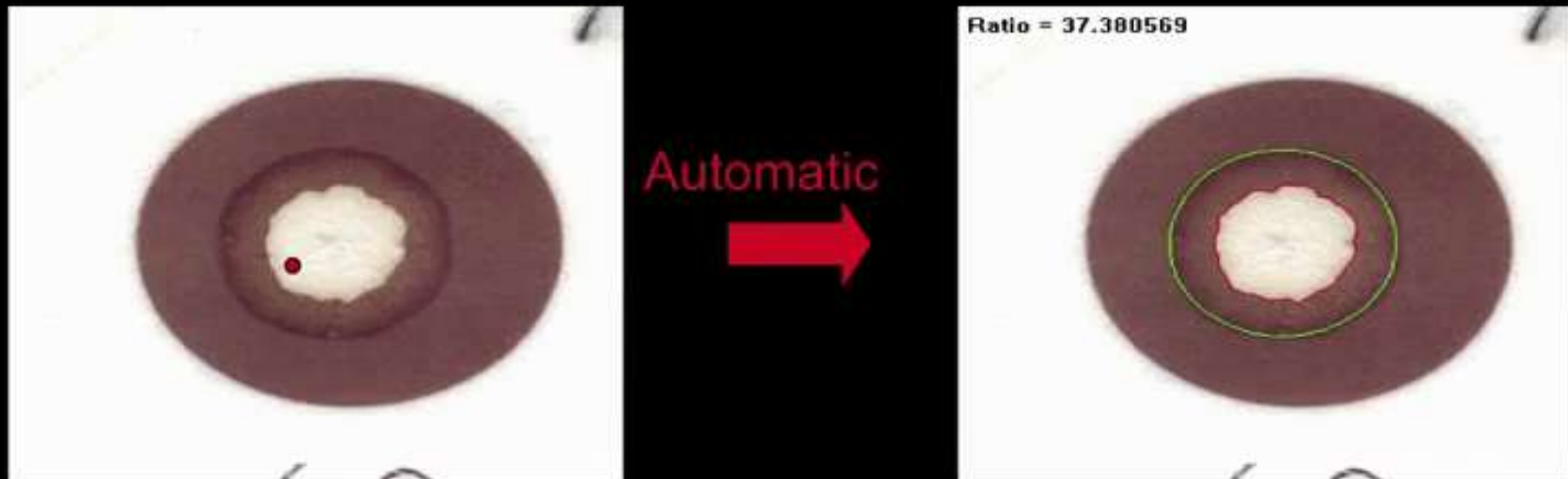


# Automatic skin lesion segmentation



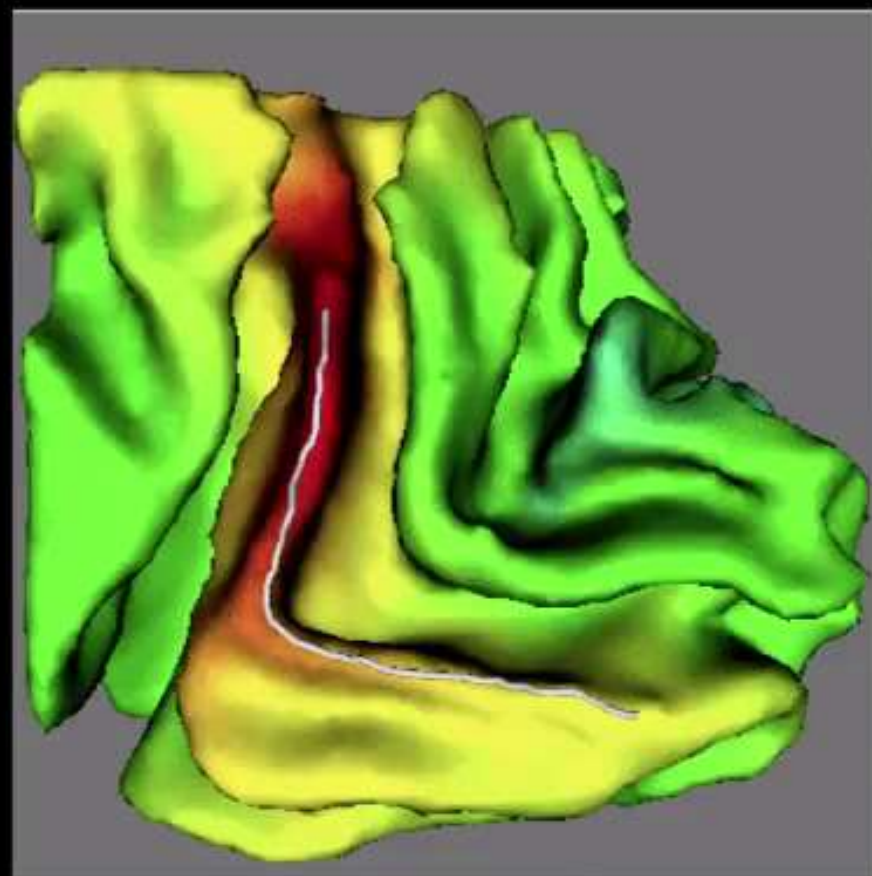
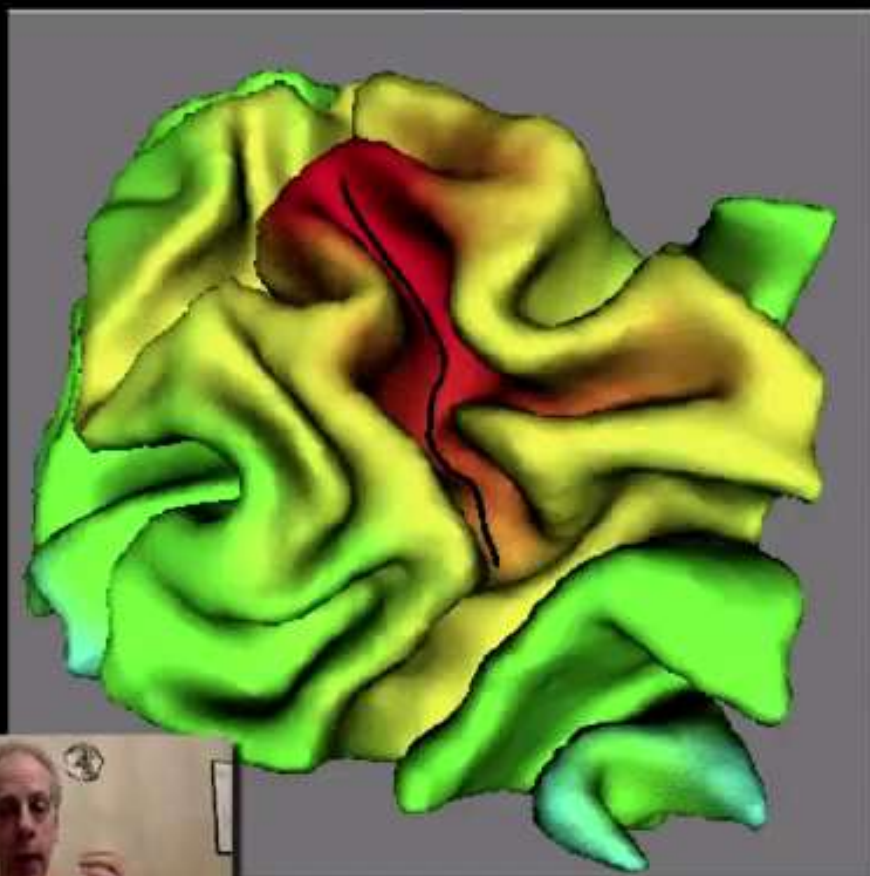
# A non-invasive test to aid in the diagnosis of cystic fibrosis: Automatic chloride patch/sensor analysis



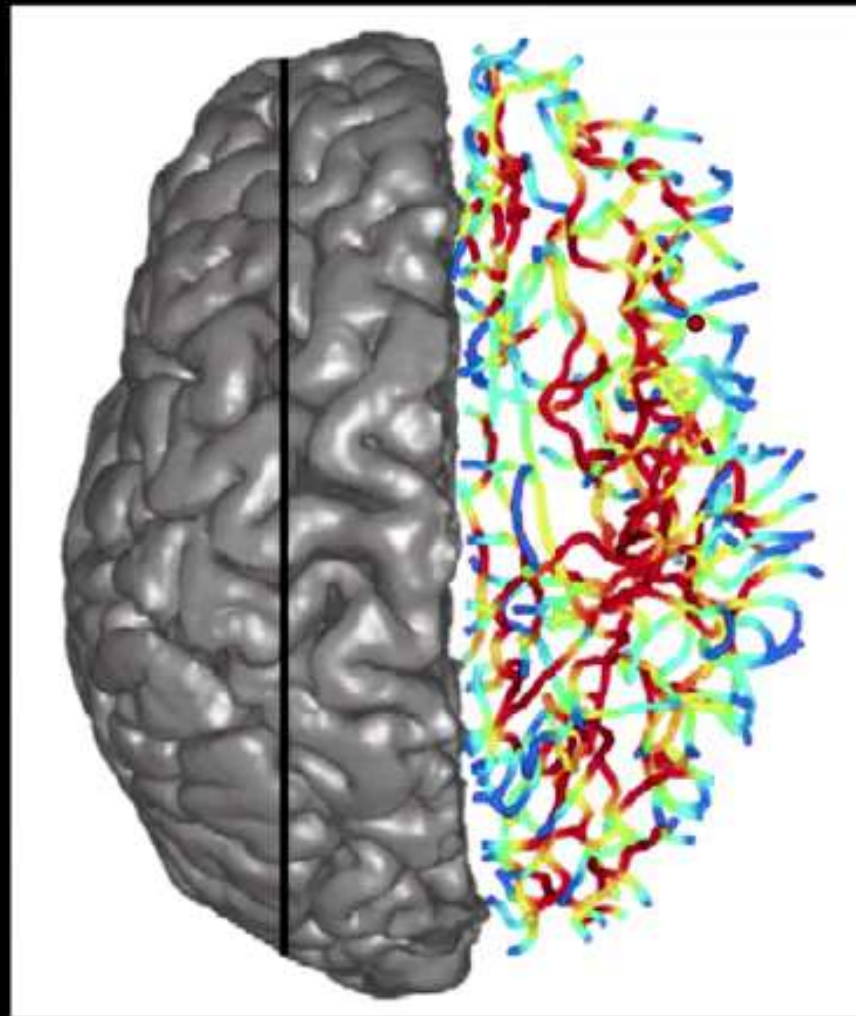
- Ratio between red and green areas is in correlation with chloride concentration, aiding in the diagnosis of CF
- Courtesy of PolyChrome and Warren Warwick



# Sulci extraction







# Image Registration, Classification and Averaging in Cryo-Electron Tomography

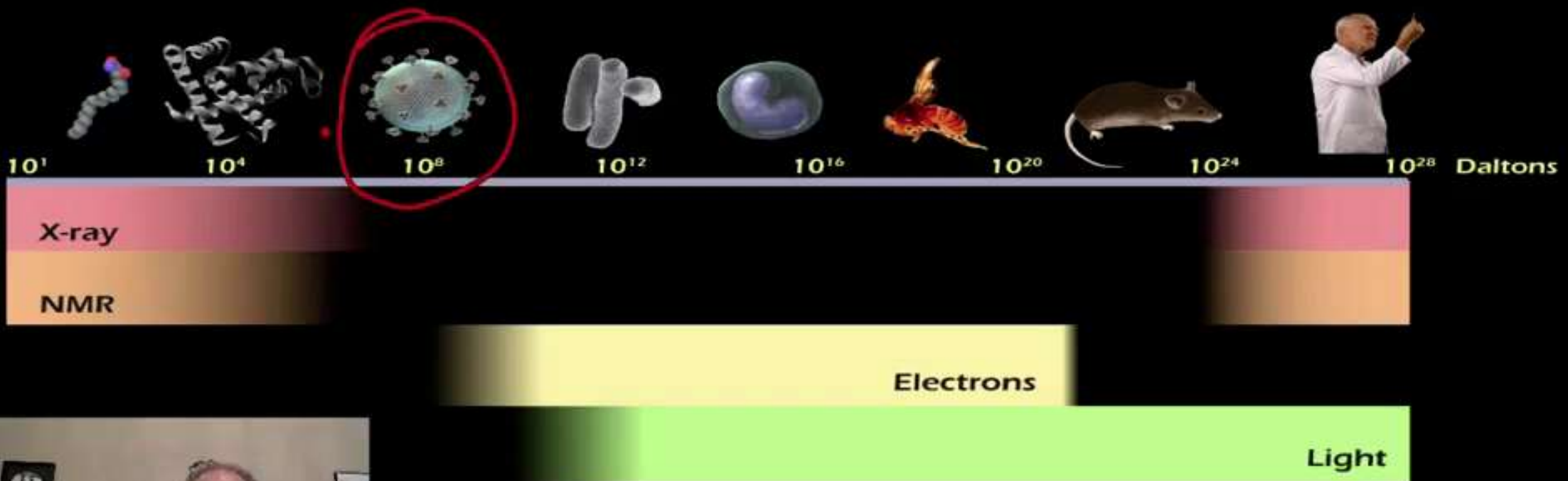
**Thanks to Alberto Bartesaghi and Sriram Subramaniam**

