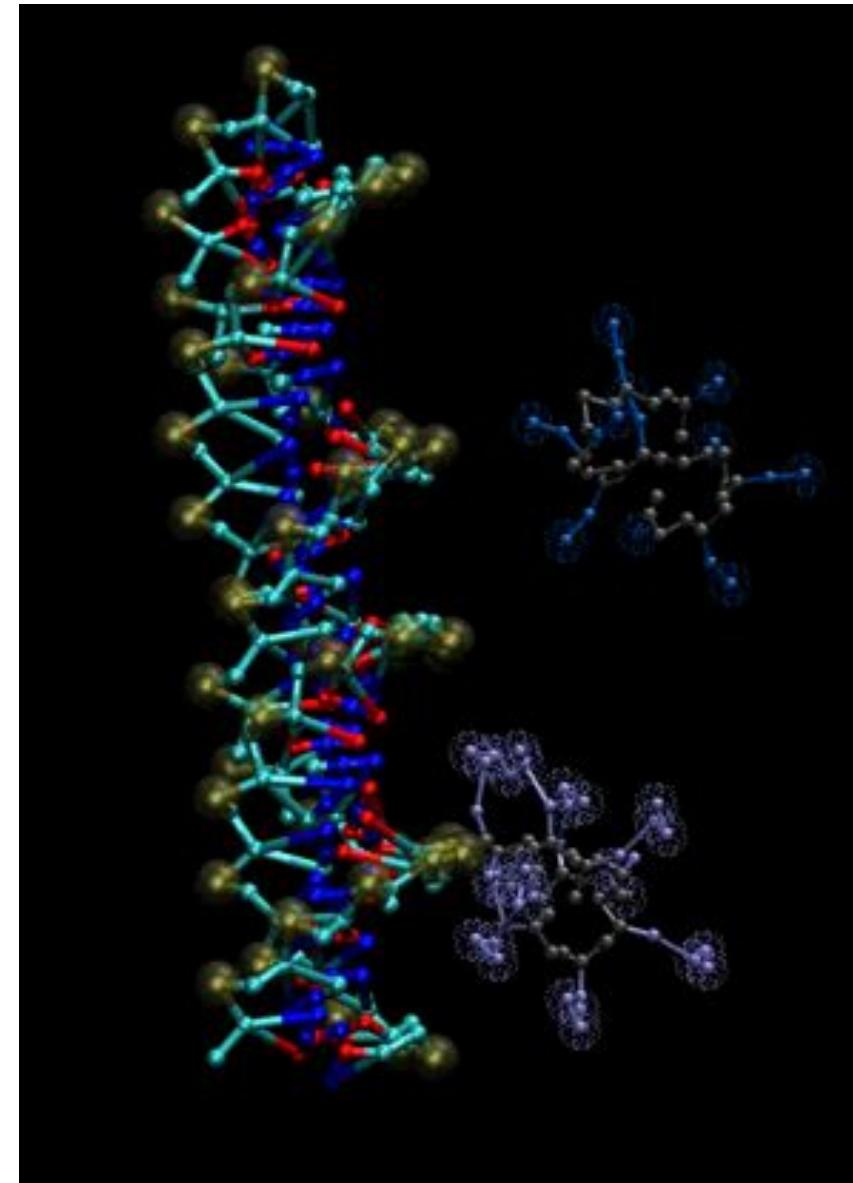
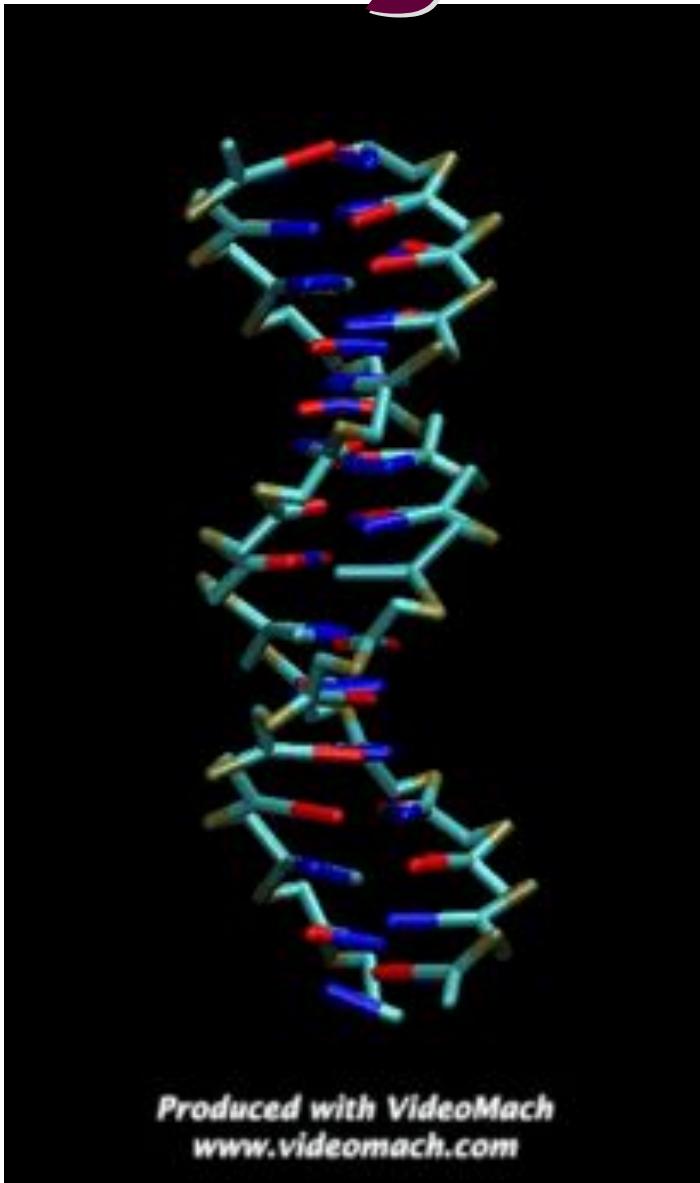
Higher CG level at side chains

