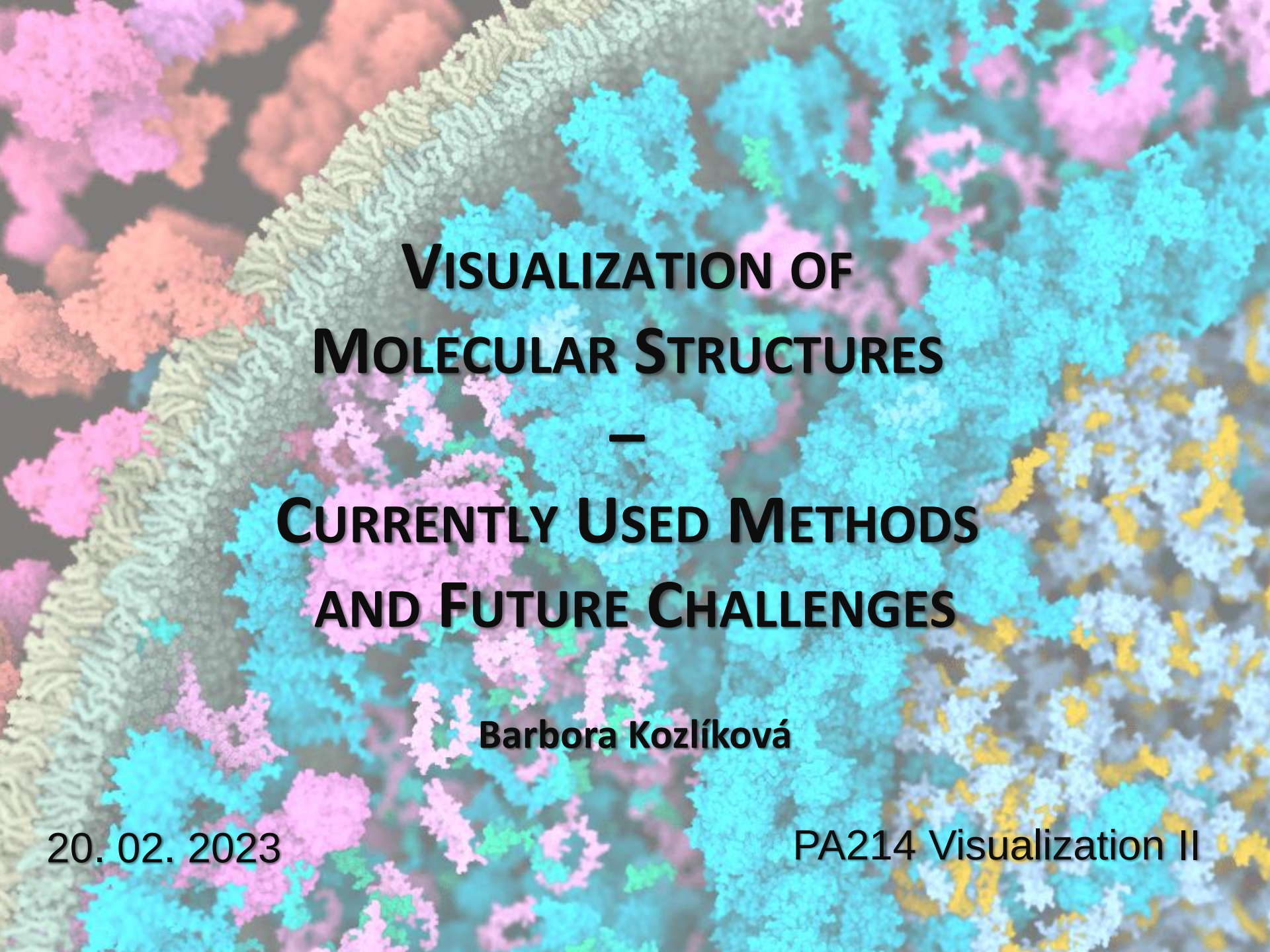


Visualization of Molecular Structures – Currently Used Methods and Future Challenges

Barbora Kozlíková

20. 02. 2023

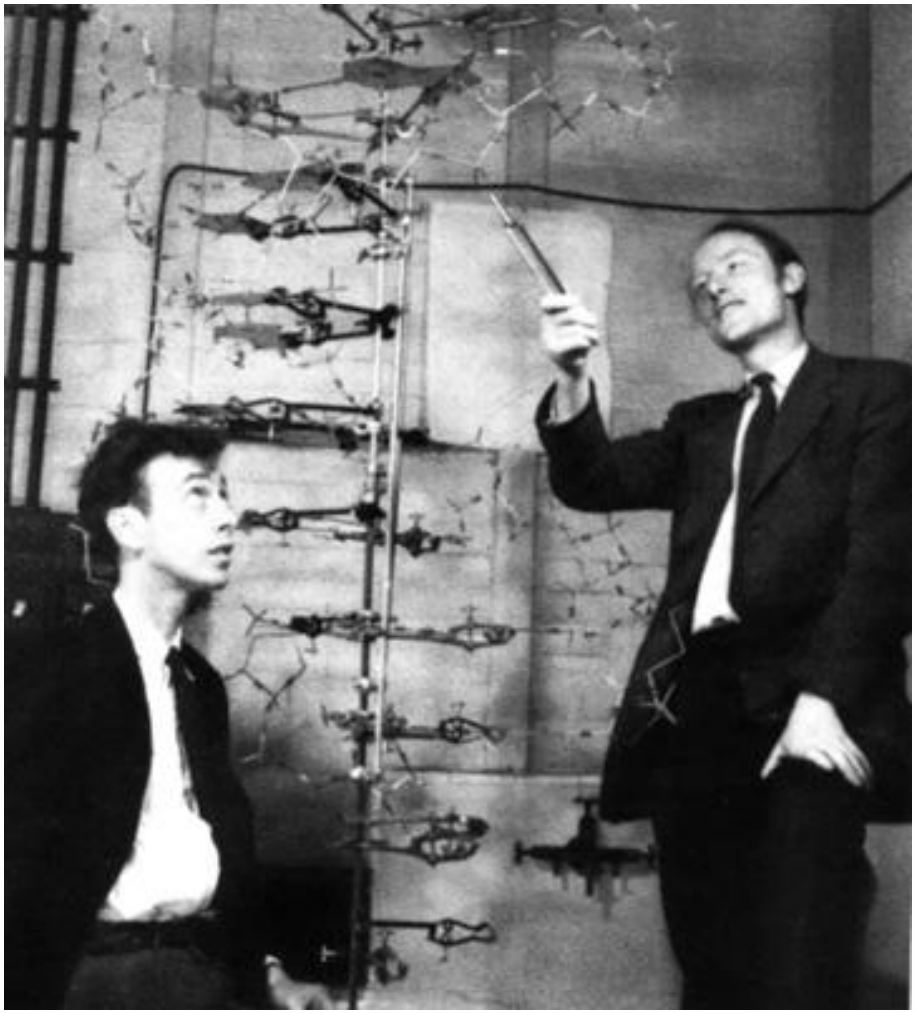
PA214 Visualization II

INTRODUCTION

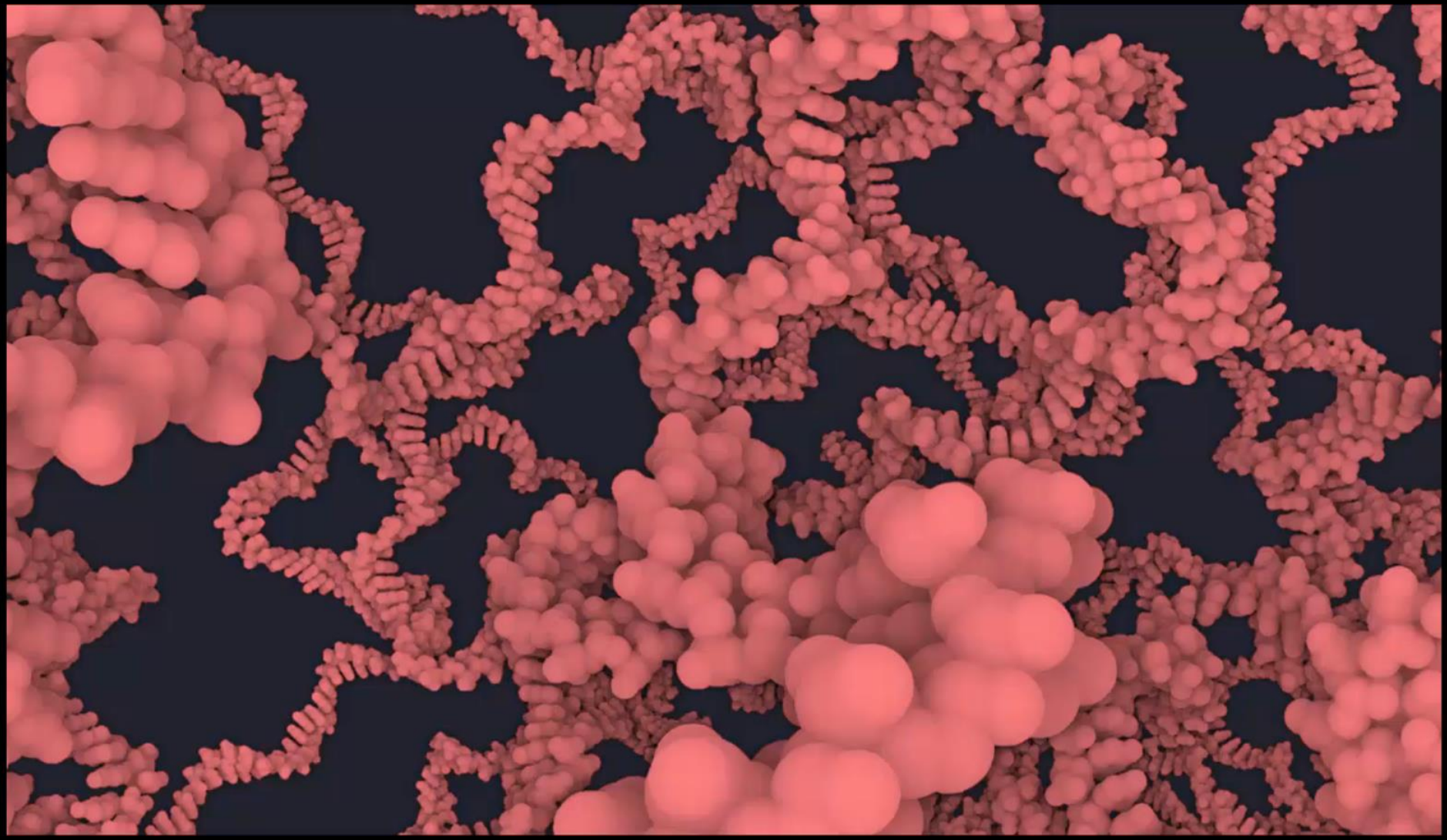
- Molecular visualization is one of the oldest branches of data visualization
  - Builds up on pre-computer era depictions and models of molecules
- *Molecular visualization is a vast and diverse field of research*

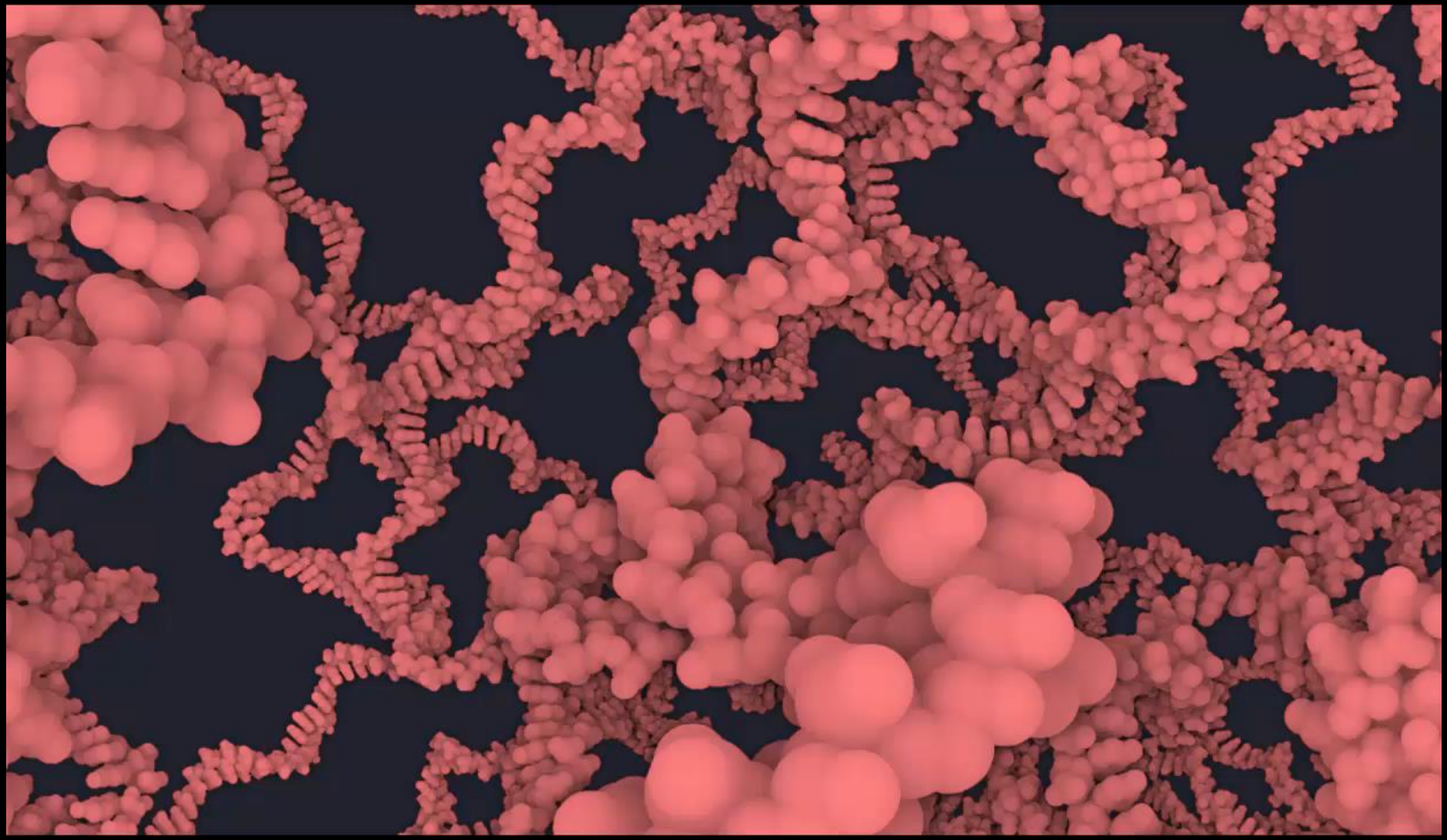
→ We will focus on
  - **Interactive 3D Visualization** of
  - **Biomolecules** (DNA, proteins, lipids etc.) described by
  - **Classical Models** (no quantum effects, atoms depicted by hard spheres)

INTRODUCTION



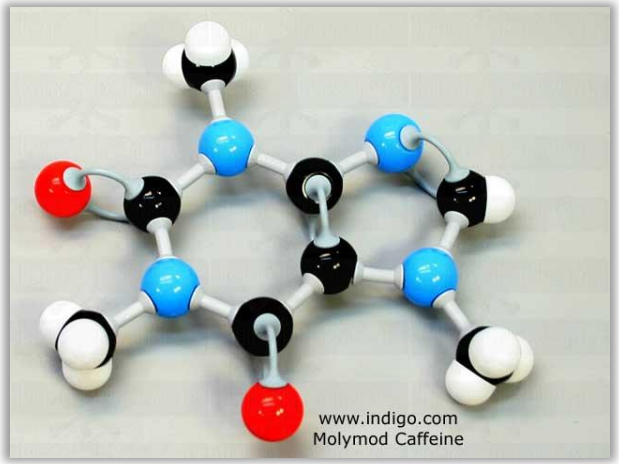
INTRODUCTION

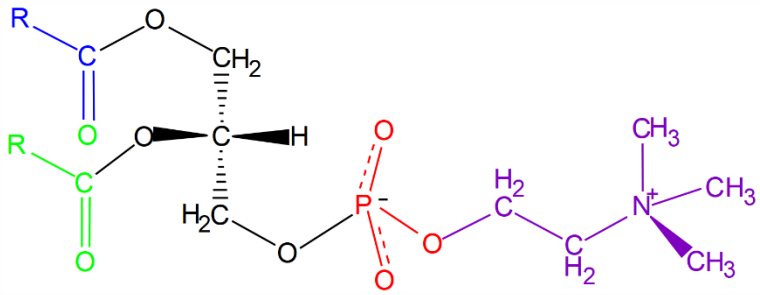




BIOMOLECULES

- Molecules
  - Atoms (117 chemical elements)
    - Oxygen, carbon, nitrogen, hydrogen
  - Bonds (e.g., covalent, disulfide, hydrogen)
- Small molecules & ions
  - Lipids (membranes)
  - Ligands/metabolites
  - Solvent molecules (e.g., water)
  - etc.

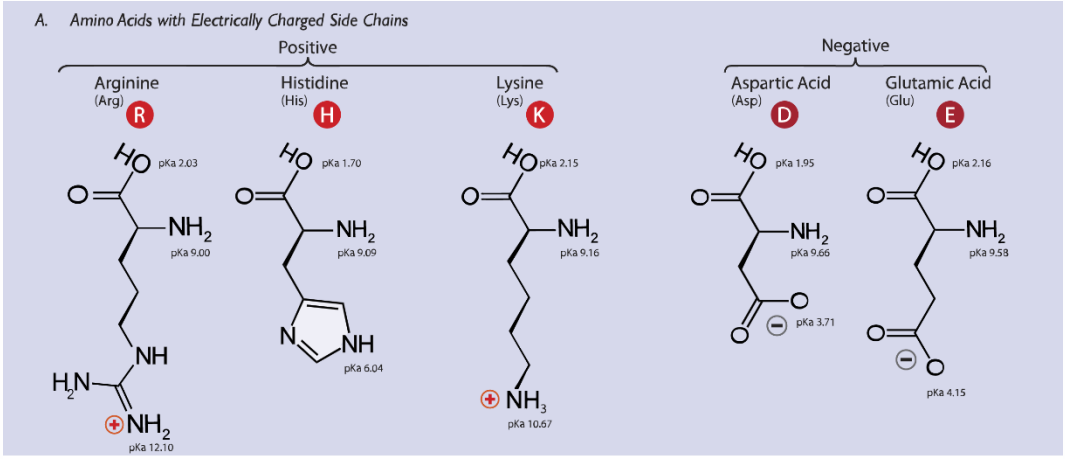




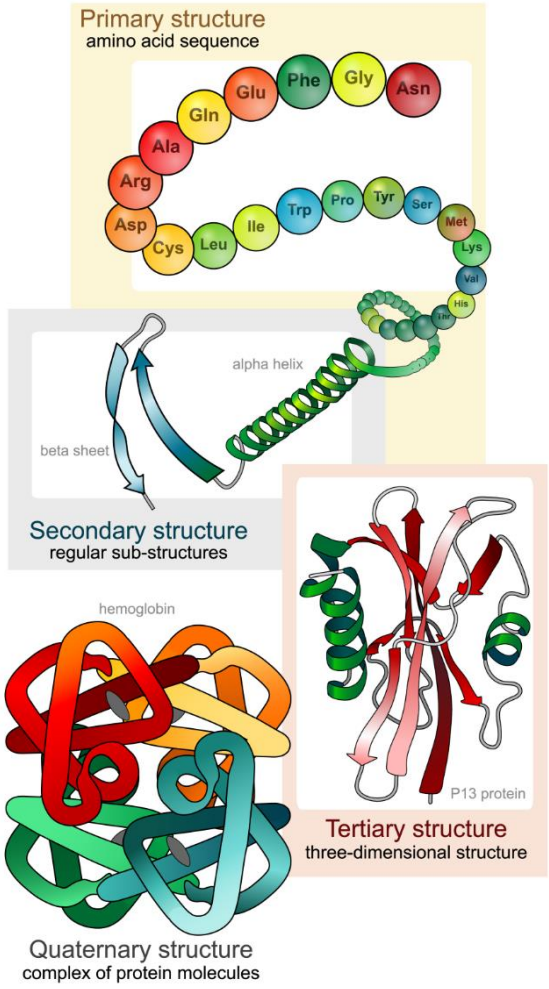
http://en.wikipedia.org/wiki/Phospholipid