Laboratory of Cell Biology

Center for Cancer Research

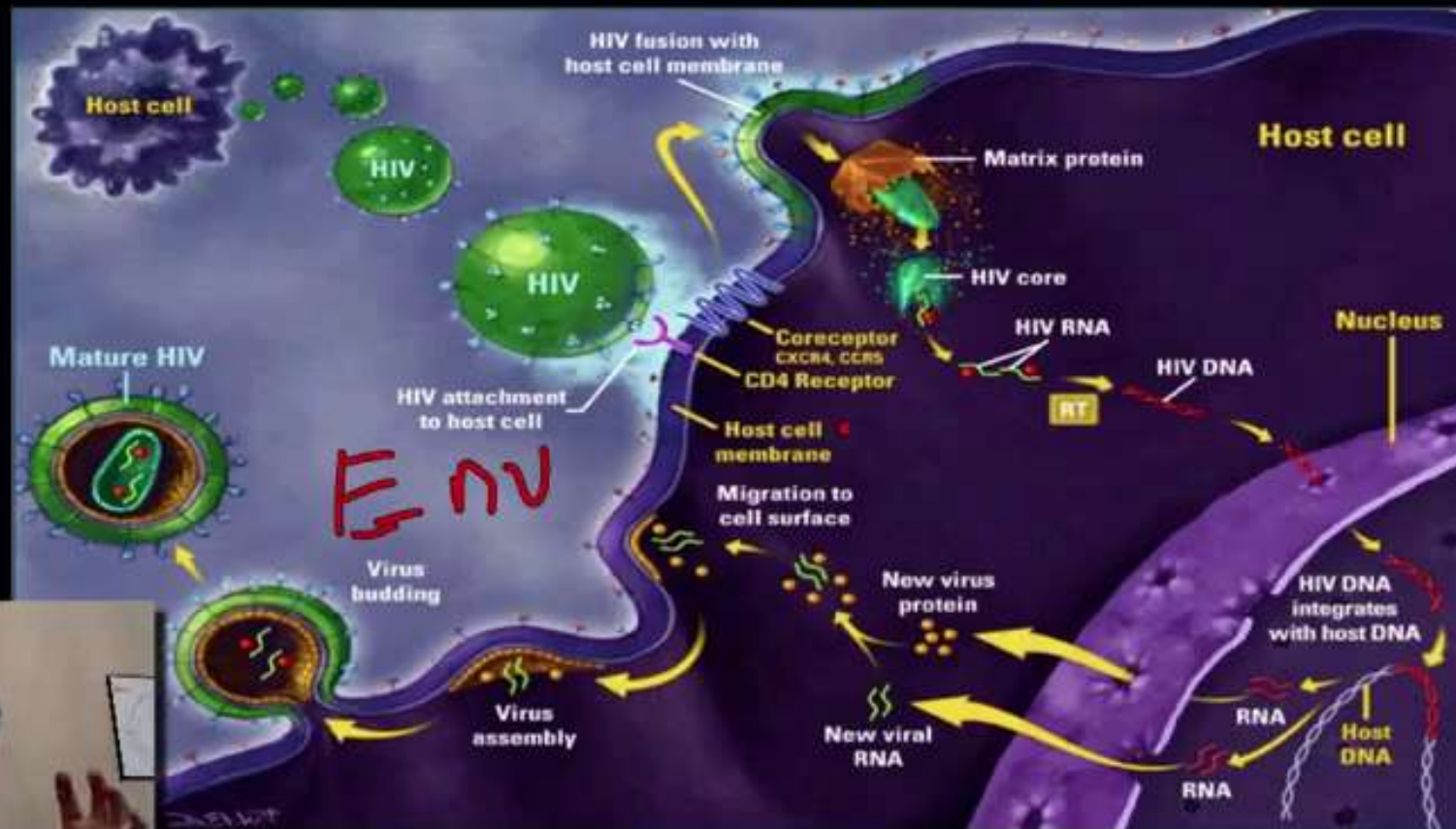


# Imaging technologies for biology



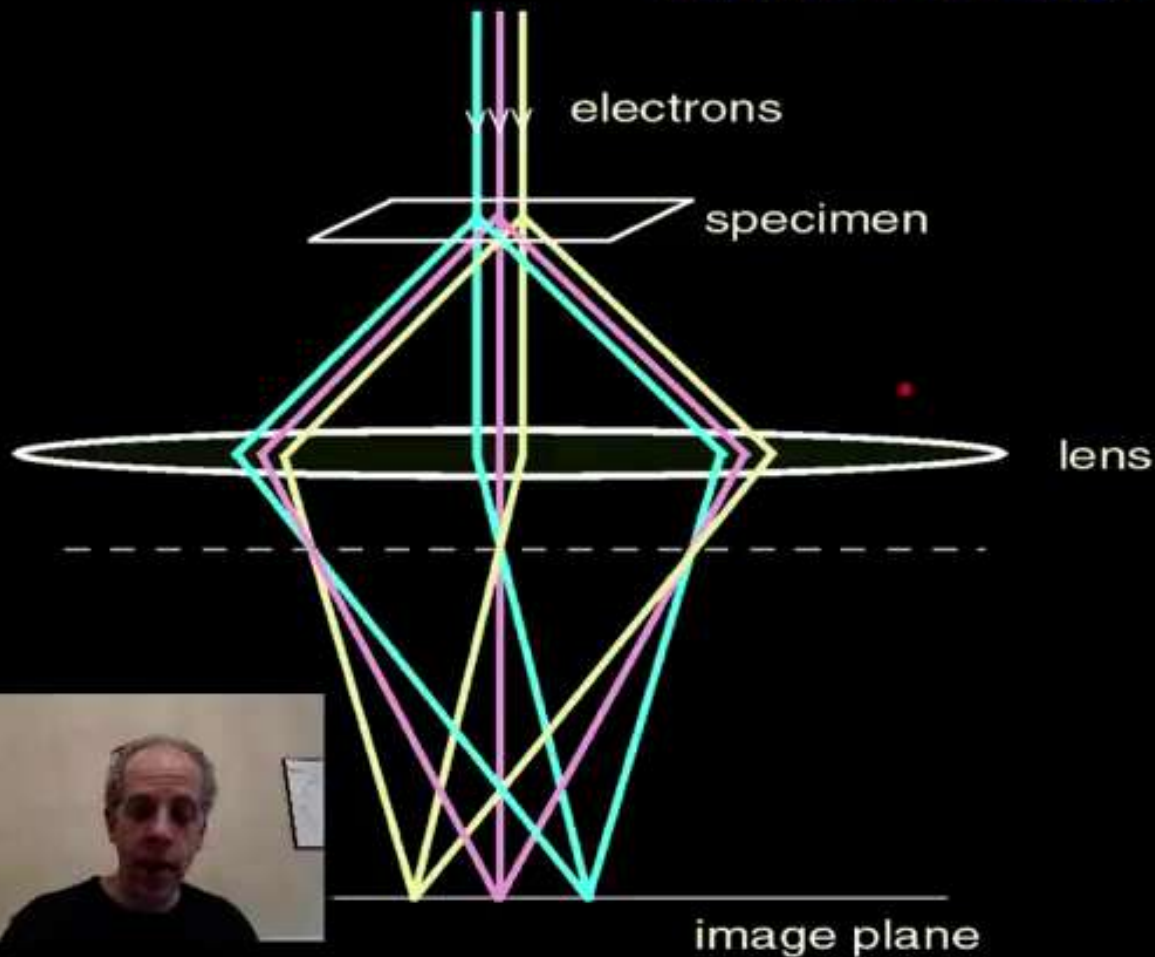
*S. Subramaniam, Curr. Opin. Microbiol. (2005)*

# Our Target: Molecular structure of HIV envelope glycoproteins



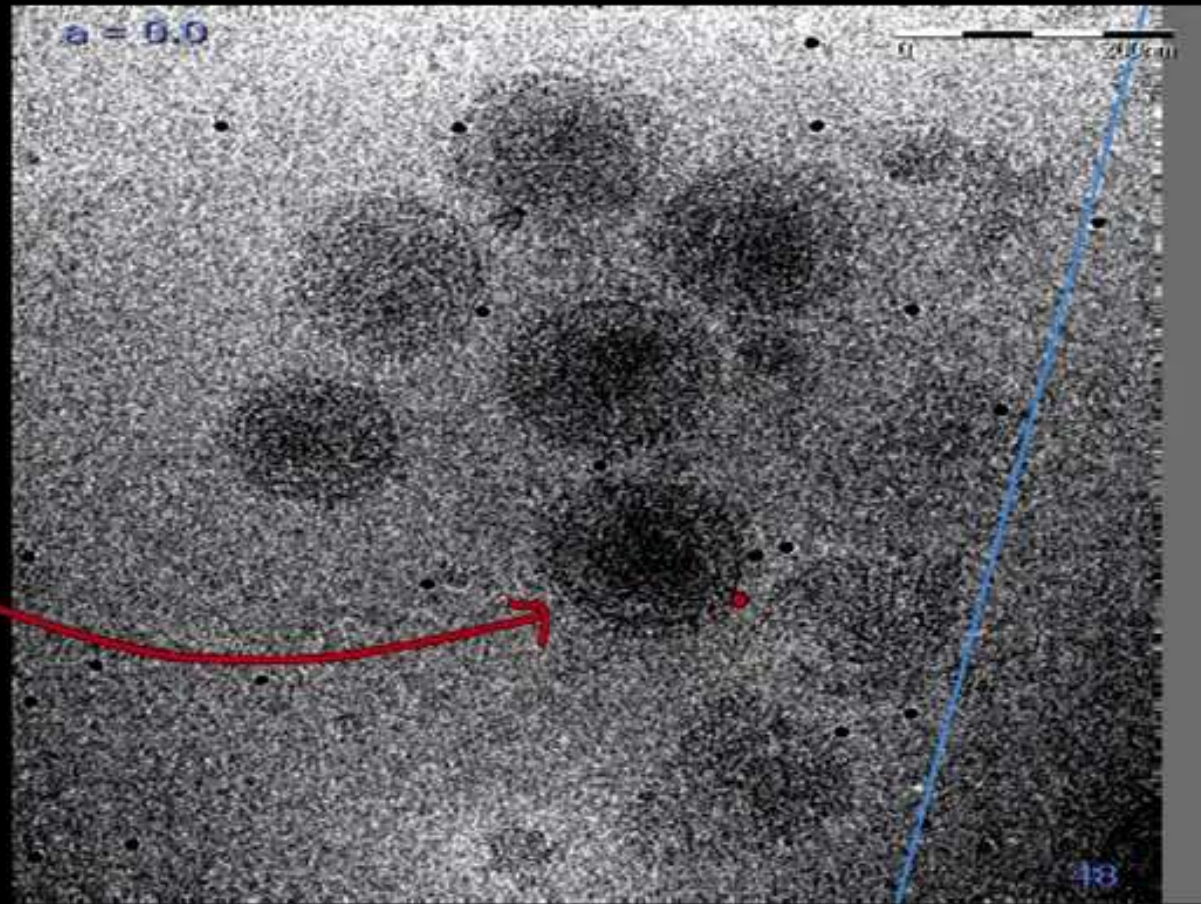


# Transmission Electron Microscopy



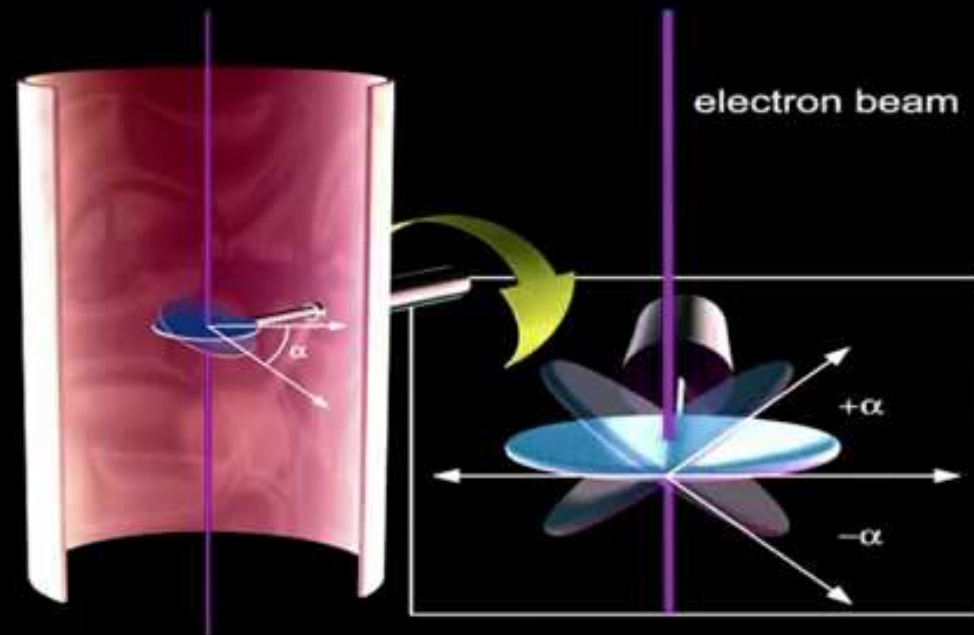


# Single Projection Image of HIV



# Cryo-Electron Tomography

- Reduce radiation damage
- Obtain 3D information



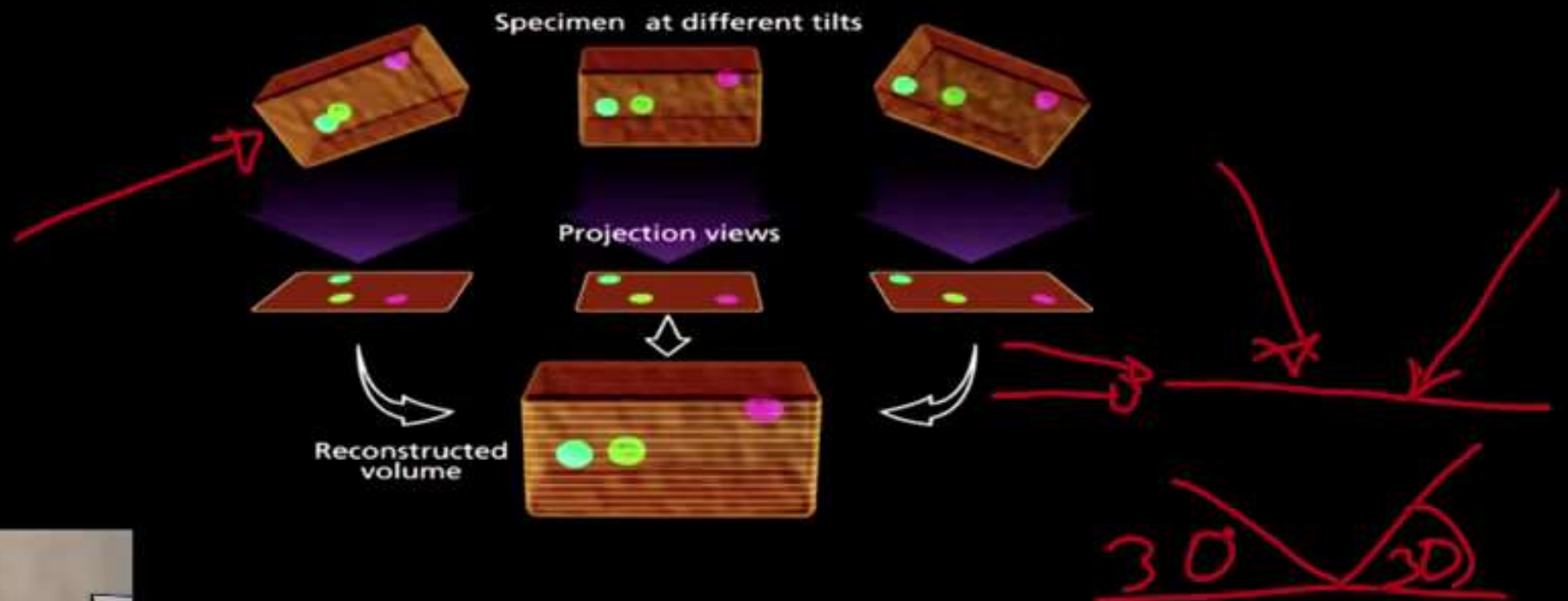


# Raw tilt-series of HIV

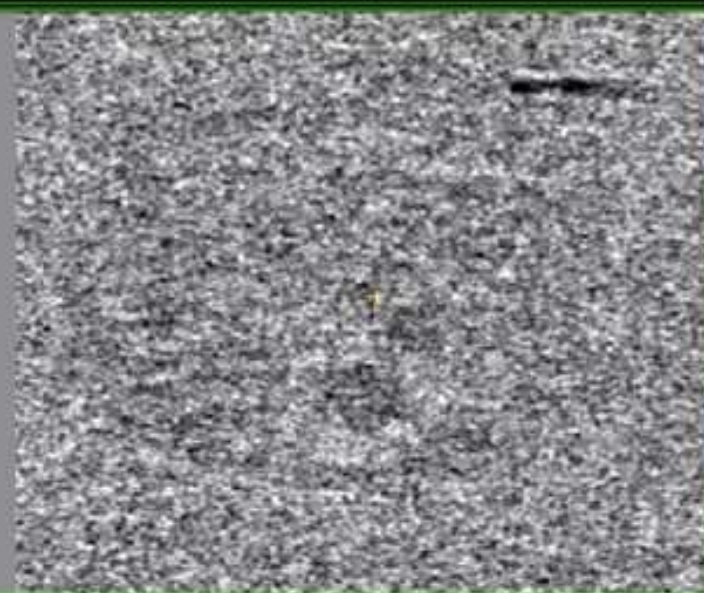
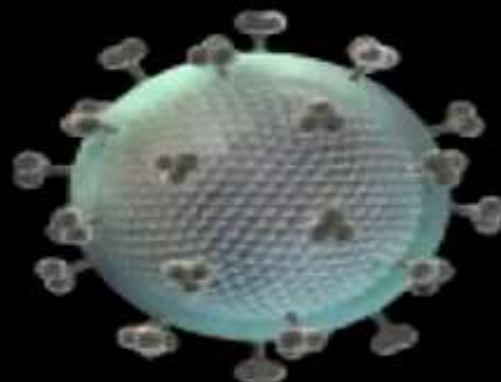




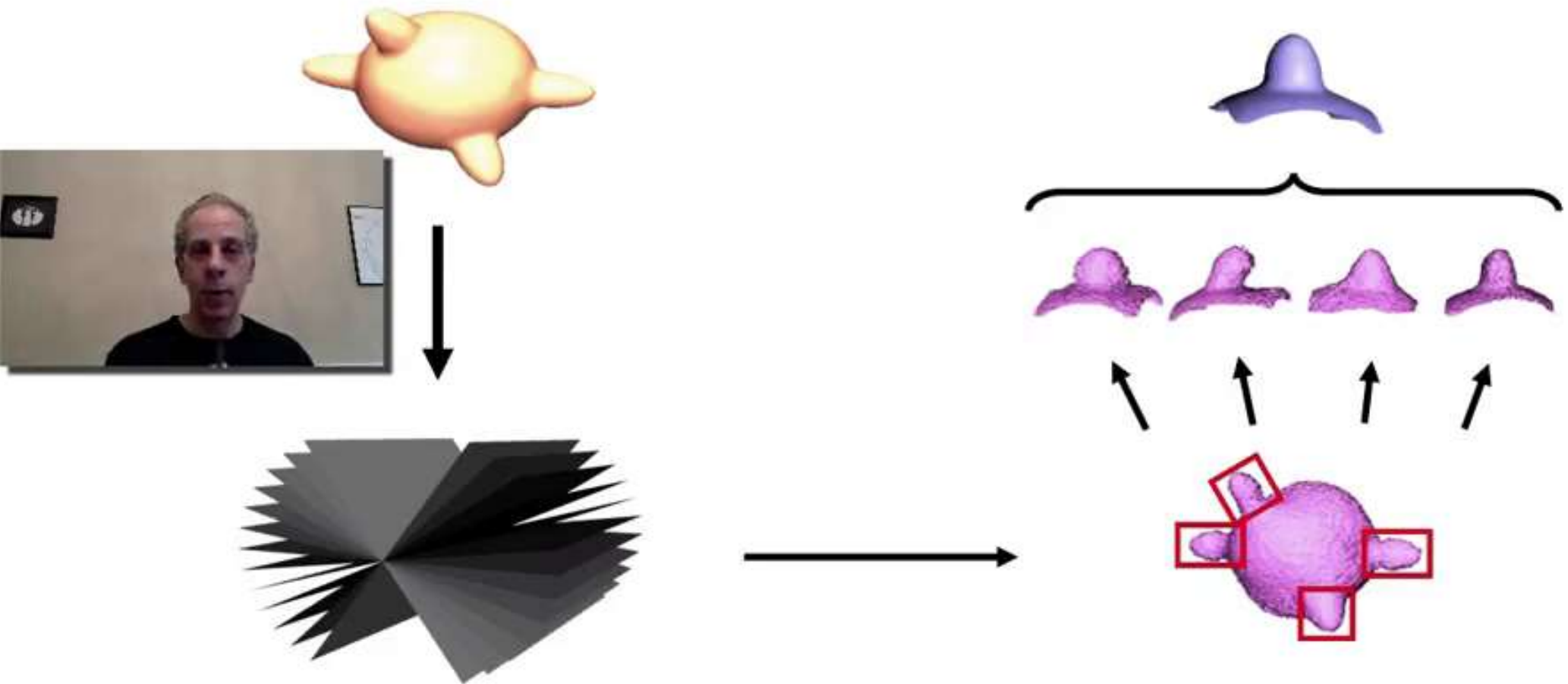
# Tomographic Reconstruction



Subramaniam et al., ASM News 60, 240-245.



