

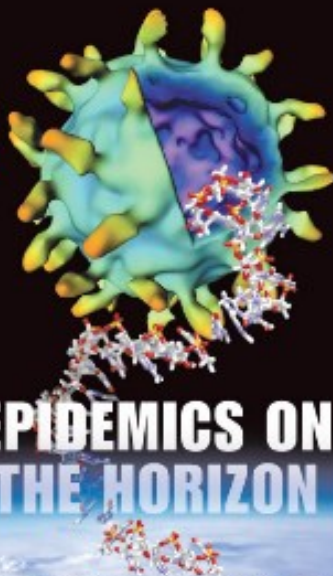
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PIOMS

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EPIDEMICS ON THE HORIZON

HIP-HOP ALUMS • WRITING SUCCESS • THE UNSETTLING SENIOR YEAR



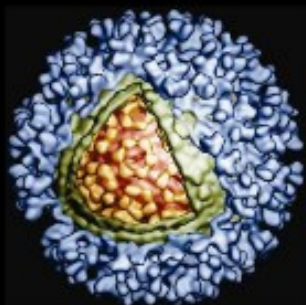
form function

120kV

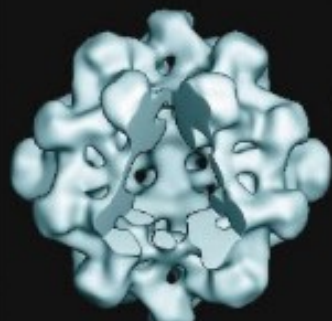
200FEG
STEM



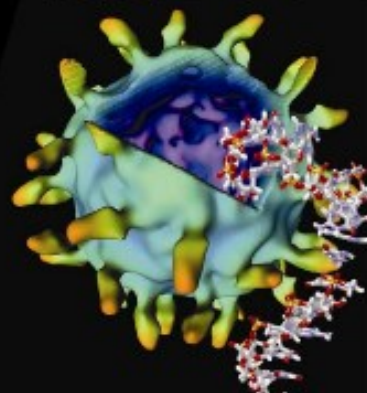
300FEG
Helium/
EELS



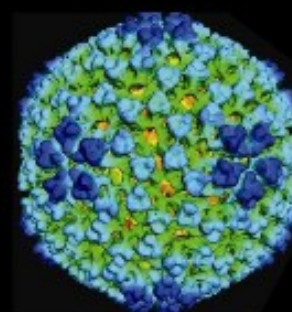
A model of an alphavirus, which is closely related to West Nile virus; diameter about 70nm.



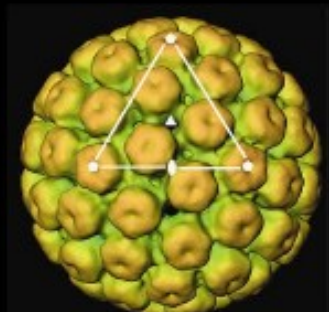
A hepatitis E virus-like particle is made of protein compounds along the edges of a 20-faced cage



The replication cycle of the polio (or common cold) virus as it releases its genome from its open shell.



A rice reovirus is composed of 780 copies of proteins on top of an inner shell; diameter about 70nm.

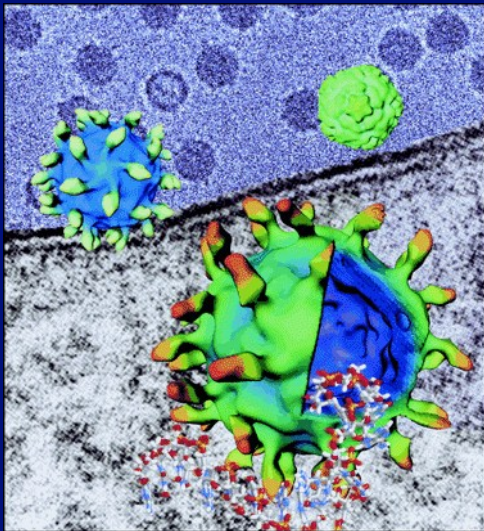


A human DNA tumor virus; diameter about 50nm.

data acquisition

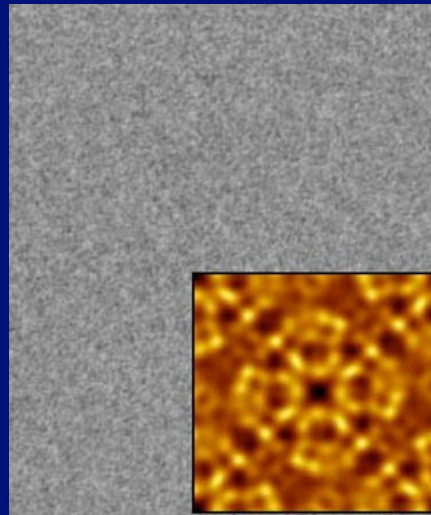
Application 1

Single Particles



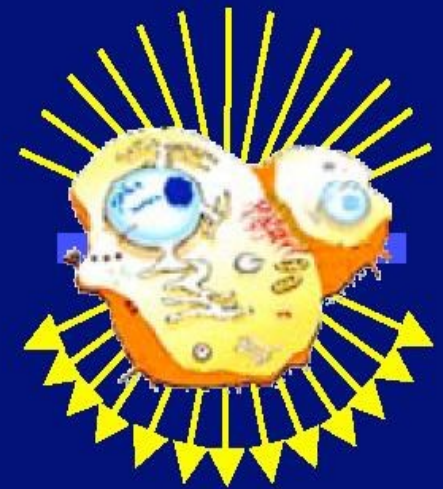
- **Sample prep**
- Cryo-TEM
- Image Processing
- **Molecular Biology**

Electron Crystallography



- **2D crystallization**
- Cryo-TEM
- **Automated** Image Processing
- Structural Biology of Membrane Proteins

Electron Tomography



- Cryo Sectionning
- Cryo-TEM
- Tomography
- Image Processing
- Data Analysis
- Cell Biology

Weak phase imaging
 Zernike phase plate
 Automation/Tele-microscopy!
 software control interface?
 FasTEM/Leginon/SerialEM

Solution 4
 Cryo-imaging

field emission gun

300kV

accelerating tube

automatic cryo specimen
 exchange mechanism

Pumping/contamination?

2x GIP
 1x CIP
 1x CDP
 1x SDP

Phase plate

field limiting aperture
 assembly

condenser lens

condenser aperture assembly

helium cooling stage

Top+side-entry tilt G6

objecture aperture assembly

objective lens

Gold / charging
 Constant objective-lens excitation

intermediate lens

entrance aperture

spectrometer

G4

Omega filter

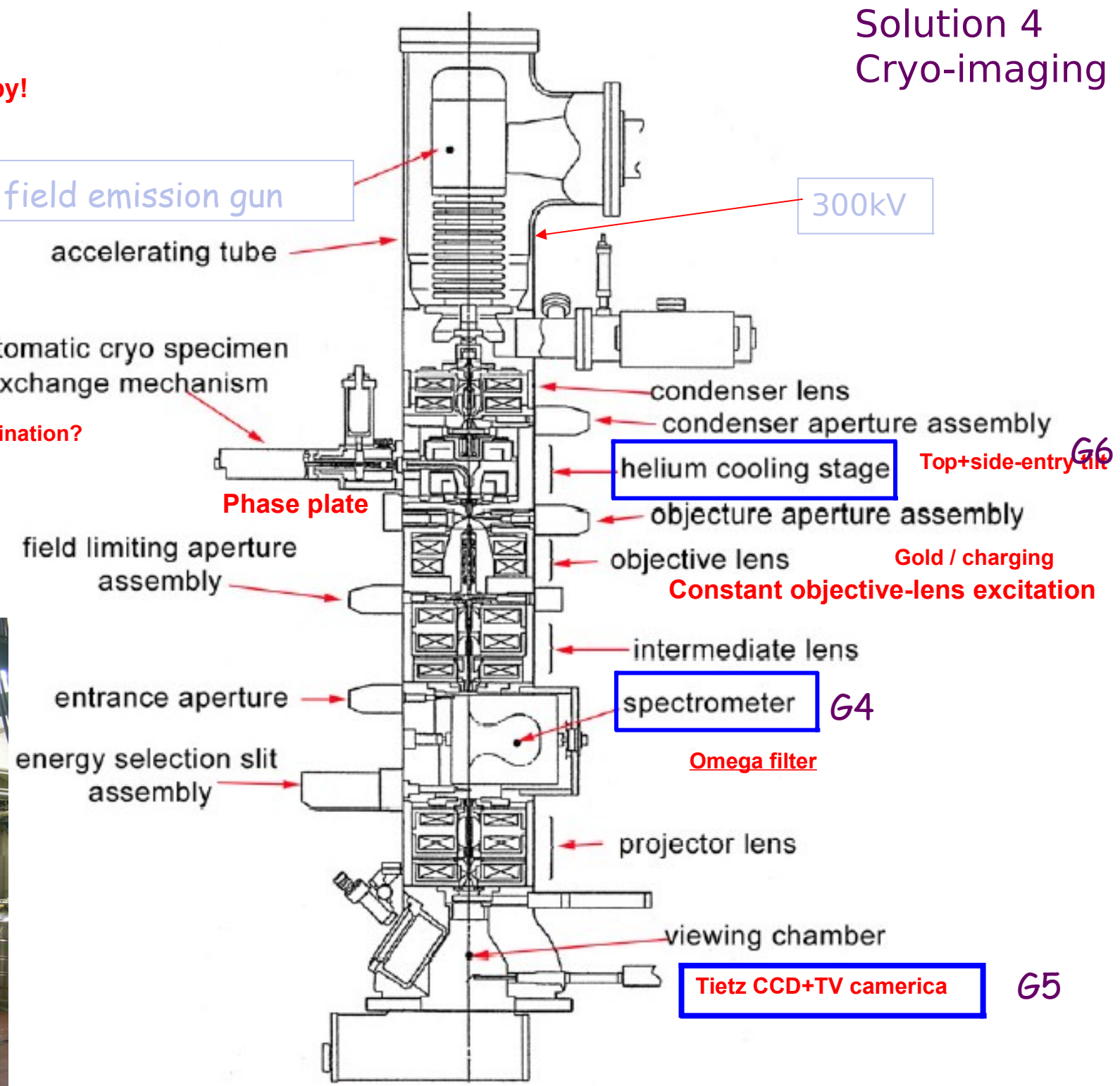
energy selection slit
 assembly

projector lens

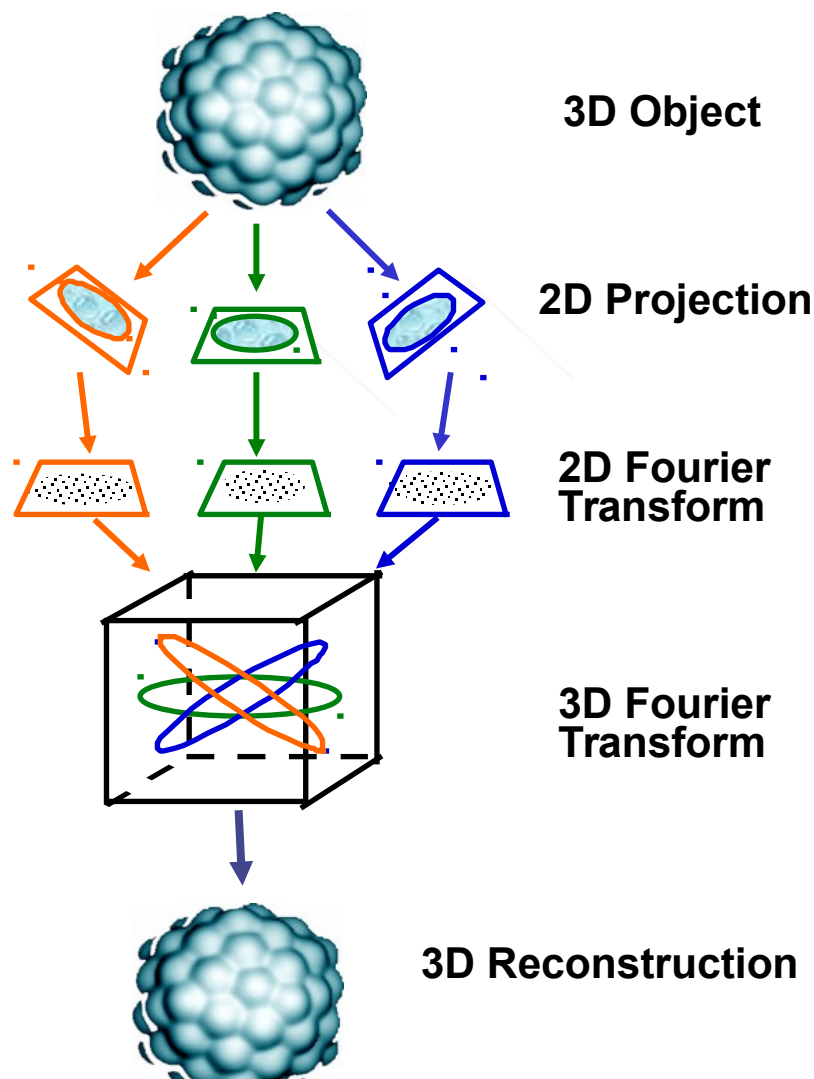
viewing chamber

Tietz CCD+TV camera

G5



Phase refinement - figure-of-merit in iterative cycles



FOM -- *crystallization in computing*

Individual filters

1. Correlation filter (refining models)
2. Size filter (interpolated models)
3. SIR variance filter
4. Contour-based weighting over CC plot to avoid false solution

