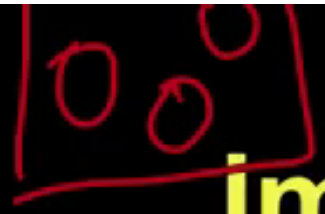
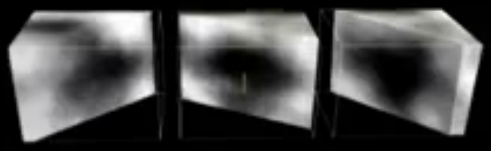
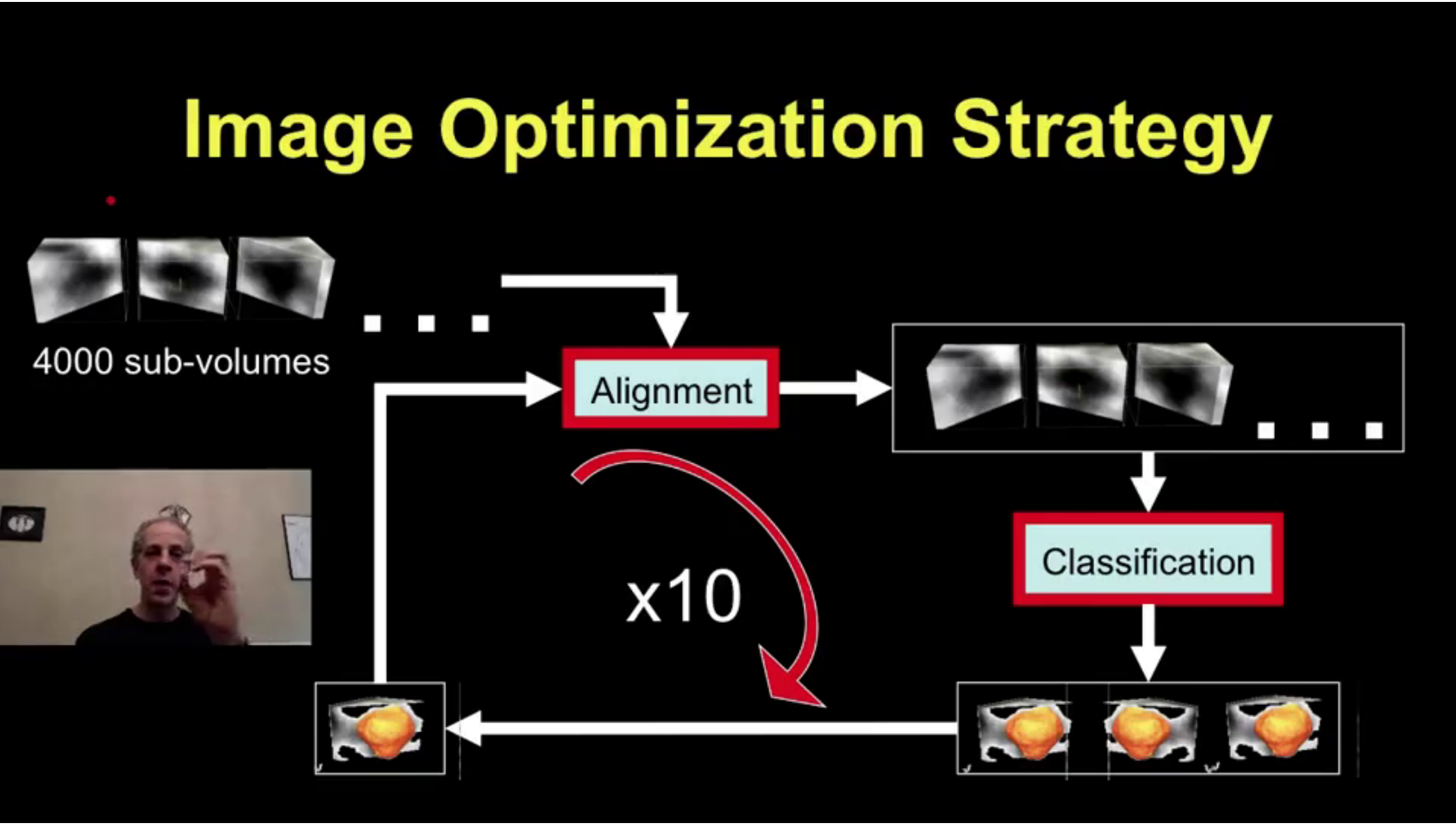