# Sub-Volume Averaging in Electron Tomography





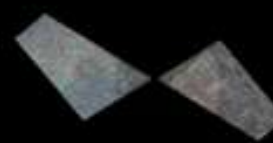
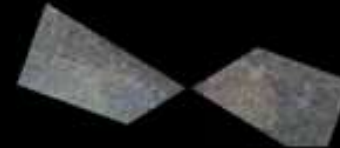
# Reconstitution From Noisy and Incomplete Images



# Reconstitution From Noisy and Incomplete Images

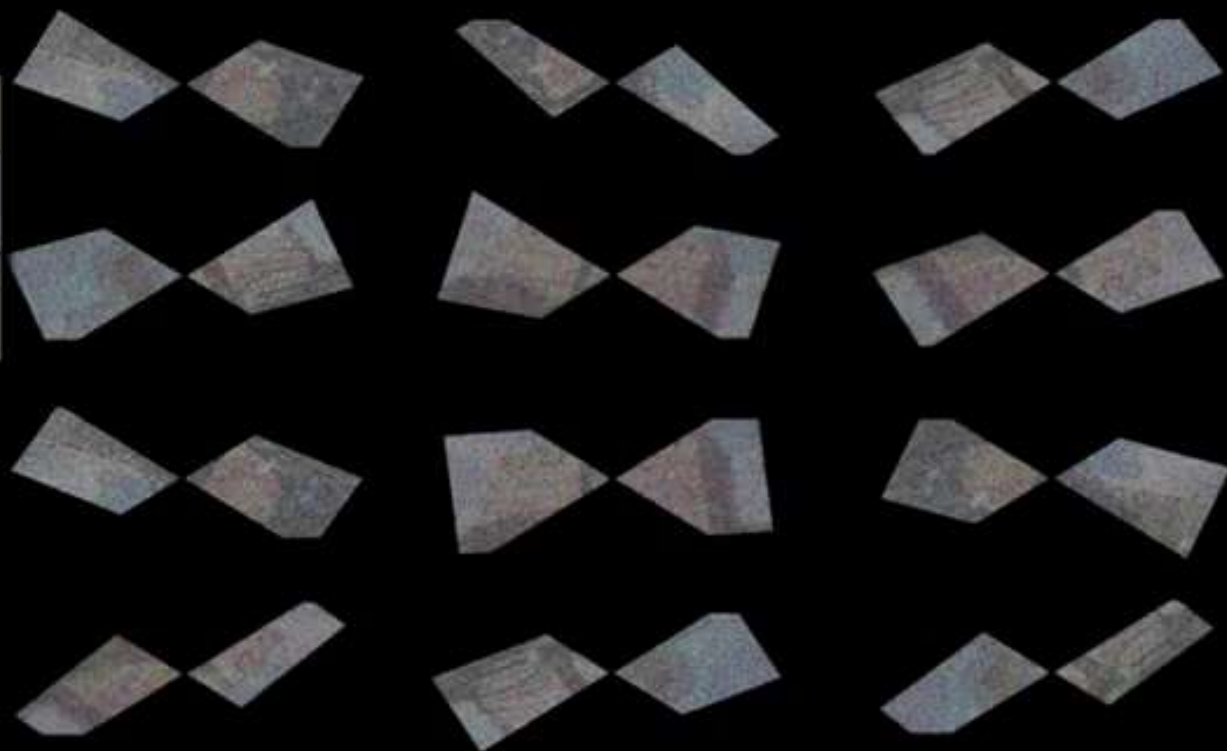


# Reconstitution From Noisy and Incomplete Images





# Reconstitution From Noisy and Incomplete Images



# Imaging Challenges of Sub-Volume Averaging in ET

- Low SNR makes alignment difficult
- Alignment ambiguities due to missing data
- 3D datasets require extensive computation



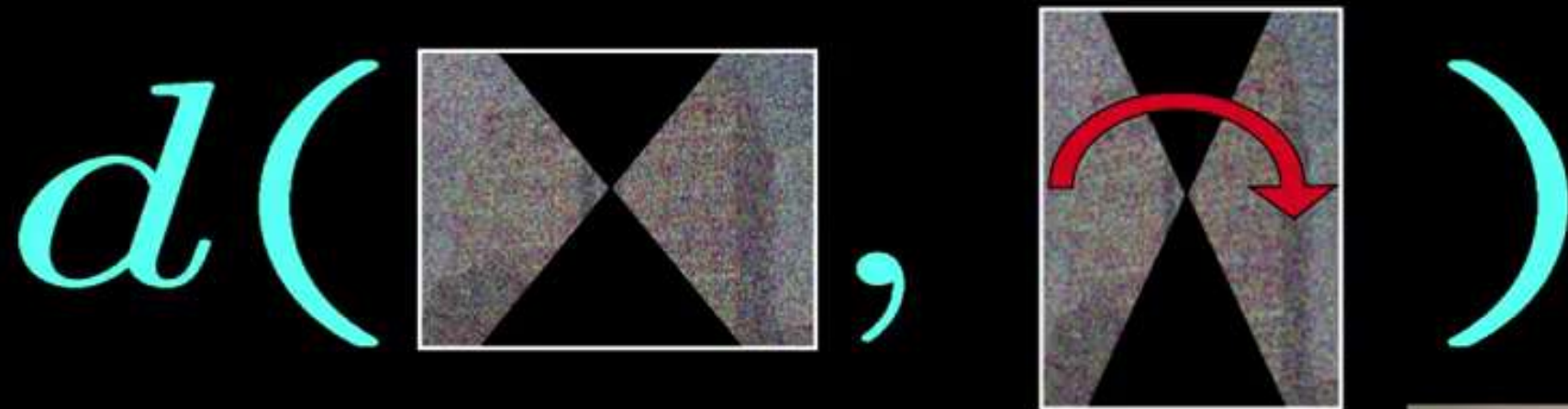
# Effects of Missing Data on Alignment

$$d(\text{[Image]}, \text{[Image]})$$

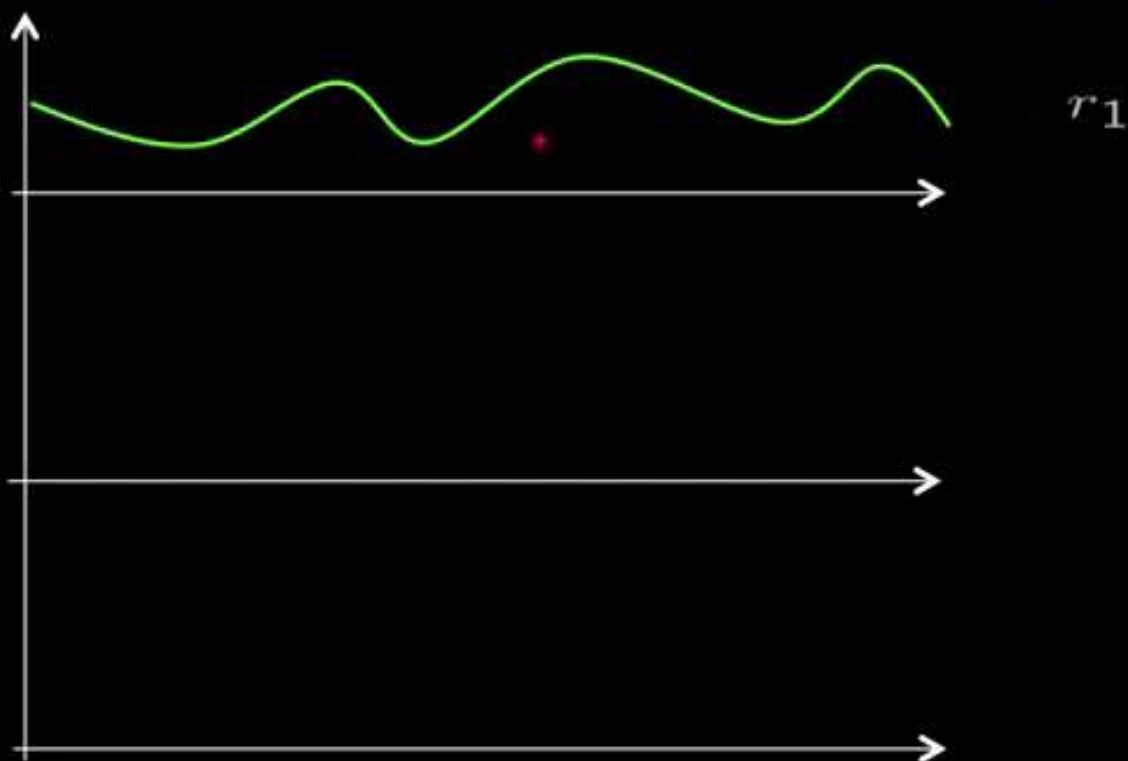




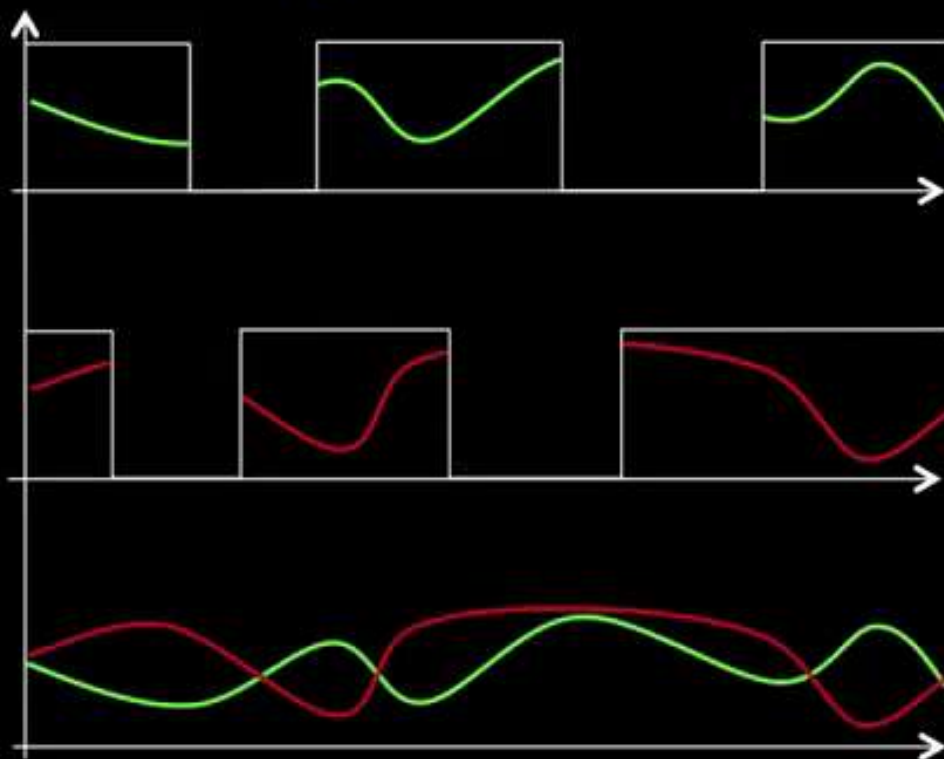
# Effects of Missing Data on Alignment



# Similarity with Missing Information



# Similarity with Missing Information



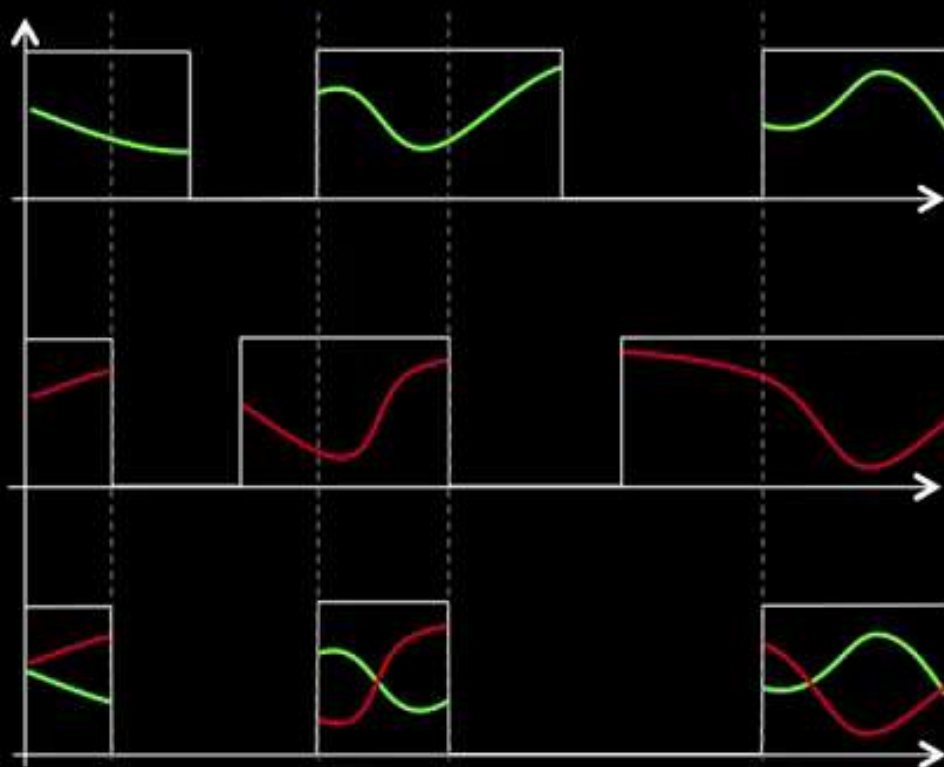
$$r_1 \cdot w_1$$

$$r_2 \cdot w_2$$





# Similarity with Missing Information



$$r_1 \cdot w_1$$

$$r_2 \cdot w_2$$

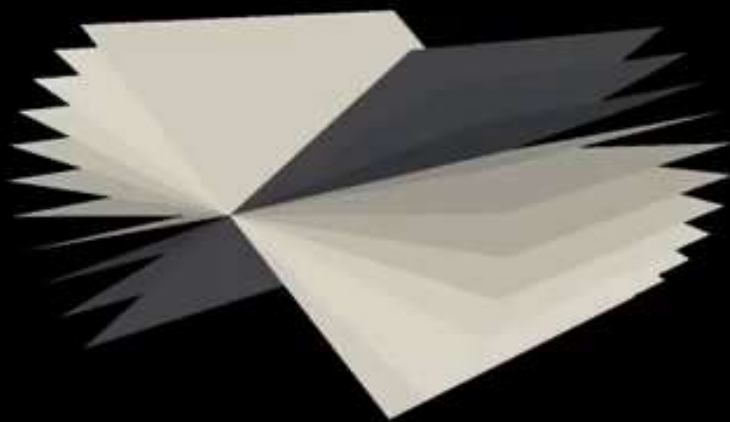
$$||r_1 - r_2|| \cdot w_1 \cdot w_2$$

$$d = \frac{\sum ||r_1 - r_2|| \cdot w_1 \cdot w_2}{\sum w_1 \cdot w_2}$$



# Similarity of partially occluded volumes in Fourier space

$$\hat{\mathcal{F}}_1 = \mathcal{F}_1 \mathcal{W}_1, \quad \hat{\mathcal{F}}_2 = \mathcal{F}_2 \mathcal{W}_2, \quad \mathcal{W}_i \rightarrow [0, 1]$$



