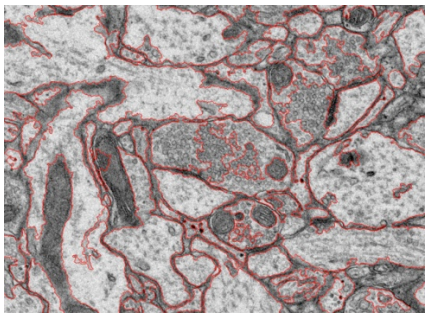
Geometric Modeling and Visualization

http://www.cs.utexas.edu/~bajaj/cs384R07/

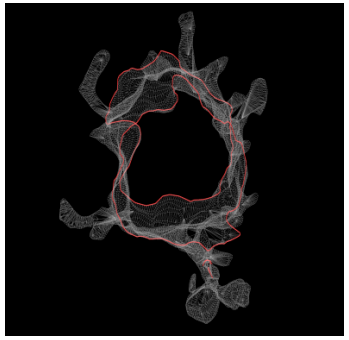
T, TH 9:30 – 10:45pm

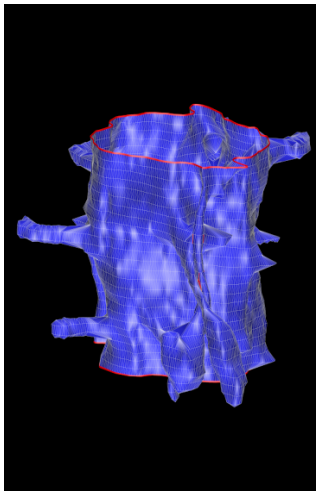
Taylor 3.114

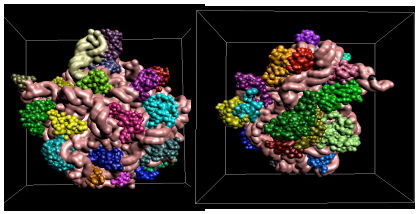
- Spatially realistic modeling to simulate and visually depict "How THINGS WORK" at multiple scales

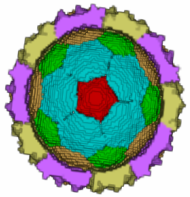


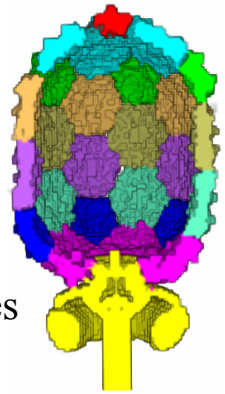
Neuronal Processes



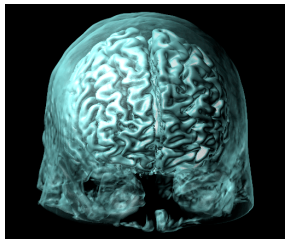


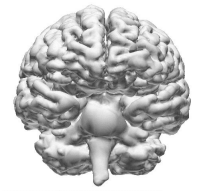


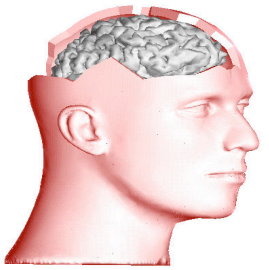




Ribosomes & Viruses







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CS384R/CAM395T/BME385J

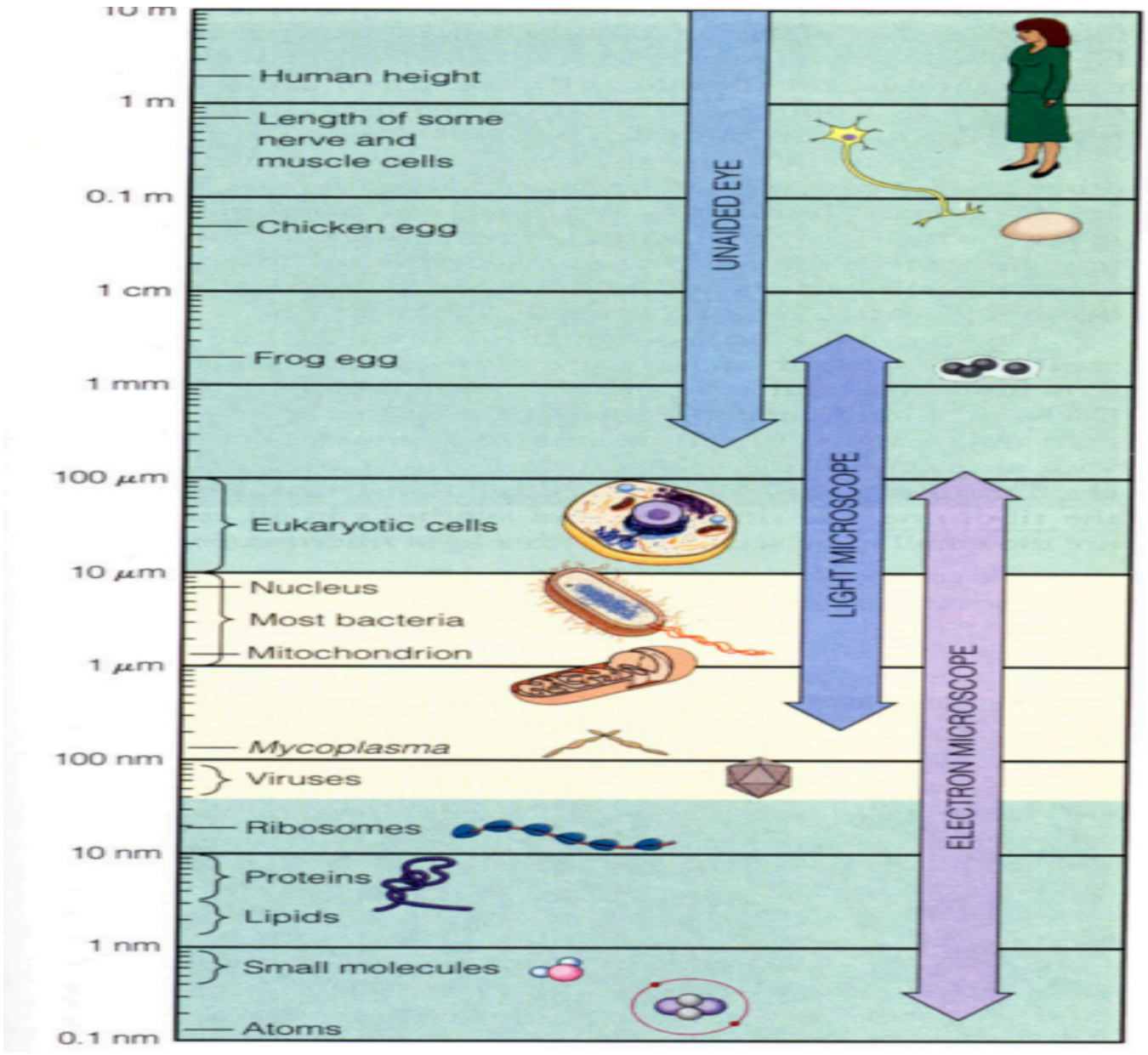
1. Imaging2Models: filtering, contrast enhancement, classification, symmetry detection, segmentation, skeletonization, subunit identification, matching, compression, reconstruction

2. Models2Analytics I: surfaces, finite element meshing, spline representations, feature identification, symmetry detection, shape segmentation, matching & complementary docking, flexibility, fluids

3. Models2Analytics II: polar and non-polar energetics, forces, torques, dynamics, cubature, discrete differential operators, sparsifiers, preconditioners

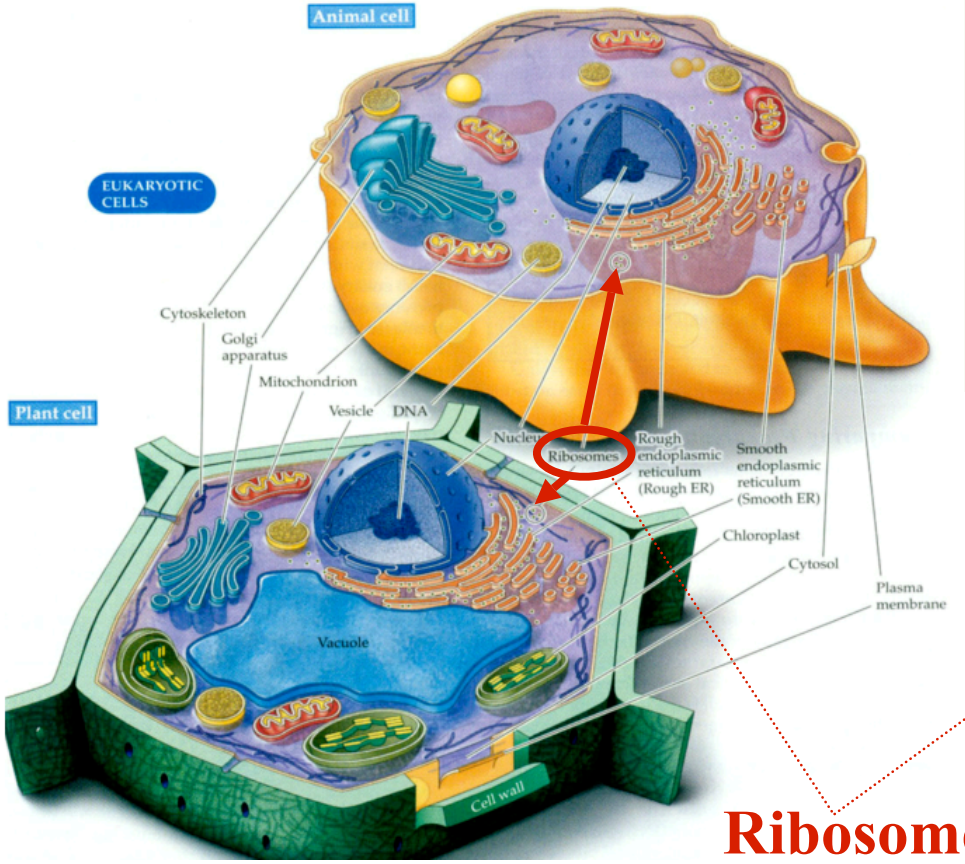
4. Analytics2Informatics I: differential/integral/ combinatorial properties, active sites, regions of interest, MACT analysis

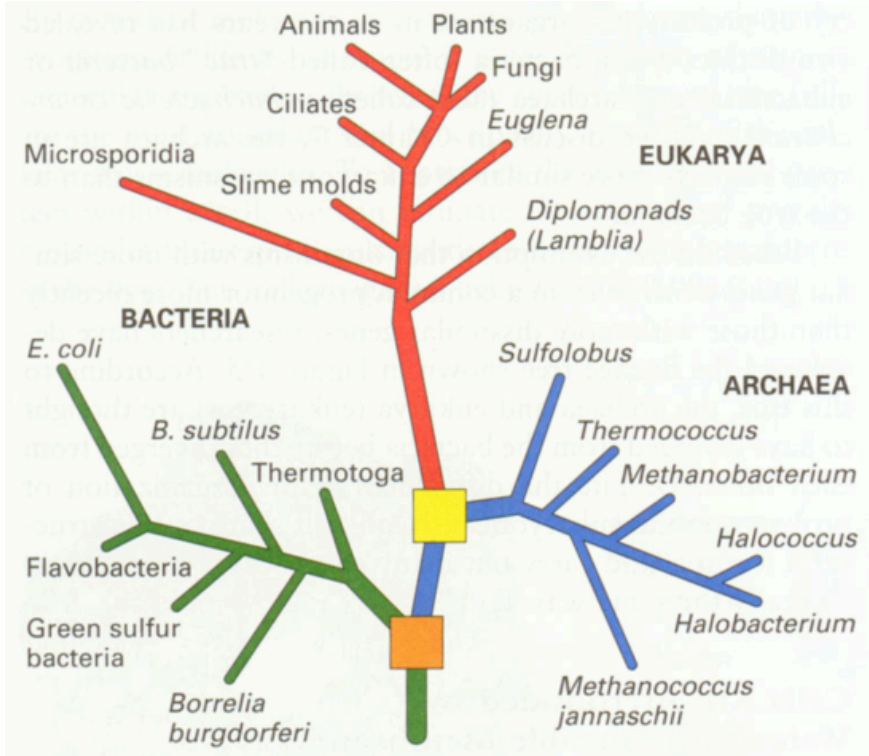
5. Analytics2Informatics II: multi-dimensional transfer functions, visible surface and volume rendering, function on surface, VisPortal


10 m
1 m
0.1 m
1 cm
1 mm
100 μm
10 μm
1 μm
100 nm
10 nm
1 nm
0.1 nm
Human height
Length of some nerve and muscle cells
Chicken egg
Frog egg
Eukaryotic cells
Nucleus
Most bacteria
Mitochondrion
Mycoplasma
Viruses
Ribosomes
Proteins
Lipids
Small molecules
Atoms
UNAIDED EYE
LIGHT MICROSCOPE
ELECTRON MICROSCOPE

The Tree of Life?