Image Optimization Strategy

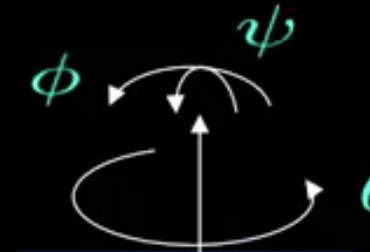


4000 sub-volumes

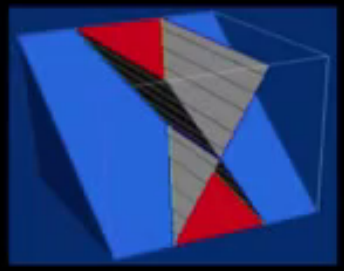
Image Optimization Strategy

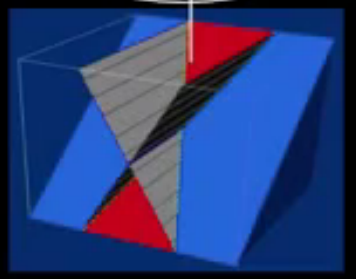


3D Image Alignment

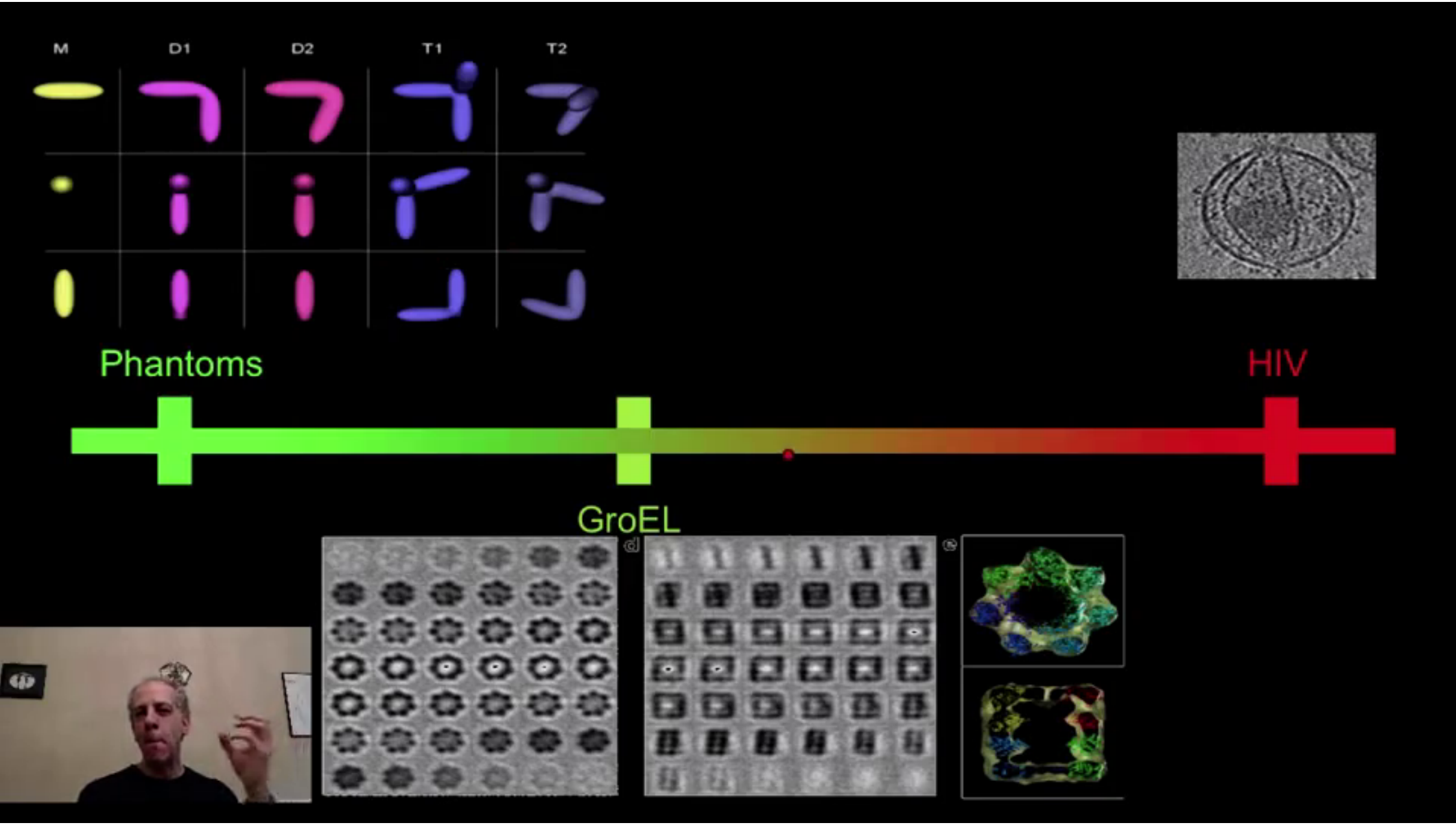


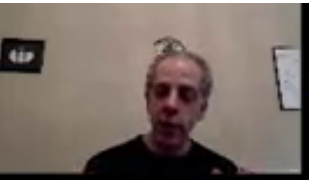
$$\min_{\theta,\phi,\psi,\vec{t}} d(\quad,\quad)$$





- 6 DOF problem: Speed-up in Fourier domain


M
D1
D2
T1
T2
Phantoms
HIV
GroEL

