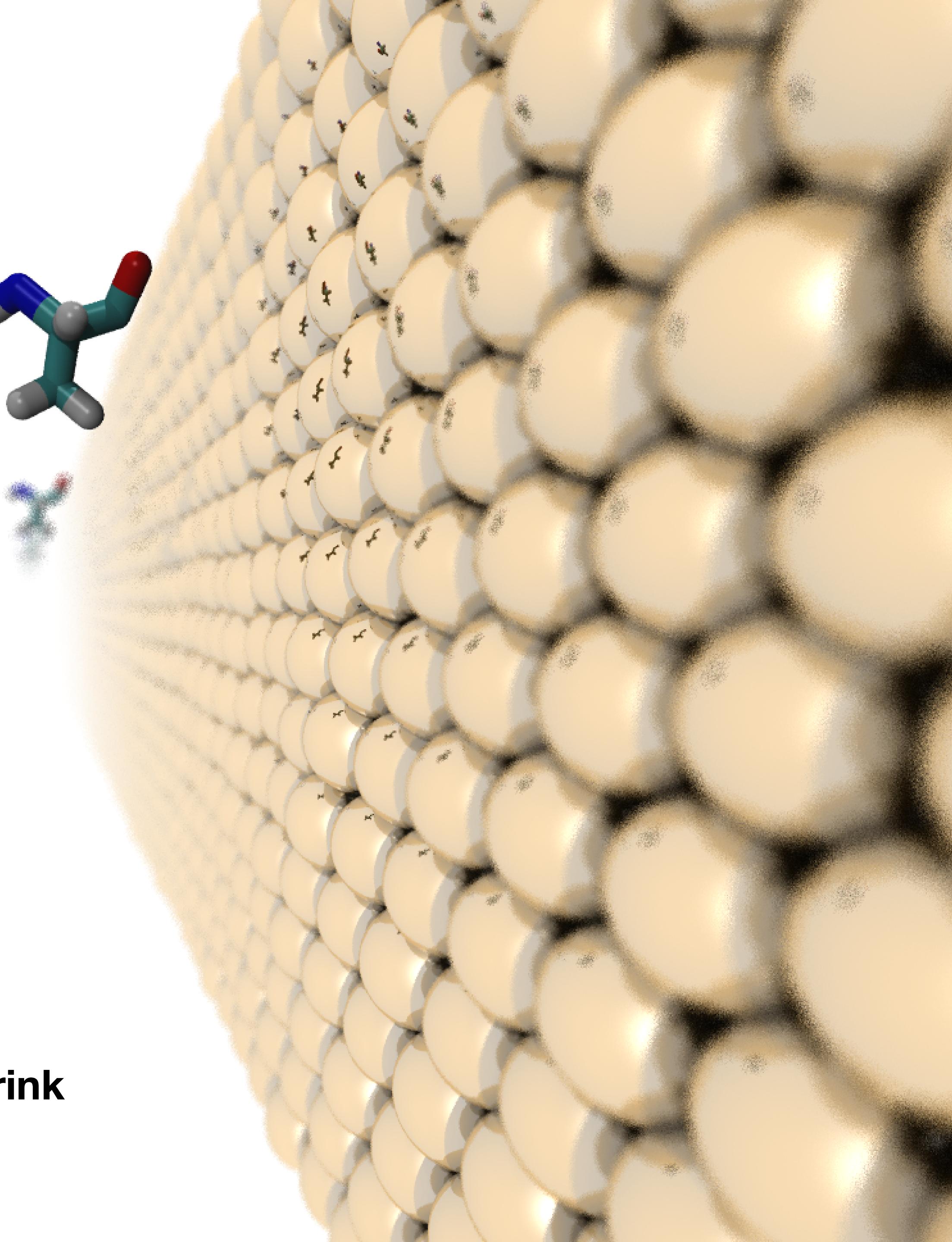


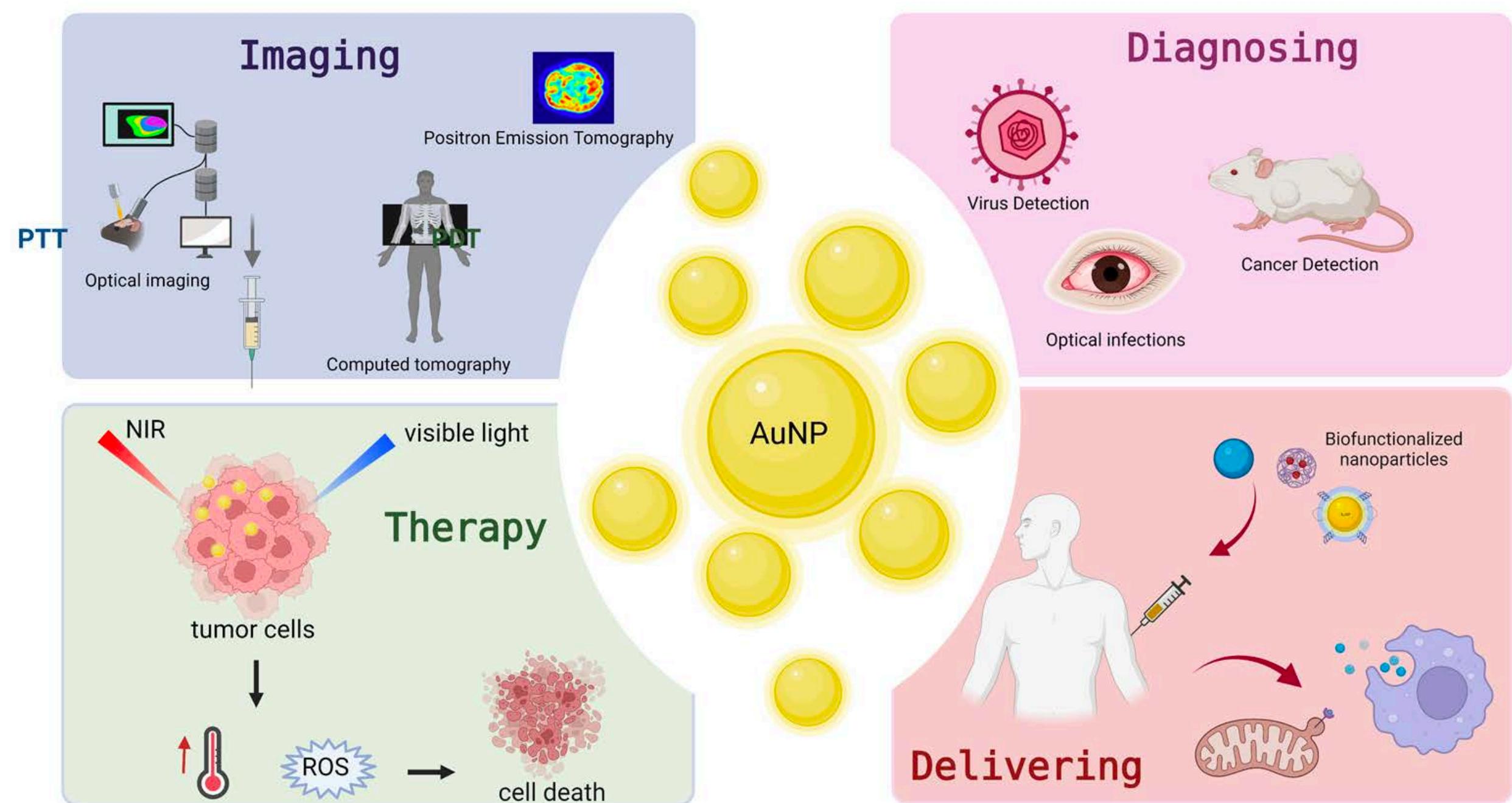
# Developing a Martini gold model for use in biological contexts



**Jahmal Ennis, Paulo Cesar Telles de Souza, Siewert-Jan Marrink  
and Grace Brannigan**

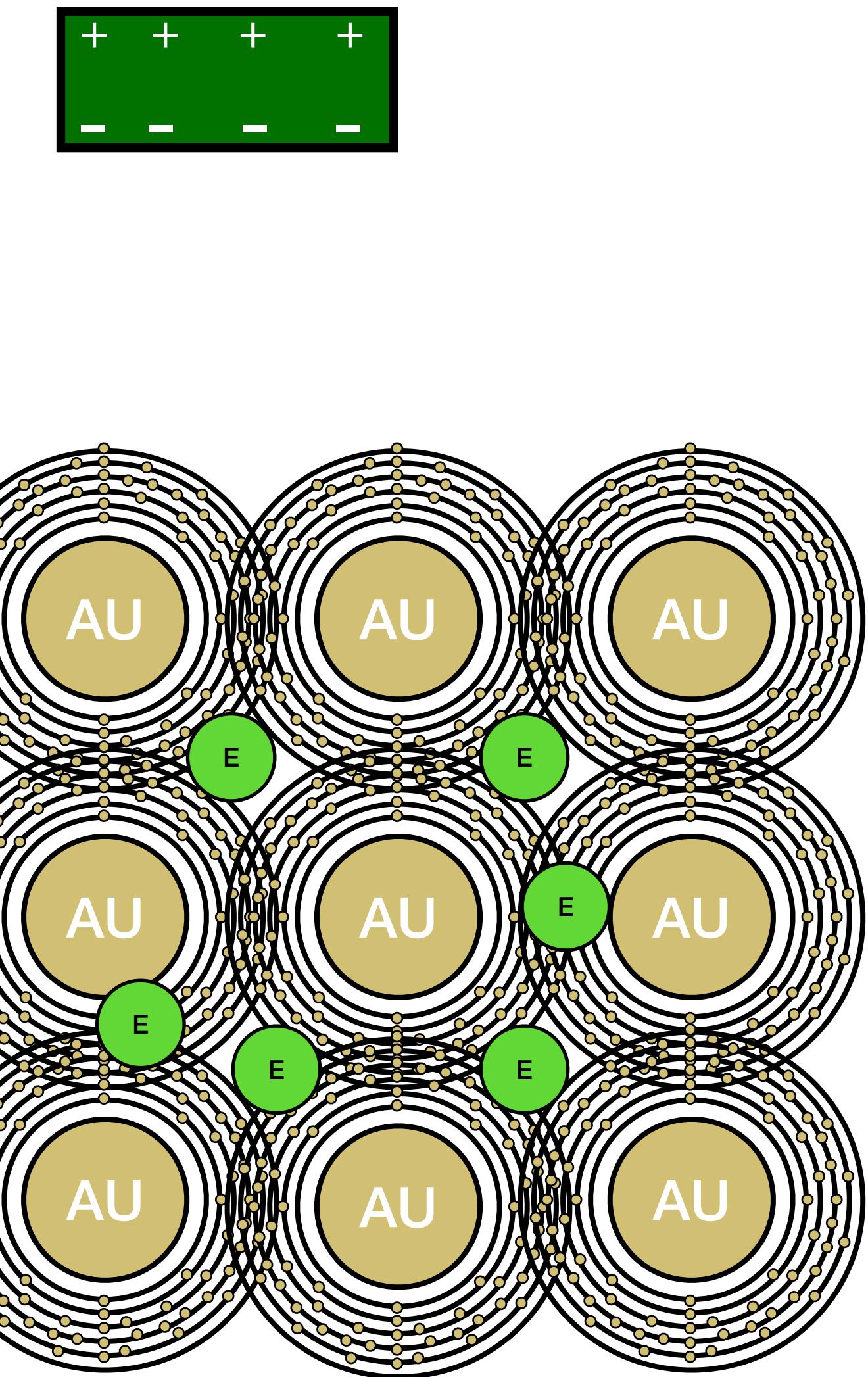
# Why do we need gold parameters in biological force fields?

