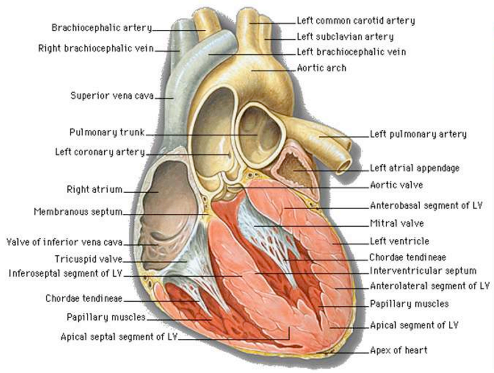
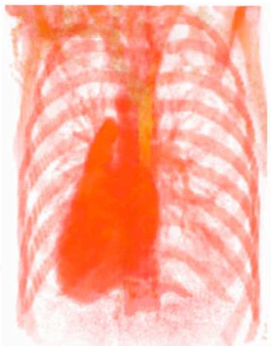
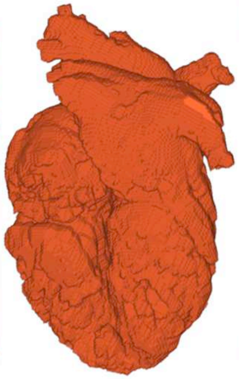
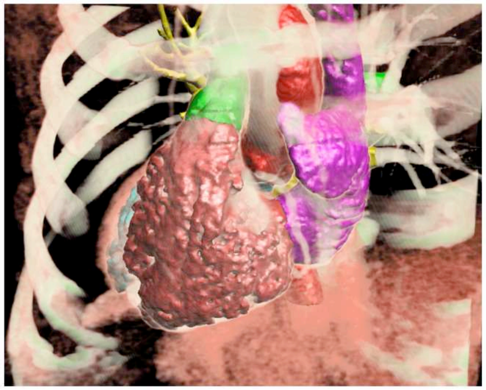
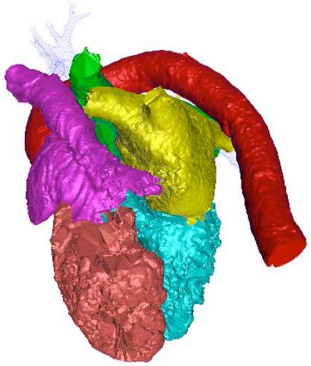
Geometric Modeling and Visualization

http://www.cs.utexas.edu/~bajaj/cs384R08/



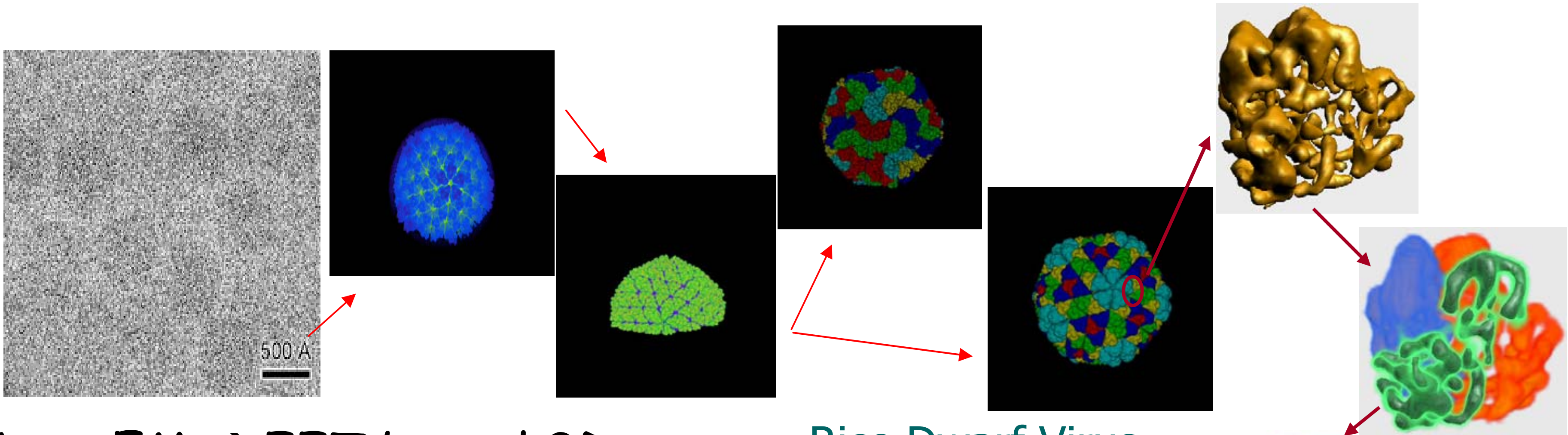
Lecture 5

Structure Elucidation: Geometric and Signal Processing Algorithms

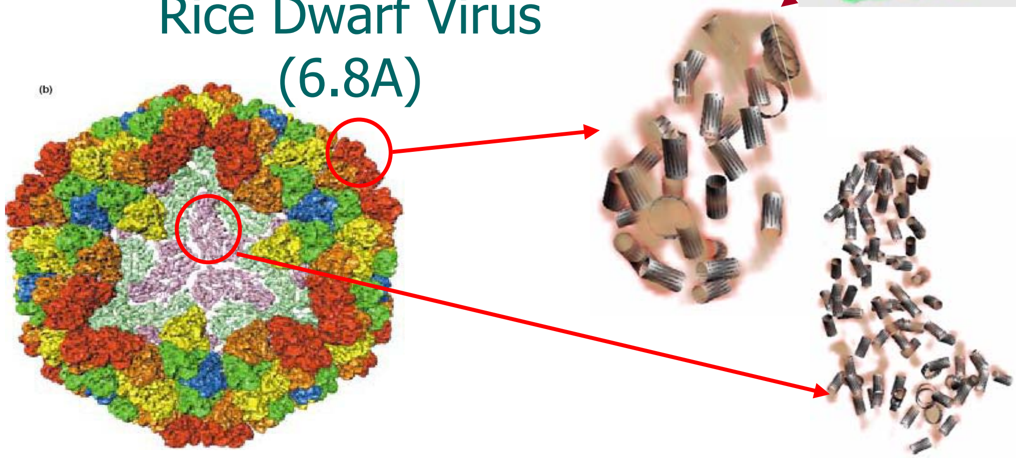
Computational Visualization Center
Institute of Computational and Engineering Sciences
Department of Computer Sciences
University of Texas at Austin

September 2008

Sub-nanometer Structure Elucidation from 3D Cryo-EM



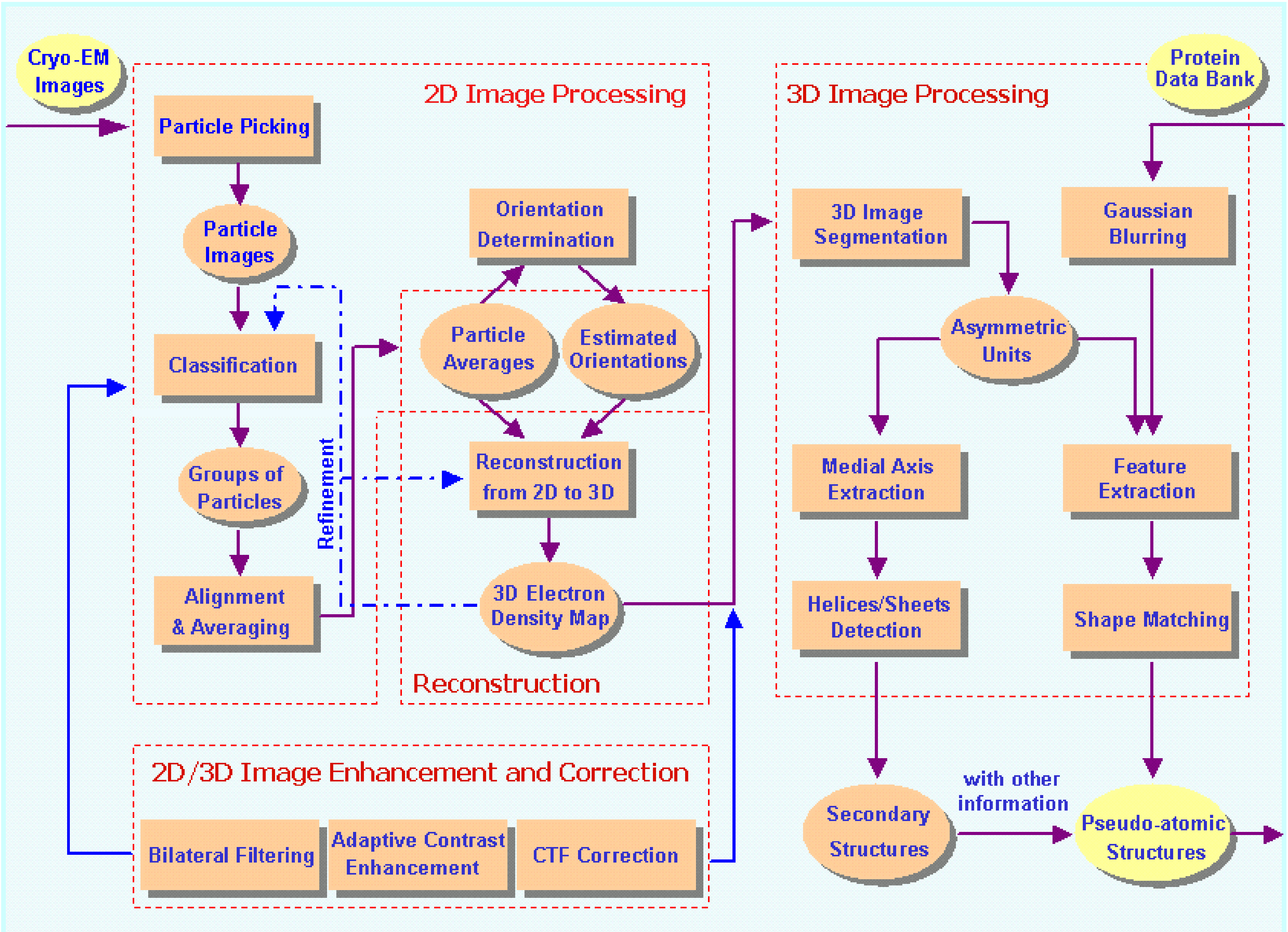
Cryo-EM →FFT based 3D Reconstruction →Anisotropic and Vector Diffusion Filtering → Structure Segmentation →Quasi-Atomic Modeling →Visualization



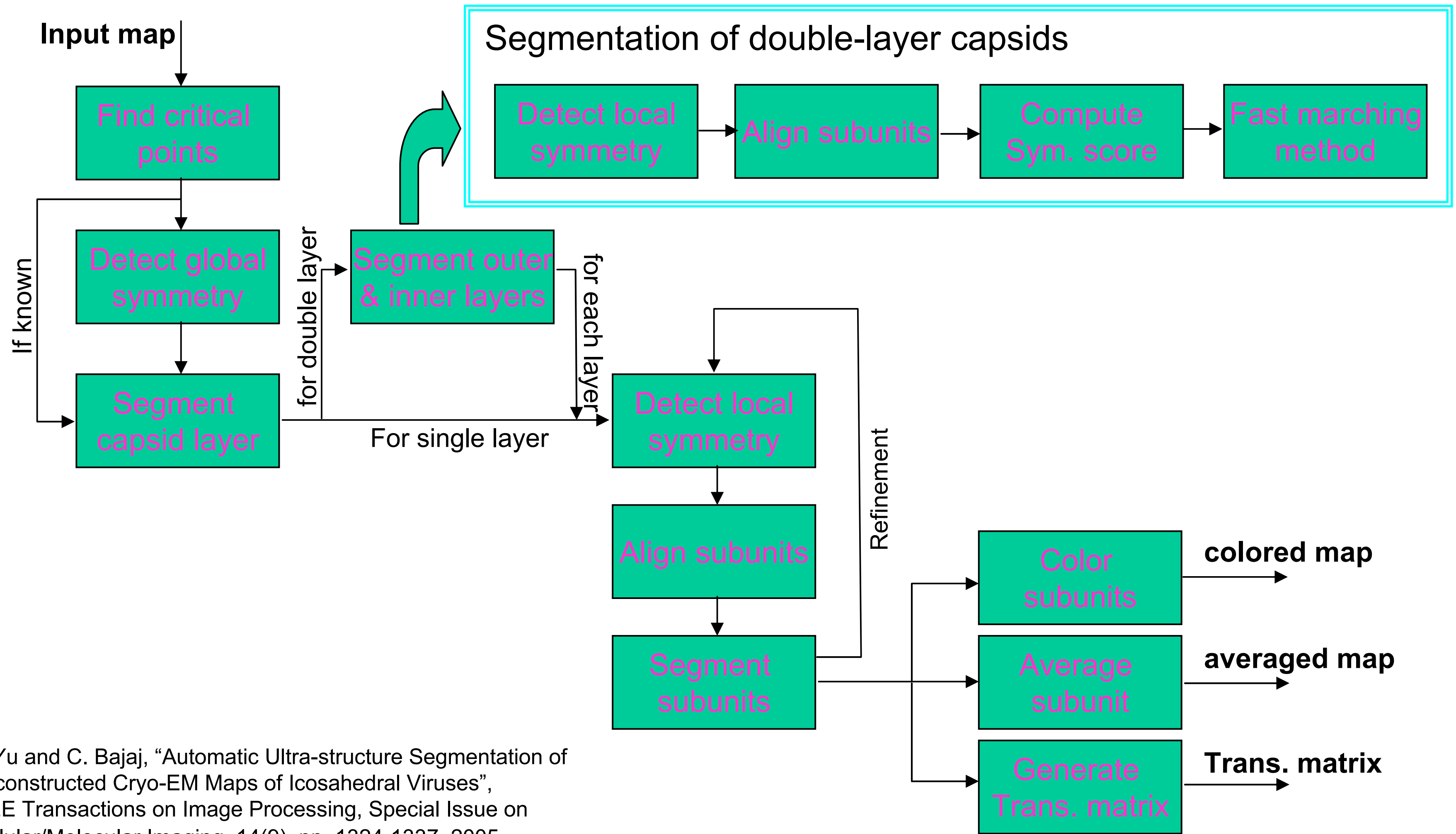
**Sponsored by NSF-ITR, NIH

(Collaborators: Wah Chiu,NCMI, Baylor College of Medicine, Andrej Sali, UCSF)

A Structure Determination Pipeline for single particle cryo-EM



Structure Elucidation for Icosahedral Viruses



Z. Yu and C. Bajaj, "Automatic Ultra-structure Segmentation of Reconstructed Cryo-EM Maps of Icosahedral Viruses", IEEE Transactions on Image Processing, Special Issue on Cellular/Molecular Imaging, 14(9), pp. 1324-1337, 2005.