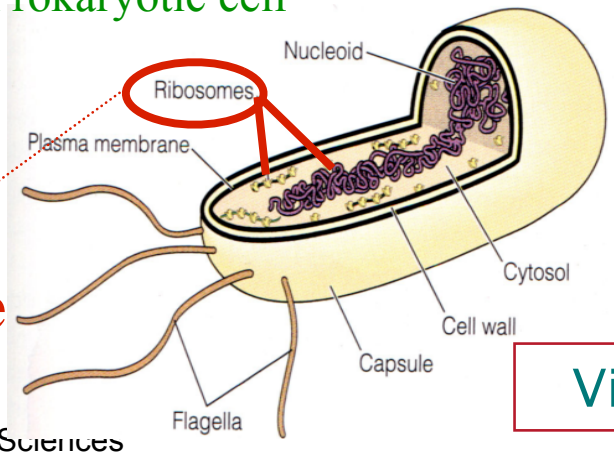
Eukaryotic cell





Archaebacteria cell

Prokaryotic cell



Ribosome

Viruses?

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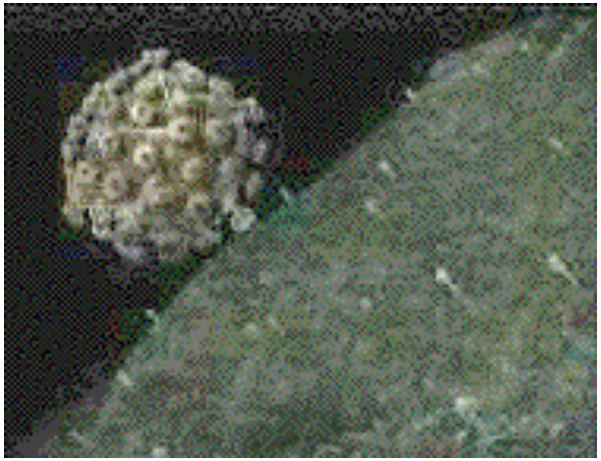
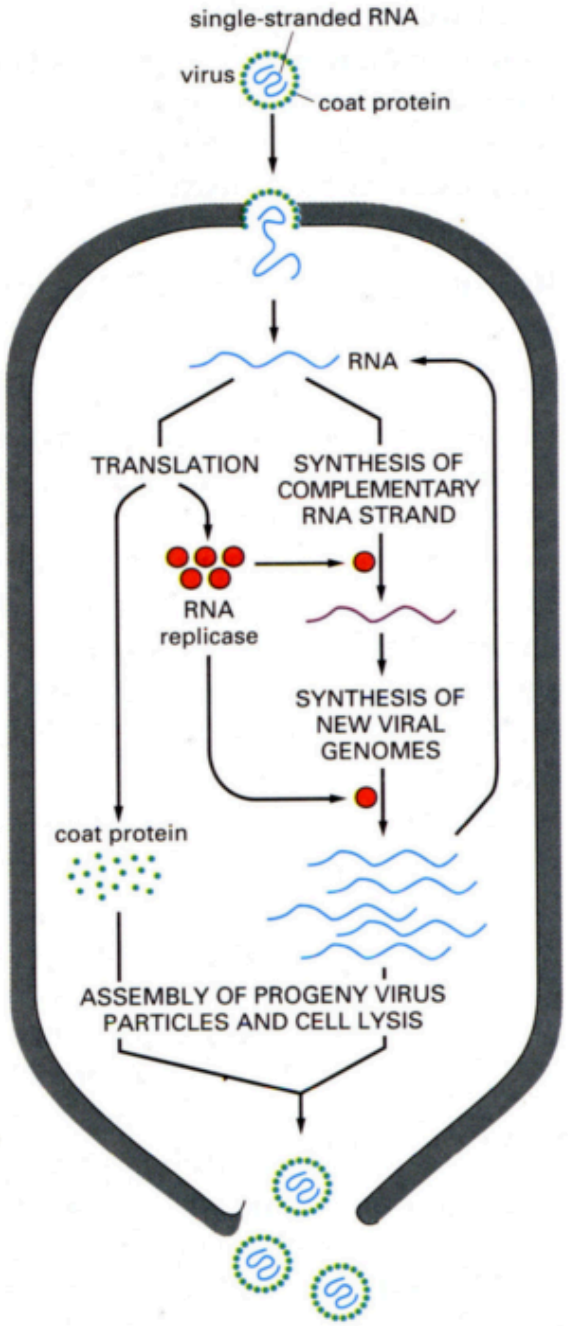
The Life Cycle of Viruses





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Imaging2Models

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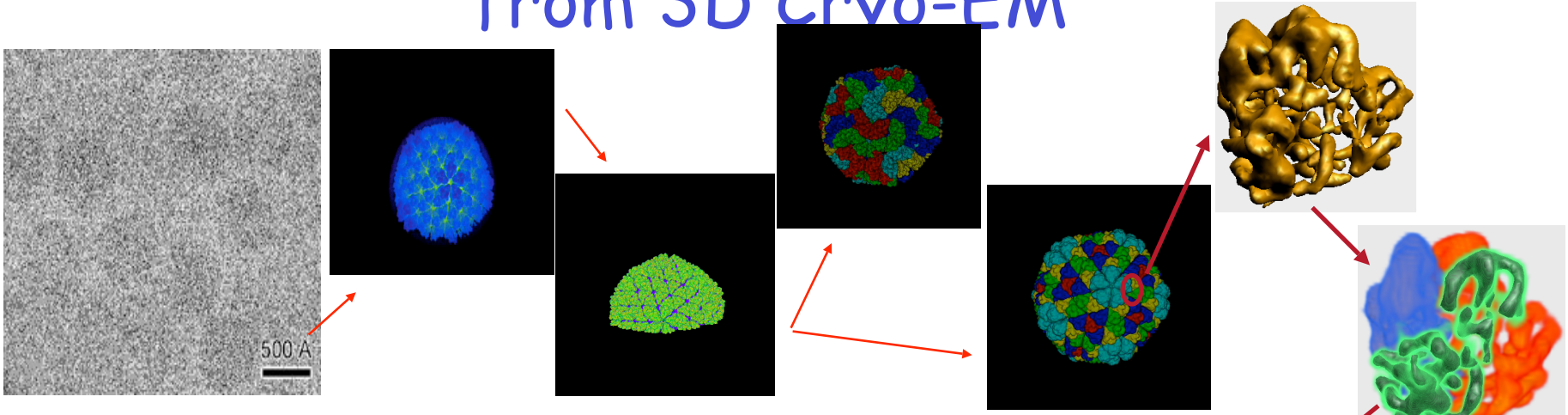
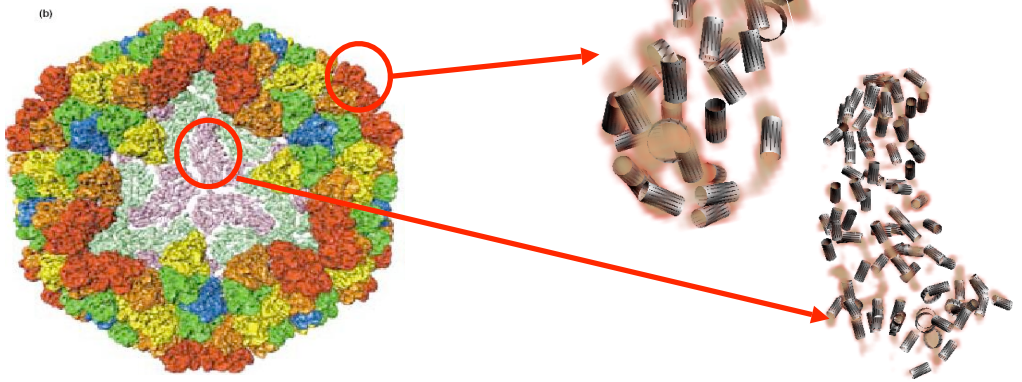
Sub-nanometer Structure Elucidation from 3D Cryo-EM



Cryo-EM →FFT based 3D Reconstruction
→Anisotropic and Vector Diffusion Filtering →
Structure Segmentation
→Quasi-Atomic Modeling
→Visualization

Rice Dwarf Virus



**Sponsor: DOE, NSF, NIH

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(Collaborators: Dr. Wah Chiu,NCMI, Baylor College of Medicine, Dr. A. Sali, UCSF, Dr. Tim Baker, UCSD)

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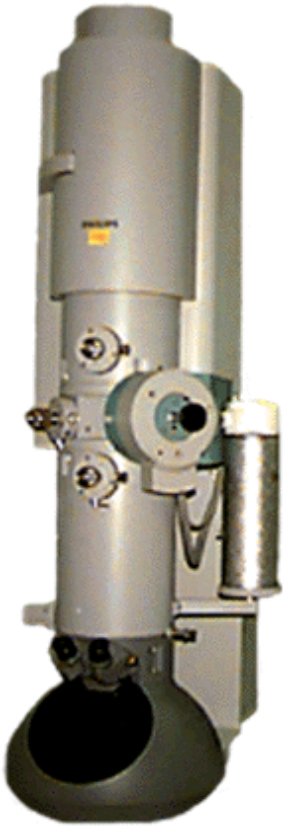
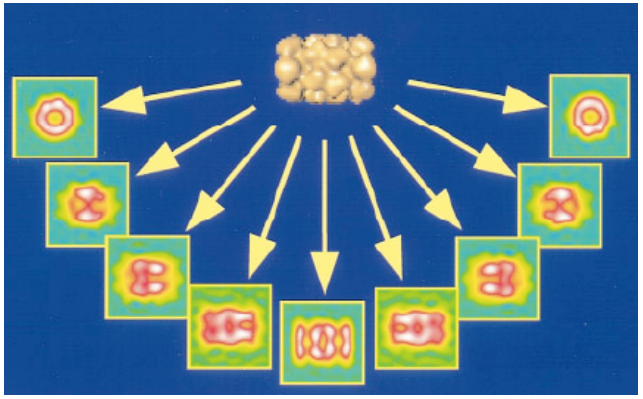
Tools for 3D Structure

- X-ray crystallography (diffraction)
  - Atomic resolution
  - Difficulties (experimental, computational)
- Nuclear magnetic resonance (NMR)
  - Atomic resolution
  - Limited to relatively small units
- Electron Microscope
  - Cryo-electron tomography
    - Low resolution (20Å – 200Å)
    - Good for whole cell or cell organelles
  - Single particle cryo-EM
    - Intermediate resolution (5Å – 20Å)
    - Computationally more complicated