- Photodynamic Imaging
- Diagnostic Tool
- Targeted Drug Delivery Systems

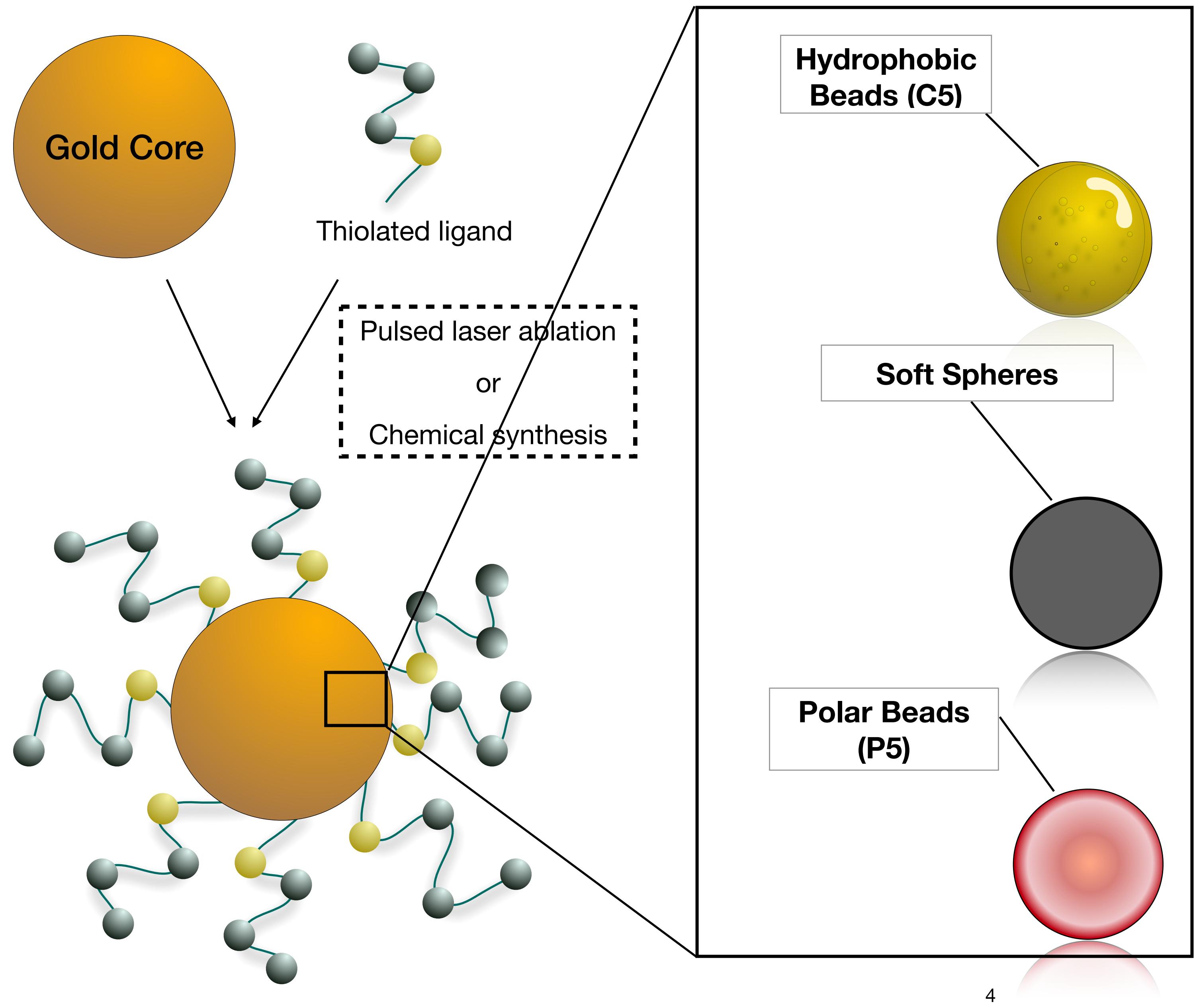


# How have atomistic force fields modeled gold?

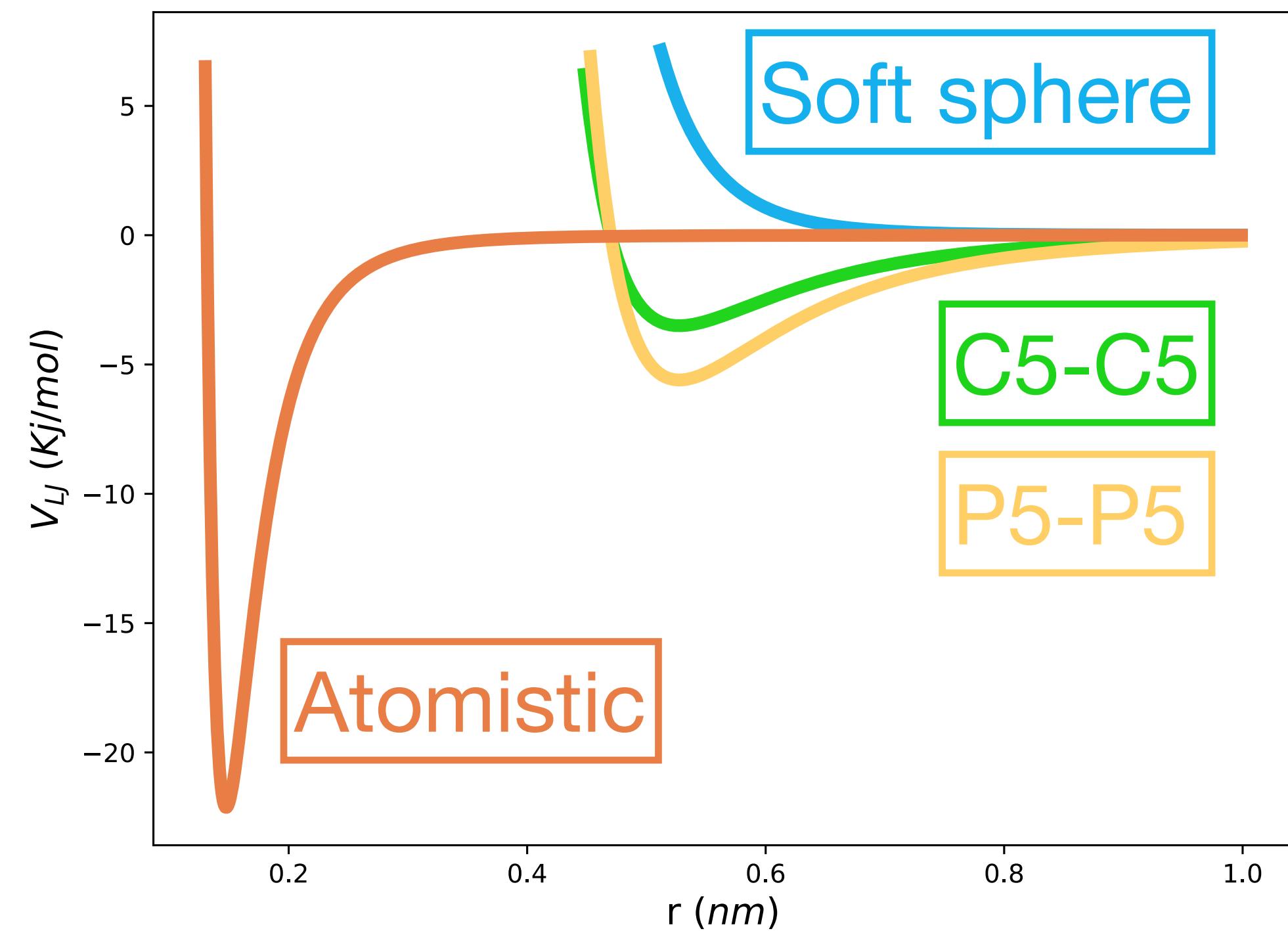
- Gold is strongly polarizable and many of the interactions depend on the moving charges
- The effect of polarizability: strong self-interactions and strong non-bonded interactions with other molecules
- The INTERFACE-FF[2] incorporates the effective polarization by deepening the Lennard Jones potential
- There have been no corresponding efforts for CG gold



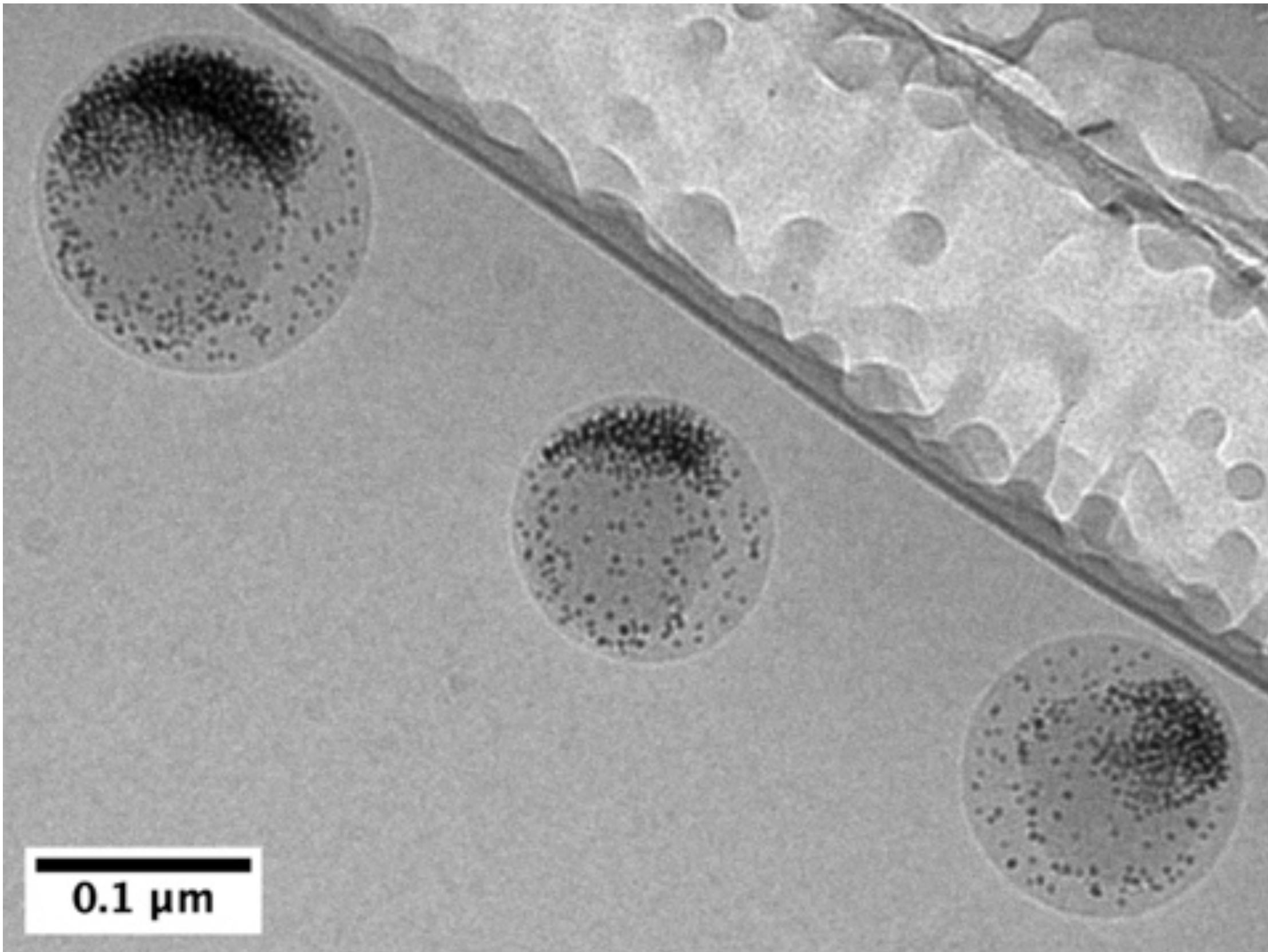
# How have users represented “gold” in Martini?