Structure Elucidation 1(A)

- Adaptive contrast enhancement
- Bilateral filtering

$$h(x,\xi) = e^{-\frac{(x-\xi)^2}{2\sigma_d^2}} \cdot e^{-\frac{(f(x)-f(\xi))^2}{2\sigma_r^2}}$$

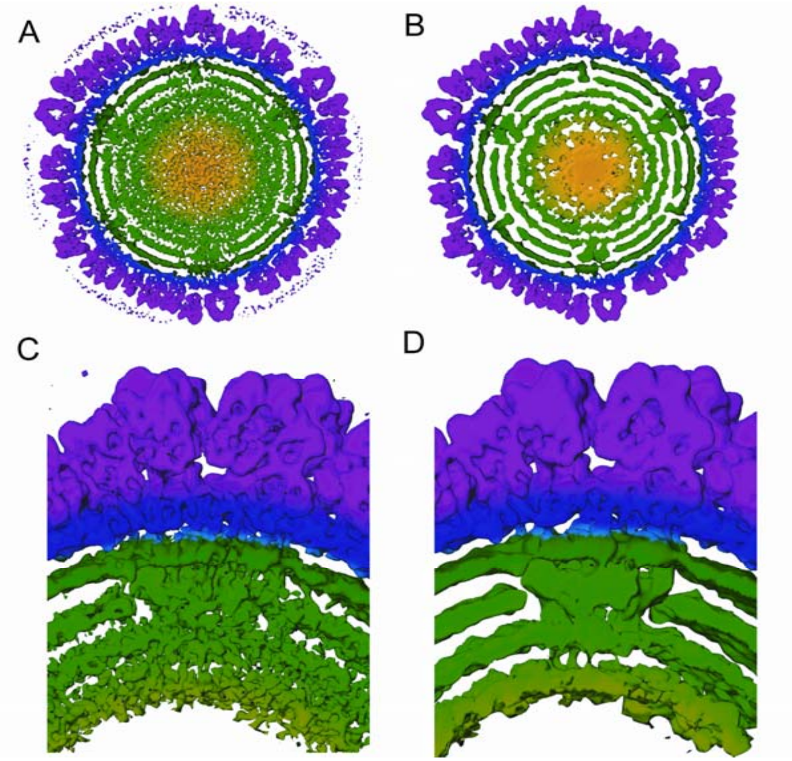
where σ_d and σ_r are parameters and $f(.)$ is the image intensity value.

- Anisotropic diffusion filtering

$$\partial_t \phi - \mathrm{div}(a(|\nabla \phi_\sigma|)\nabla \phi) = 0$$

where **a** stands for the diffusion tensor determined by local curvature estimation.

- Anisotropic gradient vector diffusion

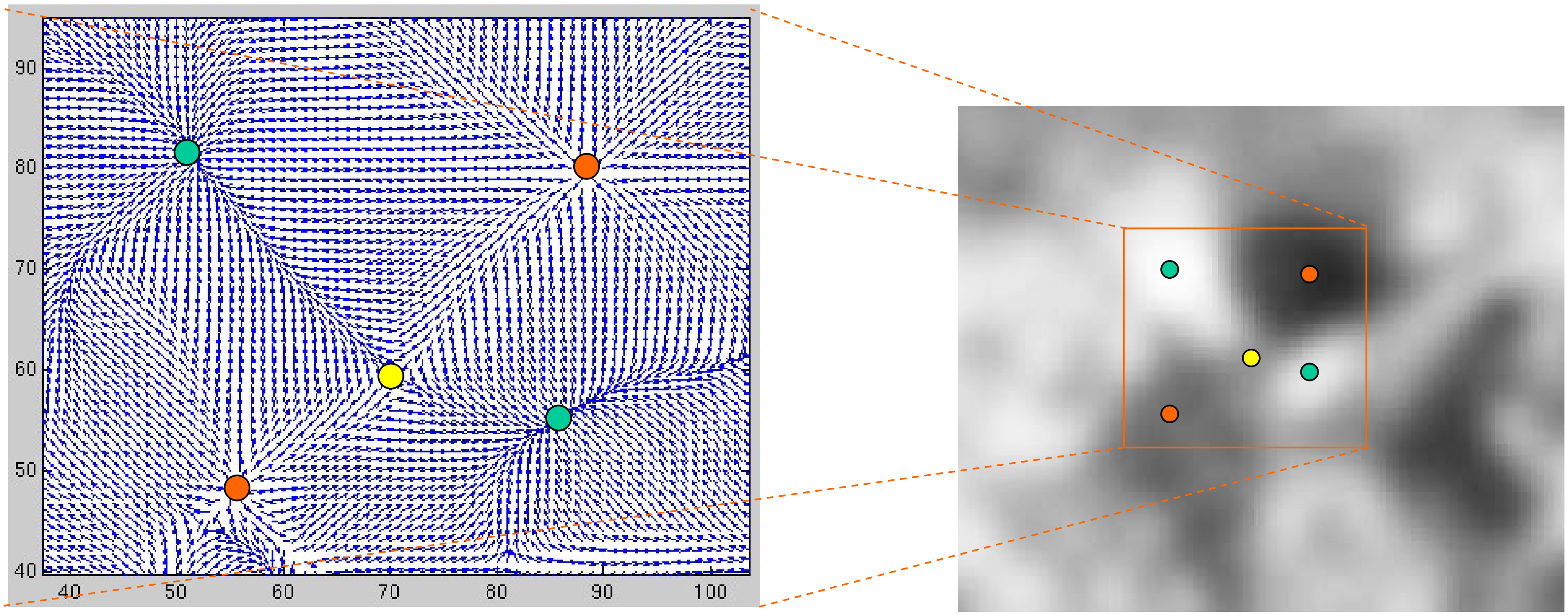


W. Jiang, M. Baker, Q. Wu, C. Bajaj, W. Chiu, Journal of Structural Biology, 144, 5,(2003),114-122

C. Bajaj, G. Xu, ACM Transactions on Graphics, (2003),22(1), 4 - 32.

Z. Yu & C. Bajaj, Proc. Int'l Conf. Image Processing, 2002. pp. 1001-1004.
Z. Yu & C. Bajaj, Proc. Int'l Conf. Computer Vision and Pattern Recognition, 2004. 415-420.

Compute Critical Points Using AGVD



: minimum (0)

: maximum (3)

: saddle (1, 2)

Anisotropic Gradient Vector Diffusion (AGVD)

Isotropic Diffusion (Xu *et al.*, 1998)

$$\begin{cases} \frac{\partial u}{\partial t} = \mu \nabla^2 u - (u - f_x)(f_x^2 + f_y^2) \\ \frac{\partial v}{\partial t} = \mu \nabla^2 v - (v - f_y)(f_x^2 + f_y^2) \end{cases}$$

Where:

(u(t), v(t)) stands for the evolving vector field;

μ is a constant;

f is the original image to be diffused;

(f_x, f_y) = (u(0), v(0)).

Anisotropic Diffusion (Yu & Bajaj ICPR'02)

$$\begin{cases} \frac{\partial u}{\partial t} = \mu \nabla (g(\alpha) \cdot \nabla u) - (u - f_x)(f_x^2 + f_y^2) \\ \frac{\partial v}{\partial t} = \mu \nabla (g(\alpha) \cdot \nabla v) - (v - f_y)(f_x^2 + f_y^2) \end{cases}$$

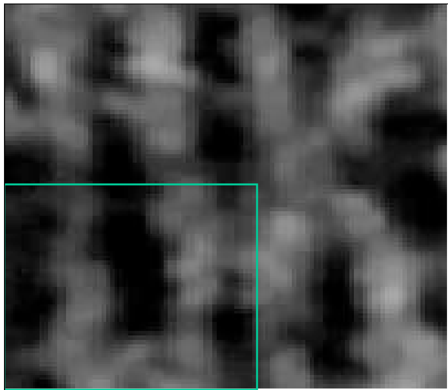
Where

(u(t), v(t)) stands for vector field;

μ is a constant; (f_x, f_y) = (u(0), v(0)).

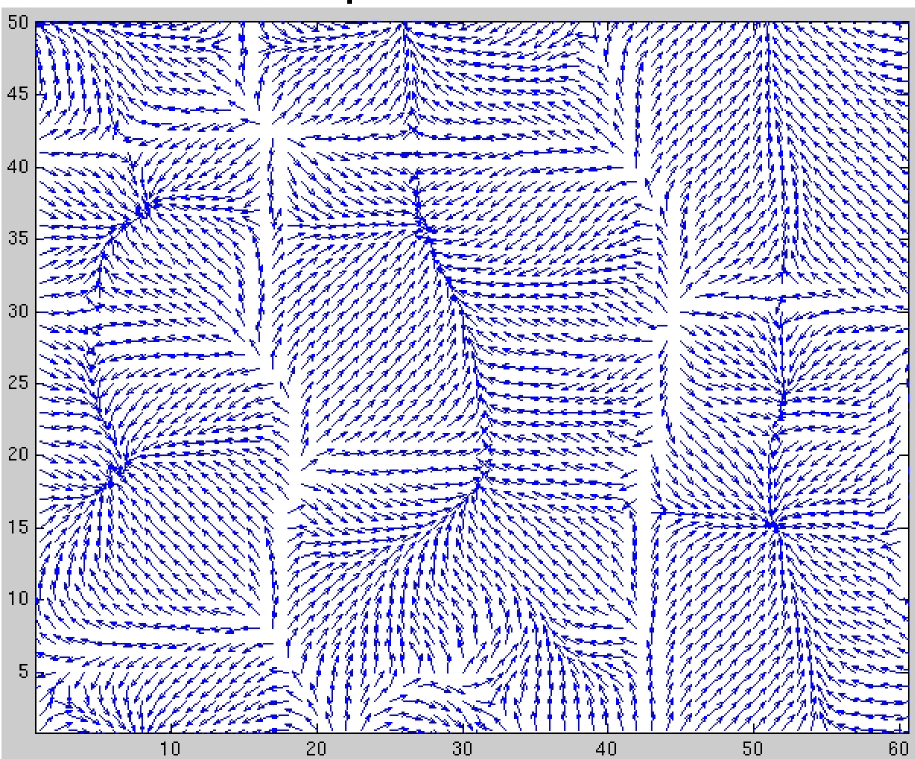
f is the original image to be diffused;

