What can we do with a bunch of spheres?

Coarse Grained Models & Applications on Protein Systems

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COMPUTE Retreat

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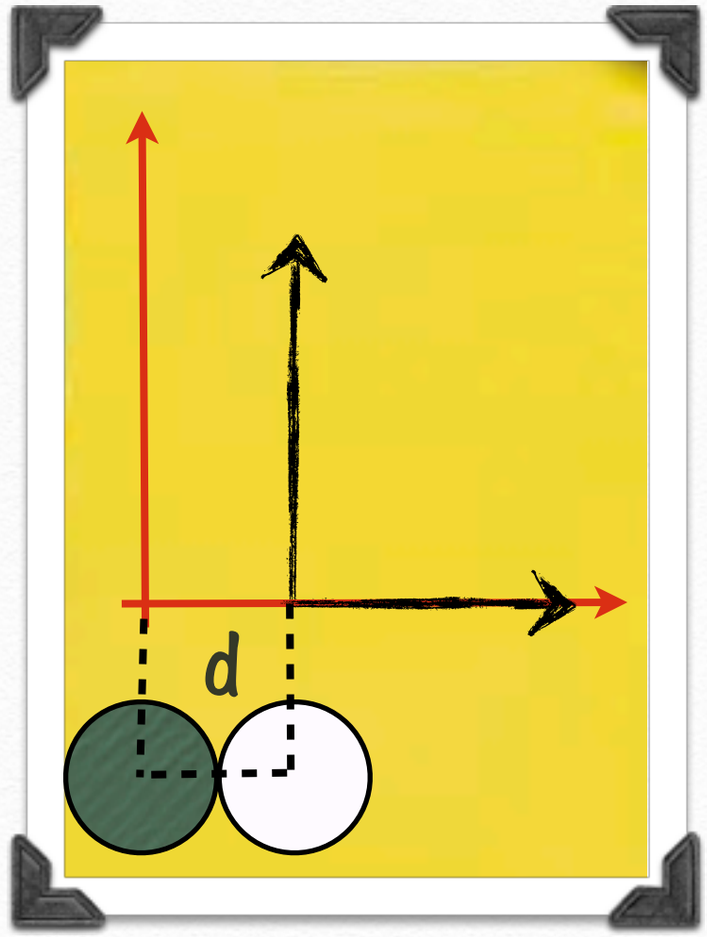
Let's model billiard balls

- Two spheres
- Simulation box with hard walls
- Interactions:
  - feel each other when they collide
  - no interactions when they are apart

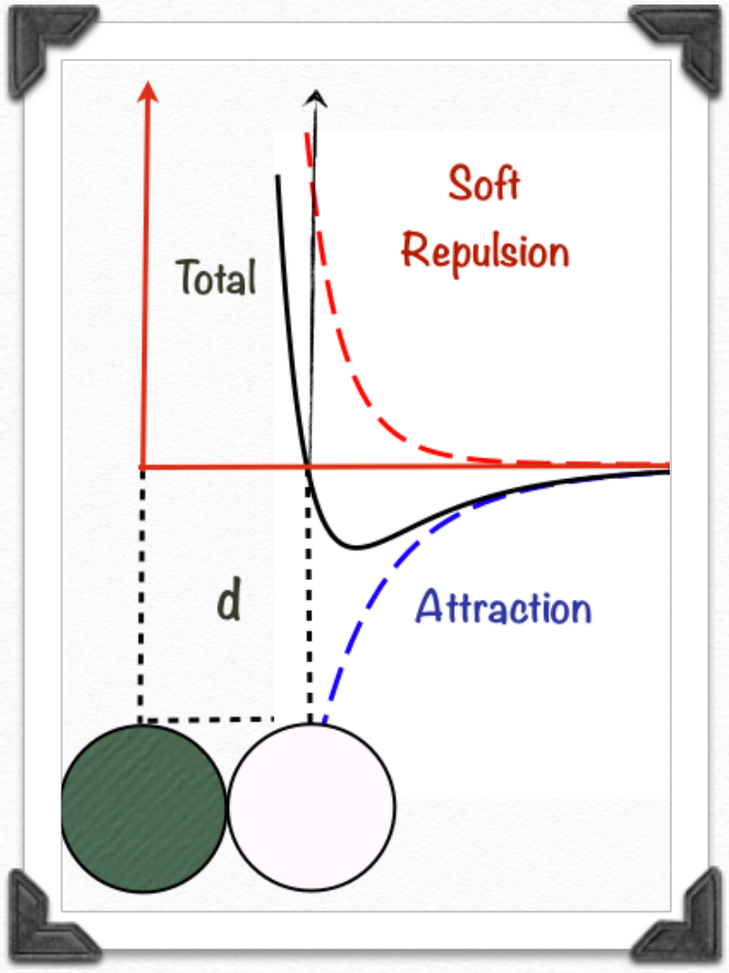
} **Hard Spheres**



Let's modify the balls

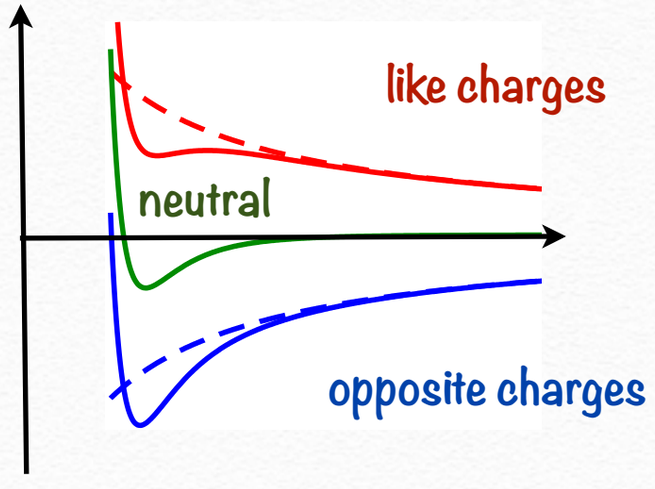
- Make the balls out of plastic
  - They will be softer
- In molecular world:
  - They have short ranged attraction

$$U(r) = 4\epsilon\left\{\left\{\frac{d}{r}\right\}^{12} - \left\{\frac{d}{r}\right\}^{6}\right\}$$