BIOMOLECULES

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



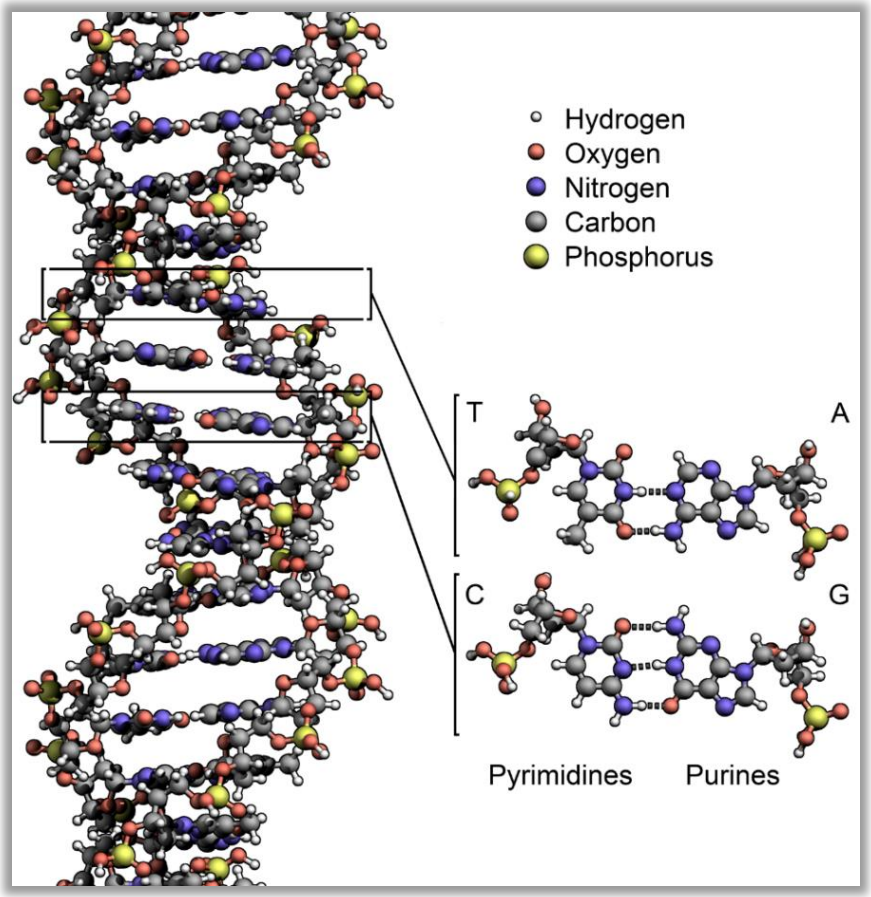
http://en.wikipedia.org/wiki/Amino_acid



http://en.wikipedia.org/wiki/Protein_structure

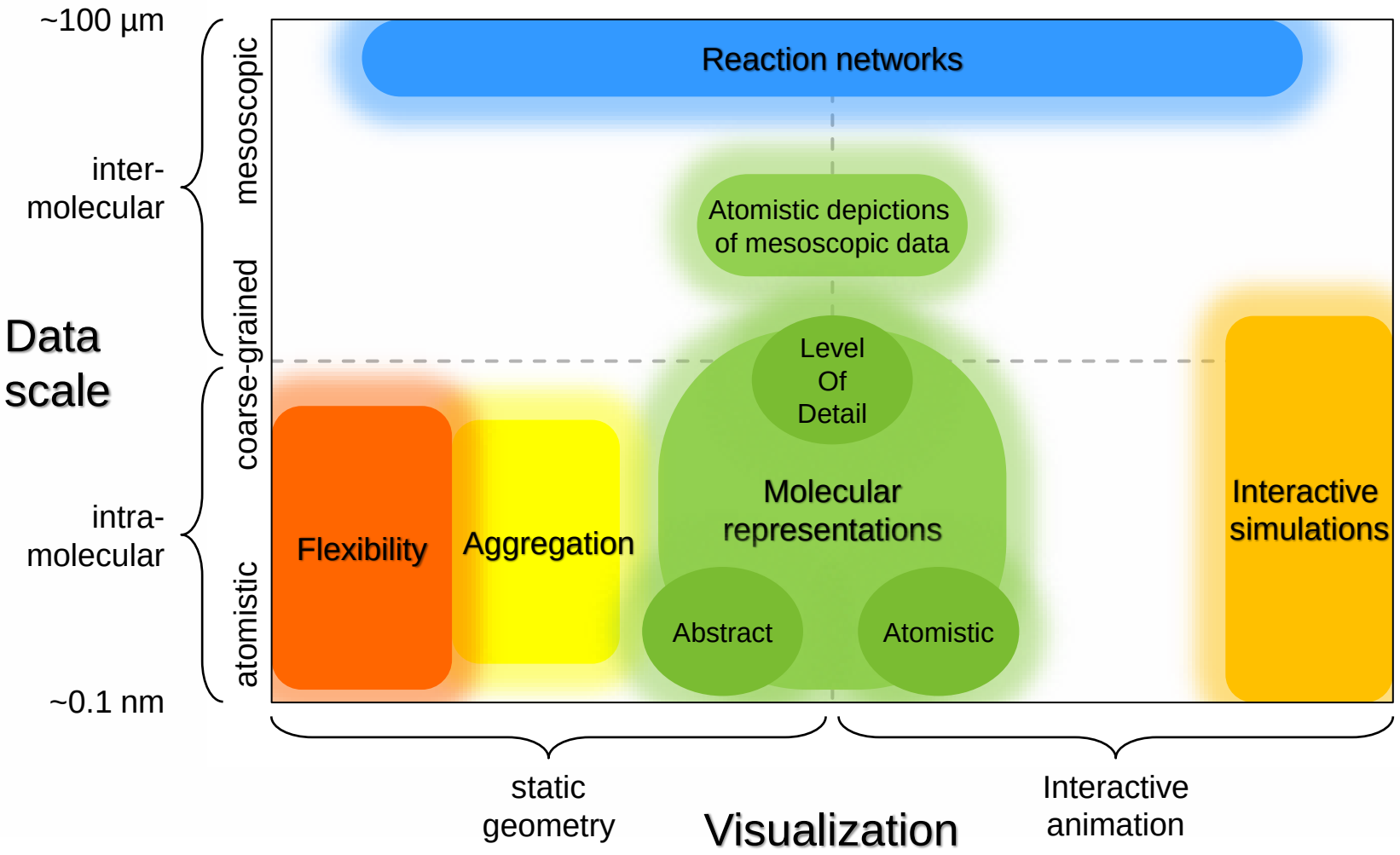
BIOMOLECULES

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



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

TAXONOMY


~100 µm
inter-
molecular
mesoscopic
coarse-grained
Data
scale
intra-
molecular
atomistic
~0.1 nm
Reaction networks
Atomistic depictions
of mesoscopic data
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Detail
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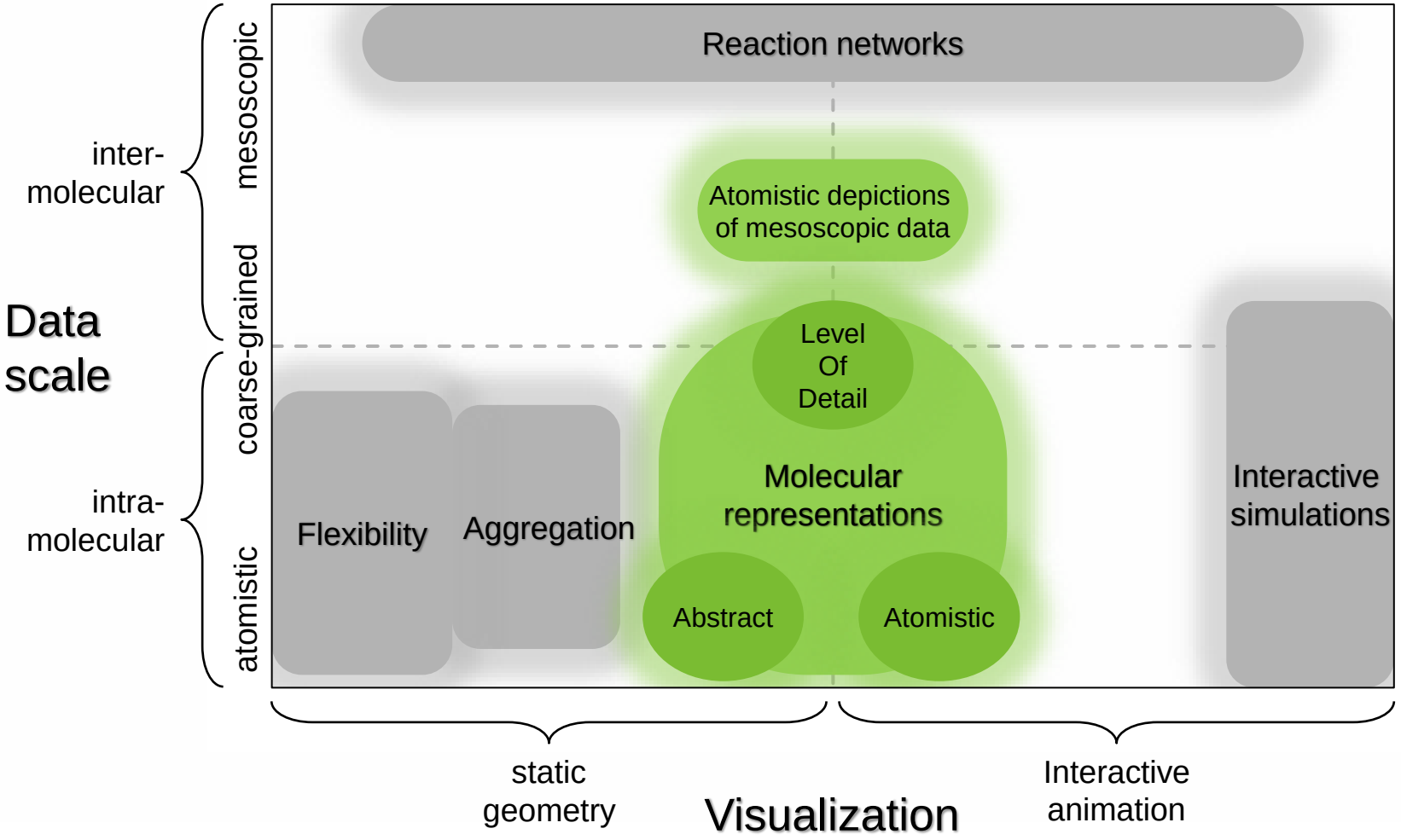
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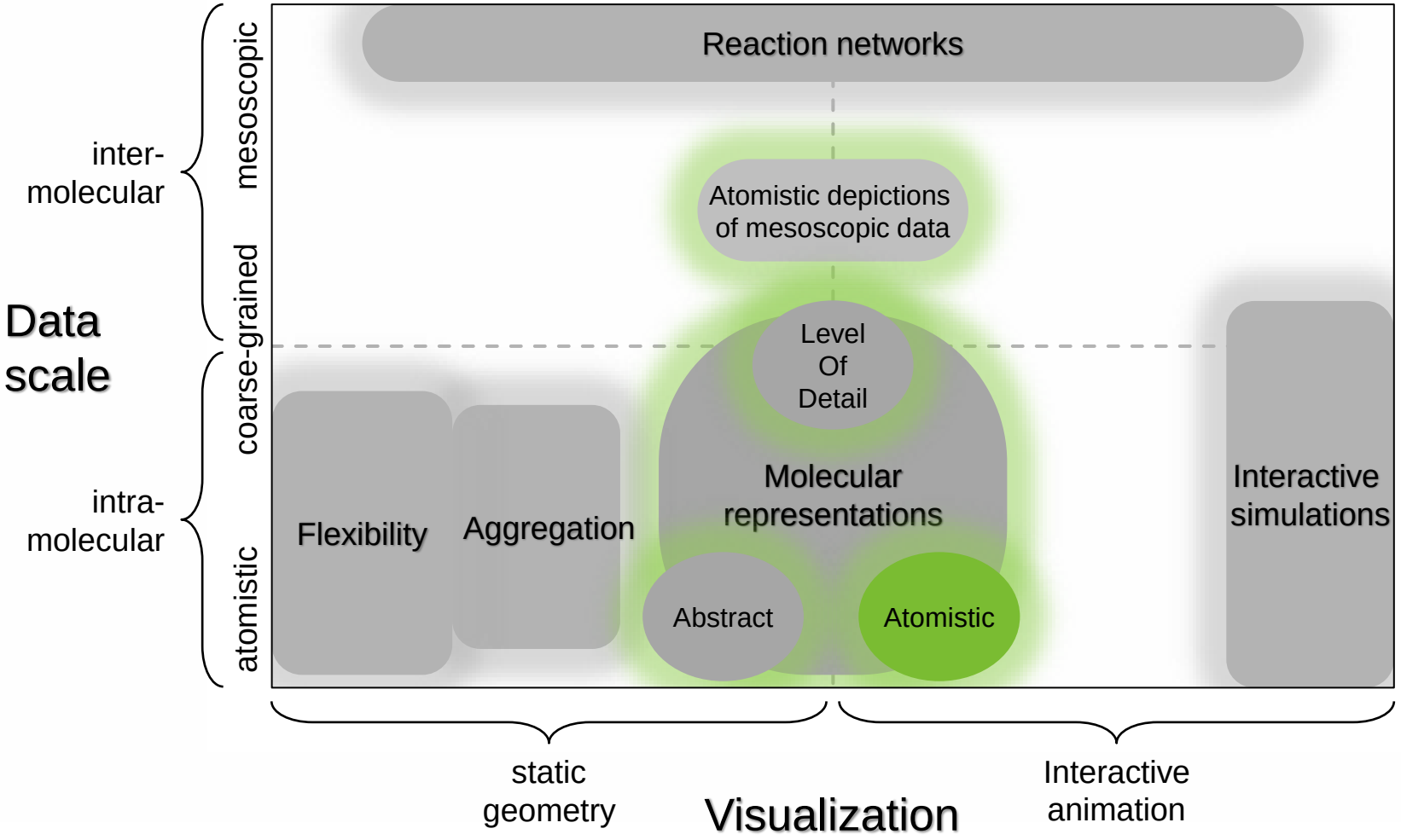
MOLECULAR REPRESENTATION MODELS

- Atomistic Representations
  - Bond-centric Models
  - Surface Models
- Abstract and Illustrative Representations
  - Representations of Molecular Architecture
  - Surface Abstractions
- Structural Level of Detail

TAXONOMY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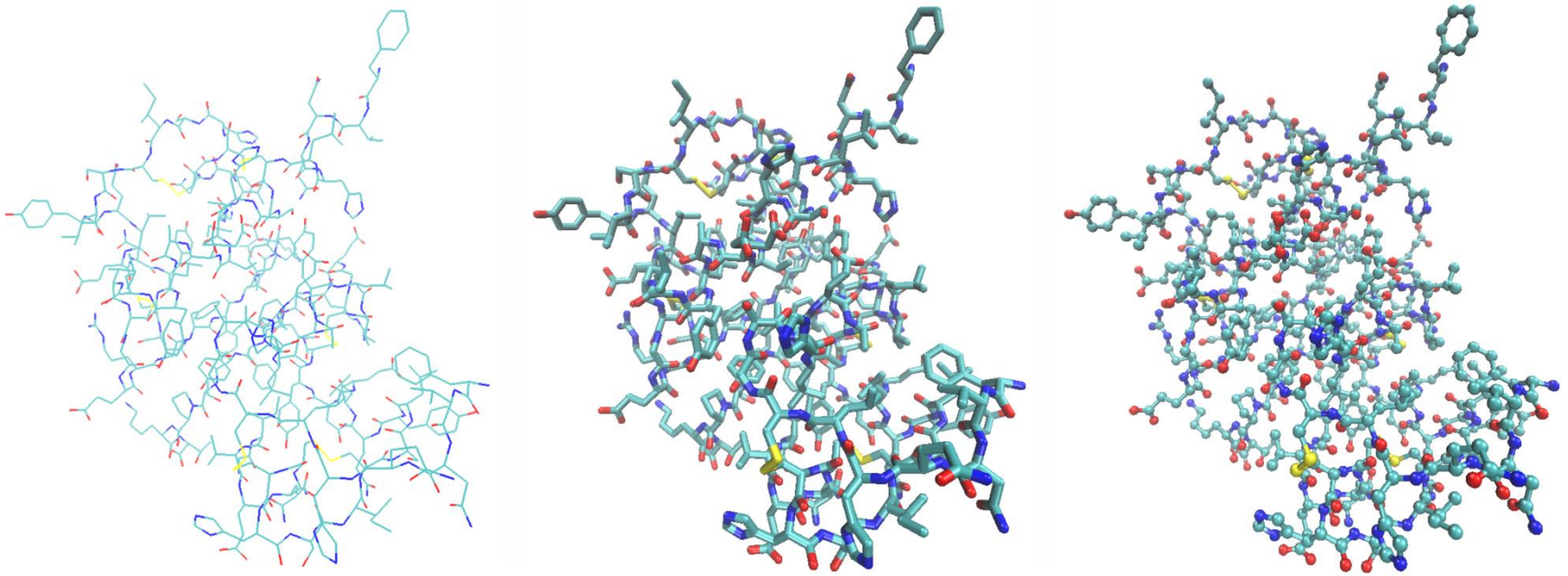
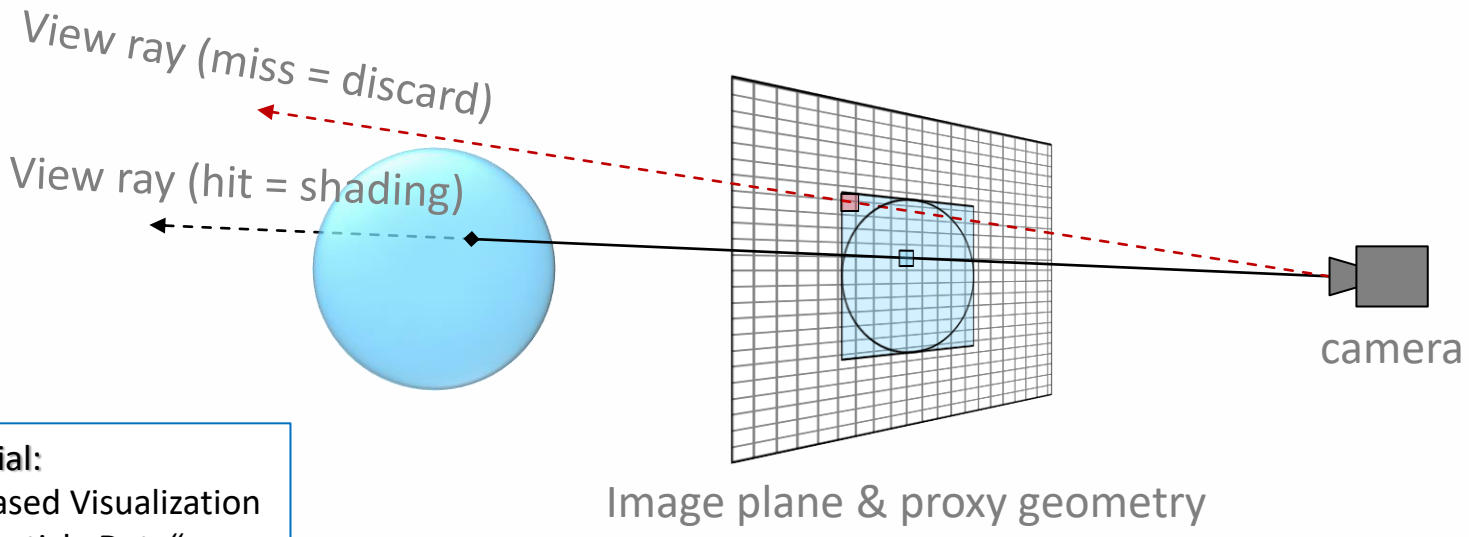
ATOMISTIC REPRESENTATIONS

- Molecular models that show the position of the atoms
- Bond-centric Models
  - Bonds define the topology of the molecule
  - Lines, Sticks, Balls-and-Sticks → spheres and cylinders



GPU-BASED GLYPH RAY CASTING

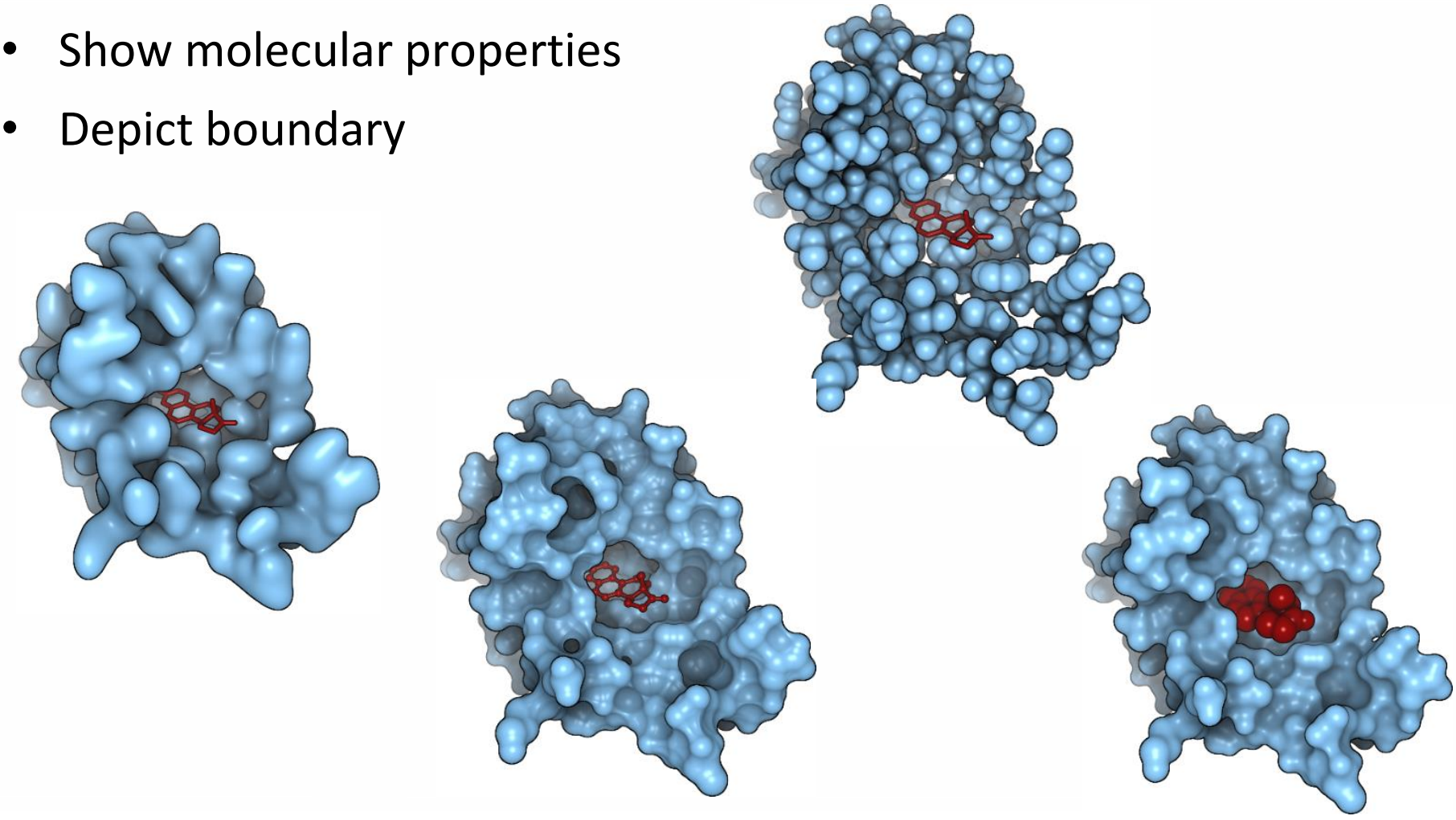
- State-of-the-art for rendering implicit objects
  - Upload implicit description of object to GPU
  - Proxy geometry that covers the object in Vertex/Geometry Shader
  - Object/ray intersection in Fragment Shader