■ Missing Wedge  
■ Measured Data

$$d = \frac{\int_{\mathcal{B}} ||\hat{\mathcal{F}}_1 - \hat{\mathcal{F}}_2|| \mathcal{W}_1 \mathcal{W}_2}{\int_{\mathcal{B}} \mathcal{W}_1 \mathcal{W}_2}$$



# Image Optimization Strategy

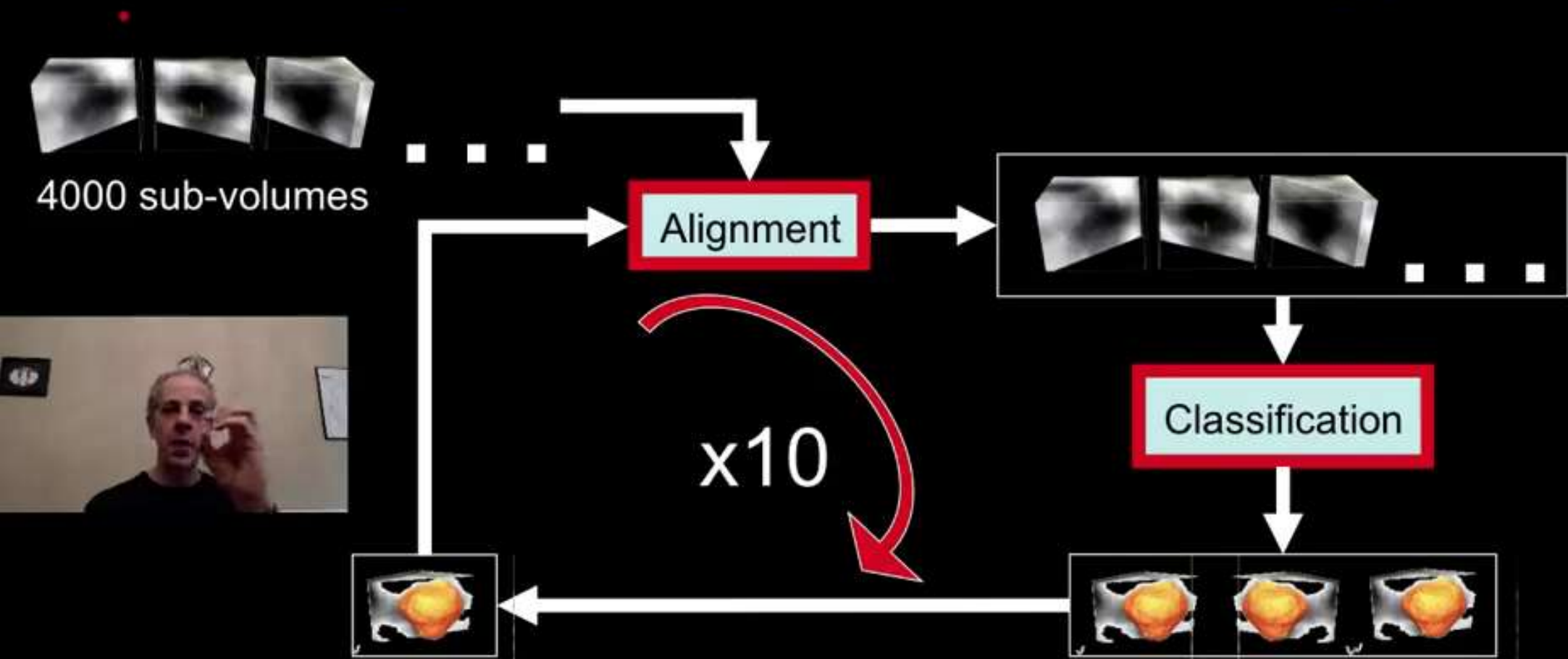


4000 sub-volumes





# Image Optimization Strategy



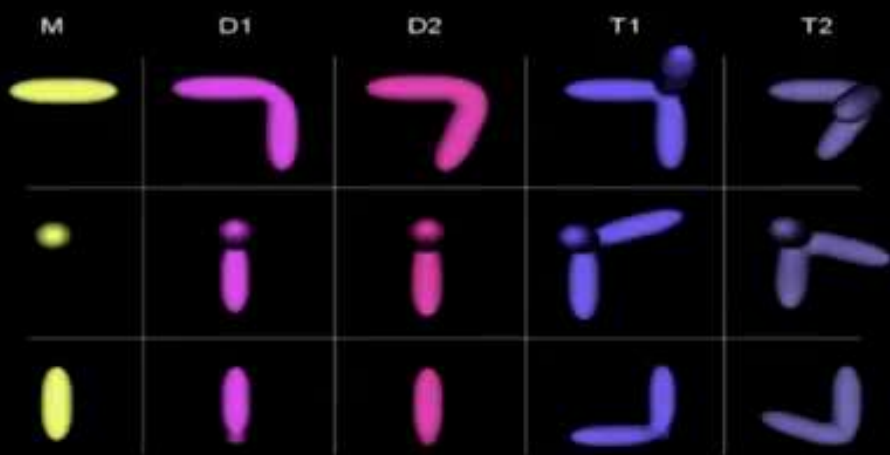
# 3D Image Alignment



$$\min_{\theta, \phi, \psi, \vec{t}} d(\text{img}_1, \text{img}_2)$$

The diagram illustrates the 6 degrees of freedom (DOF) for 3D image alignment. It shows two 3D volumes, each composed of blue, red, and gray planes. The first volume is on the left, and the second is on the right. The second volume is rotated relative to the first. The rotation is defined by three angles:  $\theta$  (roll),  $\phi$  (pitch), and  $\psi$  (yaw). A translation vector  $\vec{t}$  is also indicated, representing the displacement between the two volumes.

- 6 DOF problem: Speed-up in Fourier domain

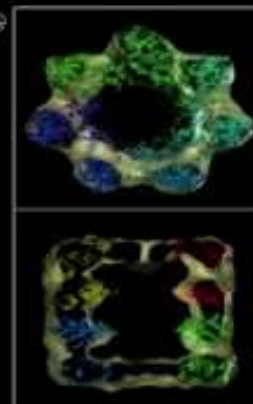
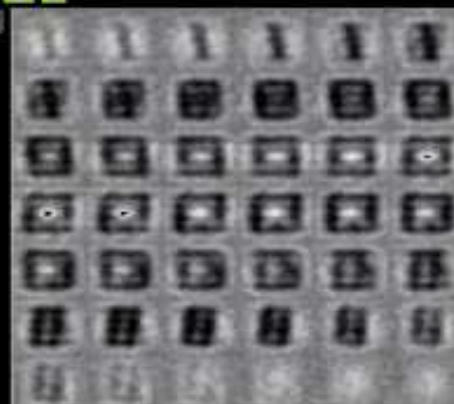
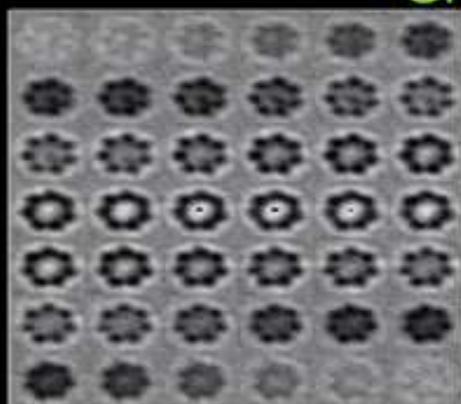


Phantoms

HIV



GroEL

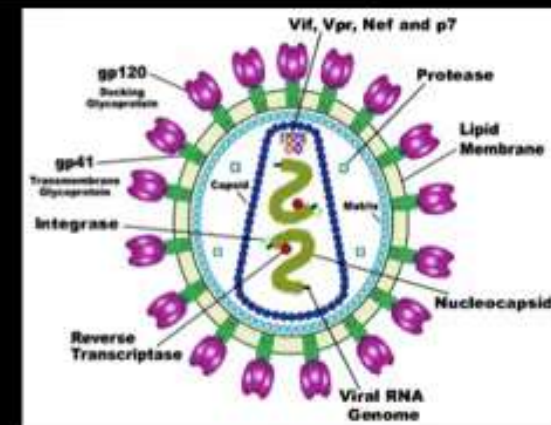
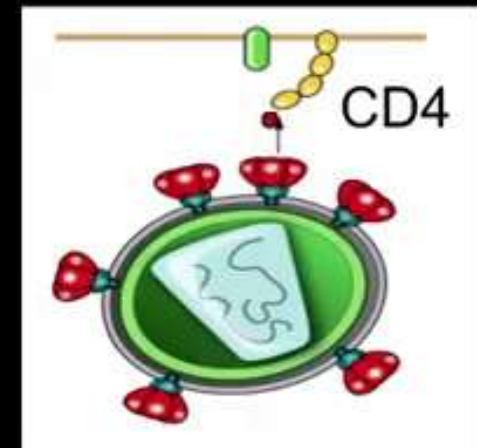






# HIV envelope glycoproteins

- Mediate virus binding to the cell surface receptor CD4 on target cells to initiate infection
- Functional unit is a trimer of **gp120** (surface glycoprotein) and **gp41** (transmembrane unit).
- Structure of components available.
- Structure of the trimer remains elusive.





## LETTERS

# Molecular architecture of native HIV-1 gp120 trimers

Jun Liu<sup>1\*</sup>, Alberto Bartesaghi<sup>1\*</sup>, Mario J. Borgnia<sup>1\*</sup>, Guillermo Sapiro<sup>2</sup> & Sriram Subramaniam<sup>1</sup>

<sup>1</sup>Laboratory of Cell Biology, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, Maryland 20892, USA. <sup>2</sup>Department of Electrical and Computer Engineering, University of Minnesota, Minneapolis, Minnesota 55455, USA.

\*These authors contributed equally to this work.

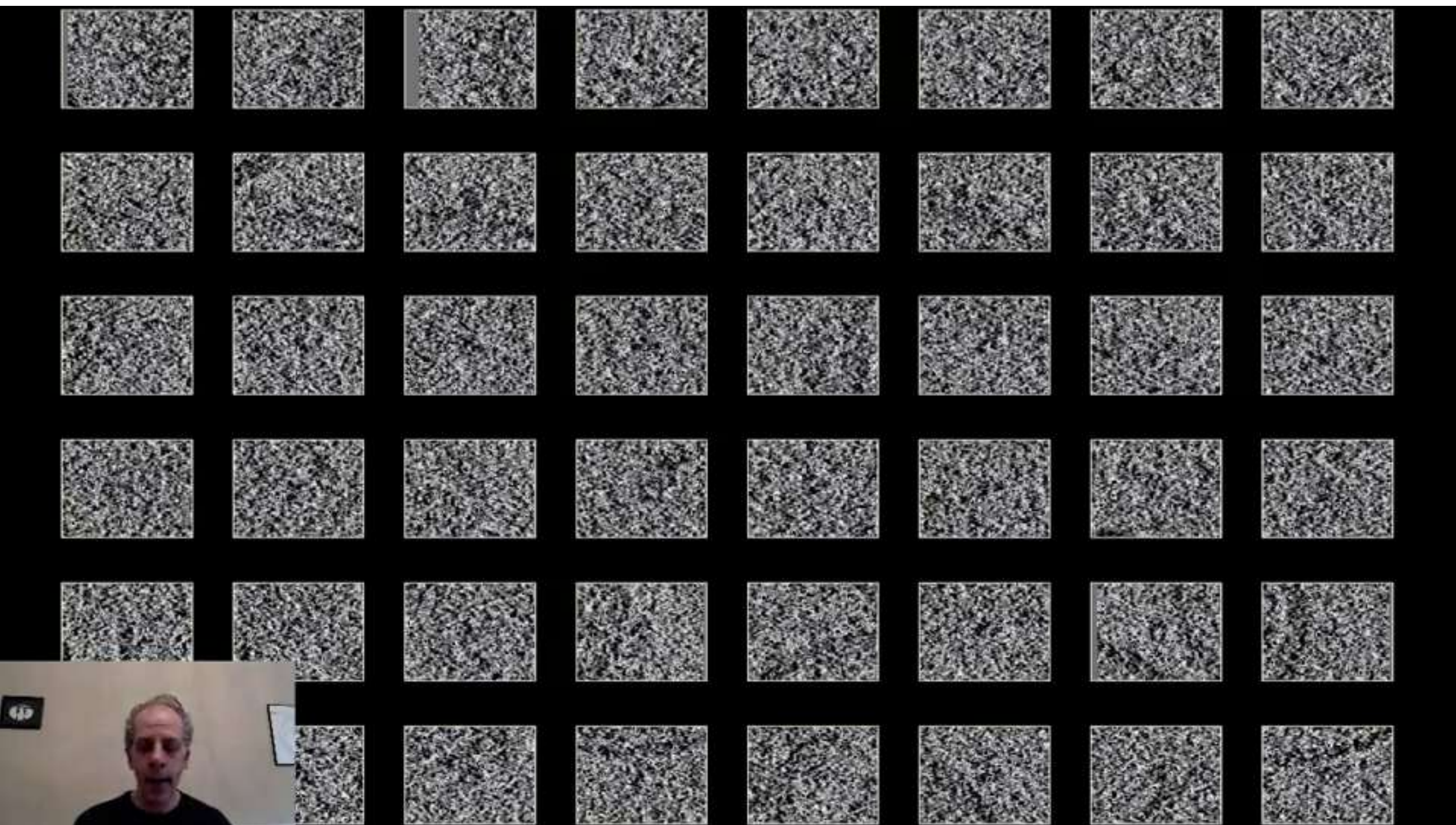
- Use cryo-electron tomography combined with 3D image averaging and classification
- Report 3D “snapshots” of trimeric spike:
  - Unliganded state
  - Complex with broadly neutralizing b12
  - Ternary complex with CD4 and 17b

# Imaging the spike at different states

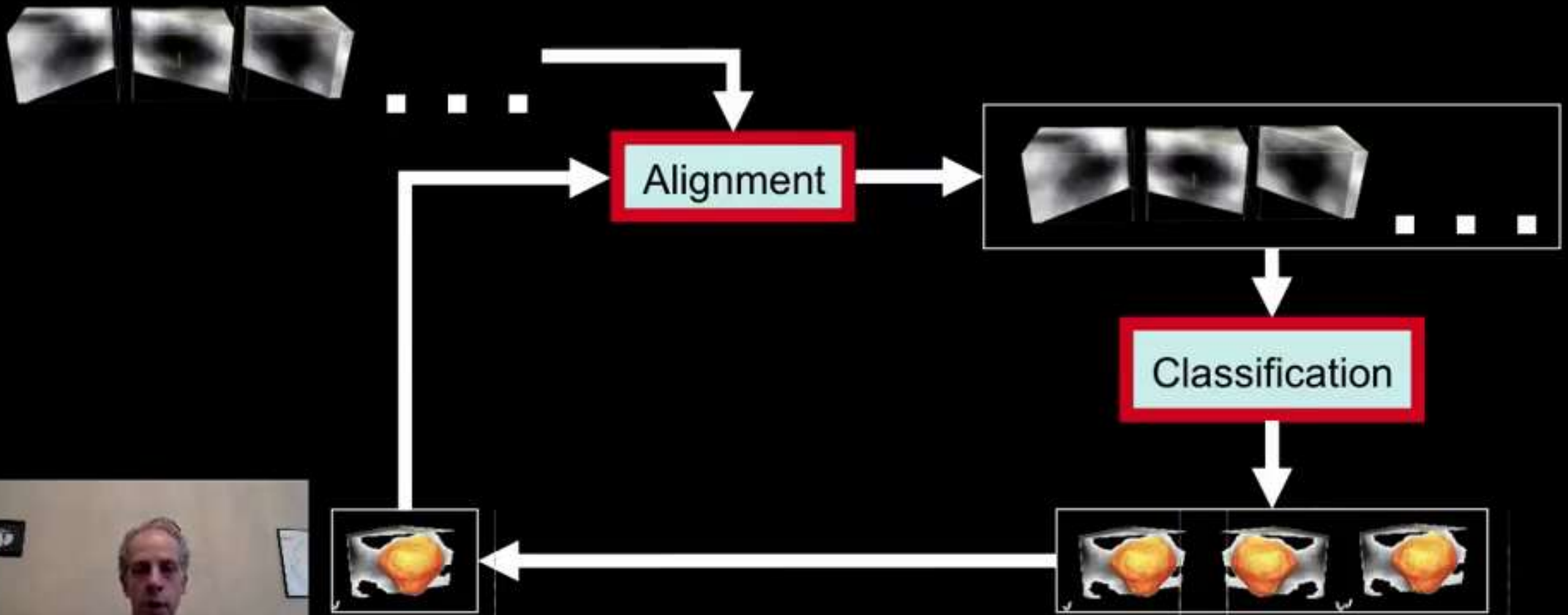
- 80 tilt series, 400 virus, 4K spikes
  1. Unliganded state
  2. Complex with b12
  3. Ternary complex with CD4 and 17b