- Make them charged

$$U_{charge}(r) = \frac{q_1 q_2}{4\Pi\epsilon_0 r}$$



- 2 spherical particles: Solution with pen and paper

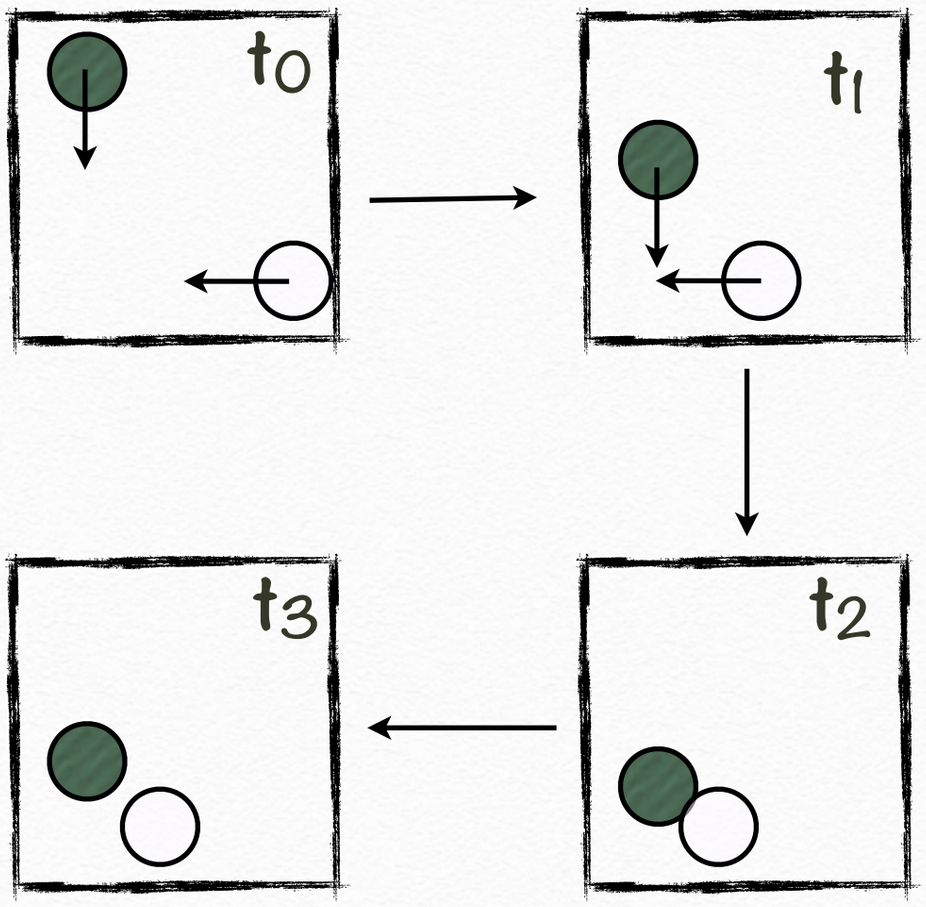
- If they were many like in billiard board: Explore all possible configurations

- If they had orientation dependent interaction: Explore all possible orientations

} Require Numerical solutions = Simulations !