Lennard Jones Potential

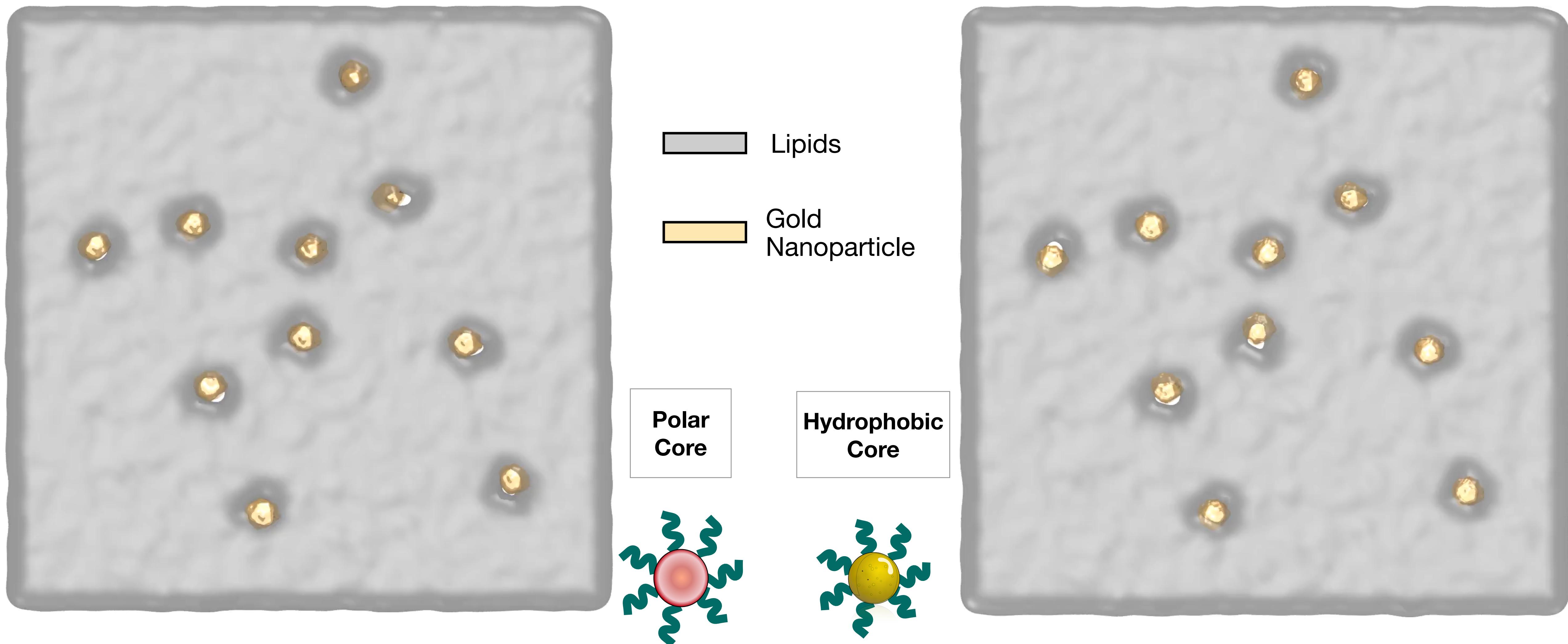


# Is gold nanoparticle aggregation in lipid membranes Martini gold model dependent?



- Why do gold nanoparticles aggregate in lipid membranes?
- Need CG-MD to observe AuNP diffusion
- Tested AuNP aggregation with both the polar bead and hydrophobic bead AuNP model

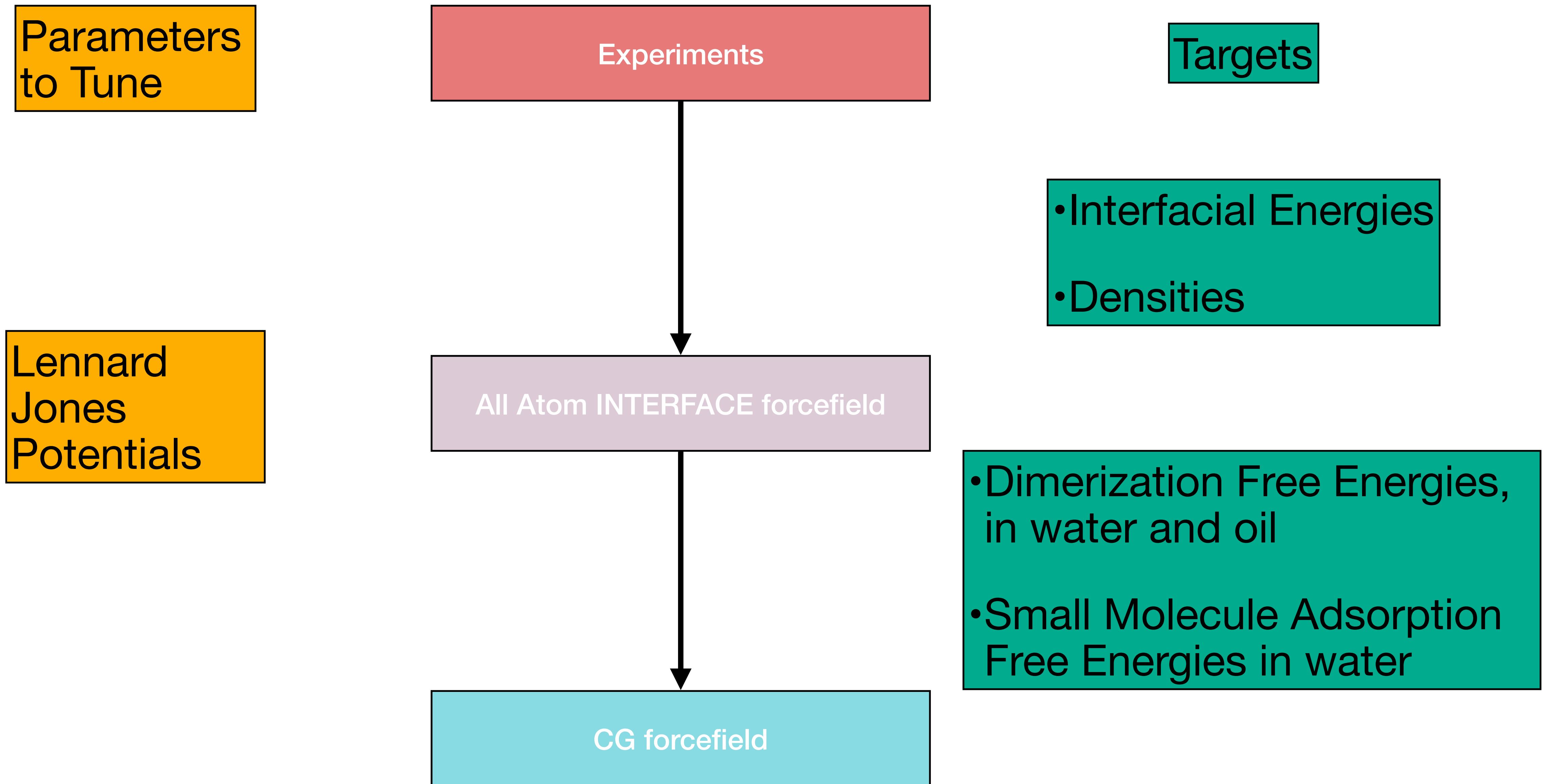
# Regardless of functionalization some properties are still affected by gold parameter choice