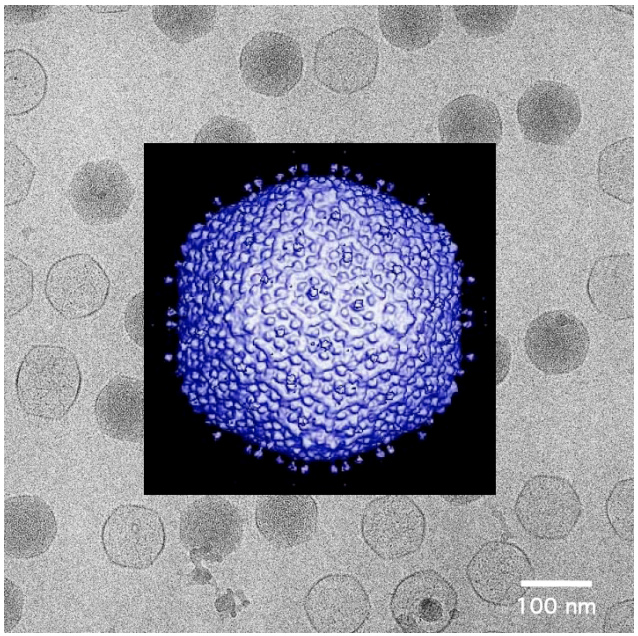


Picture from http://www.itg.uiuc.edu/ms/equipment/microscopes/tem/



Electron tomography

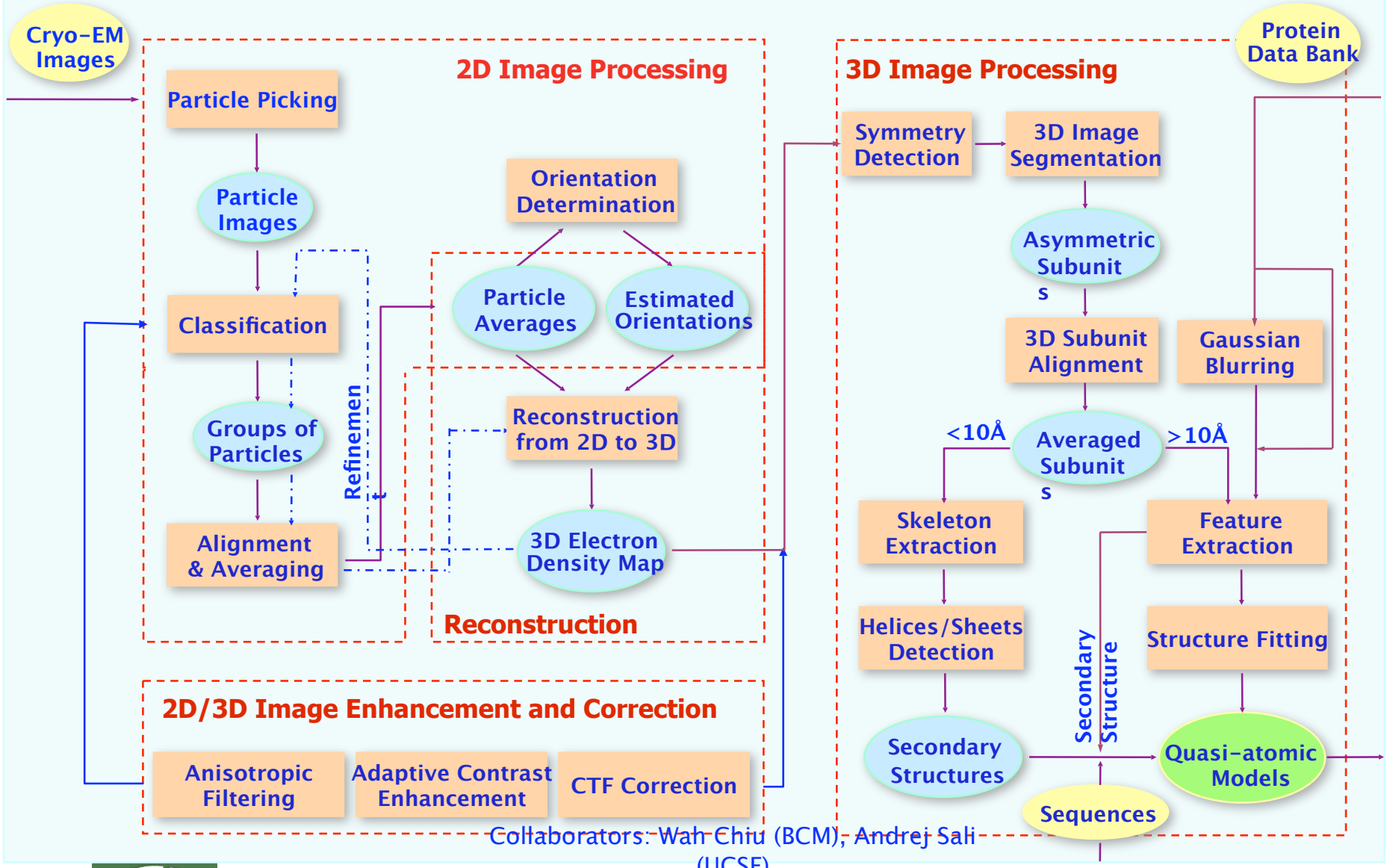
(Picture from A.J. Koster et al, JSB, 1997)



Single particle cryo-EM

(Picture from Tim S. Baker)

Sinale Particle Cryo-EM: Pipeline



Collaborators: Wah Chiu (BCM), Andrej Sali (UCSF)

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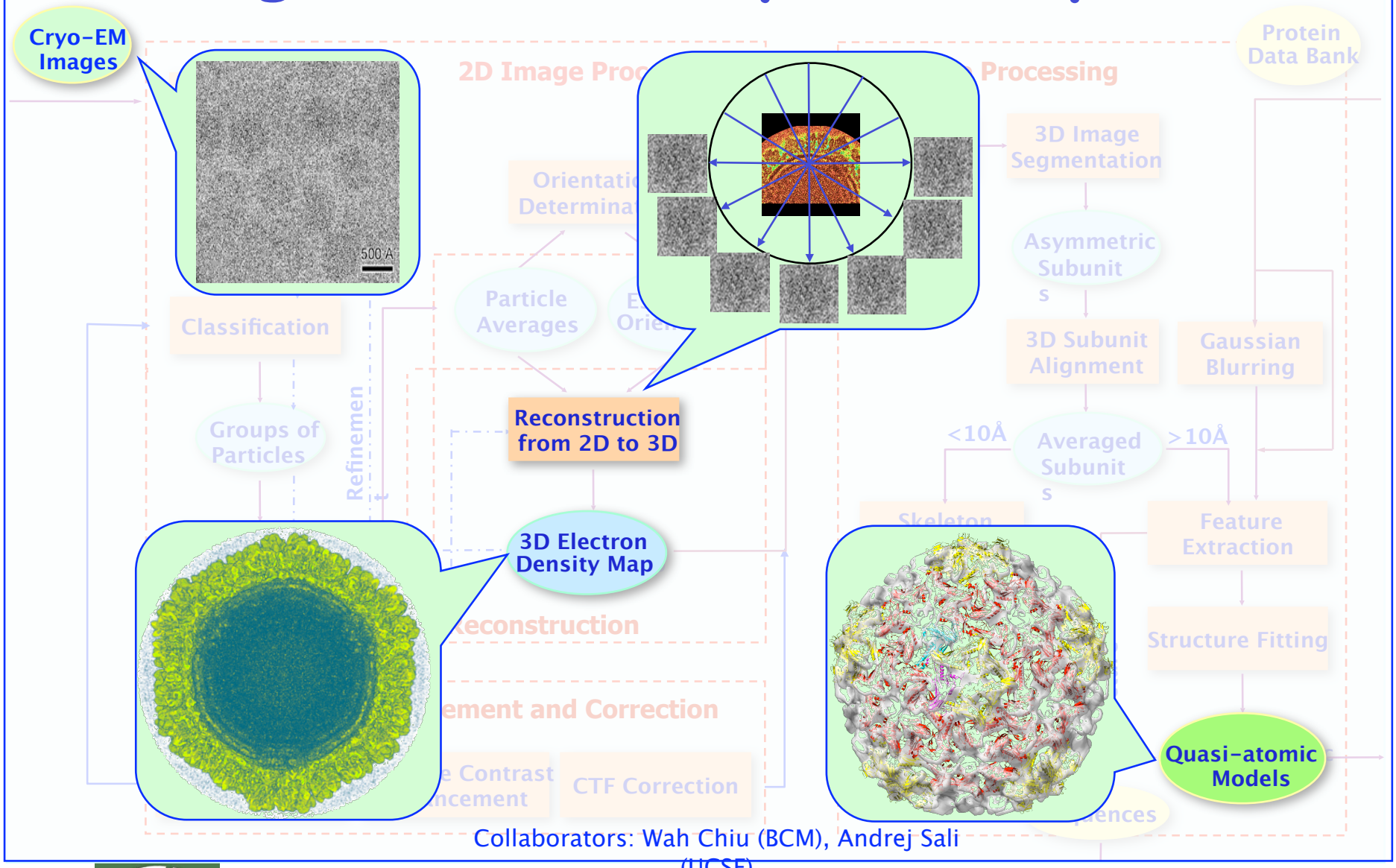
Single Particle Cryo-EM Pipeline



Collaborators: Wah Chiu (BCM), Andrej Sali (UCSF)

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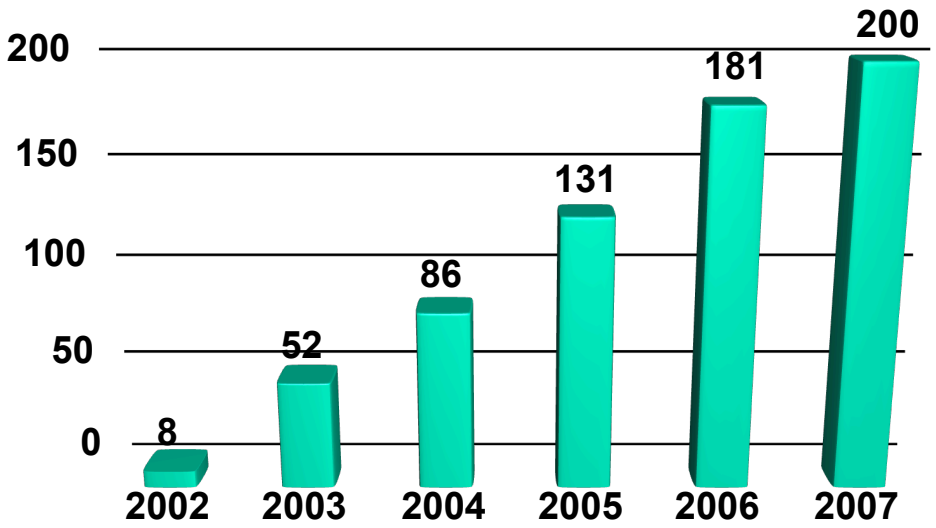
3D-Electron Microscopy DataBase