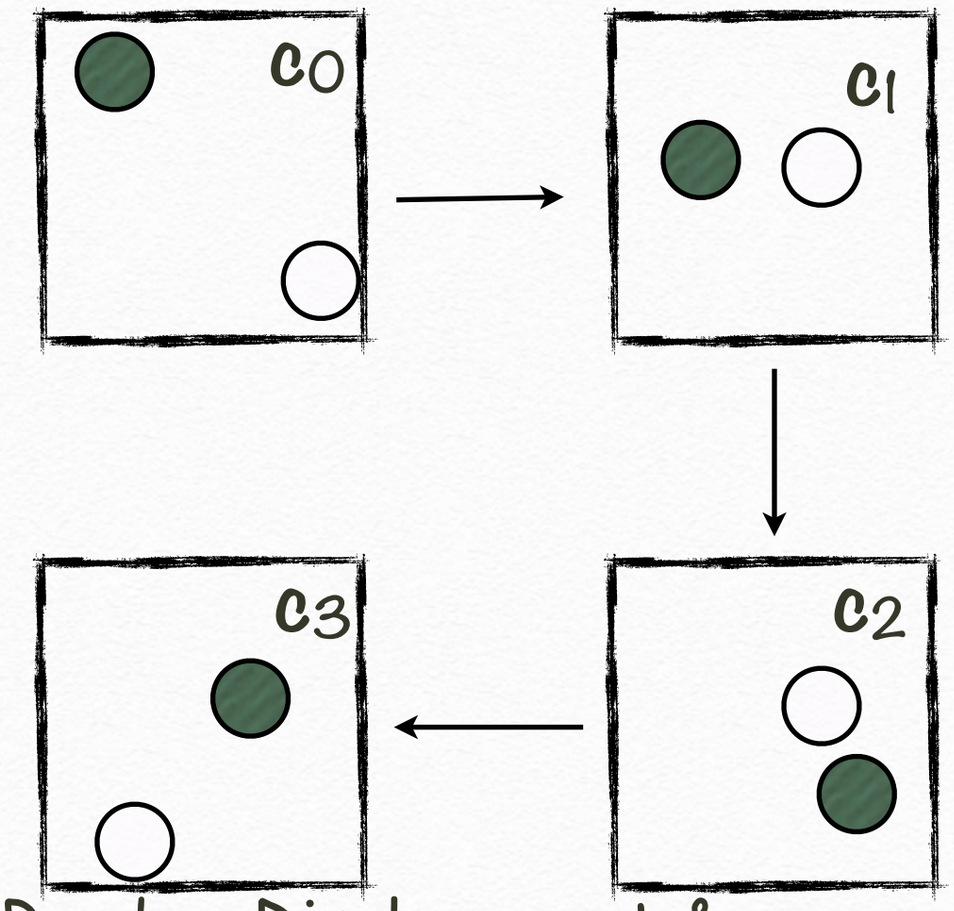
Monte Carlo Simulations

- Experimental measurements: Time averaging



Newton Equations of Motions

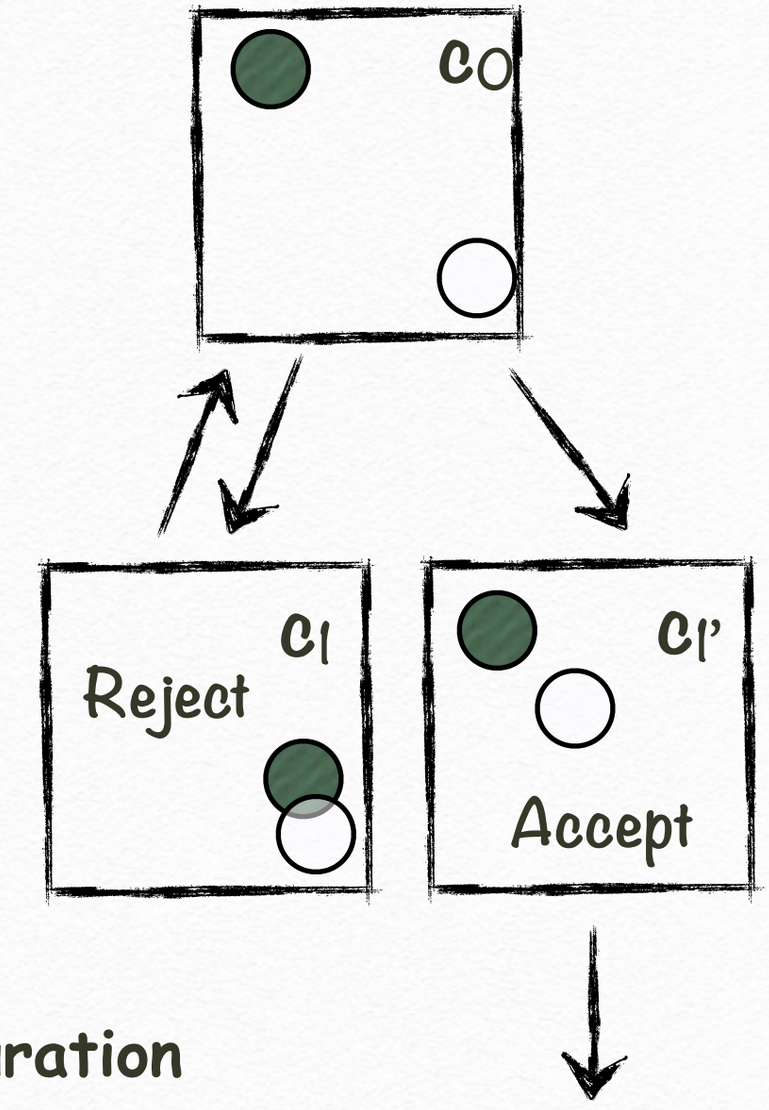
- Monte Carlo simulations: Ensemble averaging



Random Displacement & Thermal averaging: weighted by $e^{-\frac{\Delta U(r)}{kT}}$