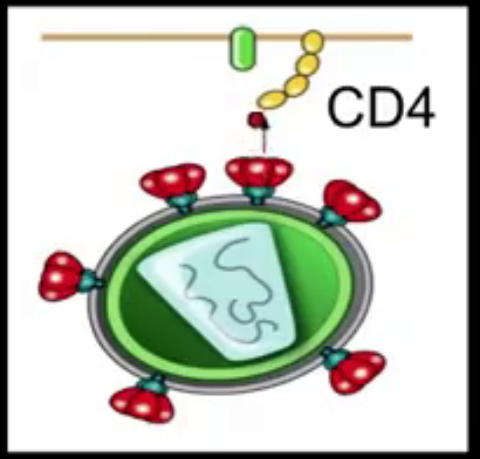


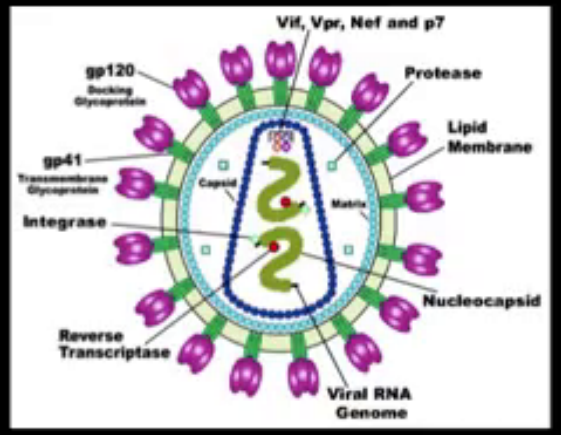
HIV envelope glycoproteins

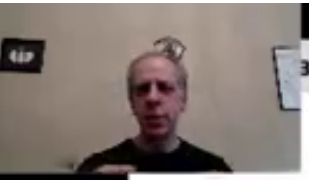
- Mediate virus binding to the cell surface receptor CD4 on target cells to initiate infection
- Functional unit is a trimer

  of **gp120** (surface glycoprotein)

  and **gp41** (transmembrane unit).
- Structure of components available.
- Structure of the trimer remains elusive.