g(.) is the angle between two vectors

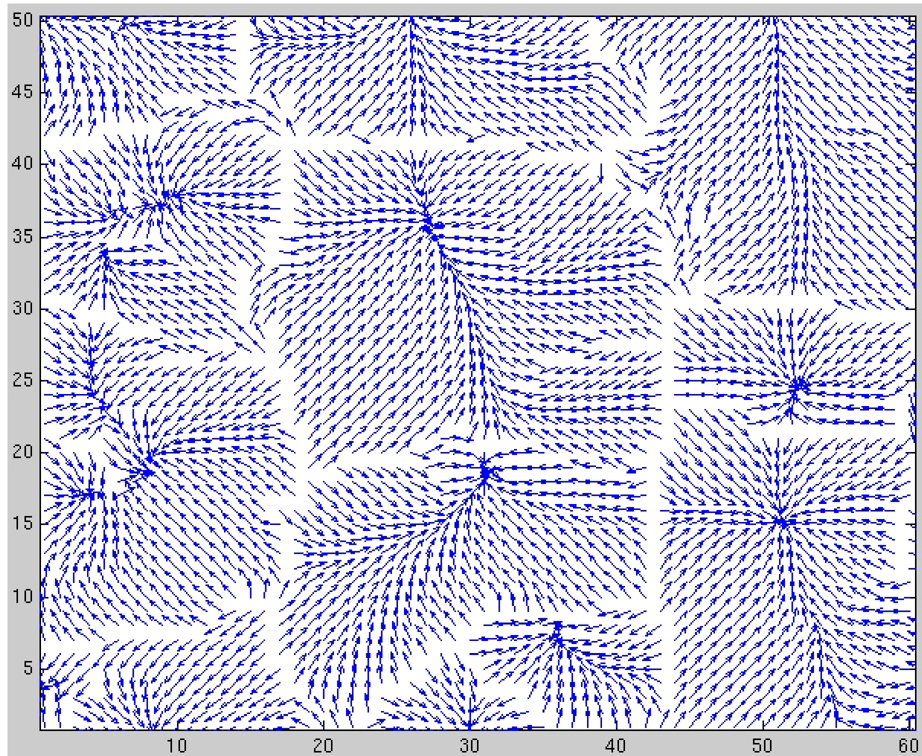


GVD v.s. AGVD

Isotropic diffusion

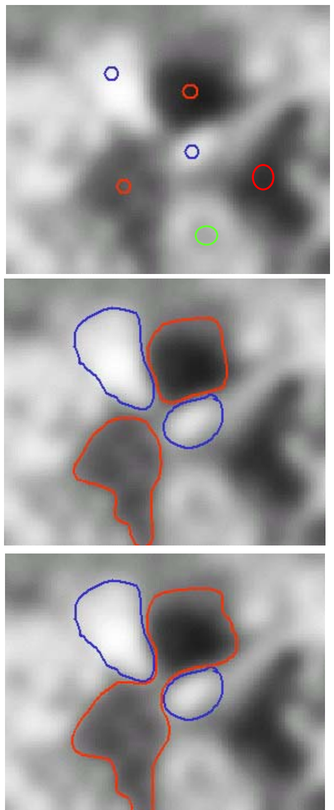


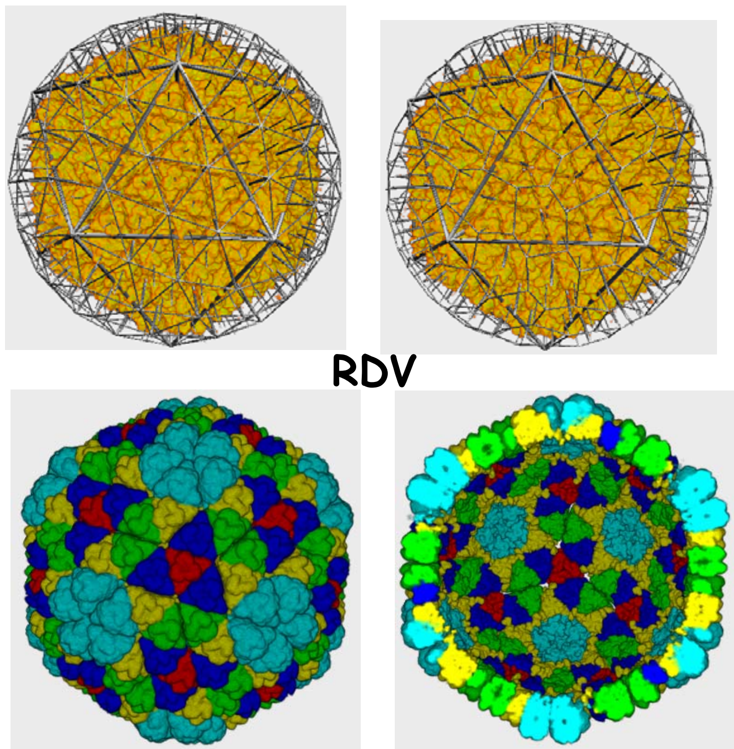
Anisotropic diffusion

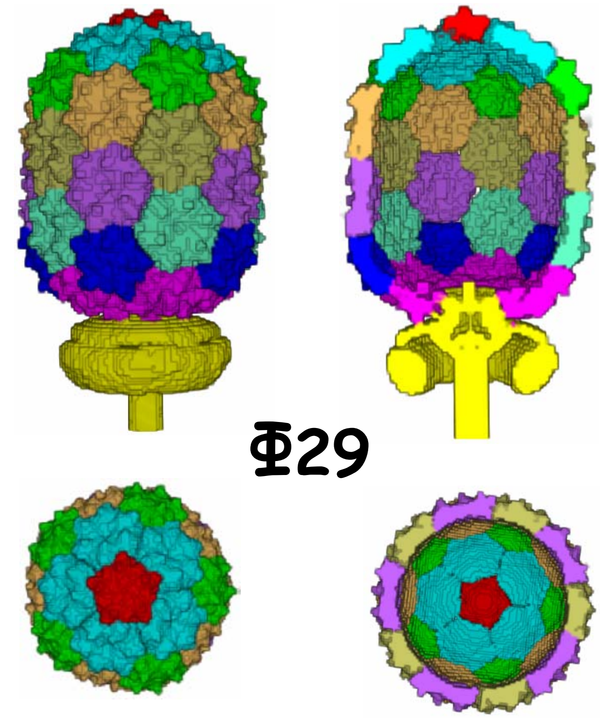


Structure Elucidation 1(B)

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



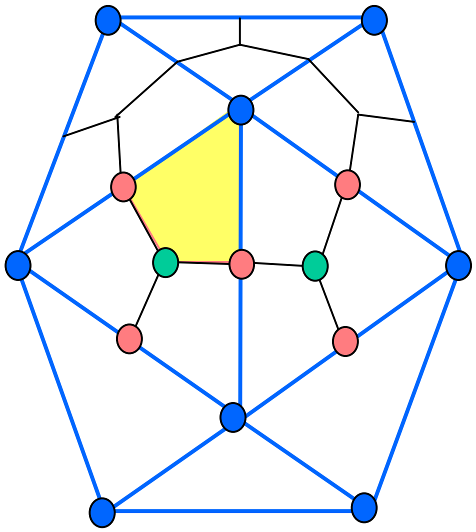


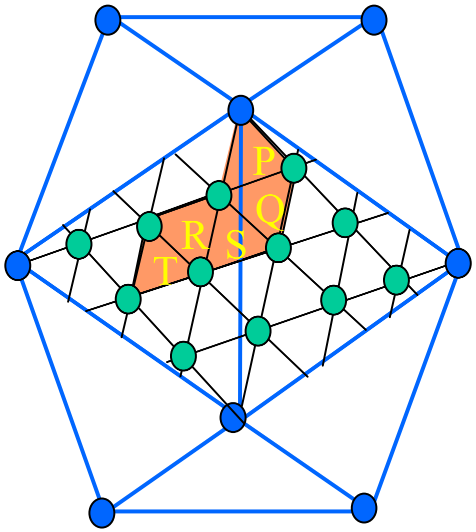


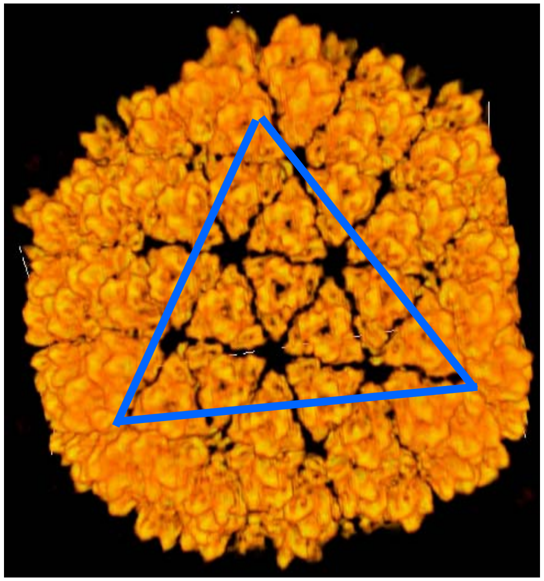
Z. Yu, and C. Bajaj, IEEE Trans.on Image Process, 2005. 144(1-2), pp. 132-143.

Global and Local Symmetry

- Automatic structure unit identification in a 3D Map







Two-fold vertices
Three-fold vertices
Five-fold vertices

Example: RDV

Symmetry Detection: Correlation Search

$$C(\theta,\varphi)=\sum_{\vec{r}\in V} f(\vec{r})f(R_{(\theta,\varphi,2\pi/5)}\cdot\vec{r})$$

- Algorithm: *detect 5-fold rotation symmetry*
  - Compute the scoring function
    - For every angular bin B_j, compute θ_j,φ_j {

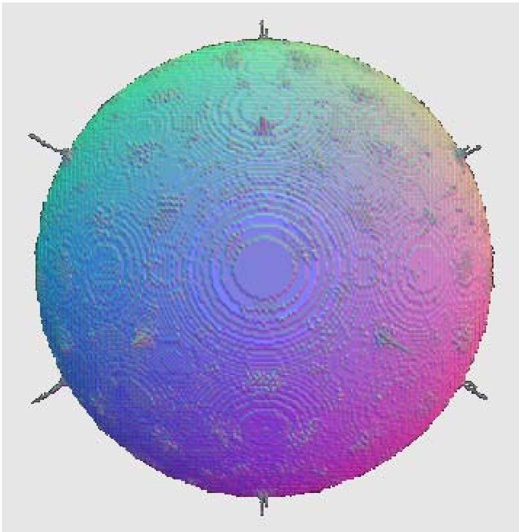
      For every critical point C_i {

$$\vec{r}_k(C_i,B_j)=R_{(\theta_j,\varphi_j,2k\pi/5)}\cdot C_i,\quad k=0,1,2,3,4$$

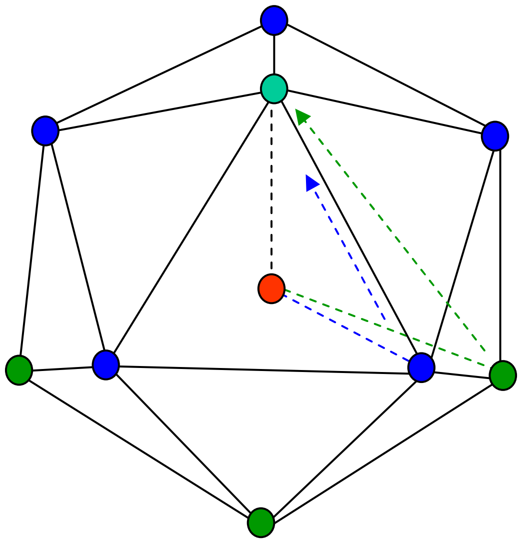
$$Dev(C_i,B_j)=\frac{1}{5}\sum_{k=0}^{4}(f(\vec{r}_k)-\bar{f})\ \}$$

$$SF(B_j)=\frac{1}{p}\sum_{i=0}^{p}Dev(C_i,B_j)\ \}$$

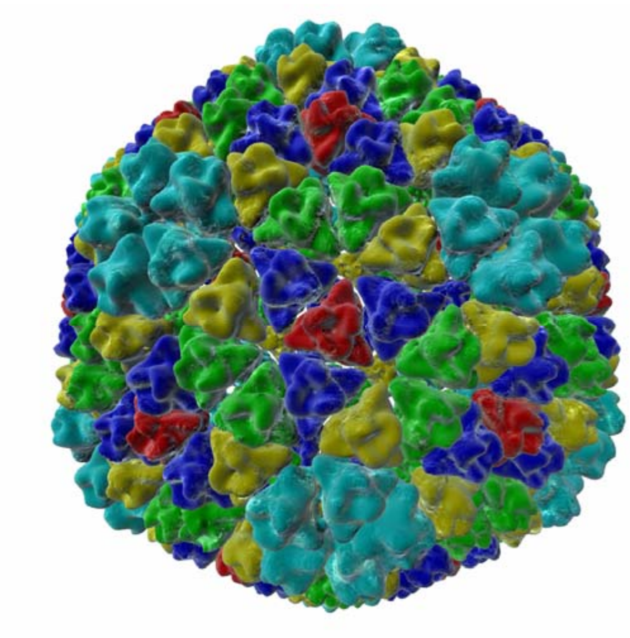
  - Locate the symmetry axes
    - The 12 peaks
  - Refine the symmetry axes
    - In order to locate a perfect icosahedron (rotate the axes by 0^0, 63.43^0, 116.57^0, 180^0)



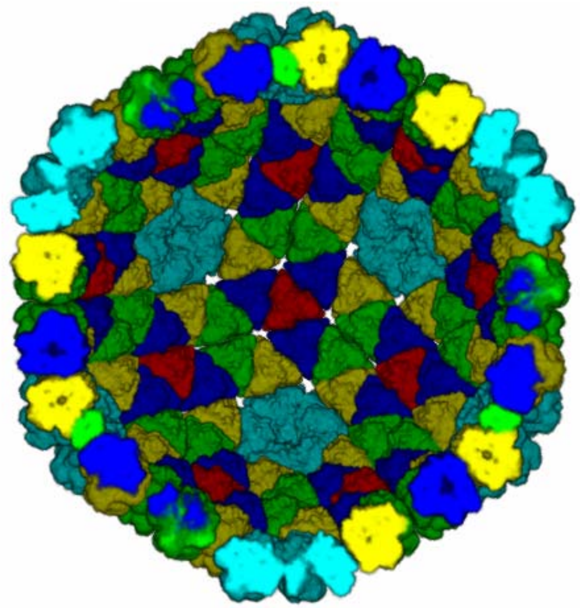
Inverted and normalized SF(Bj)



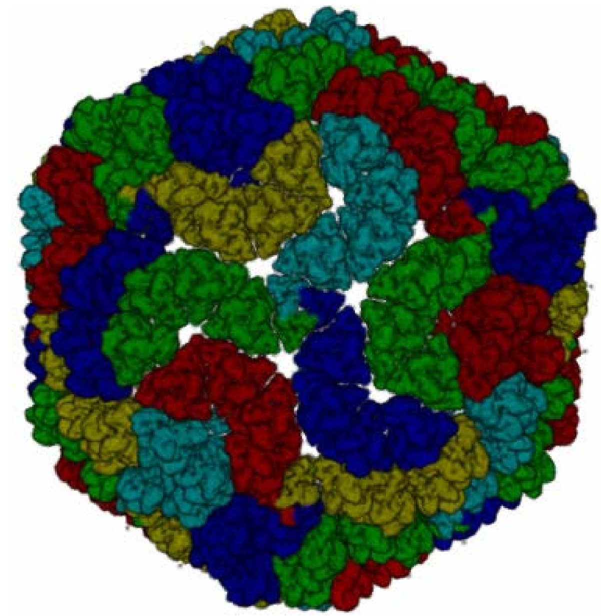
Structure Elucidation Results: RDV (Bakeoff)



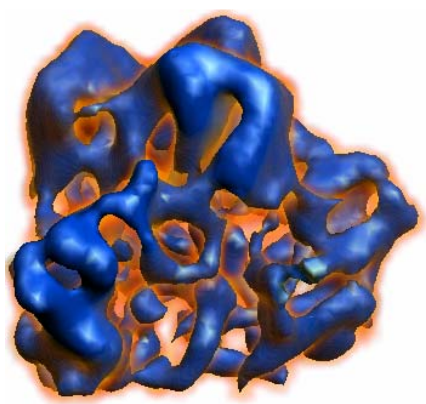
surface rendering (outside)



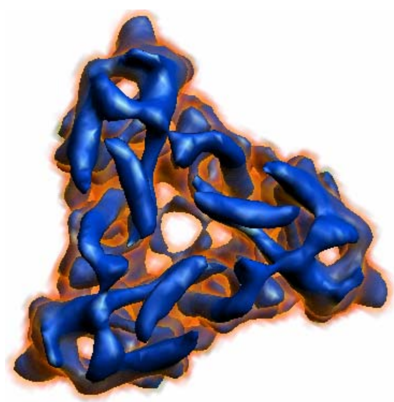
volume rendering (inside)