IEEE Vis 2015 Tutorial:
„Interactive GPU-based Visualization of Large Dynamic Particle Data“

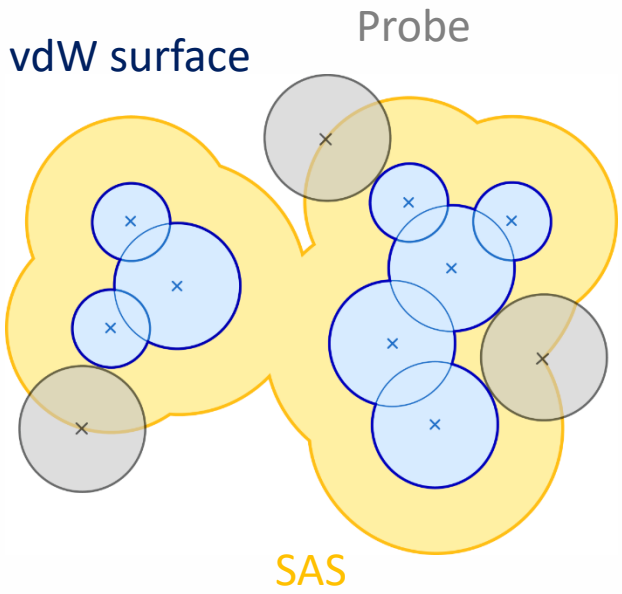
MOLECULAR SURFACES

- Show molecular properties
- Depict boundary



VDW AND SAS SURFACE

- Van der Waals (vdW) surface
  - vdW radius: 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 vdW radius by r_p

- Rendering via GPU ray casting

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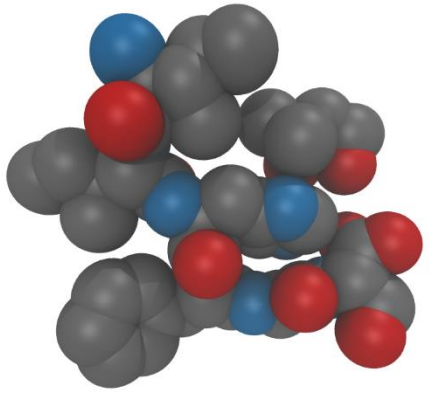

vdW surface

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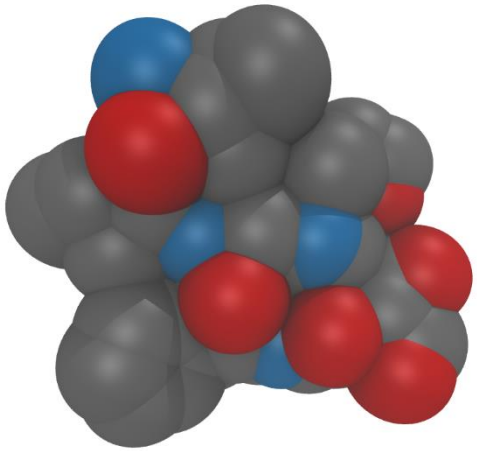
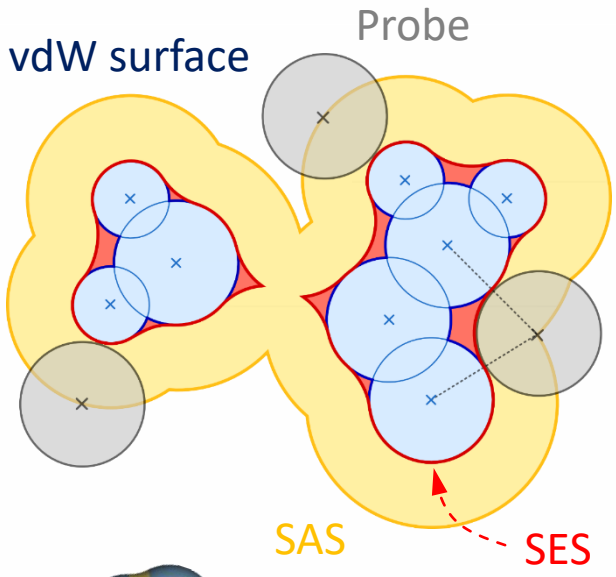


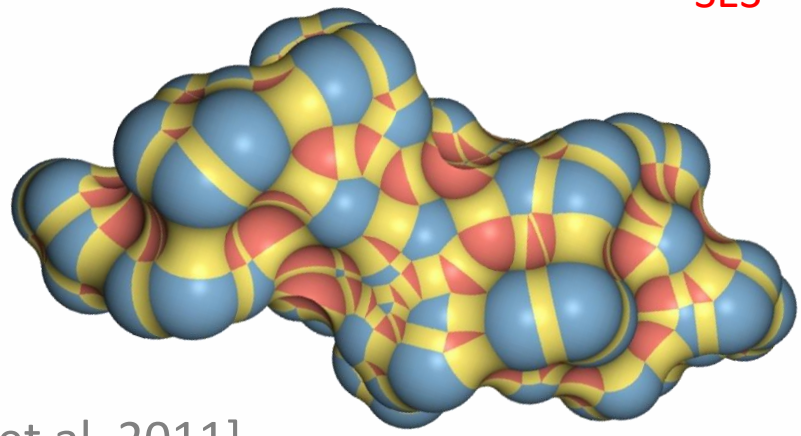
SAS

- Rendering via GPU ray casting

SOLVENT EXCLUDED SURFACE

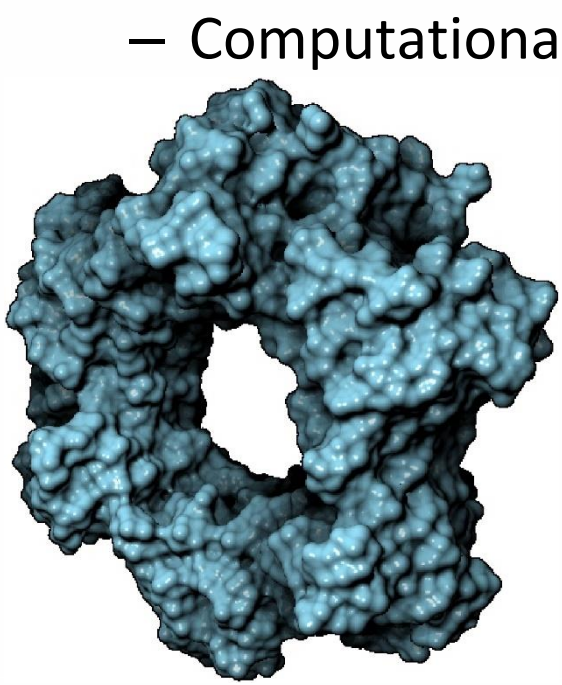
- Defined by rolling probe of radius r_p
  - Probe surface traces out SES
- Smooth, tight surface
  - Boundary with respect to solvent
  - No inflation (molecular volume is preserved)
- Three types of patches
  - Concave spherical triangles
  - Convex spherical patches
  - Saddle-shaped toroidal patches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

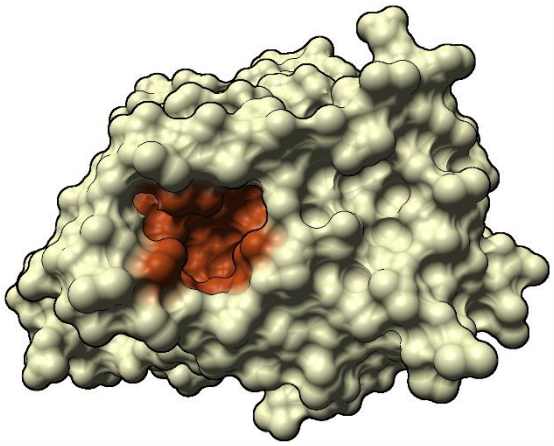




SOLVENT EXCLUDED SURFACE

- GPU ray casting of patches
- Implicit description [Parulek et al. 2012]
  - Direct ray casting via sphere tracing
  - Computationally expensive





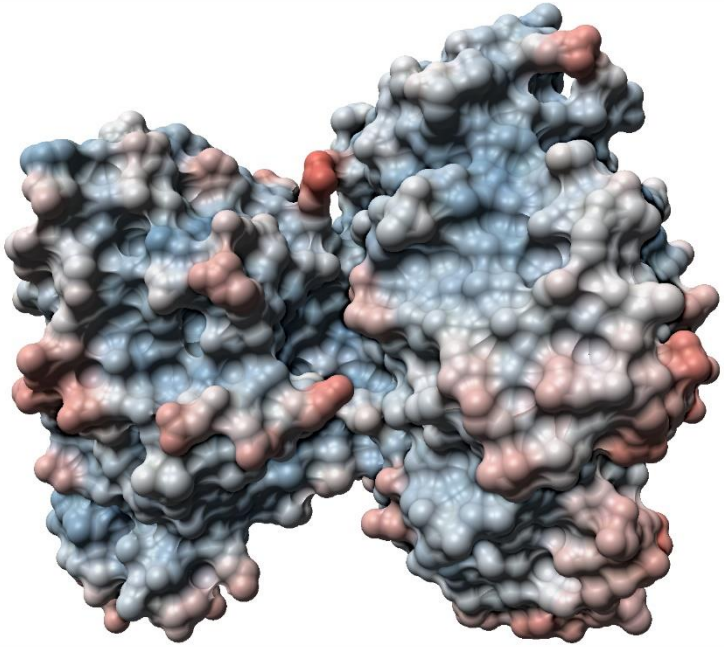


Image: [Krone et al. 2010]

SOLVENT EXCLUDED SURFACE

- Interactive CPU-based Ray Tracing of Solvent Excluded Surfaces [Rau et al. 2019]

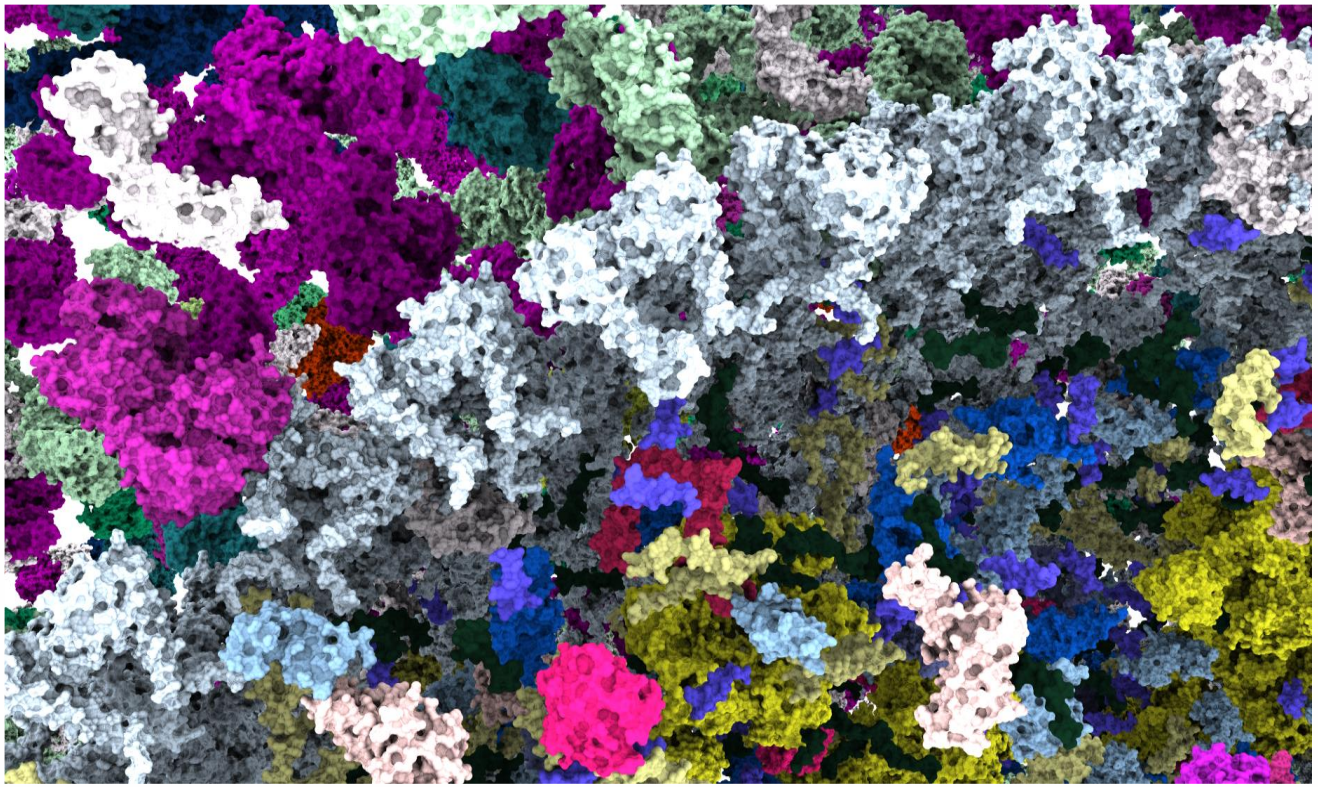


Image: [Rau et al. 2019]

SOLVENT EXCLUDED SURFACE

- Dynamic visibility-driven molecular surfaces [Bruckner 2019]
  - Fully operating in image space, no preprocessing

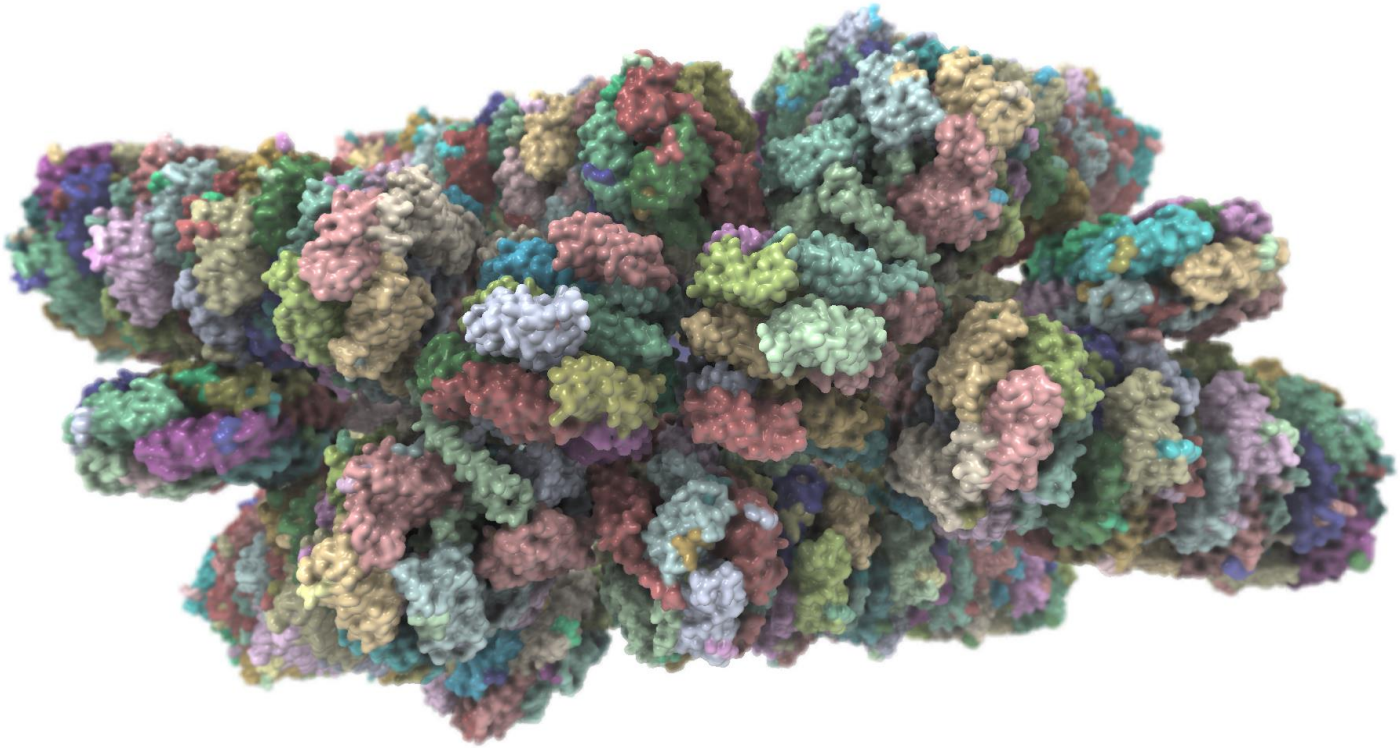
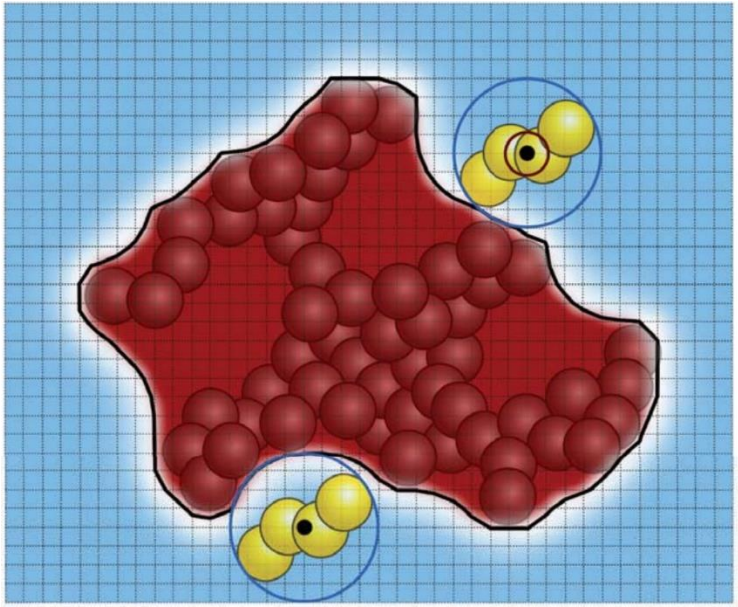
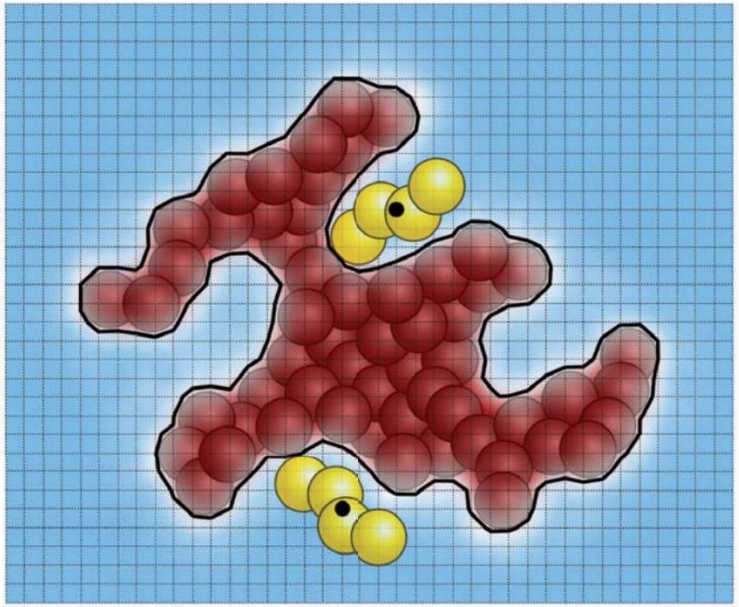


Image: [Bruckner 2019]

LIGAND EXCLUDED SURFACE

- Extension of the SES [Lindow et al. 2014]
  - Shows a more accurate contact surface with respect to a specific ligand
- No analytic computation (yet?)
  - Computationally expensive, grid-based sampling method