Population filters

1. Handedness consistency
2. Phase consistency if with geometry constraint
3. Completeness of unique phases
4. Accuracy in averaging (scaling & interpolation)
5. Model assessment and occupancy (if with symmetrical objects)



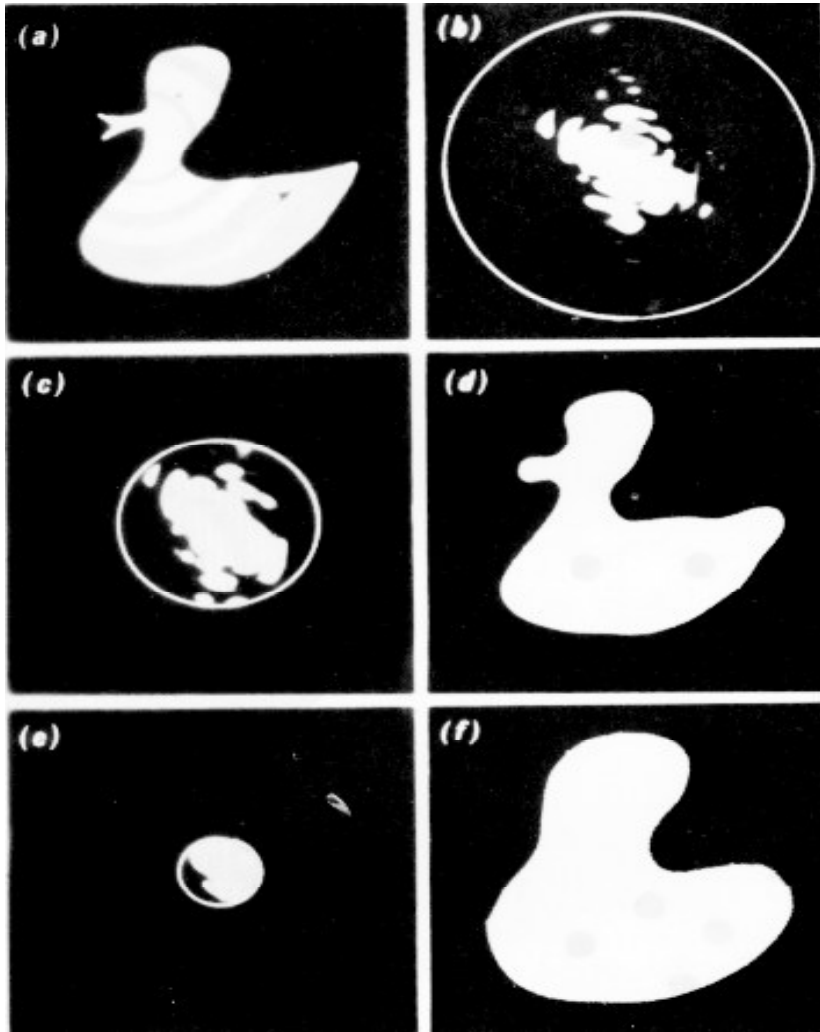
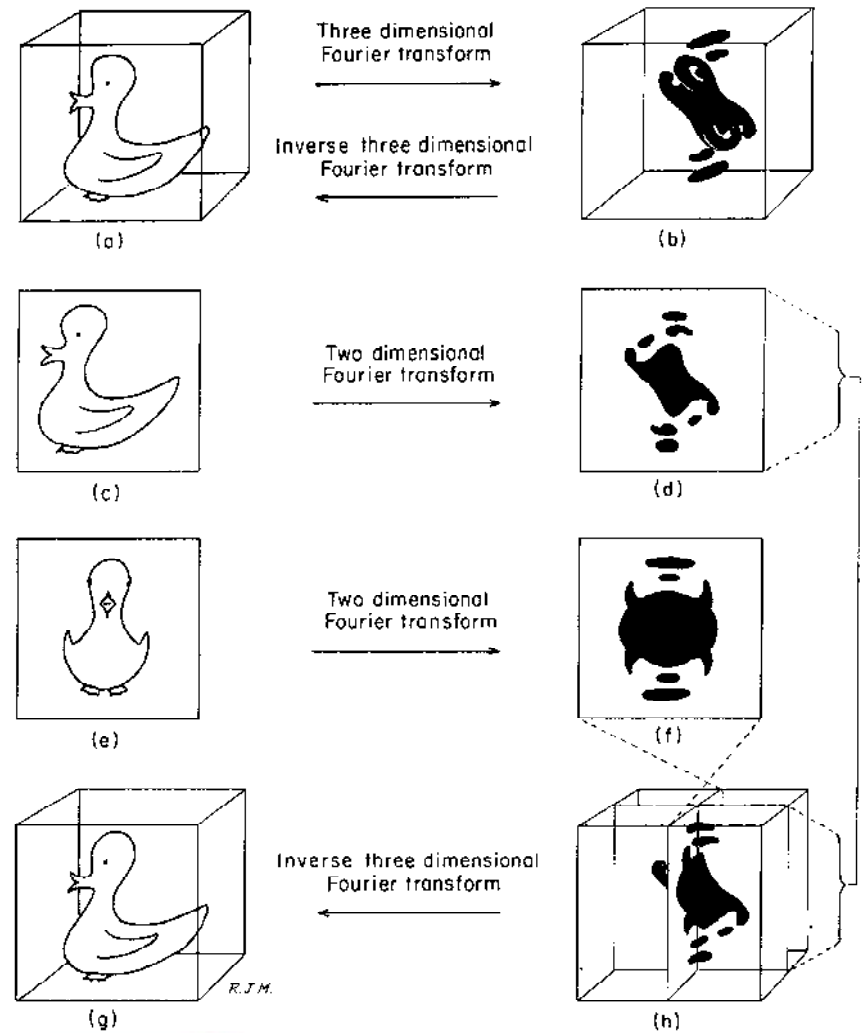
US20120301494 A1 (2012)

US20120064169 A1 (2012)

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Classical Fourier filter

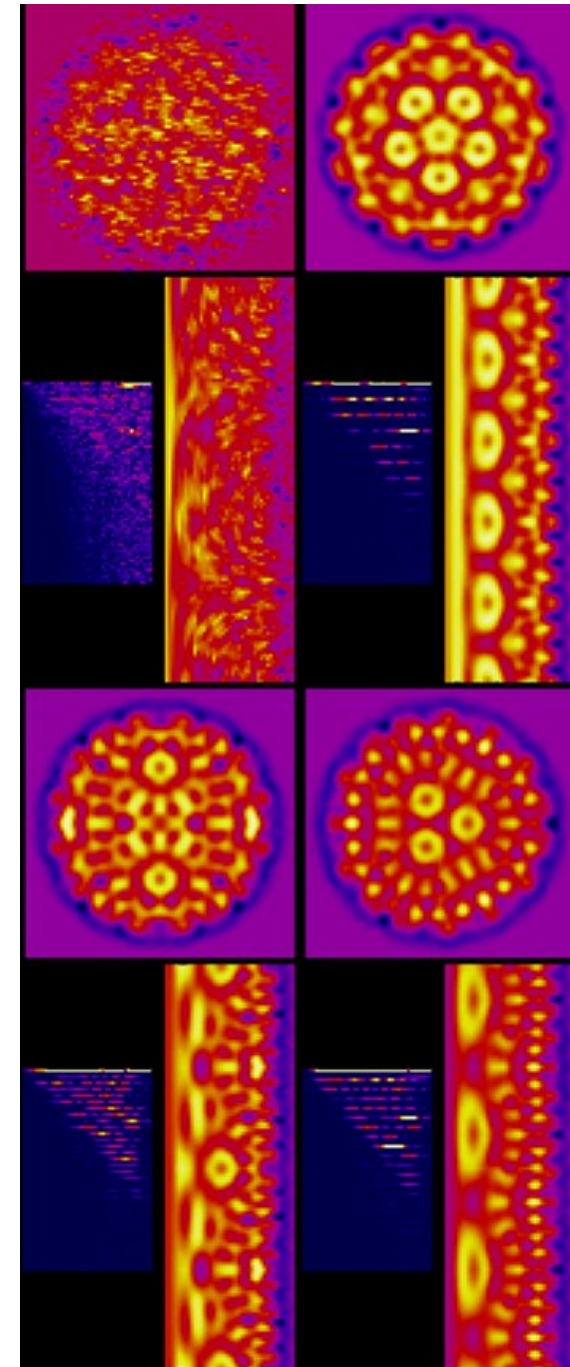
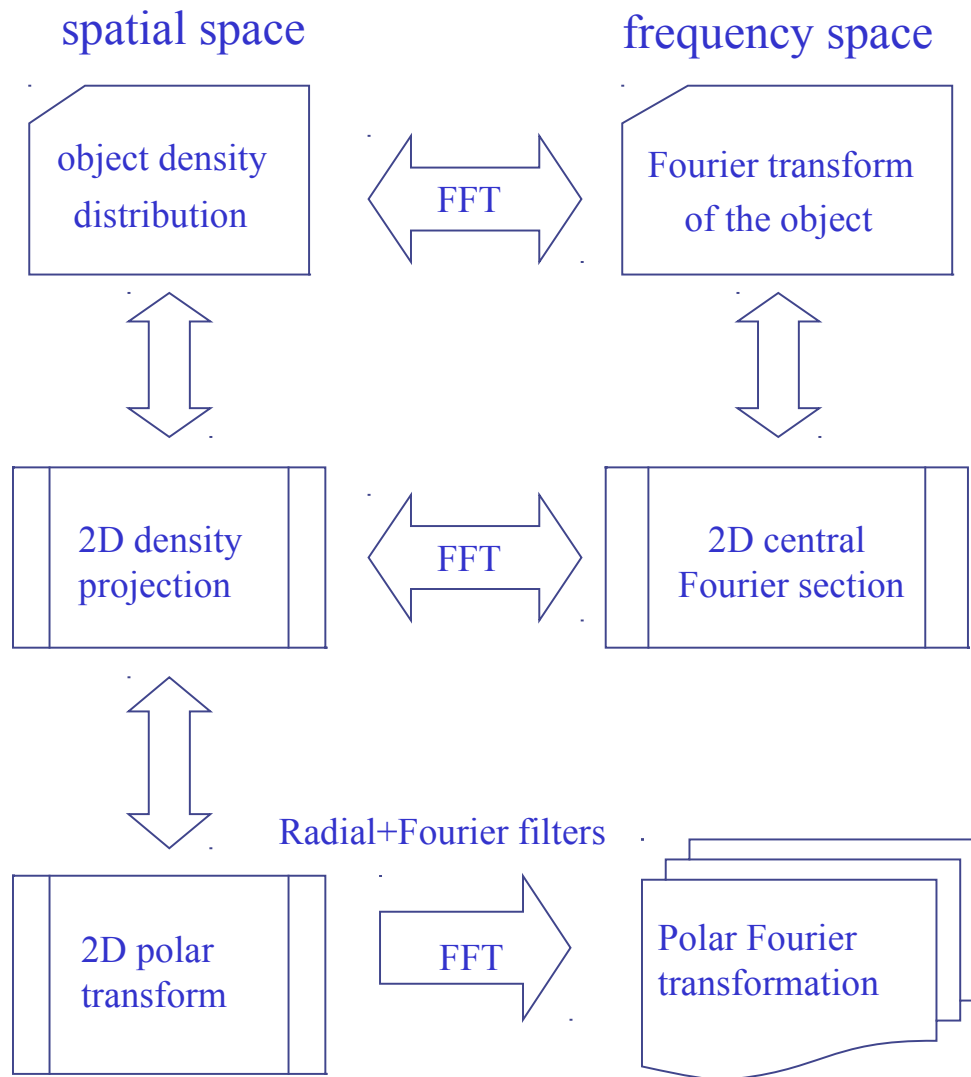