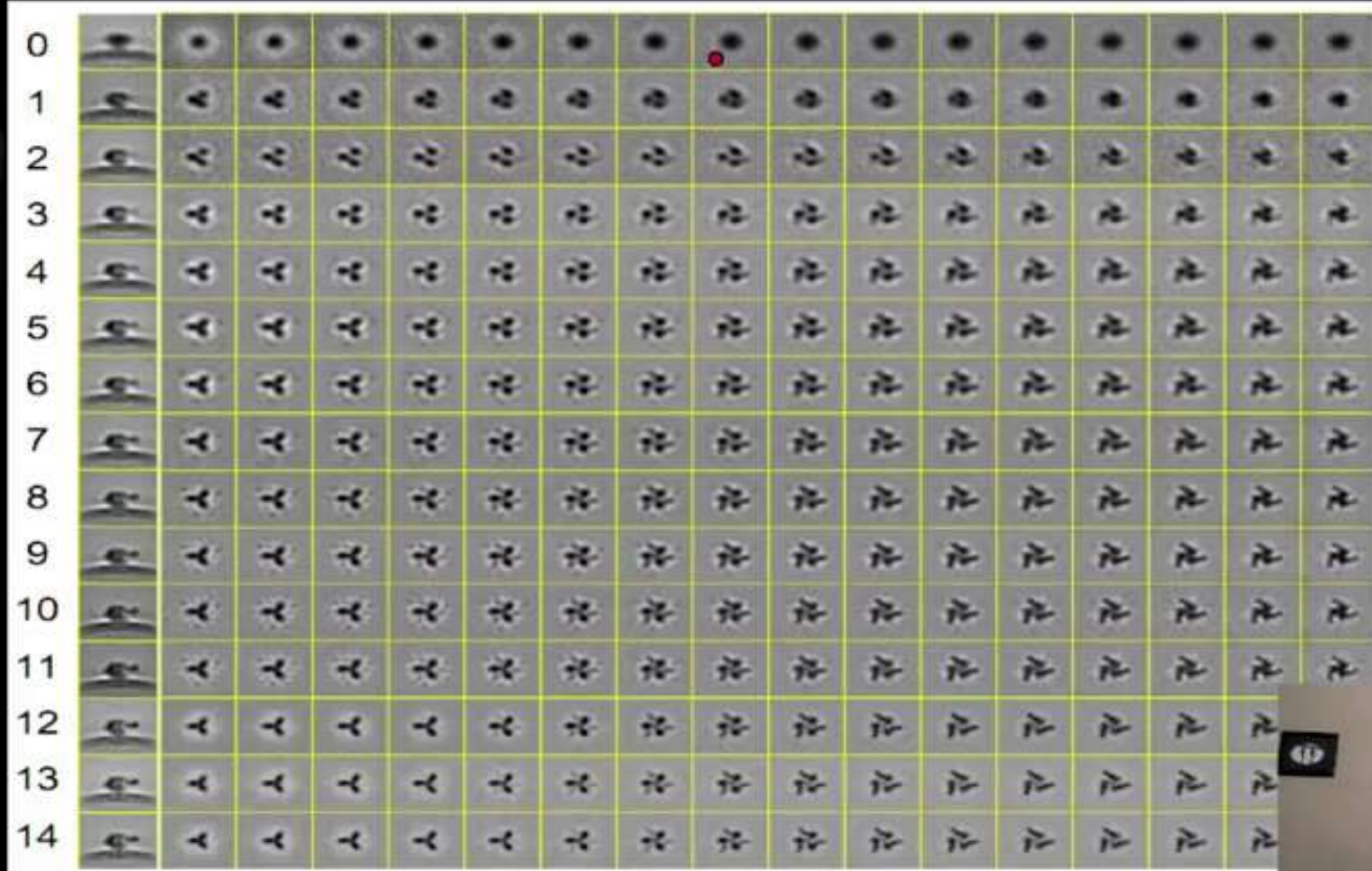
# Image Refinement Loop

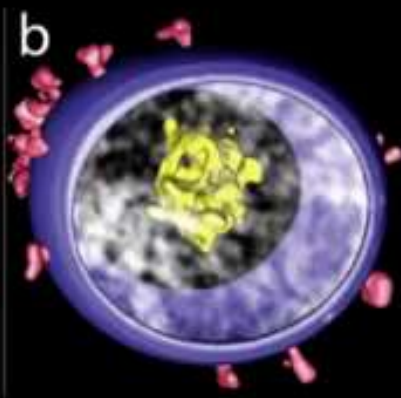
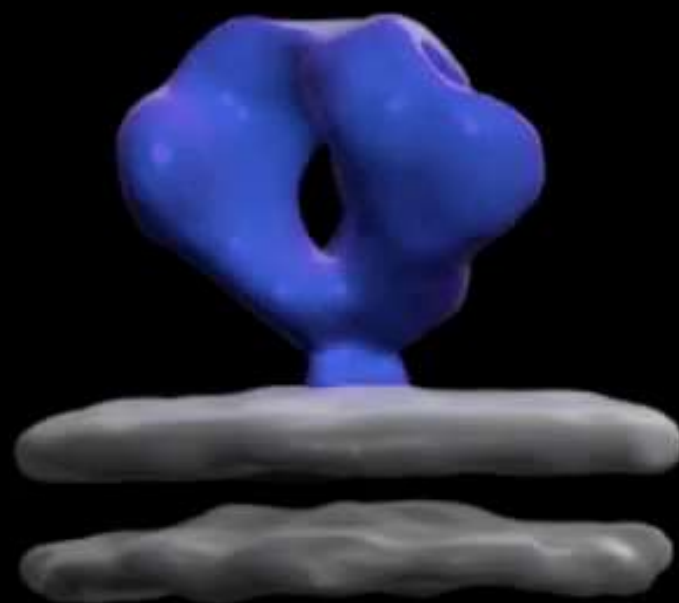
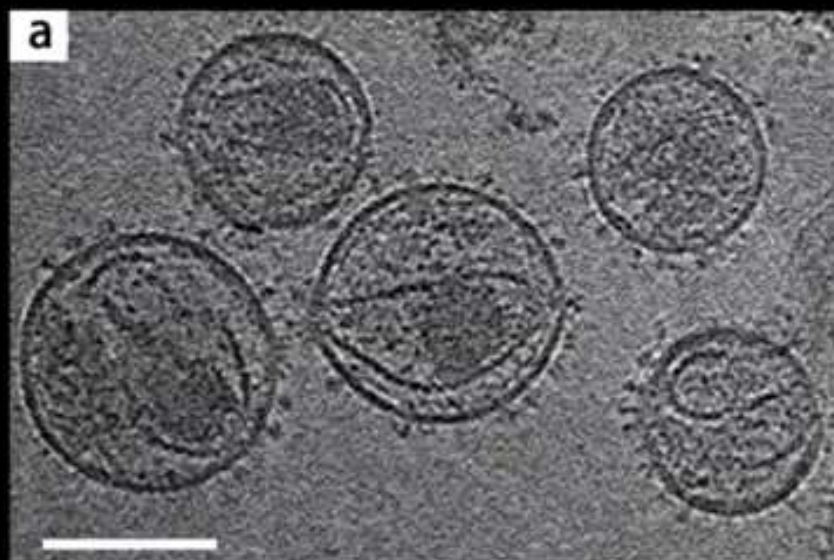




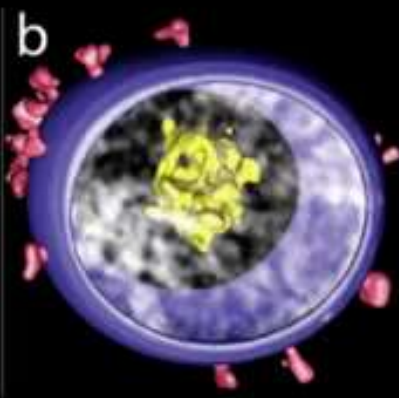
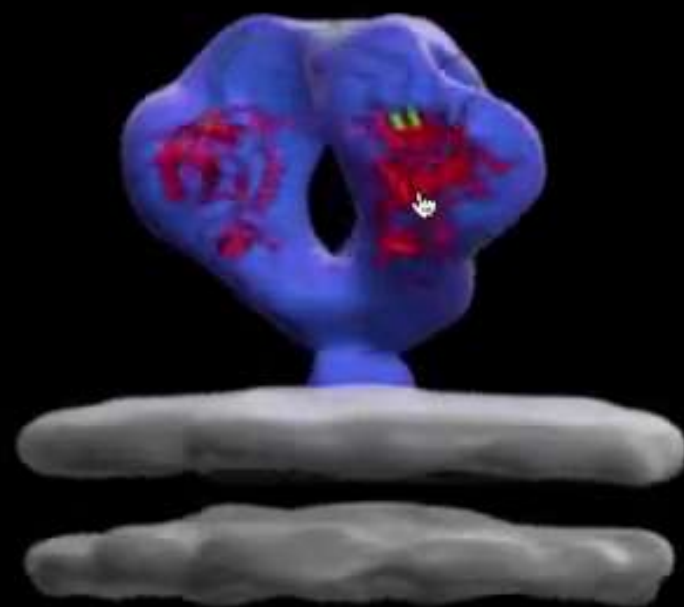
# Image Refinement Loop

Refinement Iterations



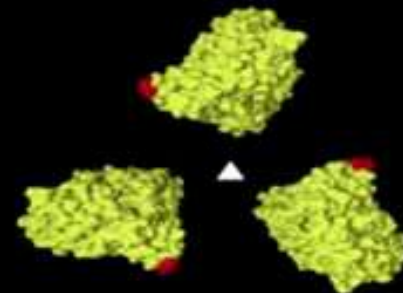
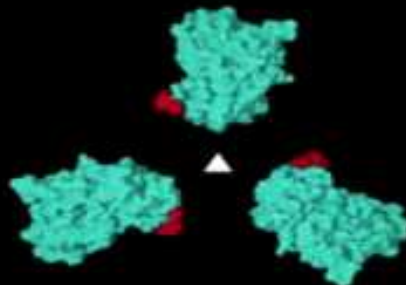
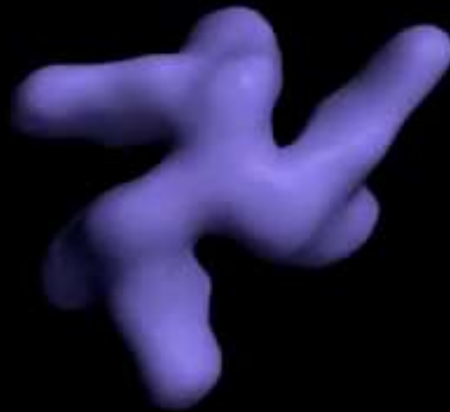








# Piecing it all together

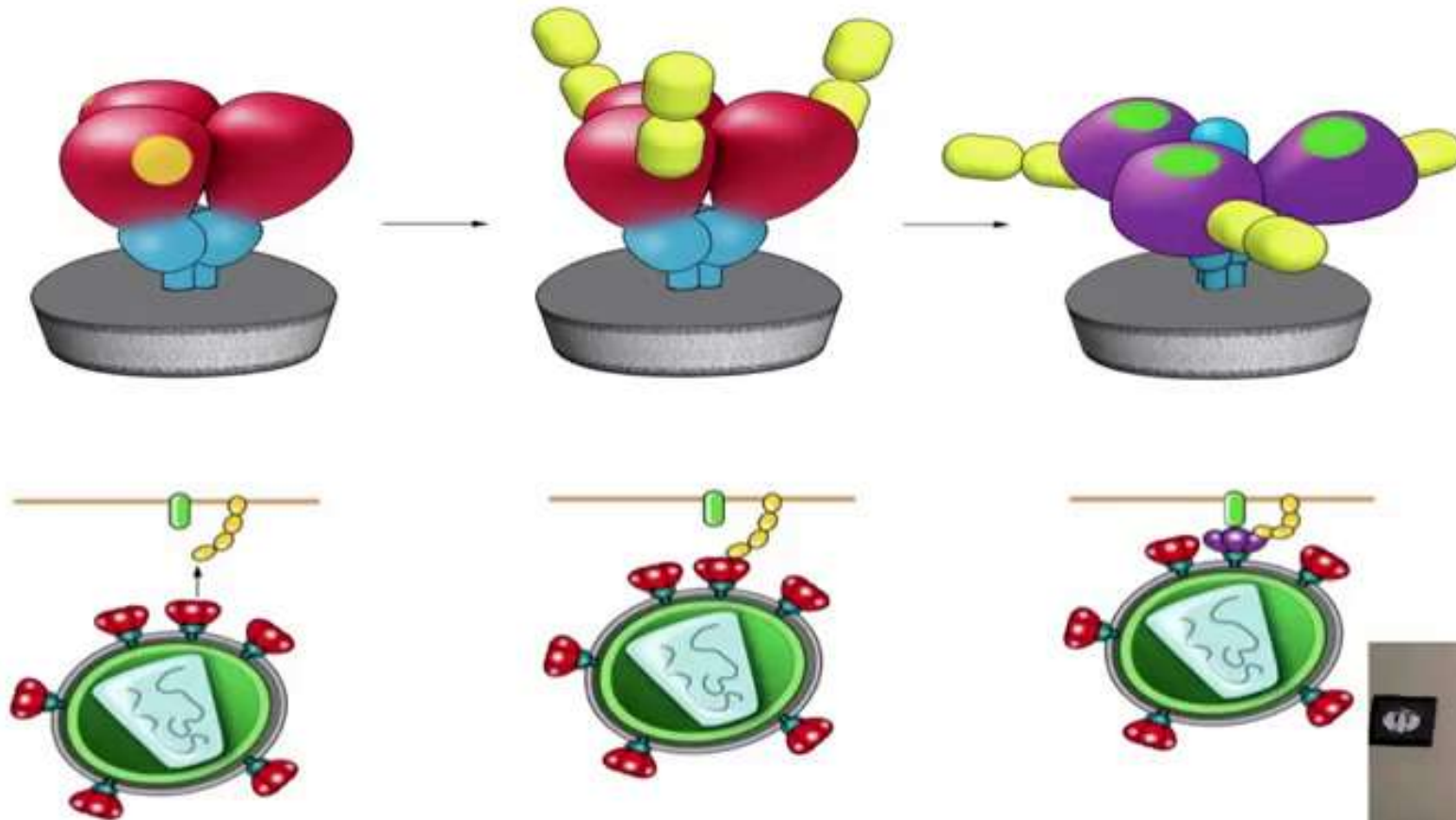


unliganded

b12-bound

CD4-bound

# Conformational changes of the trimeric spike that occur upon CD4 binding



# Diffusion-Weighted MRI

**Provides architecture of biological tissues**



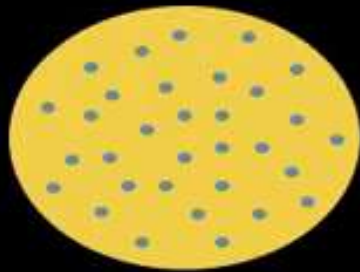
**Used to study:**

- **Neurological disorders**
- **Brain development**
- **Structure of brain fiber bundles**