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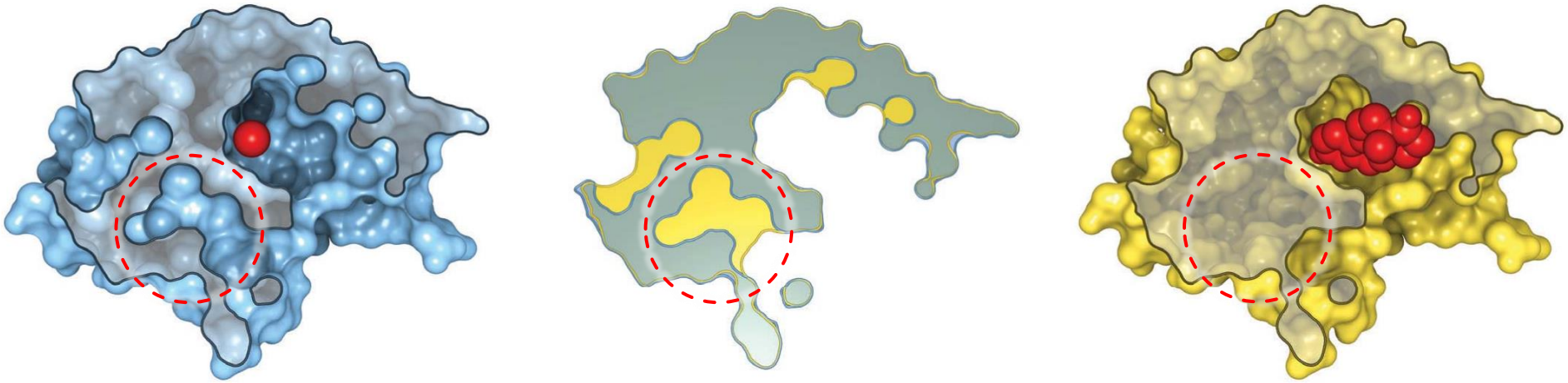
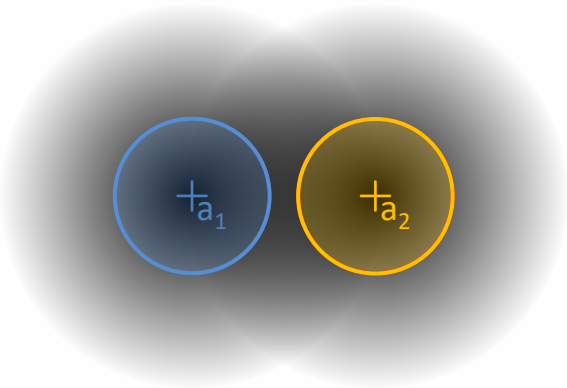
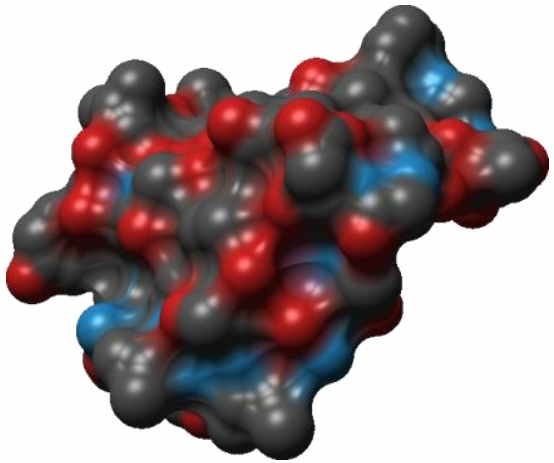


GAUSSIAN SURFACES

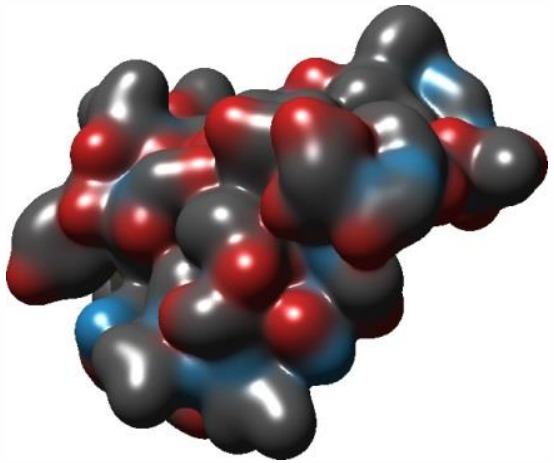
- Defined in 1982 by Jim Blinn (aka Metaballs/Convolution Surfaces)
  - Sum of Gaussian radial basis function for each atom ($\Rightarrow$ density field in $\mathbb{R}^3$)
  - Model electron density
  - Isosurface can approximate SES (surface shape and surface area)



Two atoms with radial symmetric Gaussian density kernels



SES

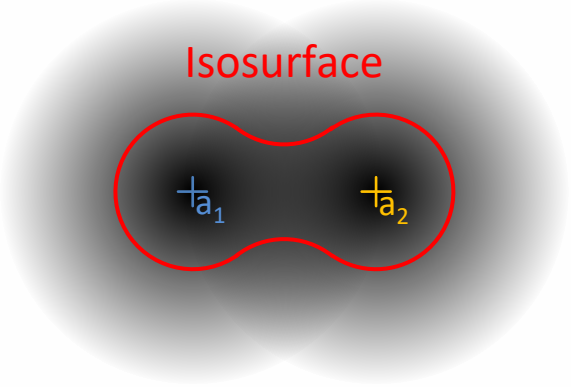


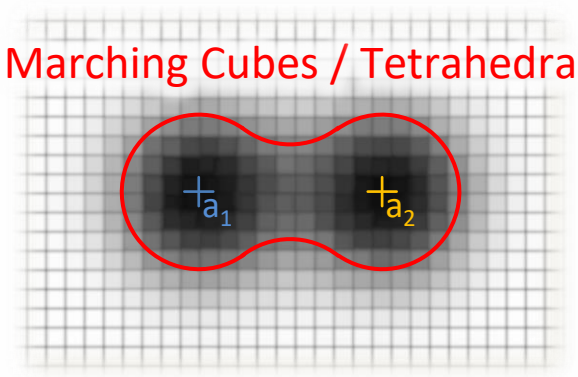
Gaussian surface

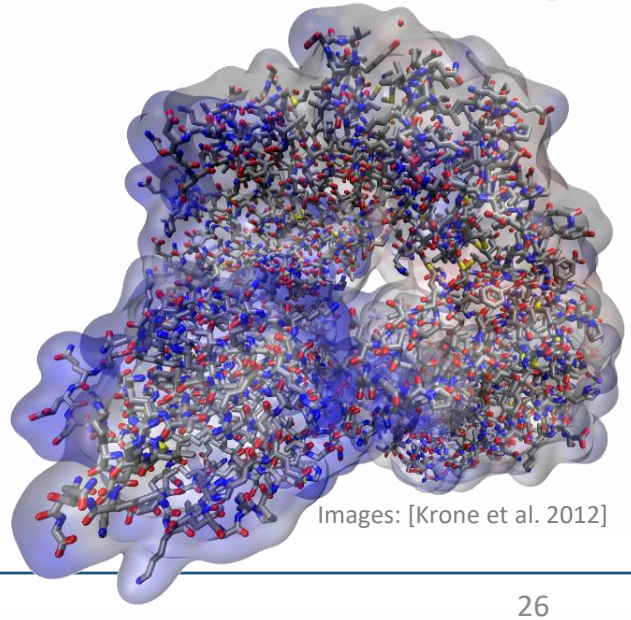
Images: [Krone et al. 2012]

GAUSSIAN SURFACES

- Interactive Rendering
  - Direct ray casting using depth peeling (~1M atoms) [Kanamori et al. 2008]
  - Grid-based sampling of the density (GPU-parallelized: ~10M atoms)
    - Isosurface extraction via Volume Ray Marching or Marching Cubes/Tetrahedra
  - Interactive image-based method for molecular dynamics [Bruckner, 2019]

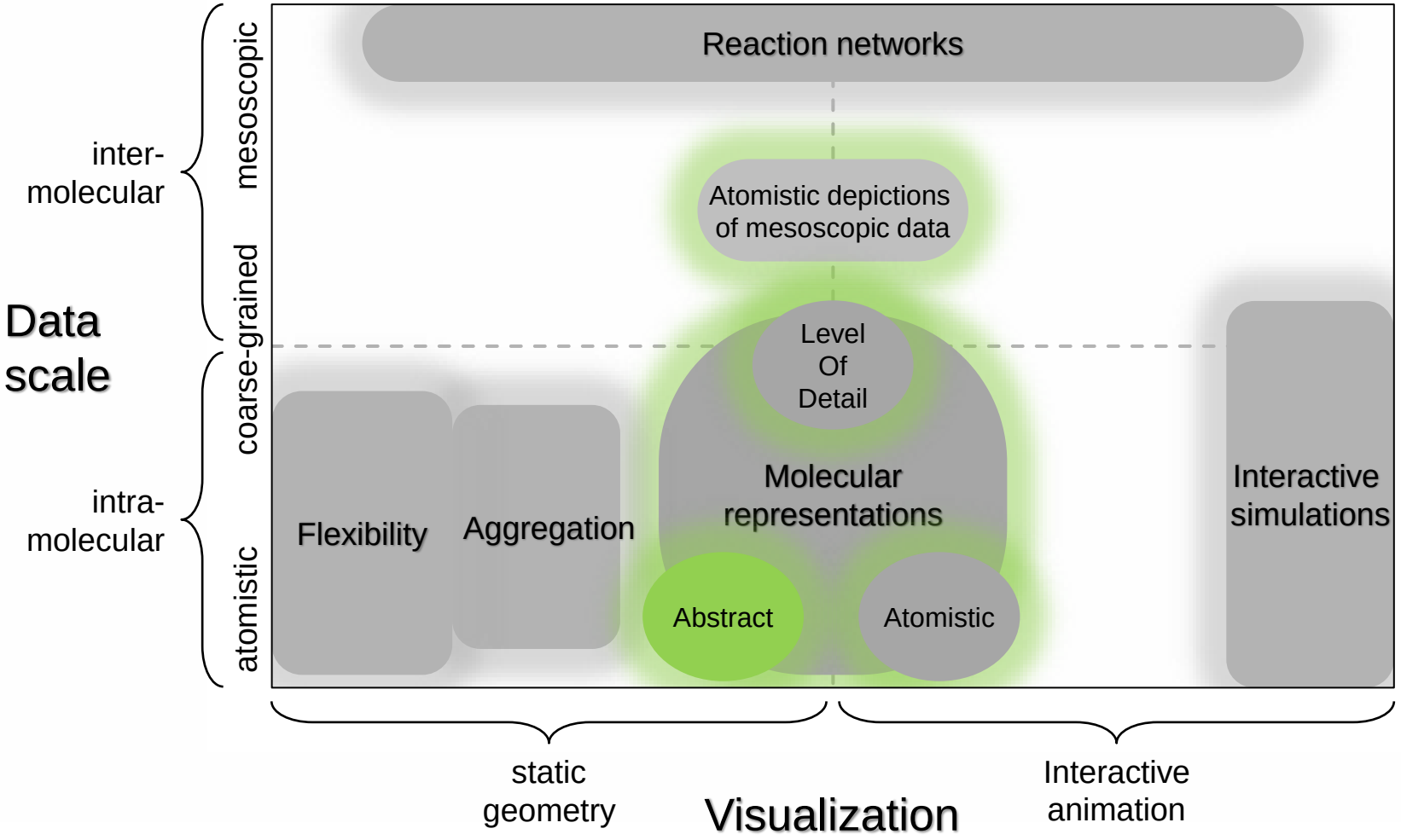






Images: [Krone et al. 2012]

TAXONOMY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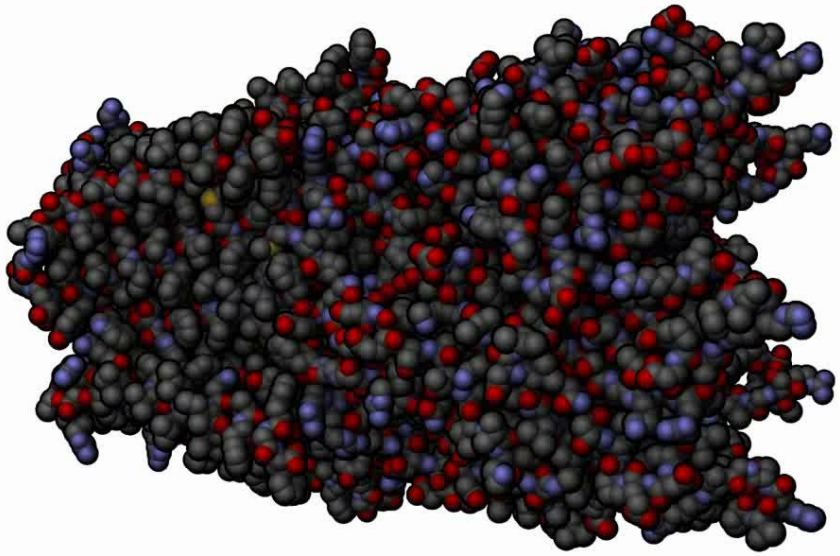
ABSTRACT AND ILLUSTRATIVE REPRESENTATIONS

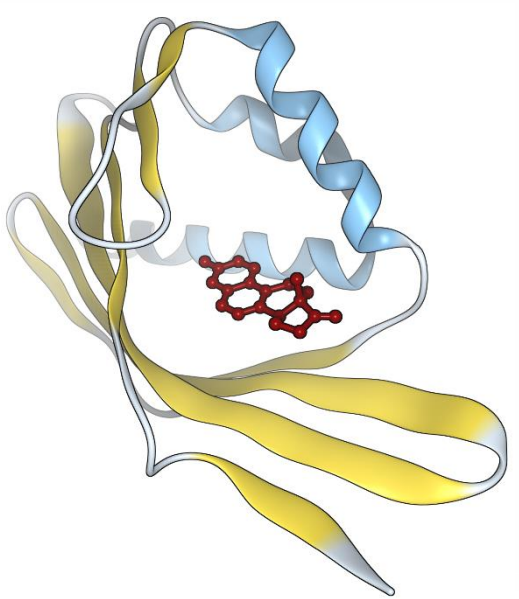
- Representations of Molecular Architecture
  - Show functional structure (derived from atom positions)
  - Cartoon Representation for DNA and proteins
    - Seamless transition [van der Zwan et al. 2011]

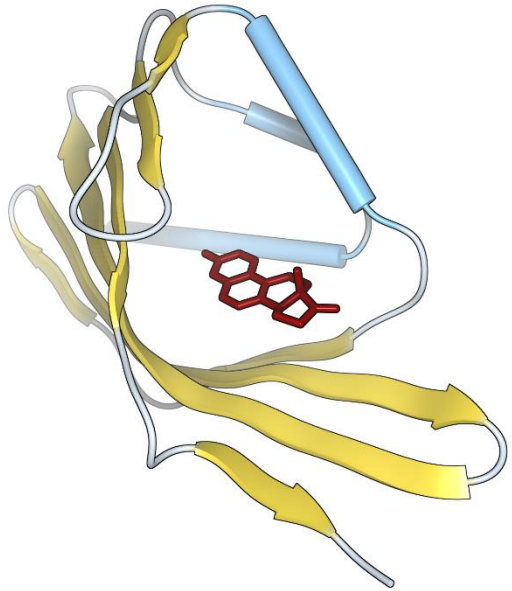


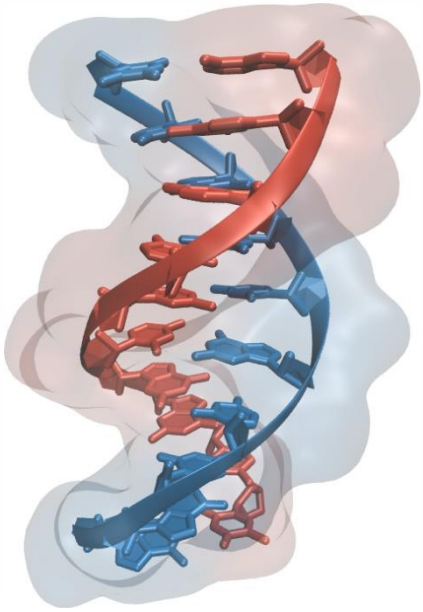
http://tobias.isenberg.cc/VideosAndDemos/Zwan2011IMV

ABSTRACT AND ILLUSTRATIVE REPRESENTATIONS

- Cartoon Rendering
  - Complex shapes → no ray casting
  - GPU-acceleration polygonal rendering
    - Vertex shader [Wahle et al. 2011]
    - Geometry shader [Krone et al. 2008]

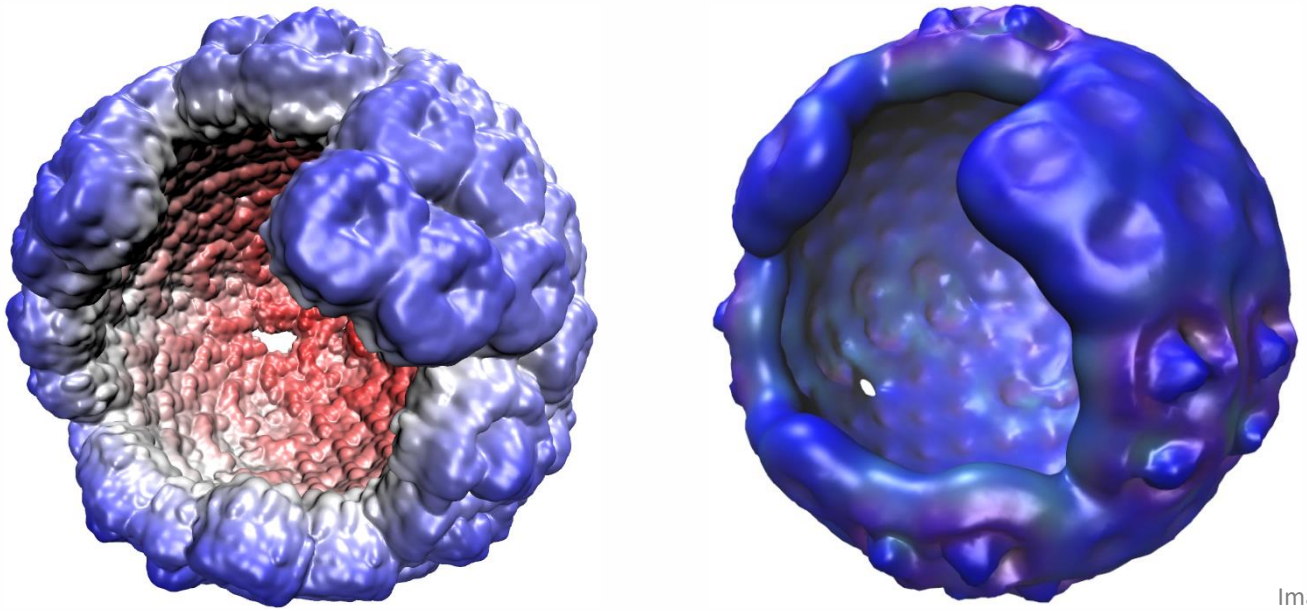






ABSTRACT AND ILLUSTRATIVE REPRESENTATIONS

- Surface Abstractions
  - Coarsening of Gaussian surfaces (LoD, bounding spheres) [Krone at al. 2012]
  - Smoothing of high-frequency surfaces like SES [Cipriano, Gleicher 2007]
  - Mapping of molecular surface to a sphere (e.g., [Rahi, Sharp 2014])



Images: [Krone et al. 2012]

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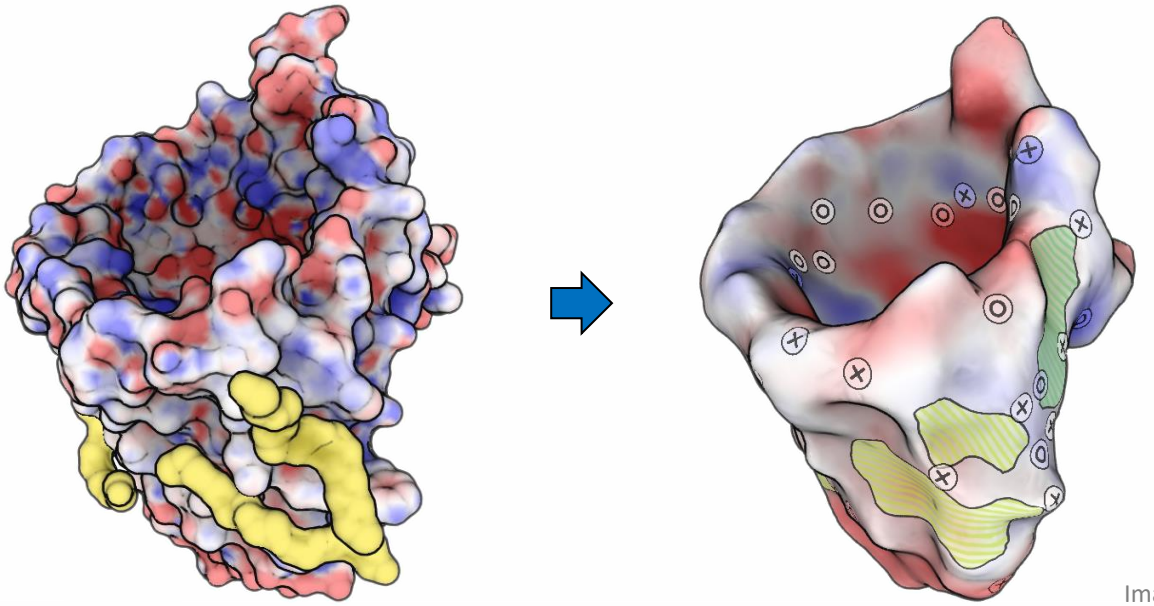

Images: [Cipriano, Gleicher 2007]