**Our goal is to develop a Martini 3 bead that meets several criteria:**

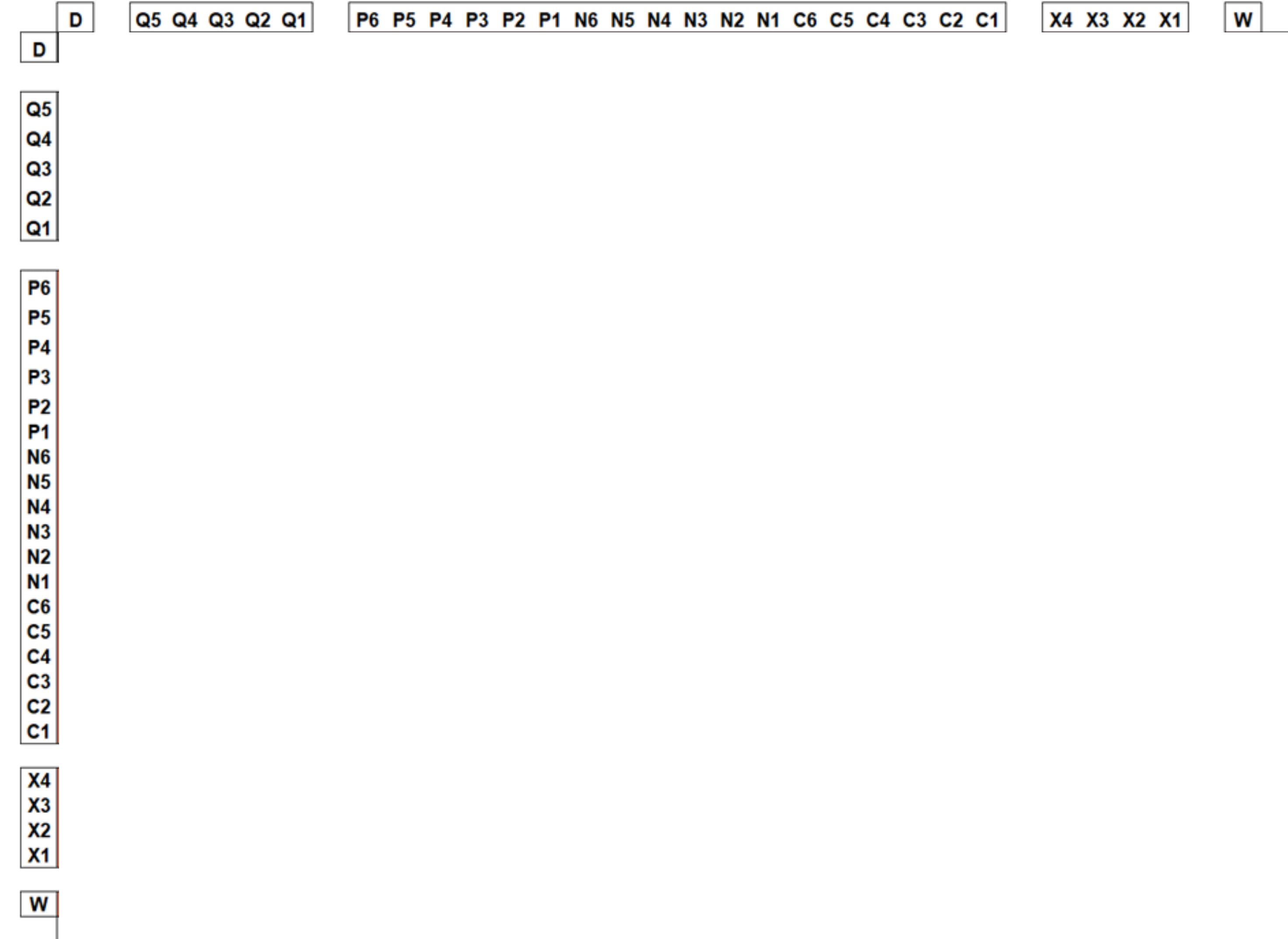
- Preserves strong gold-gold interactions
- Accurately reproduce atomistic and experimental data for small molecule adsorption
- Full compatibility with the Martini 3 CG force field

# Using All-Atom models as a base for coarse grained



# There are a lot of bead options in Martini 3, would any of them work out the box?

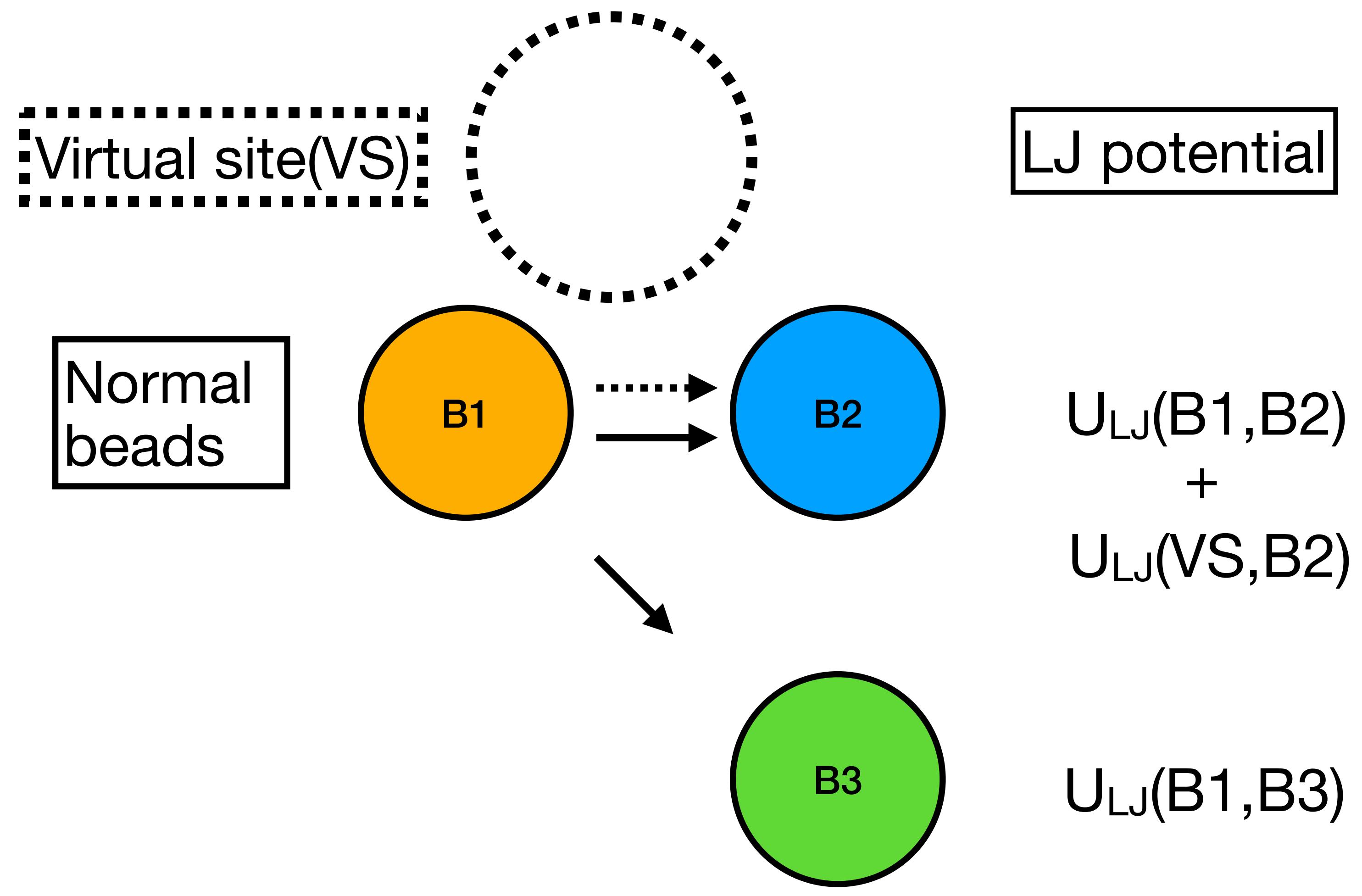
Blocks with different balance when we reduce the bead size:



## Dream Martini Gold Bead

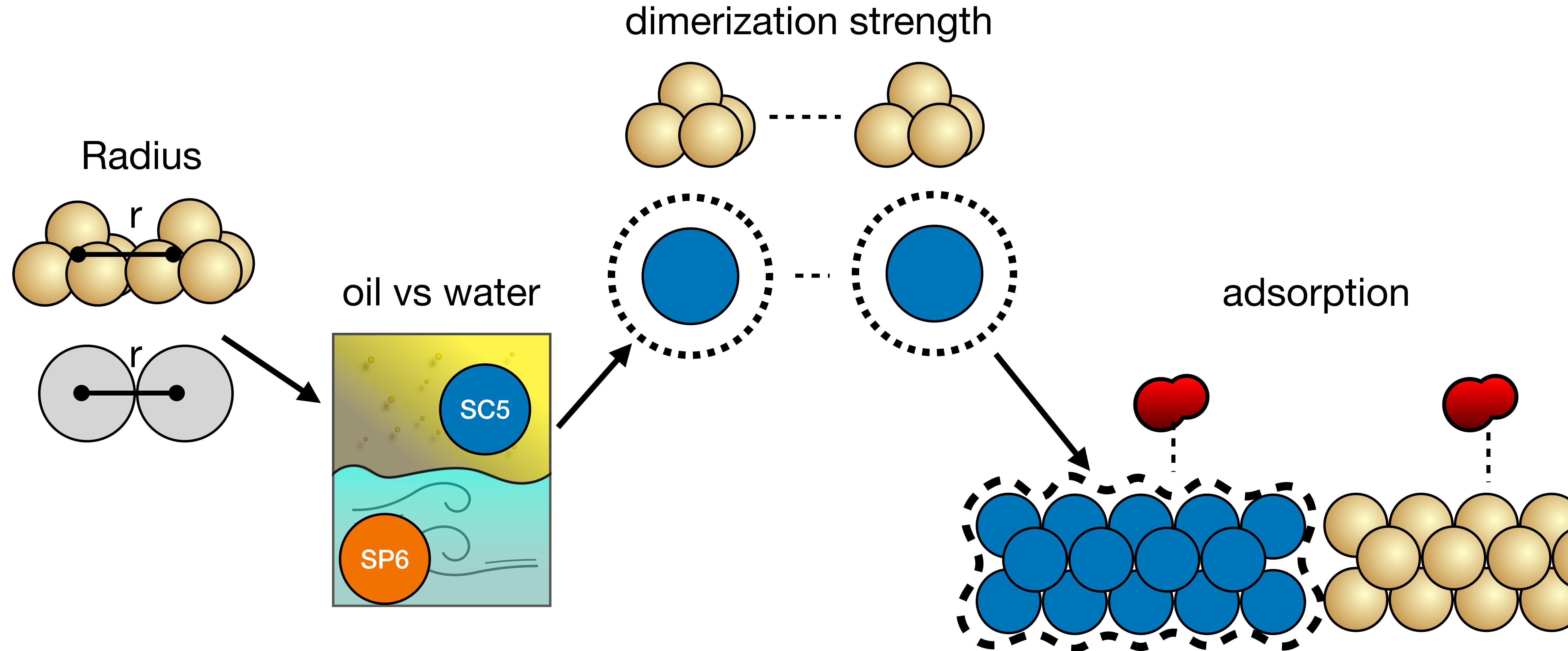
- Really strong self-interaction
- Really strong interactions with Amino Acids like Arg and Trp
- Strong interactions with charge groups
- Relatively strong interactions with alkanes...

