

# Molecular Visualization

Pere-Pau Vázquez  
ViRVIG Group – UPC

# Outline

- Introduction & background
- Computer Graphics Challenges
- Visualization Challenges
- Examples

# Outline

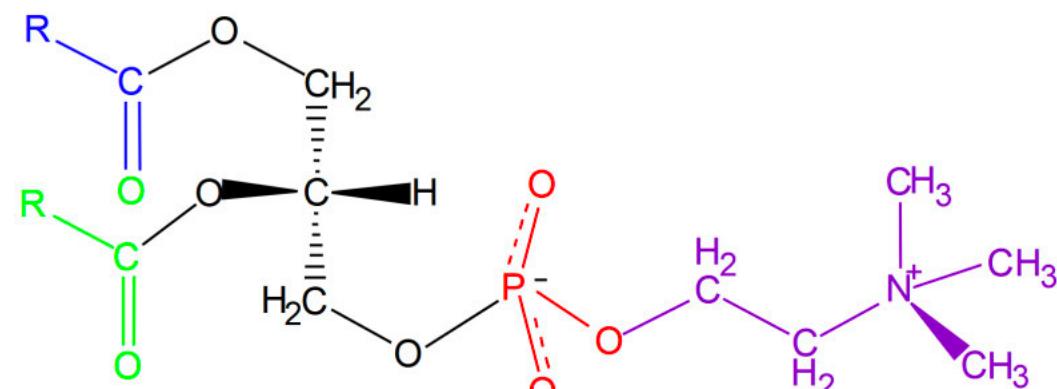
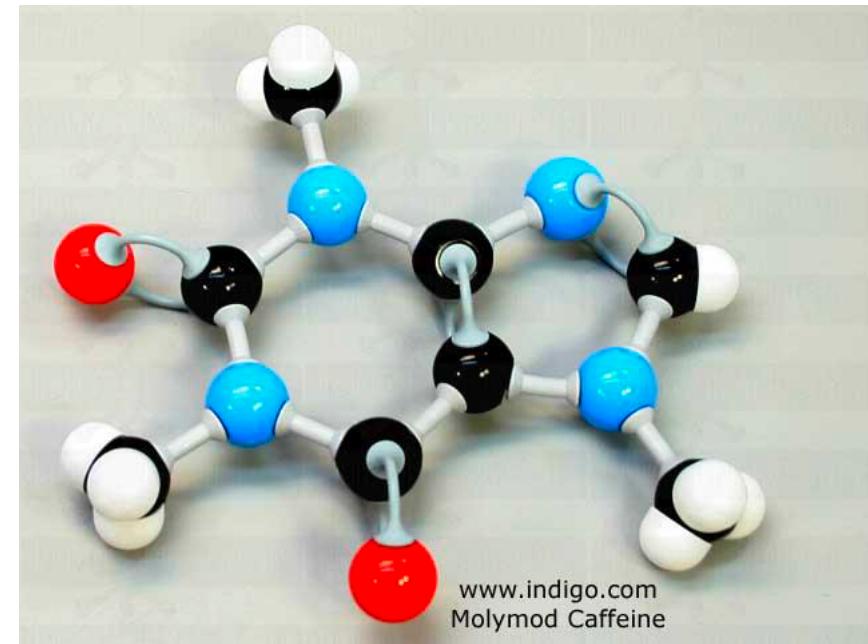
- **Introduction & background**
- Computer Graphics Challenges
- Visualization Challenges
- Examples

# Introduction & background

- Molecules are sets of atoms
  - With certain properties
    - Might be interested in visualizing
  - With certain arrangements
    - Might be interested in visualizing
  - With certain interactions
    - Might be interested in visualizing

# Introduction & background

- Molecules
  - Atoms (117 chemical element)
    - Protons and electrons
  - Bonds (e.g., covalent, disulfide, hydrogen)
- Small molecules & ions
  - Lipids (membranes)
  - Ligands/metabolites
  - Solvent molecules (e.g., water)
  - etc.



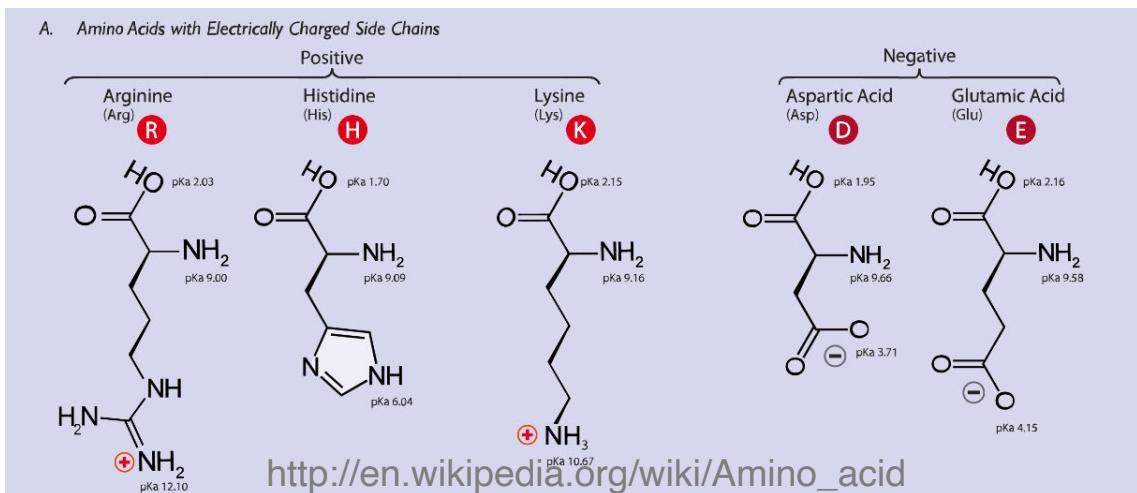
<http://en.wikipedia.org/wiki/Phospholipid>

# Introduction & background

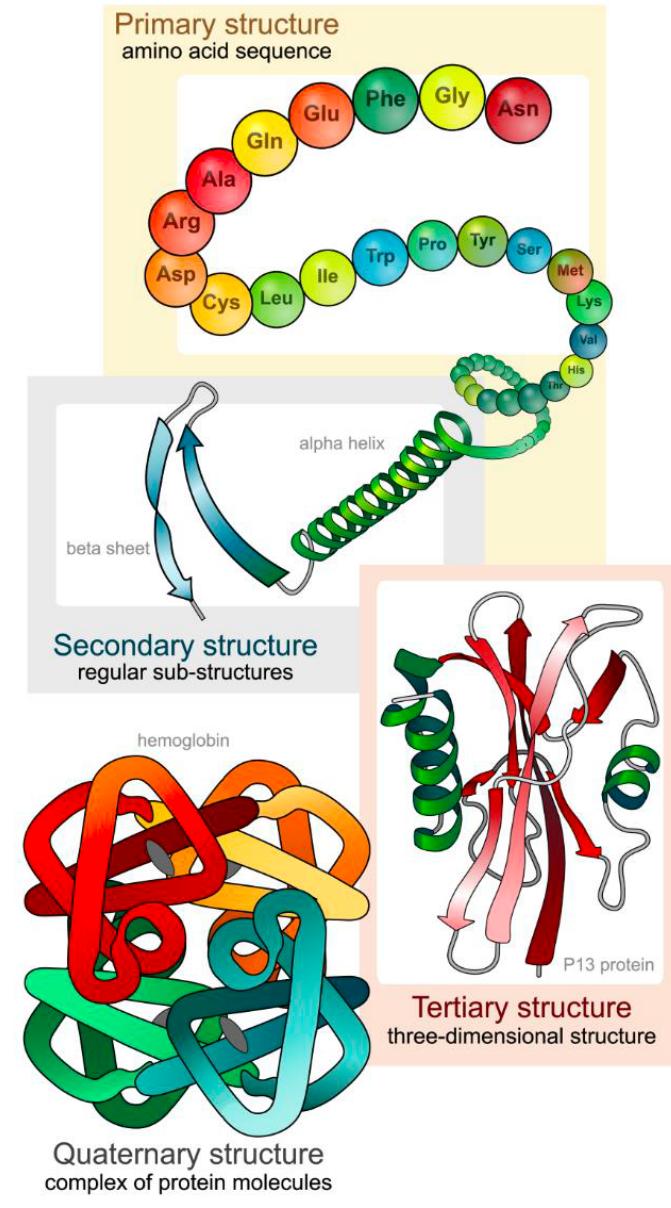
- Proteins
  - Sequences of residues
    - Each residue can be one of a set of 20 possible aminoacids.
  - All residues are divided into
    - The backbone
    - The side chain
    - This structure is based on a scaffold of  $\alpha$ -helices and  $\beta$ -sheets, kept in place by a network of internal h-bonds between backbone atoms

# Introduction & background

- Proteins
  - Building blocks of the „machinery of life“
  - Consists of amino acids
    - One or more linear chains of amino acids that form a functional complex
  - Secondary Structure (helix, sheet, turn, coil)