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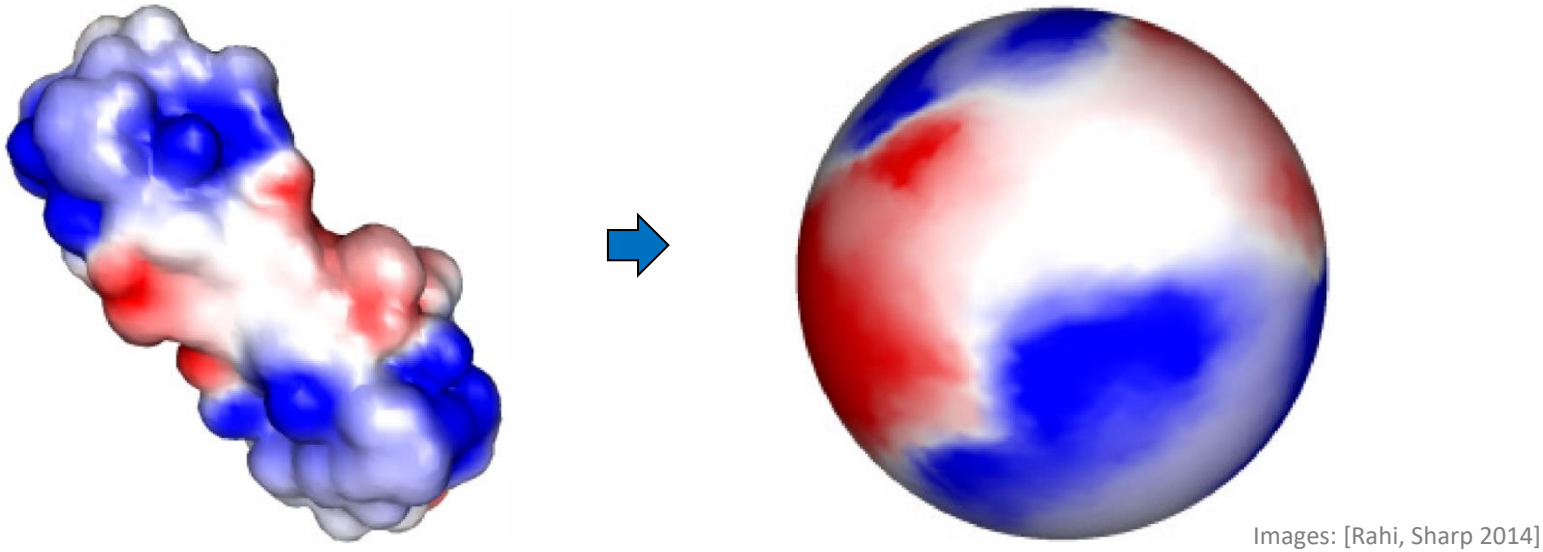
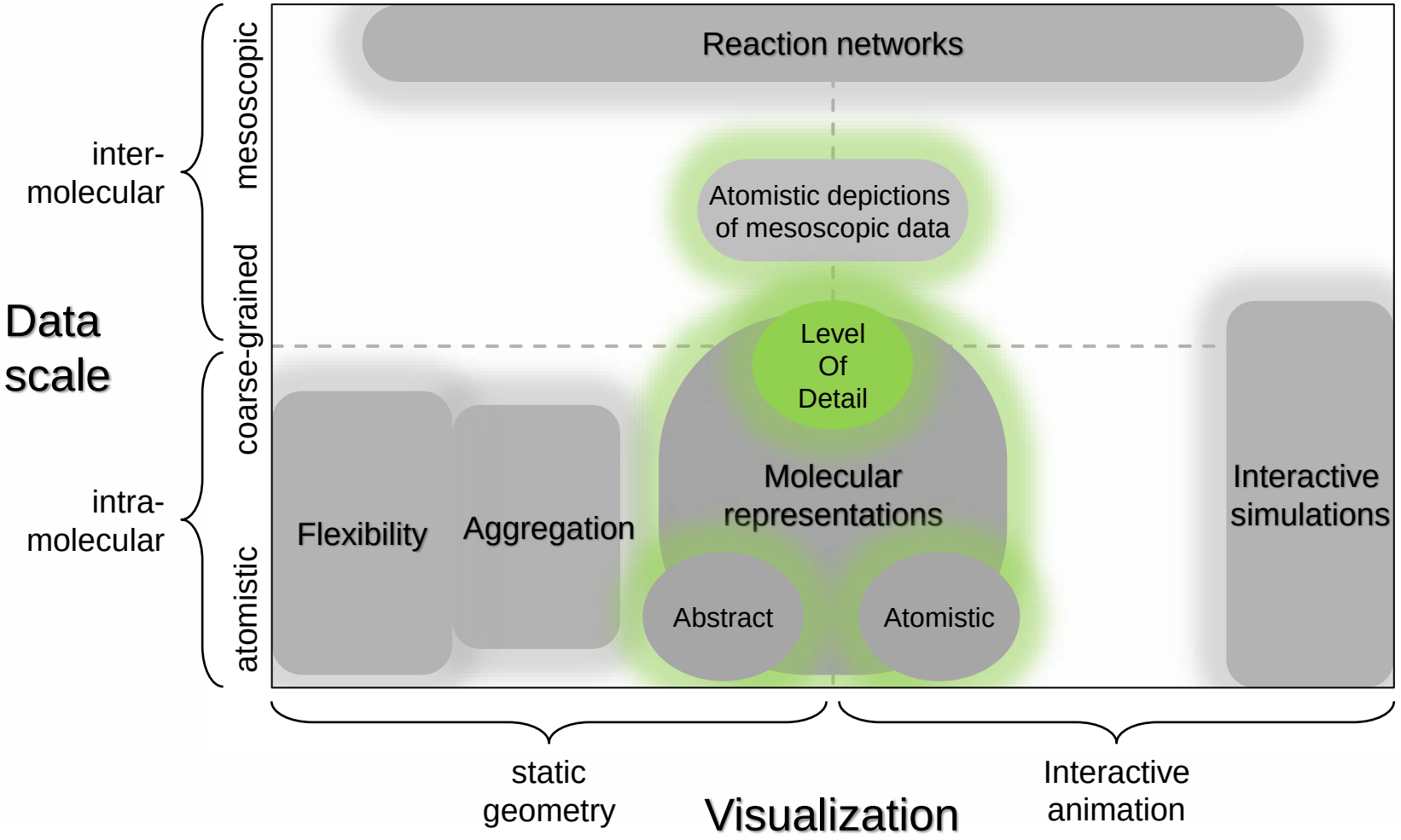
  - Molecular surface maps [Krone at al. 2017]



Images: [Rahi, Sharp 2014]

TAXONOMY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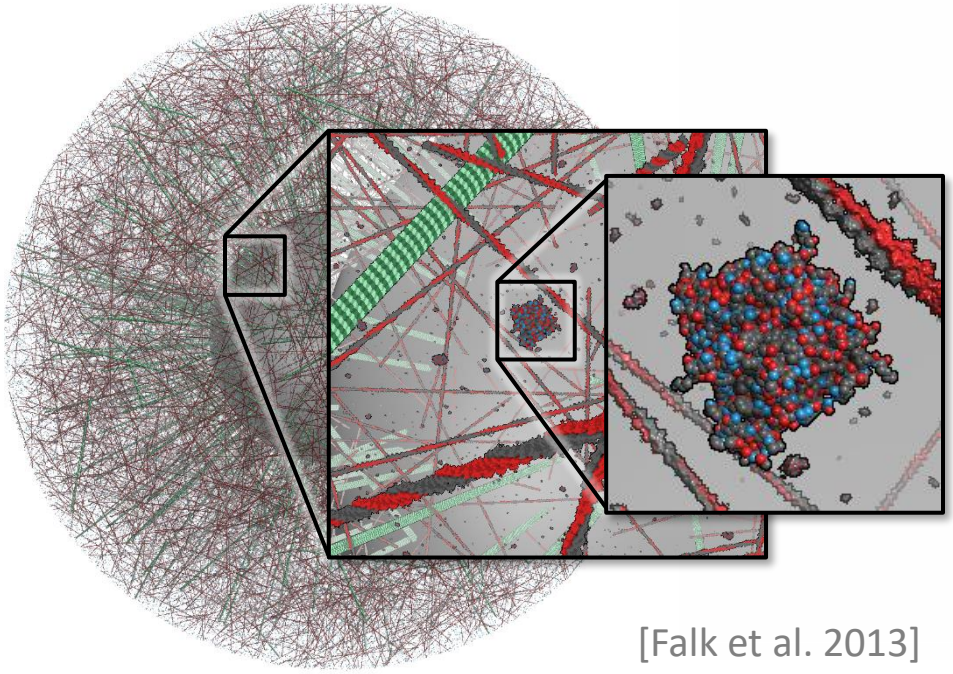
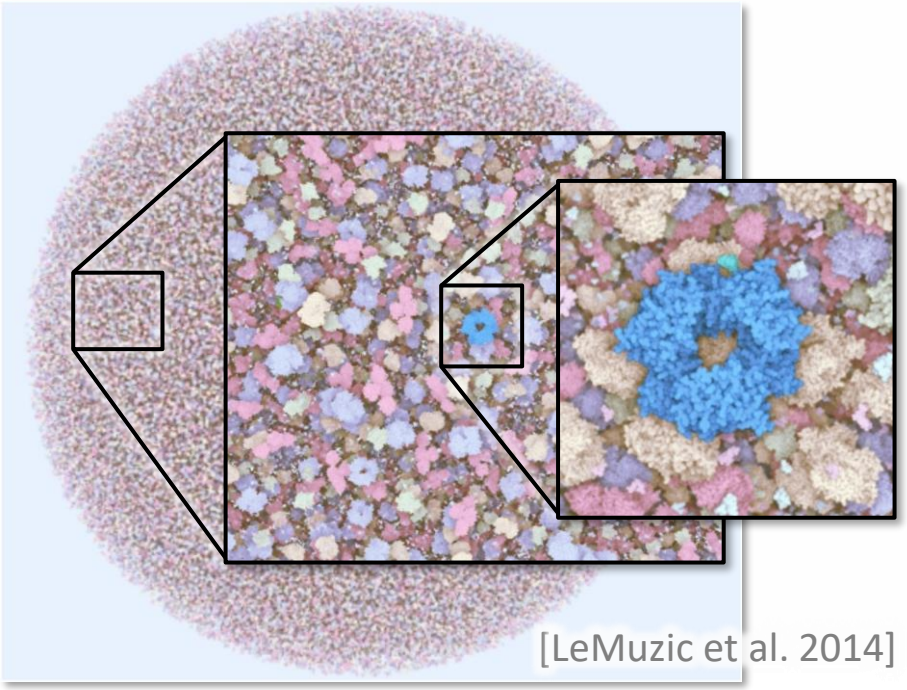
STRUCTURAL LEVEL OF DETAIL

- 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]



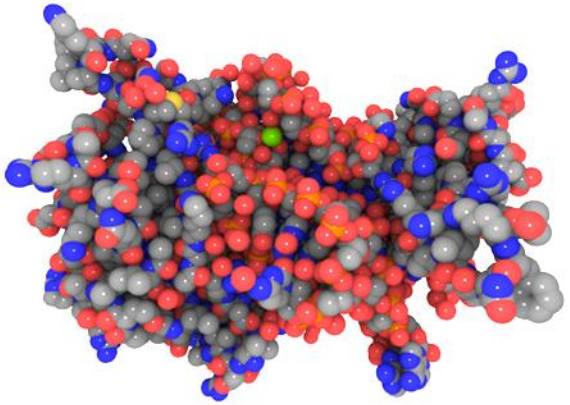
[LeMuzic et al. 2014]

MOLECULAR RENDERING

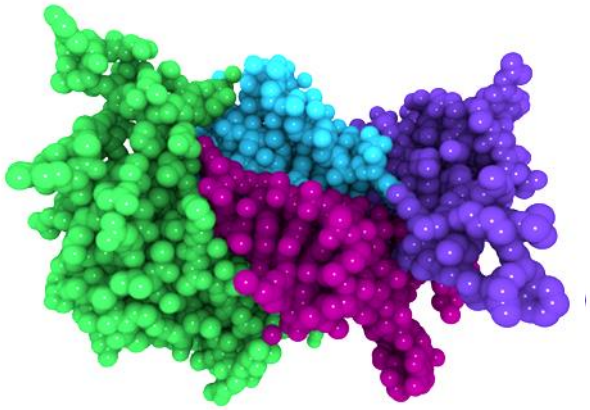
- Enhances
  - Image quality
  - Perception of geometric shapes and depth complexity
- Achieved by
  - Shading
  - Depth cues
- Computable for dynamic data in real-time

COLOR

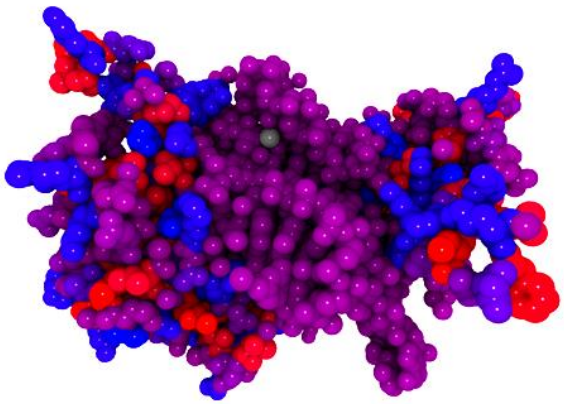
type of atoms



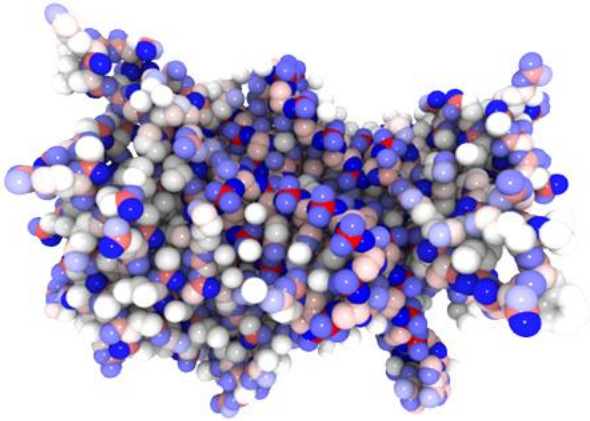
chains



hydrophobicity

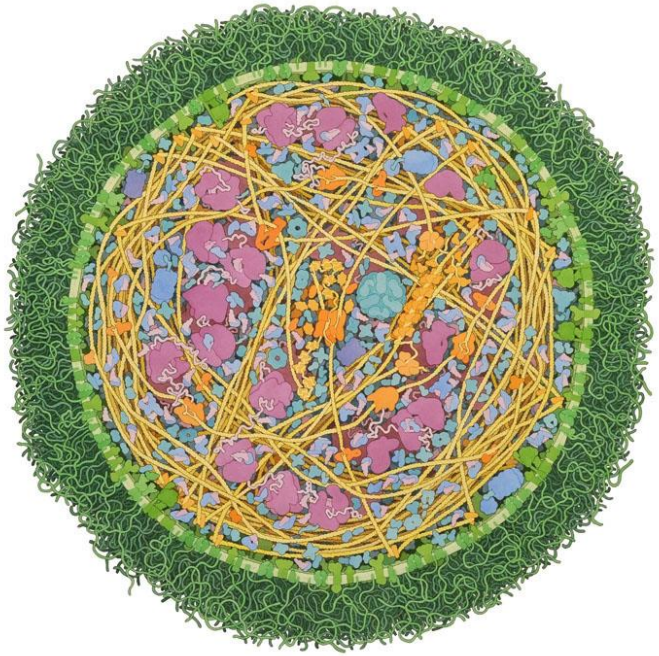


partial charge

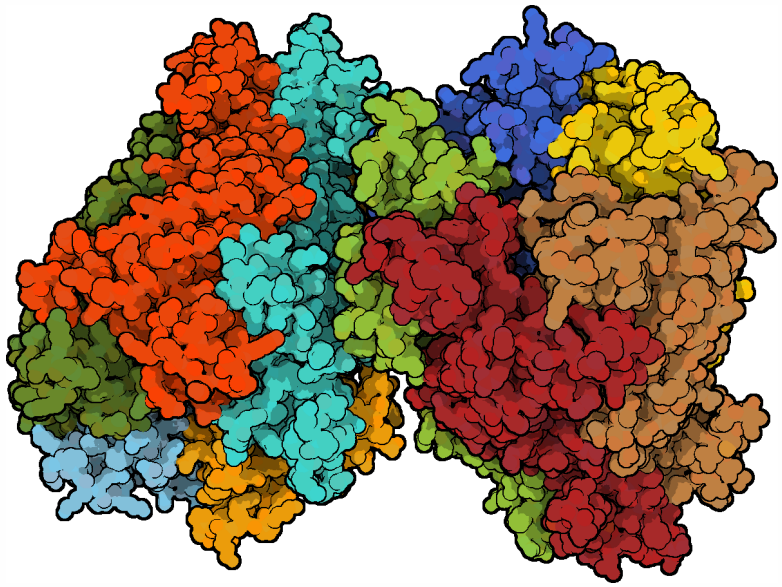


CEL SHADING

- Artistic or non-photorealistic renderings with a comic-like look
- Resembles hand-drawn illustrations



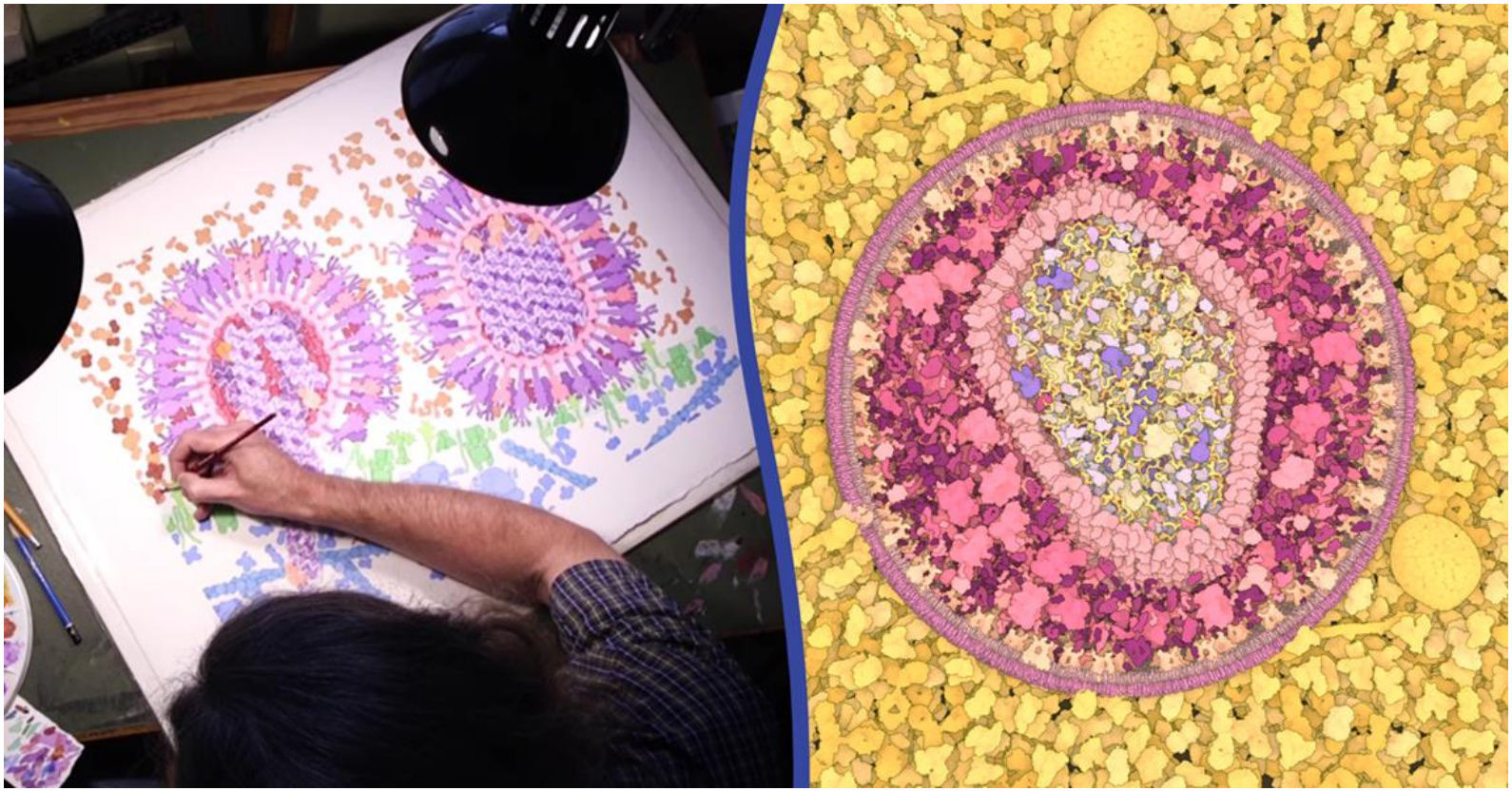
Mycoplasma cell
[Goodsell]



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

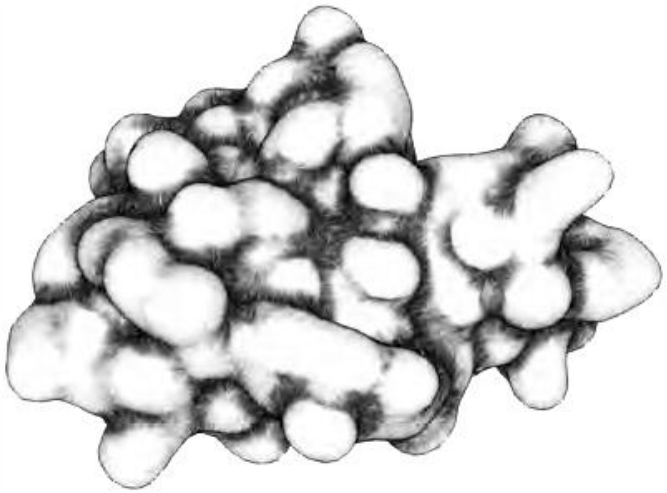
CEL SHADING

- cellVIEW
  - Aiming to resemble hand-drawn illustrations of David Goodsell



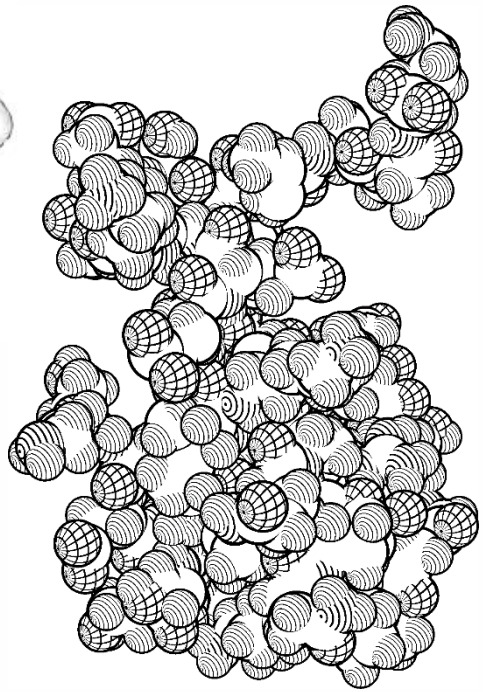
FEATURE LINES AND HATCHING

[van der Zwan et al. 2011]