US20120301494 A1 (2012)
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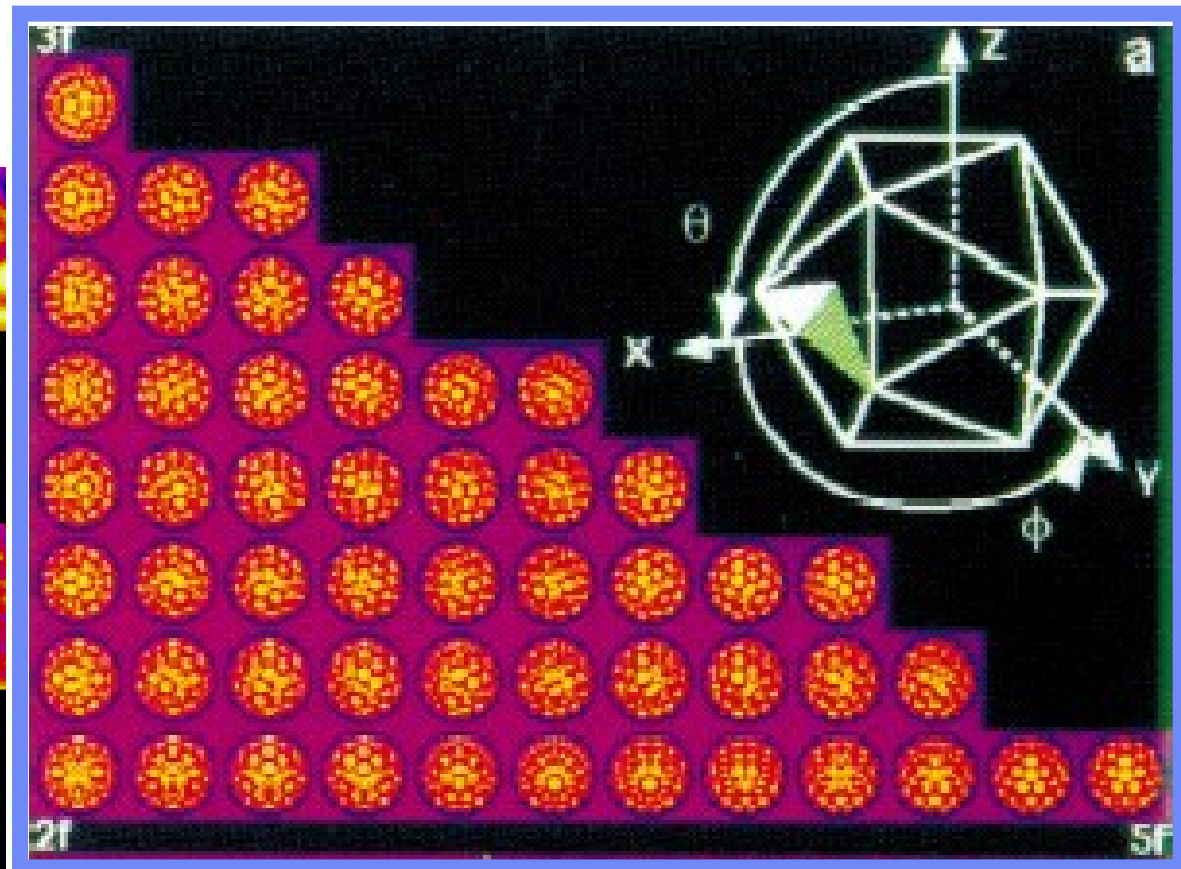
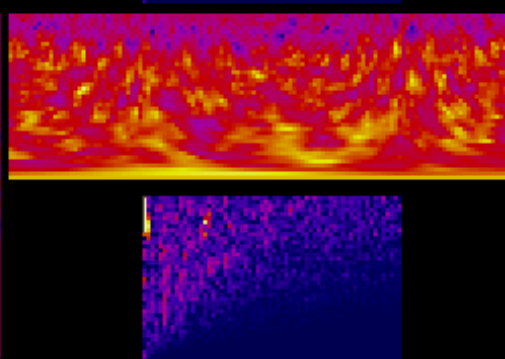
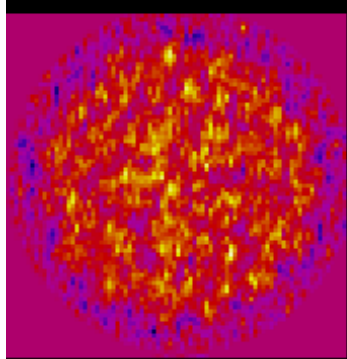
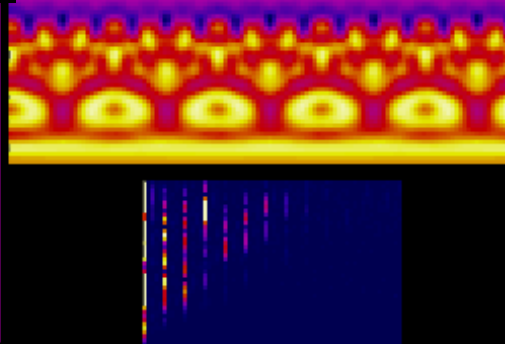
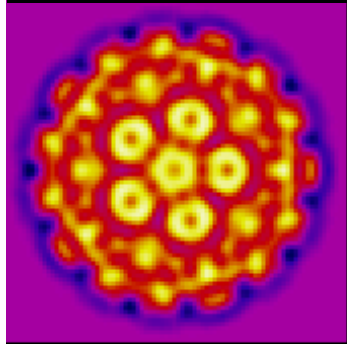
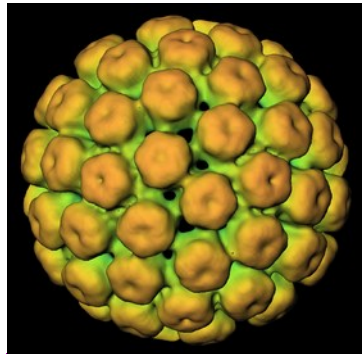
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cross-domain double filters