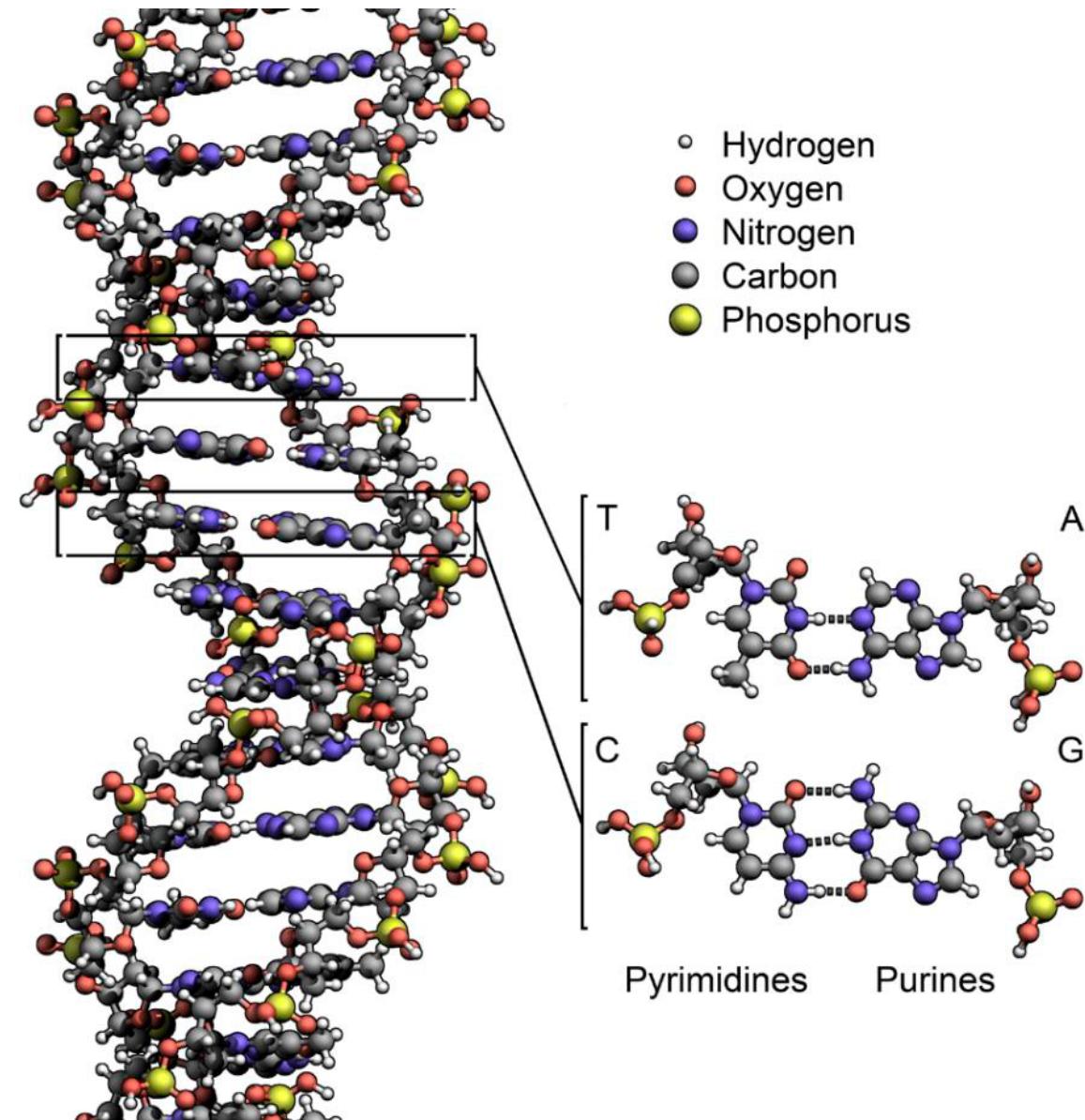


up, UPC



# Introduction &

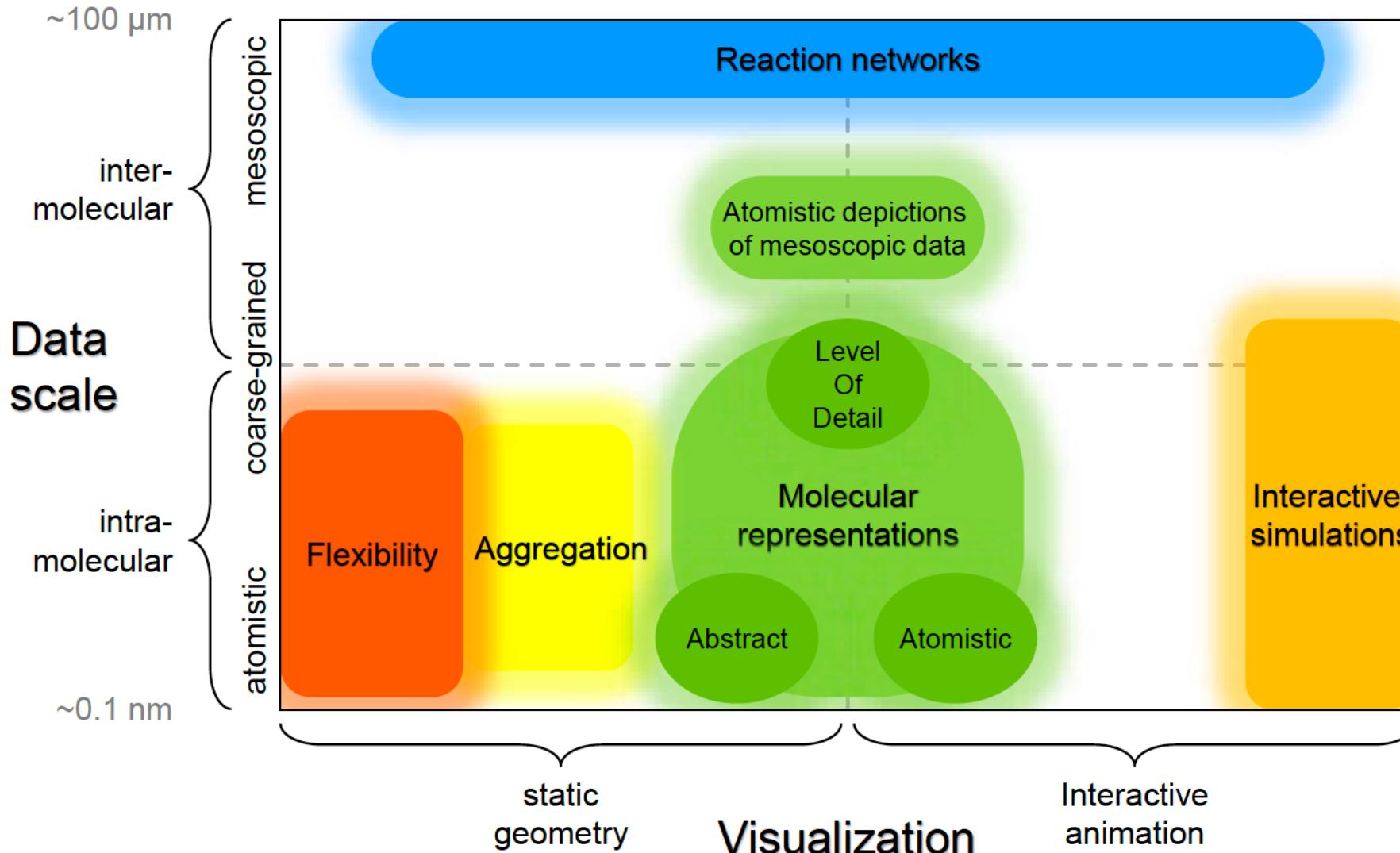
- DNA & RNA
  - DNA stores the “genetic code”
    - Blueprint for proteins
  - Chain of nucleotides
    - Sugar backbone (Desoxy-/Ribose)
    - Phosphate
    - Nucleobase
      - cytosine, guanine, adenine, thymine/uracil)
  - 3 nucleotides encode 1 amino acid



<http://en.wikipedia.org/wiki/DNA>

# Introduction & background

## Taxonomy



# Introduction & background

- Molecular Simulations (MS):
  - Use computers to simulate whether a small molecule (ligand) can bind to a larger biomolecule (the protein)
    - Activate or inhibit a certain biomolecule function
  - Ligands developed to provide a therapeutic benefit for the patient
  - Result is a trajectory
    - Atoms' positions
    - Energy of the system
      - E.g. solvation, Coulomb electrostatic

# Introduction & background

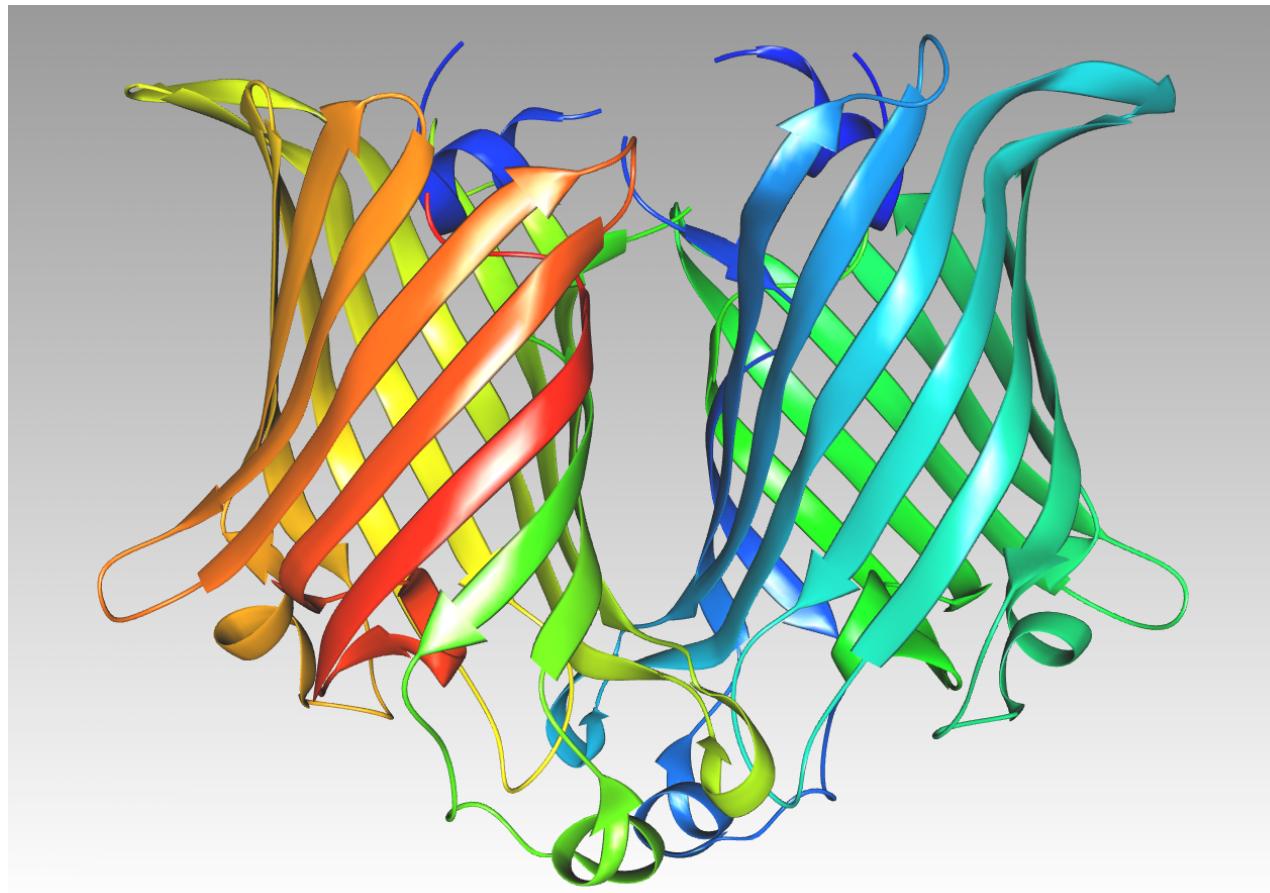
- Simulation energy
  - Strength of the binding (aka binding affinity)
  - Can be approximated as the sum of the interaction energies between the protein residues and ligand
  - Low level conformations are more stable
  - Three main types (additive):
    - Van der Waals (short range)
    - Electrostatic energy in the vacuum (long-range)
    - Screening of that electrostatic energy due to the solvent

# Introduction & background

- Root Mean Square Fluctuation
  - Average fluctuation of a residue's atom around a reference position
  - Induced by the potential energies of interaction
  - Residues with high RMSF may indicate that they move to interact with the ligand guiding it towards the binding site
  - Its units are angströms

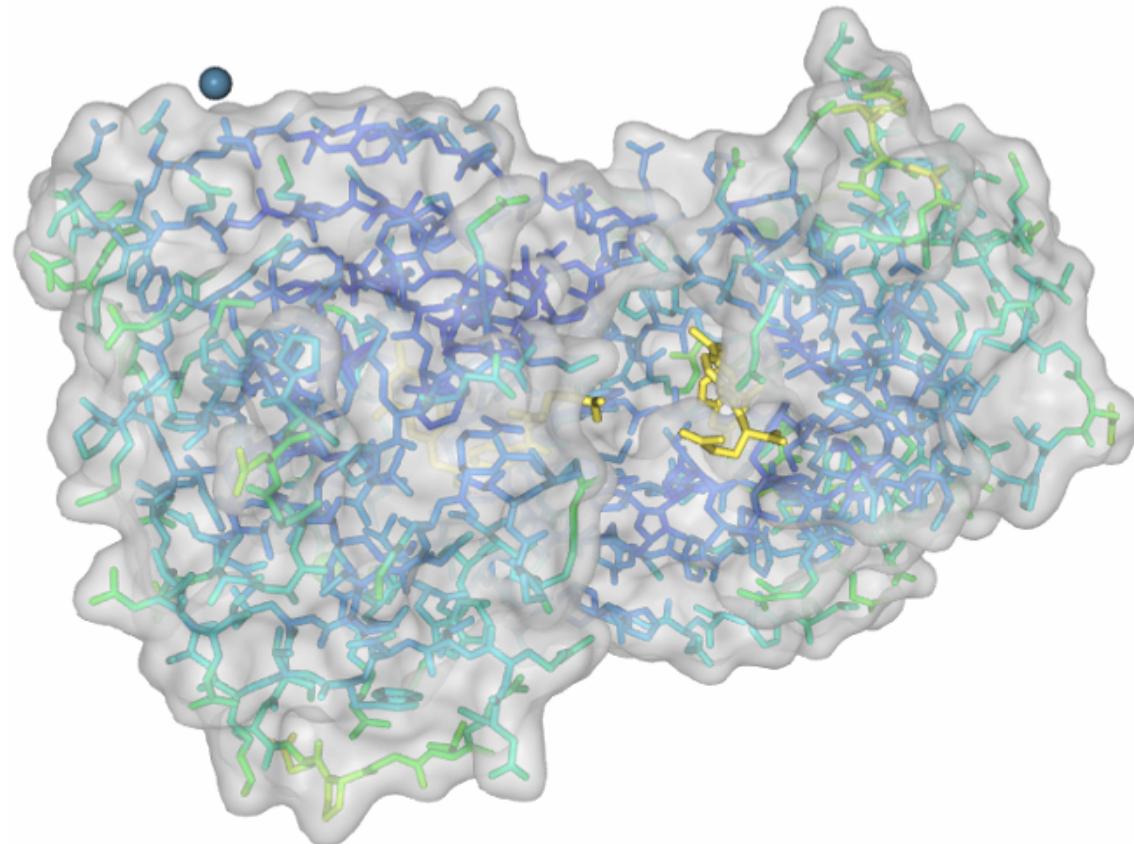
# Introduction & background

- Molecular representations



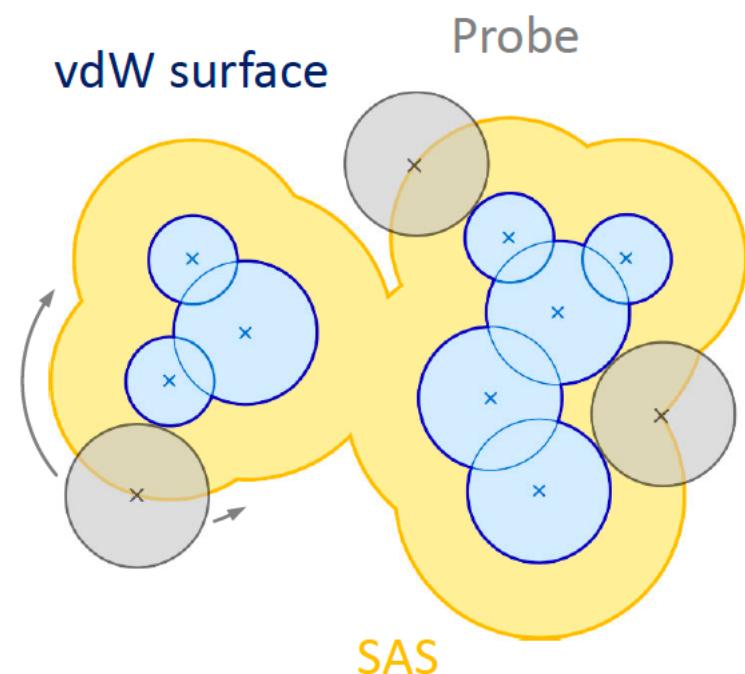
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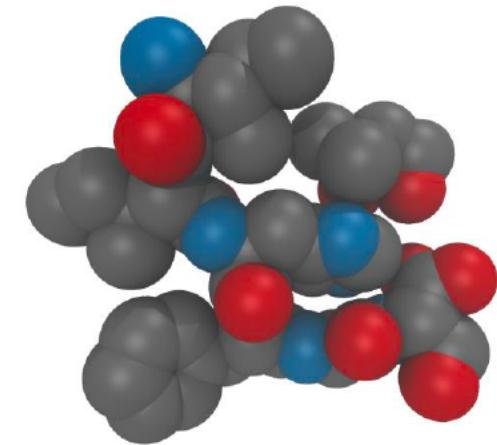
# Introduction & background