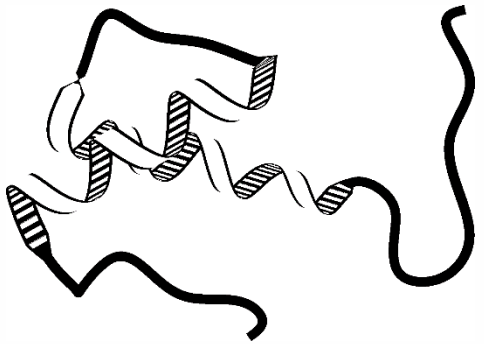
molecular surfaces

[Lawonn et al. 2014]

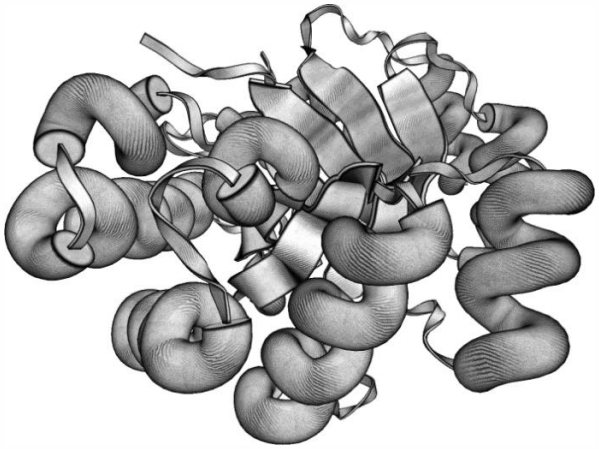


space filling models

[van der Zwan et al. 2011]



cartoon representations



[Weber 2009]

DEPTH CUE TECHNIQUES

- Sihouettes, halos, depth darkening
- Ambient Occlusion

  Real-time Ambient Occlusion
- Depth of Field

ORDINAL DEPTH CUES

- **Silhouettes**

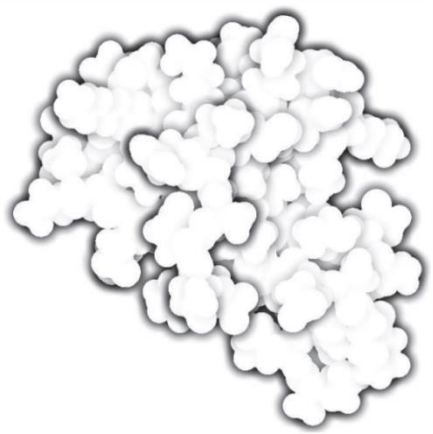
  Computed in image space in postprocessing

- **Halos**

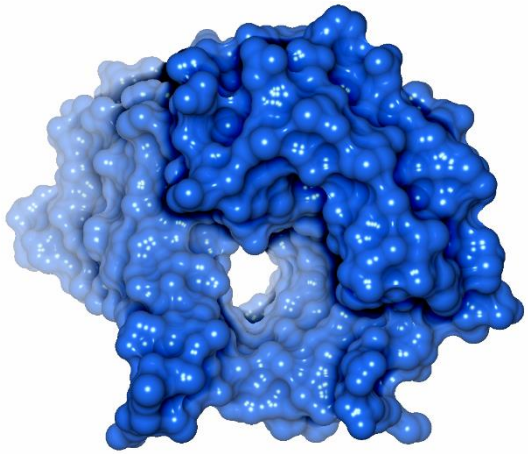
  Extended from the object boundaries

- **Depth darkening**

  Visually separates distant overlapping objects



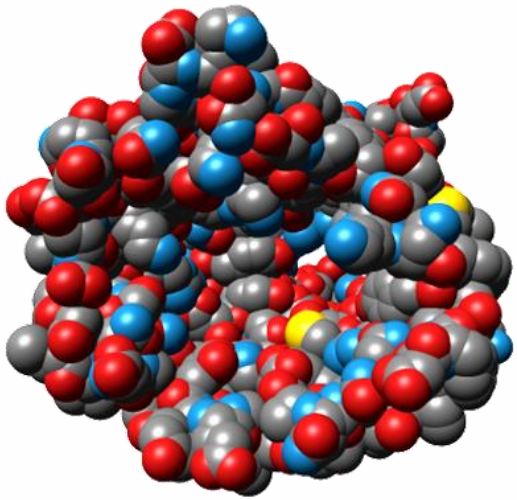
[Tarini et al. 2006]



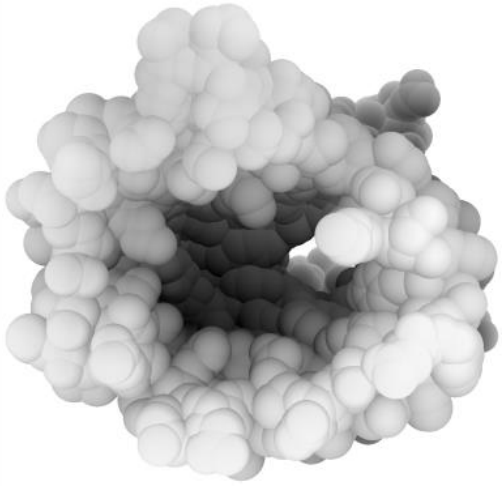
[Krone et al. 2009]

RELATIVE DEPTH CUES - AMBIENT OCCLUSION

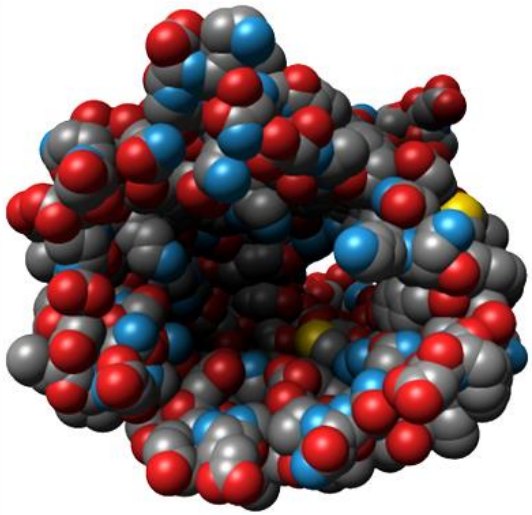
- Mimicking the transport of diffuse light between objects
- Local shadowing, increases depth perception



Local lighting



Ambient Occlusion

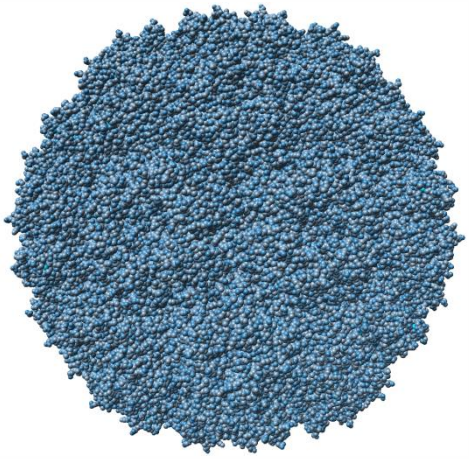


Combined

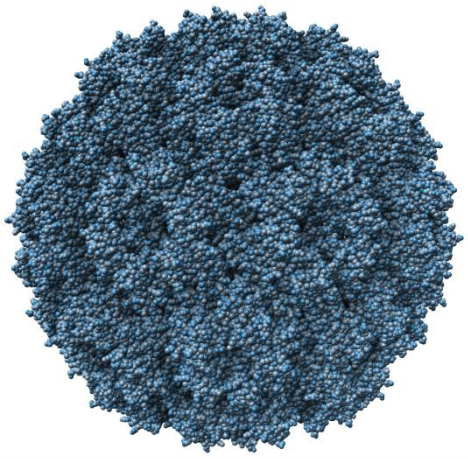
- Computationally expensive, accelerated approaches developed

REAL-TIME AMBIENT OCCLUSION

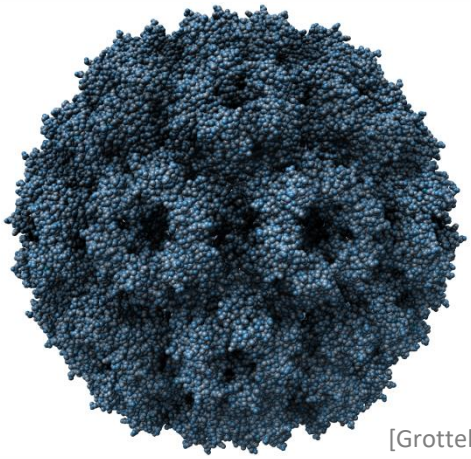
- Screen-Space Ambient Occlusion
  - Image space technique, approximates the effects in postprocessing
  - Considers the visible neighborhood of fragments
- Object-Space Ambient Occlusion
  - Considers the entire local neighborhood of atoms



Local lighting



Screen Space AO
[Kajalin 2009]

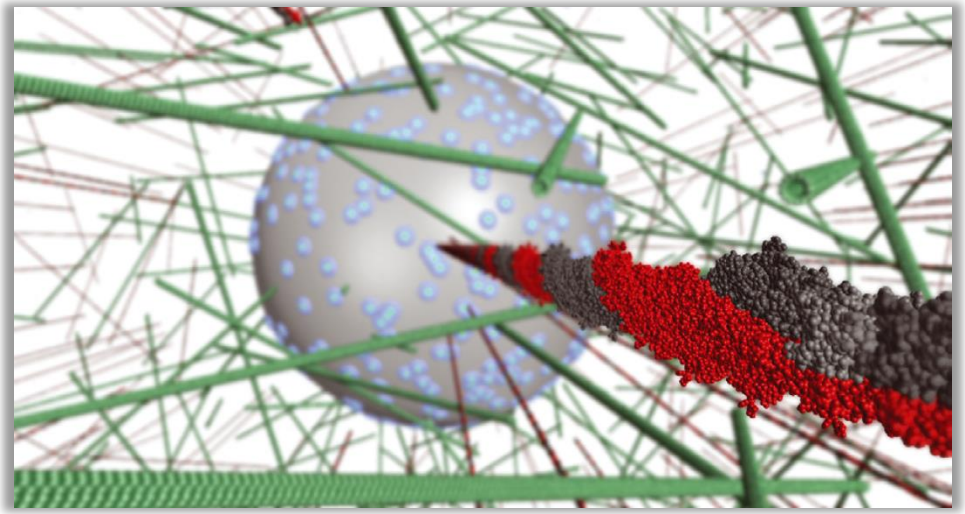


Object Space AO
[Grottel et al. 2012]

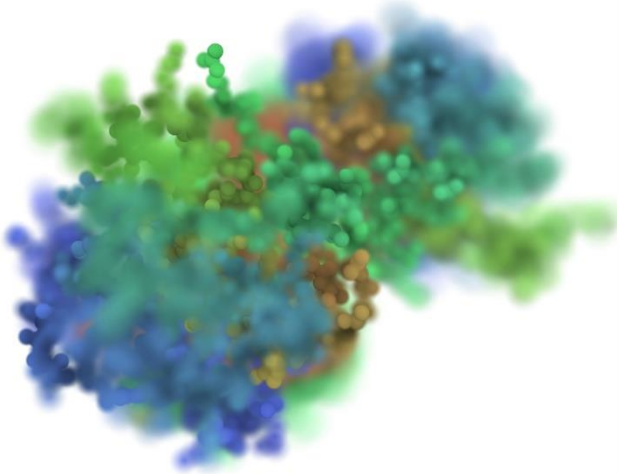
Images:
[Grottel et al. 2012]

DEPTH OF FIELD

- Separating foreground from background
- Image-space and object-space based approaches
- Draw the attention to a specific region or semantic properties

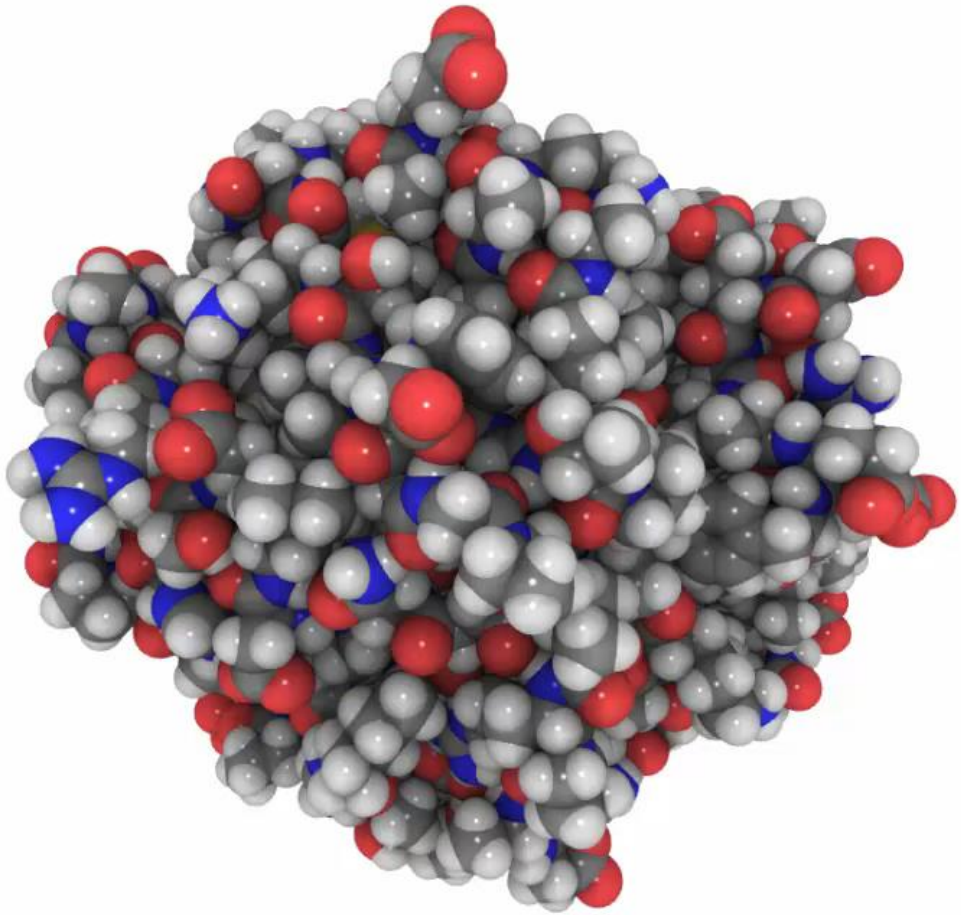


Region-based
[Falk et al. 2013]

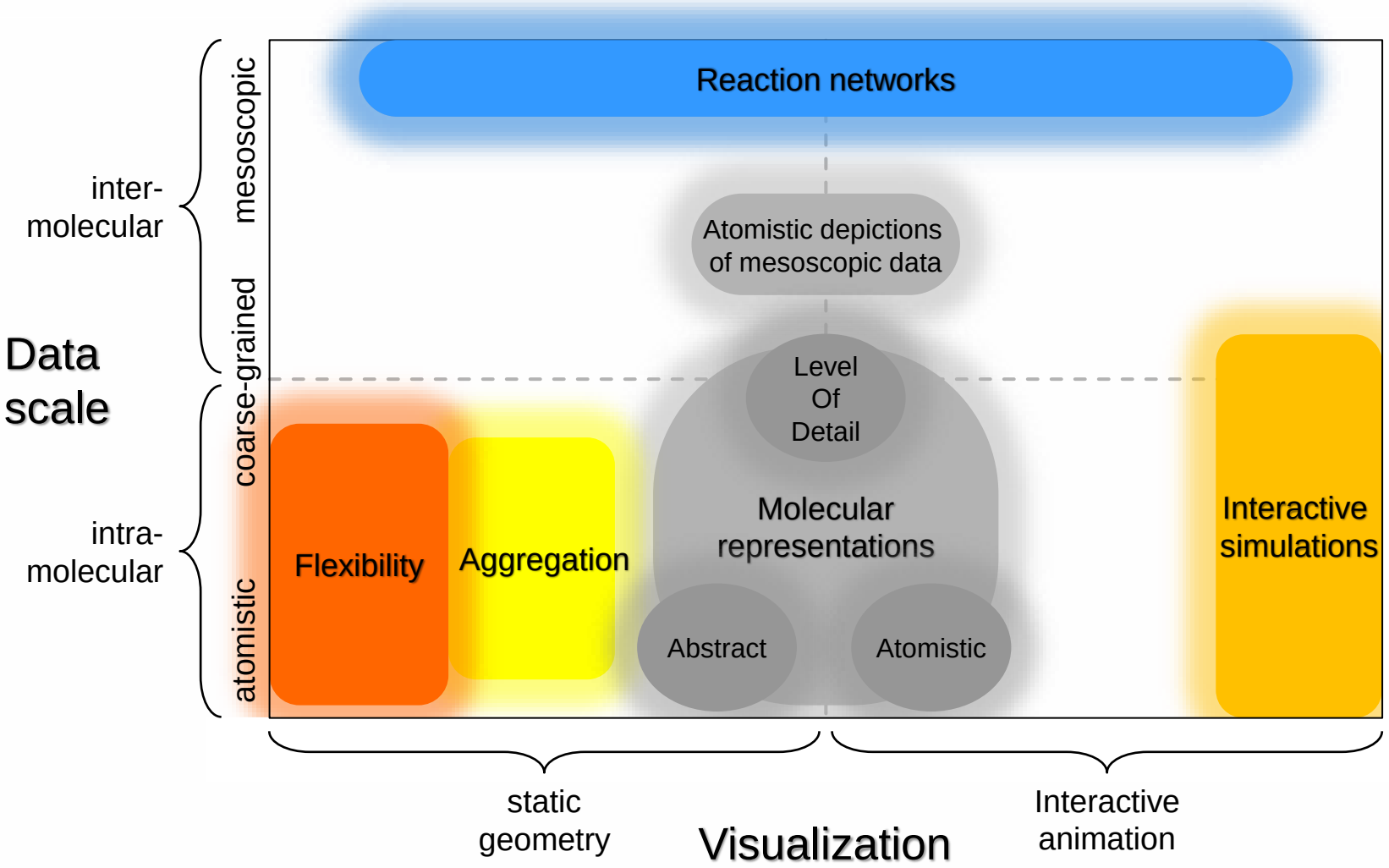


Semantic-based
[Kottravel et al. 2015]

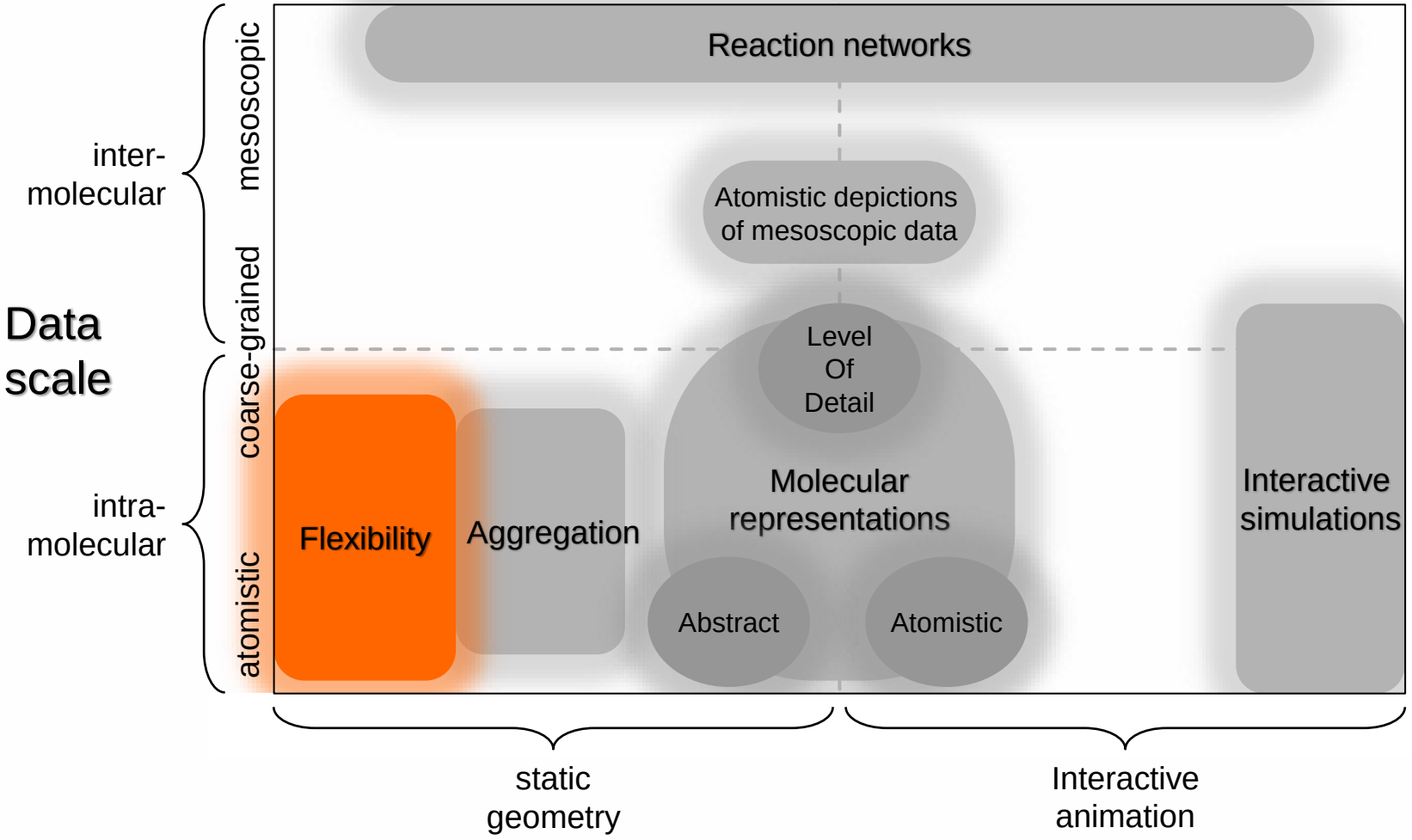
VISUALIZATION OF MOLECULAR DYNAMICS



VISUALIZATION OF MOLECULAR DYNAMICS

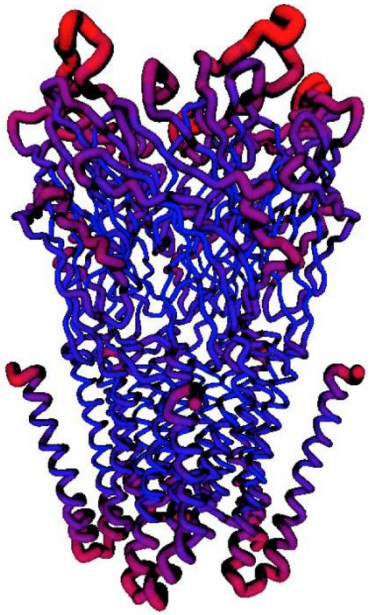


TAXONOMY

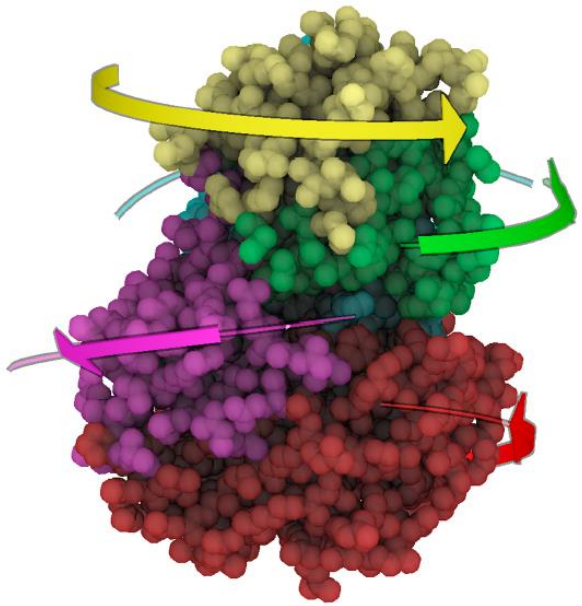

Reaction networks
Atomistic depictions of mesoscopic data
Level Of Detail
Molecular representations
Abstract
Atomistic
Flexibility
Aggregation
Interactive simulations
mesoscopic
coarse-grained
atomistic
inter-molecular
intra-molecular
Data scale
static geometry
Interactive animation