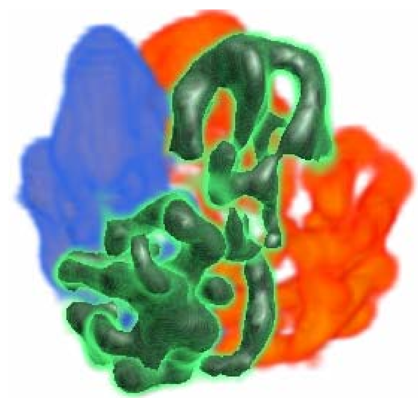
volume rendering (asymmetric unit)



averaged trimer (side)

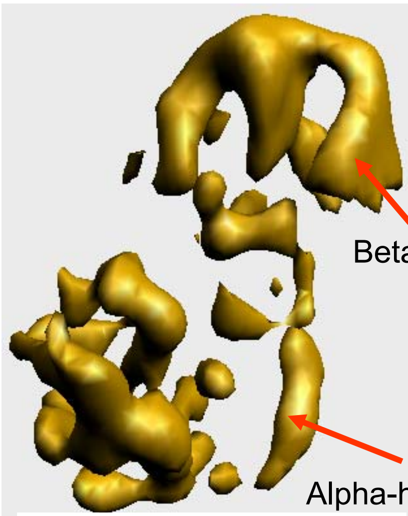


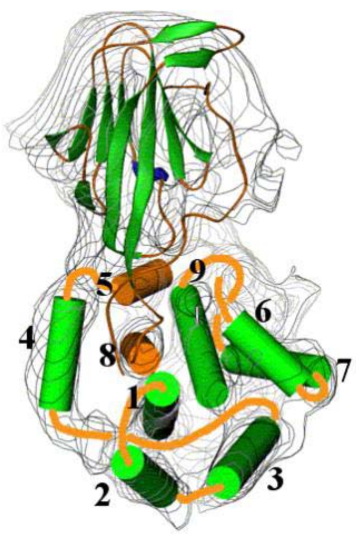
averaged trimer (bottom)

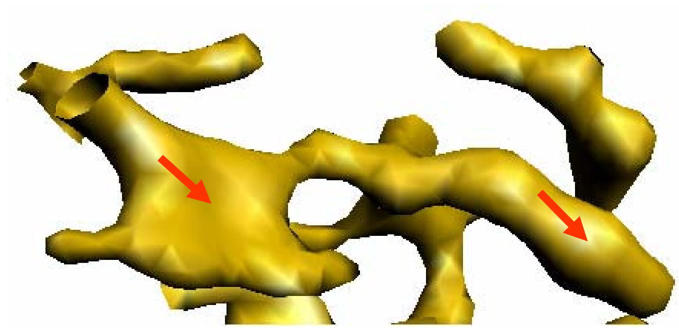


segmented monomers

Structure Elucidation 1(C): Secondary Structure Identification

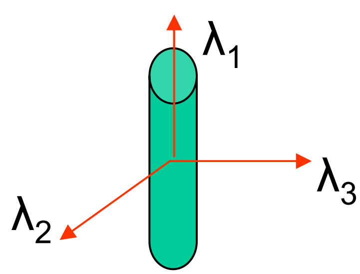


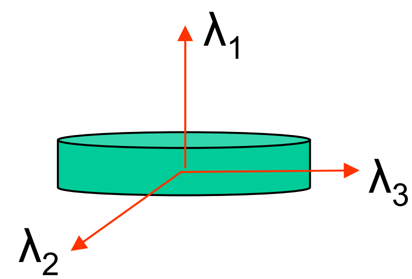




$$G_\sigma * \begin{pmatrix} I_x^2 & I_x I_y & I_x I_z \\ I_x I_y & I_y^2 & I_y I_z \\ I_x I_z & I_y I_z & I_z^2 \end{pmatrix}$$

The eigenvectors of the local structure tensor give the principal directions of the local features:





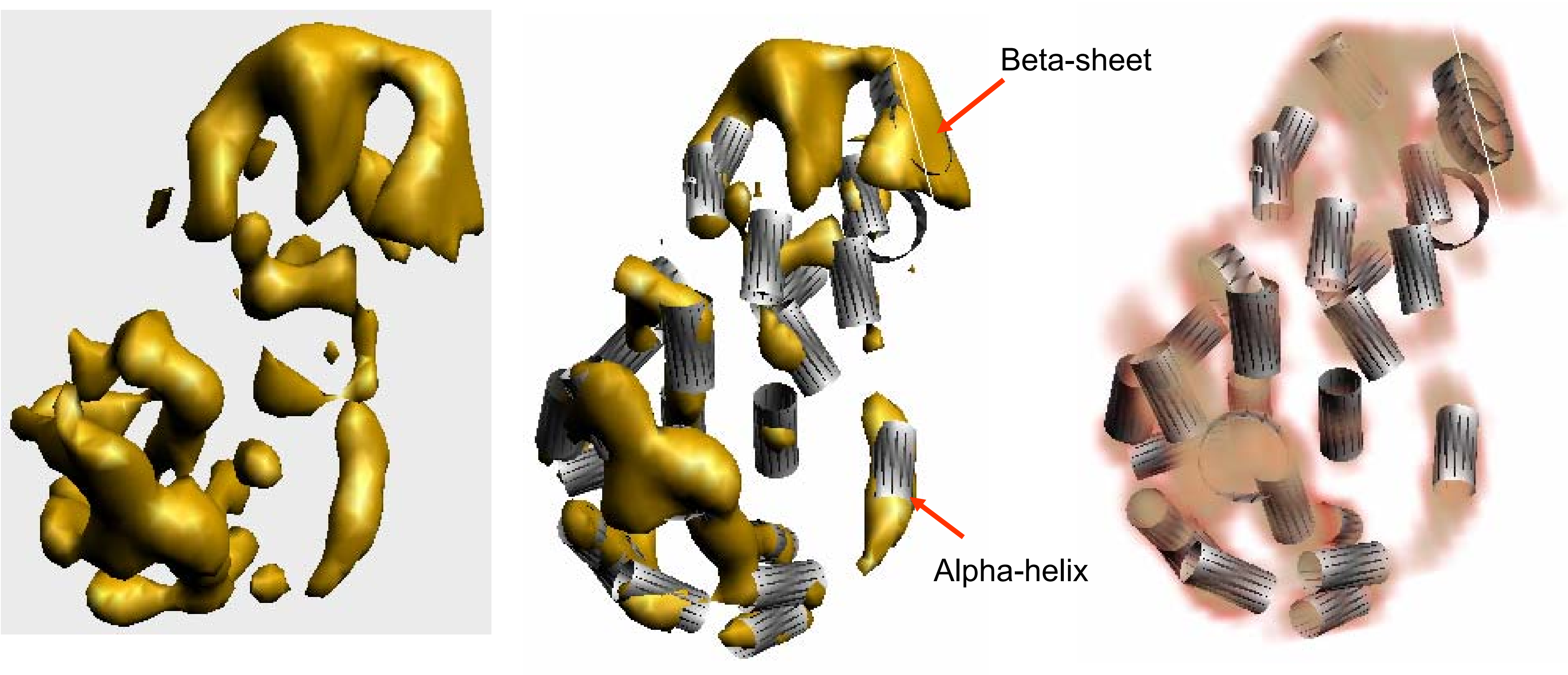
Line structure (alpha-helix)

$$\lambda_2 \approx \lambda_3 >> \lambda_1 \approx 0$$

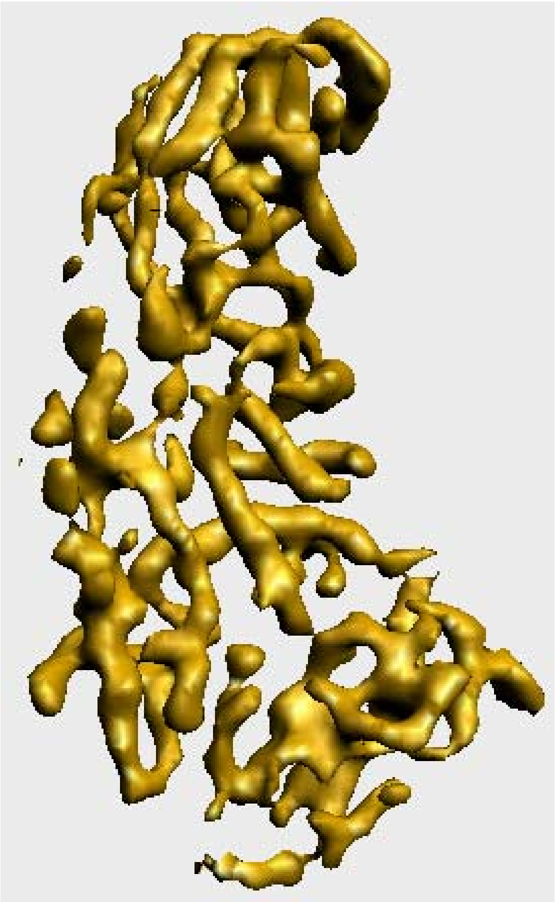
plane structure (beta-sheet)

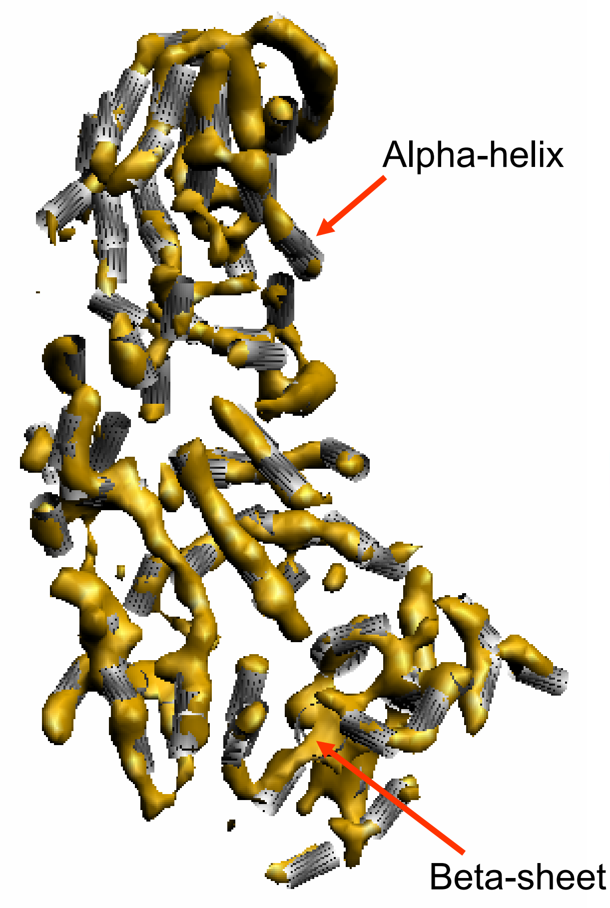
$$\lambda_1 >> \lambda_2 \approx \lambda_3 \approx 0$$