3D-EM Maps Deposited in EMDB

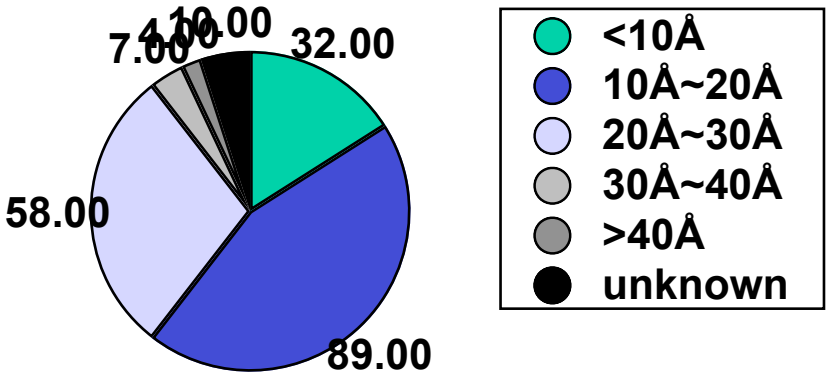


Data from: http://www.ebi.ac.uk/msd-srv/emsearch/, as of March 14th, 2006

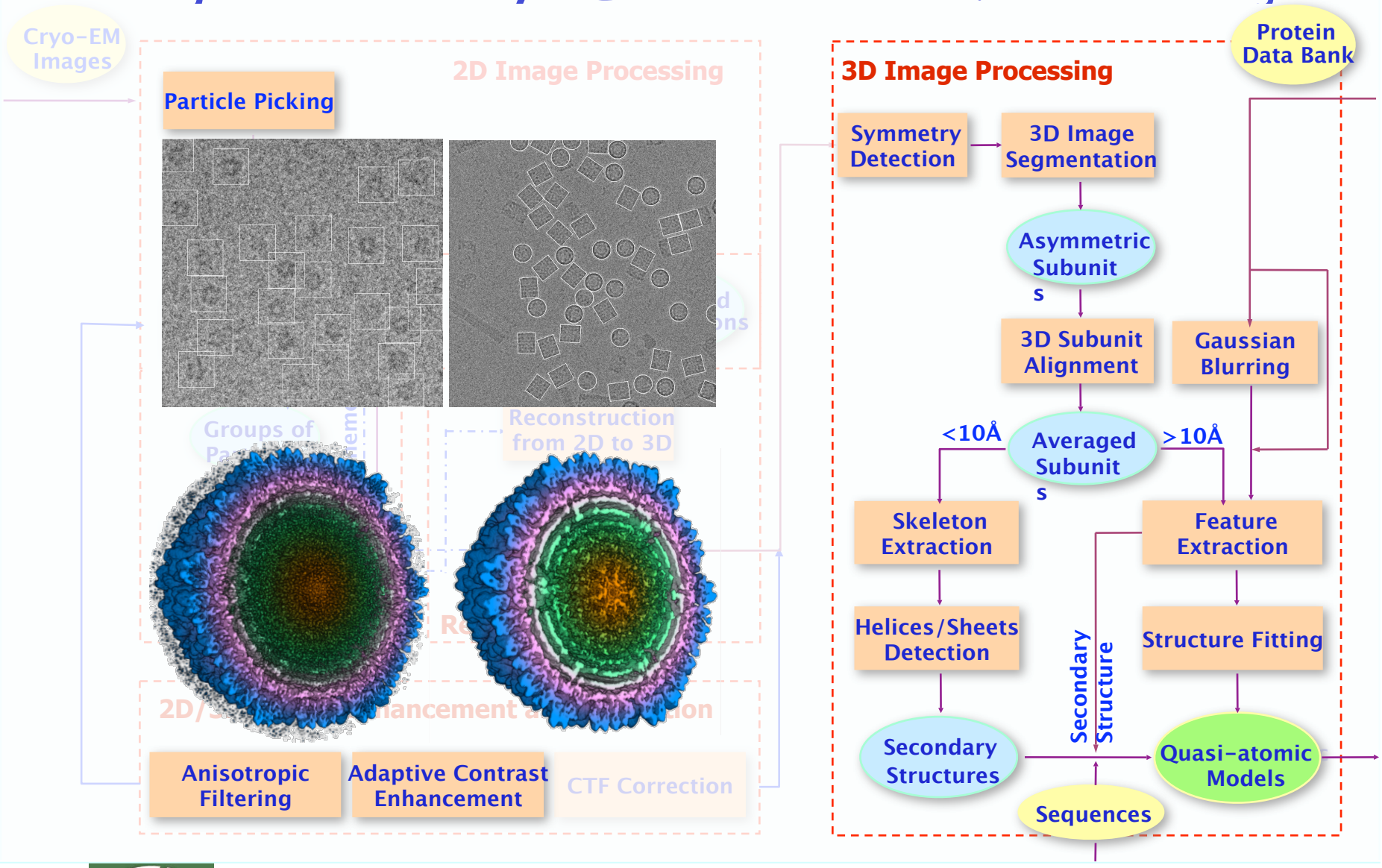
Automatic interpretation?

Quantitative analysis?

Resolution Distribution



Single Particle Cryo-EM: Towards Automatic Processing



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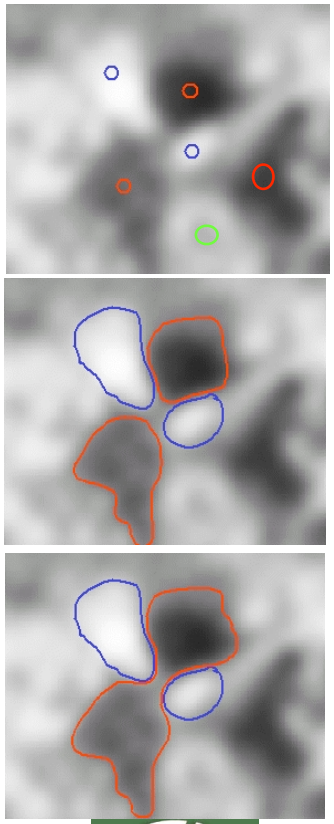
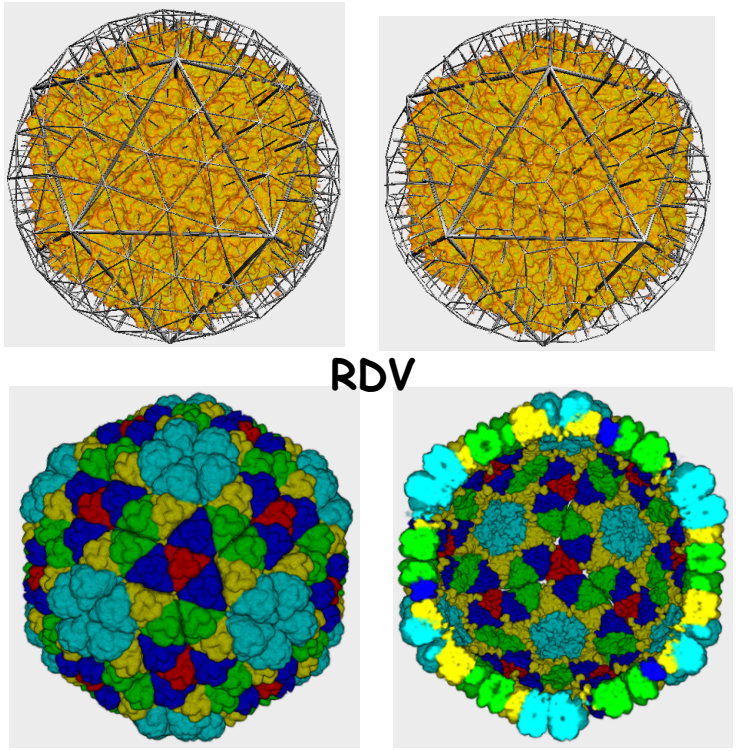
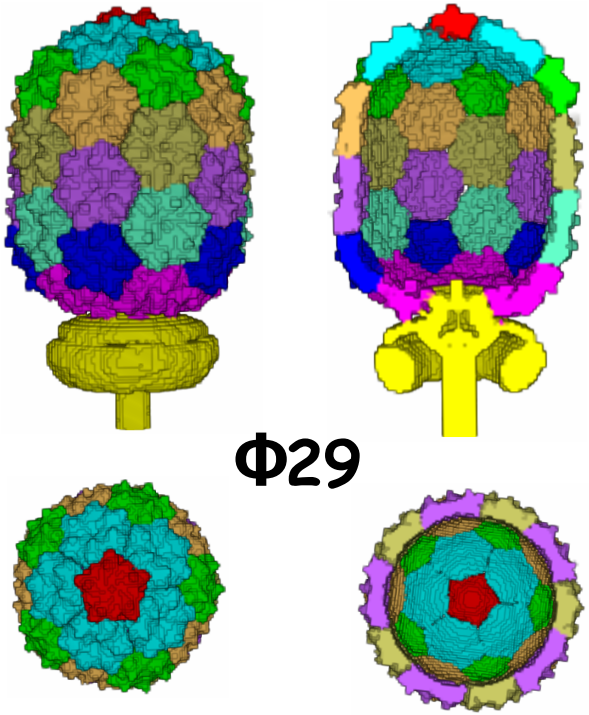
Structure Elucidation 1(B): Boundary Segmentation

- Multi-seed Fast Marching Method
  - Classify the critical points based on local symmetry.
  - Each seed initializes one contour, with its group's membership.
  - Contours march simultaneously. Contours with same membership are merged, while contours with different membership stop each other.





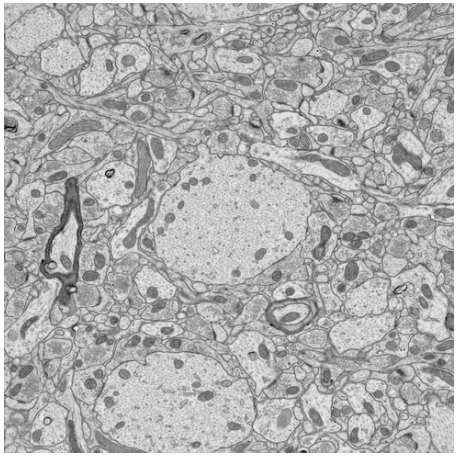
RDV

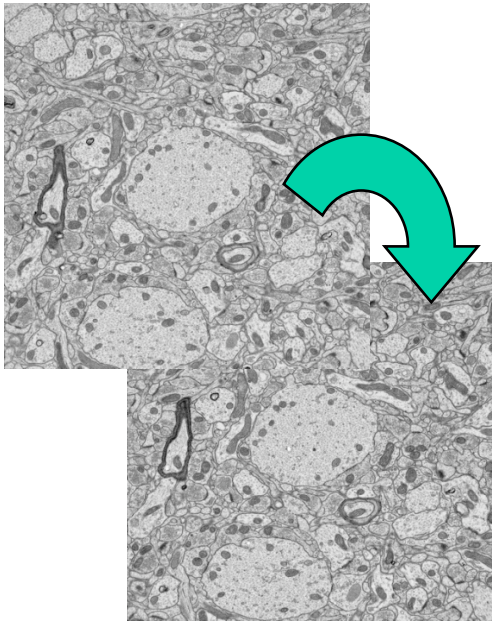


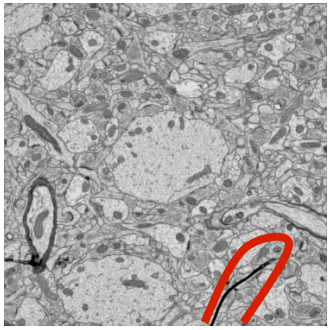
Φ29

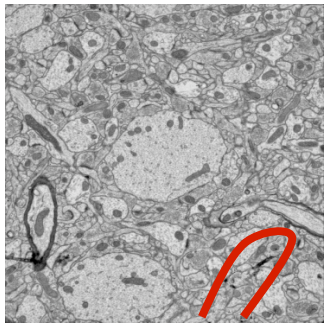
Z. Yu, and C. Bajaj, IEEE Trans.on Image Process, 2005. 144(1-2), pp. 132-143.

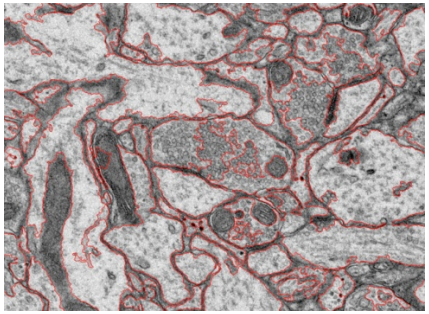
Quantitative Morphology of Hippocampal Neurons

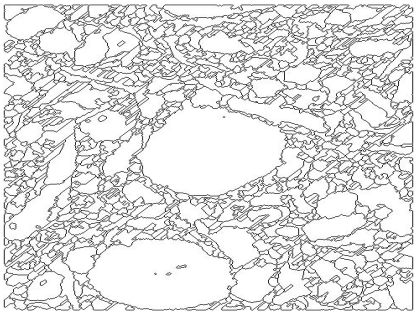






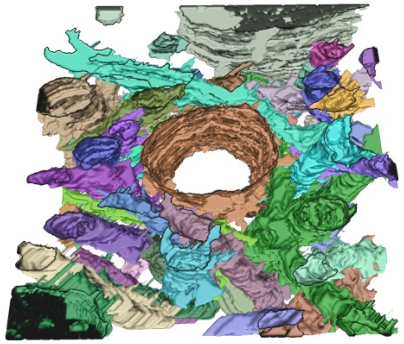


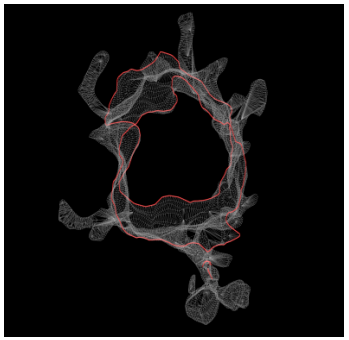


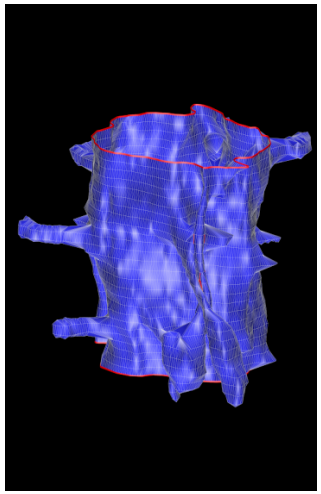


Transmission Electron Microscopy, Thin Sections:

Kristen Harris, University of Texas at Austin







Addtl. Collab: Tom Bartol, Salk Institute

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Models2Analytics

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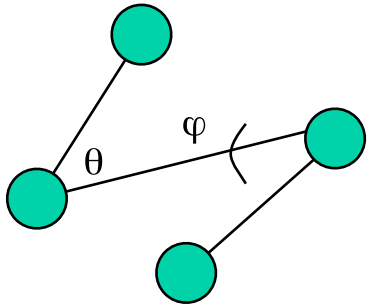
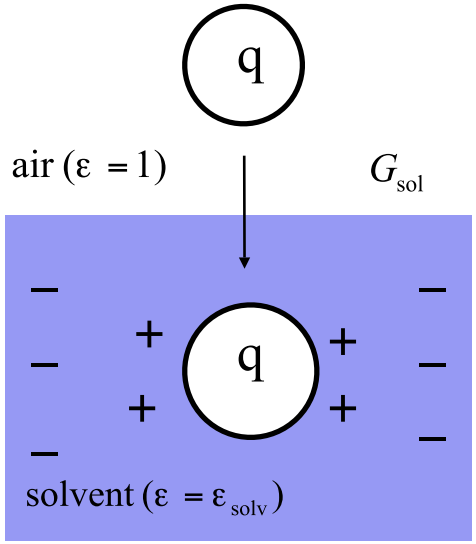
Free Energy of a Macromolecule in Solvent

Total free energy : $G = E_{MM} + G_{sol} - TS$

$$E = E_b + E_\theta + E_\varphi + E_{vdw} + E_{elec}$$

$$G_{sol} = G_{cav} + G_{vdw} + G_{pol}$$





How to Compute G_{pol} ?

$$G_{\text{pol}} = \frac{1}{2}\int [\phi_{\text{solvent}}(\mathbf{r}) - \phi_{\text{air}}(\mathbf{r})]\rho(\mathbf{r})\,dV$$

- Poisson-Boltzmann (PB) Theory

$$-\nabla\cdot[\varepsilon(\mathbf{r})\nabla\phi(\mathbf{r})] = 4\pi\rho(\mathbf{r}) + 4\pi\lambda(\mathbf{r})\sum_{j=1} c_j^{\infty} q_j \exp(-q_j\phi(\mathbf{r})/k_B T)$$

finite difference, boundary element, finite element

ε	dielectric constant
ϕ	electrostatic potential
ρ	solute charge density
λ	ion accessibility parameter
c_j^{∞}	ion bulk concentration
q_j	ion charge
k_B	Boltzmann's constant
T	temperature

- Generalized Born (GB) Theory
  - Born formula (Born 1920), Generalized Born formula (Still 1990)

$$G_{\text{pol}} = -\frac{\tau}{2}\sum_{ij}\frac{q_i q_j}{[r_{ij}^2 + R_i R_j \exp(-\frac{r_{ij}^2}{4R_i R_j})]^{\frac{1}{2}}} \qquad R_i^{-1} = \frac{1}{4\pi}\int_{\text{ex}}\frac{1}{|\mathbf{r}-\mathbf{x}_i|^4}\,dV$$

$\tau = 1 - \frac{1}{\varepsilon_{\text{solv}}}$ r_{ij} : distance between atom i and j

q_i : charge of atom i R_i : effective Born radius of atom i

ex: exterior to molecule

How to Compute G_{pol} ?

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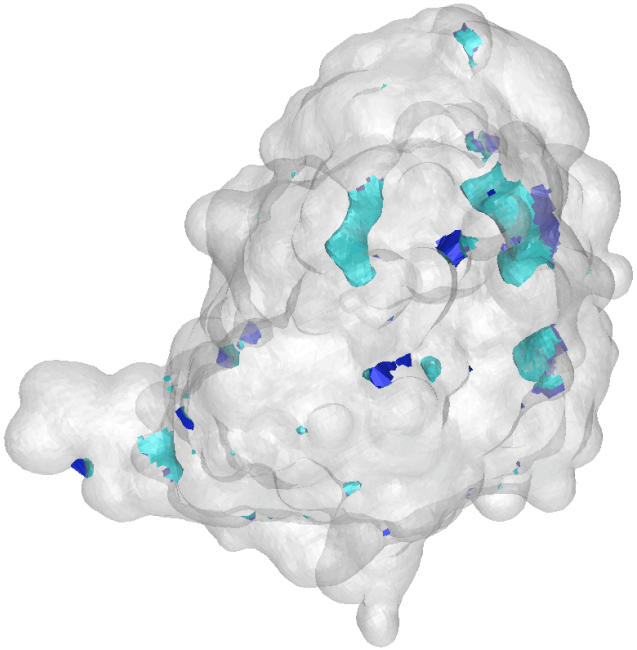
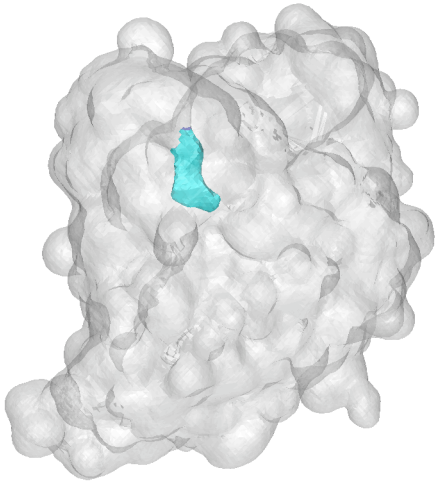
finite difference, boundary element, finite element

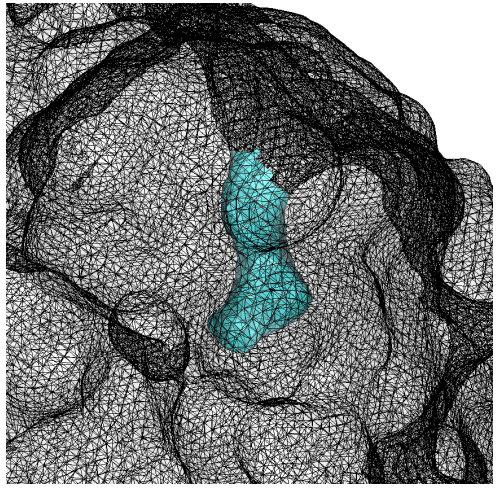
ε	dielectric constant
ϕ	electrostatic potential
ρ	solute charge density
λ	ion accessibility parameter
c_j^{∞}	ion bulk concentration
q_j	ion charge
k_B	Boltzmann's constant
T	temperature

- Generalized Born (GB) Theory
  - Born formula (Born 1920)
    generalized Born formula (Still 1990)
  - methods to compute the Born radii:
    - pairwise summation methods: fast but not easy for force calculation
    - analytic integration methods: slow but straight forward for force

Topological Noise Removal







C.Bajaj, A. Gillette, S. Goswami, **Topology Based Selection and Curation of Level Sets** , 2007

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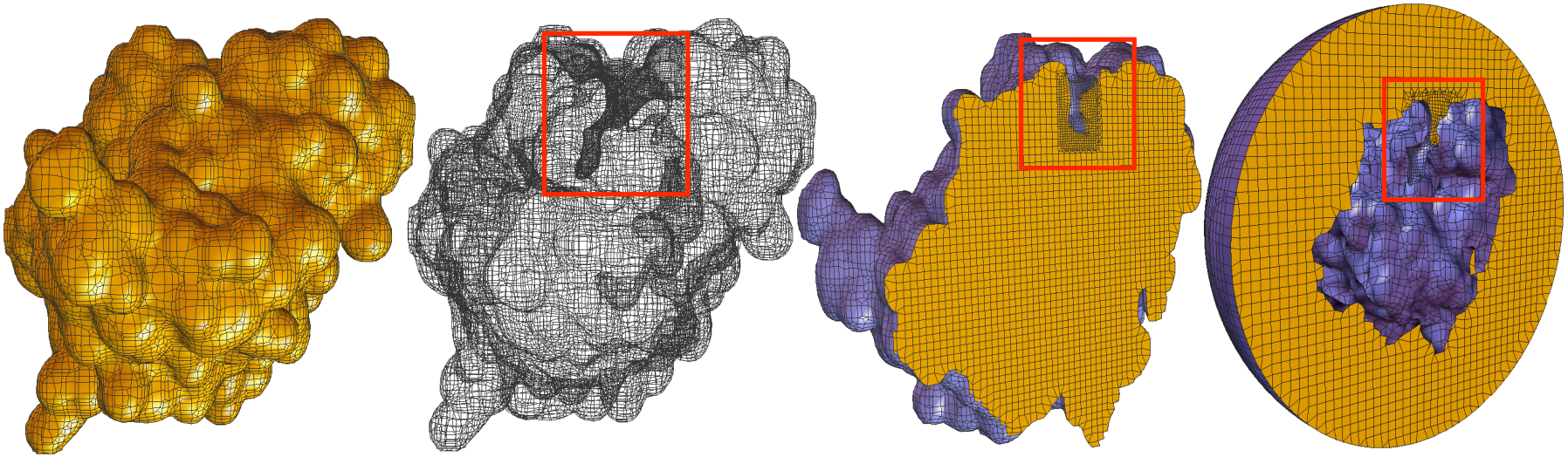
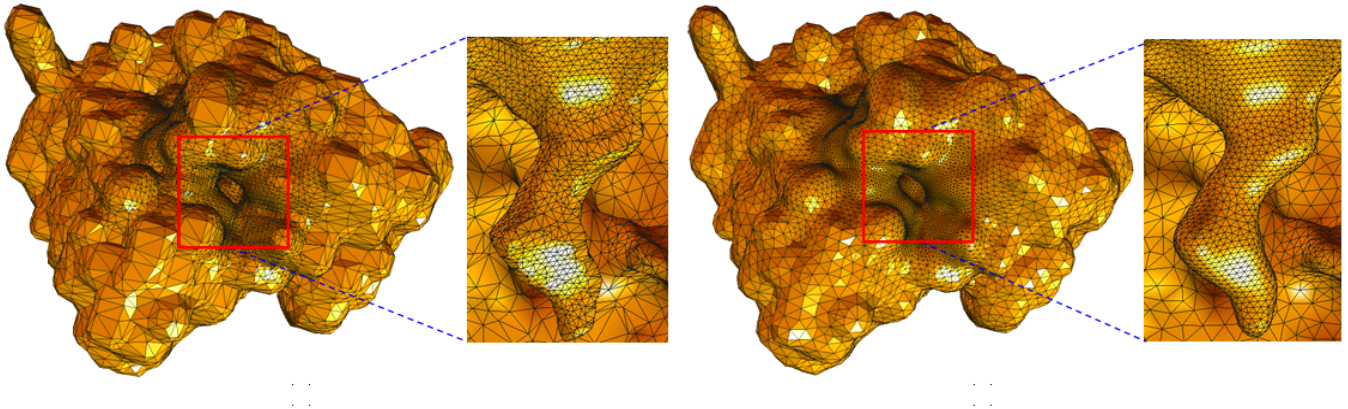
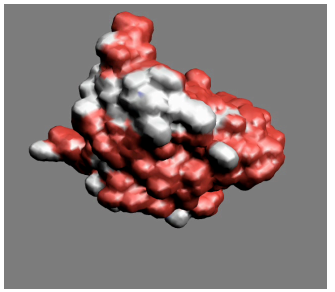
Quality Boundary, Interior-Exterior Meshing







Y. Zhang, G. Xu, C. Bajaj
Quality Meshing of Implicit Solvation Models of Biomolecular Structures,
Computer Aided Geometric Design (CAGD) , 23, 6, 2006, 510-530

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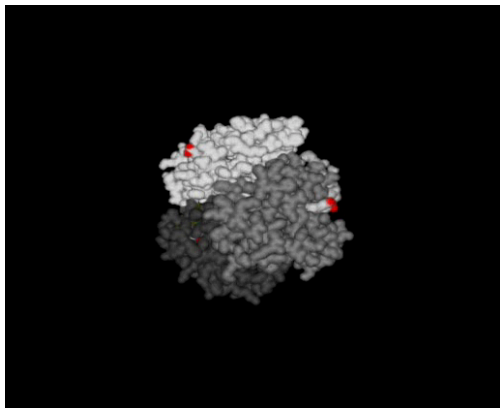
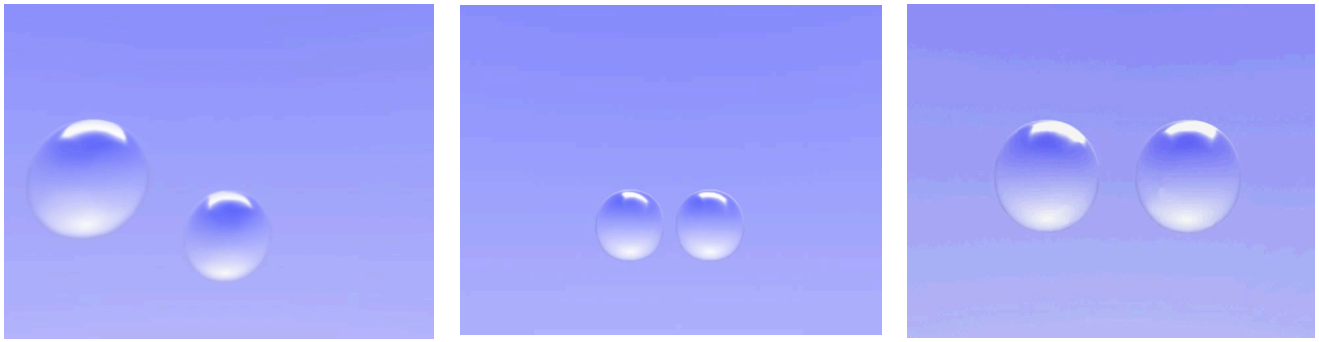
Fast Dynamic BEM Electrostatics of Molecular and Cell Membrane Models