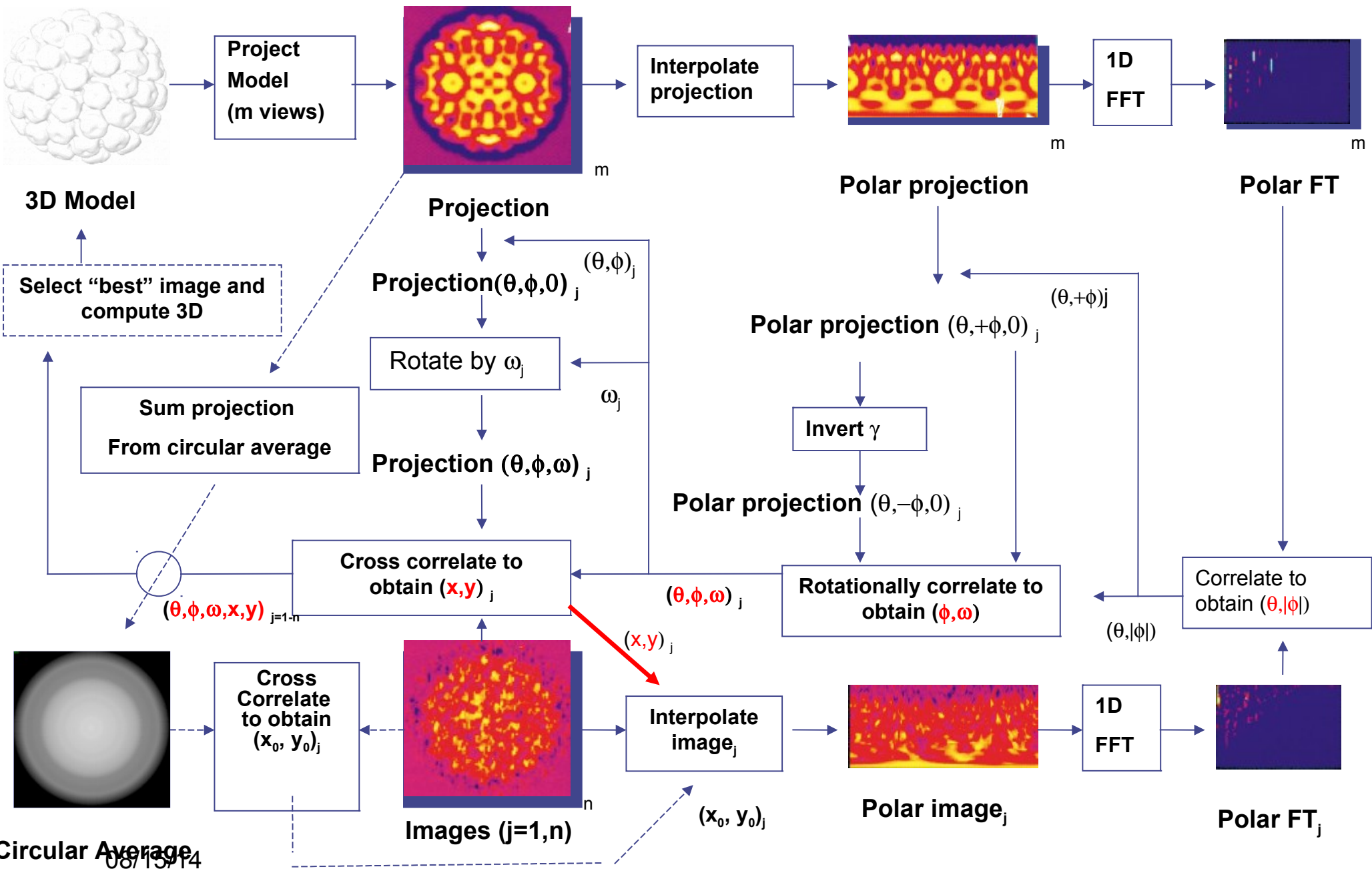


phasing with dual digital filters

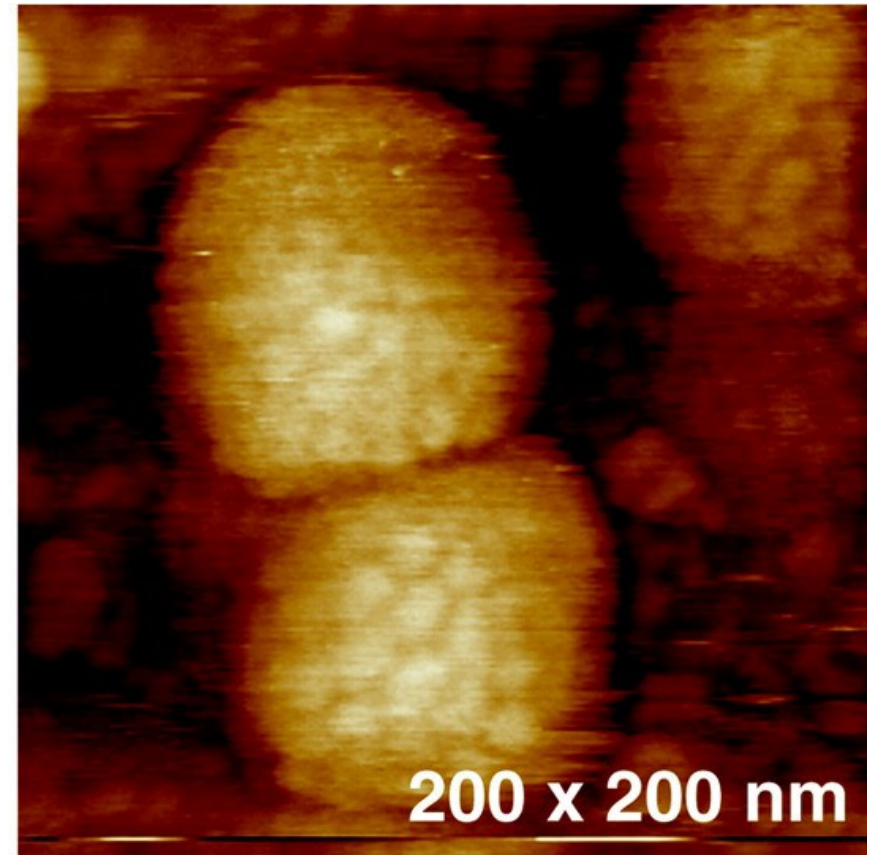
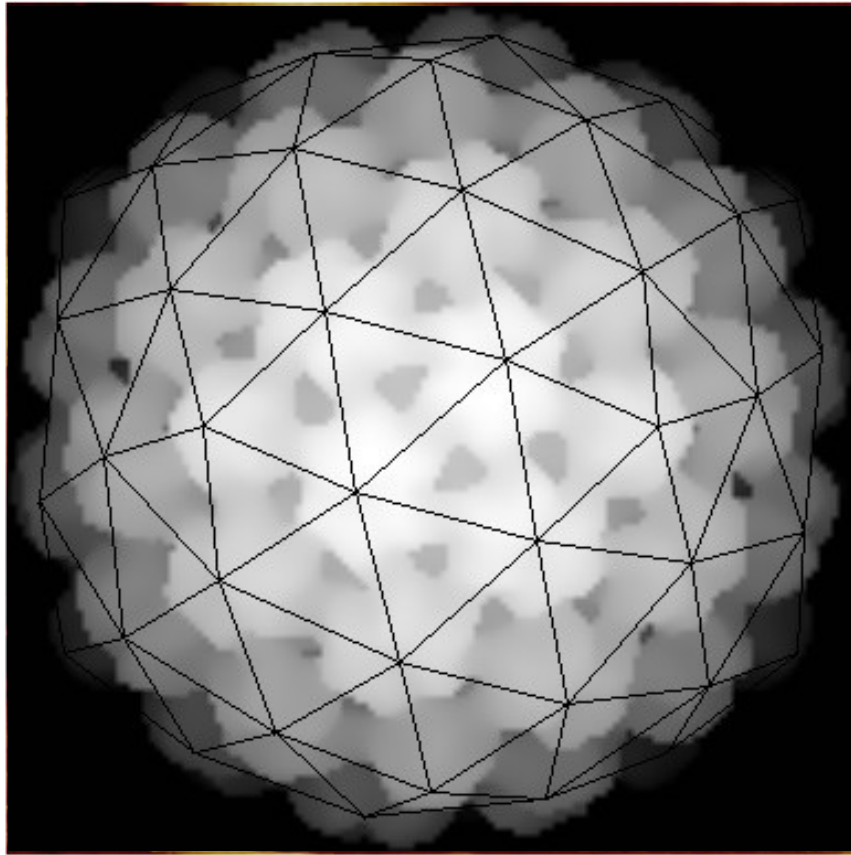
Image alignment via Polar Fourier Transform



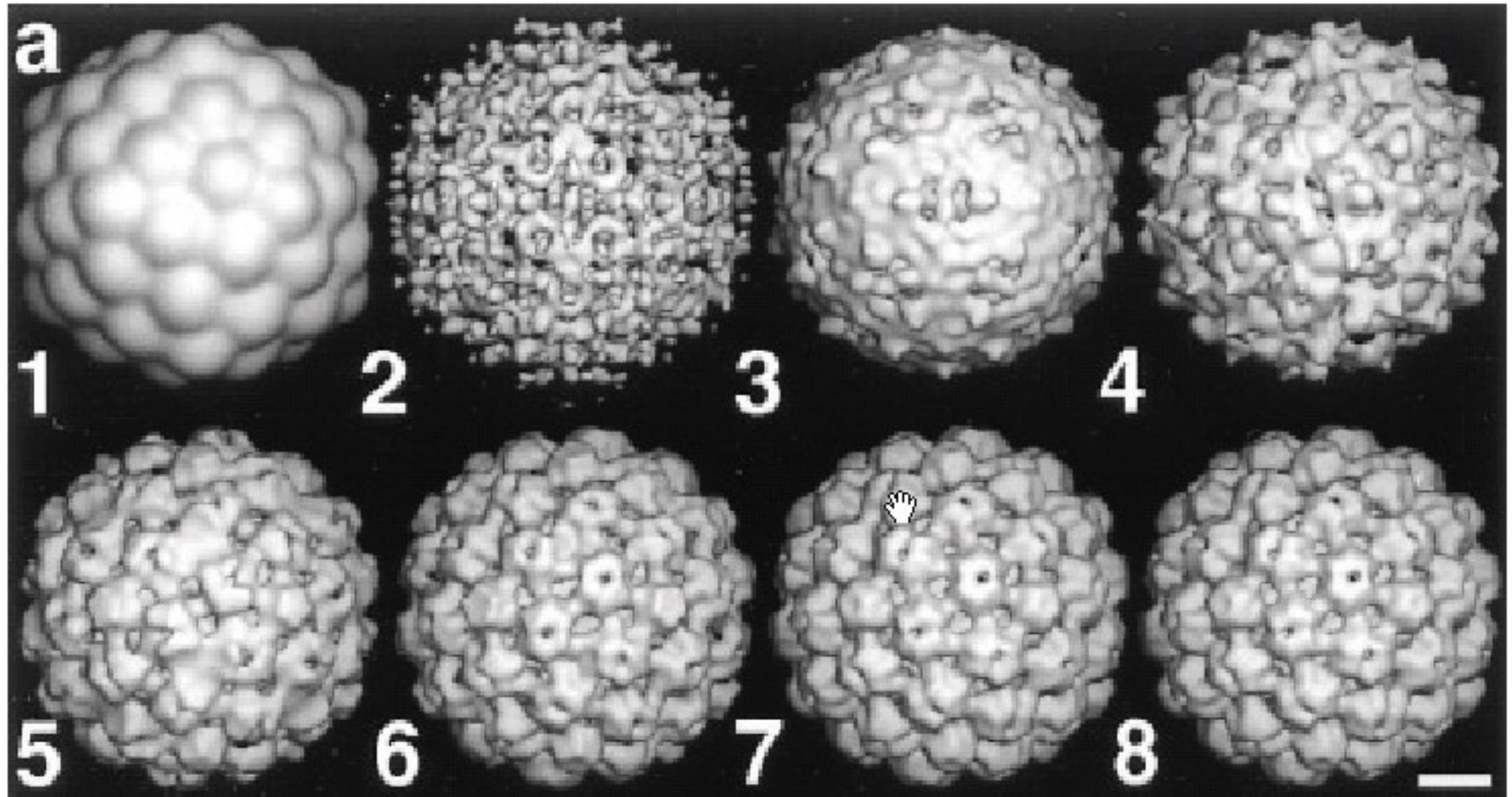
Algorithms of double transforms



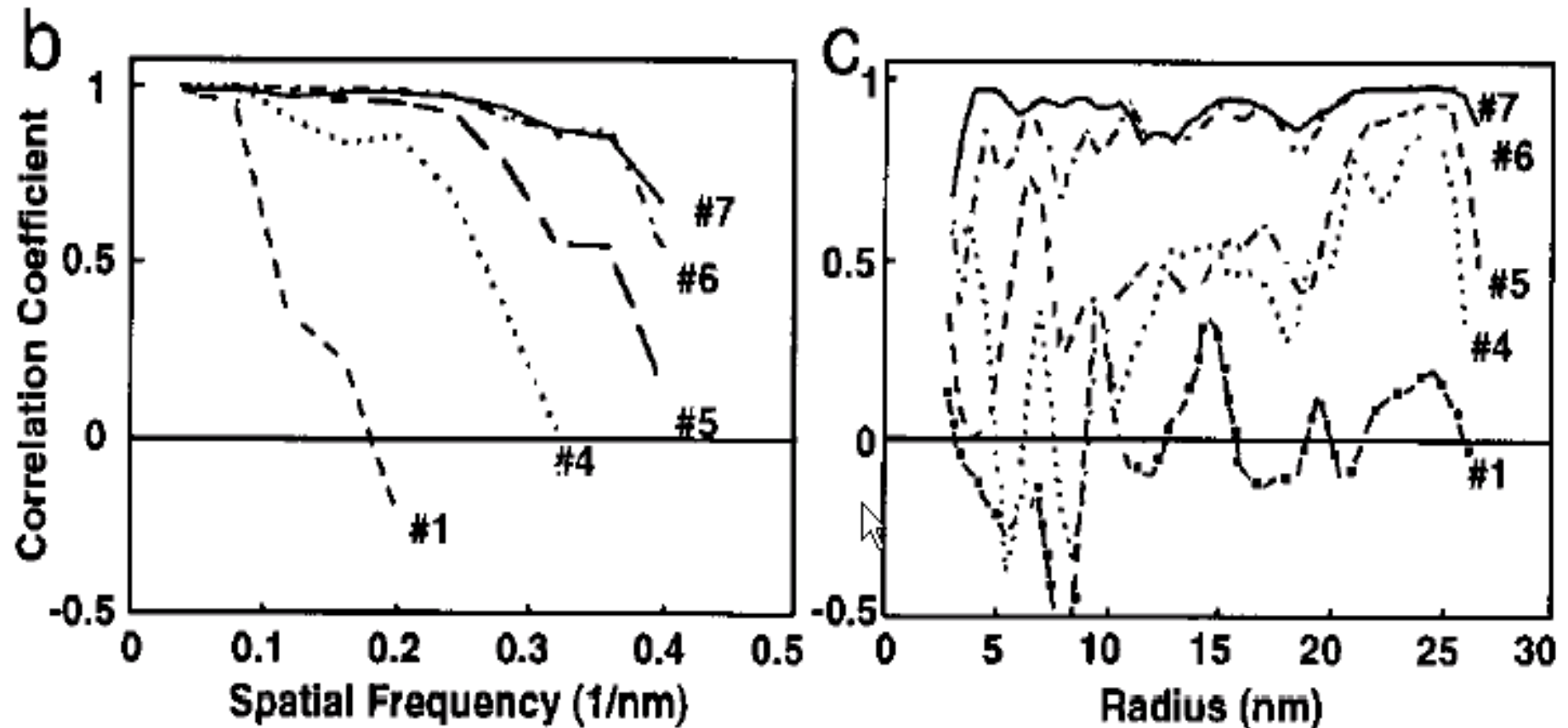
stained image can only show topological features — e.g. AFM