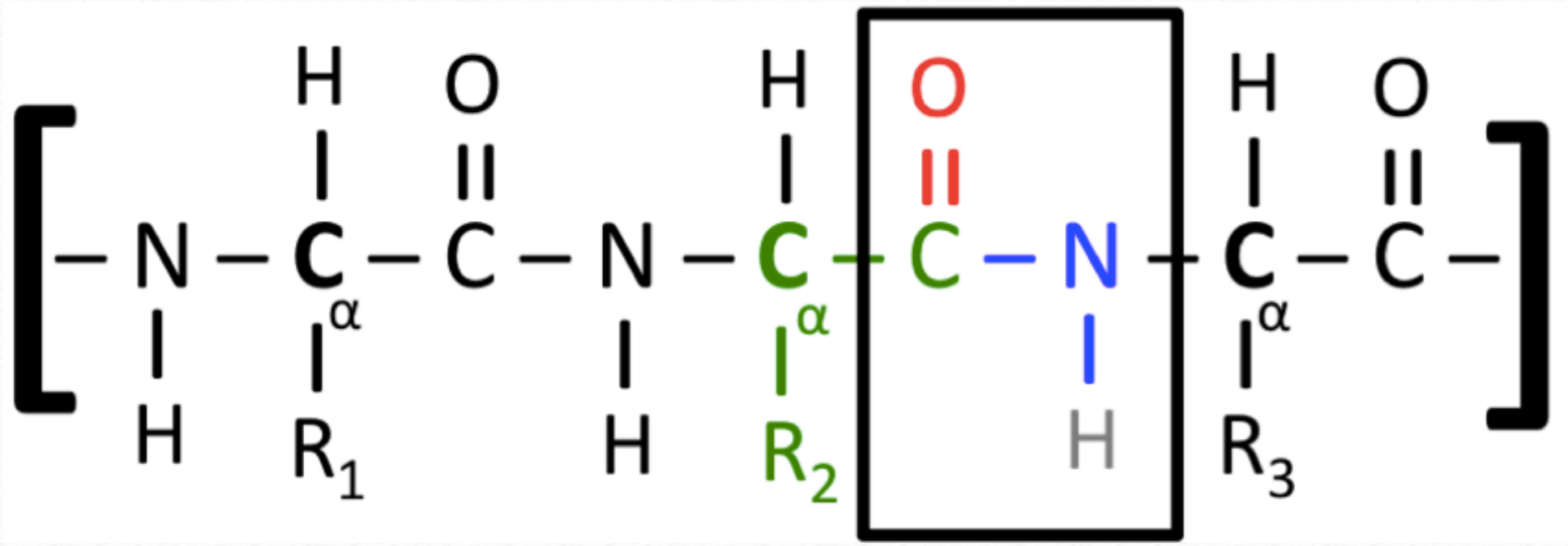
Metropolis Monte Carlo Algorithm

- Pick a random particle
- Move it to a random position
- Calculate the difference in total energy
  - by summing all pair interactions
  - calculation time is proportional to N^2
- Generate a random number R between 0 and 1
- If R < $e^{-\frac{\Delta U(r)}{kT}}$ → **Accept the new configuration**
  - otherwise → **move it back**

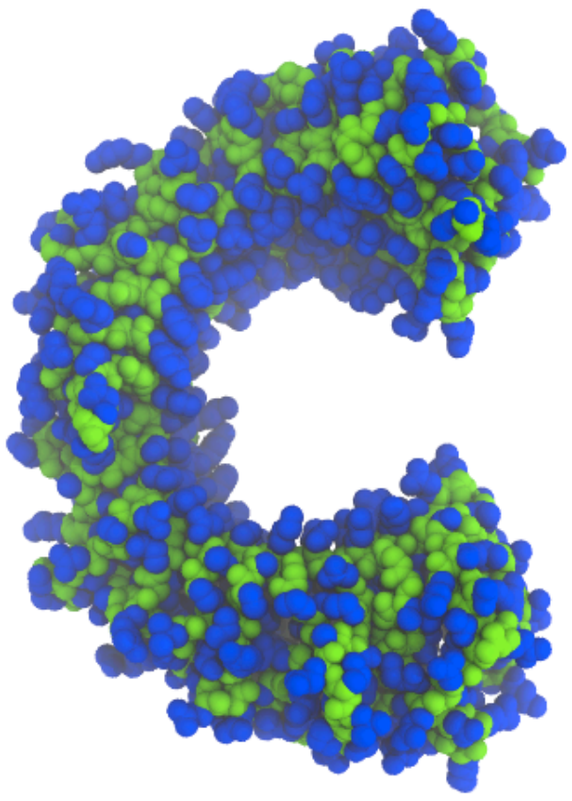


More interesting systems: Proteins

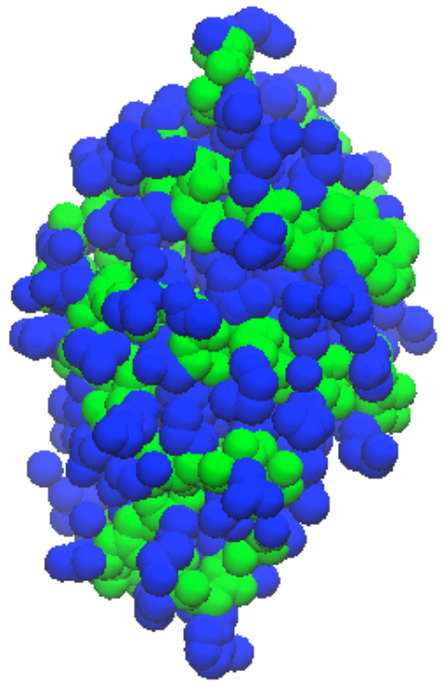
- Sequence of building blocks called amino acids bound to each other by peptide bonds



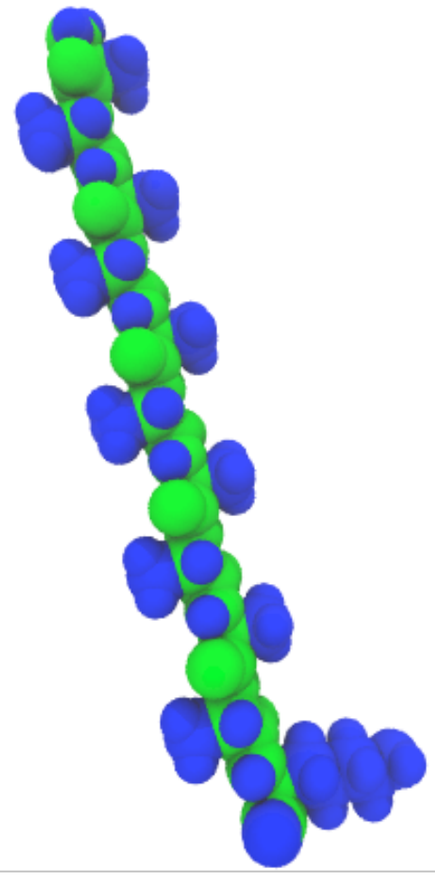
Horse shoe shaped protein:
314 amino acids
2336 particles