VISUALIZATION OF FLEXIBILITY

- Probability distribution depicting the varying molecular conformations

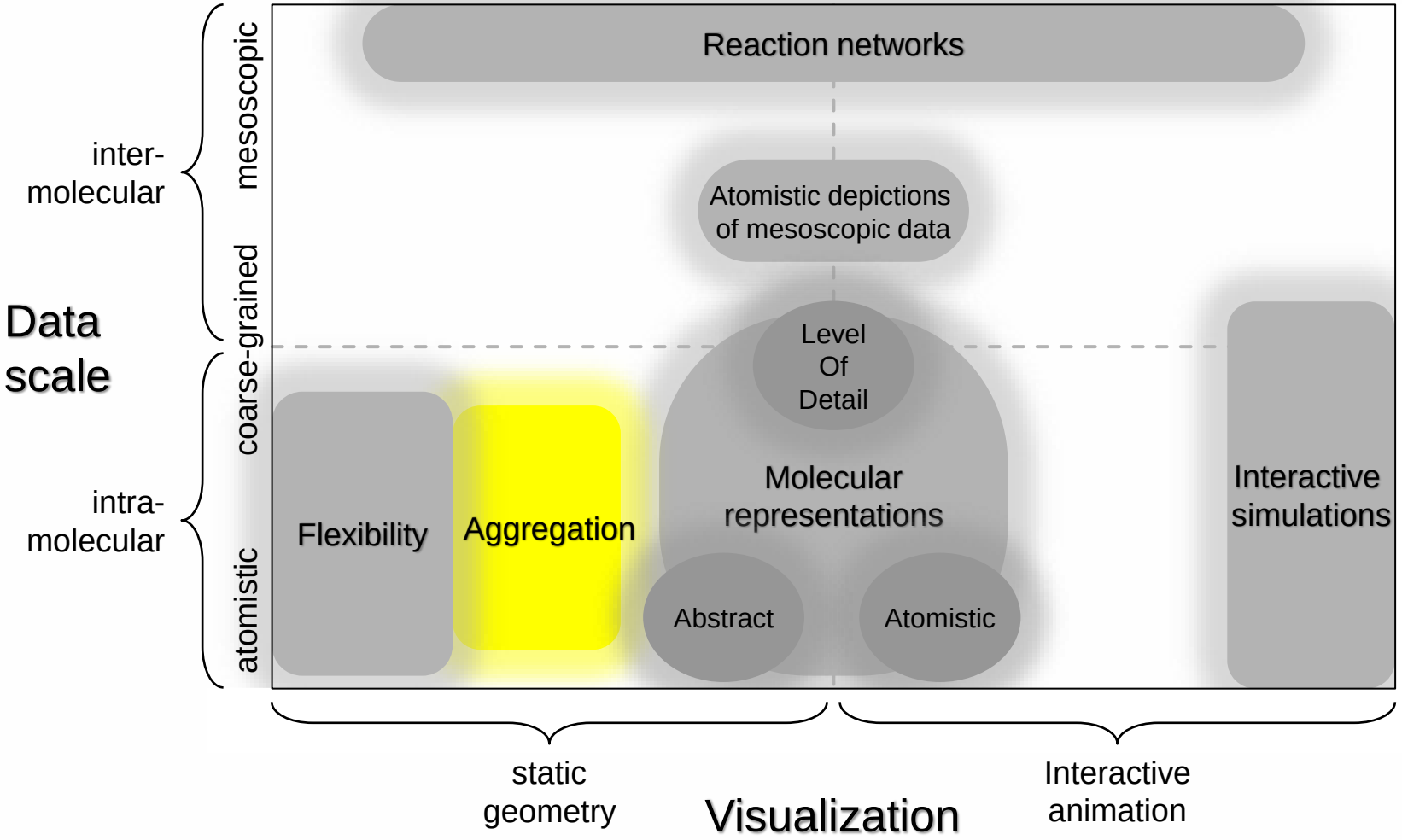


Modulated tube
[Lv et al. 2013]



Normal Mode Analysis
[Bryden et al. 2012]

TAXONOMY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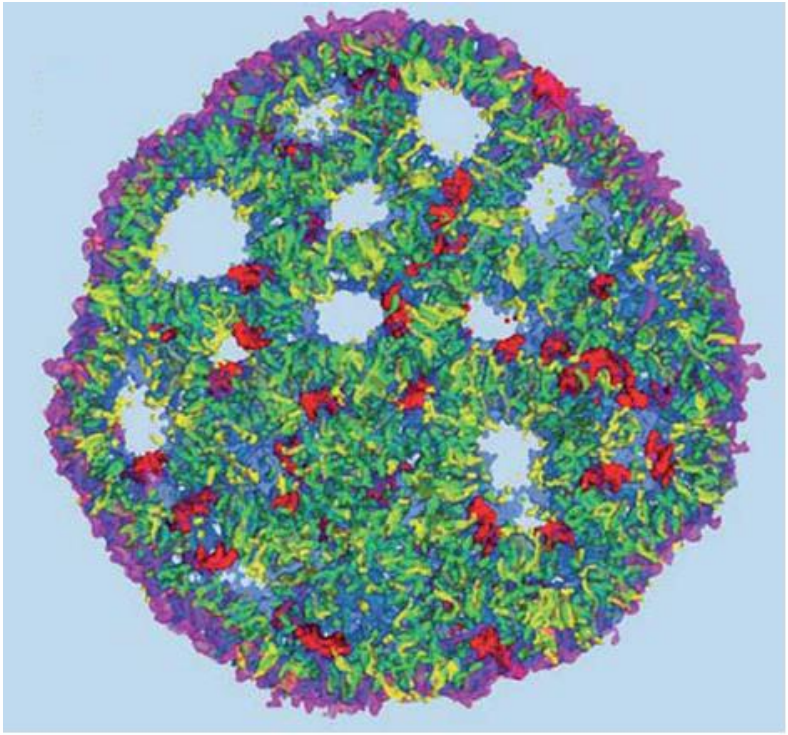
Visualization
Interactive animation

AGGREGATION

- **Spatial**

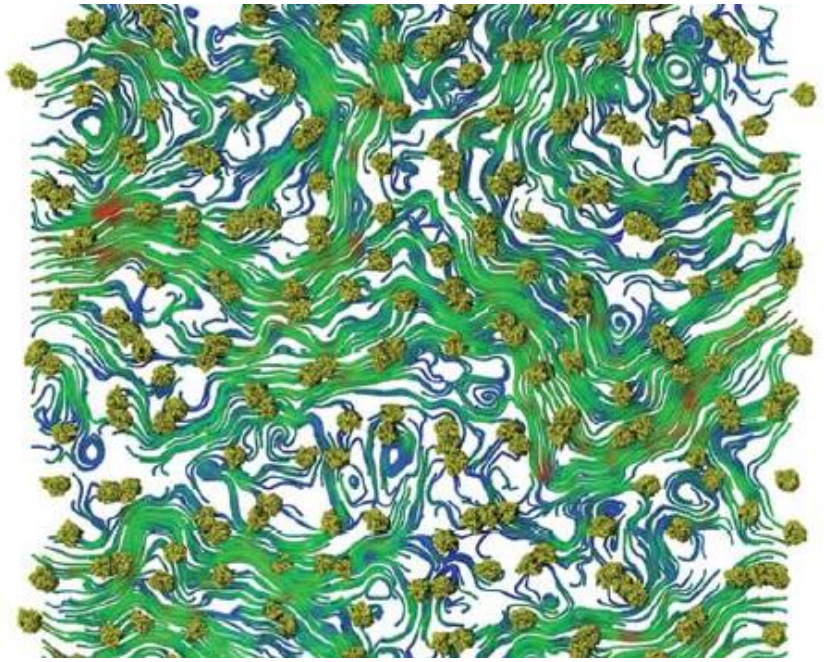
  Aggregating atom densities using property grids



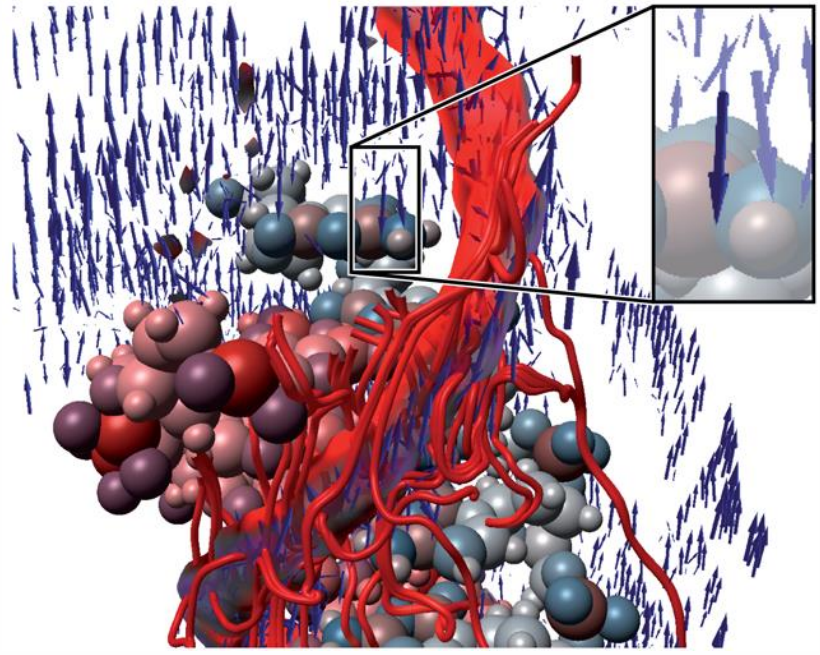
[Rozmanov et al. 2014]

AGGREGATION

- **Temporal**
  - Aggregated diffusional motion
  - Combination of temporal and spatial aggregation

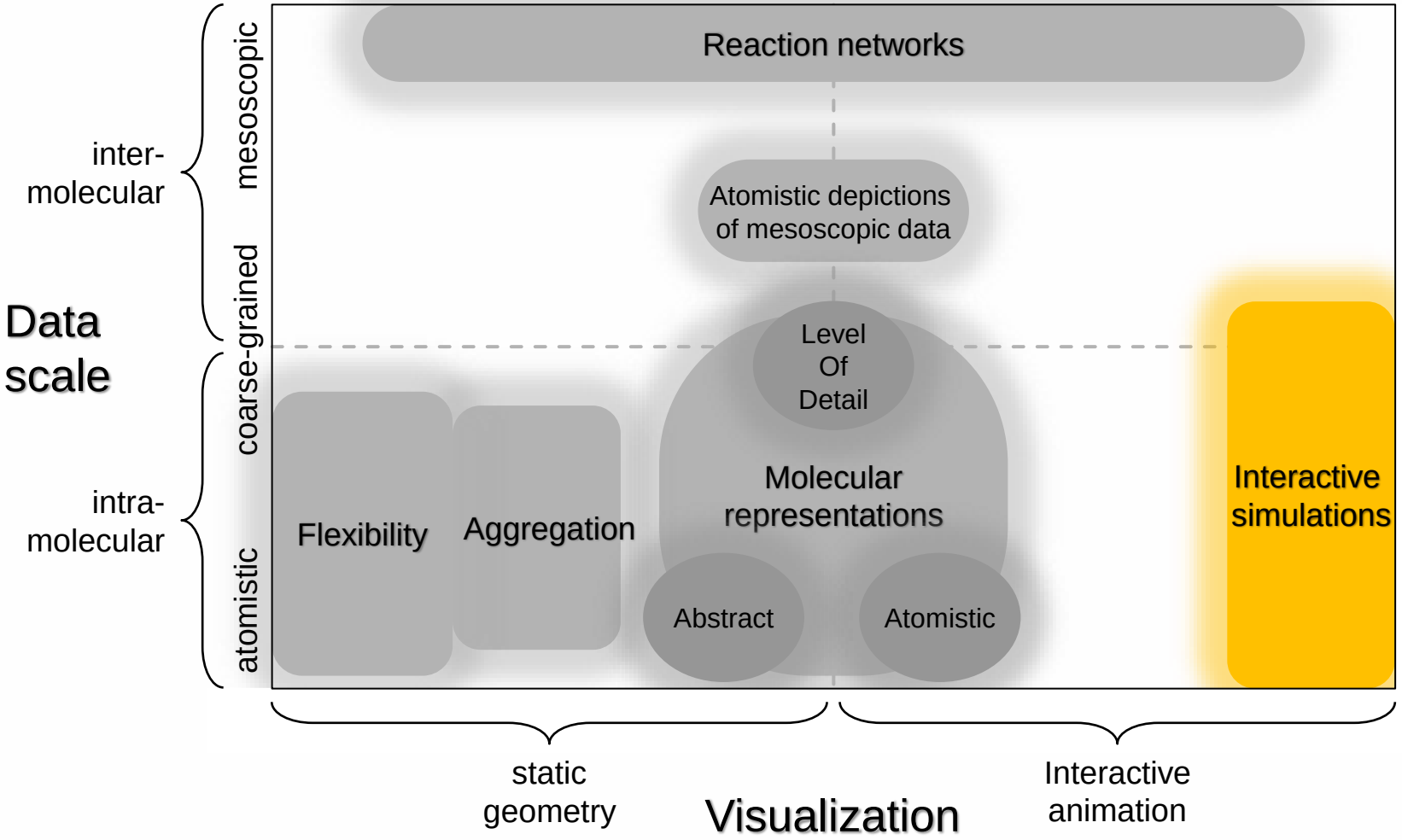


[Chavent et al. 2014]



[Ertl et al. 2014]

TAXONOMY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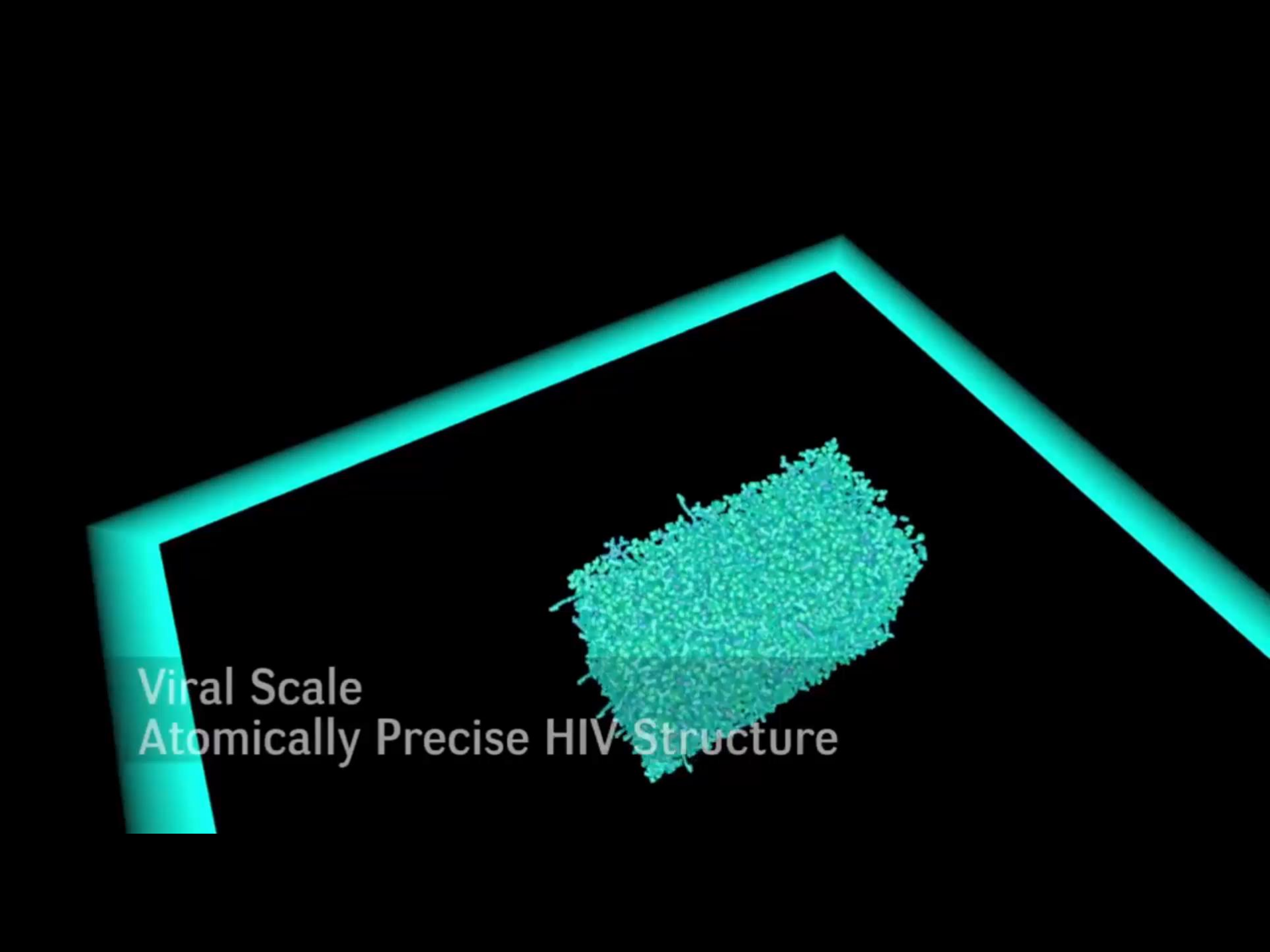
INTERACTIVE SIMULATIONS