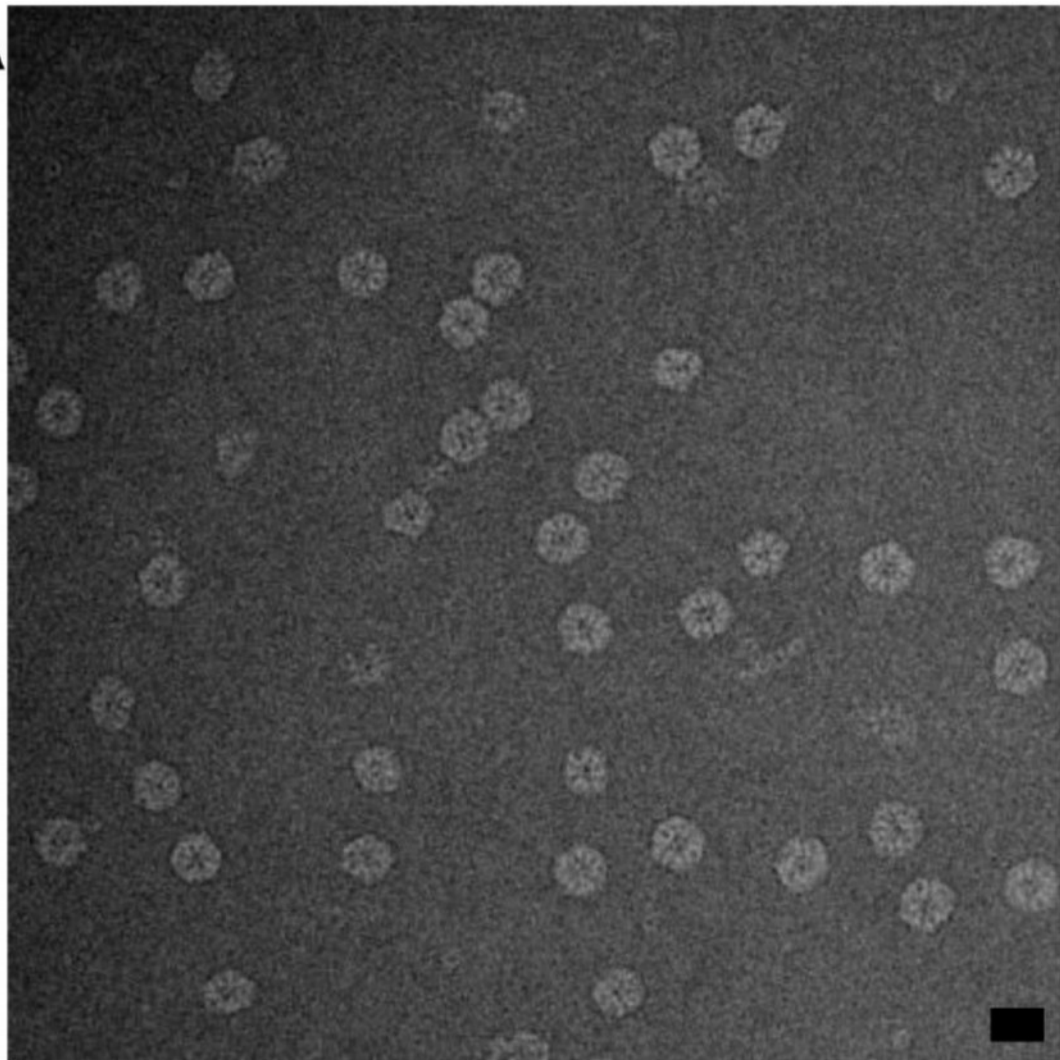
Build model from symmetry lattice



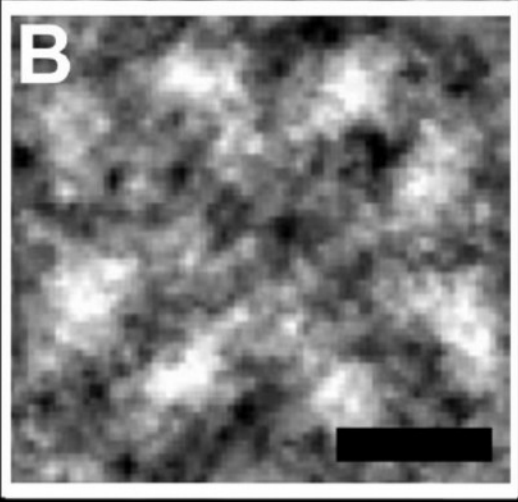
Monitor in both Fourier & real spaces



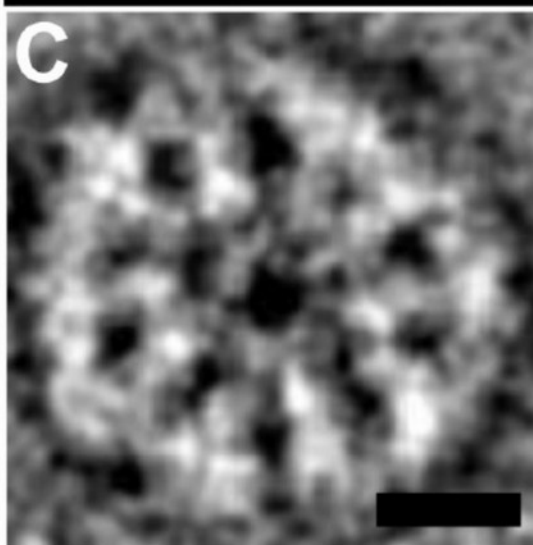
A



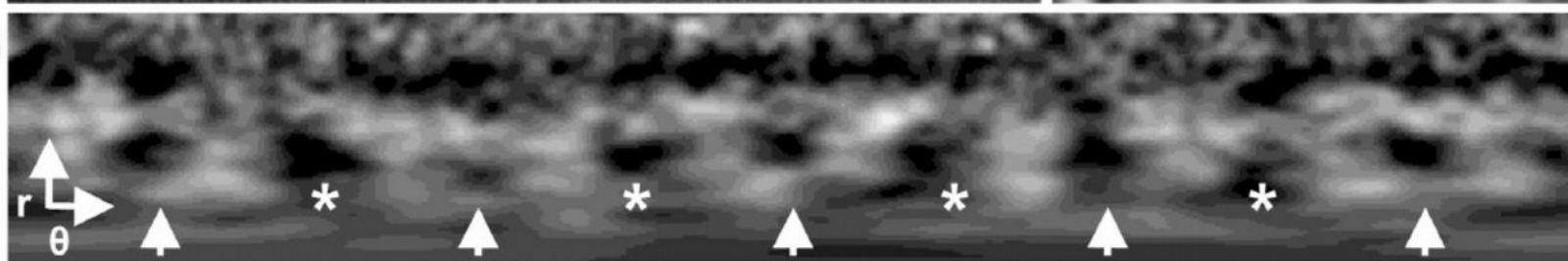
B



C

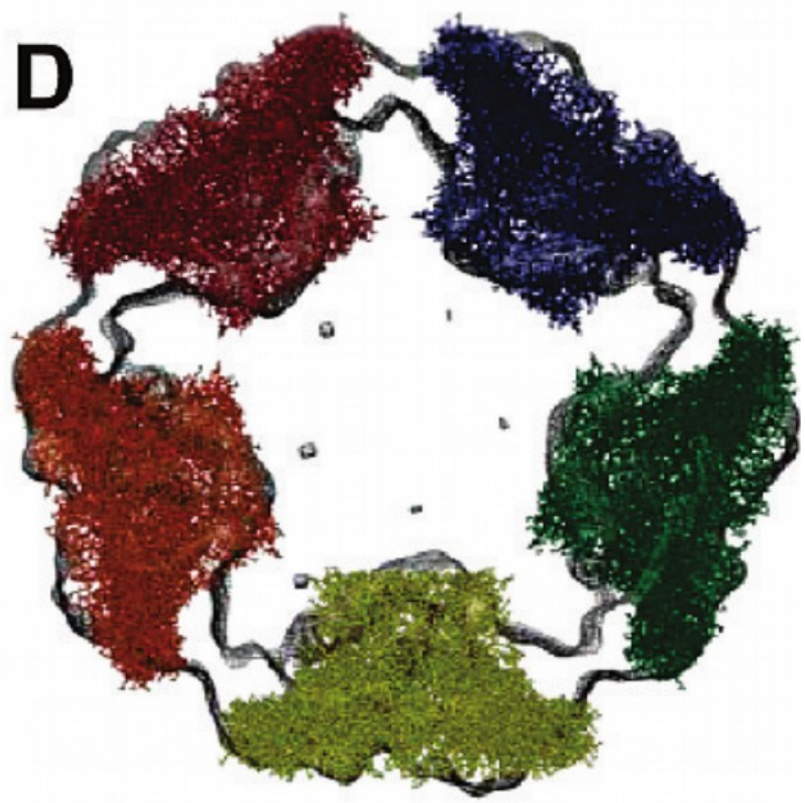
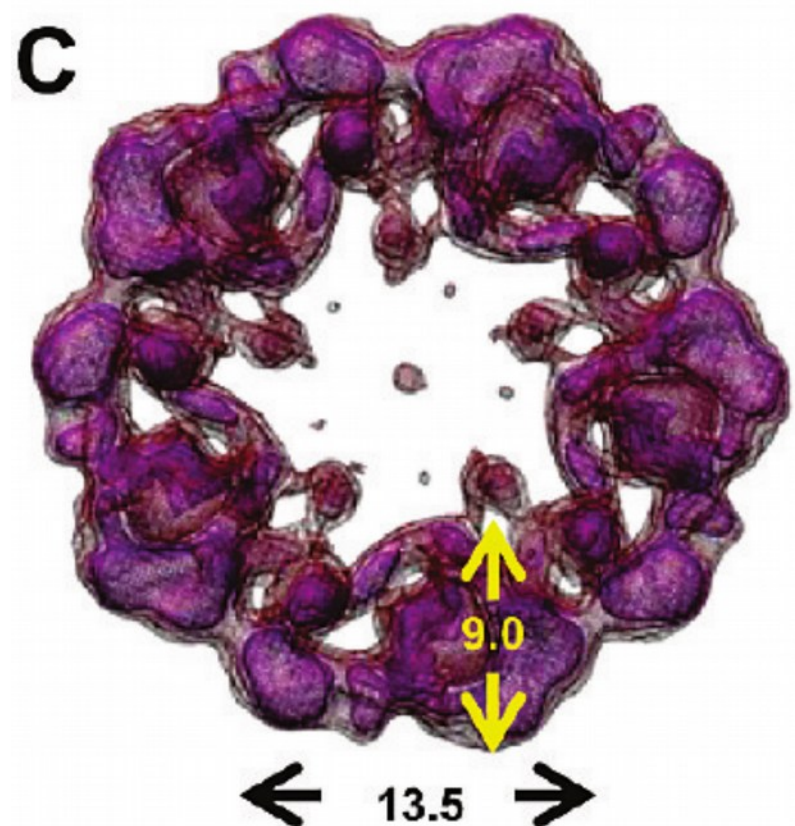
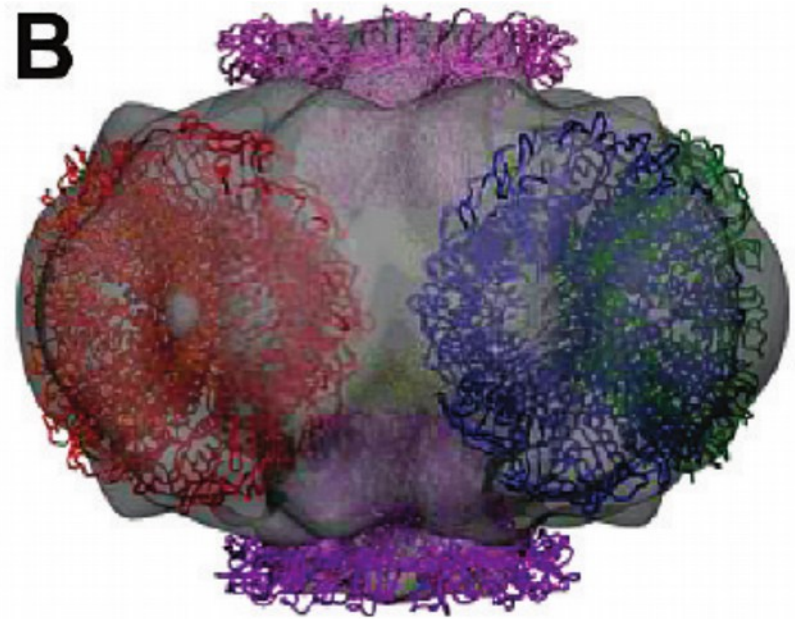
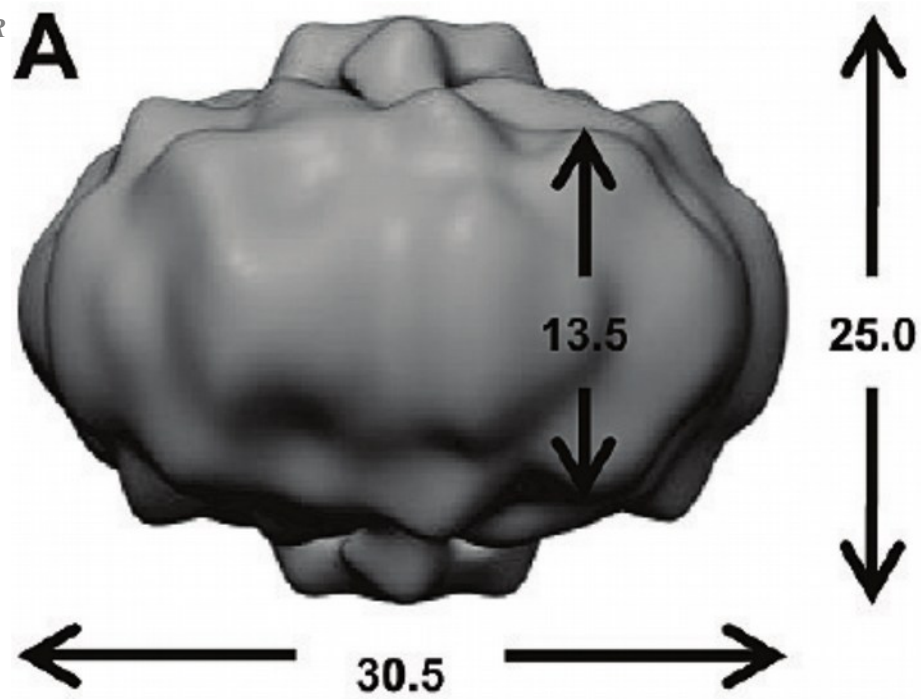