Globular protein:
123 amino acids
990 particles

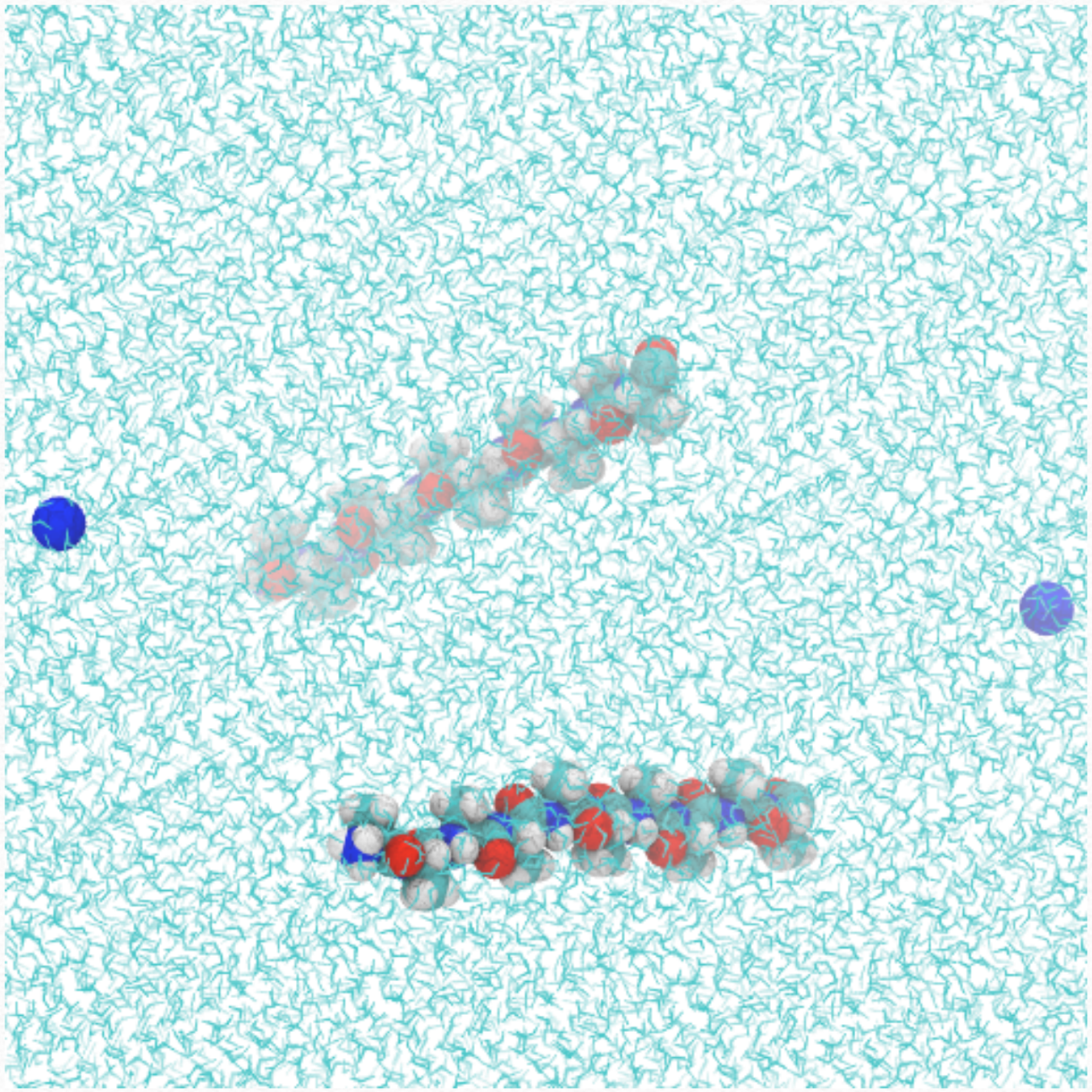


Chain like protein:
11 amino acids
250 particles



Proteins in solution

Proteins + water + ions
=67628 particles



Number of Particles
in the system
needs to be reduced
to study

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binding of bigger
proteins,
protein self assembly,
phase separation

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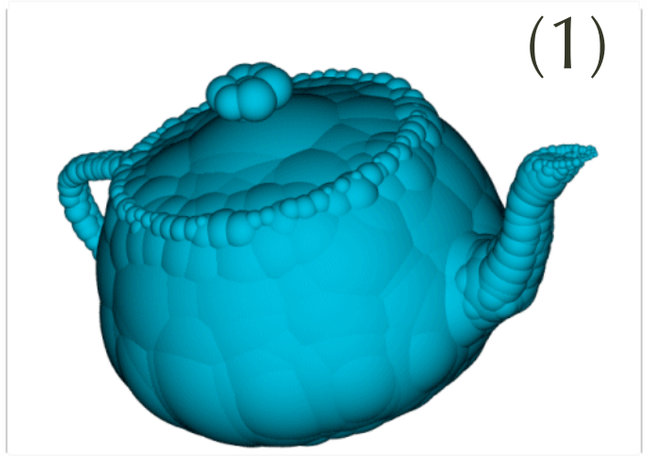
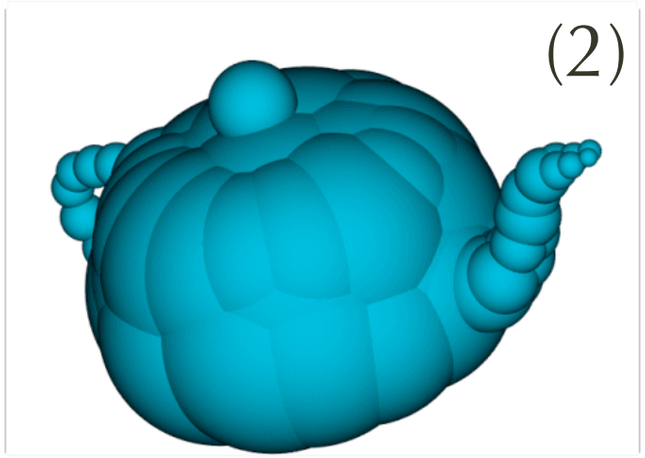
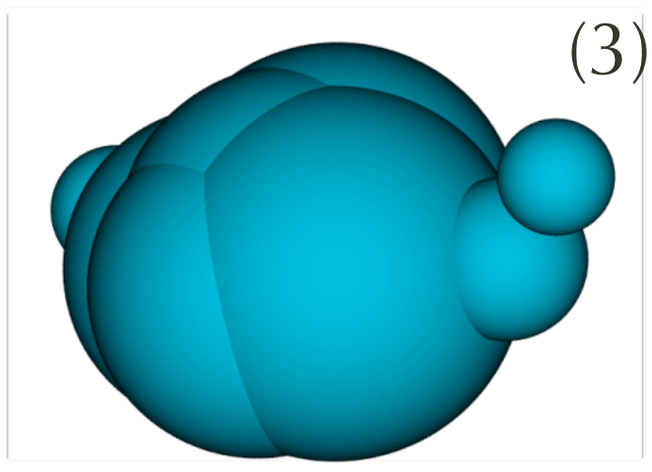
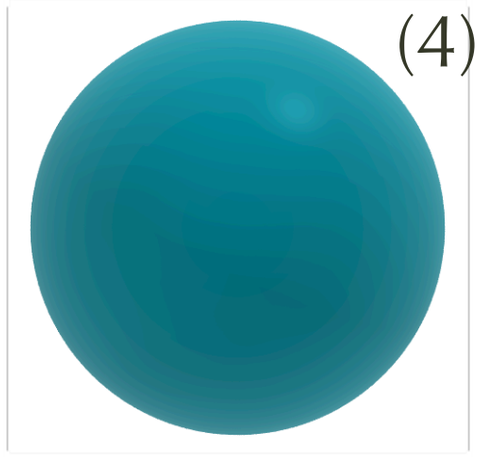
COARSE GRAINED
MODELS