- Van der Waals (vdW) surface
  - vdWradius: distance between non-bonded atoms
  - Molecular volume
  - Does not consider ligands or solvent molecules
- Solvent Accessible Surface (SAS)
  - Surface with respect to a certain solvent radius
    - Interior not reachable by solvent
  - Theory: Rolling probe (radius  $r_p$ )
  - Practice: Inflation of vdWradius by  $r_p$
- Rendering via GPU ray casting

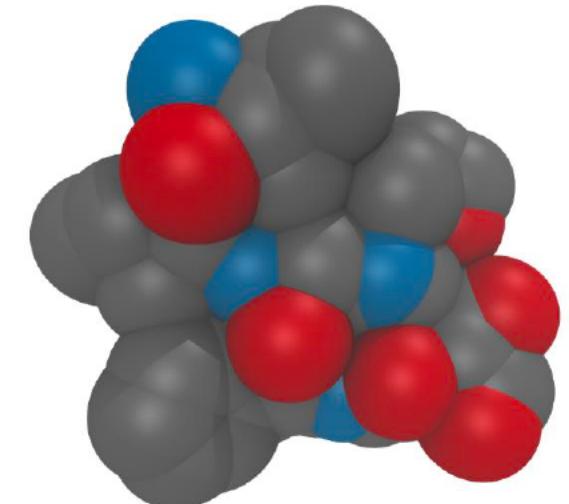


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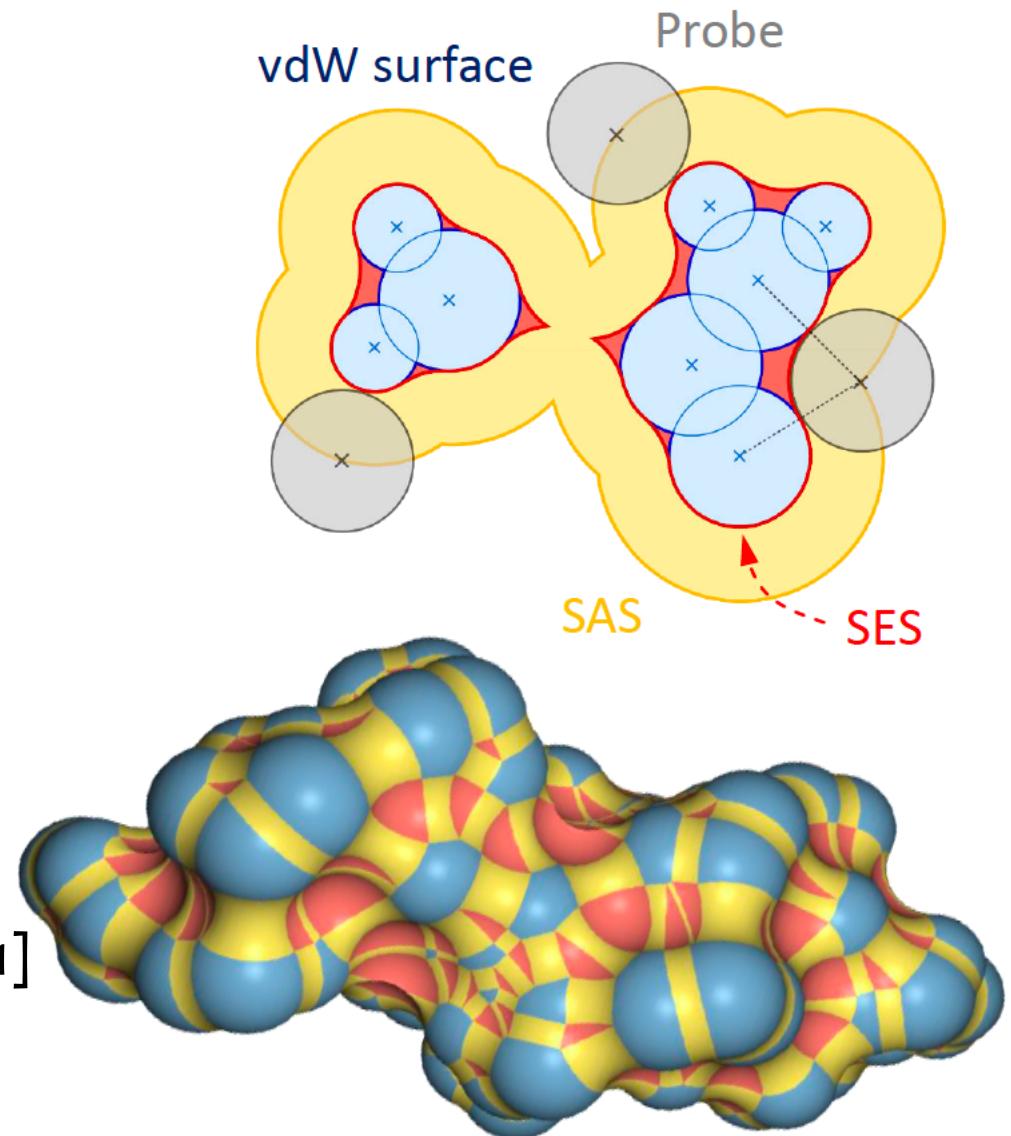
vdW surface



SAS

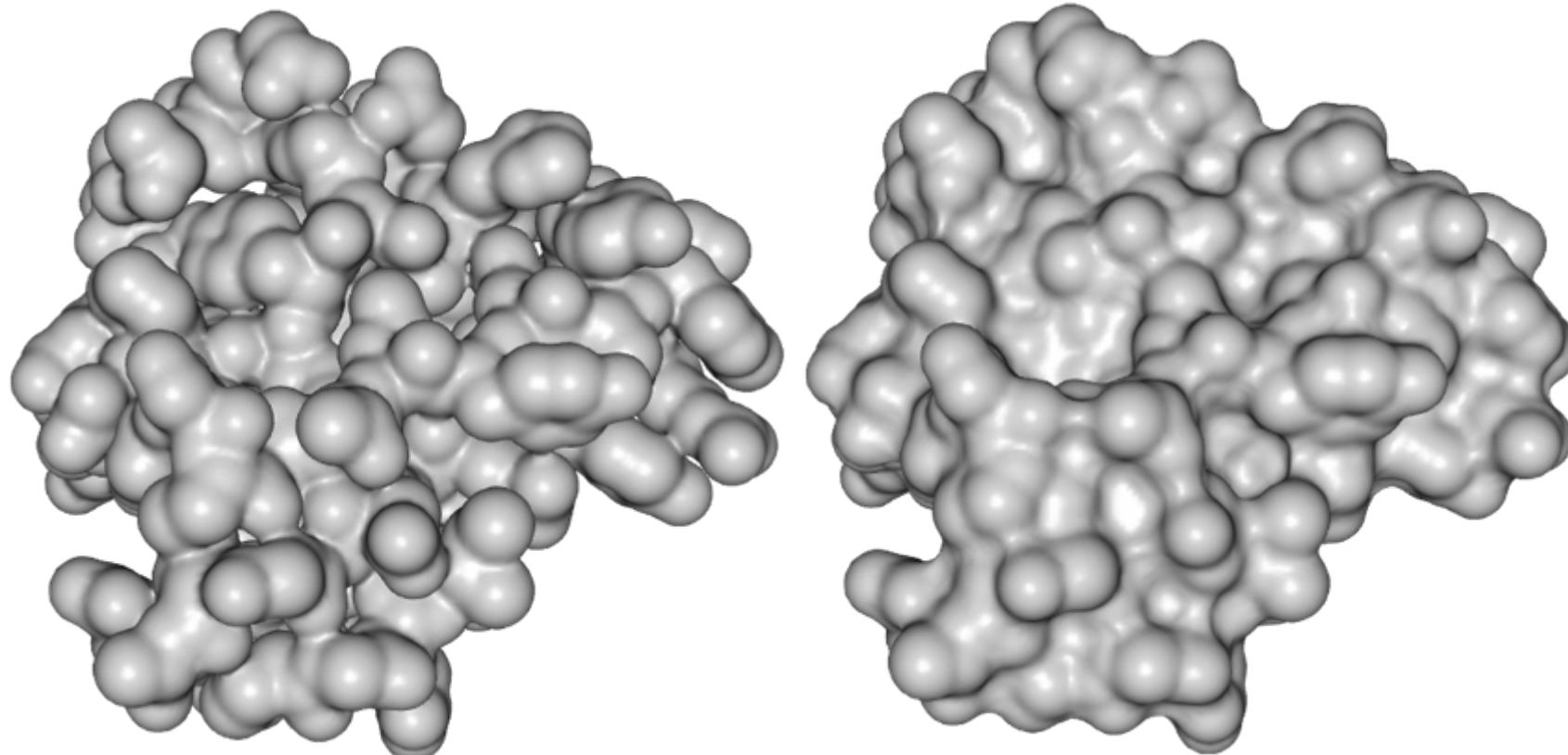
# Introduction & background

- Defined by rolling probe of radius  $r_p$ 
  - Probe surface traces out SES
- Smooth, tight surface
  - Boundary with respect to solvent
  - No inflation (molecular volume is preserved)
- Three types of patches
  - Concave spherical triangles
  - Convex spherical patches
  - Saddle-shaped toroidal patches
- Parallel computation
  - Interactive for 100k atoms
  - CPU [Lindow et al. 2010] or GPU [Krone et al. 2011]