- vdW radii \sim gyration radius of side chains
- Hydrophobic / hydrophilic
- HBond-like interactions
- Protonation states





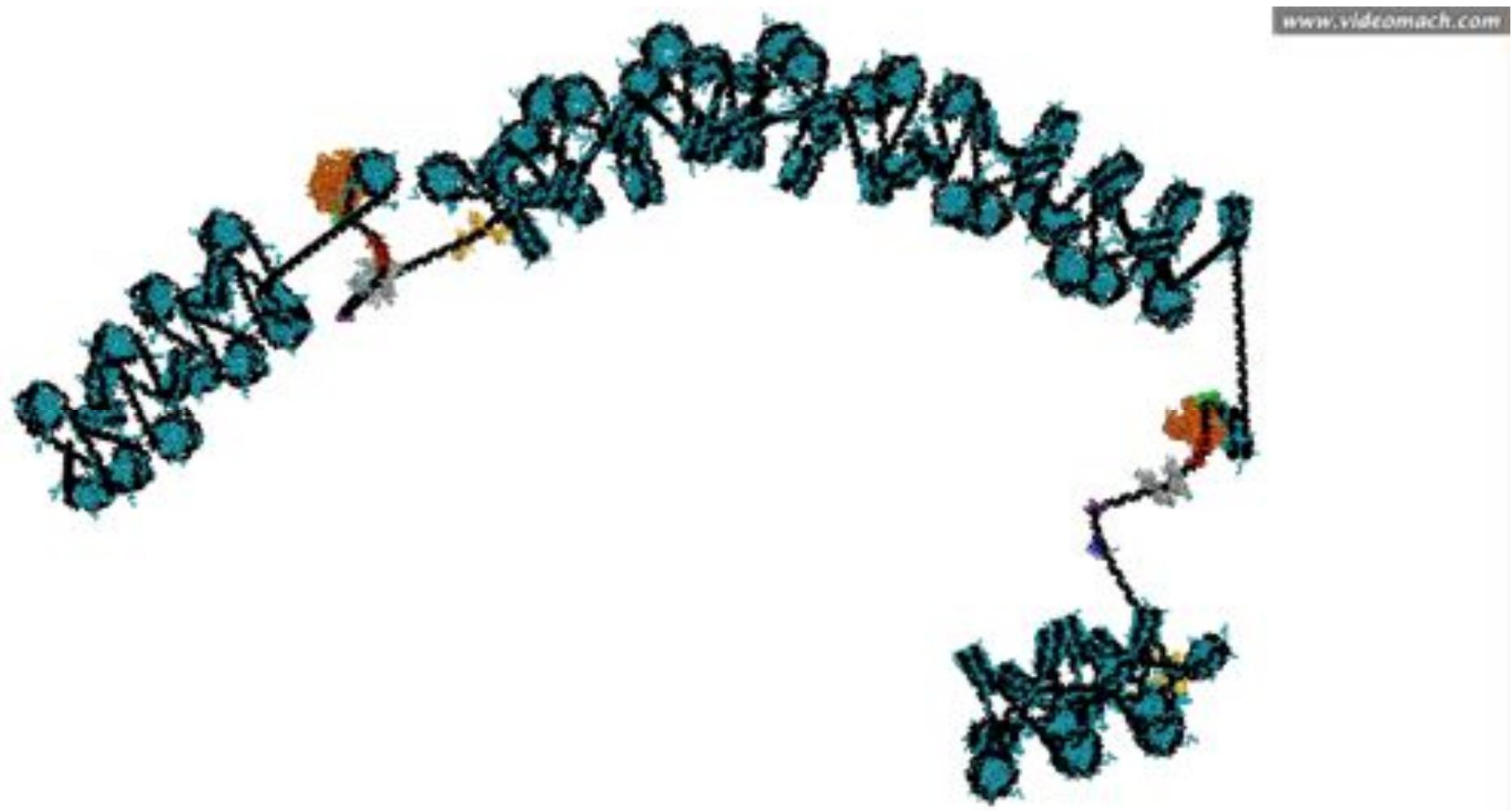
Melting and Protein/DNA

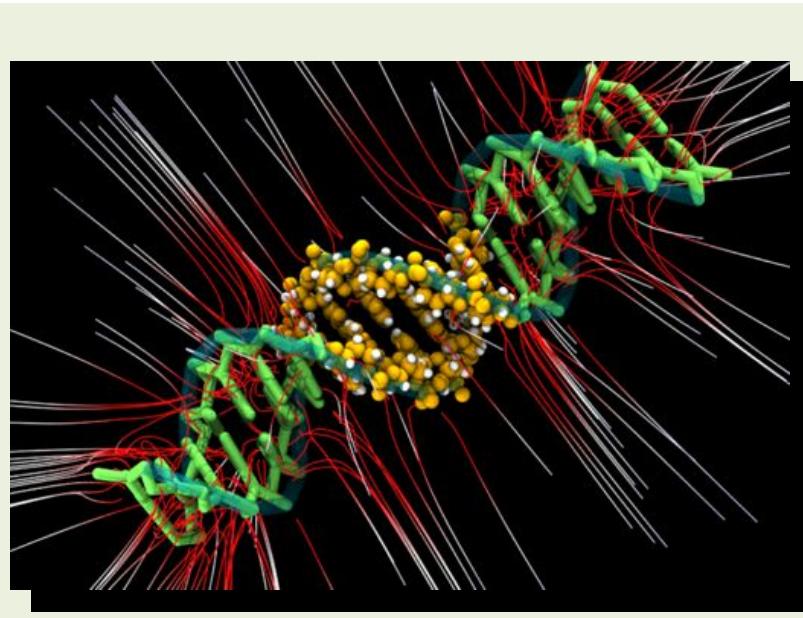
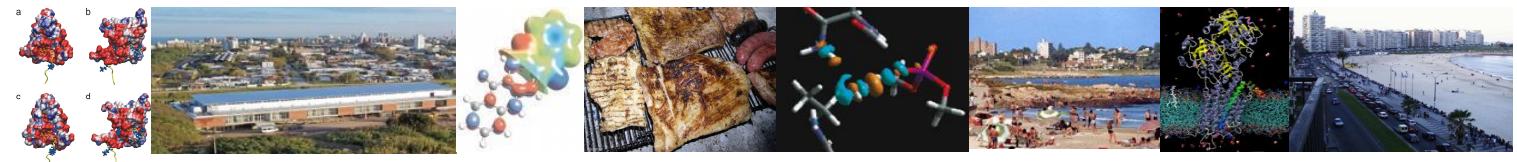