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How to Compute G_{pol} ?

$$G_{pol} = \frac{1}{2}\int [\phi_{solvent}(\mathbf{r}) - \phi_{air}(\mathbf{r})]\rho(\mathbf{r})\,dV$$

- Poisson-Boltzmann (PB) Theory

$$-\nabla\cdot[\varepsilon(\mathbf{r})\nabla\phi(\mathbf{r})] = 4\pi\rho(\mathbf{r}) + 4\pi\lambda(\mathbf{r})\sum_{j=1} c_j^{\infty} q_j \exp(-q_j\phi(\mathbf{r})/k_B T)$$

finite difference, boundary element, finite element

ε	dielectric constant
ϕ	electrostatic potential
ρ	solute charge density
λ	ion accessibility parameter
c_j^{∞}	ion bulk concentration
q_j	ion charge
k_B	Boltzmann's constant
T	temperature

- Generalized Born (GB) Theory
  - Born formula (Born 1920), Generalized Born formula (Still 1990)

$$G_{pol} = -\frac{\tau}{2}\sum_{ij}\frac{q_i q_j}{[r_{ij}^2 + R_i R_j \exp(-\frac{r_{ij}^2}{4R_i R_j})]^{\frac{1}{2}}} \qquad R_i^{-1} = \frac{1}{4\pi}\int_{ex}\frac{1}{|\mathbf{r}-\mathbf{x}_i|^4}\,dV$$

$\tau = 1 - \frac{1}{\varepsilon_{solv}}$ r_{ij} : distance between atom i and j

ex: exterior to molecule

q_i : charge of atom i R_i : effective Born radius of atom i

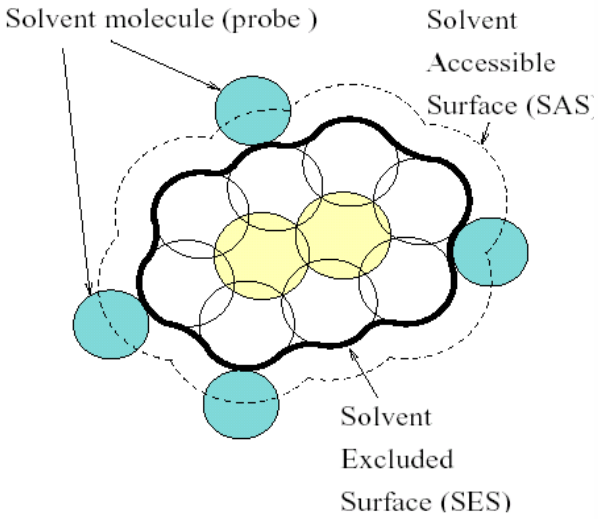
Fast Computation of Born Radii

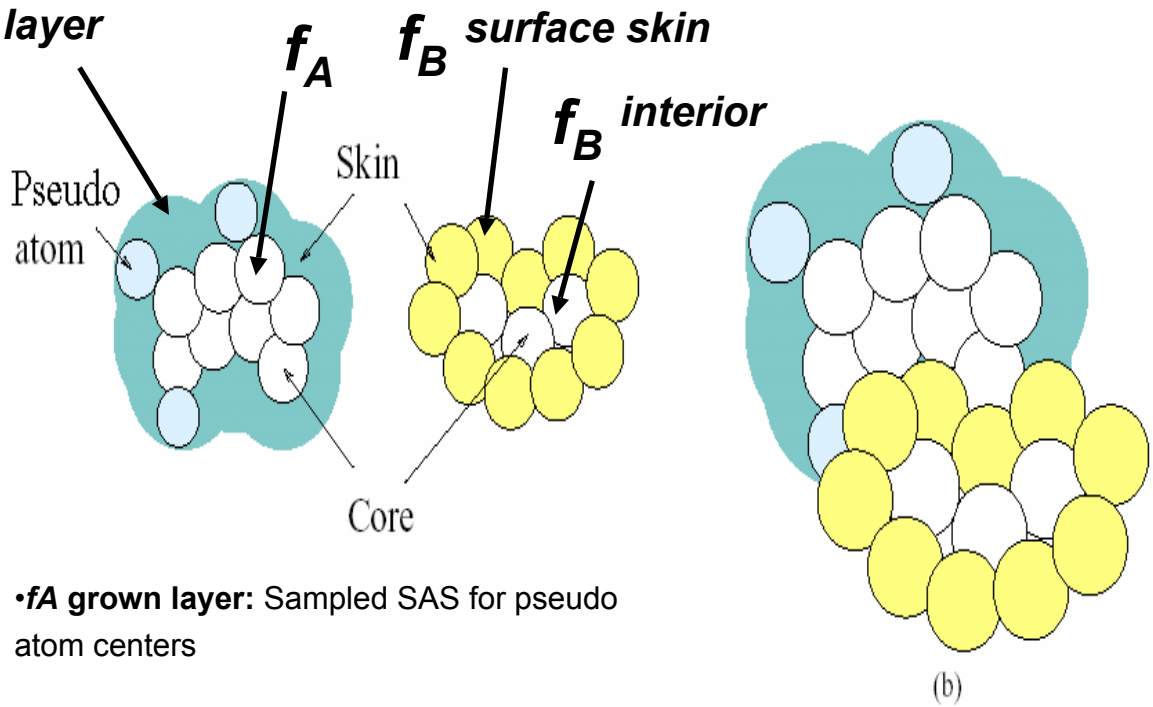
$$R_i^{-1} = \frac{1}{4\pi}\int_\Gamma \frac{(\mathbf{r}-\mathbf{x}_i)\cdot\mathbf{n}(\mathbf{r})}{|\mathbf{r}-\mathbf{x}_i|^4}\,dS \approx \frac{1}{4\pi}\sum_{k=1}^{N} w_k \frac{(\mathbf{r}_k-\mathbf{x}_i)\cdot\mathbf{n}(\mathbf{r}_k)}{|\mathbf{r}_k-\mathbf{x}_i|^4}, \qquad \mathbf{r}_k \in \Gamma$$

Algorithm:

1. Generate a model for the molecular surface Γ .
2. Cubature: choose w_k and $\mathbf{r}_k$ for higher order accuracy to be obtained for small N.
3. Fast Fourier summation to evaluate R_i , $i = 1,\ldots,M$.

F^3 Dock: Fast Flexible Fourier Docking





(a) Skin and Core regions. Atoms are drawn as soi and white. (b) Docking of molecular (A) & (B).

- ***fA* grown layer:** Sampled SAS for pseudo atom centers
- ***fA***: Atom centers of the protein
- ***fB surface skin***: Surface atoms
- ***fB* interior atoms**:Atoms of B which are not surface atoms

Stable Docking

Collaborators: Art Olson, Michel Sanner (TSRI)

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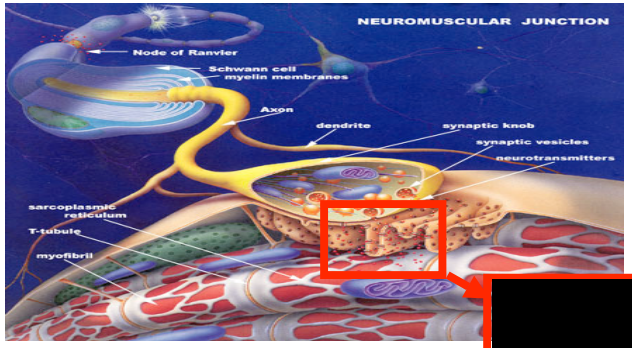
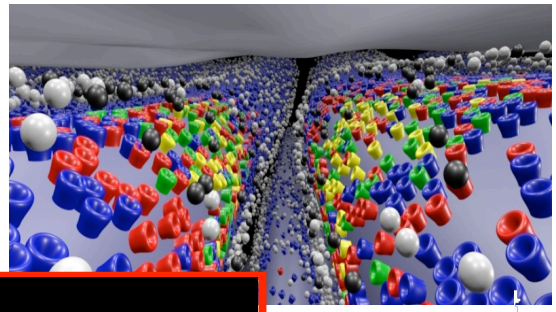
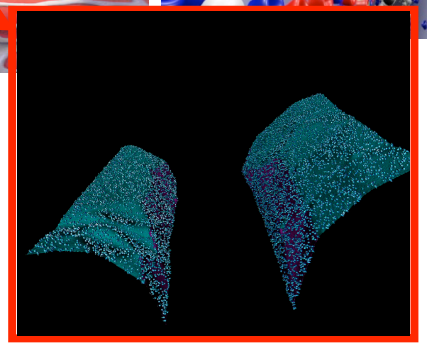
Multiscale Modeling of the Neuro-Muscular Junction

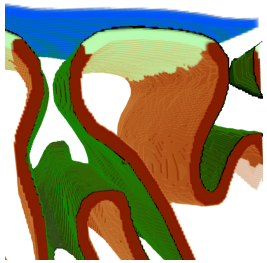


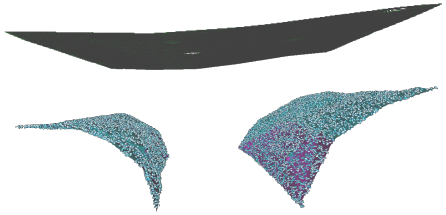


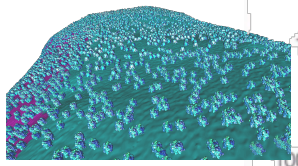


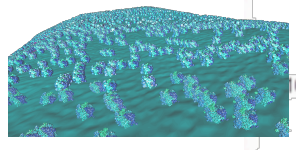
http://fig.cox.miami.edu/~cmallery/150/neuro/neuromuscular-sml.jpg http://mcell.salk.edu/

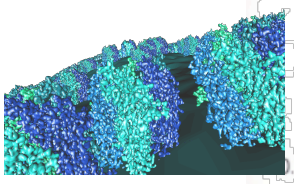
Multi-scale LOD

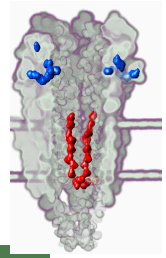


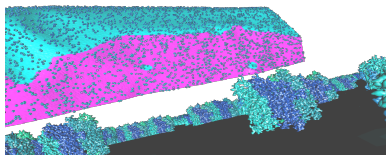


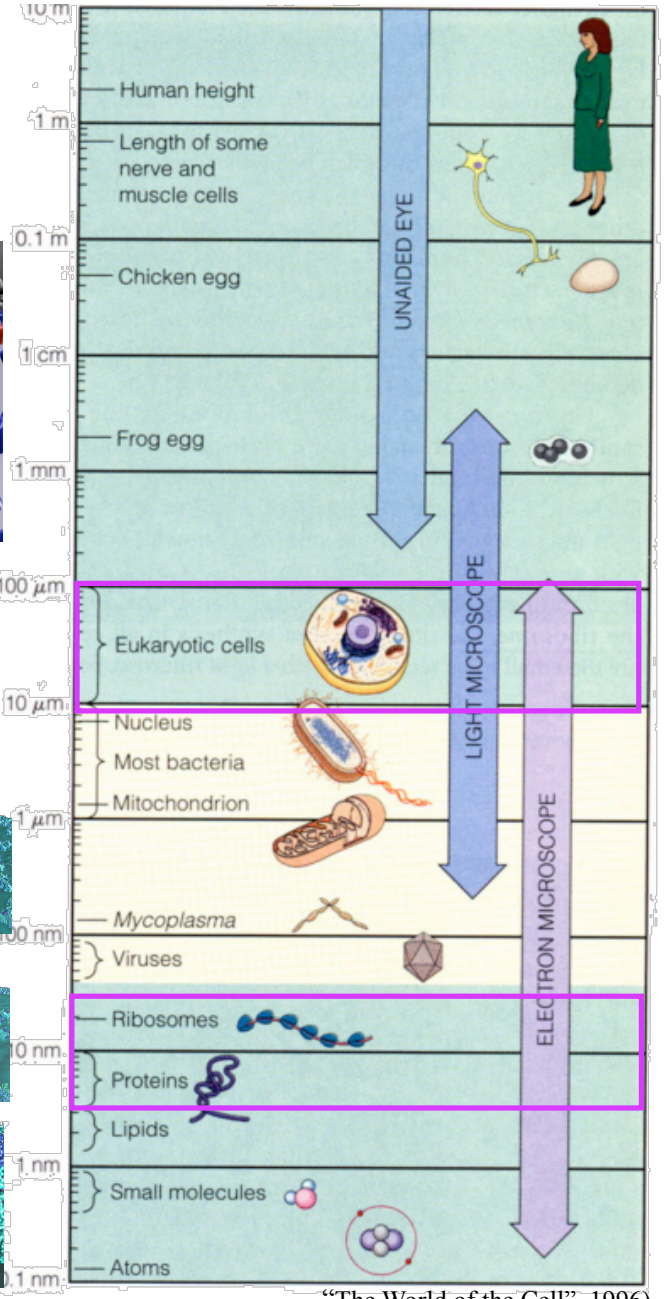












"The World of the Cell", 1996)