# Using virtual sites to tune existing interactions



- We can use virtual sites to modify existing Martini beads
- We overlay a massless particle on our particle and give it extra potentials
- We have the original potential and the virtual site potential contributing to the pair interactions
- Tune some interactions while keeping others consistent

# The roadmap to developing gold

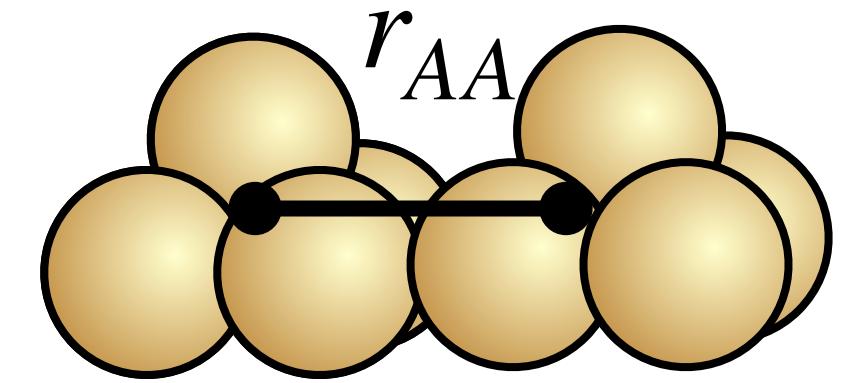


# **Validation and Model Refinement**

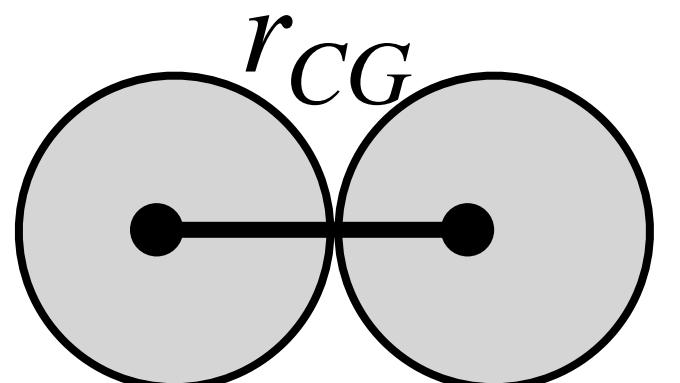
# The roadmap to developing gold

$r$  = global minimum

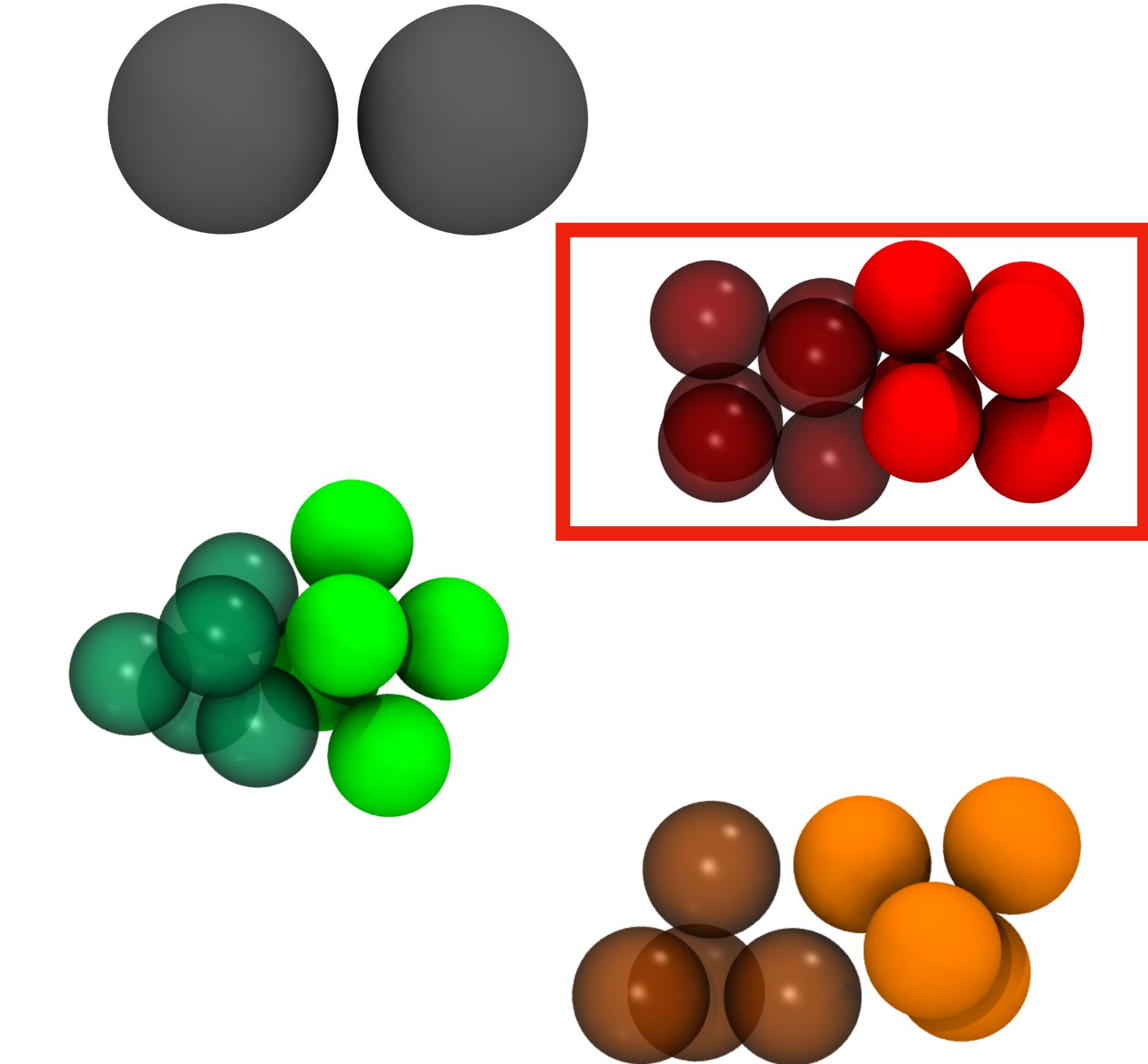
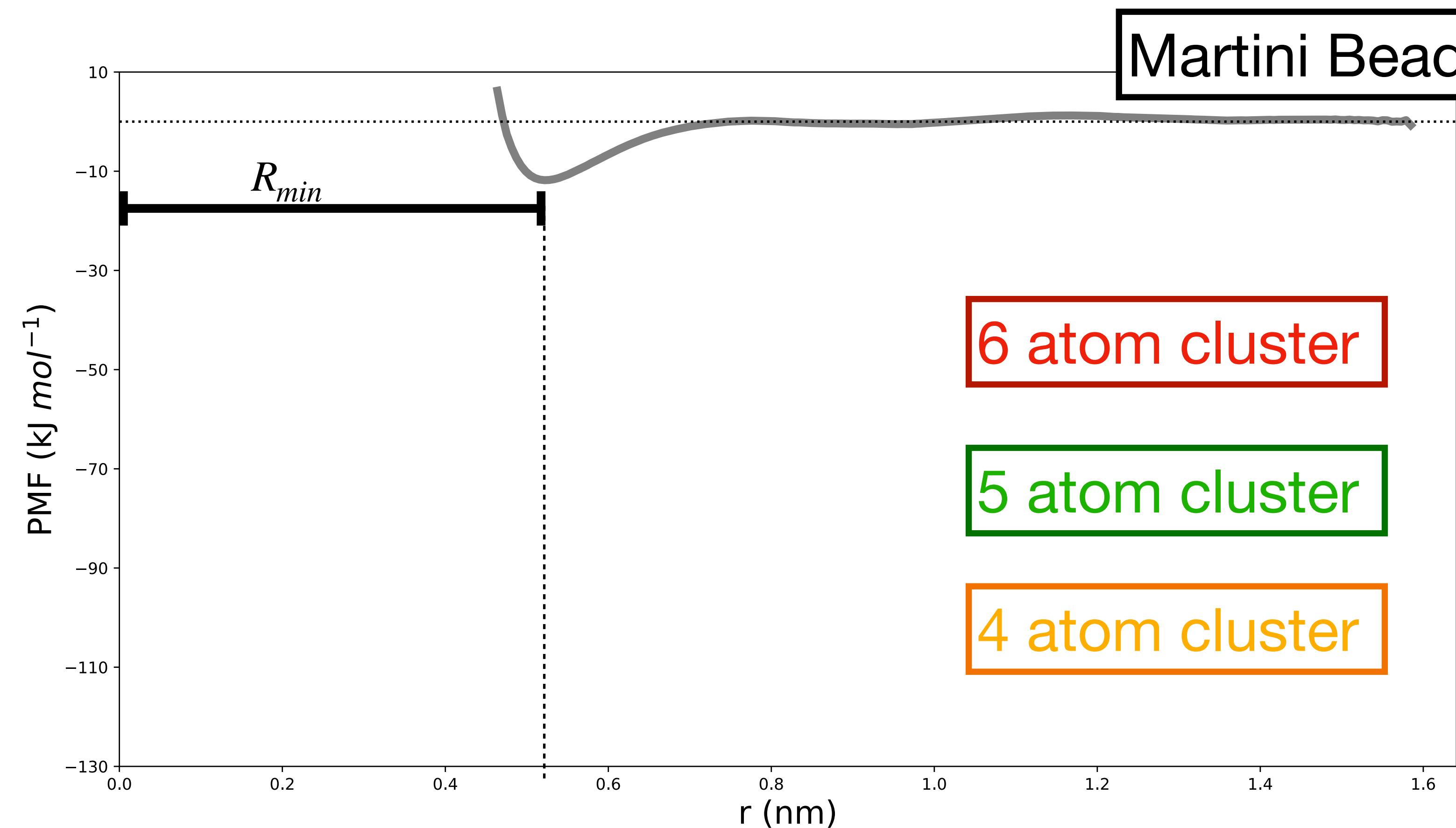
$r_{cg} = r_{AA}$