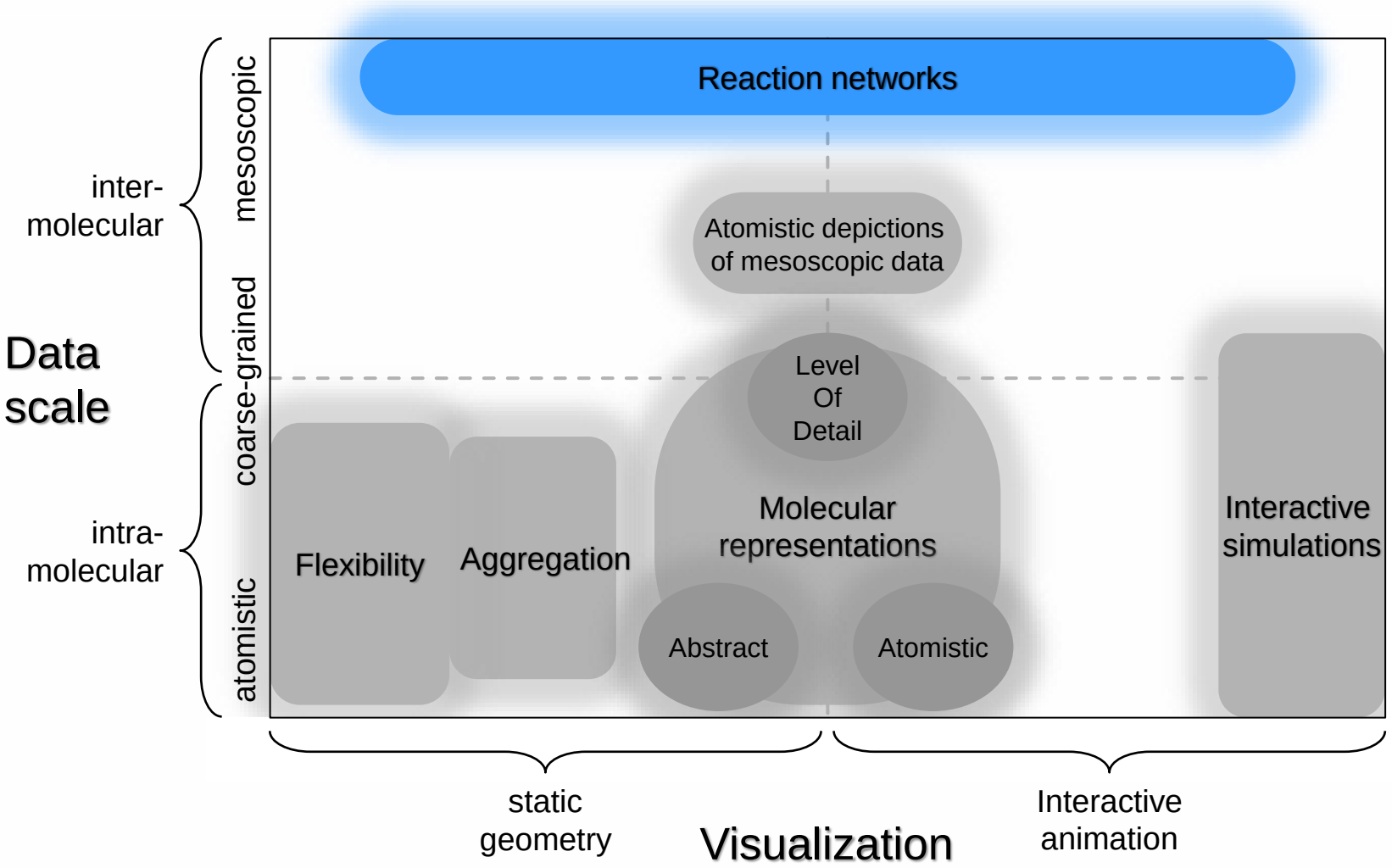
- Visualization has to be interactive → simulation performance has to be the limiting factor
- Haptic rendering – 1000 Hz refresh rates
- Cheaper and better hardware → haptic steering is very attractive

  Applied to systems with more than 1 million atoms

[Dreher et al. 2013]


Viral Scale
Atomically Precise HIV Structure

TAXONOMY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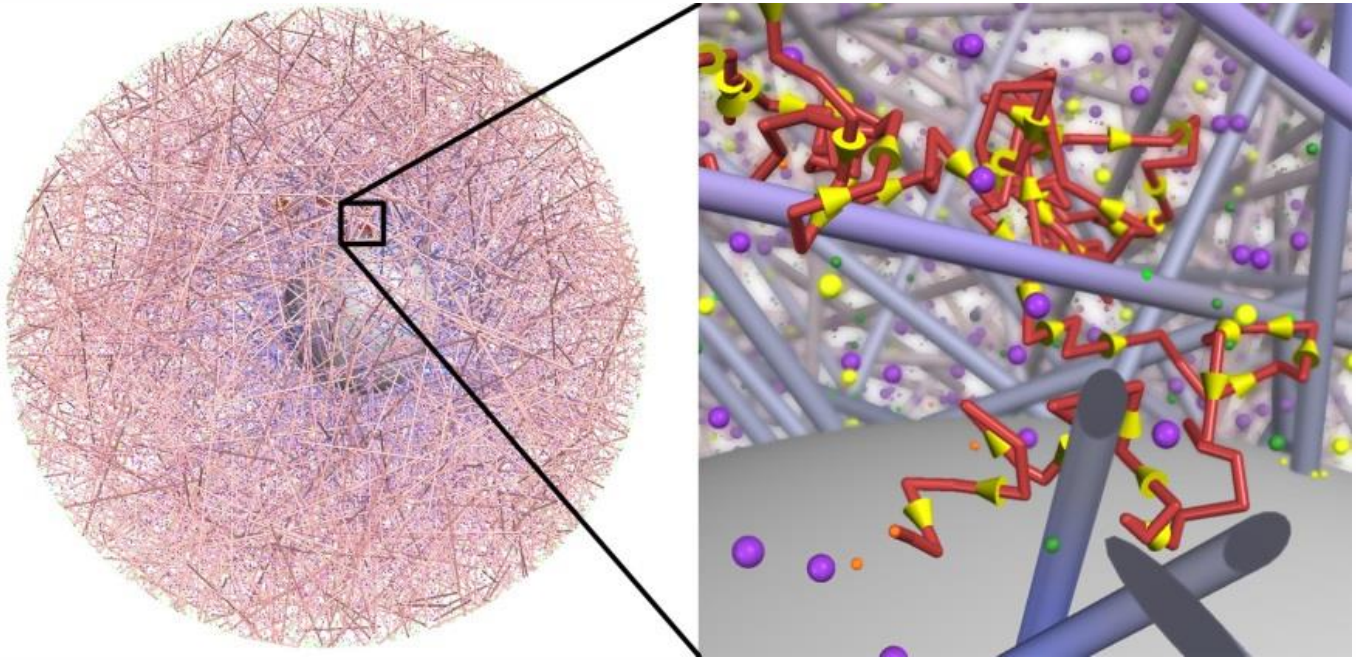
MOLECULAR REACTIONS

- Several existing tools for the visualization of reaction networks
- Particle simulations are very crowded

Methods visually emphasizing interesting aspects of simulations



particle trajectory [Falk et al. 2009]

MOLECULAR REACTIONS

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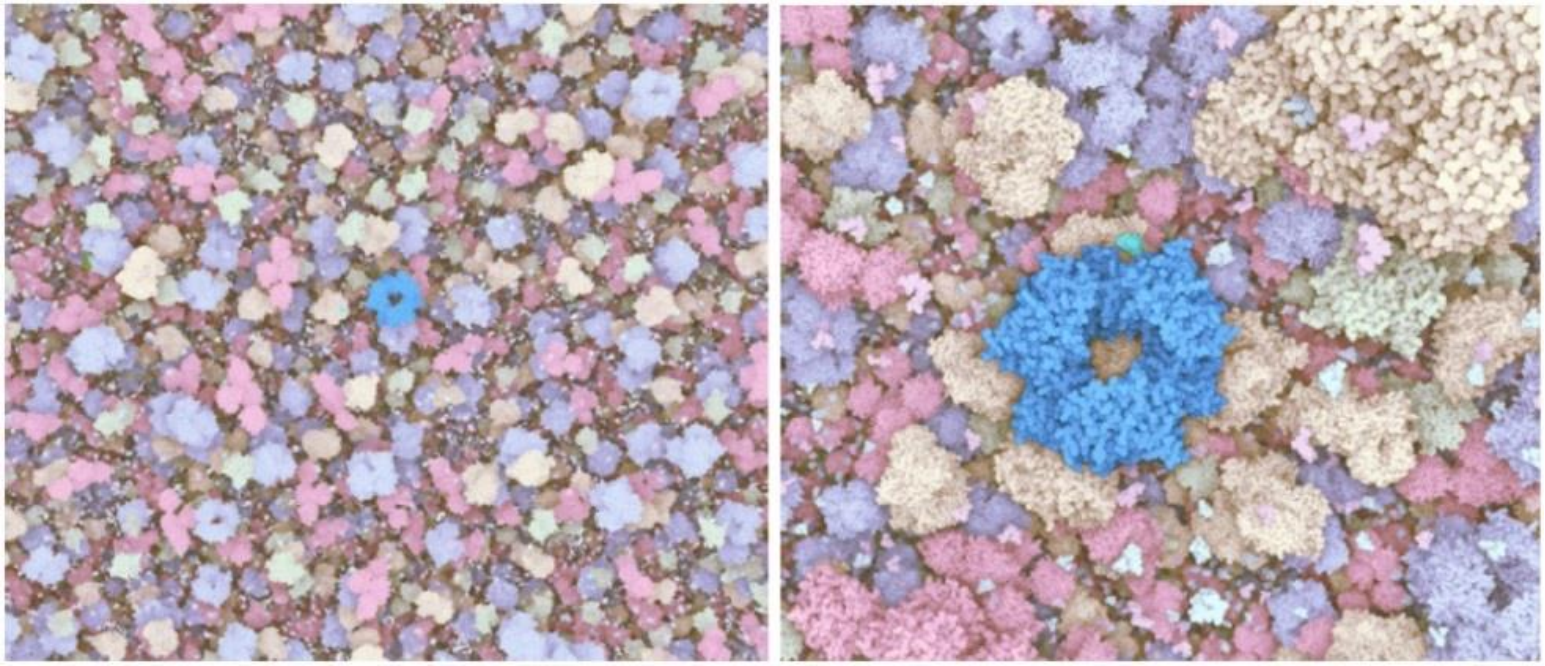
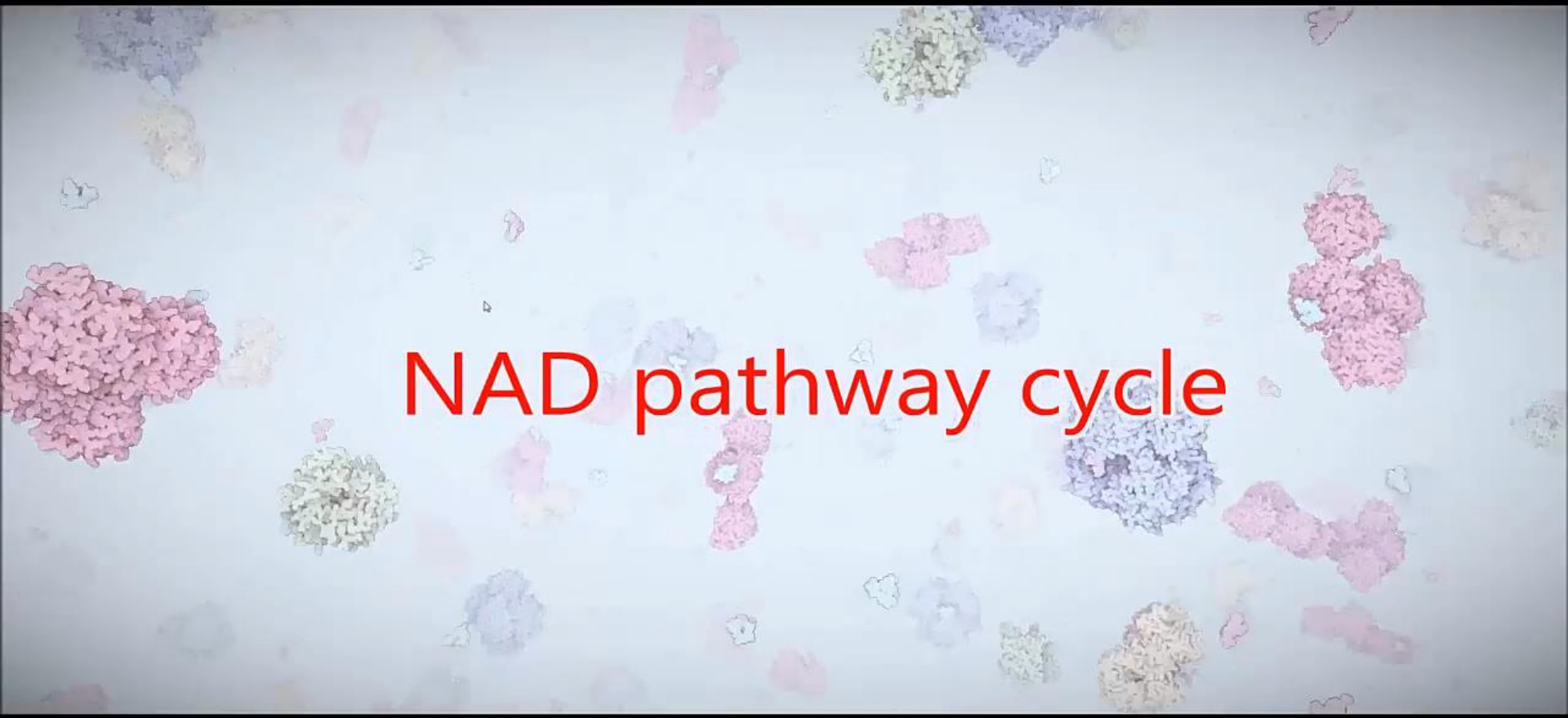


focus on reactions [Le Muzic et al. 2014]

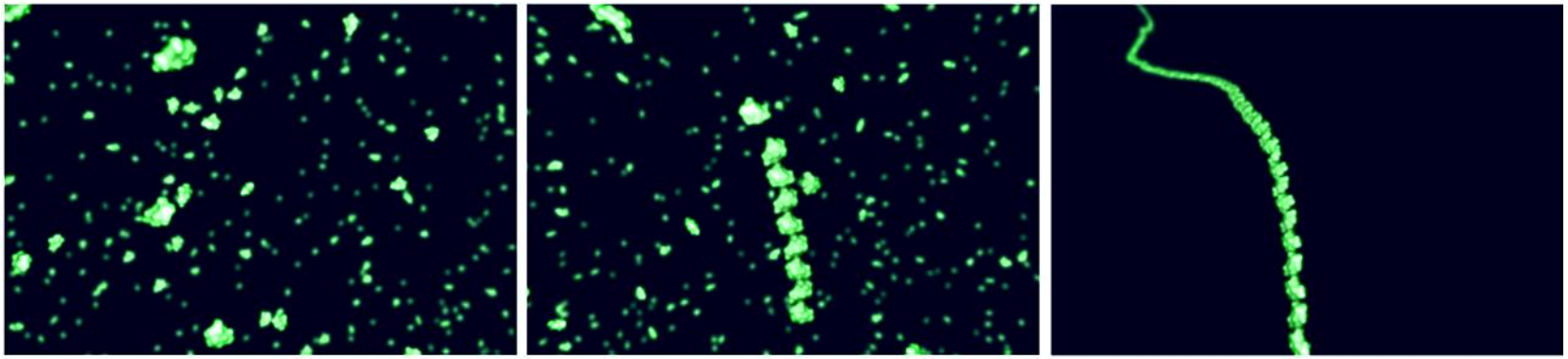
MOLECULAR REACTIONS



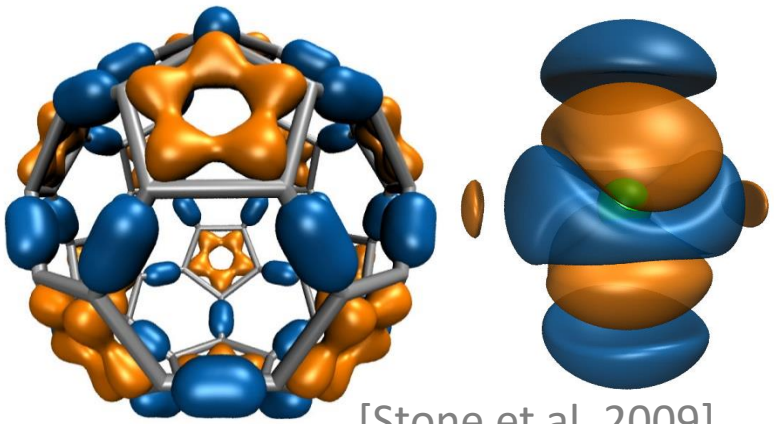
MOLECULAR REACTIONS

- Visualization of polymerization

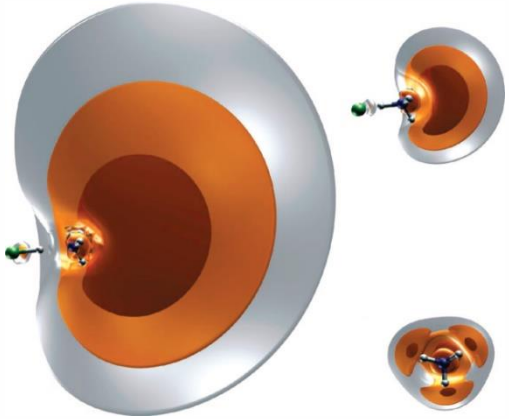
[Kolesár et al. 2014]



- Visualization of molecular orbitals, electron densities, bonds



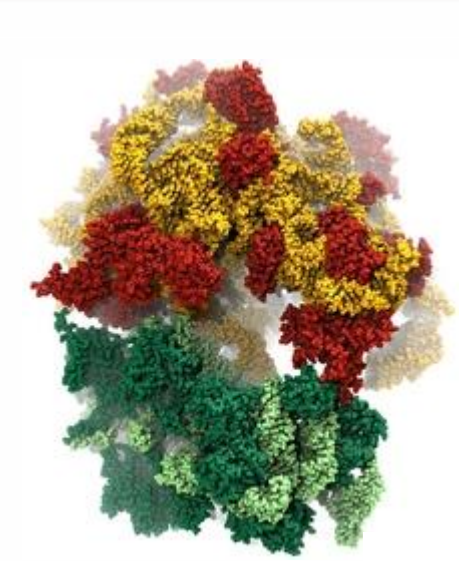
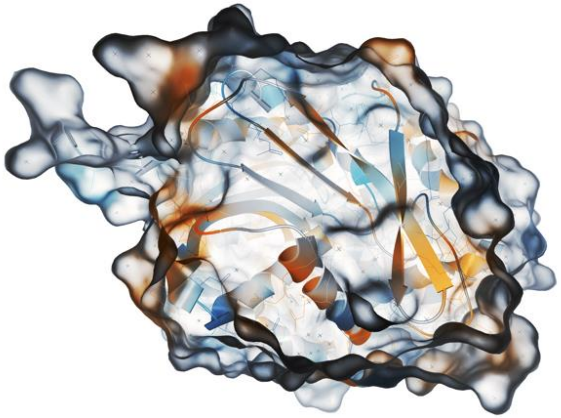
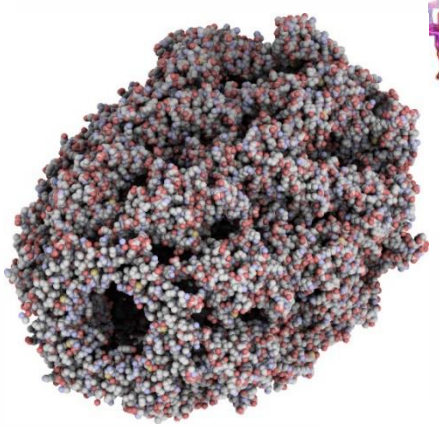
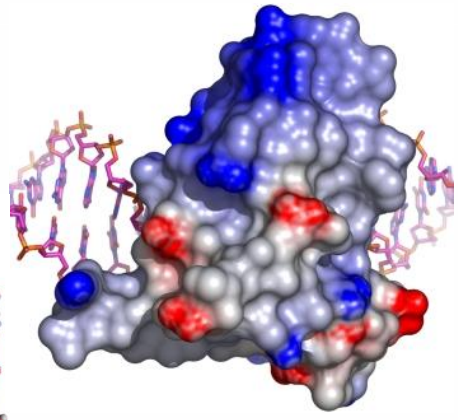
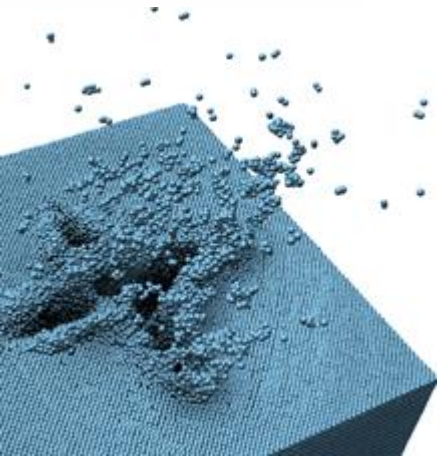
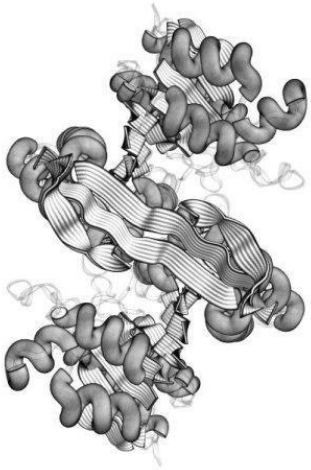
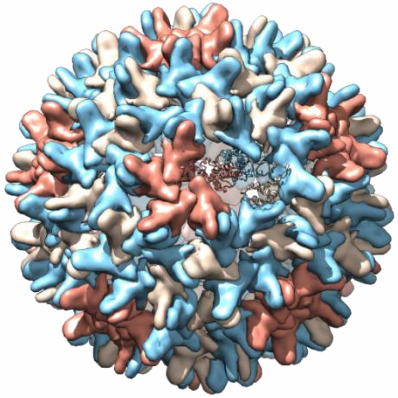
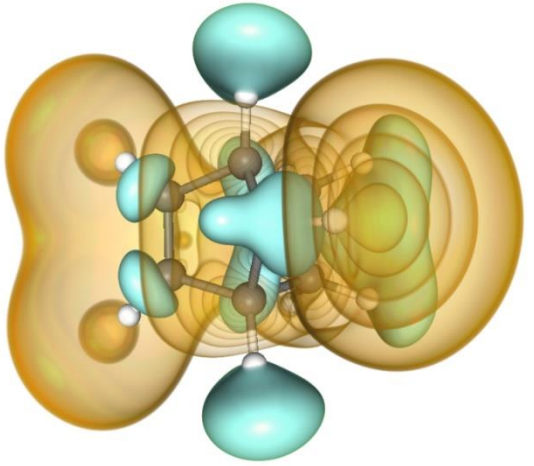
[Stone et al. 2009]



[Haranczyk, Gutowski 2008]

MOLECULAR VISUALIZATION SYSTEMS

MOLECULAR VISUALIZATION SYSTEMS

FUTURE CHALLENGES

- Prevailing trend is to use GPU based rendering and computations
  - Programmable GPUs and multi-core GPUs enable parallelization
- Increasing amount of captured data sets in terms of particle numbers and time steps
- Complexity of data will require new visual representations
  - Visual analysis
- Quantum mechanics simulations will require novel visualization methods
- Visual language for biomolecules