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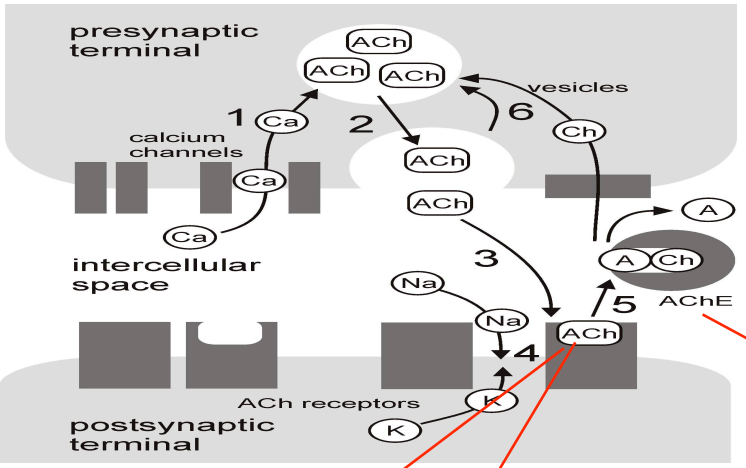
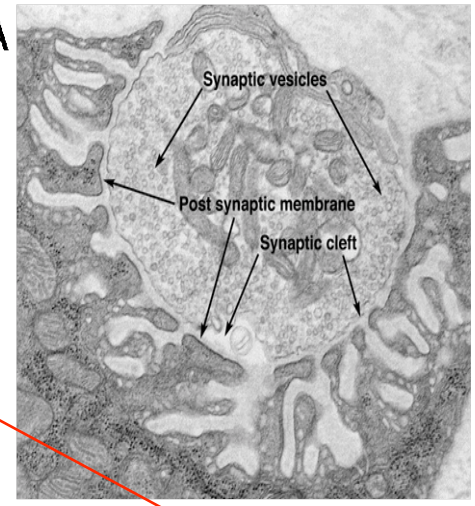
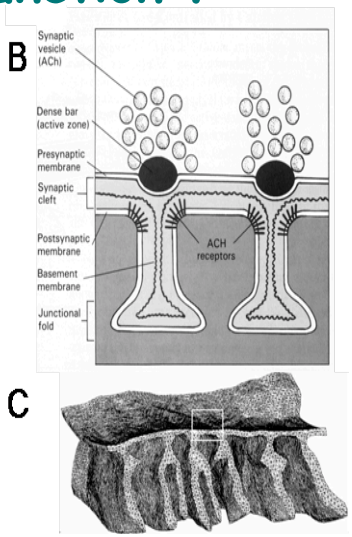
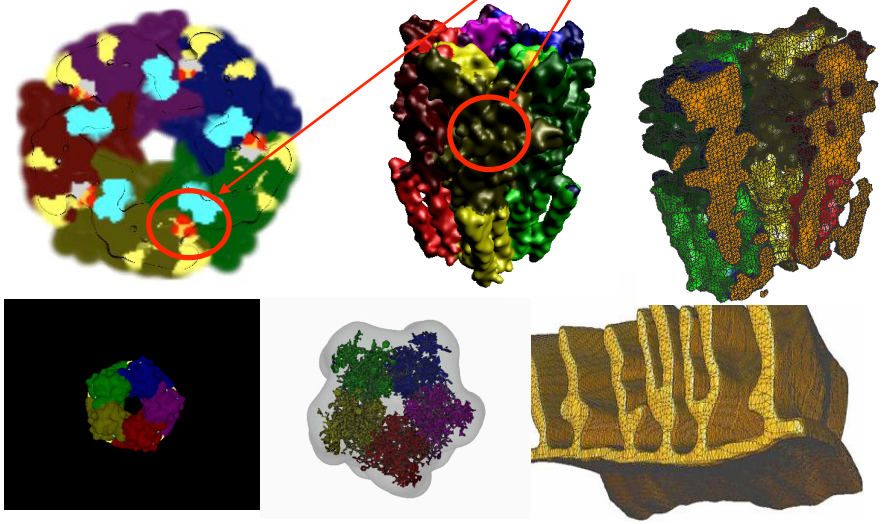
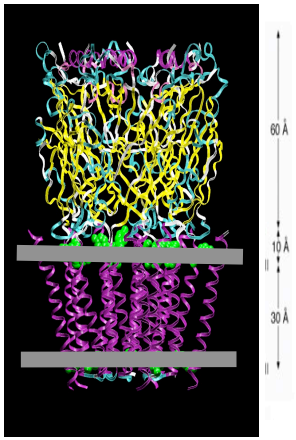
How do Synapses Occur at the Neuro-Muscular Junction ?

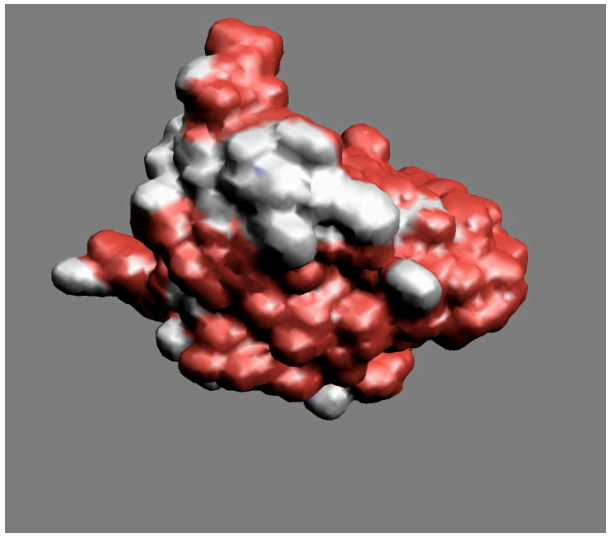












•Y. Zhang, C. Bajaj, B. Sohn, *Special issue of Computer Methods in Applied Mechanics and Engineering (CMAME) on Unstructured Mesh Generation, 2004.*

•Y. Song, Y. Zhang, T. Shen, C. Bajaj, J. A. McCammon and N. A. Baker, *Finite Element Solution of the Steady-State Smoluchowski Equation*, *Biophysical Journal, 86(4):2017-2029, 2004.*

Collaborators: Nathan Baker (Wash. U), Andy McCammon, Mike Holst, Mark Ellisman (UCSD)

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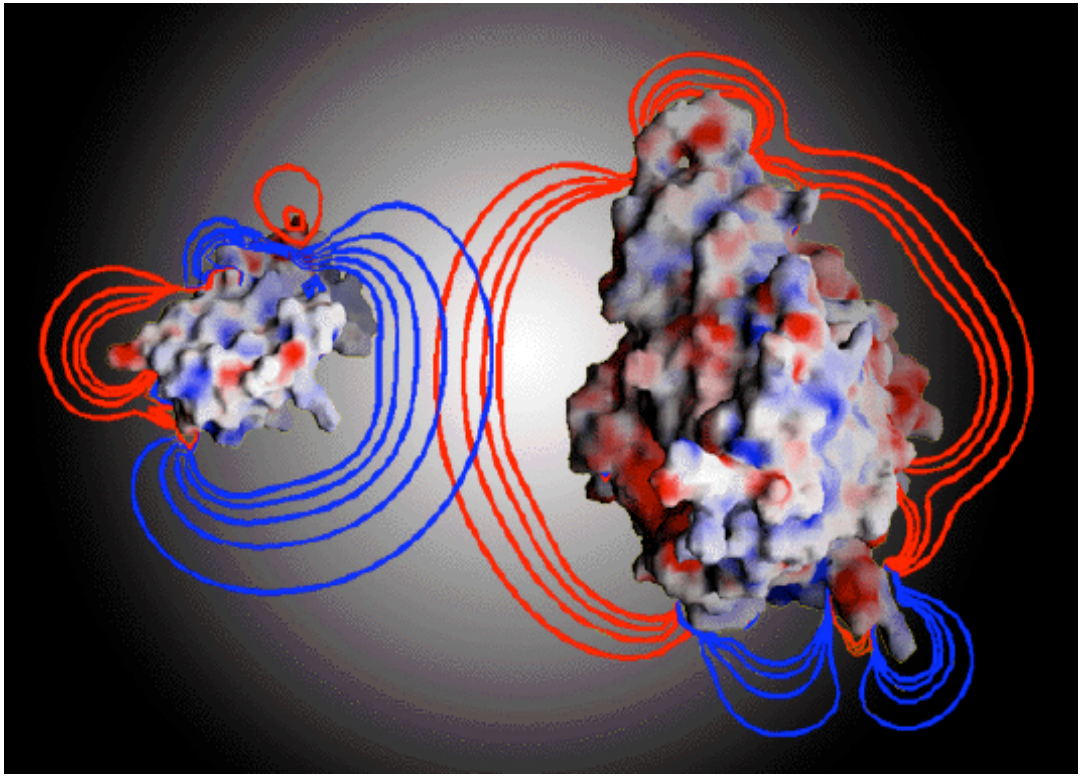
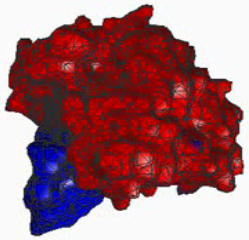
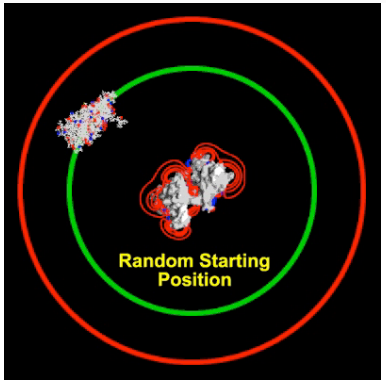
Fas2 meets AChE



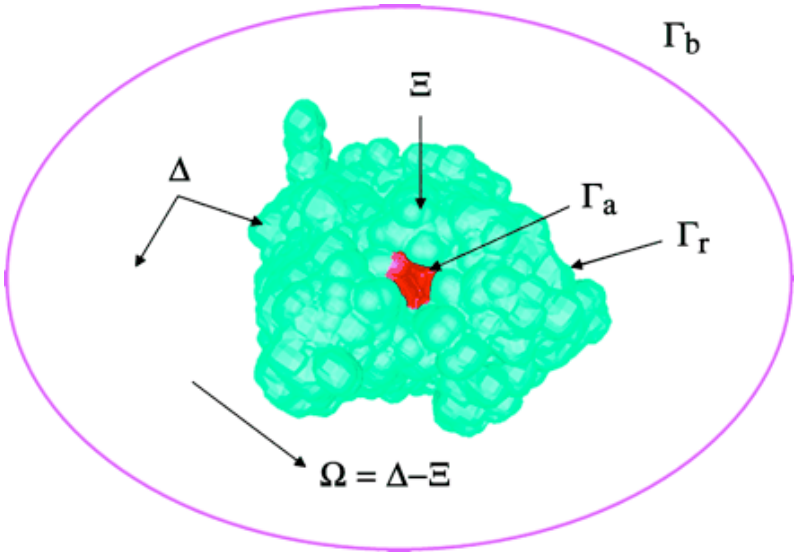




Steady State Smulochowski Equation

(Diffusion of multiple particles in a potential field)

$$\vec{J}p(\vec{r}) = D(\vec{r})[\nabla p(\vec{r}) + \beta p(\vec{r})\nabla U(\vec{r})]$$



- Δ -- entire domain
- Ξ -- biomolecular domain
- Ω -- free space in Δ
- Γ_a – reactive region
- Γ_r – reflective region
- Γ_b – boundary for Δ

$$p(\vec{r}) = p_{bulk} \text{ for } \vec{r} \in \Gamma_b$$

$$p(\vec{r}) = 0 \text{ (Dirichlet BC) for } \vec{r} \in \Gamma_a$$

$$\text{or } \vec{n} \times \vec{J}p(\vec{r}) = \alpha(\vec{r})\, p(\vec{r}) \text{ (Robin BC)}$$

$$\vec{n} \times \vec{J}p(\vec{r}) = 0 \text{ for } x \in \Gamma_r$$

Diffusion-influenced biomolecular reaction rate constant :

$$k = \frac{\int_{\Gamma_a} \vec{n} \times \vec{J}p(\vec{r})\, dS}{p_{bulk}}$$

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How does the Brain function ?