D



E

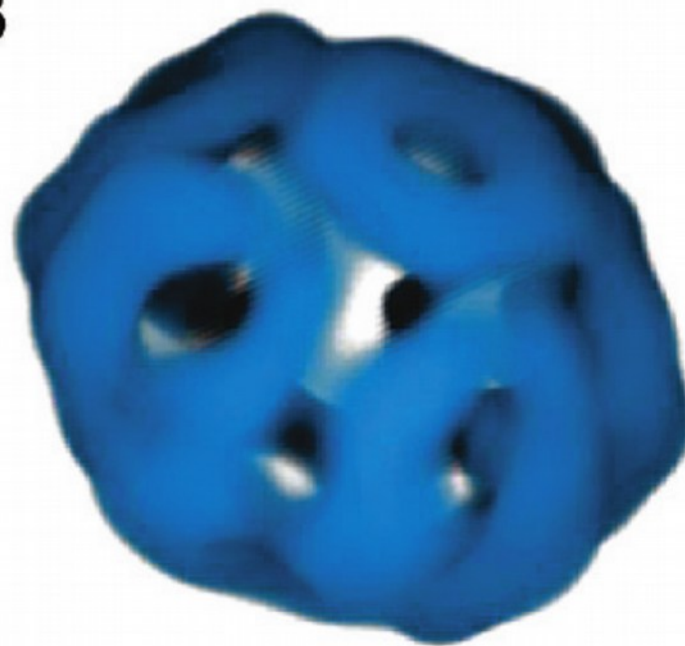




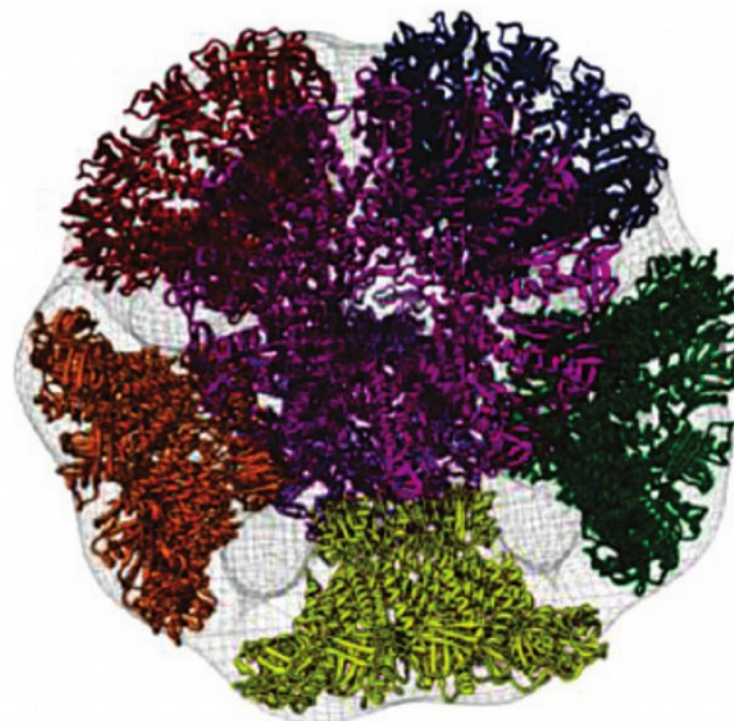
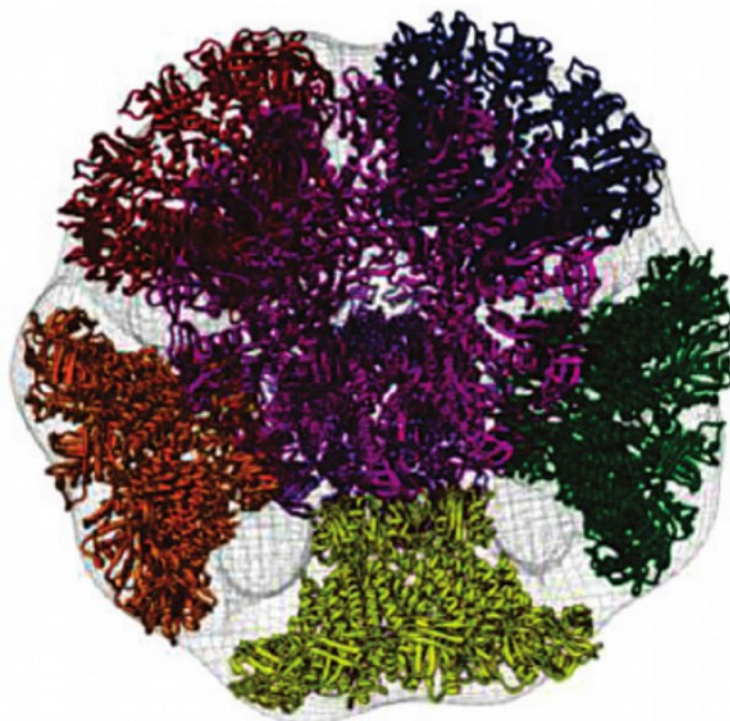
A

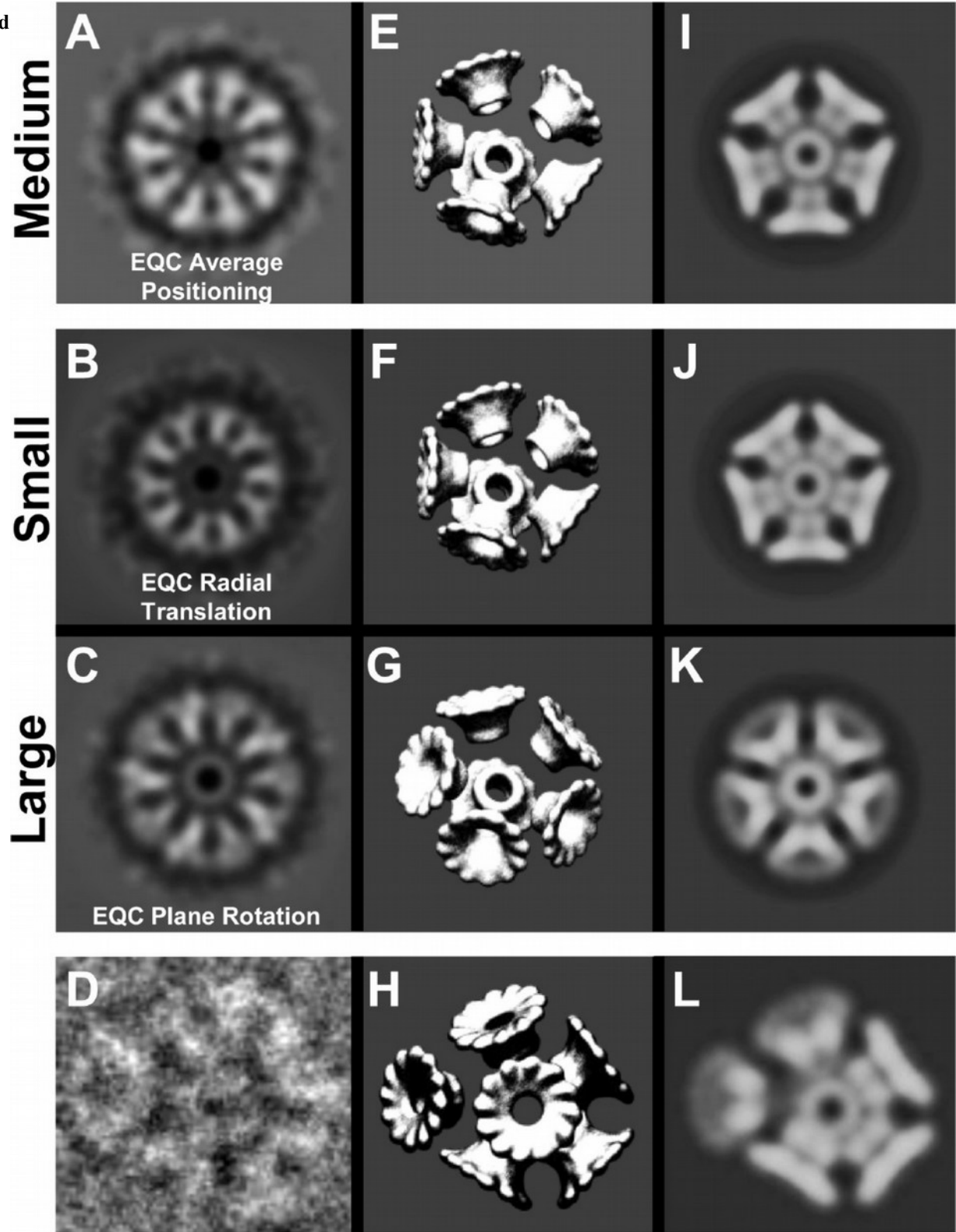


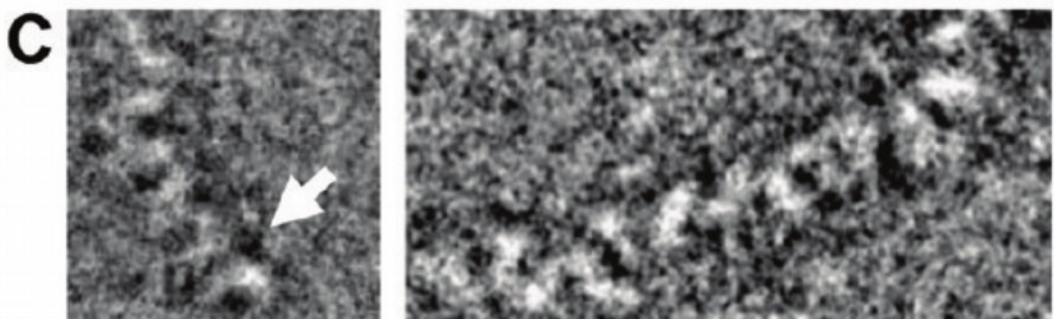
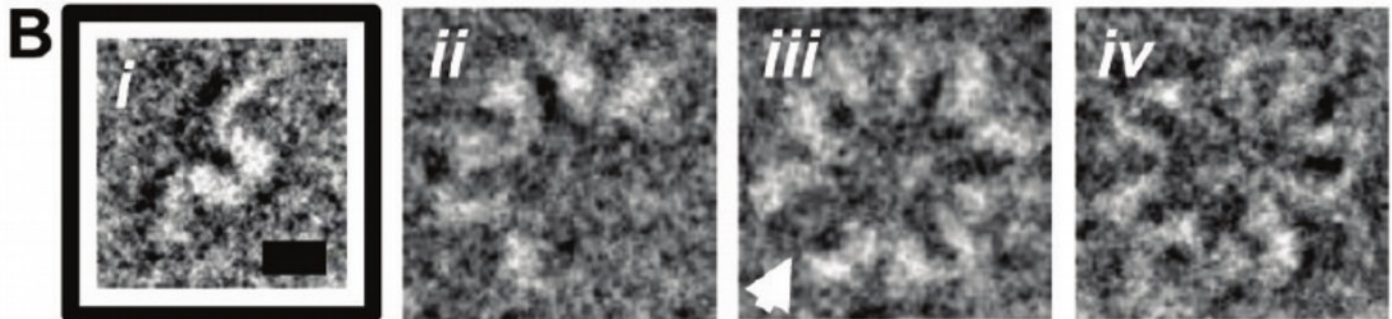
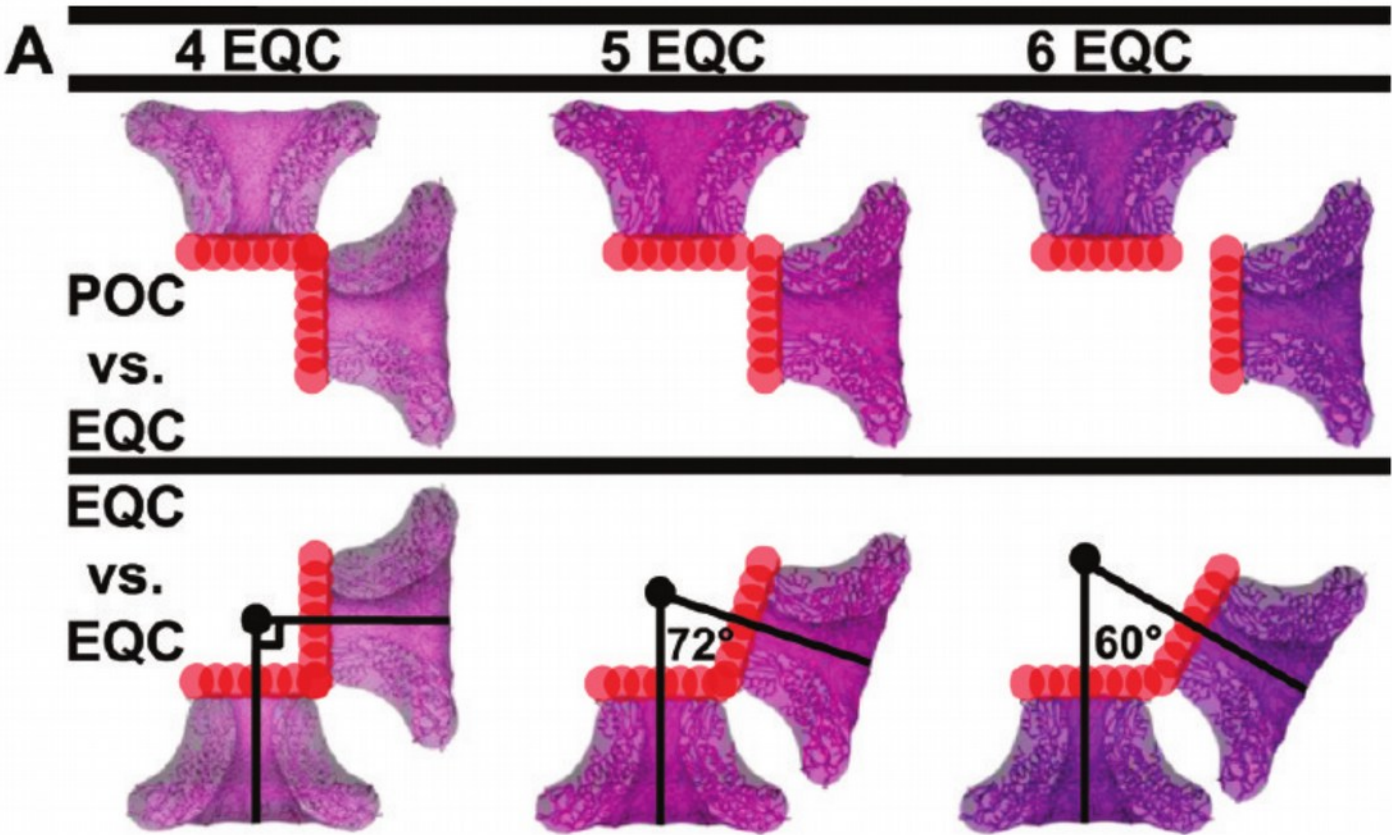
B