What is coarse graining?







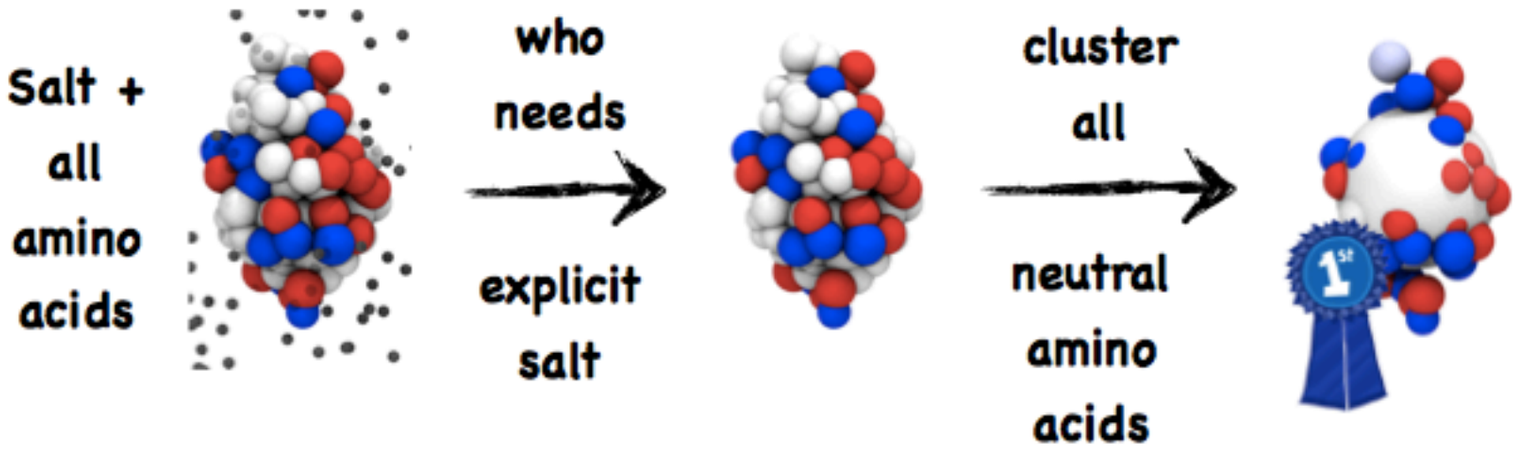


(5)

implicit

Effect of charge anisotropy on phase separation of proteins

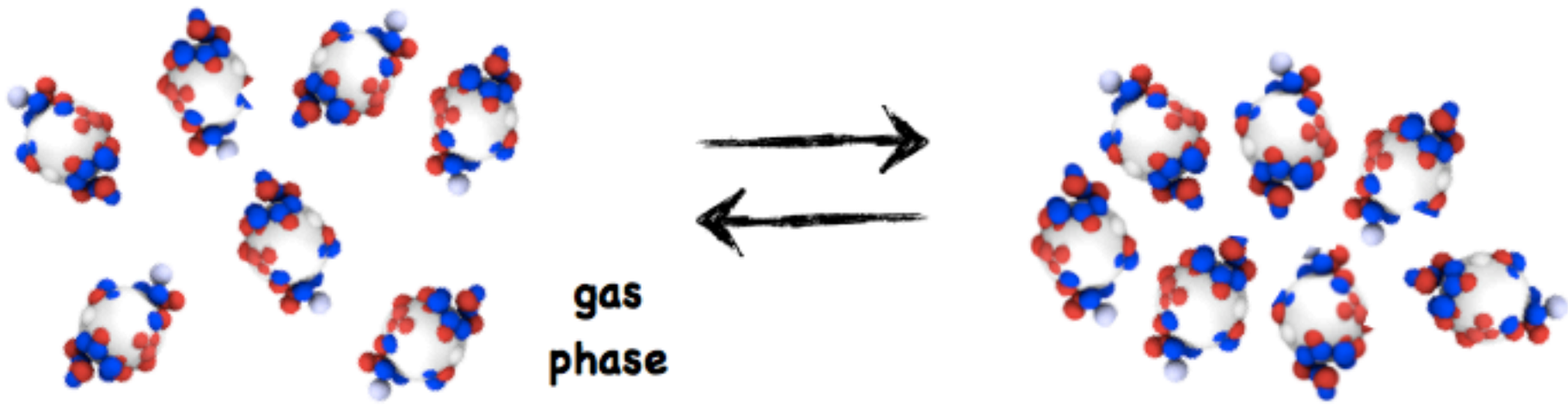
1 Step: Development of proper model = FAST+DETAILED enough