Step 1: Figure out  
how many gold atoms  
fit into a Martini bead

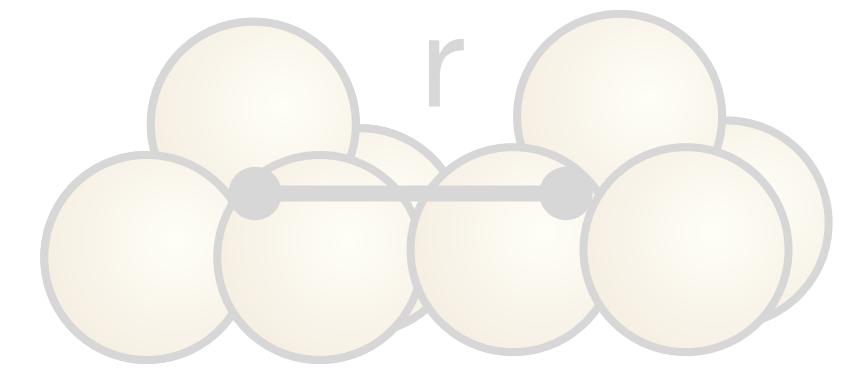


# What size atomistic cluster fits into a Martini bead?

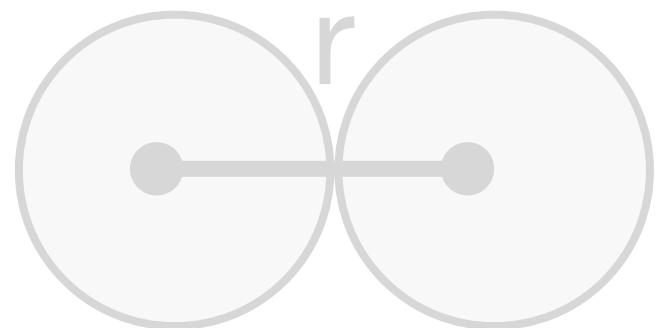


# The roadmap to developing gold

Match the radius

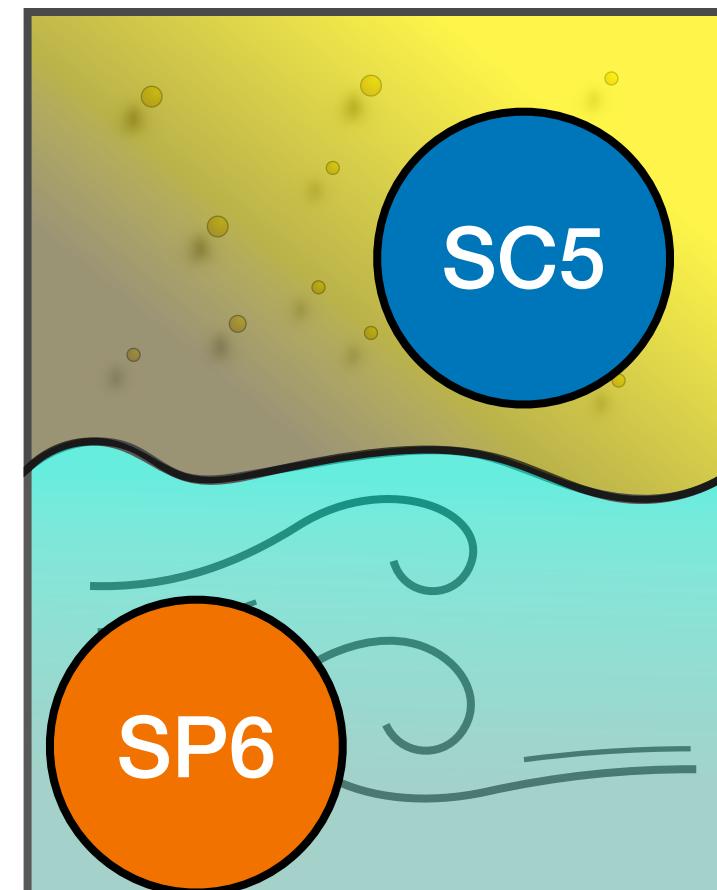


Step 1: Figure out  
how many gold atoms  
fit into a Martini bead



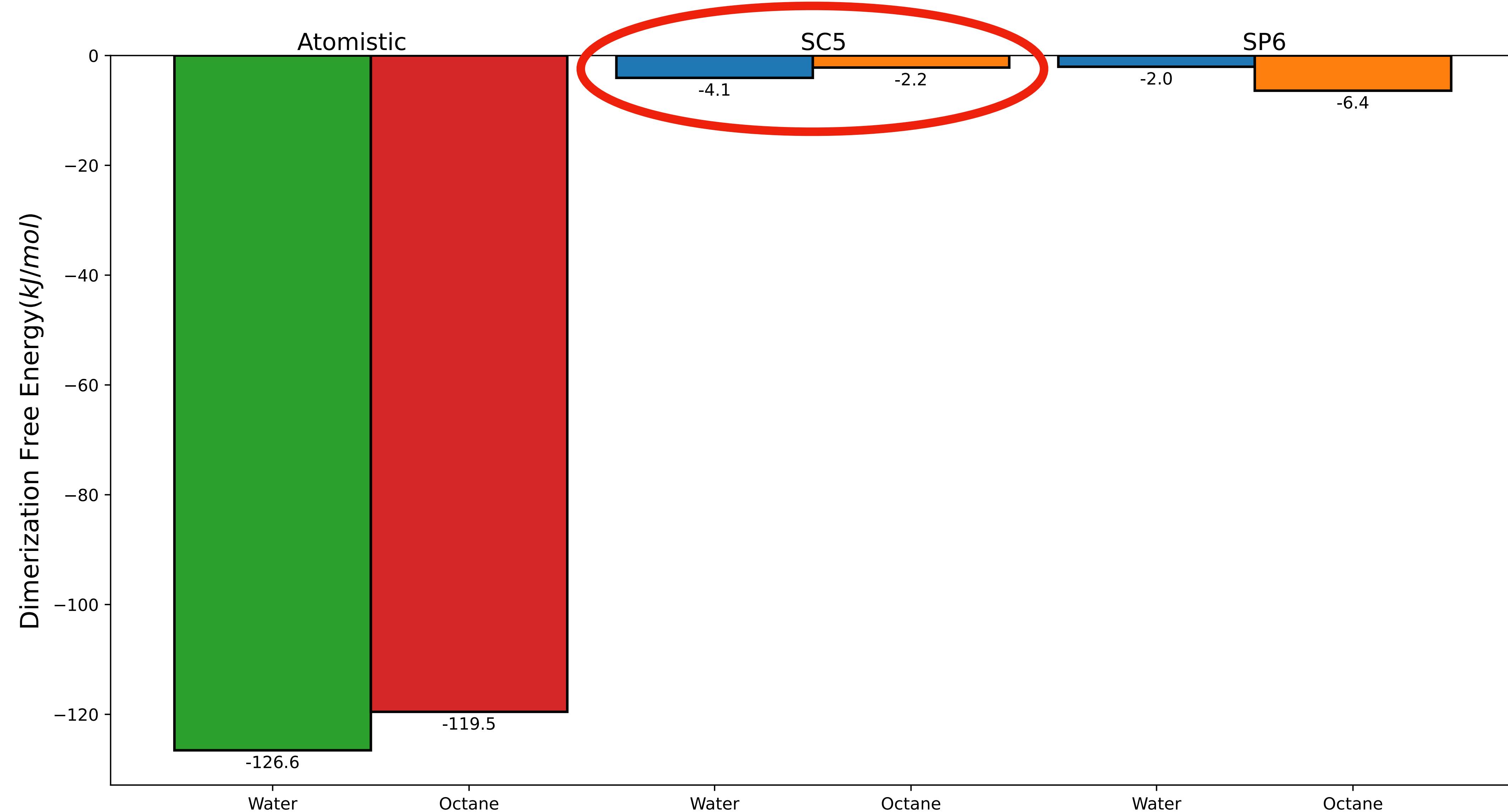
6 atoms

Match the oil-  
water rank



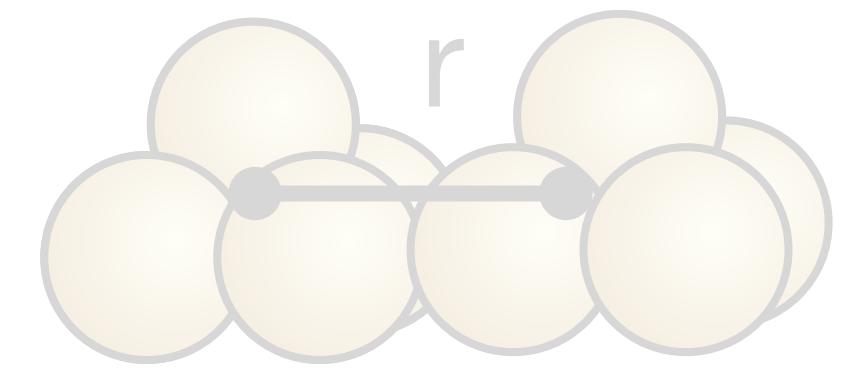
Step 2: Choose a  
base bead

# Choosing the right base bead

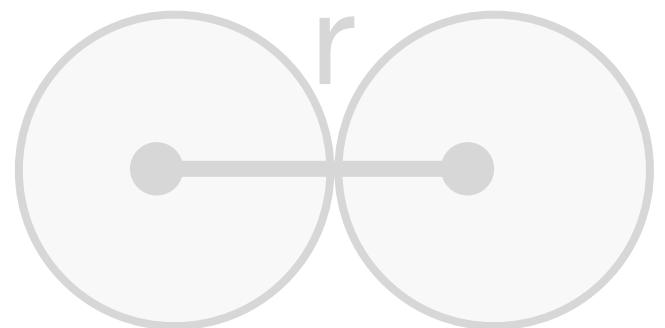


# The roadmap to developing gold

Match the radius

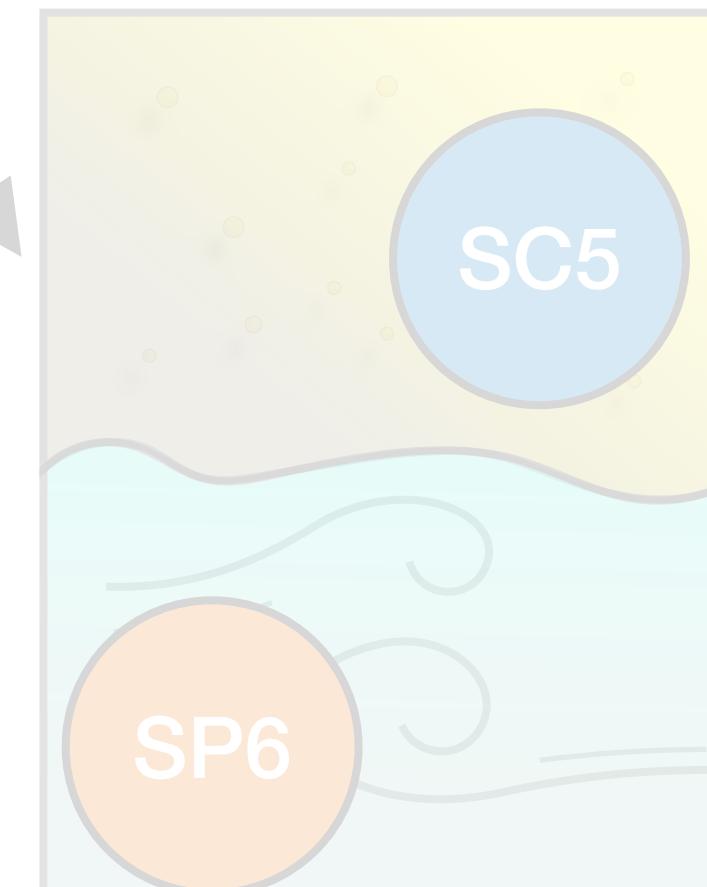