38/nature07159 nature

LETTERS

Molecular architecture of native HIV-1 gp120 trimers

Jun Liu[1]*, Alberto Bartesaghi[1]*, Mario J. Borgnia[1]*, Guillermo Sapiro[2] & Sriram Subramaniam[1]

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*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

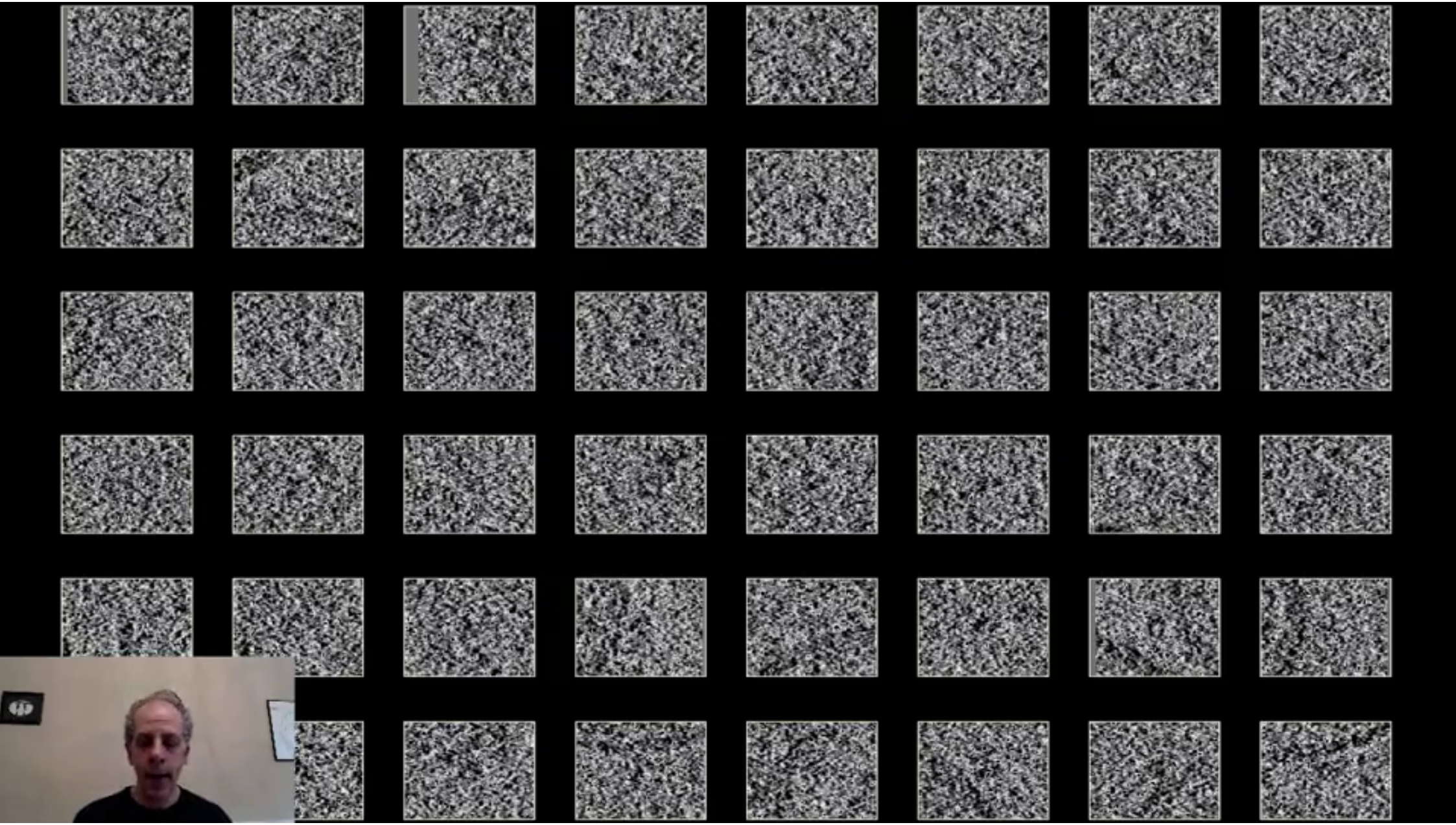


Image Refinement Loop

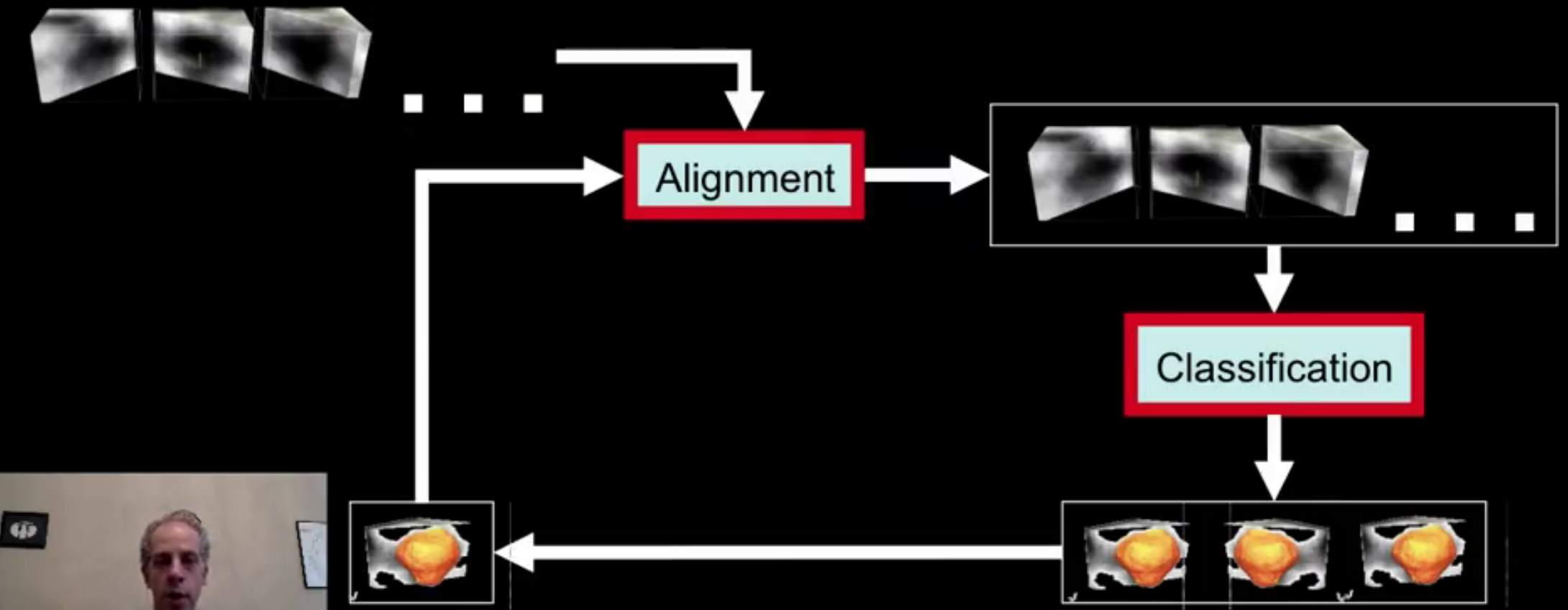
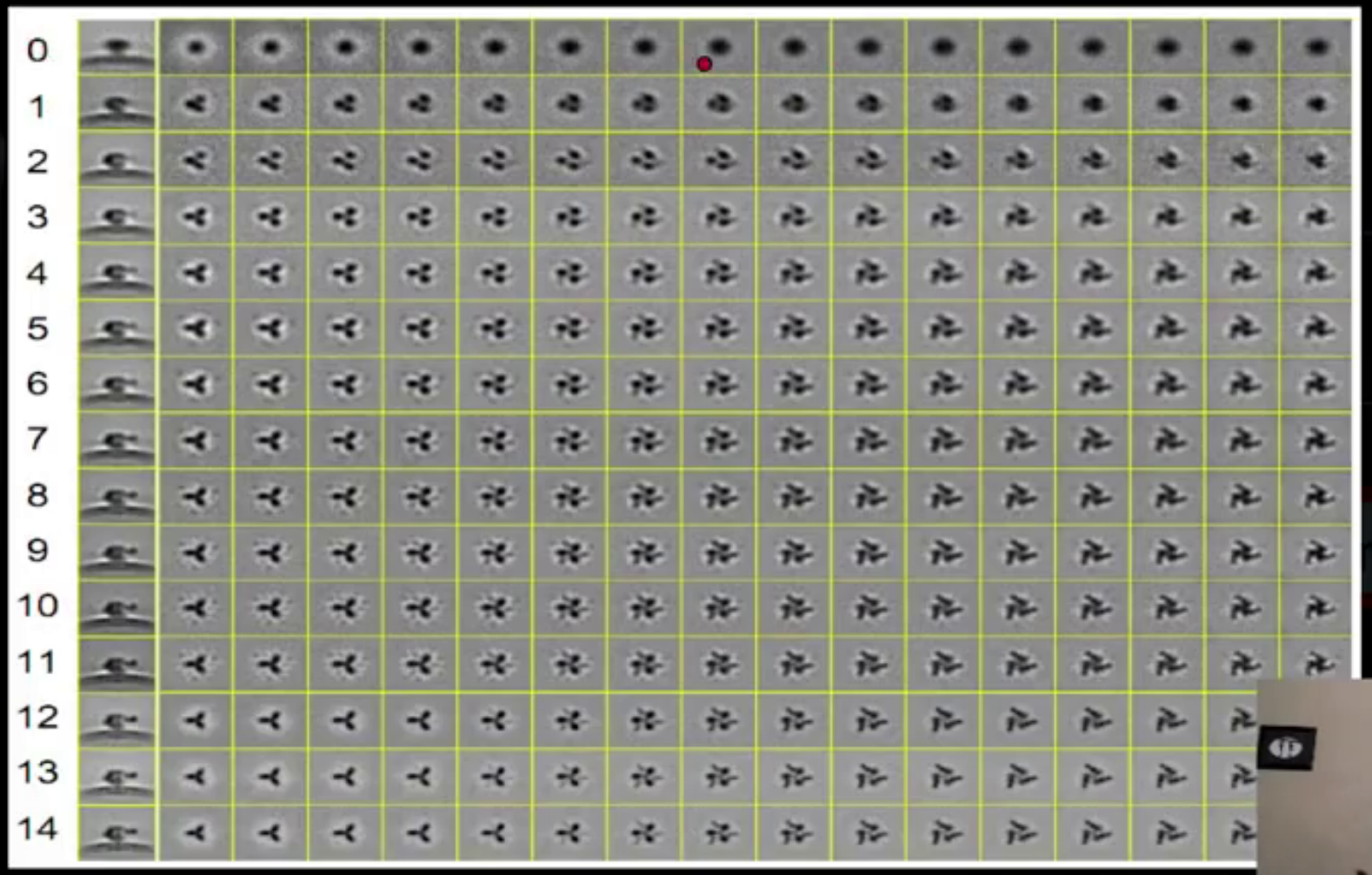