Chromatin Modeling

HIV-1 integrated provirus

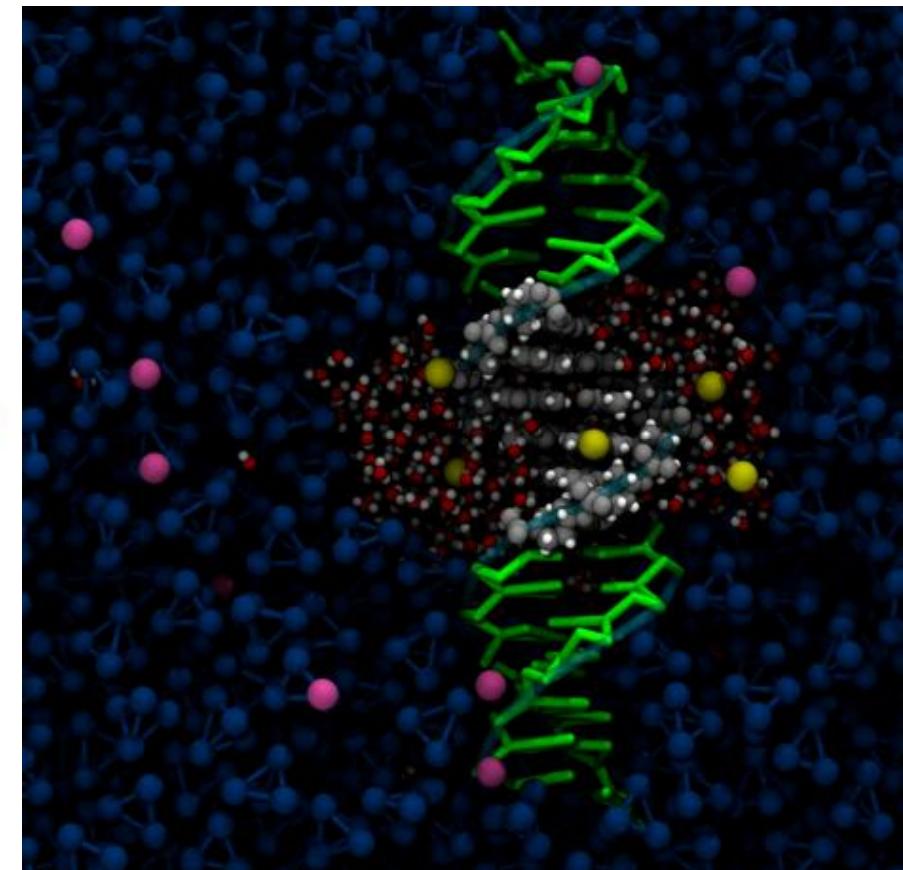
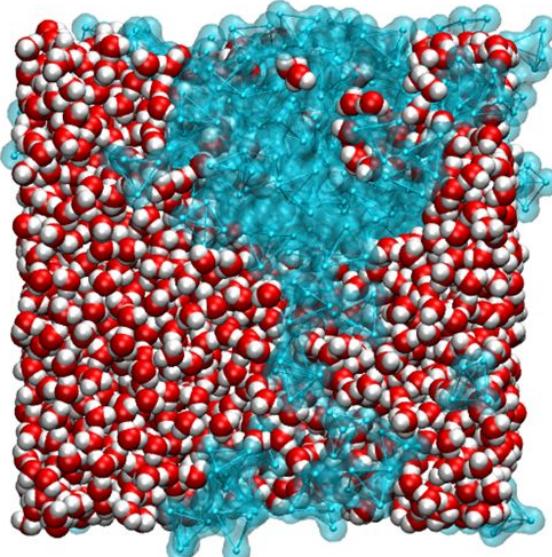
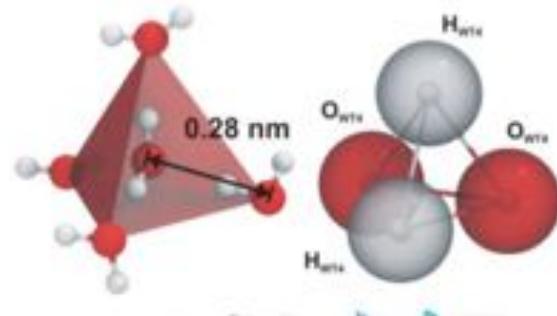