Step 1: Figure out  
how many gold atoms  
fit into a Martini bead



6 atoms

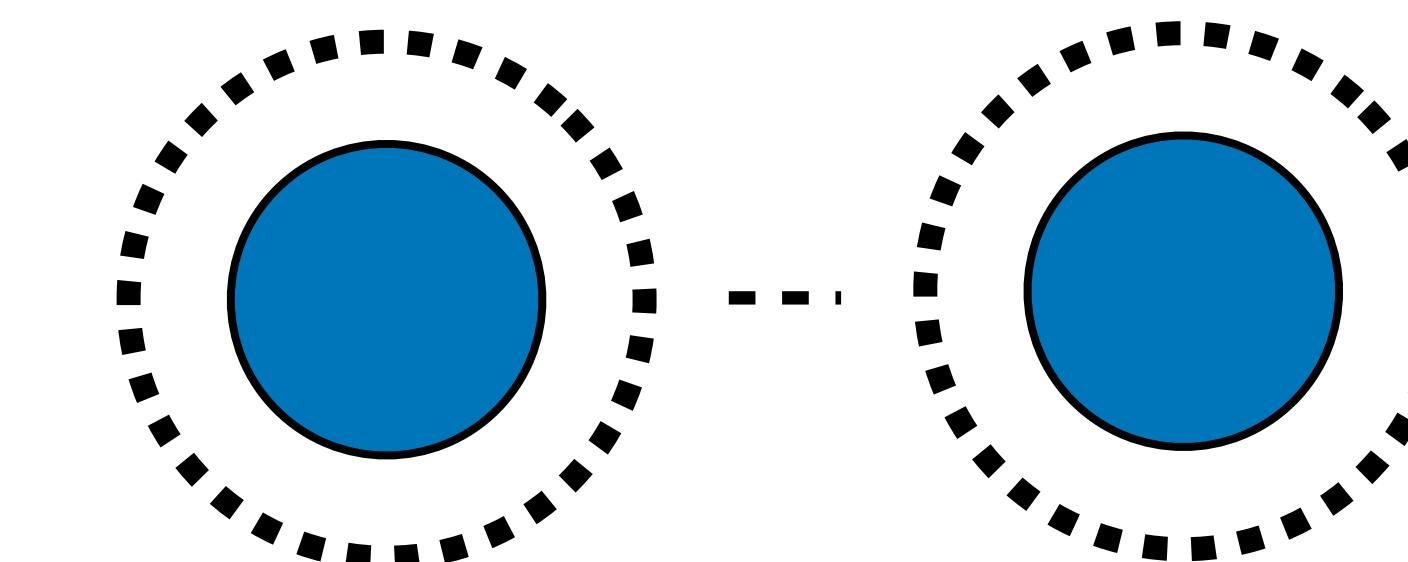
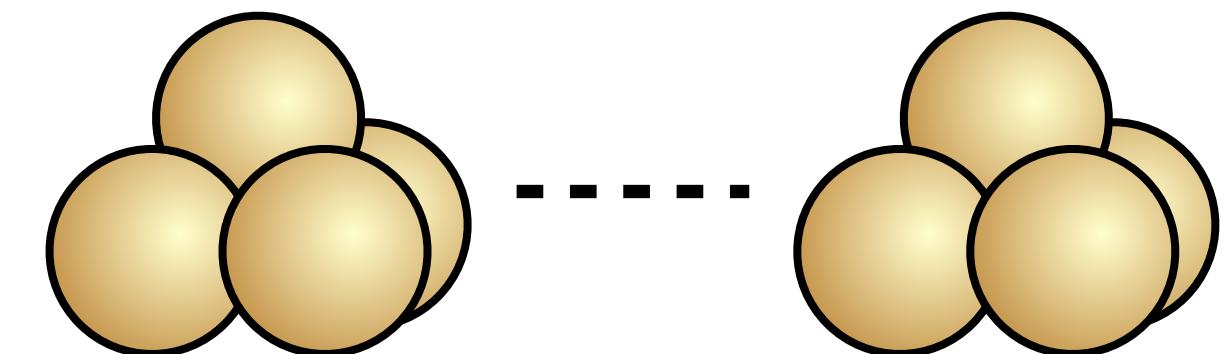
Match the oil-  
water rank



Step 2: Choose a  
base bead

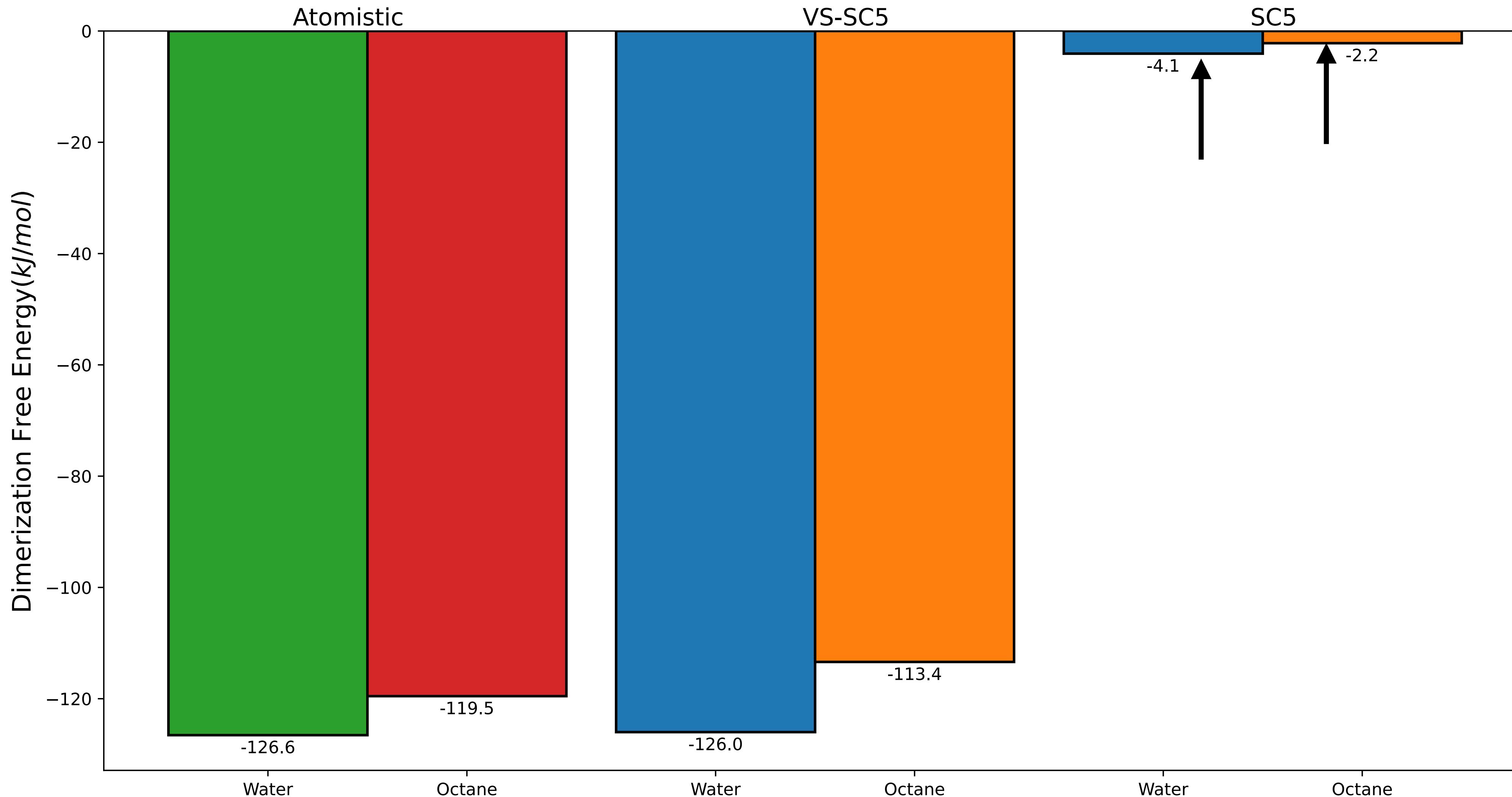
SC5

$$\Delta G_{dimer,CG} = \Delta G_{dimer,AA}$$



Step 3: Apply virtual  
sites and match  
dimerization free energy  
between clusters or  
beads

# Matching the dimerization free energy between AA gold cluster and virtual site bead

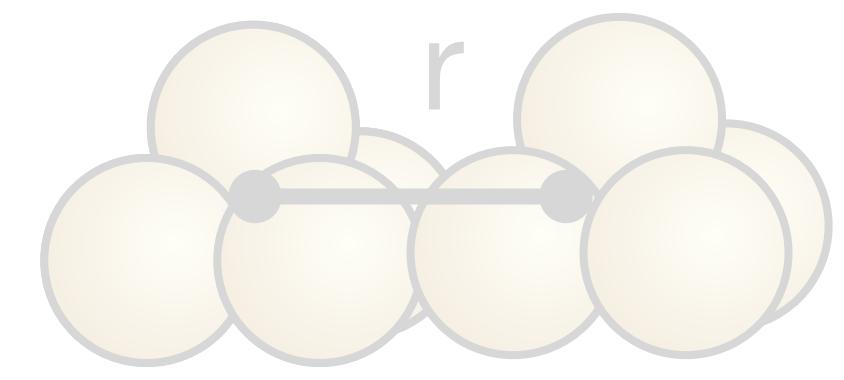


Virtual Site  
Modification

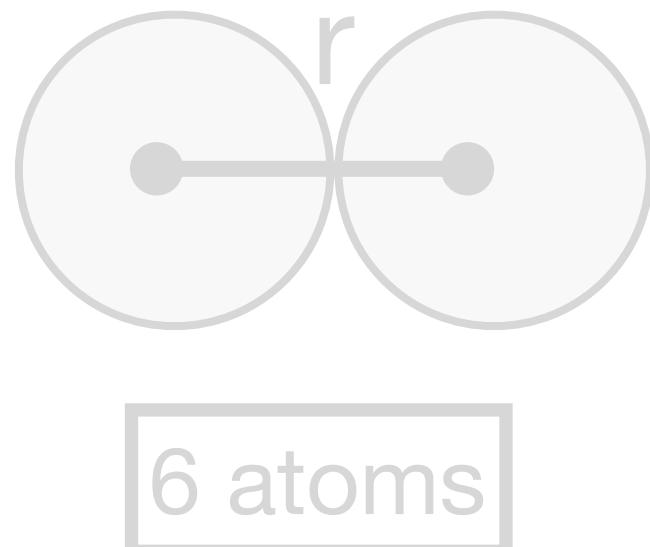
Strengthened gold-gold LJ interactions by about 60 times the original SC5-SC5 bead strength.