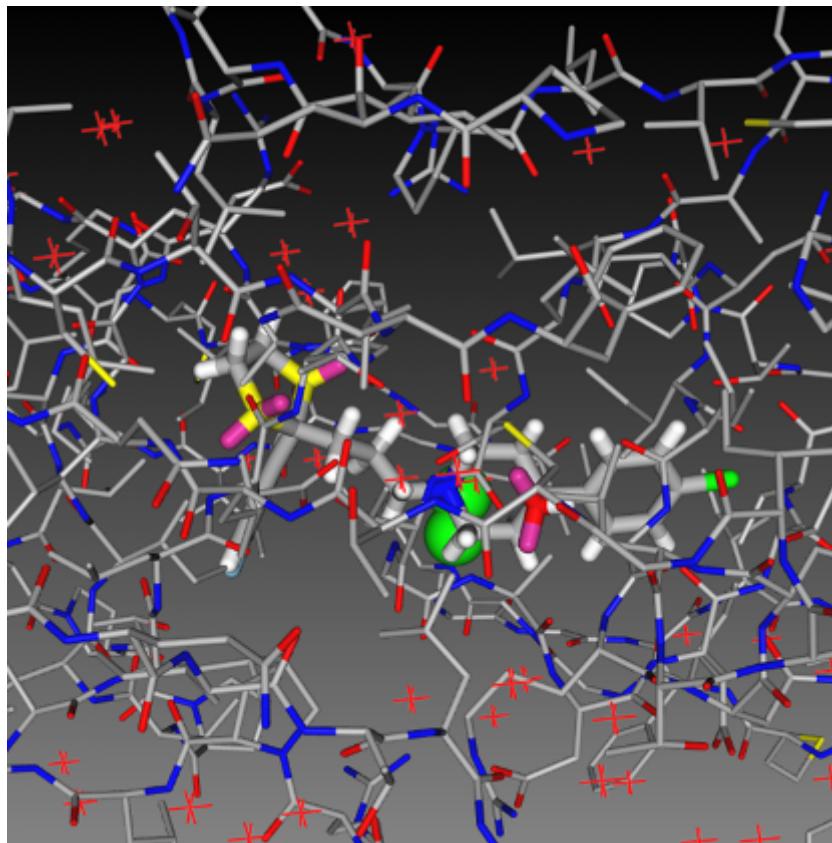
# Introduction & background

- Molecular representations



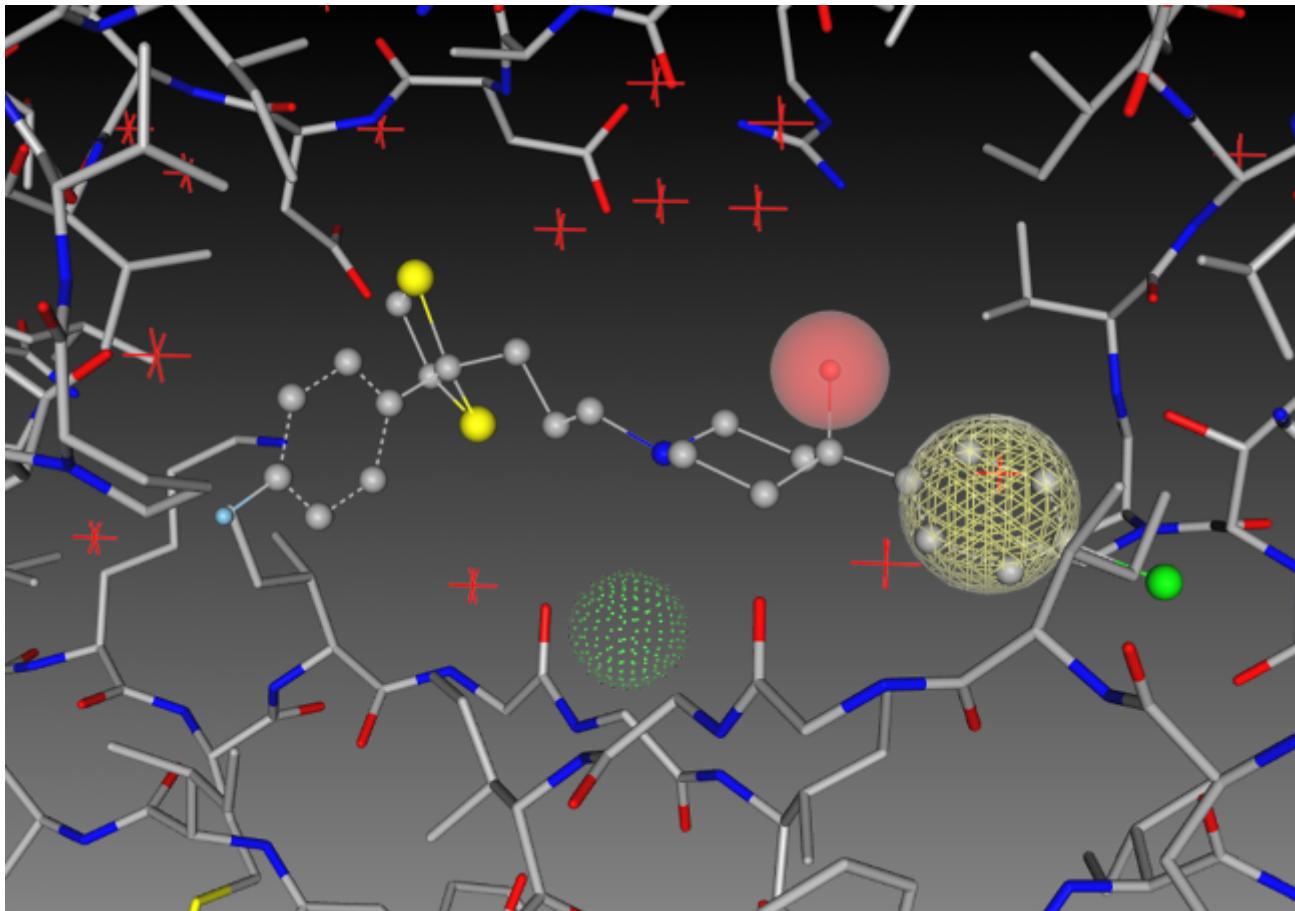
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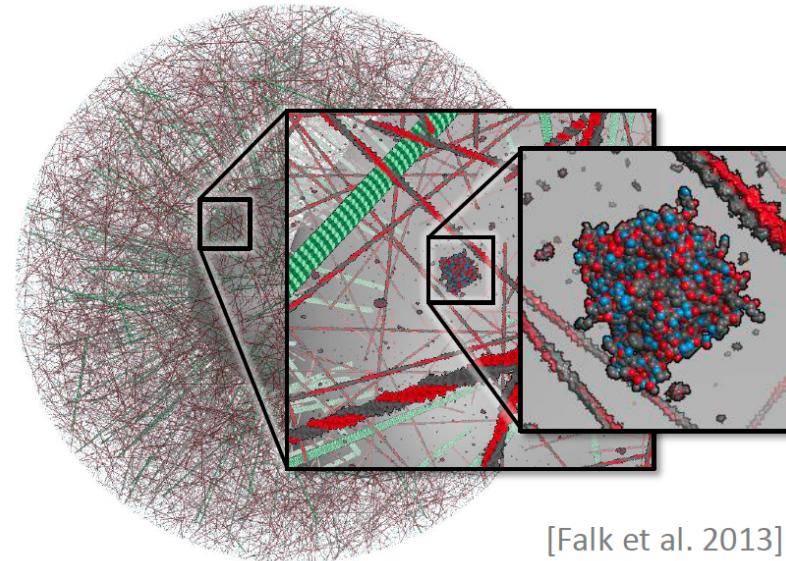
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- Molecular representations

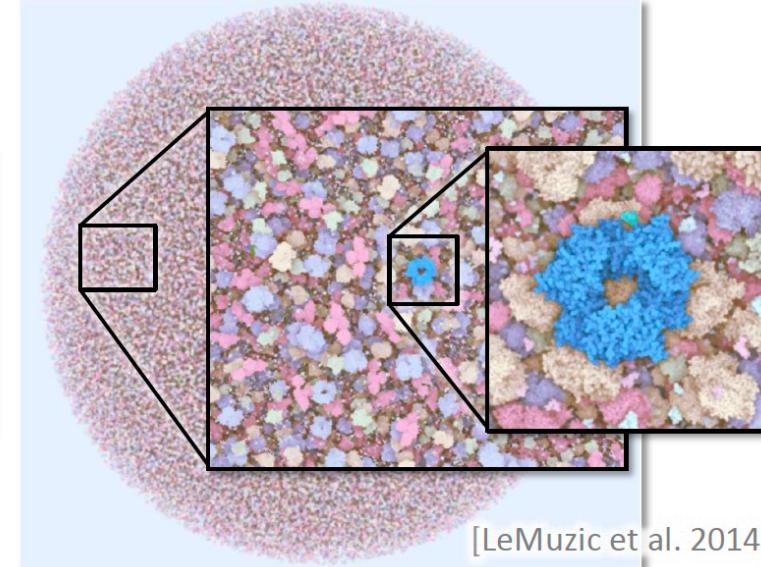


# Introduction & background

- Molecular representations: Structural Level of Detail
  - Derive all-atom representation from coarse-grained simulations
    - Cellular environment: Many instances of the same molecules
    - Special GPU-accelerated rendering methods
    - Interactive rendering of up to 10 billion particles



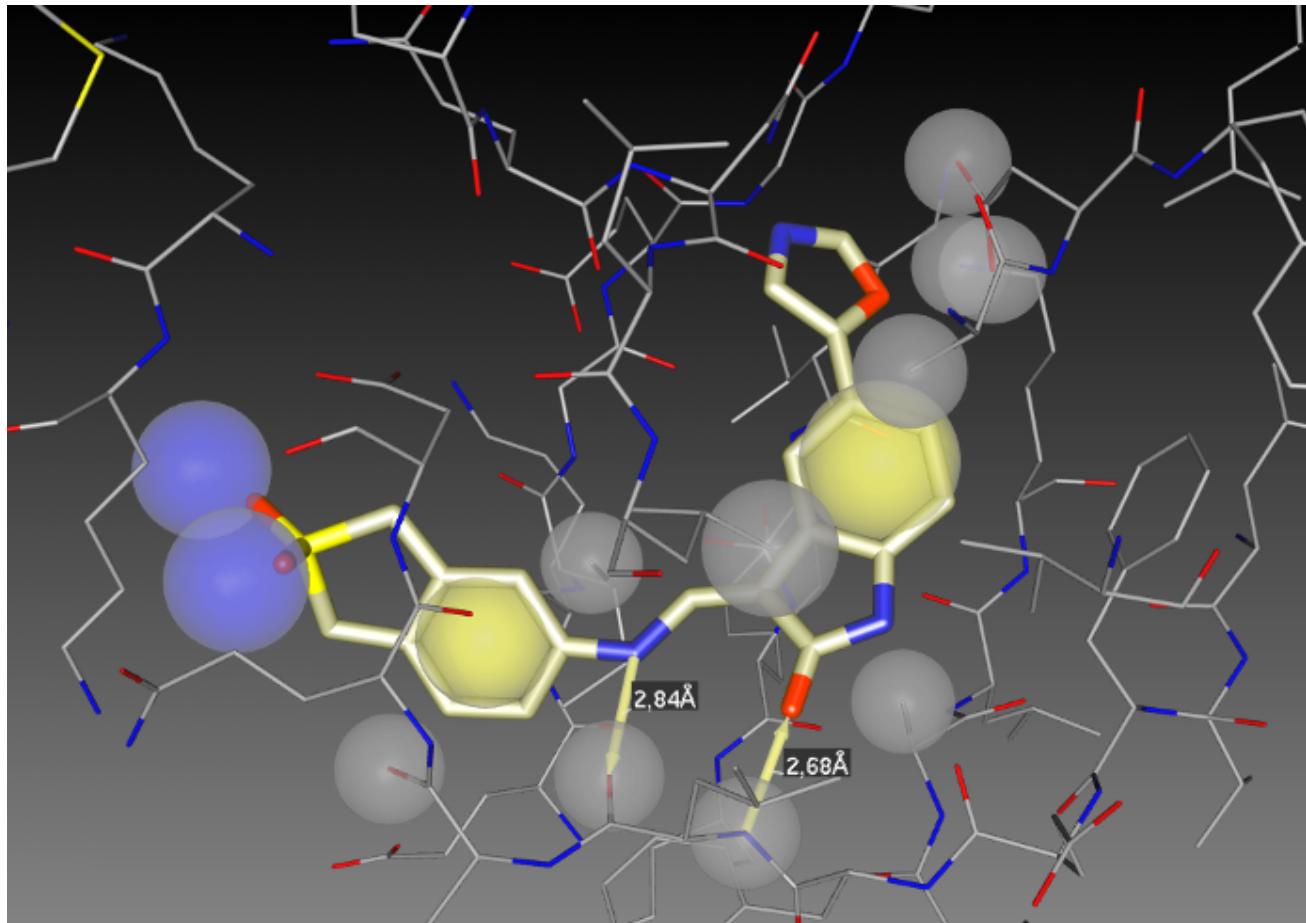
[Falk et al. 2013]



[LeMuzic et al. 2014]

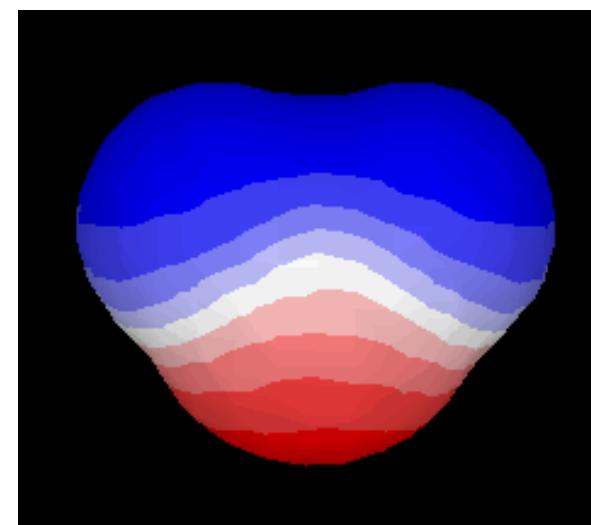
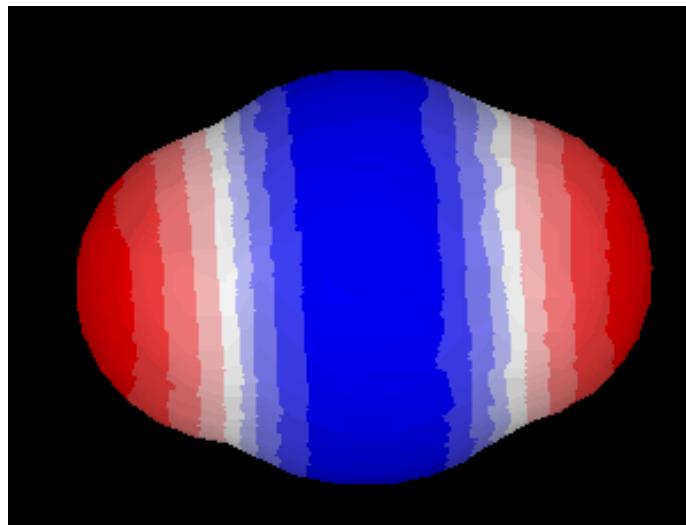
# Introduction & background