Monomeric Unit of Outer Capsid of RDV

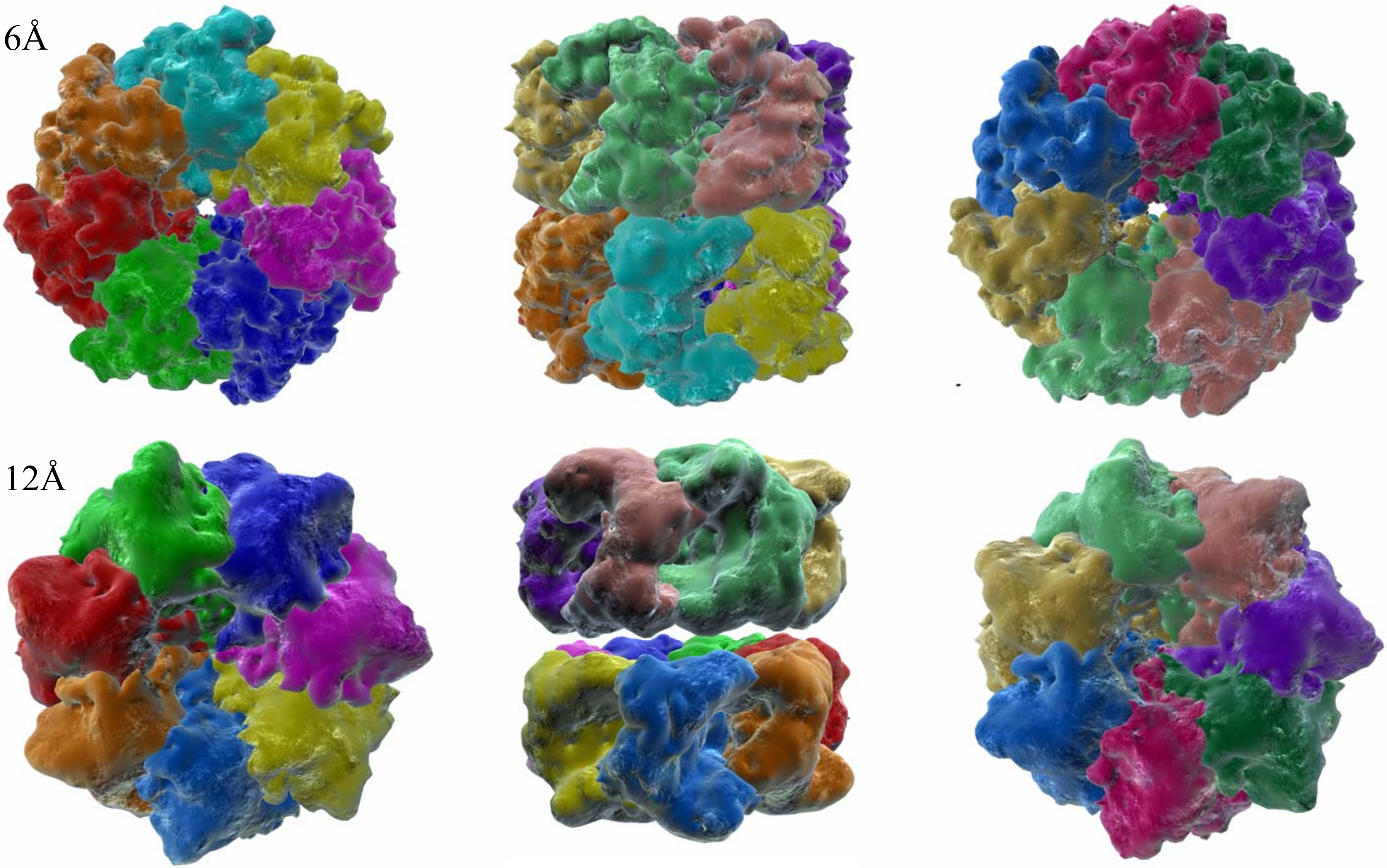


Monomeric Unit of Inner Capsid of RDV





Structure Elucidation Results: GroEL



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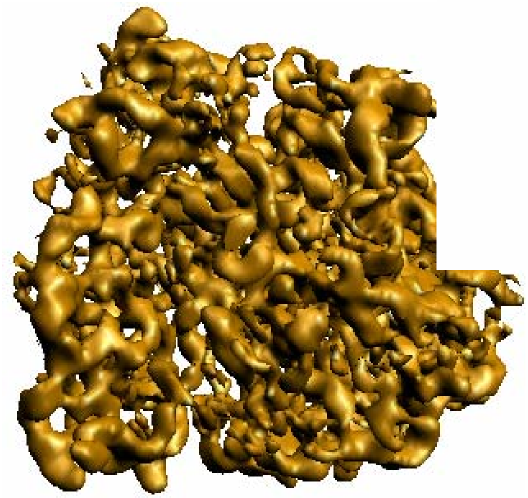
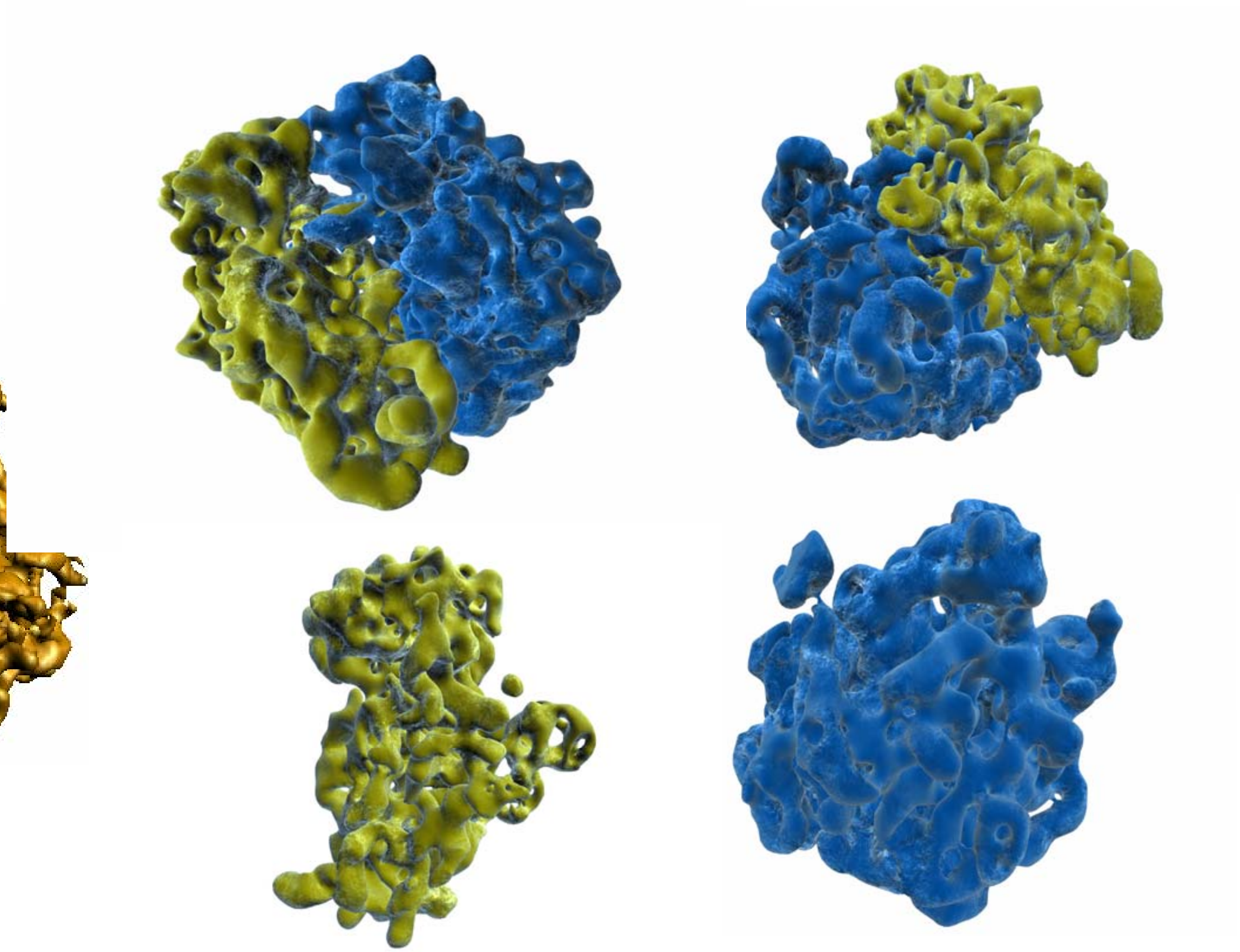
University of Texas at Austin

Data courtesy: Dr. Wah Chiu

September 2007

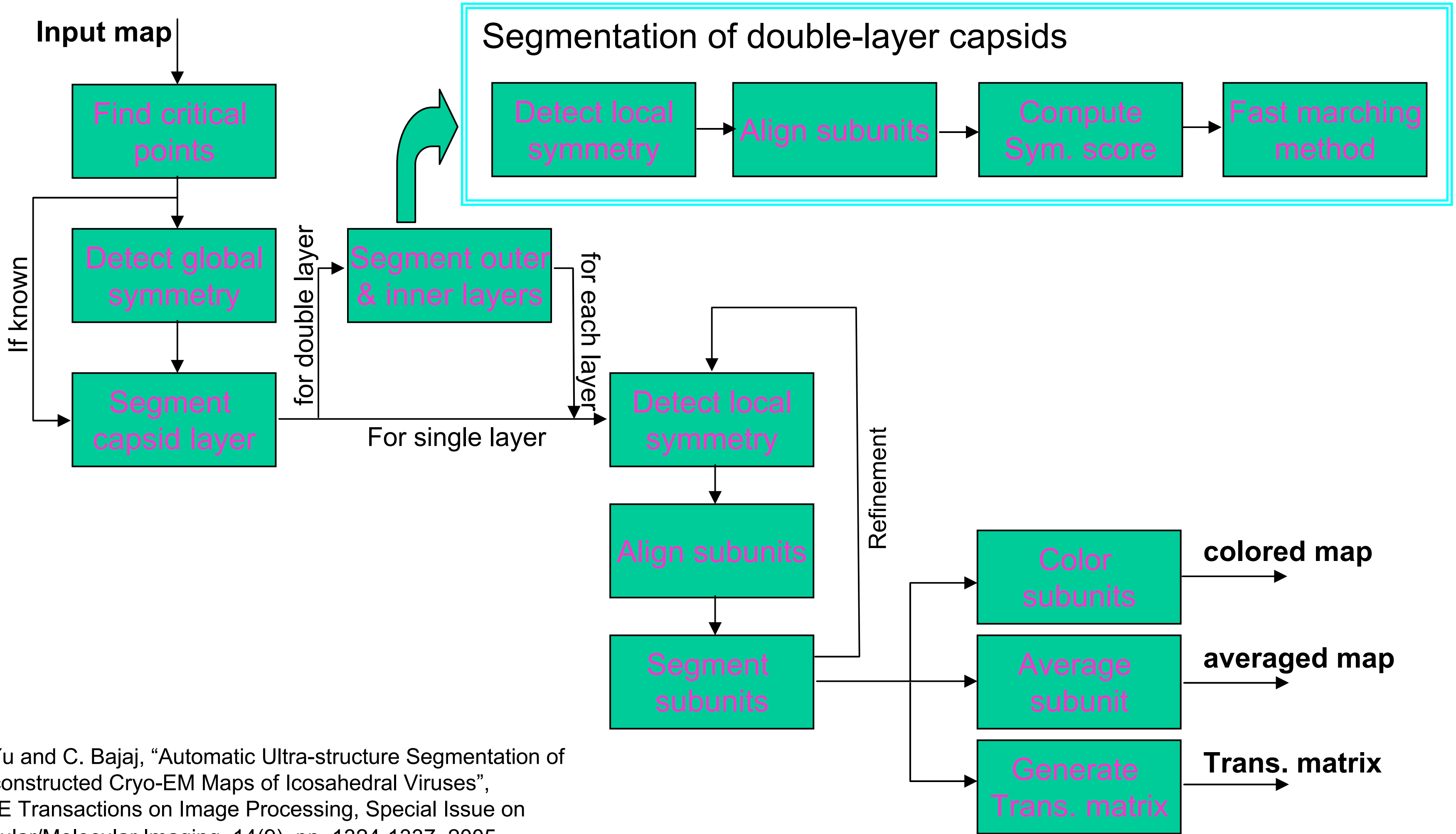
Segmentation Results: Ribosome (Bakeoff)





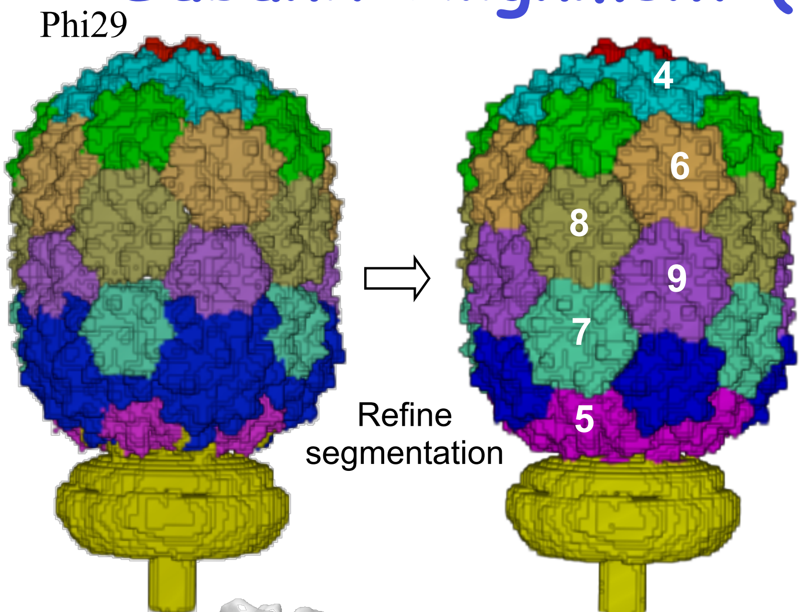
70S ribosome from E. coli complex. 70S-tRNAfMet-MF-tRNAPhe. Data courtesy: EBI & J.Frank

Structure Elucidation for Symmetric Capsid Viruses



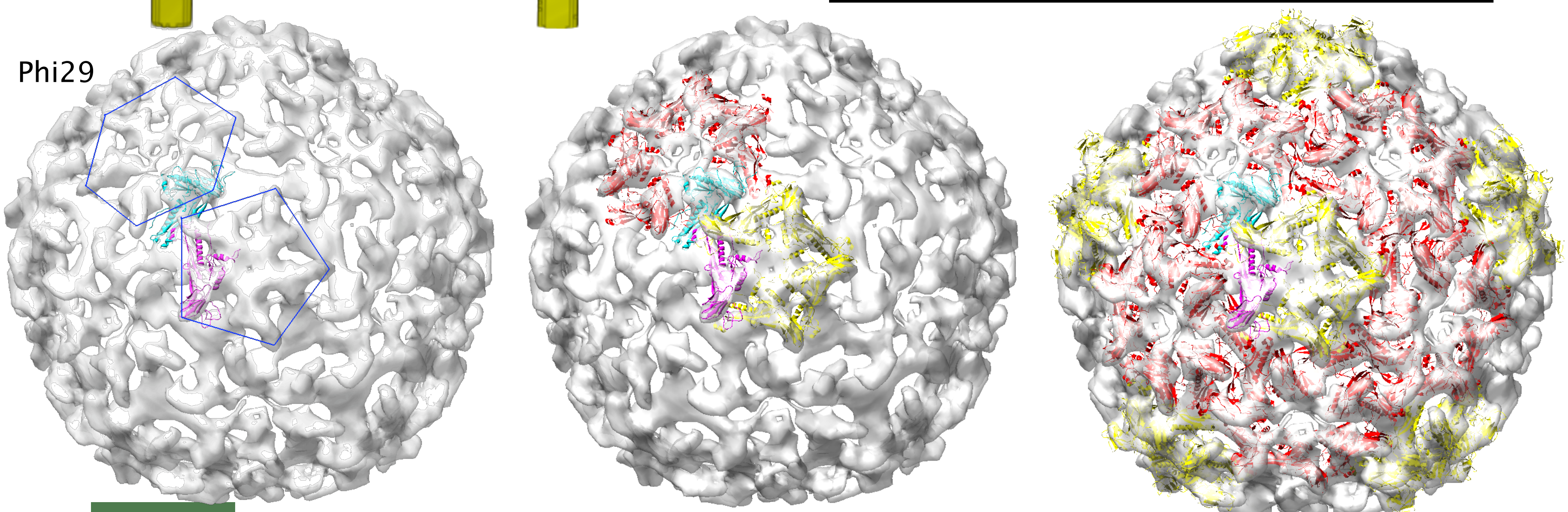
Z. Yu and C. Bajaj, "Automatic Ultra-structure Segmentation of Reconstructed Cryo-EM Maps of Icosahedral Viruses", IEEE Transactions on Image Processing, Special Issue on Cellular/Molecular Imaging, 14(9), pp. 1324-1337, 2005.