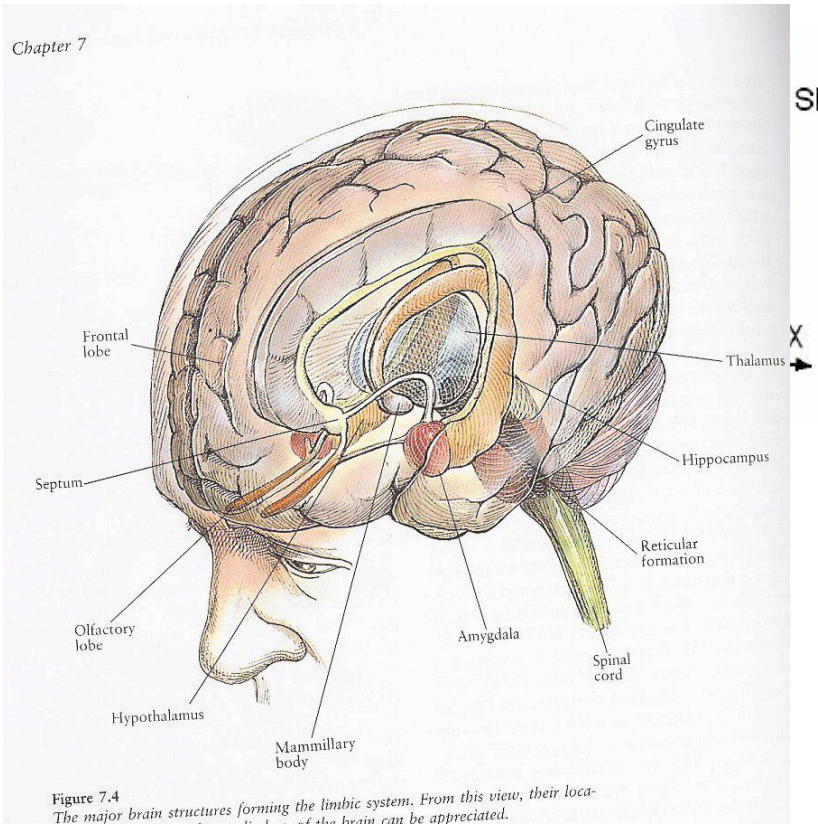
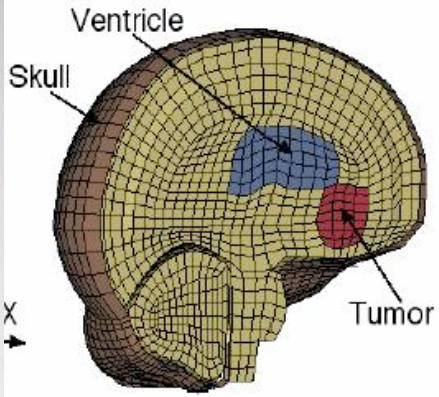
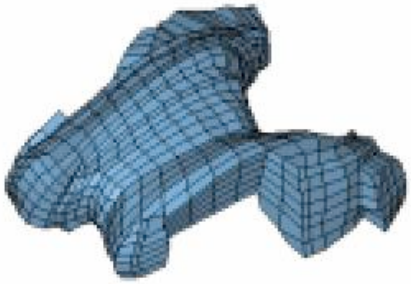
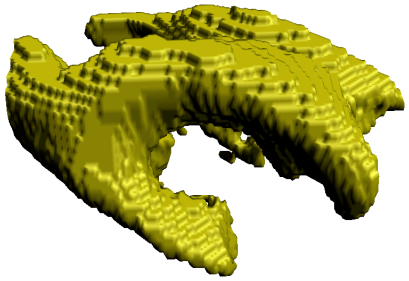
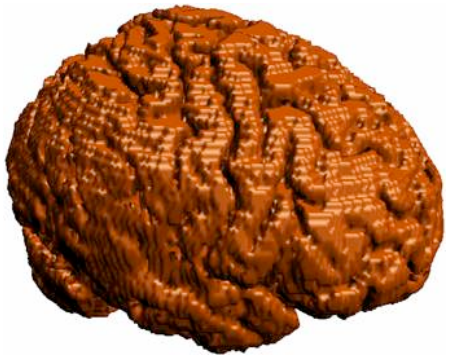


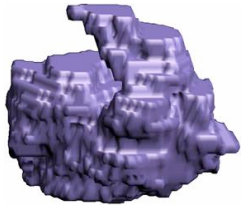
Figure 7.4
The major brain structures forming the limbic system. From this view, their loca-











How does the Brain pulse the Musculature ?

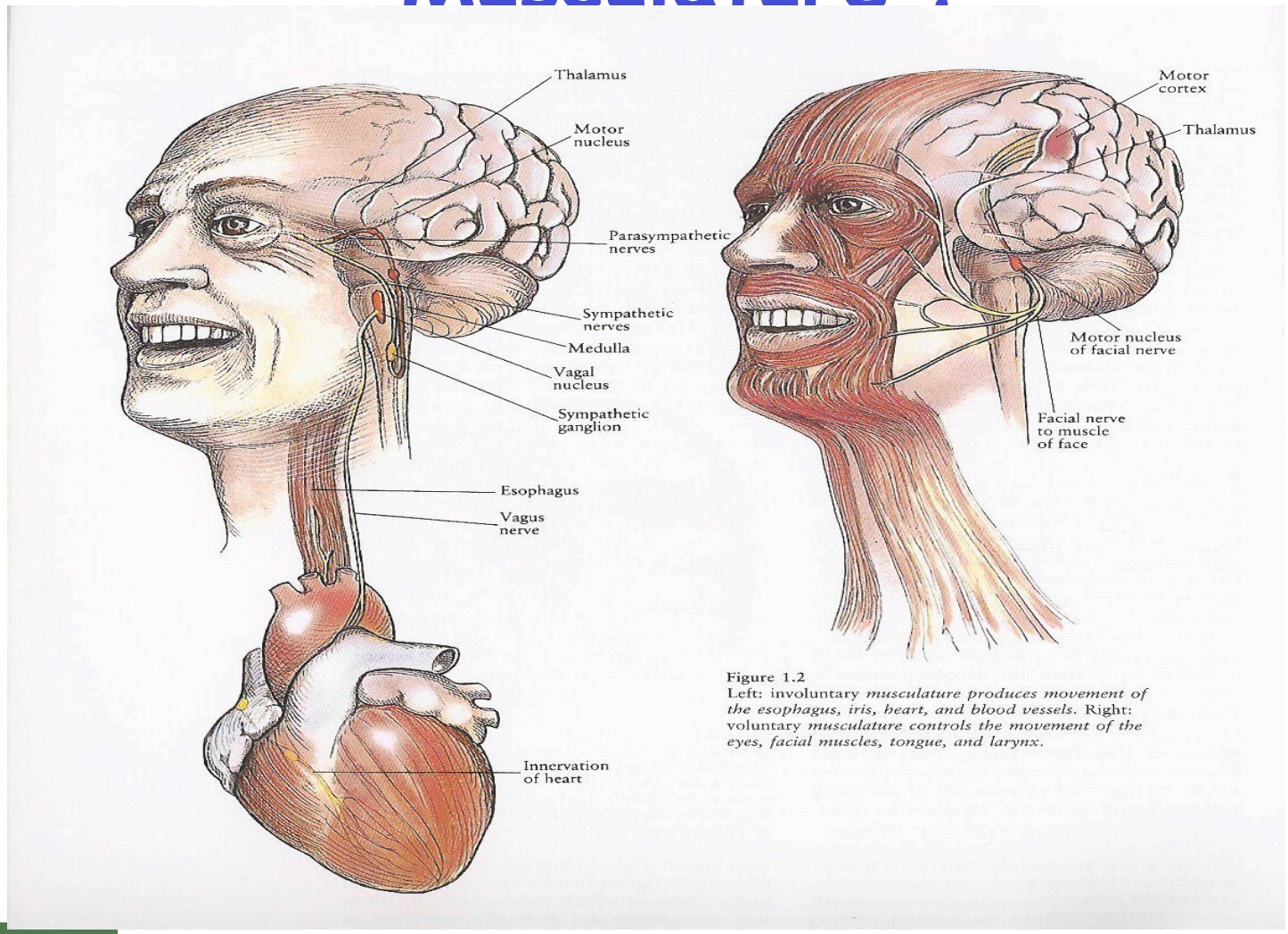


Figure 1.2
Left: involuntary *musculature produces movement of the esophagus, iris, heart, and blood vessels.* Right: voluntary *musculature controls the movement of the eyes, facial muscles, tongue, and larynx.*

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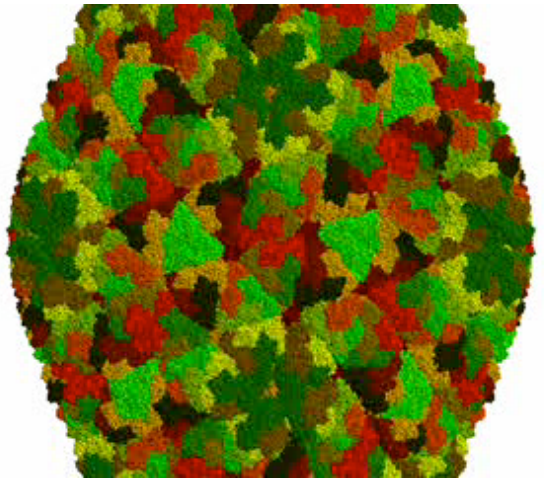
Interrogative Scalable Visualization

- **Novel techniques**
  - Surface/2D Textures/3D Texture based rendering exploit hardware acceleration
  - Multi-dim Transfer Functions for Regions of Interest
  - Compressed data processing
  - Parallelism (back-end PC cluster)
  - Hierarchical processing and rendering



TexMol

C.Bajaj, I. Ihm, S. Park, *ACM Trans. on Graphics*, 20, 1, 10-28, 2001

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C. Bajaj, J. Castrillon-Candas, S. Vinay, A. Xu, *Structure*,13,3,2005,463-471

X. Zhang, C. Bajaj, *IEEE Symp. On Parallel, Large Data Visualization*, 2001, 51-58
X. Zhang, C. Bajaj *Eurographics-IEEE TVCG Symposium on Visualization 2002, 9-18*

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GroEL Data courtesy: Dr. Wah Chiu

Today's Examples

- Ss TEM, Cryo-EM and Tomographic Imaging to Ultra-Structure to Geometry (Volumetric Image Processing)
- Geometry to Finite Element Meshes (Geometric Modeling)
- Faster Solvers (Geometry Adaptive Integral / Differential Equations Solving)
- Quantitative Analysis of Structure & Properties - Topological, Combinatorial, Metric (Comp. Geometry)
- Immersive/Exploratory Visualization

What could you learn from this course ?

- Techniques and tools to generate computer structure (geometry) models of life forms with spatial realism
- Techniques and tools to computationally model and simulate physiological function
- Techniques and tools to visualize & analyze structure and function

Additional Reading for the Next Lectures

- C. Bajaj "Modeling and Visualizing Virus Ultrastructure"

http://www.cs.utexas.edu/~bajaj/cs395T05/reading/b05-virus-arch.pdf

- C. Bajaj and Z. Yu "Geometric Processing of 3D Cryo-EM"

http://www.cs.utexas.edu/~bajaj/cs395T05/reading/by05-hndbk.pdf