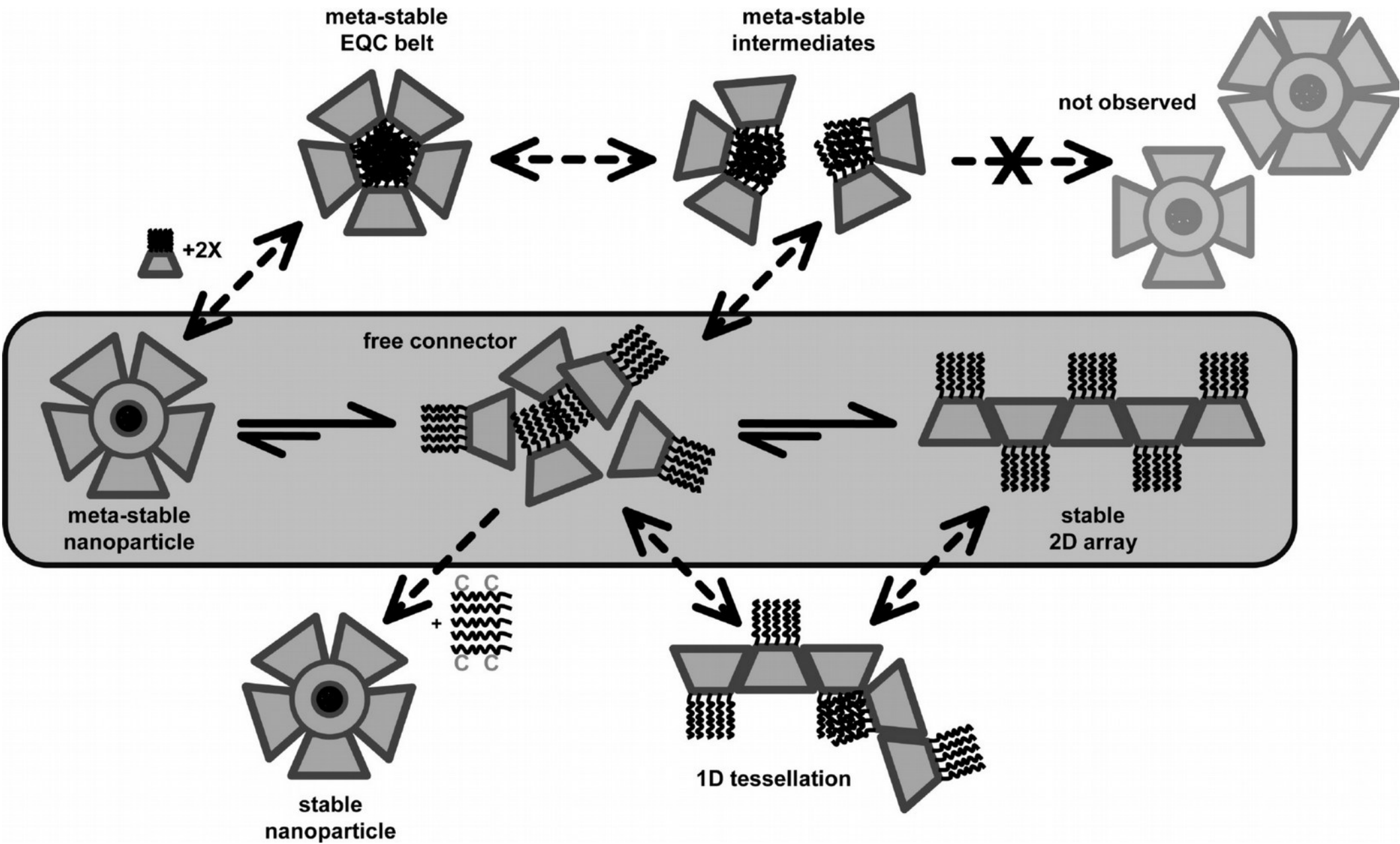


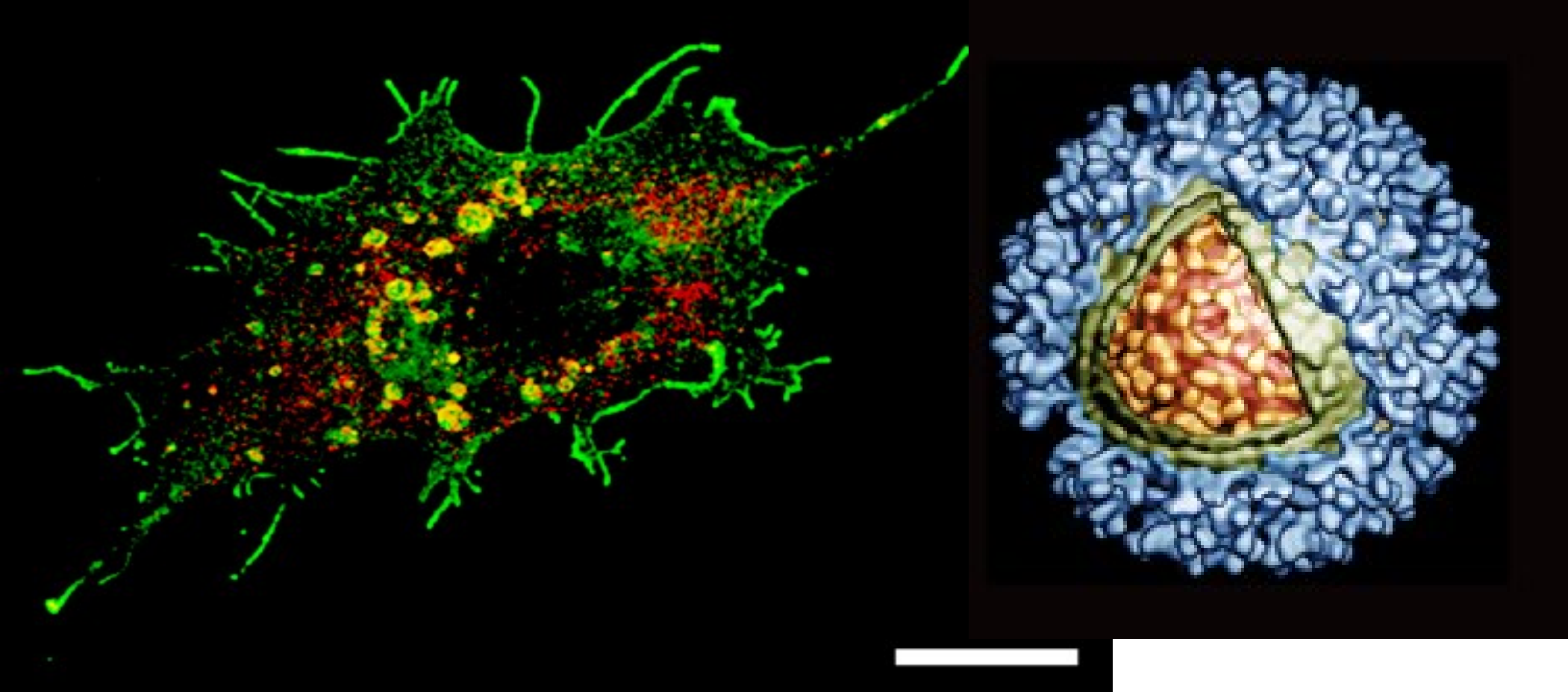
C











membrane-mediated sorting

Packaging cell line to deliver vaccines

Relearn from virus infection



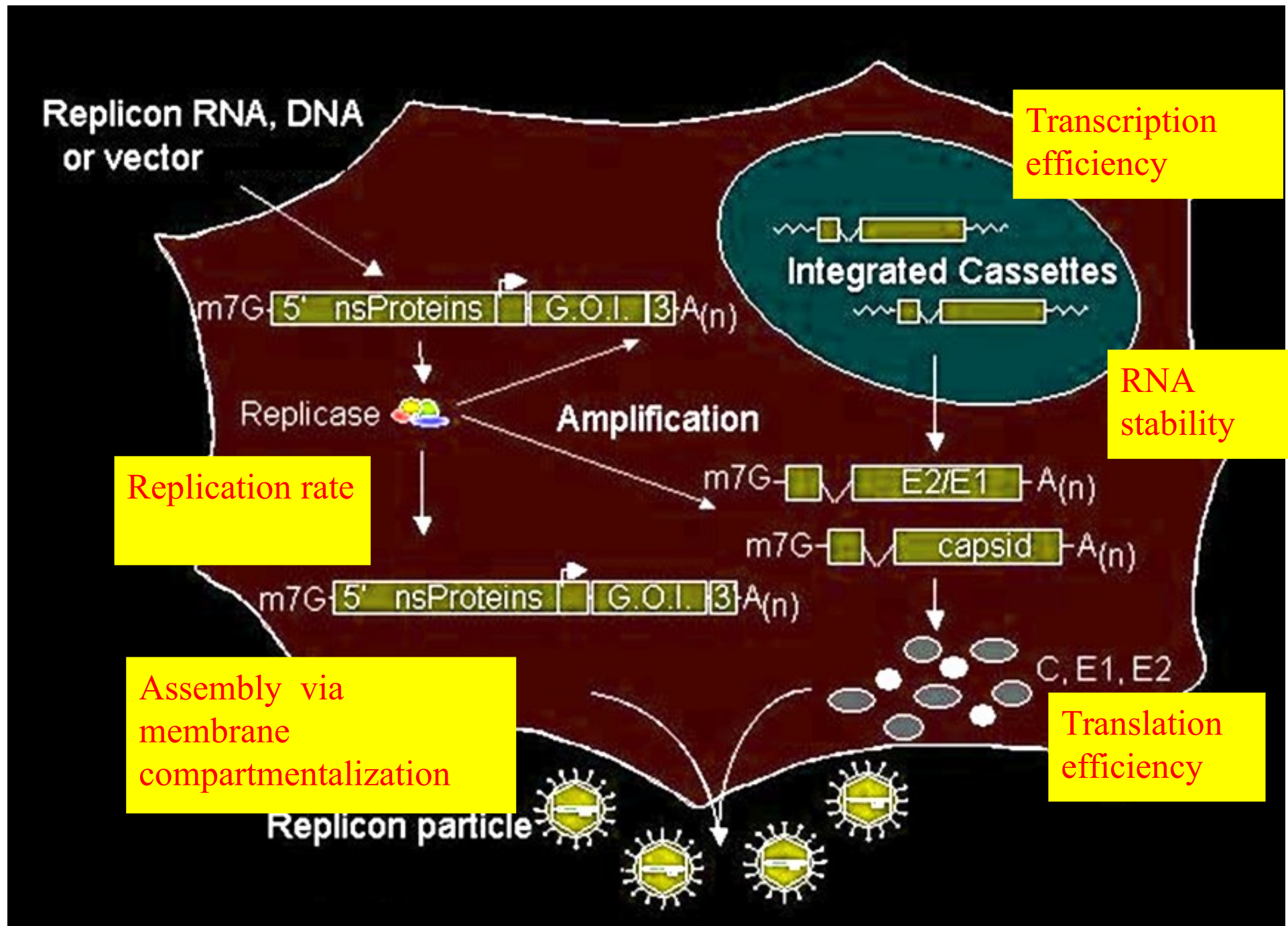
US20120301494 A1 (2012)