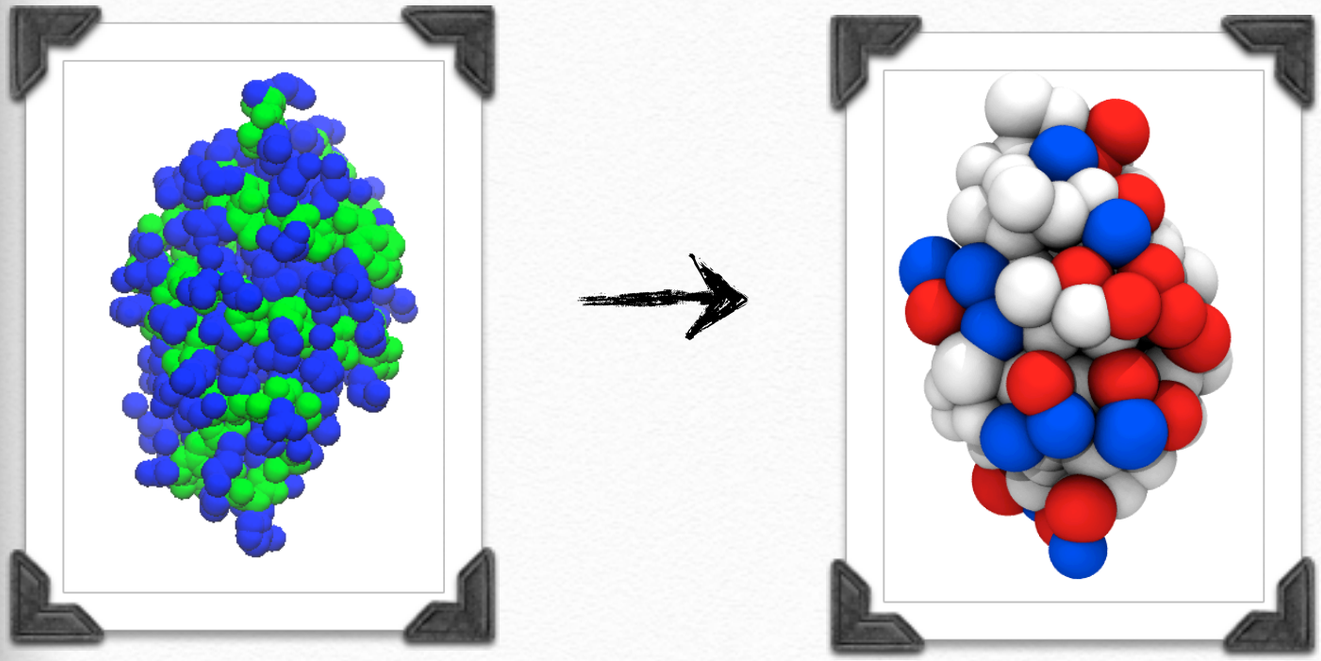
Winner: Fastest and captures essential physics

2 Step: Play with MC simulations =

Play ground: pH, salt concentration, mutations on protein structures



Protein-protein binding



Need all amino acids

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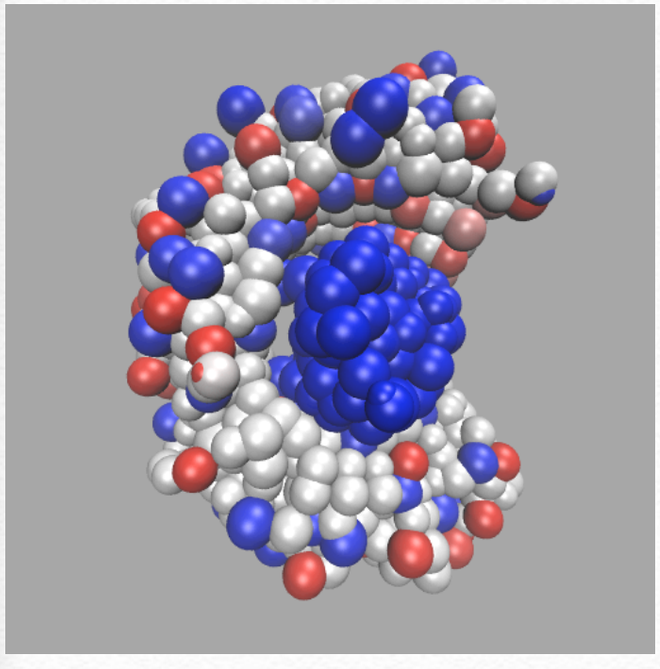
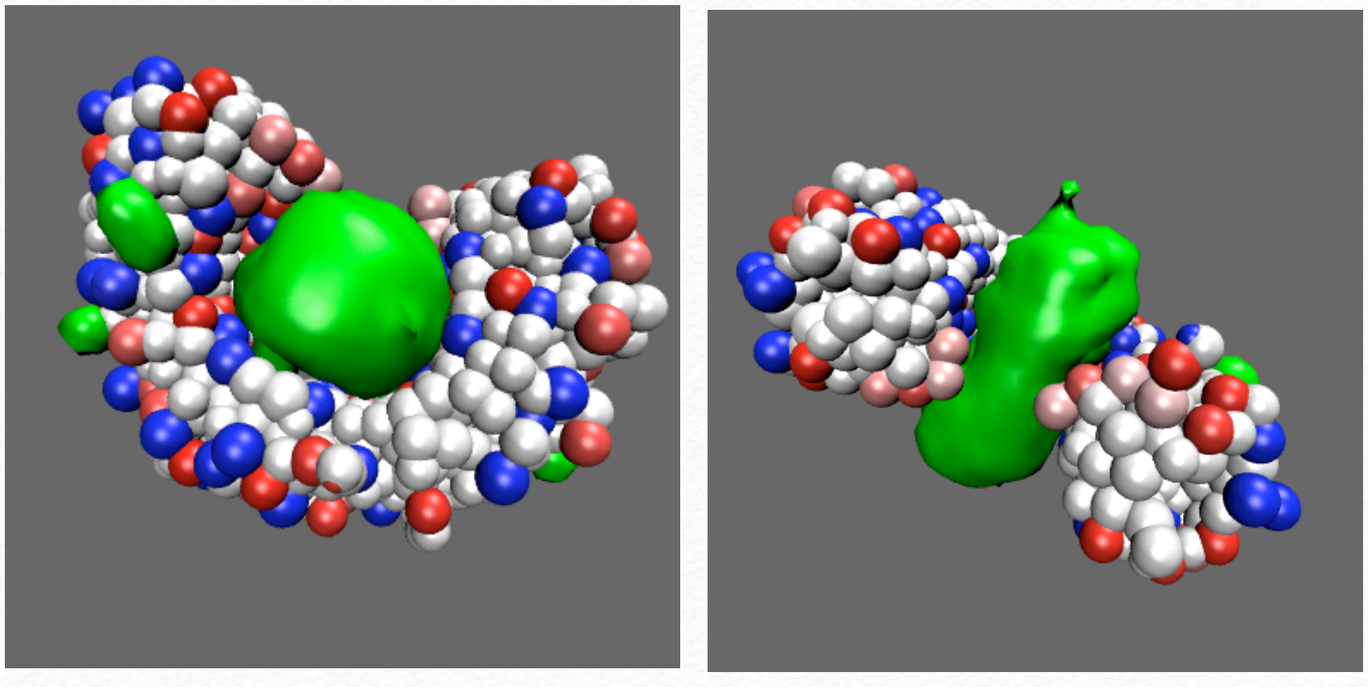
to capture the ones involved in the binding