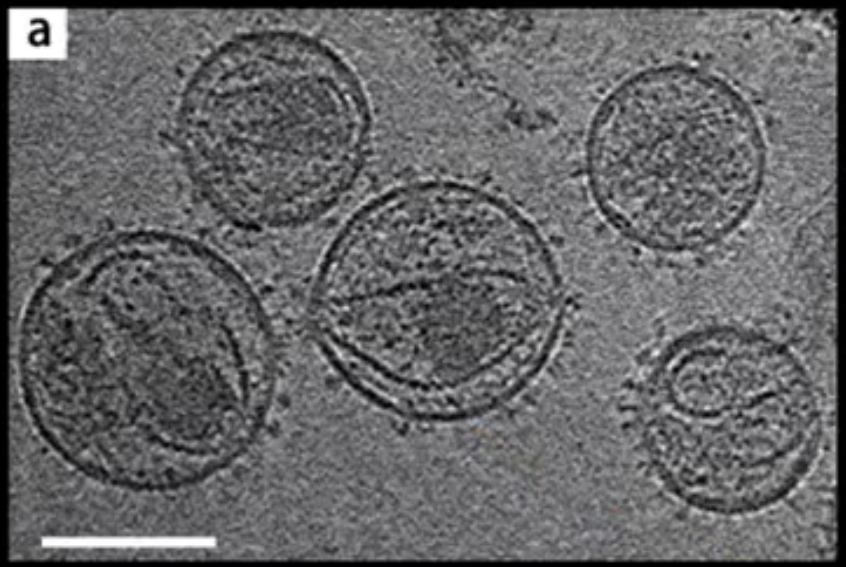
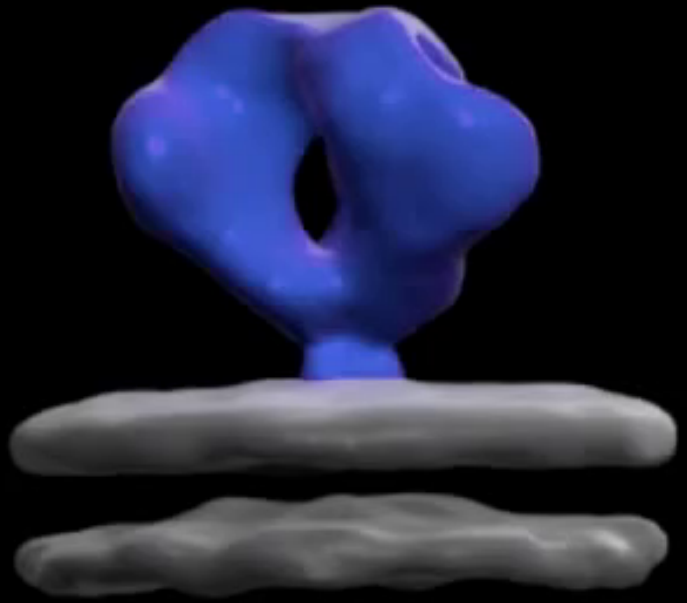
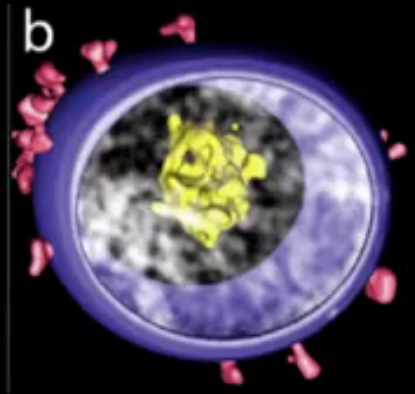