Subunit Alignment (Simul. Structure Fitting)



Similarity table

	#4	#5	#6	#7	#8	#9
#4	**0.97**	0.79	0.95	0.94	0.87	0.88
#5		**0.81**	0.79	0.78	0.77	0.79
#6			**0.98**	0.96	0.88	0.88
#7				**0.96**	0.89	0.88
#8					**0.87**	0.94
#9						**0.81**



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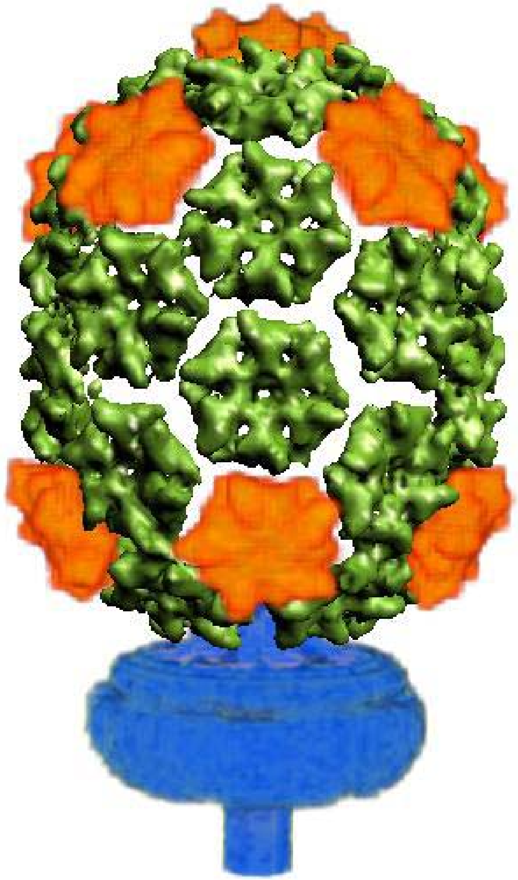
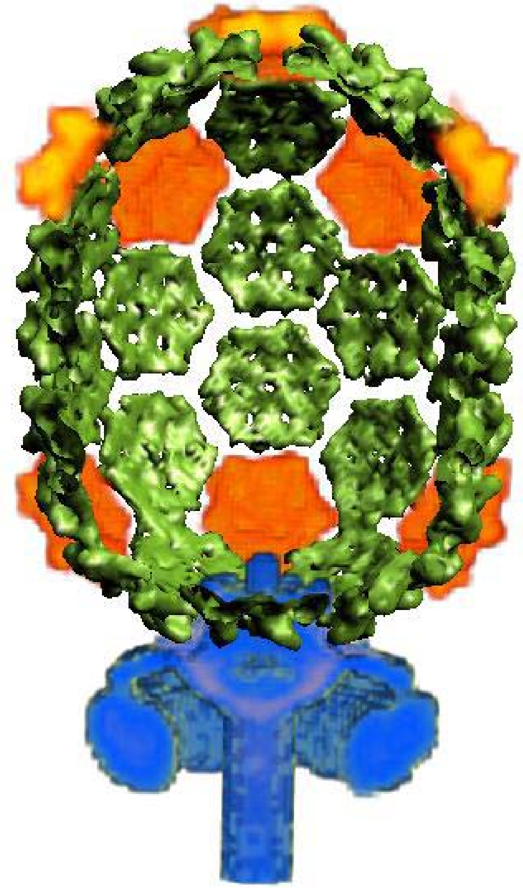
Subunit alignment (1): averaging



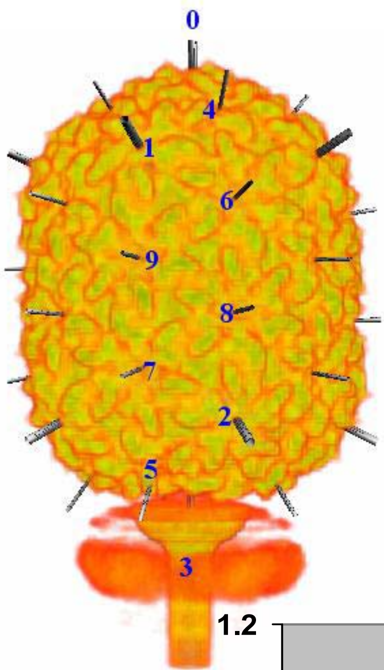
Φ29



The above two pictures (left: outer; right: inner) show the averaged capsid layer, calculated from one 5-fold subunit (orange) and one 6-fold subunit (green). The tail structure (blue) is augmented after the averaging.

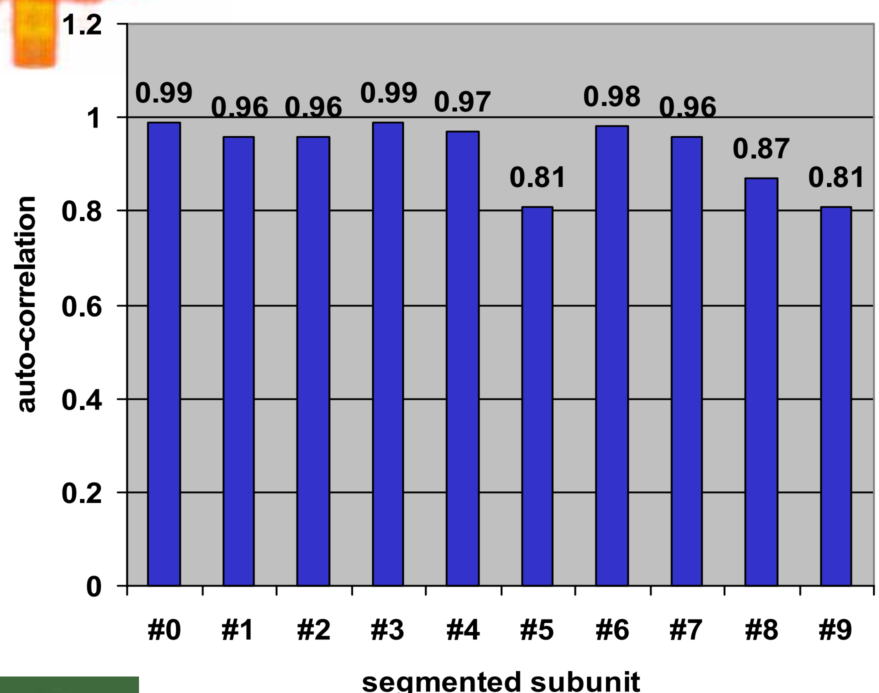
Data courtesy: Tim Baker

Structure Elucidation 1(C): Subunit Alignment



Φ29

- Symmetry score



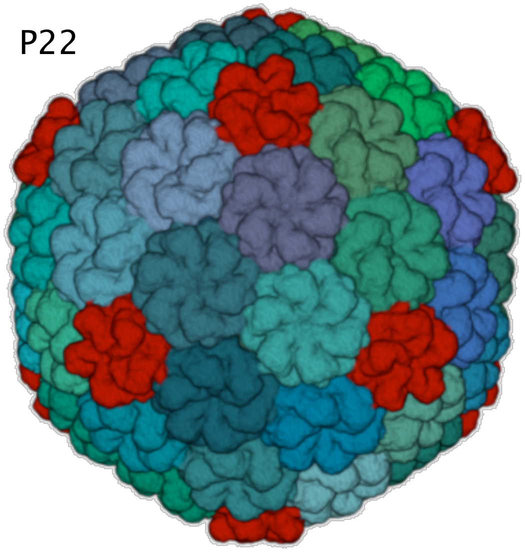
- Cross-correlation

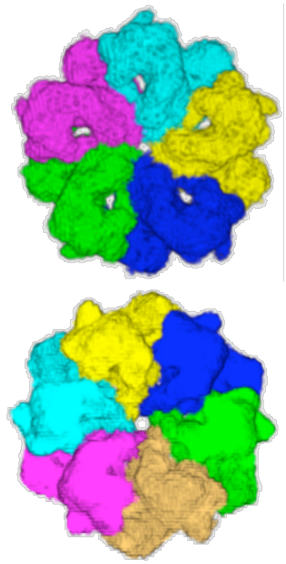
	#0	#1	#2	#3
#0	1	0.95	0.95	0.34
#1	0.95	1	0.96	0.31
#2	0.95	0.96	1	0.31
#3	0.35	0.31	0.32	1

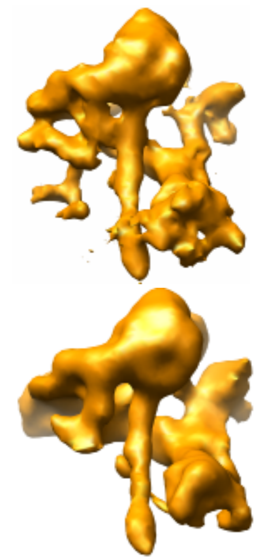
	#4	#5	#6	#7	#8	#9
#4	1	0.79	0.95	0.94	0.87	0.88
#5	0.79	1	0.79	0.78	0.77	0.79
#6	0.95	0.79	1	0.96	0.88	0.88
#7	0.94	0.78	0.96	1	0.89	0.88
#8	0.87	0.77	0.88	0.89	1	0.94
#9	0.88	0.79	0.88	0.88	0.94	1

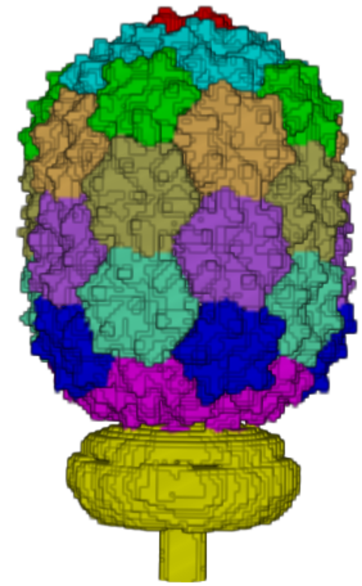
Subunit Segmentation

P22



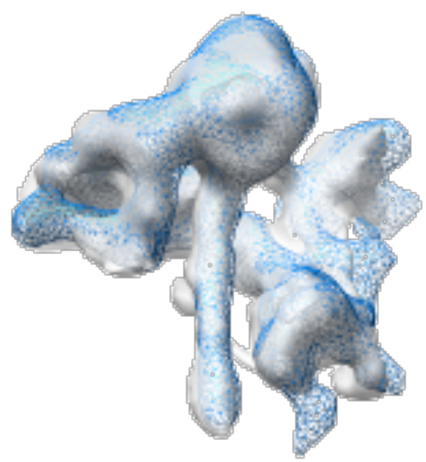


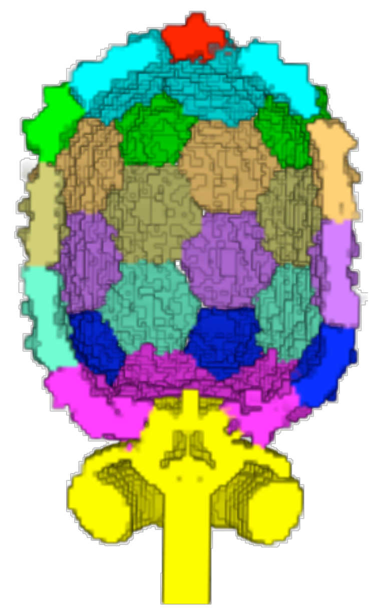




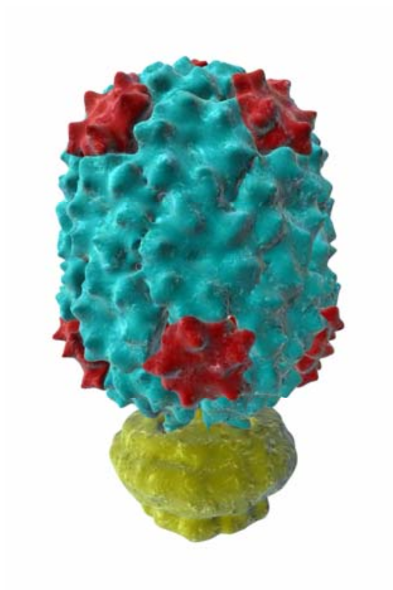
Correlation Score with manually segmented subunits:

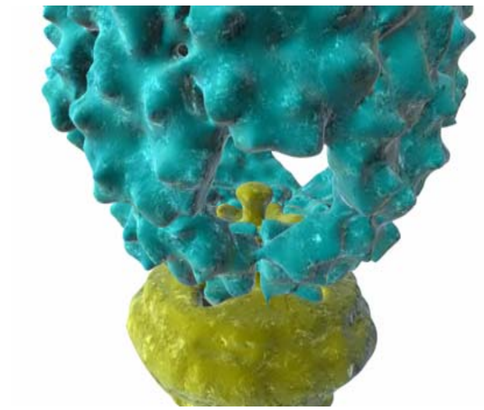
5-fold: **0.72**
6-fold: **0.79**

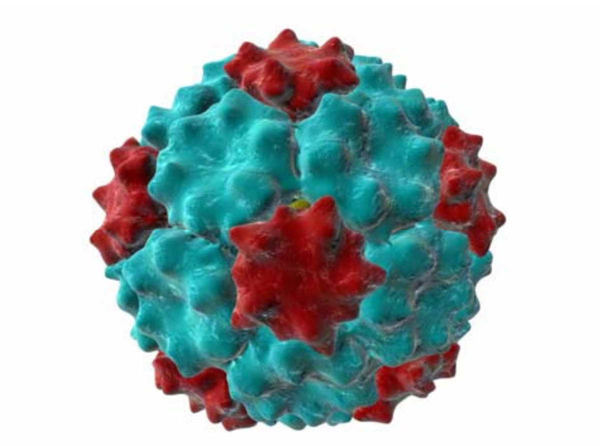




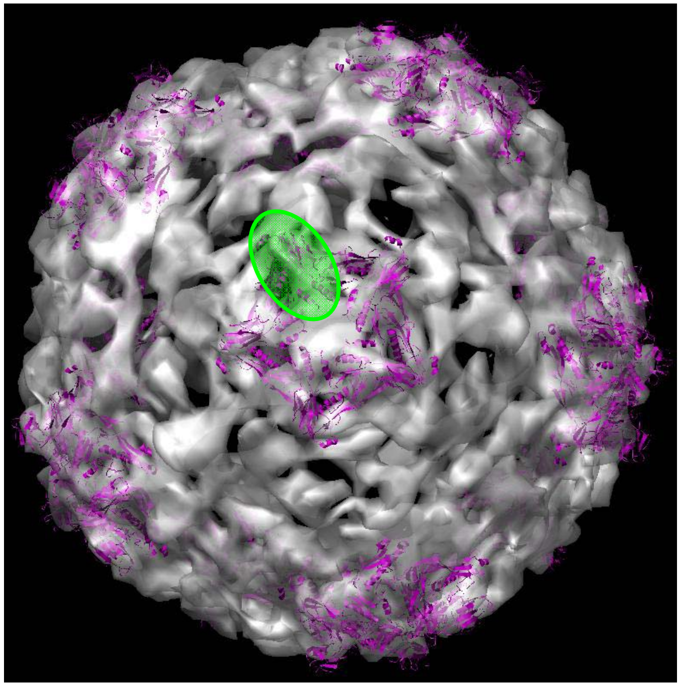
Structure Elucidation Results: **Φ29**

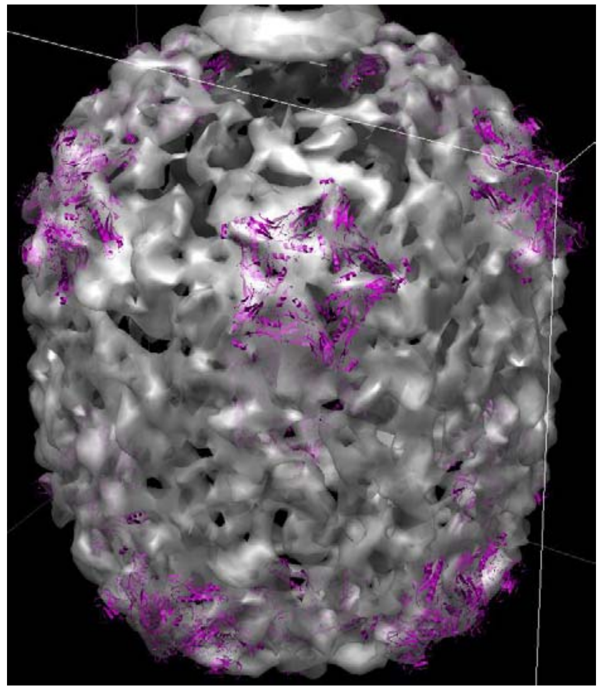


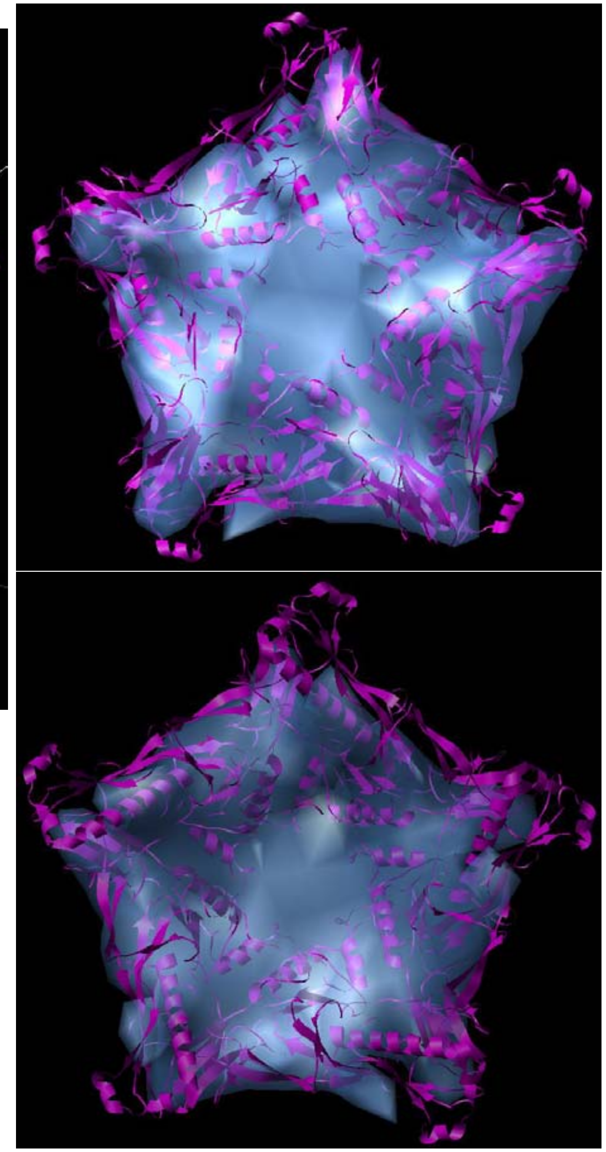




Subunit alignment (2): Fitting

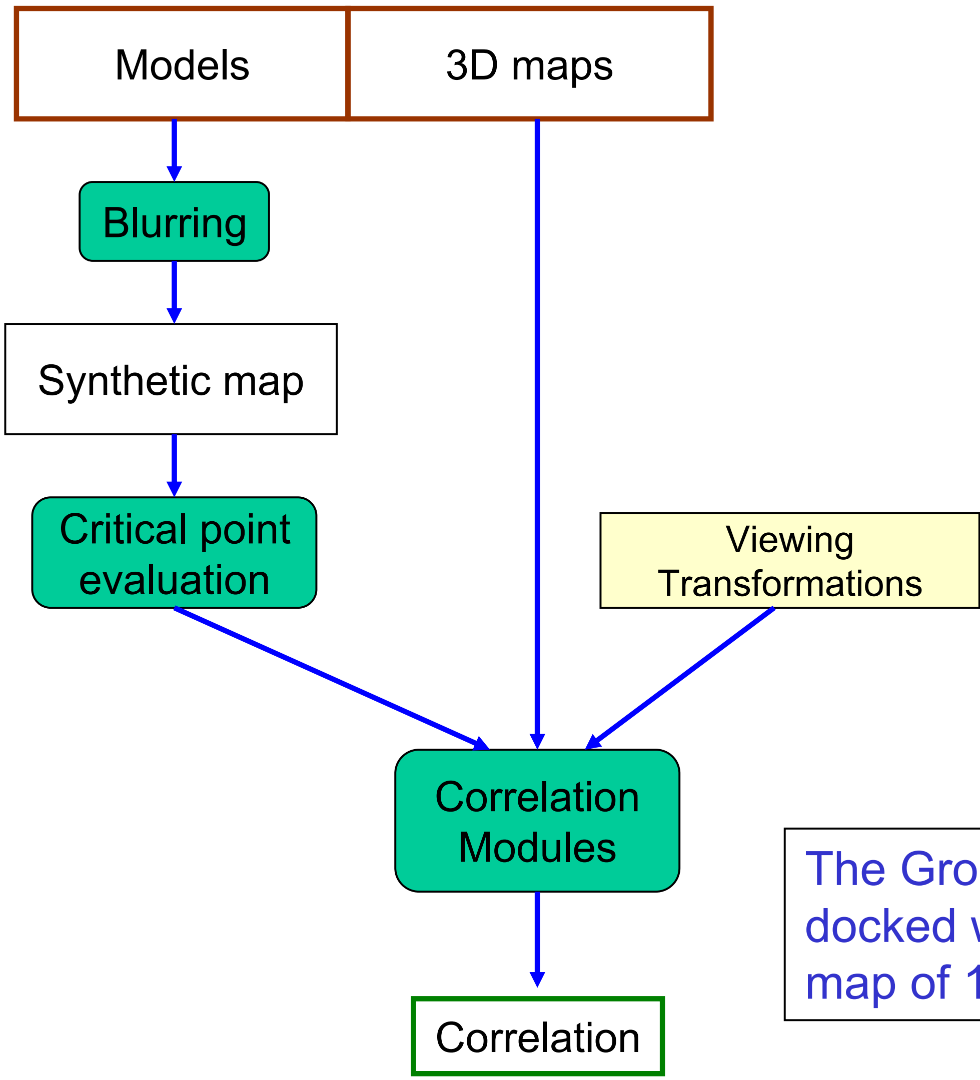


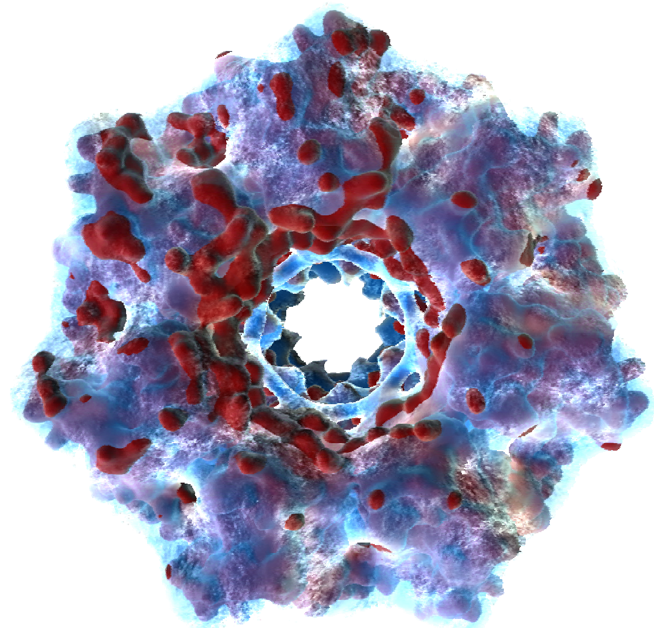


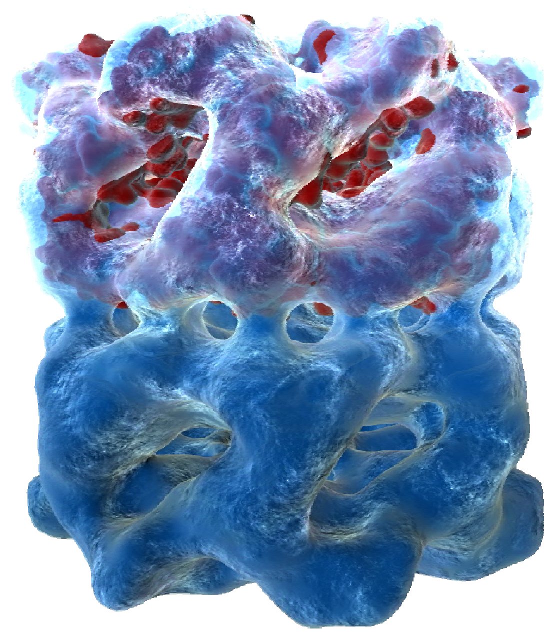


The PDB structure of one monomer is matched & fit into the cryo-EM map (as shaded in green in the left figure). Then all the quasi-symmetric 5-fold subunits are computationally fit with the PDB structure using the transform matrices obtained in subunit alignment. Similar procedure can be applied to all 6-fold subunits.

"Interactive" Fitting

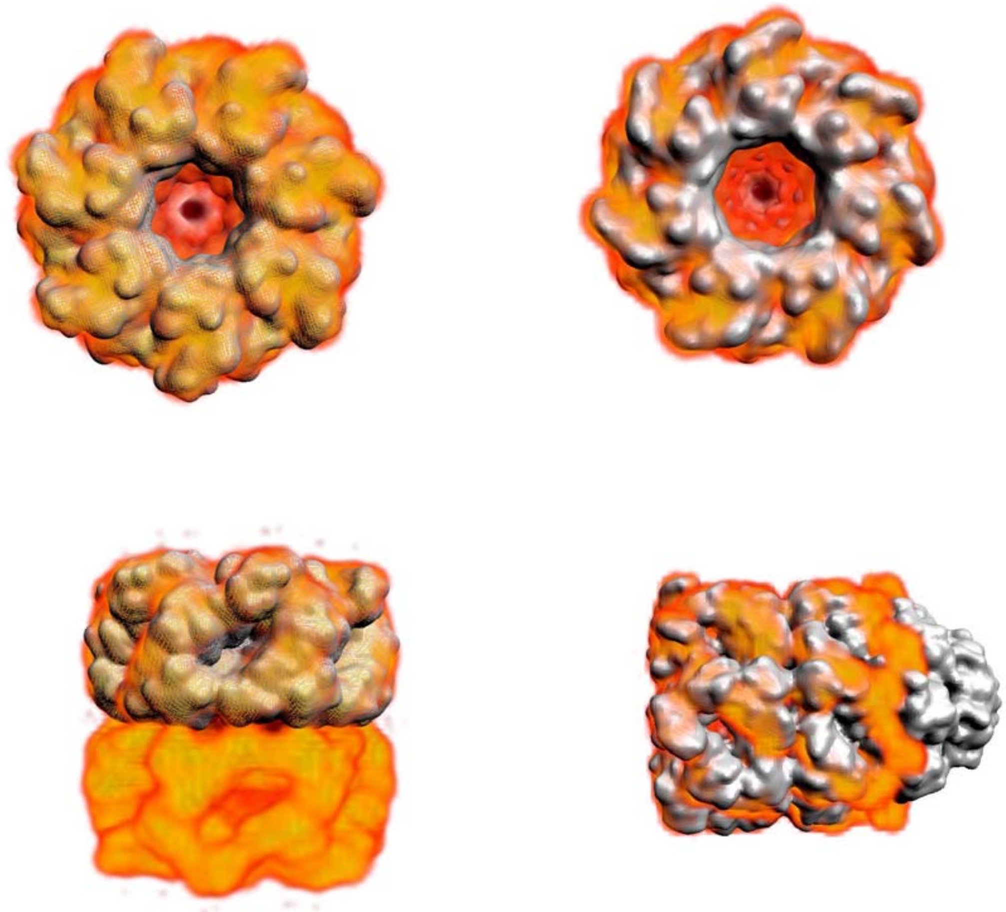






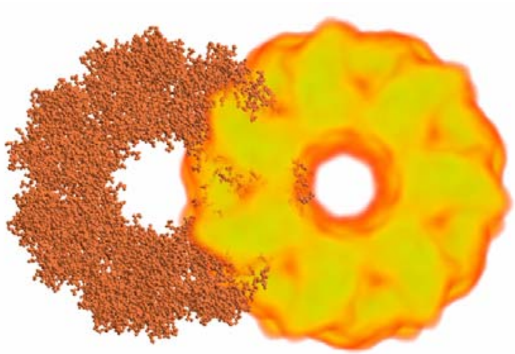
The GroEL map docked with a blur map of 1OEL.PDB