Hybrid SIRAH (dual resolution schemes)



Dual Resolution Simulations

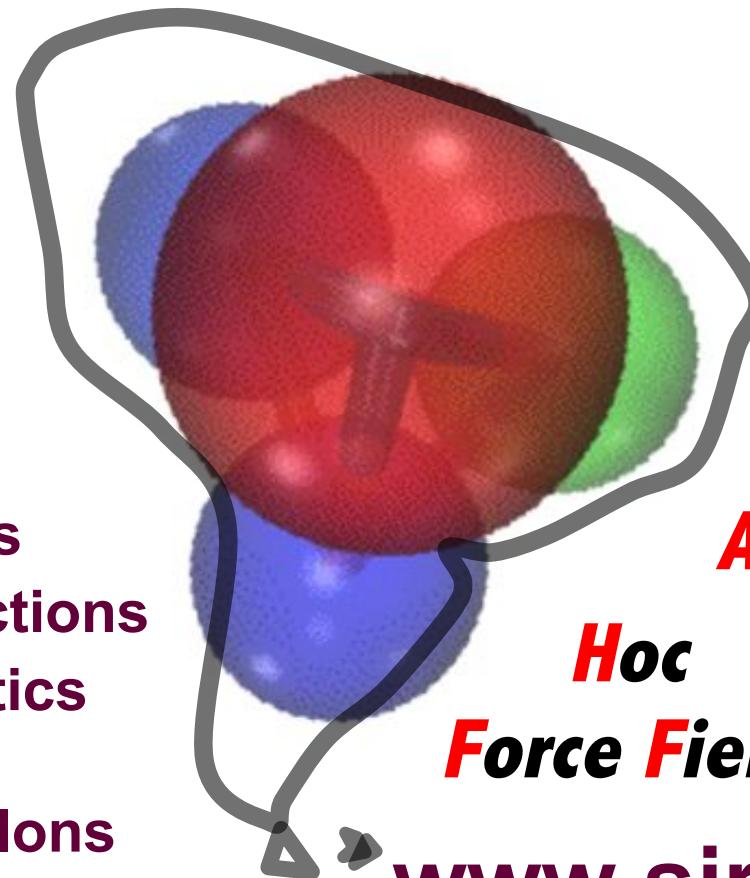


Darre et al. JCTC, 2012



SIRAH FF

- **Easy-to-use**
(straightforward in GROMACS and AMBER)
- **800 to 2500 speed-up**
(explicit and implicit solvation, respectively)
- **Back-mappable**
- **Multi Scale simulations**
- **All Hamiltonian interactions**
- **Long range electrostatics**
(Ewald summation)
- **DNA, Proteins, Water, Ions**
(lipids will arrive, eventually)



Simulate
Rapidly and
Ad
Hoc
Force Field
www.sirahff.com



Molecular dynamics simulations of BPTI *McCammon & Karplus, 1974*

Atomistic Force Fields:

AMBER
CHARMM
GROMOS/GROMACS
OPLS

Coarse Grain Force Fields:

MARTINI

SIRAH ?