- Molecular properties



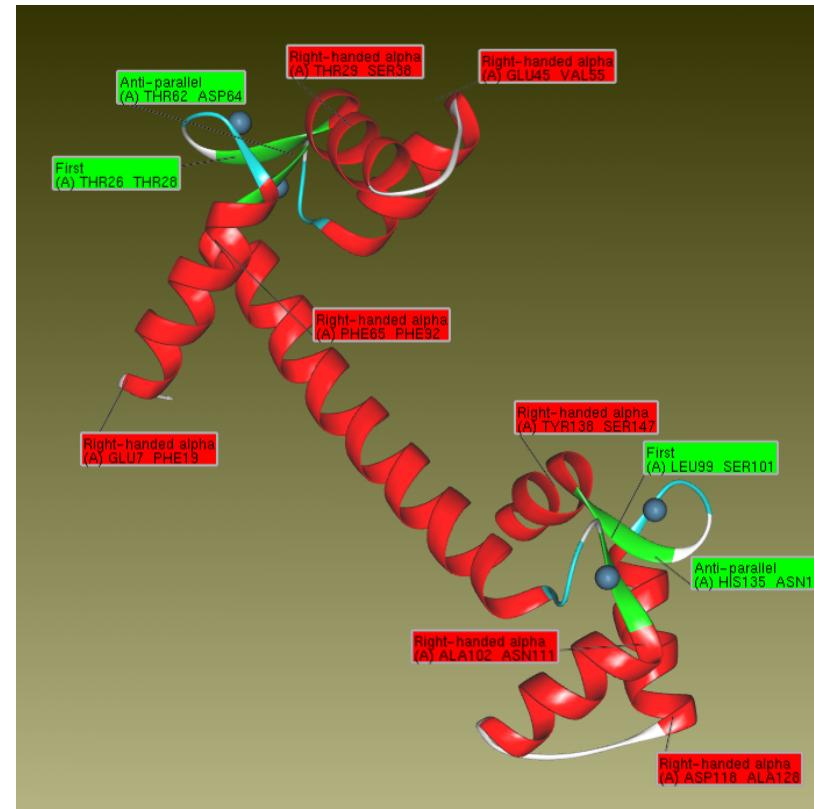
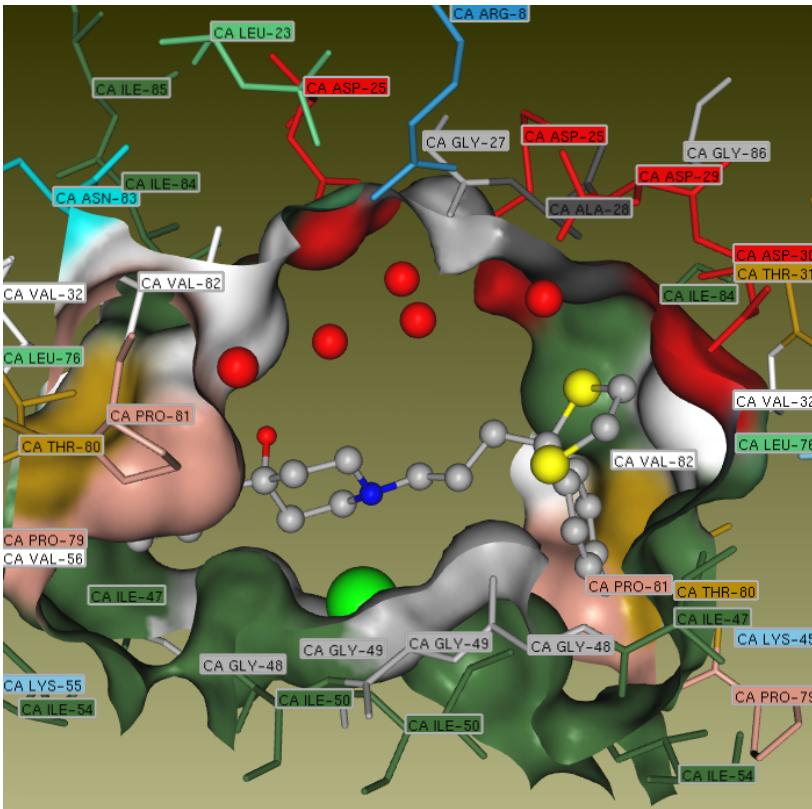
# Introduction & background

- Molecular properties
  - Molecular geometry and polarity using electrostatic potential maps



# Introduction & background

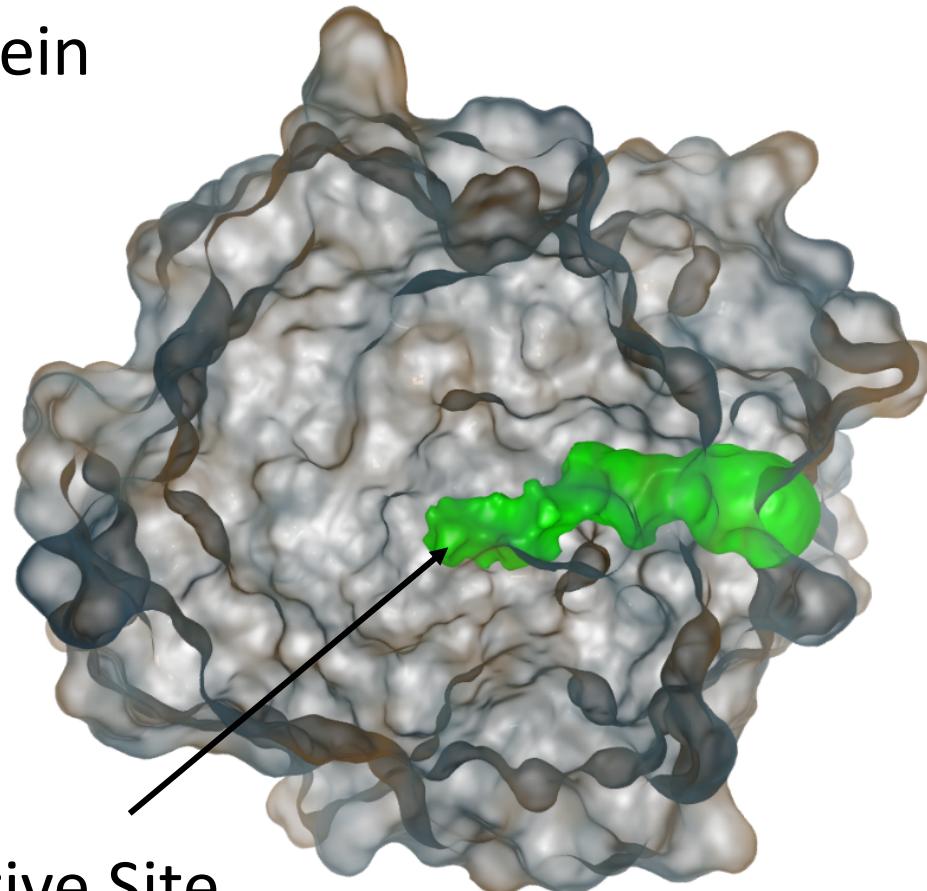
- Molecular properties



# Introduction & background

- Molecular properties

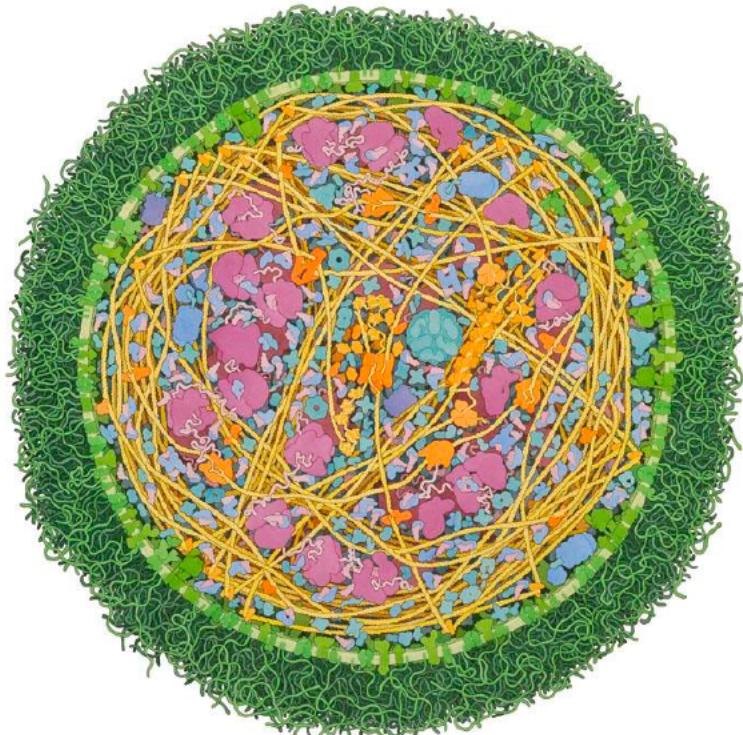
Protein



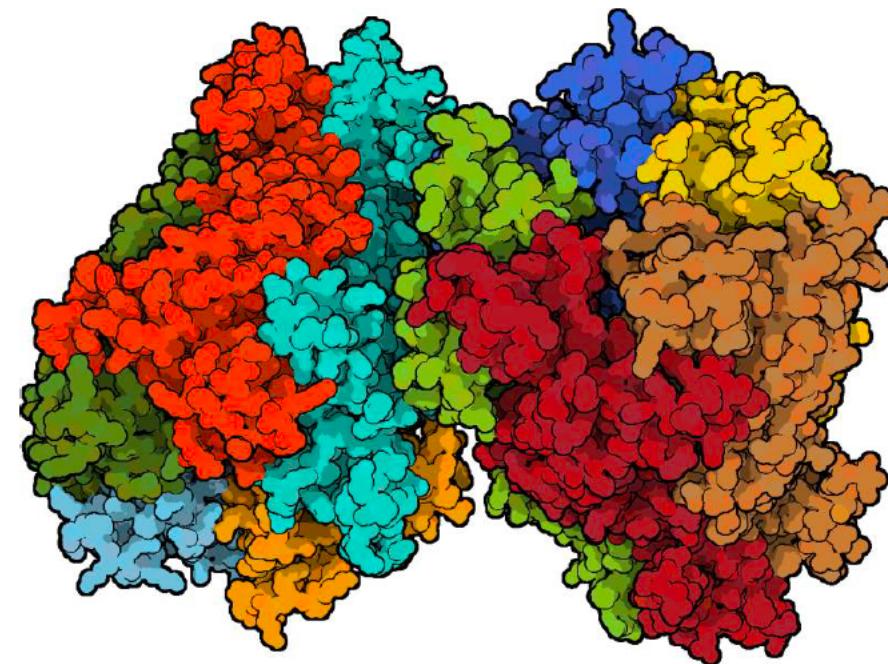
Active Site

# Introduction & background

- Rendering: Artistic



Mycoplasma cell  
[Goodsell]

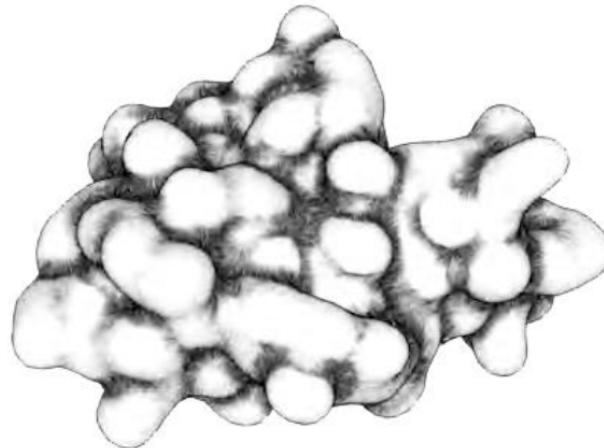


B-Raf protein rendered in MegaMol  
[Grott et al. 2015]

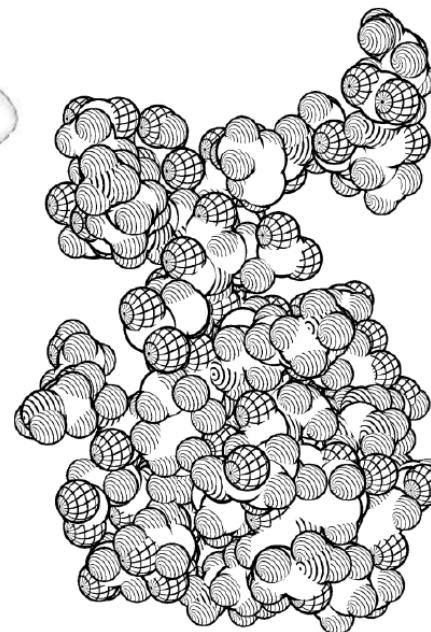
# Introduction & background

[van der Zwan et al. 2011]

- Rendering: Hand-drawn like



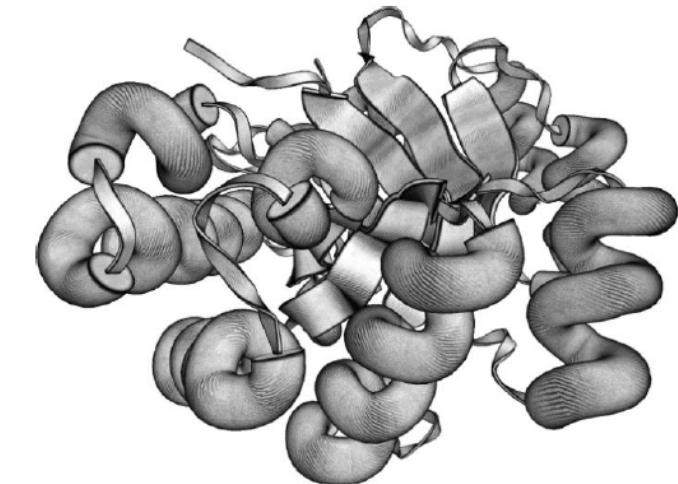
molecular surfaces  
[Lawonn et al. 2014]



space filling models  
[van der Zwan et al. 2011]



cartoon representations



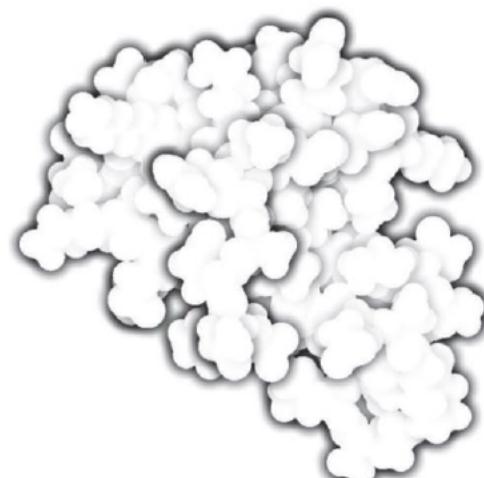
[Weber 2009]

# Introduction & background

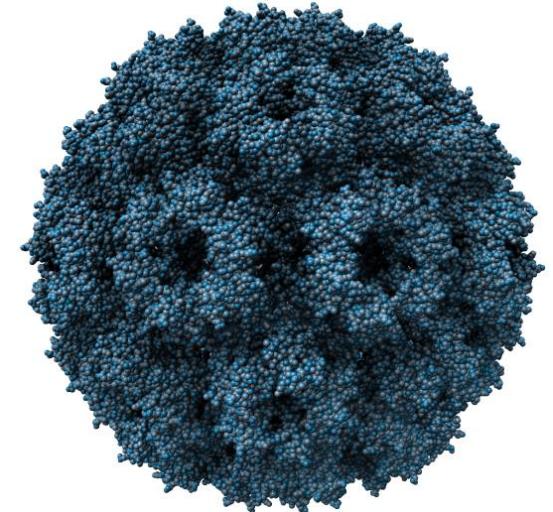
- Rendering: CG-based techniques
  - Ambient occlusion
  - Depth of field
  - Silhouettes
  - Halos...