Gro-EL: X-ray structures docked in Cryo-EM

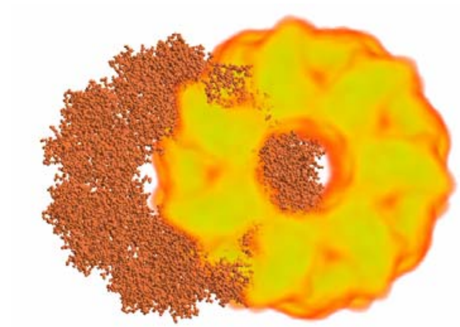


Interactive Correlation Analysis

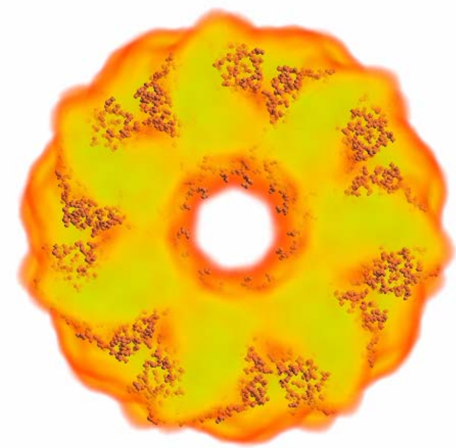
C = 0.2235



C = 0.269

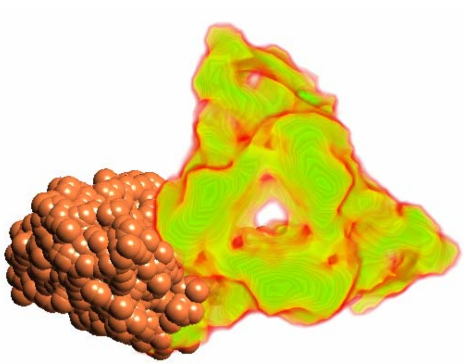


C = 0.593

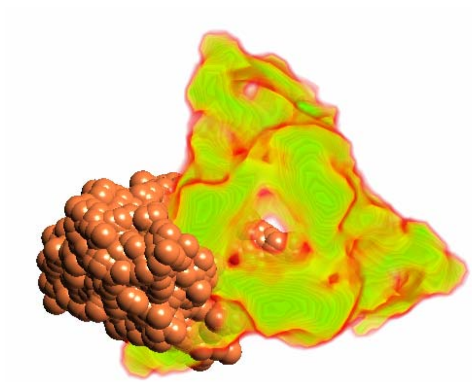


12A GroEL map and 1OEL.pdb

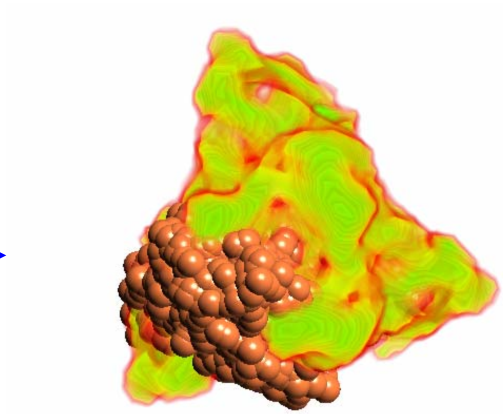
C = 0.208



C = 0.387



C = 0.542

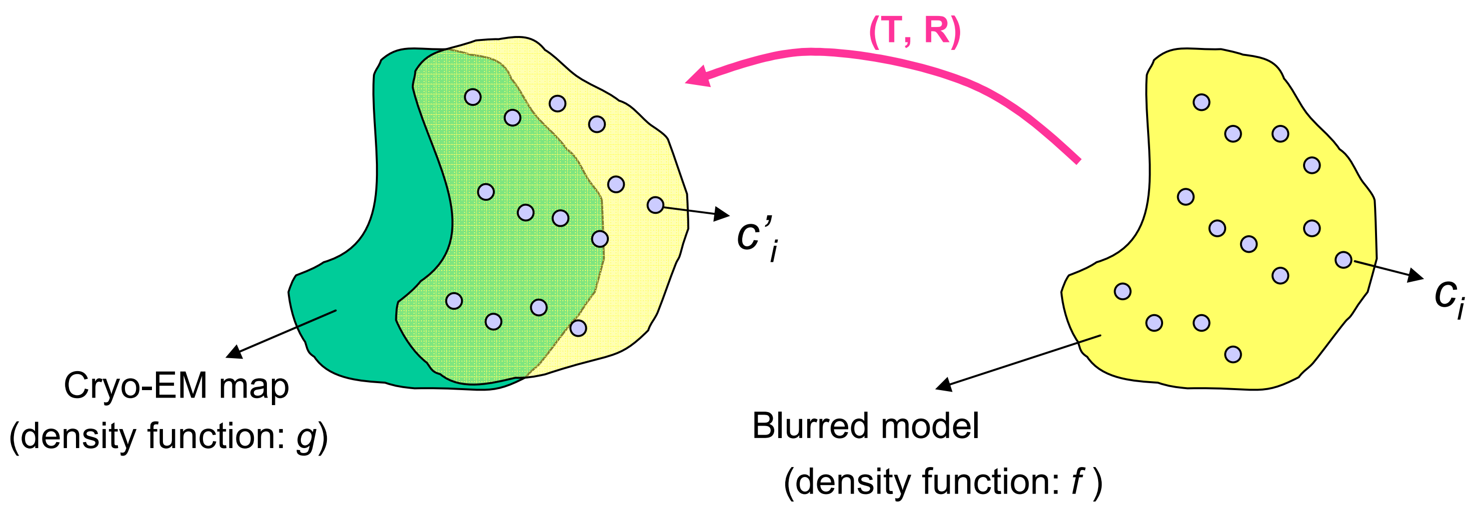


6.8A RDV map and 1UF2.pdb

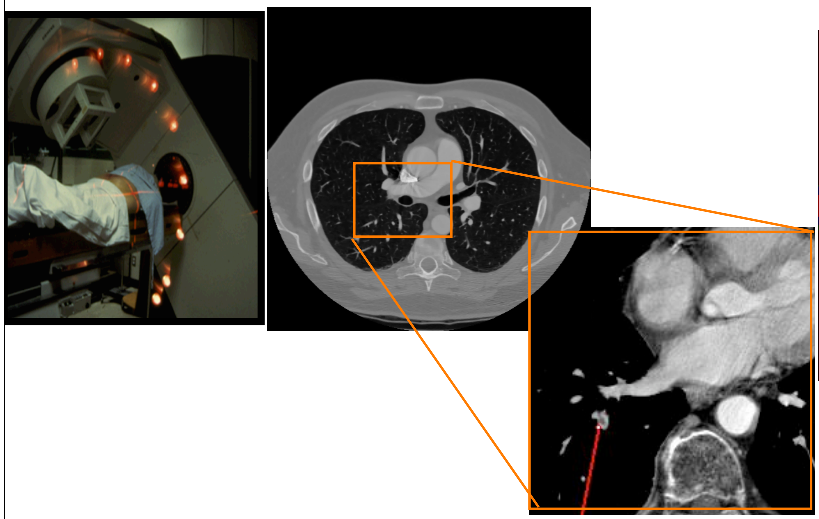
Approximate Correlation Analysis

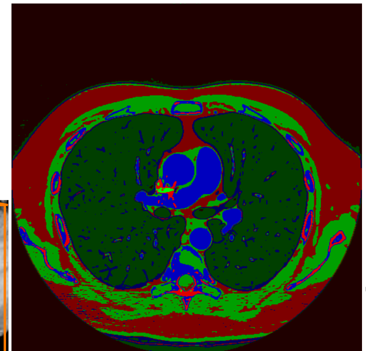
$$score = 1 - \frac{\sum_{i=1}^{N} | f(c_i) - g(c_i^{'}) |}{\sum_{i=1}^{N} \max(f(c_i), g(c_i^{'}))}$$

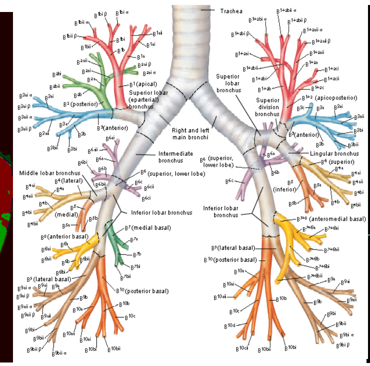
Where ***f*** is the normalized density function of the blurred crystal structure;
g is the normalized density function of the cryo-EM map;
c$_i$, i=1,2,…N, are the critical points of the blurred crystal structure;
c'$_i$, i=1,2,…N, are the transformations of the critical points.

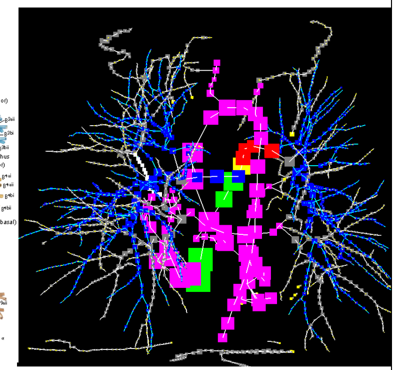


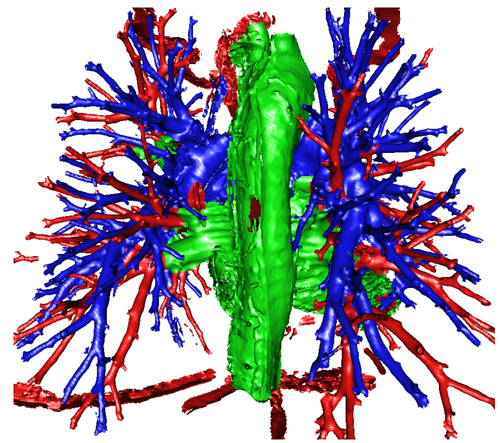
Computer Assisted Radiology: Pulmonary Embolus Cancer Detection











CTA/MRA →Contrast Enhancement, Anisotropic Filtering → Atrial/ Venal Classification & Segmentation → Vasculature Skeltonization → PE Diagnosis/ Quantification

S. Park, CS, Ph.D.

(Collaborator: Dr. Gregory Gladish : MD Anderson Cancer Center)

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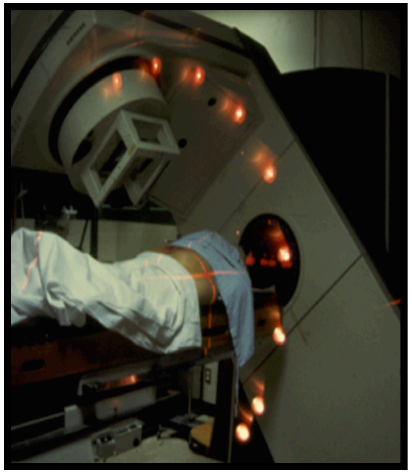
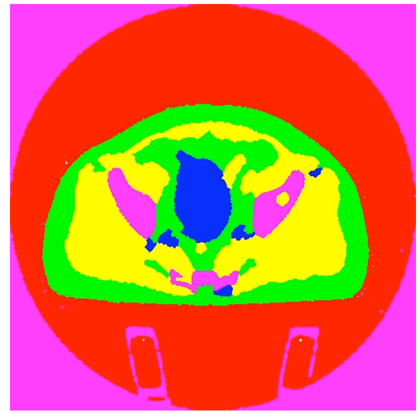
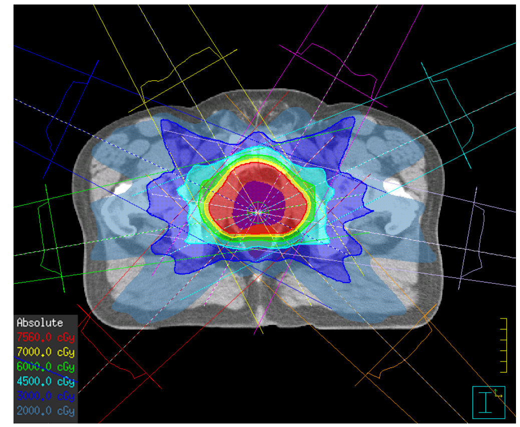
University of Texas at Austin

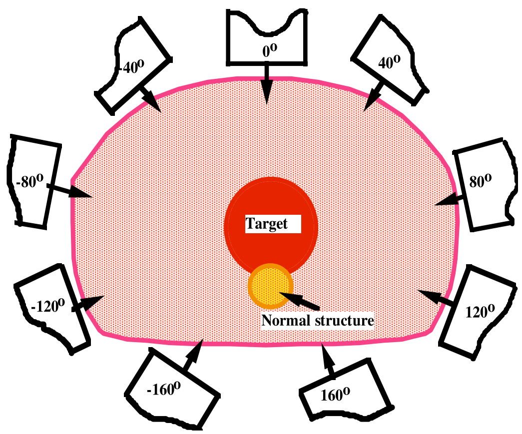
August 2008

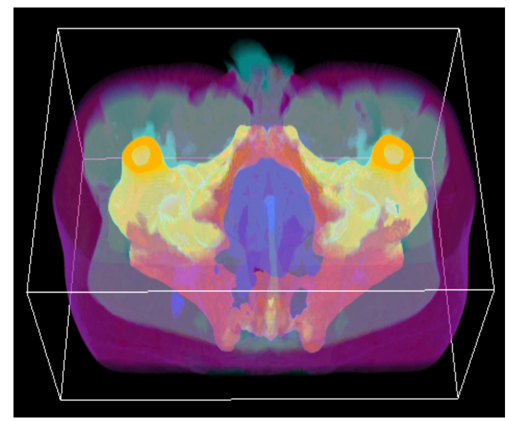
4DRT: Radiation Treatment Planning



CT/MRI → Anisotropic and Vector Diffusion Filtering → Classification & Segmentation → Radiation Dosage Estimation → Treatment Plan → 4DRT (mapping)





(Collaborators: Dr. Radhe Mohan, Dr. Lei Dong, Dr. John Hazle : MD Anderson Cancer Center)

**Sponsored by NSF-DDDAS

Additional Reading

- The references given below include the ones cited in the lecture slides. Please check for pdf's of these references on university computers from http://cvcweb.ices.utexas.edu/cvc/papers/papers.php

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