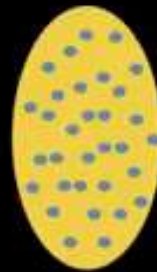




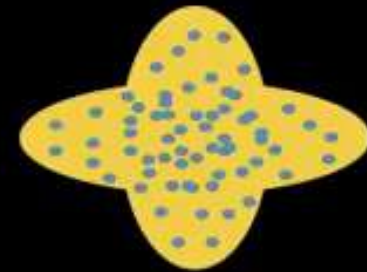
# Diffusion of Water Molecules



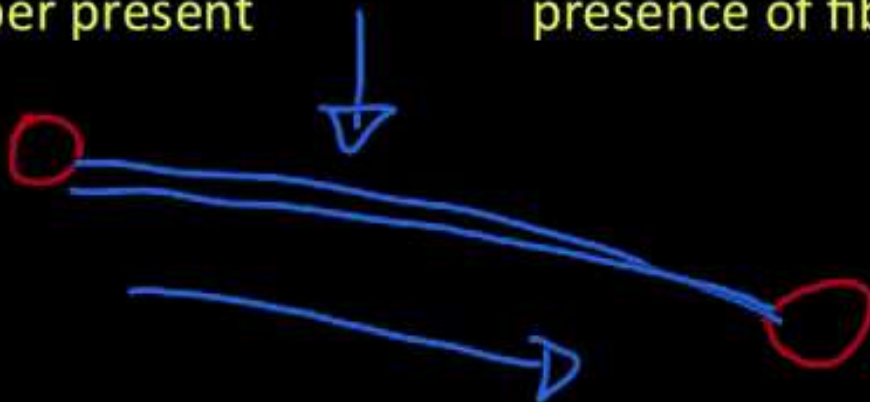
Isotropic Diffusion  
no fiber present



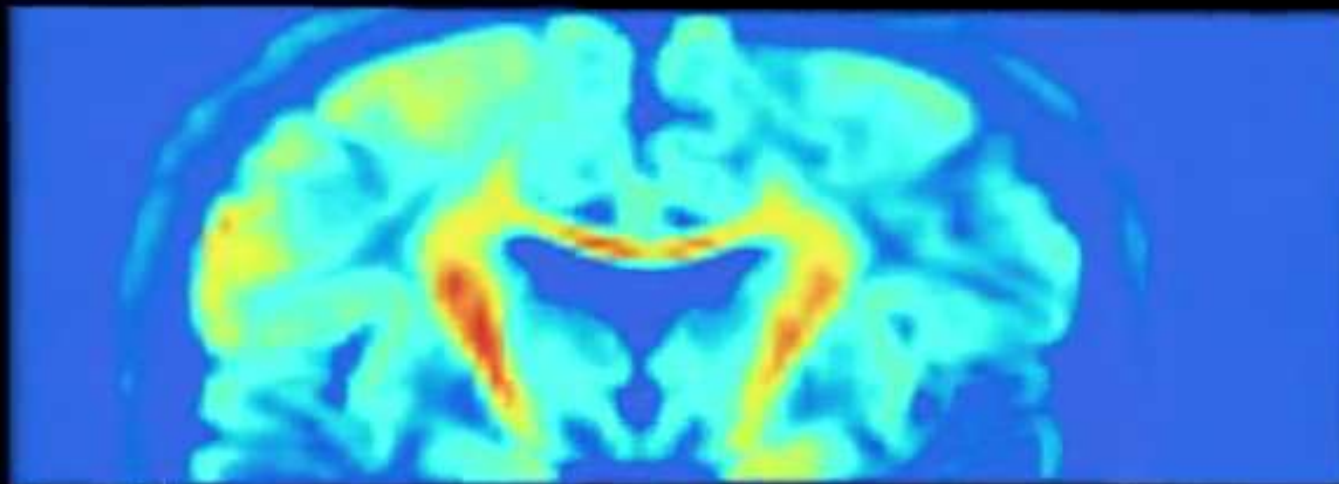
Anisotropic Diffusion  
presence of fiber