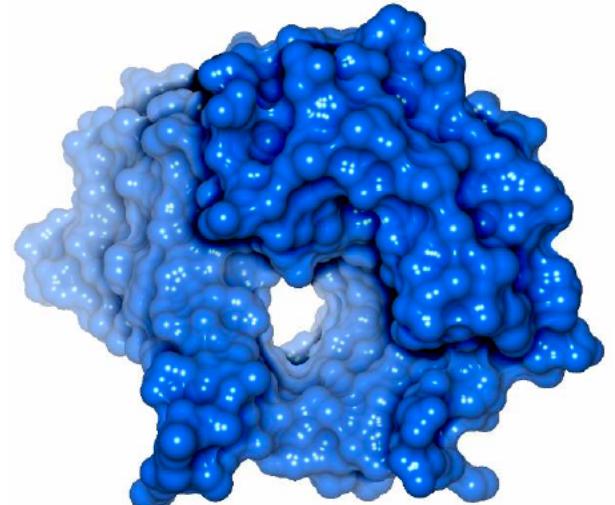
[Tarini et al. 2006]



JPC



[Grott et al. 2012]



[Krone et al. 2009]

# Outline

- *Introduction*
- **Computer Graphics Challenges**
- Visualization Challenges
- Examples

# Computer Graphics Challenges

- High number of triangles
  - From several thousands to million atoms
    - Each atom many triangles
    - Scales badly!
  - Techniques to:
    - Simplify: Reduce number of triangles
    - Use impostors
    - Cluster
- Dynamic information
  - Difficult to use acceleration techniques
  - Ad-hoc techniques using GPU tricks

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# Visualization Challenges

- Improve the overall perception
  - Models may be complicated
    - Structure is difficult to perceive
    - Relationship between protein-ligand difficult to see

# Visualization Challenges

- Improve the overall perception
  - Specific techniques to:
    - Improve shading (e.g. ambient occlusion)
    - Depict boundaries
    - Element of interest enhancement
- Examples:
  - AO and edge cueing (Tarini et al. 2006)
  - Dynamic AO & halos (Hermosilla et al., 2015)

# Visualization Challenges

- Depict the properties
  - Initial model is 3D
    - Quite complicated/cluttered/depth-complex initial view
  - Need to add information at different levels
    - Surface properties
    - Space properties/attributes
    - Difficult to add over the rendering

# Visualization Challenges

- Depict the properties
  - Specific techniques to:
    - Focus, clip, defocus, cutaway
    - Interact, explore
    - Accelerate rendering to allow for those tricks
- Examples:
  - Tunnel visualization (Byška et al., 2015)
  - Interactive energies visualization (Hermosilla et al., 2016)
  - Molecular structure abstraction for trajectory analysis (Vázquez et al., 2018)

# Visualization Challenges

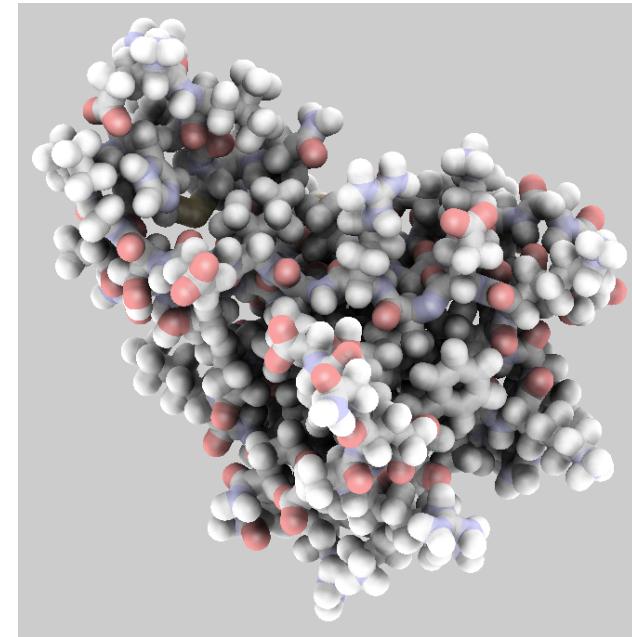
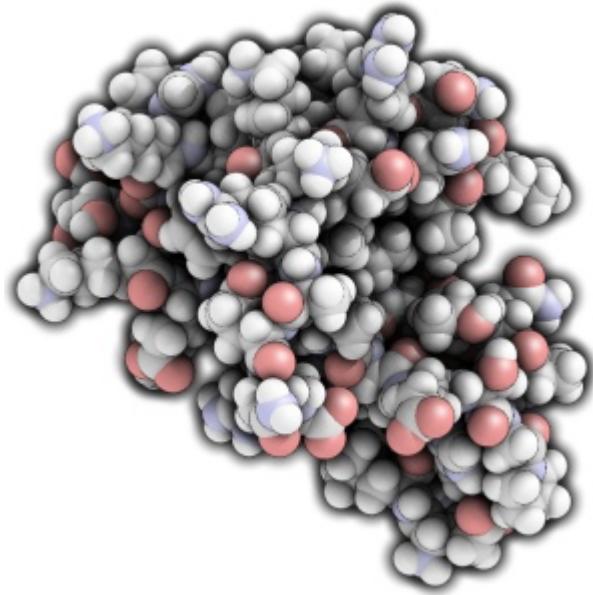
- Visualize extremely large trajectories (1B steps)
  - Specific techniques to:
    - Visualize large (up to 1M time steps)
- Examples:
  - Visualization of large simulation trajectories (Duran et al., 2018)

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- *Computer Graphics Challenges*
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- **Examples**

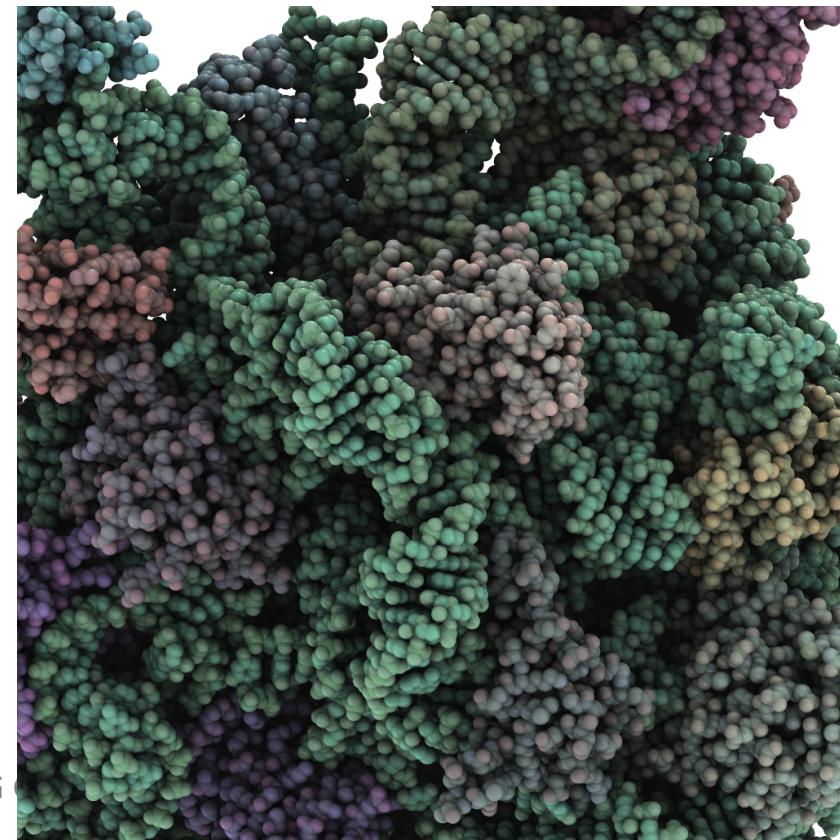
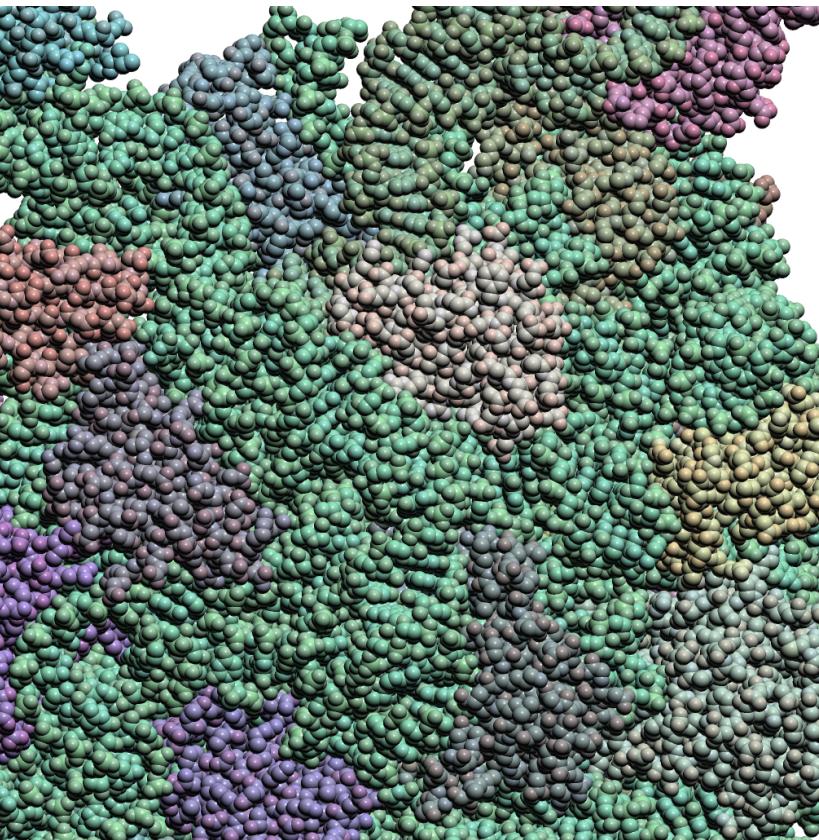
# Examples

- Improving perception of molecules (Tarini et al., 2006, QuteMol)



# Examples

- Improving perception of molecules (Tarini et al., 2006, QuteMol)



# Examples

- Improving perception of molecules
  - Real time AO, depth cueing... (Tarini et al., 2006)
- Contributions:
  - Fast rendering: Using impostors
  - Ambient Occlusion: Precomputed, using textures
  - Borders: Realtime, fragment shader
  - Edge Cueing (aka halos): Realtime, extra rendering step with alpha-blending

# Examples

- Improving perception of dynamic pharmacological simulations
  - Realtime AO, halos (Hermosilla et al., 2015)