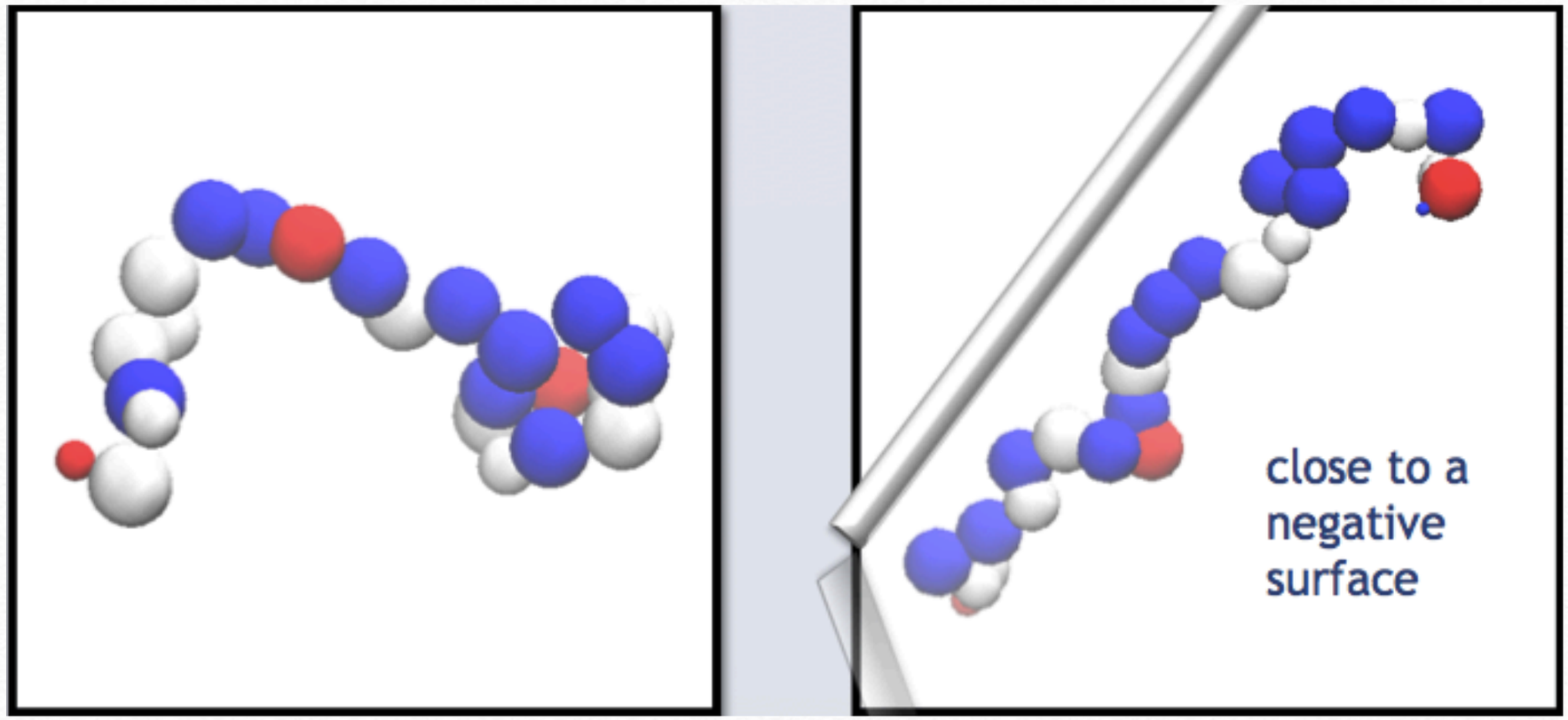
Snapshot from simulation



Green: Isodensity map



Effect of charge regulations on adsorption of flexible proteins



MODEL

Flexible chain: Harmonic bonds between each adjacent particles

Charges are allowed to fluctuate

Implicit: Surface charges, ions and water molecules

Conclusion

- Determine essential physics
- Develop proper model: **Fast** and **detailed** enough
  - **Fast** = Decrease the number of particles
  - **Detailed** = Capture essential physics
- Verify the coarse grained model:
  - Compare with more detailed models and experiments
- **Let the simulations run !**

Thank you for your attention

Any implicit questions?