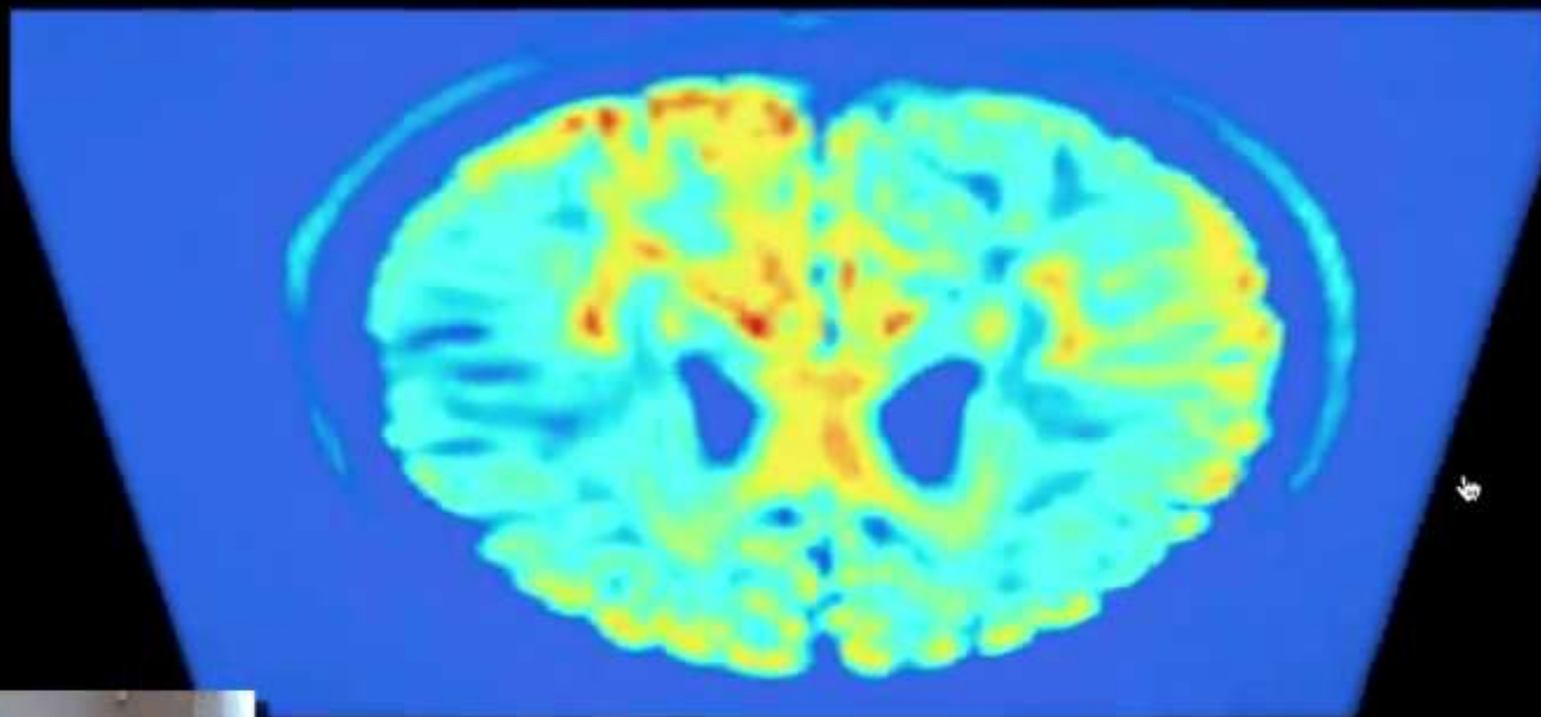
Orthogonal Diffusion  
fiber crossing



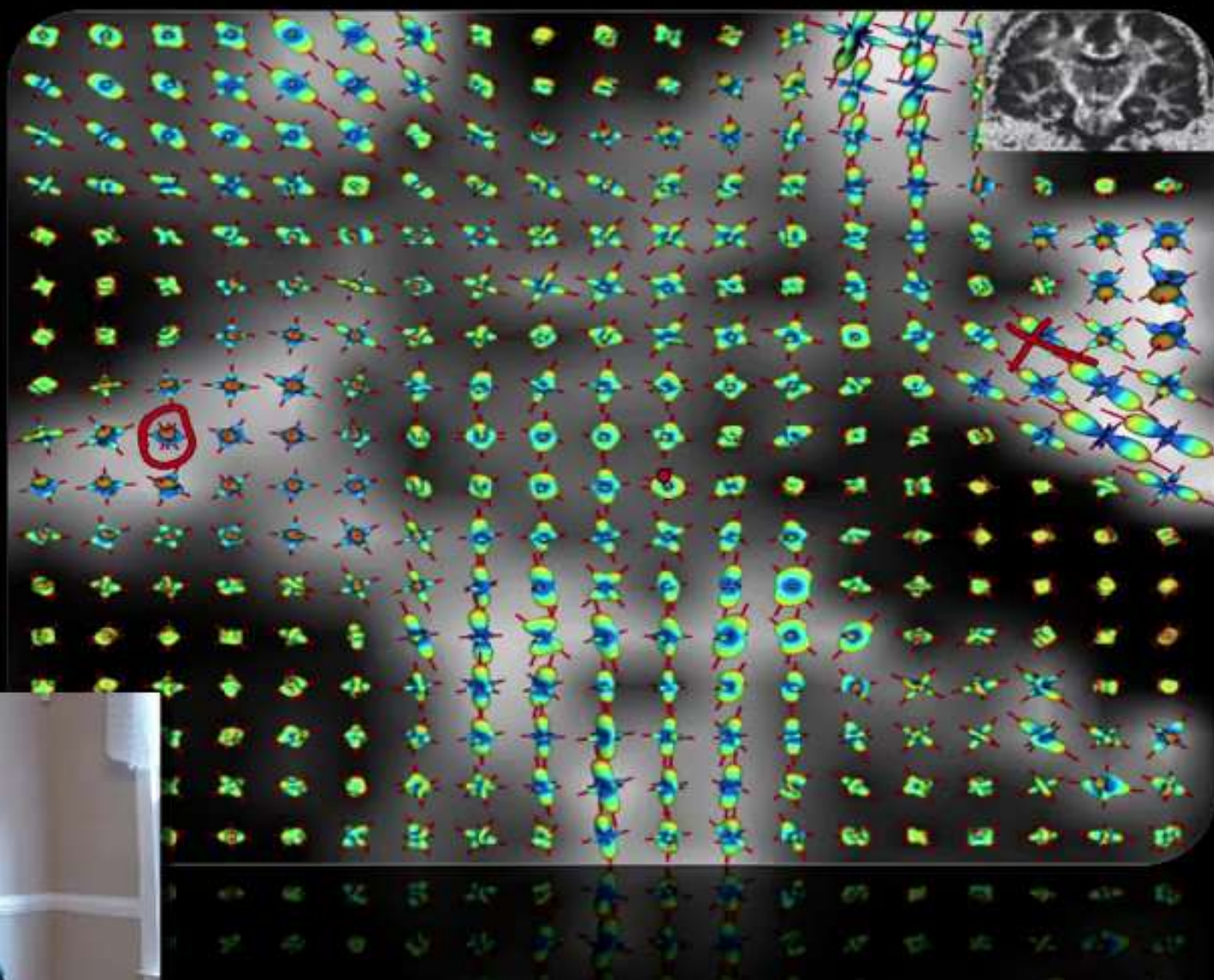
# Diffusion-Weighted MR Image



# Diffusion-Weighted MR Image

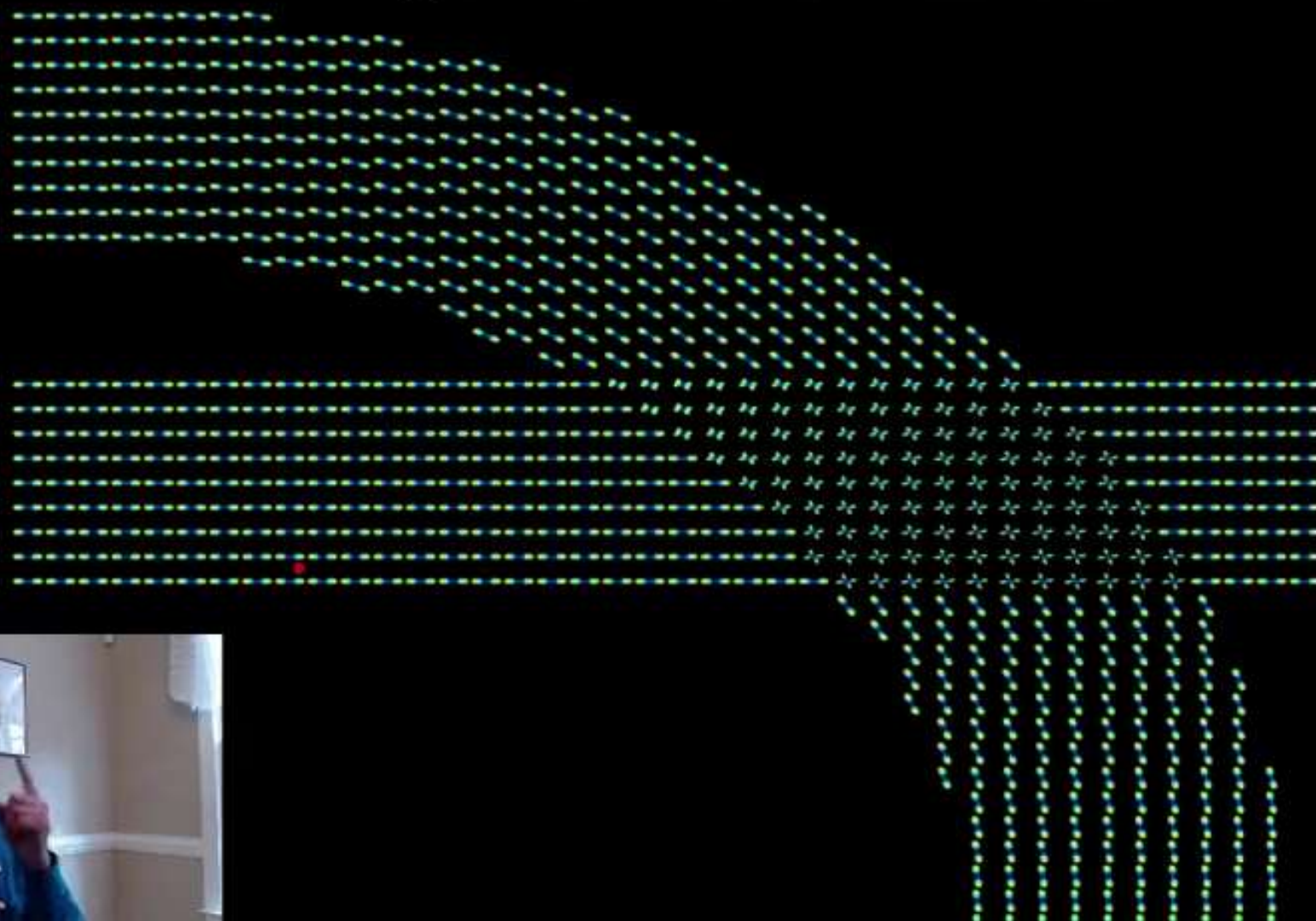




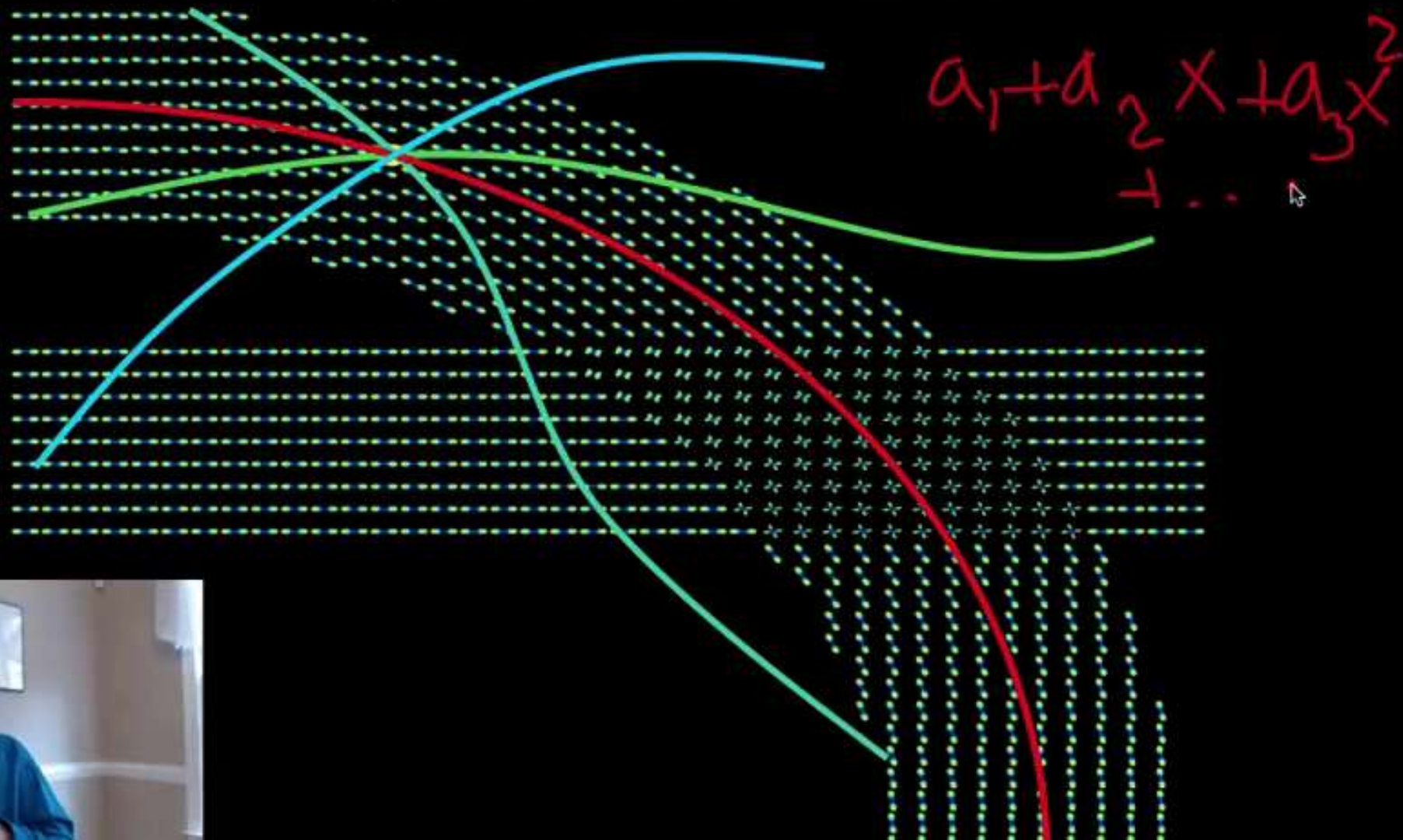




# Hough Transform !!!

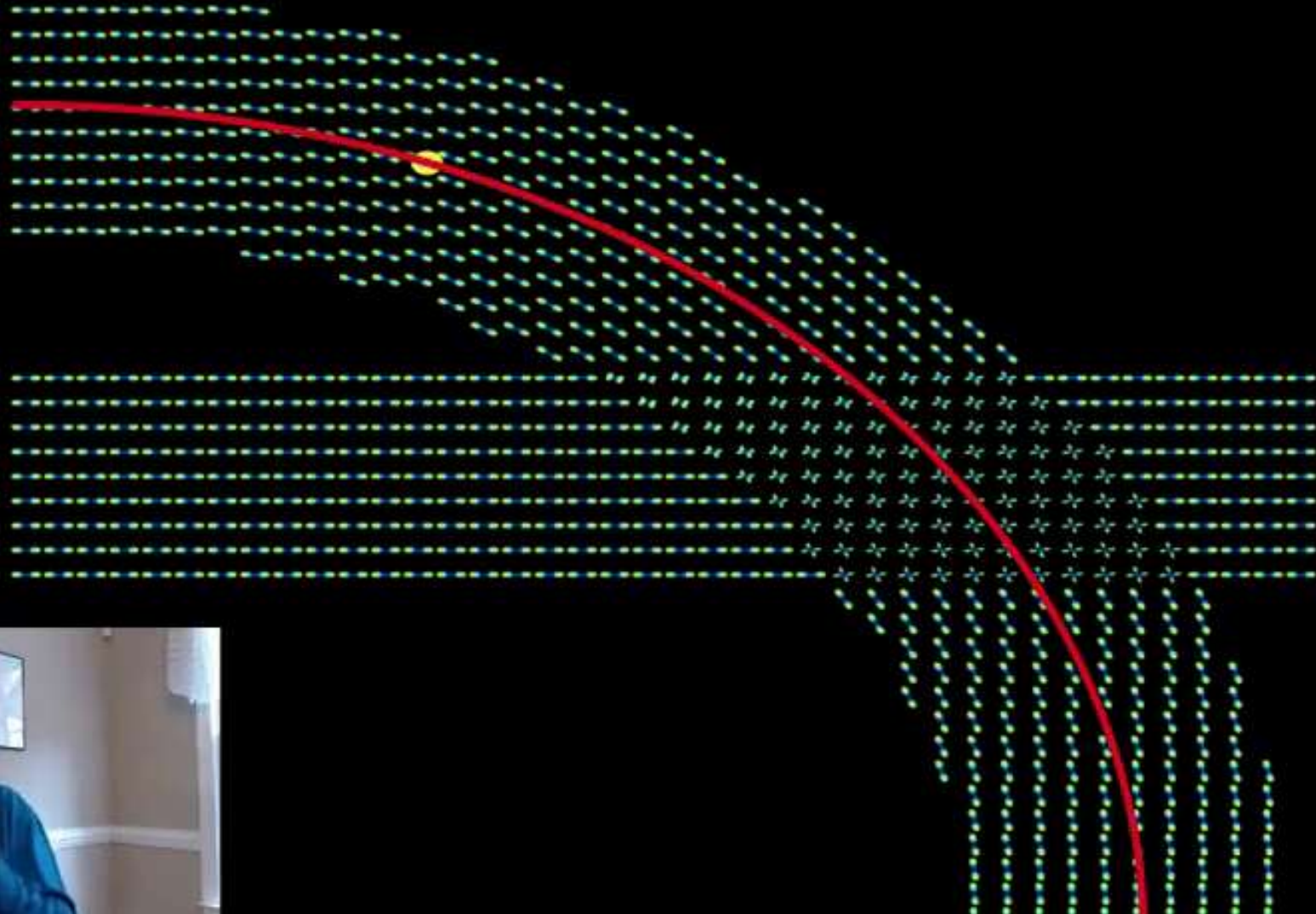


# Hough Transform !!!

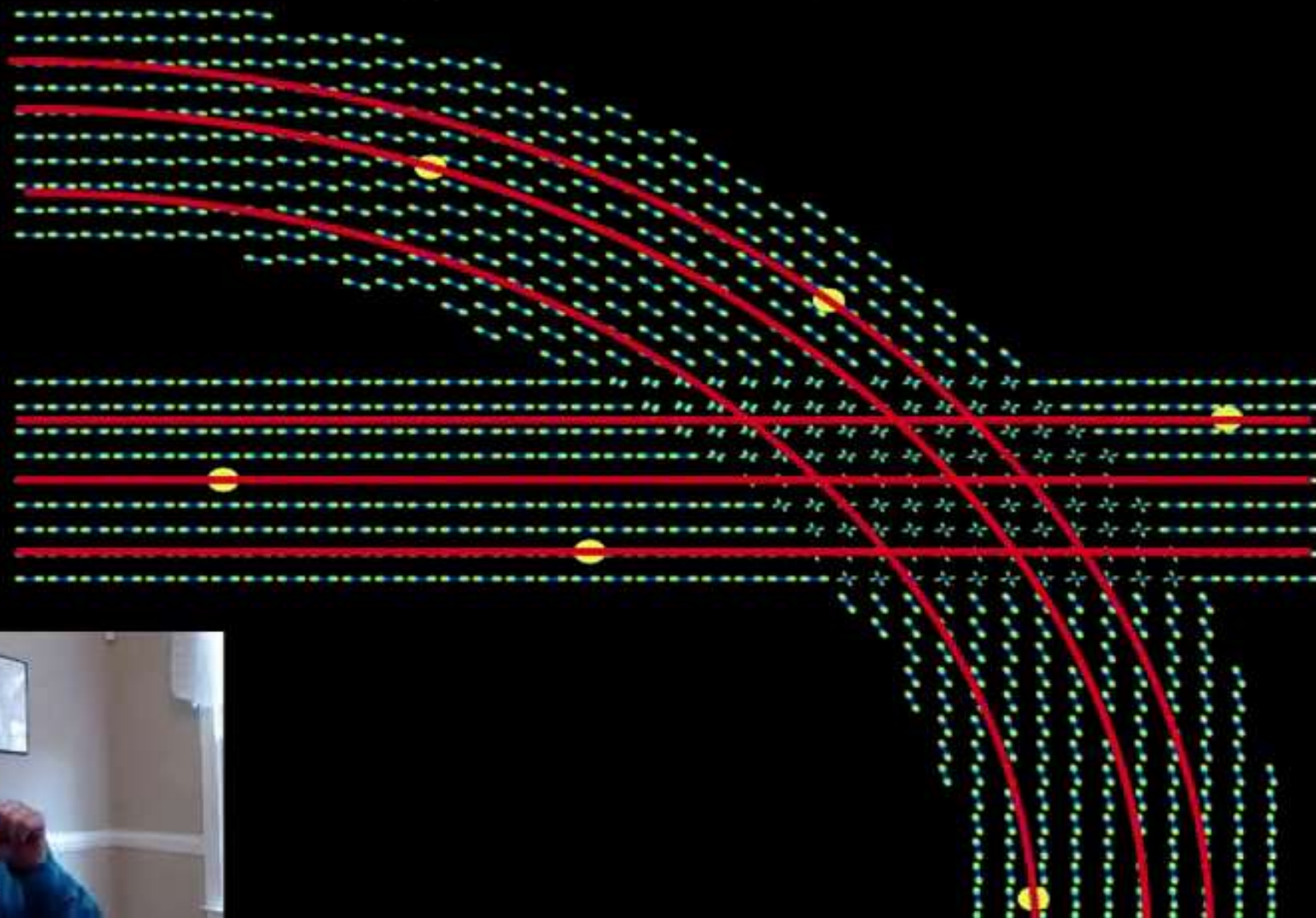




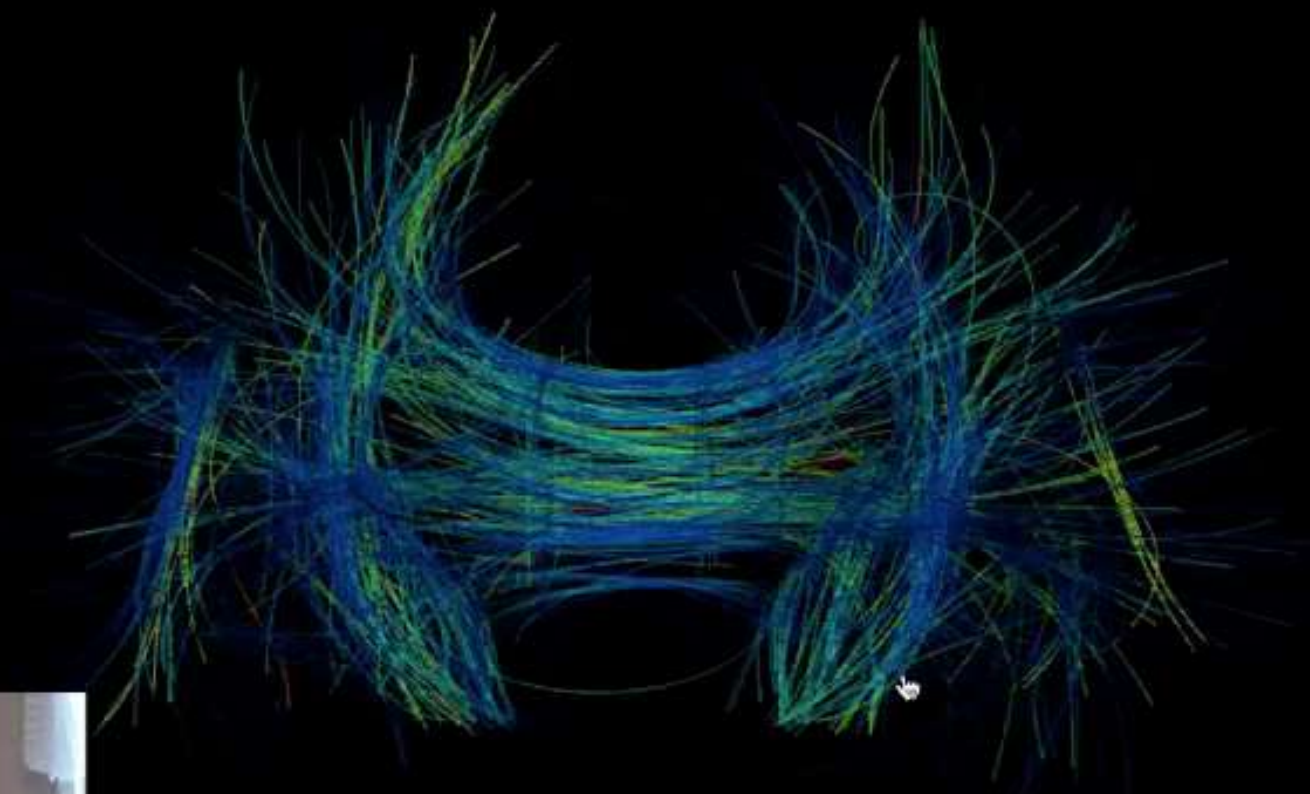
# Hough Transform !!!



# Hough Transform !!!







## Brain Imaging: Deep Brain Stimulation

# Image and Video Processing: From Mars to Hollywood with a Stop at the Hospital

Guillermo Sapiro

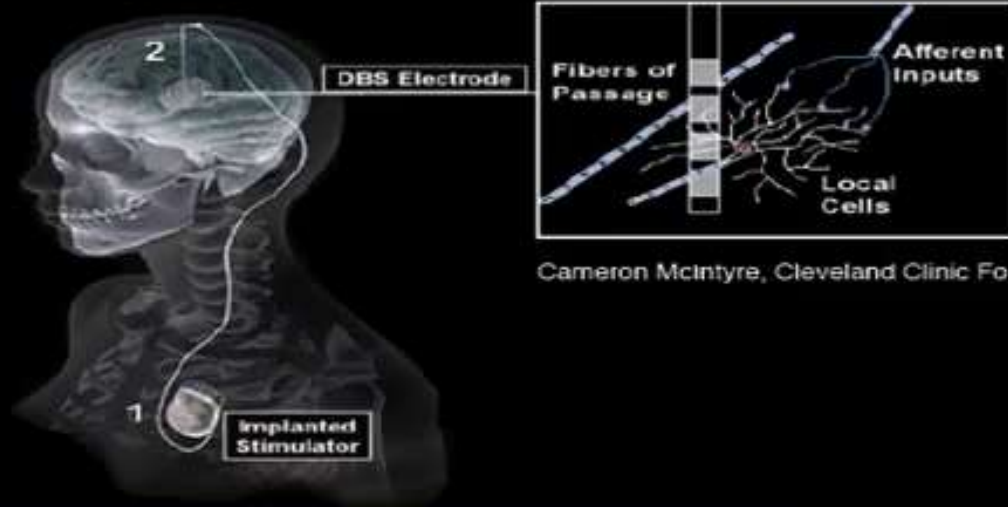


Thanks to Lenglet, Aganj, Harel, Duchin, SIS

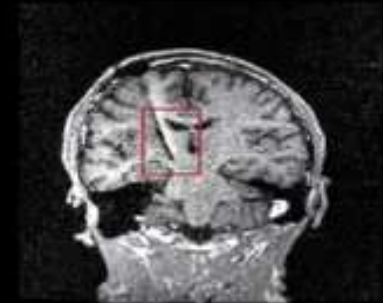




# Deep Brain Stimulation (DBS)



Cameron McIntyre, Cleveland Clinic Foundation

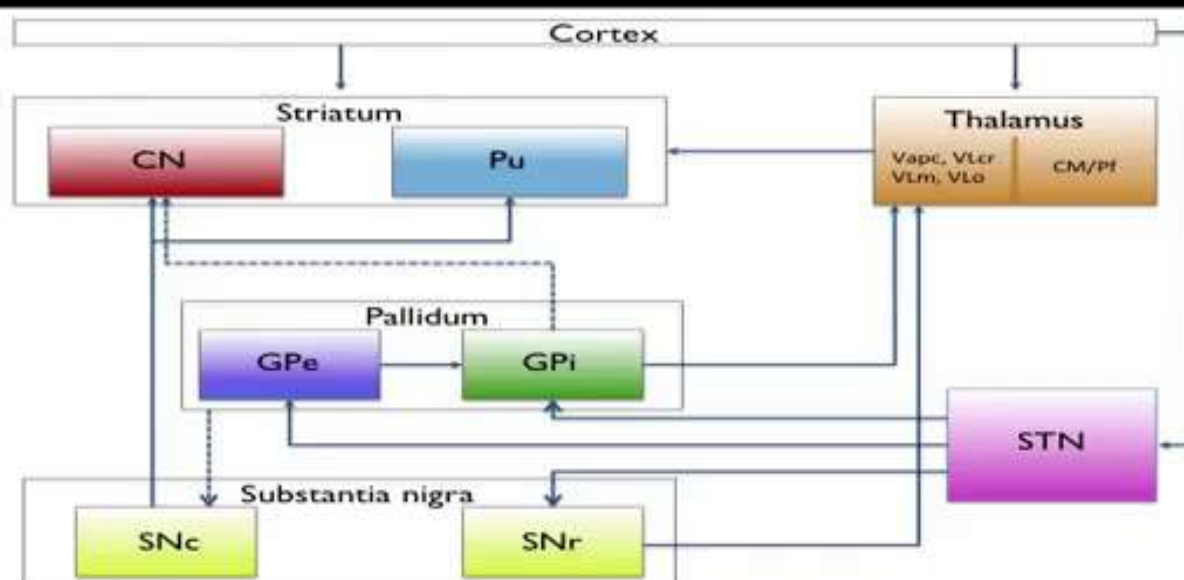


Successful DBS surgery is critically dependent on precise placement of DBS electrodes into target structures

Students: A good place to take a break if needed.