# The roadmap to developing gold

Match the radius



Step 1: Figure out how many gold atoms fit into a Martini bead



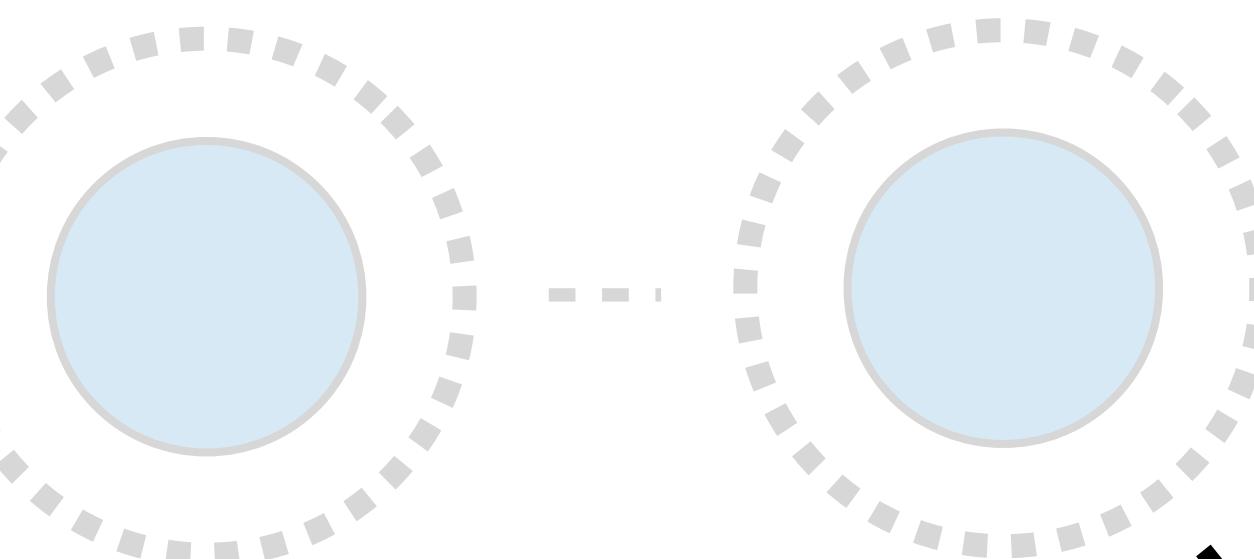
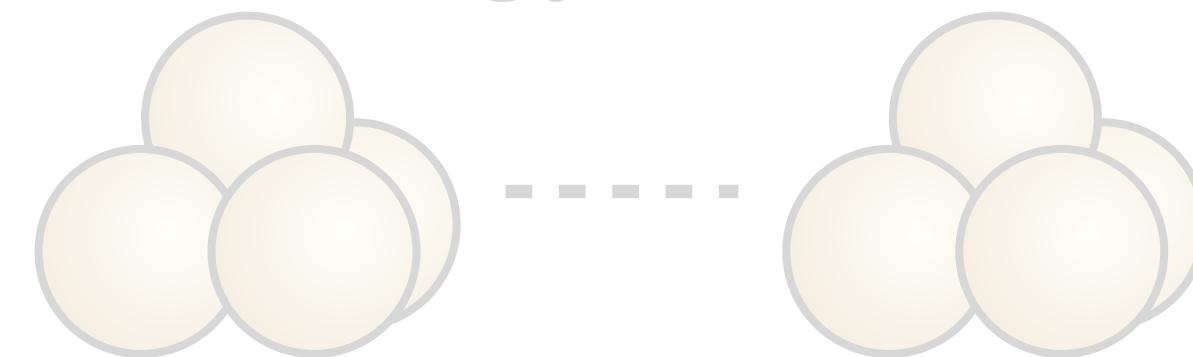
Match the oil-water rank



Step 2: Choose a base bead

SC5

Match the dimerization free energy



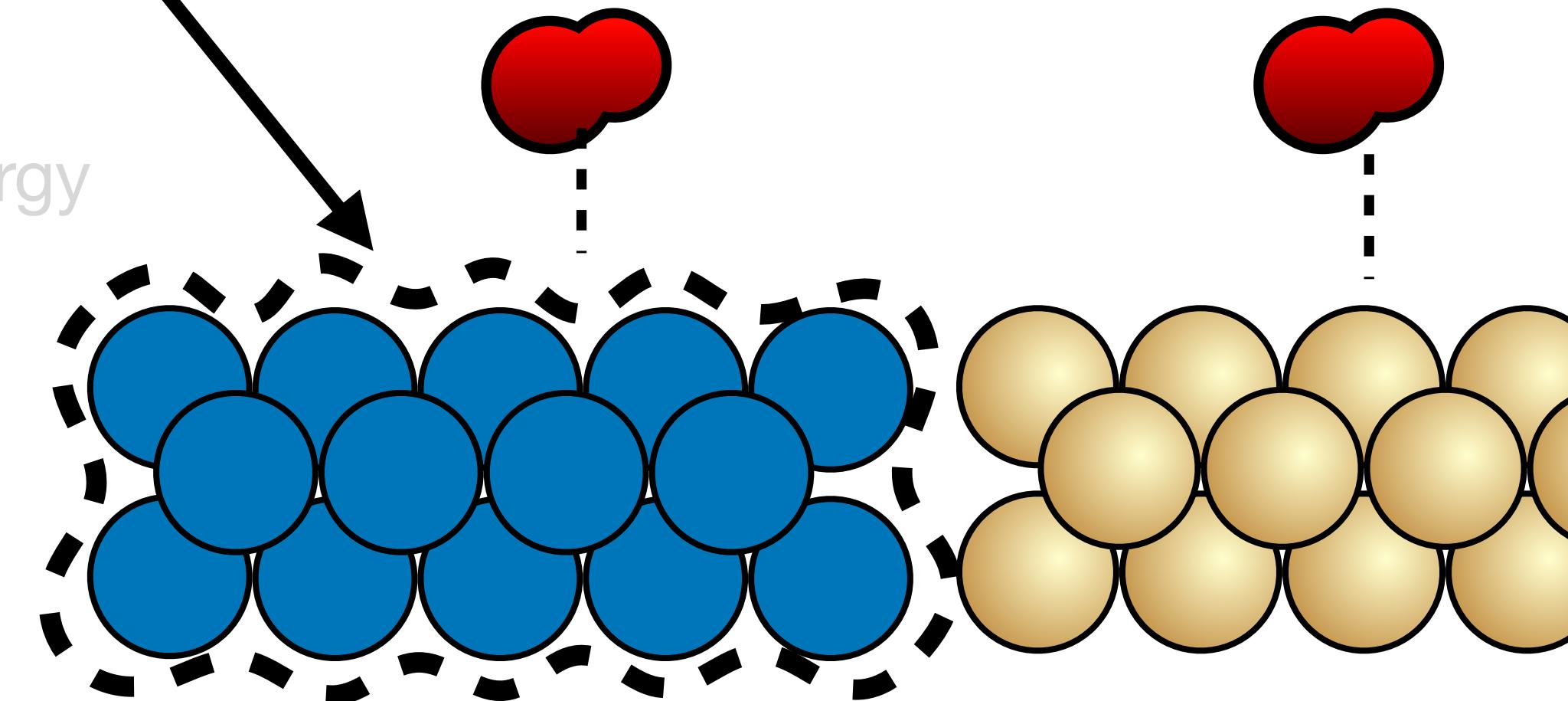
Step 3: Apply virtual sites and match dimerization free energy between clusters or beads

Approx. 120 kJ/mol

Martini Amino Acid Beads

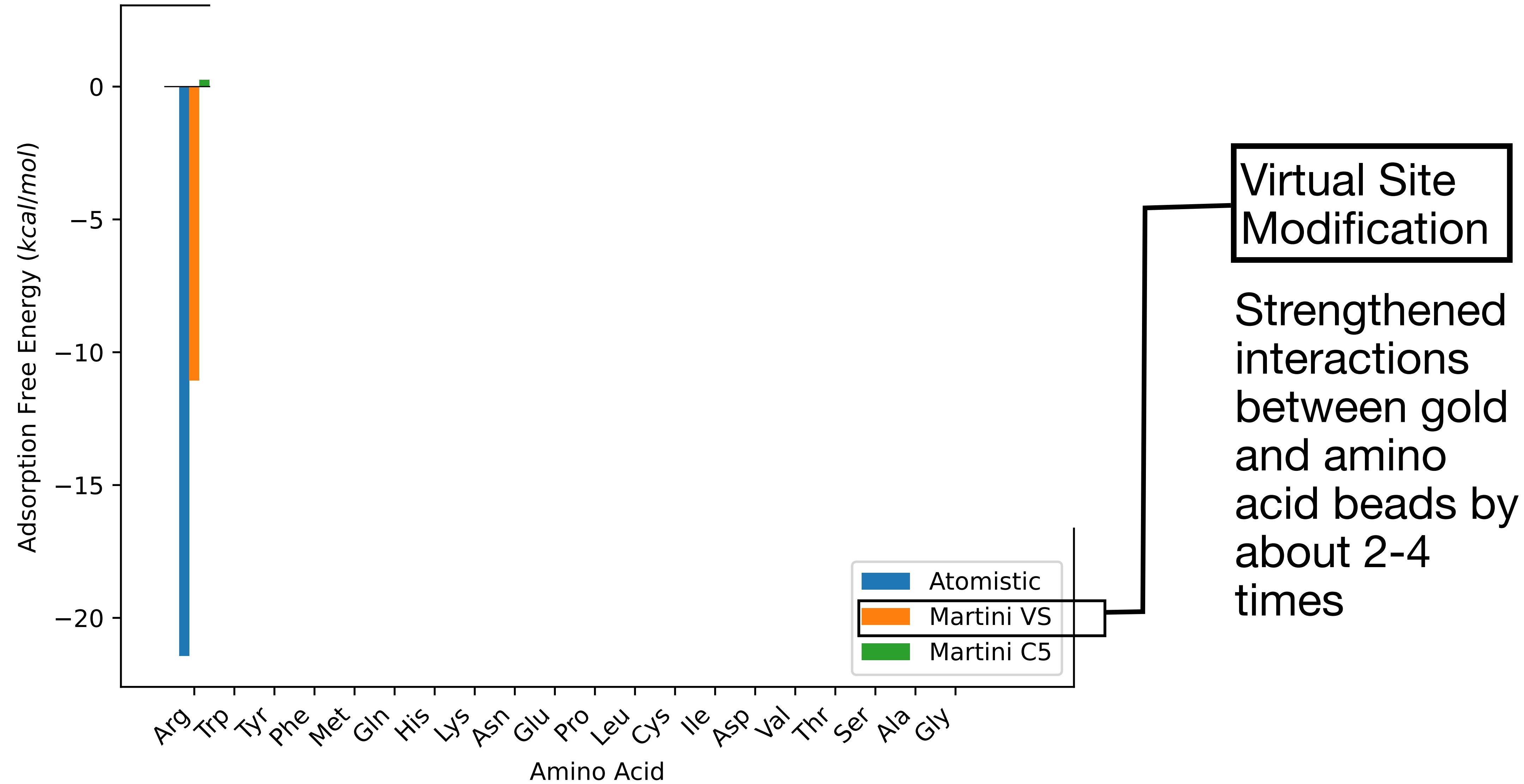
Q5n, P6, P5, P2, P1, SQ5n, SQ4p, SQ3p, SP5, SP2, SP1, SC4, SC3, SC2, TP1, TN6, TN6d, TN5a, TC6, TC5, TC4, TC3, TC2

$$\Delta G_{ads,CG} = \Delta G_{ads,AA}$$



Step 4: Match small molecule adsorption free energies

# Matching adsorption free energies of amino acids between AA and virtual site gold slabs



# Summary & model refinement

- Present a method for developing Martini metal parameters that relies on free energy comparisons to atomistic simulation
- Present a Martini model for gold that:
  - Matches 6 atom cluster size
  - Uses a virtual site as a base to modify LJ potentials
  - Matches dimerization free energies of atomistic gold clusters
  - Incorporates polarization effects into interactions with small molecules
- Further refinement of the model will include:
  - \* Adsorption free energies for Halogens, other charged molecules, etc...
  - \* Extrapolate interactions to the entire Martini Matrix
  - \* Comparison to experimental data

# Acknowledgements



- Dr. Paulo C.T. Souza
- Dr. Grace Brannigan
- Dr. Siewert-Jan Marrink
- Regina Salzer
- Dr. Julianne Griepenburg



22



National  
Science  
Foundation