# Examples

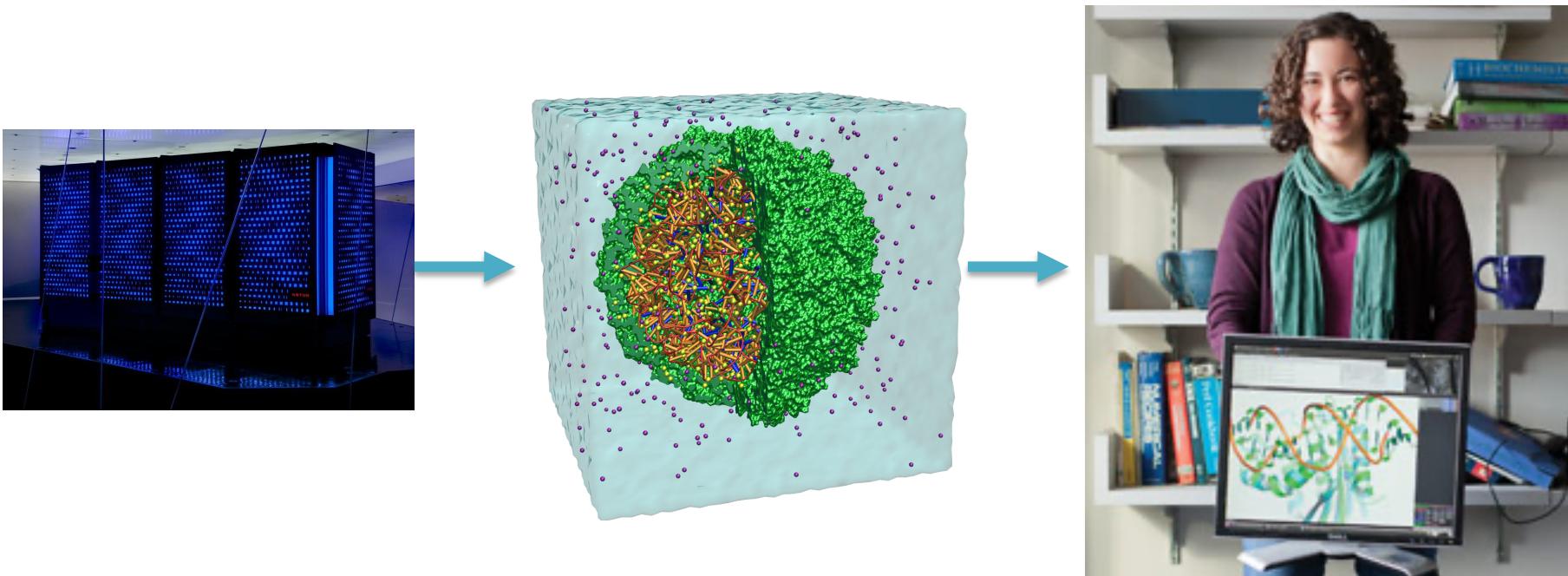
- Improving perception of ***dynamic*** pharmacological simulations
  - Realtime AO, halos (Hermosilla et al., 2015)
- Providing interactive information on the interaction forces
  - Hermosilla et al., 2016

# Examples

- Dynamic vs static
  - Molecules are received **dynamically** from the simulation process
  - Cannot take advantage of many acceleration structures:
    - Cannot precompute and store spatial data structures
      - Atoms change every frame
    - Cannot take advantage of abstract structures
      - Need to be recomputed every time

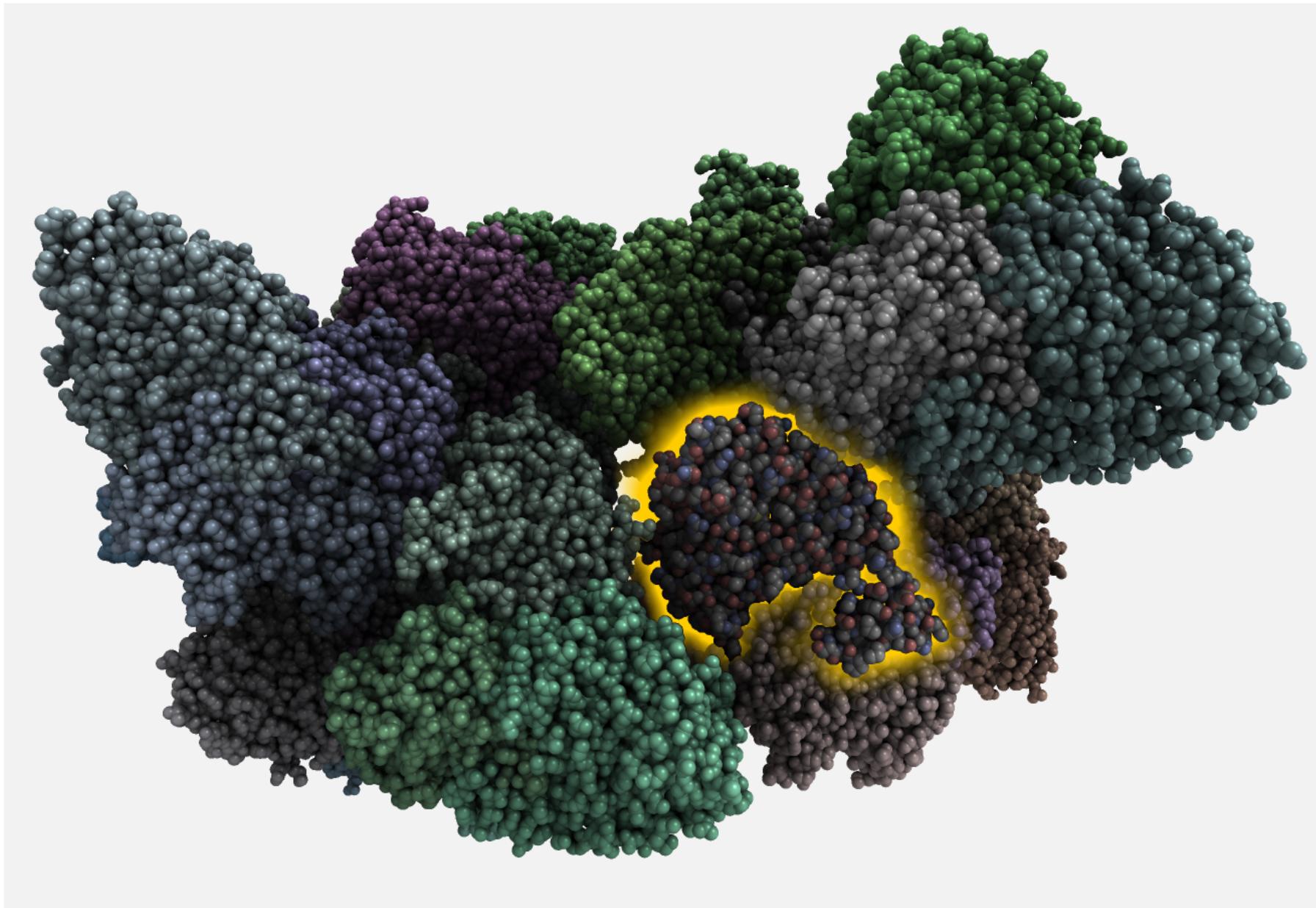
# Examples

- Dynamic vs static



# Examples

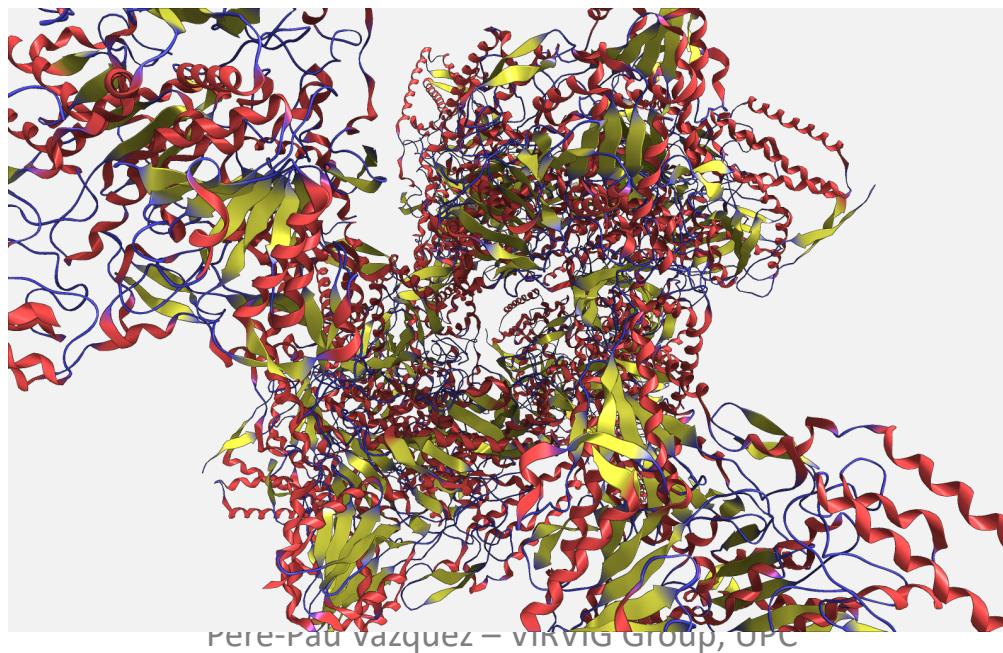
- Dynamic vs static
  - Process can take hours
  - Throughout the process results may be inspected
    - The simulation can be reconfigured to search for more promising steps
  - Need to visualize instantly what the simulation is doing
    - The information received is only the positions of atoms



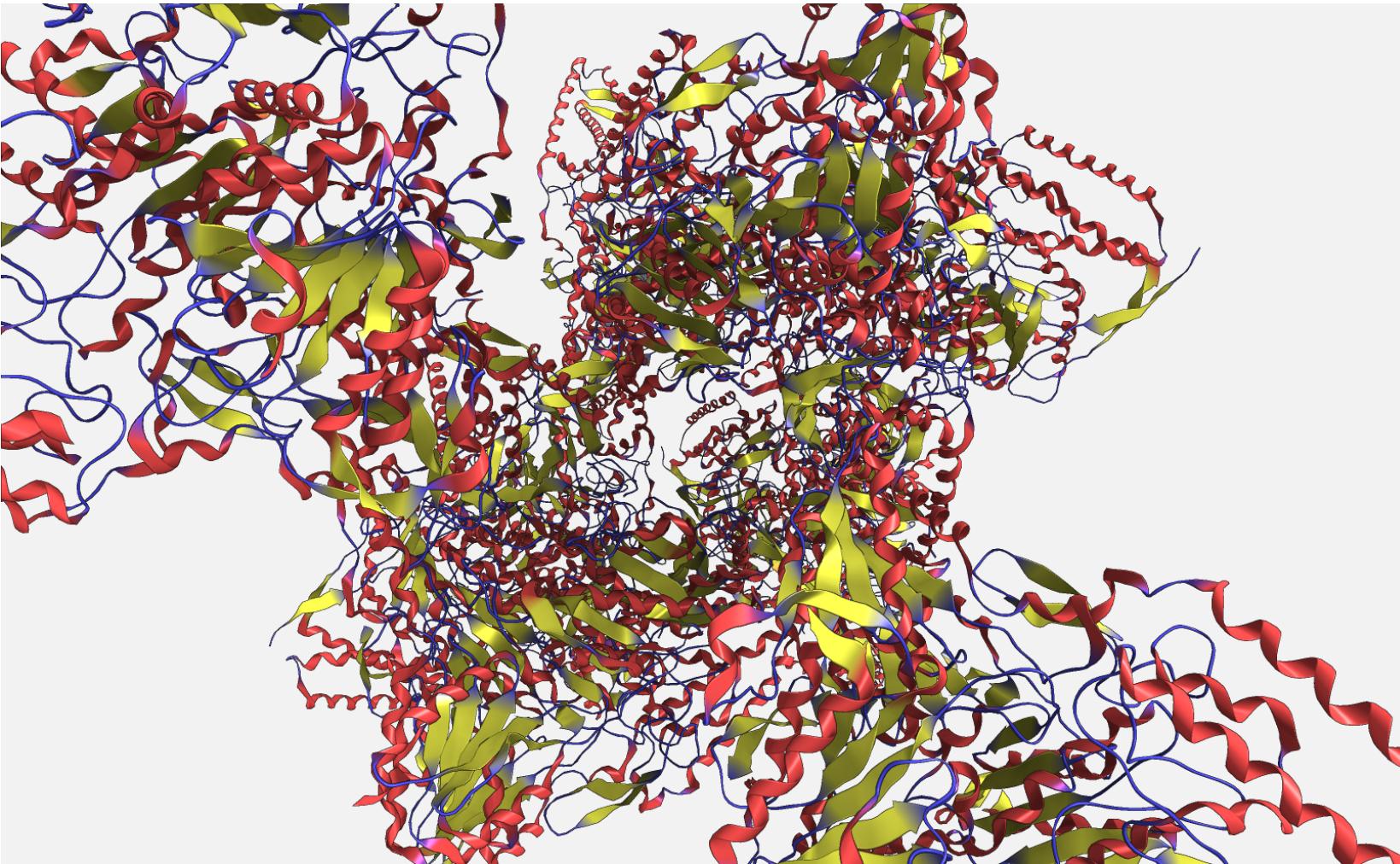
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# Examples

- Improving perception of dynamics pharmacological simulations
  - Realtime secondary structures & AO (Hermosilla et al., 2015)