Image Refinement Loop




a

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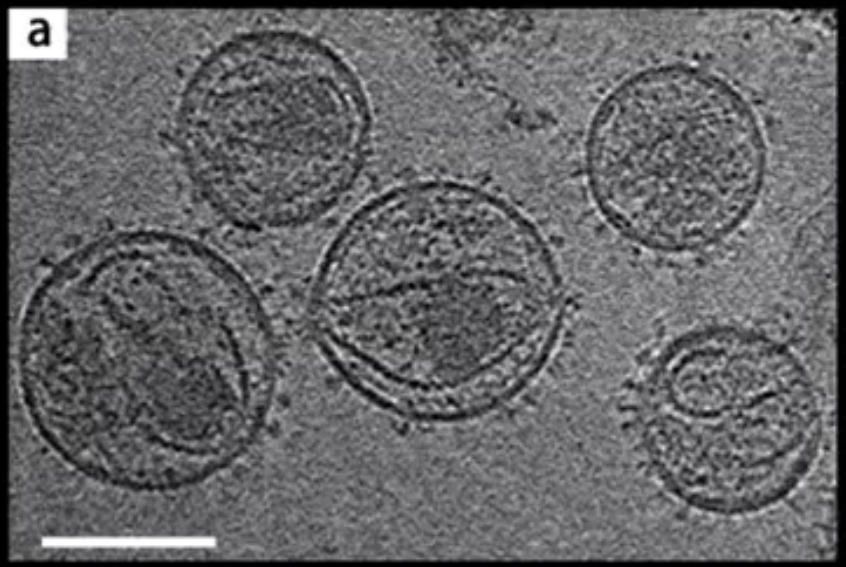
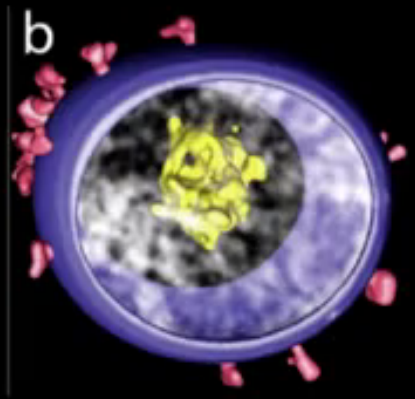
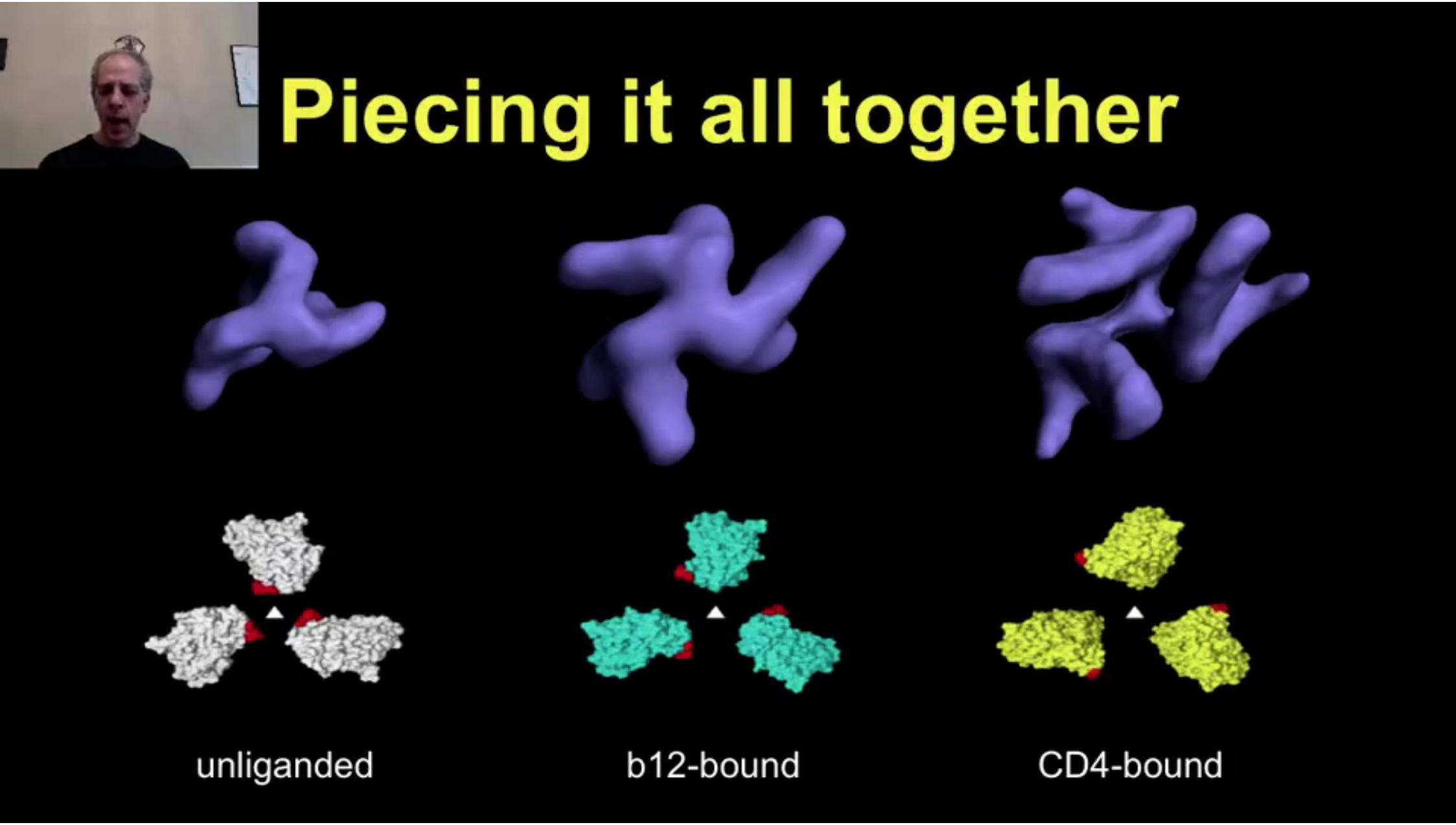

a


b


Piecing it all together
unliganded
b12-bound
CD4-bound

Conformational changes of the trimeric spike that occur upon CD4 binding