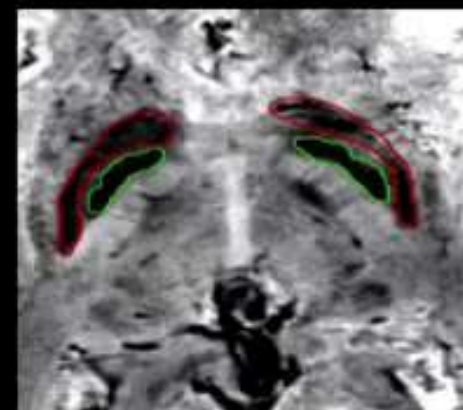
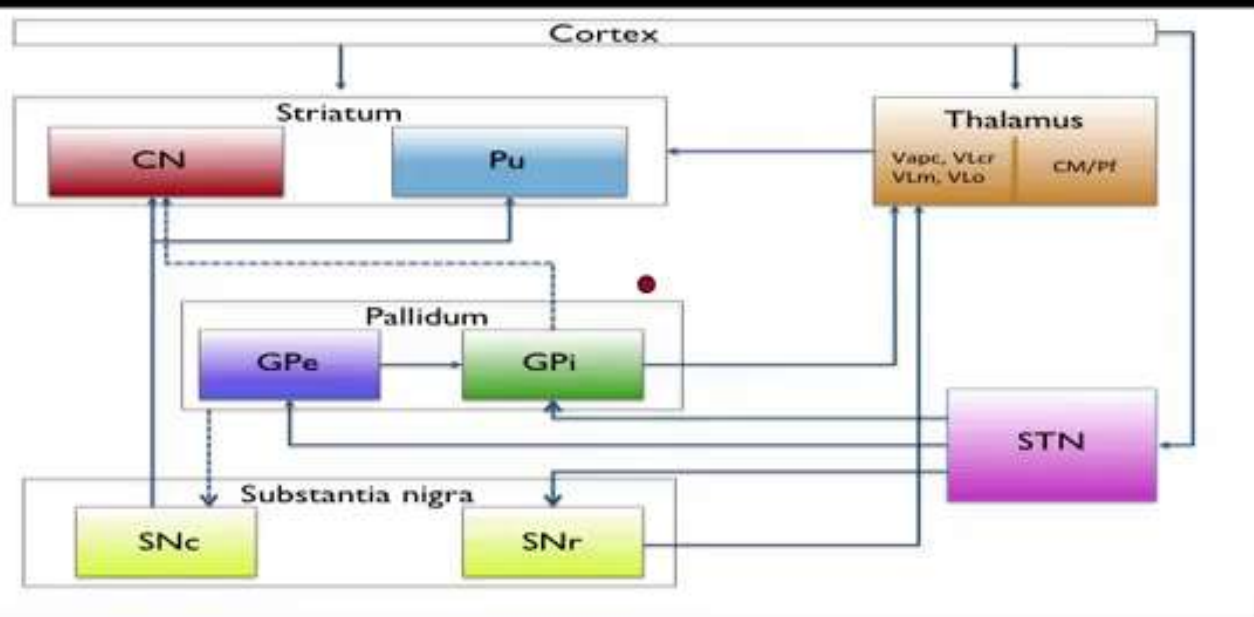
# Brain Imaging and DBS





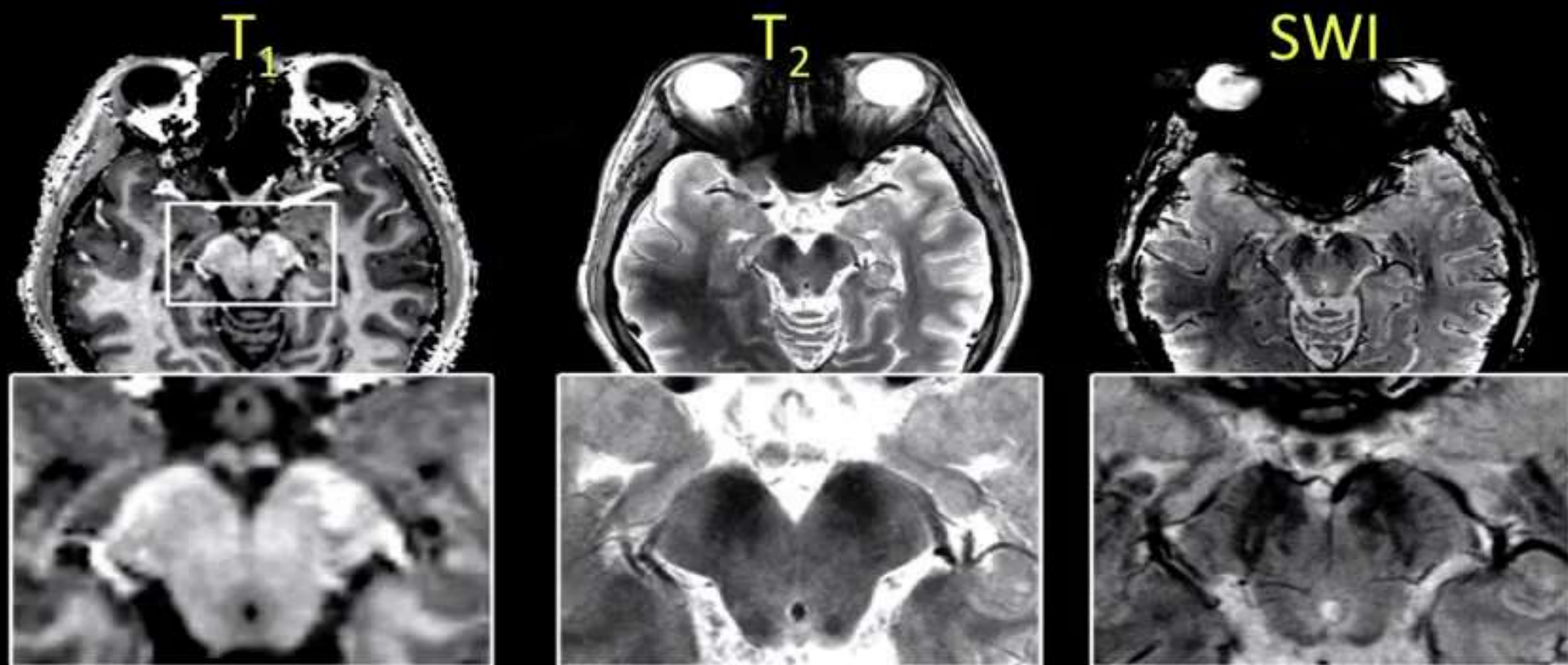


# Brain Imaging and DBS

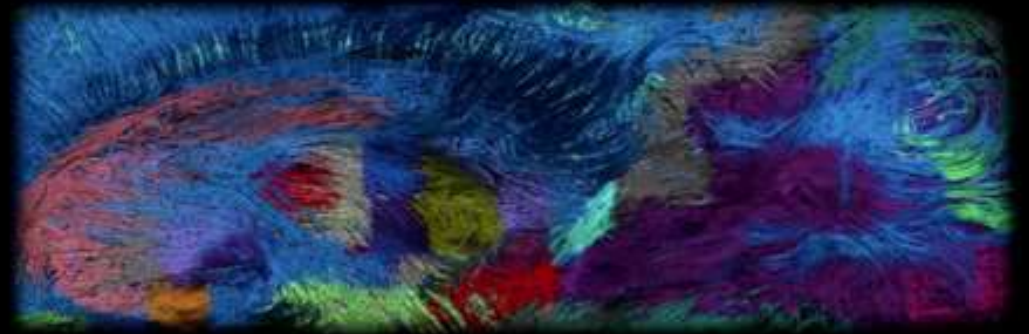
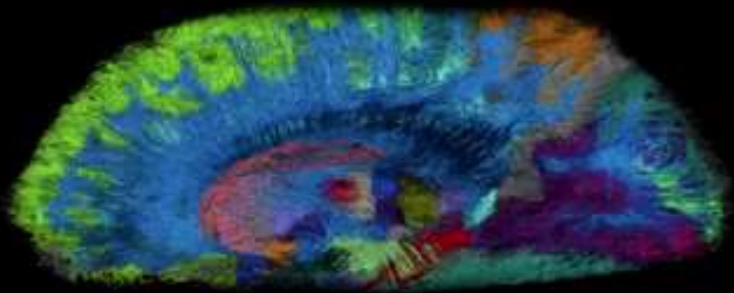
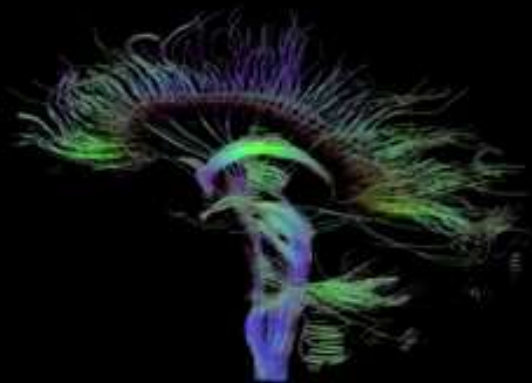
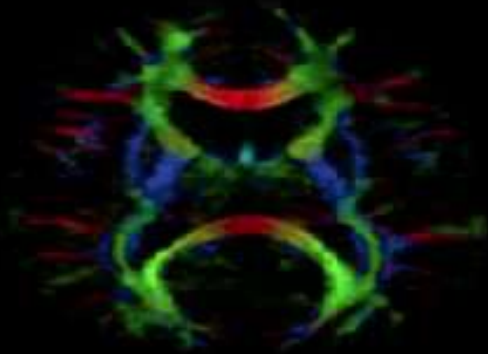




# Brain Imaging and DBS



# Brain Imaging and DBS

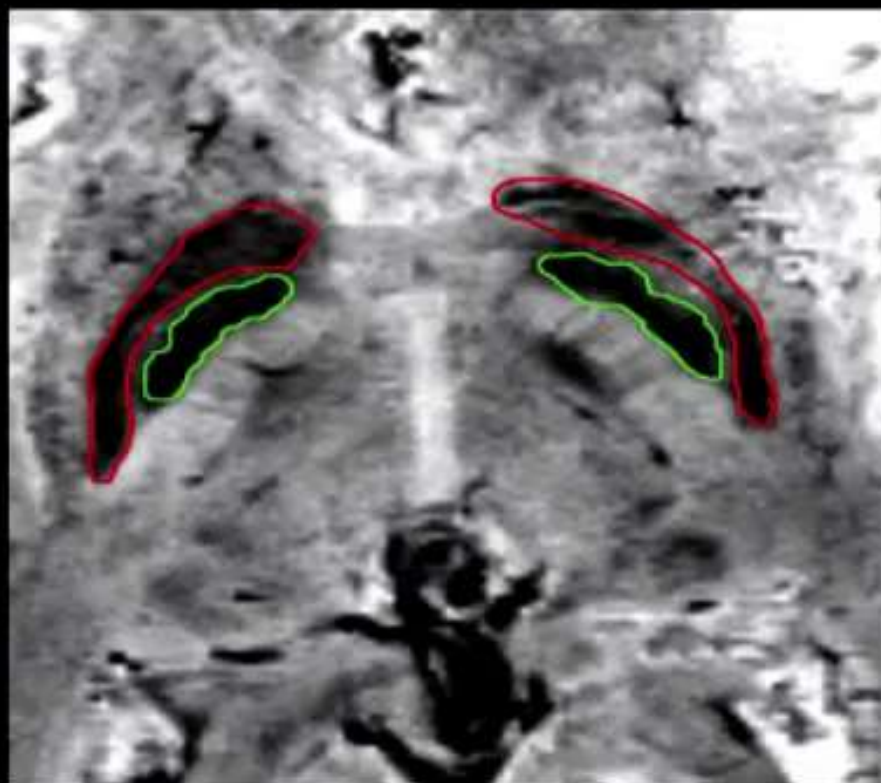


Human, 7T,  $1.5 \times 1.5 \times 1.5 \text{ mm}^3$   
Tractography – Paul Thompson, UCLA





# Brain Imaging and DBS



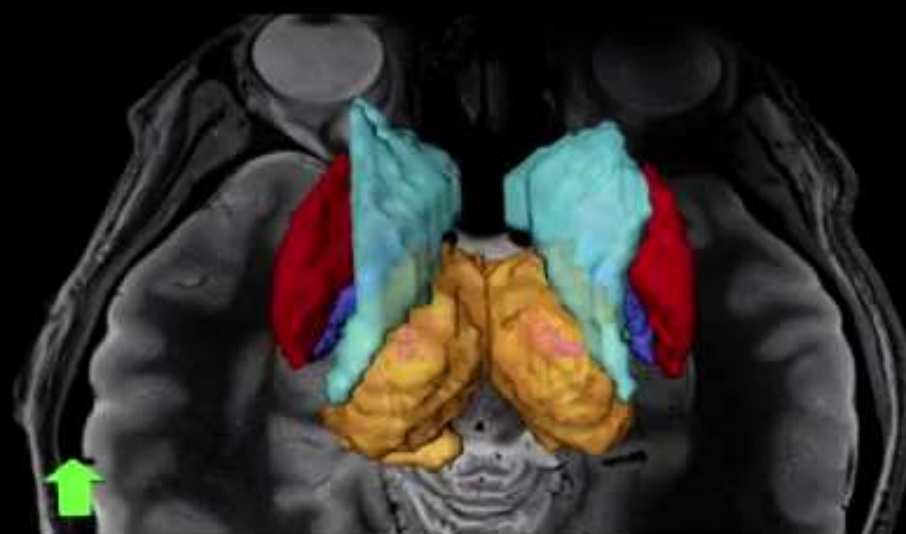
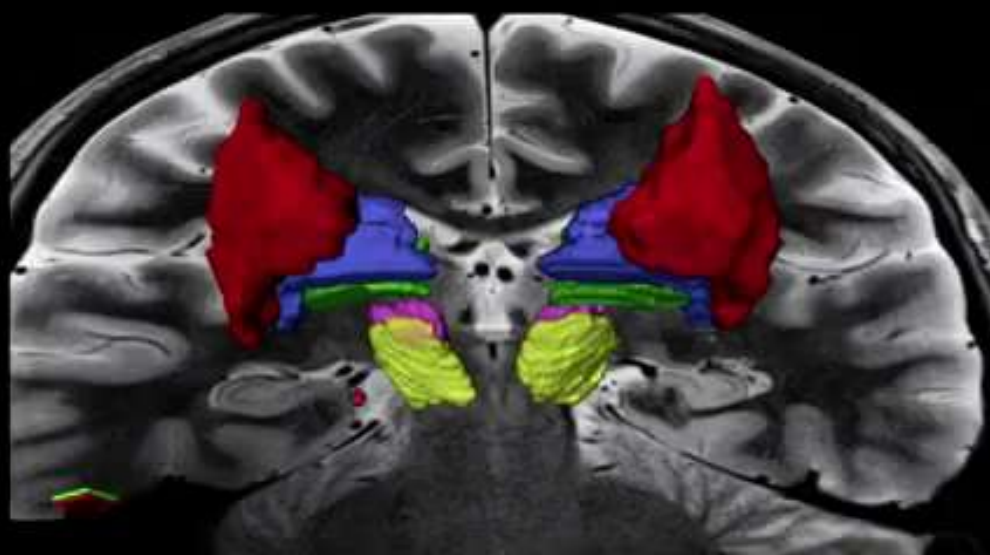
GP = Globus pallidus

GPi = DBS Target for Dystonia





# Brain Imaging and DBS: ROI





# Brain Imaging and DBS: DWI