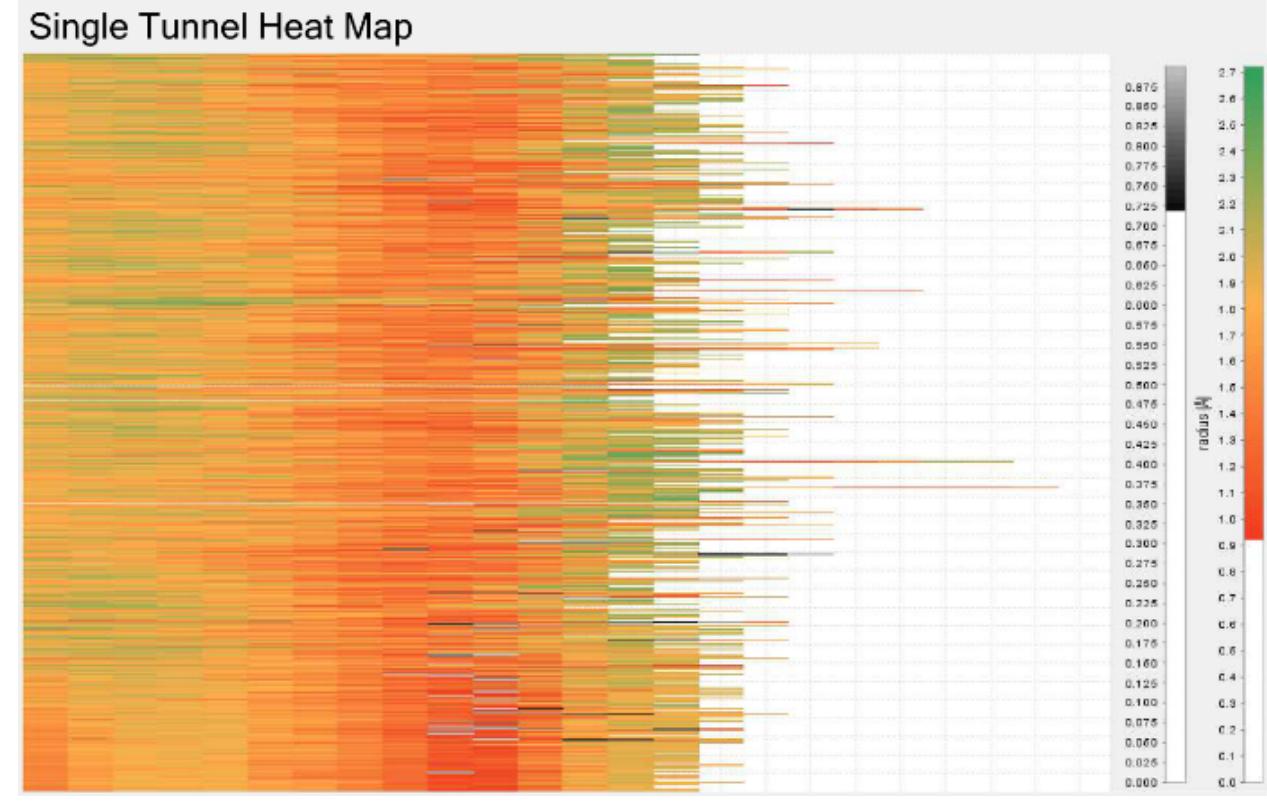
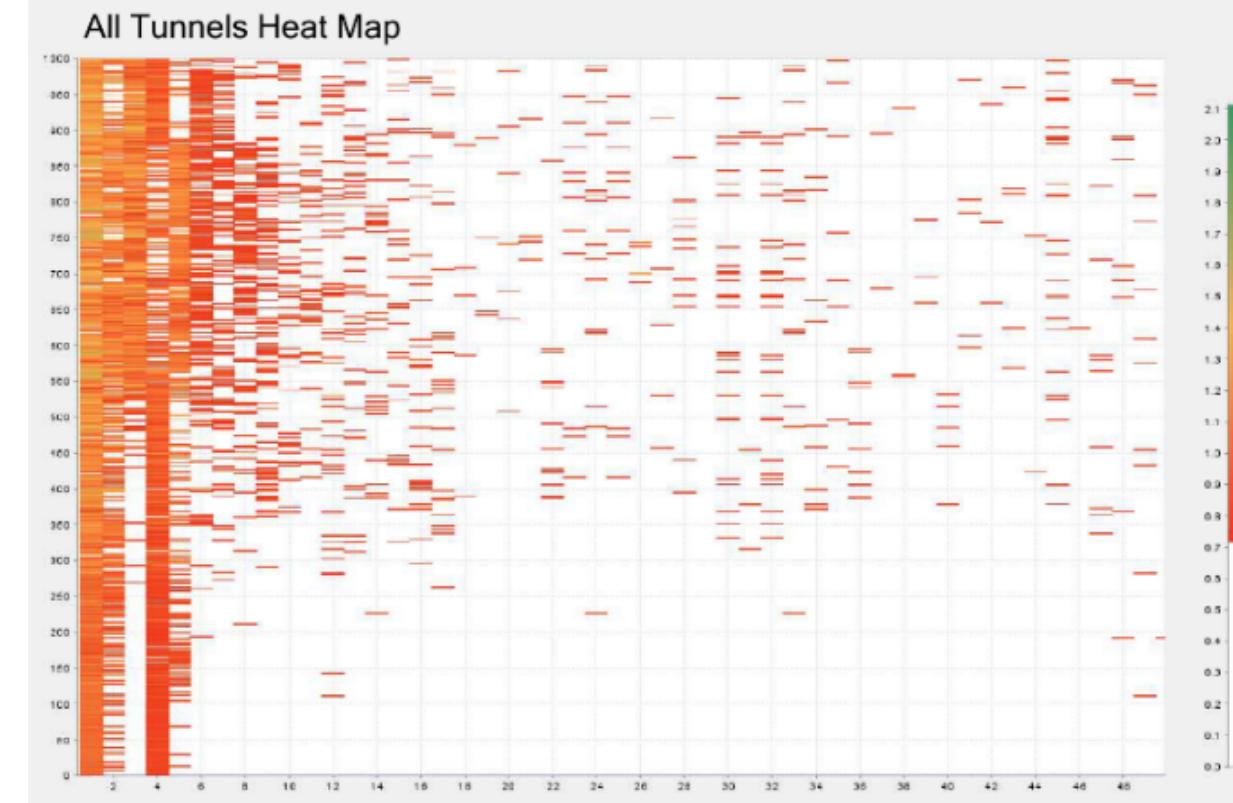
# Examples



# Examples

- Improving the understanding of tunnels and energies
  - Tunnel visualization (Byška et al., 2015)

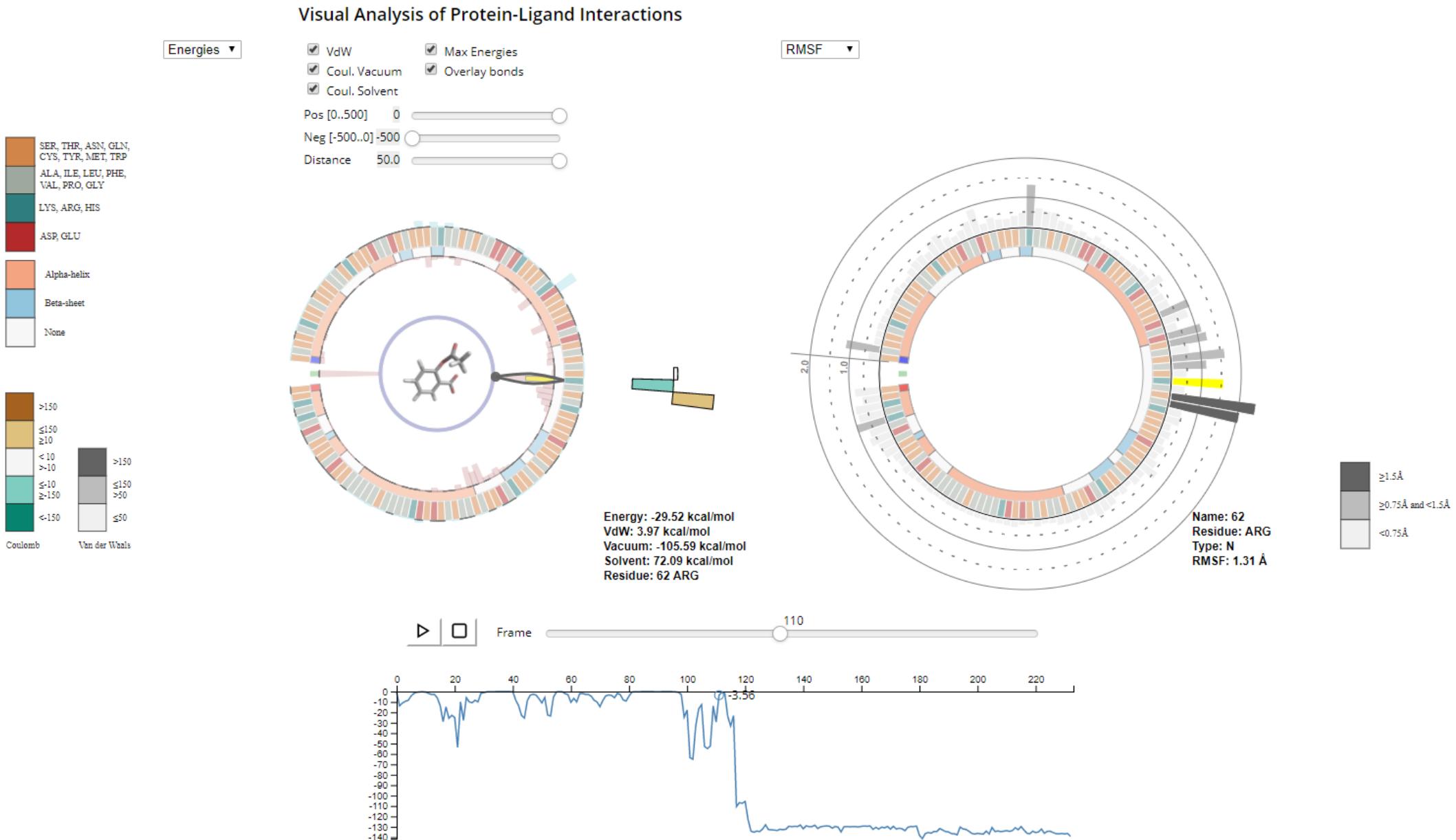
# Examples



# Examples

- Visualization interactions in molecular simulation
  - Residue-based energy interactions (Vázquez et al., 2018)

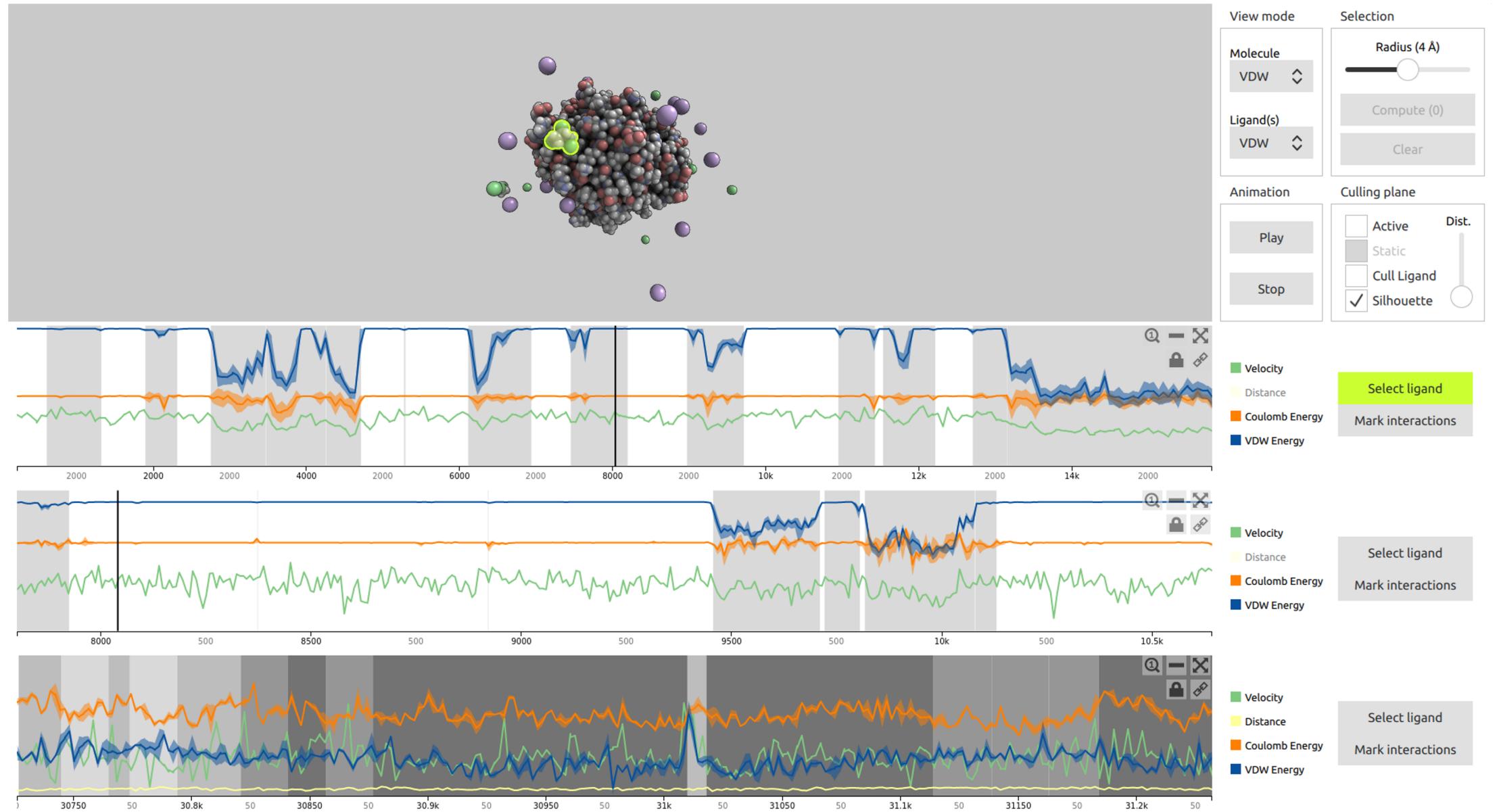
# Examples



# Examples

- Visualization of large simulations
  - Progressive exploration of large charts (Duran et al., 2018)

# Examples



# Molecular Visualization

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