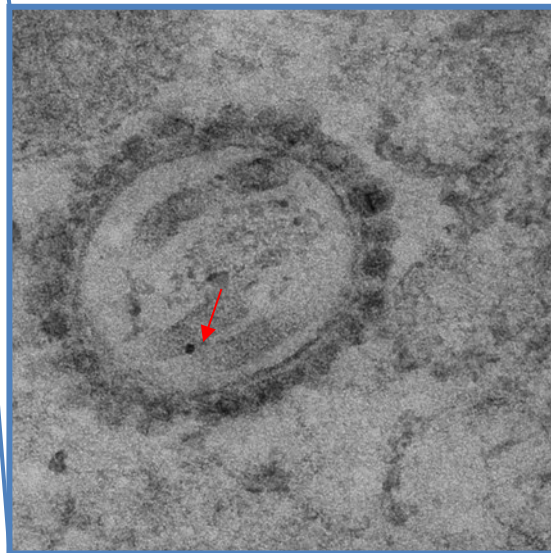
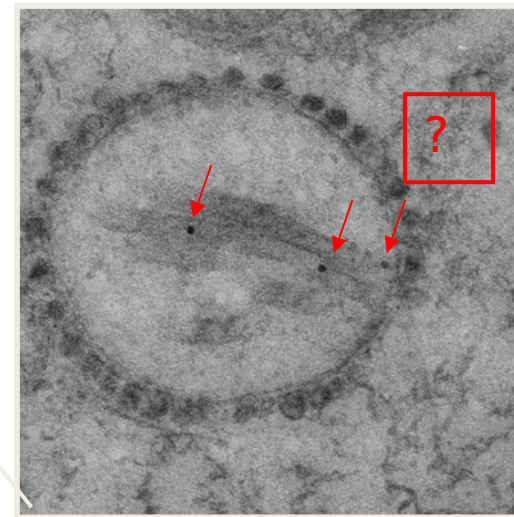
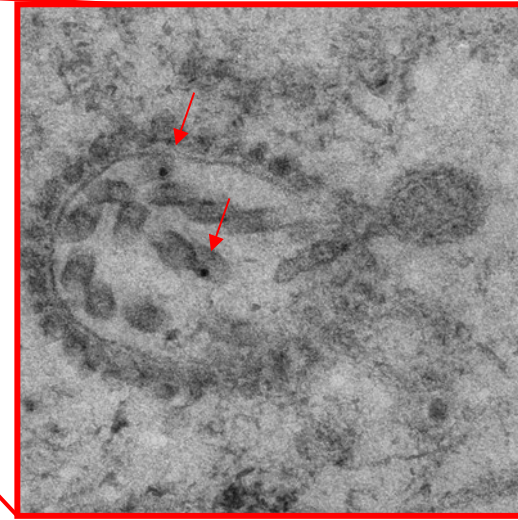
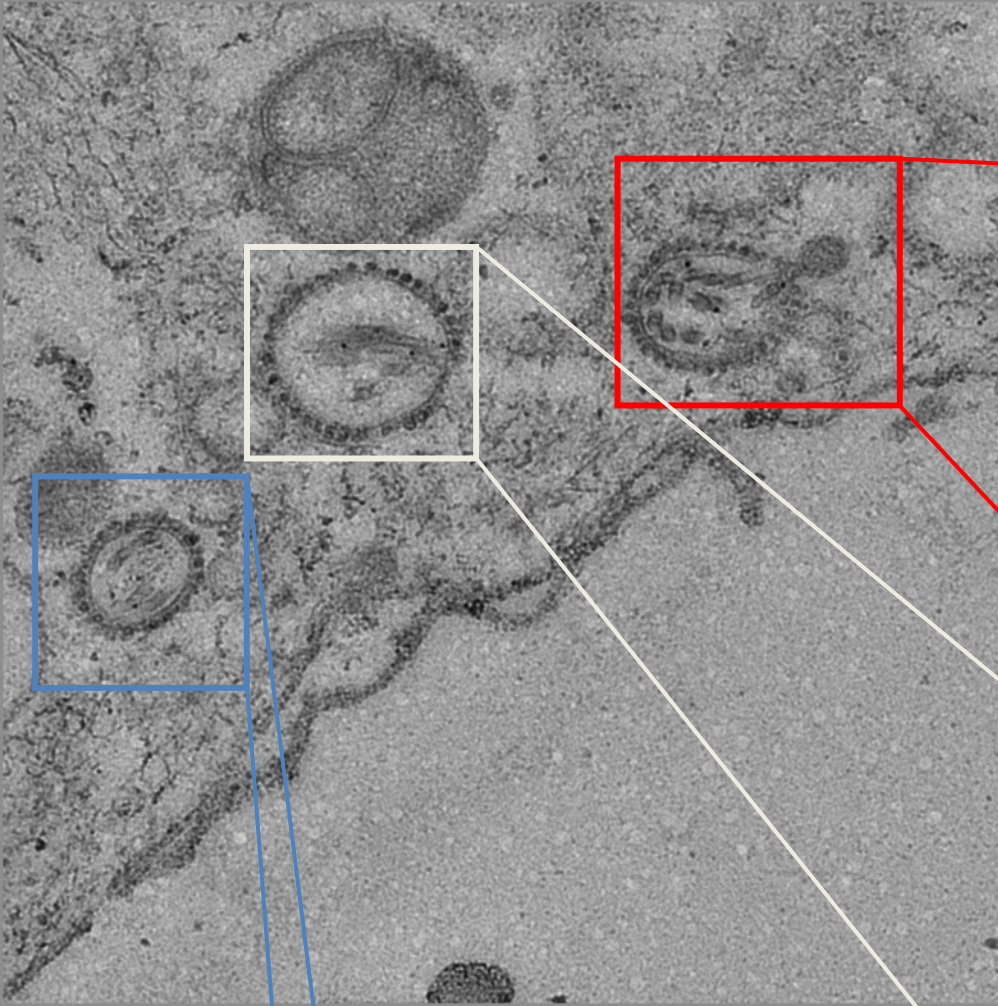
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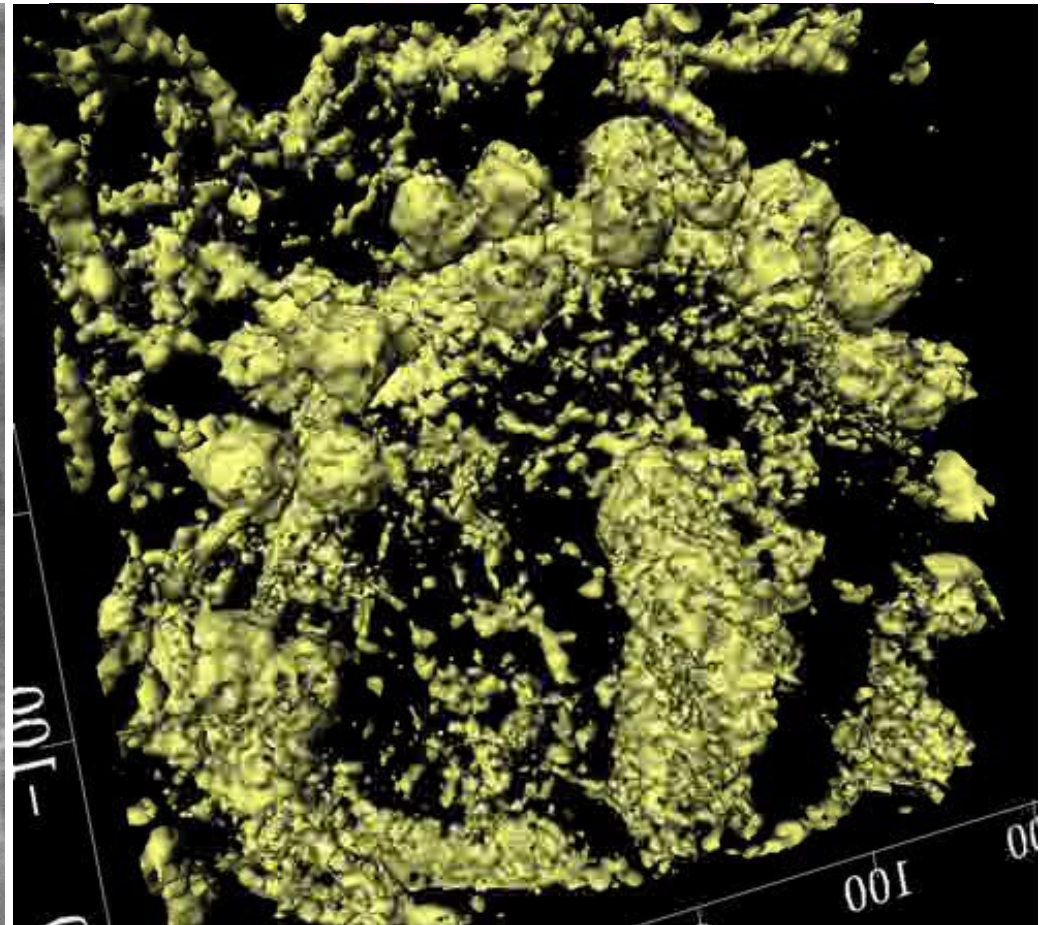
PCL engineering to produce vaccine





2001: *Microsc Microanal*, 7S, 104 (Cheng R.H.)
2010: PCL vaccine application (Soonsawad et al)

cytopathic vacuole - II / RNP & tubes

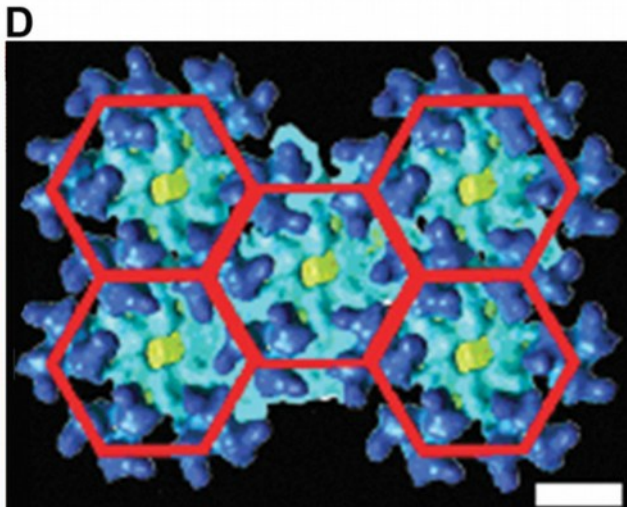
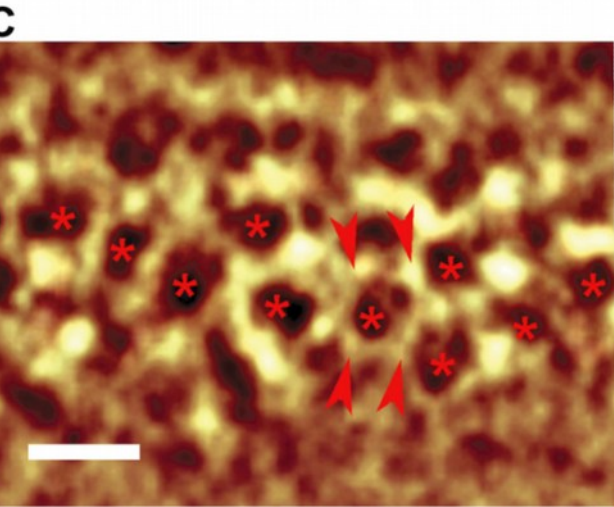
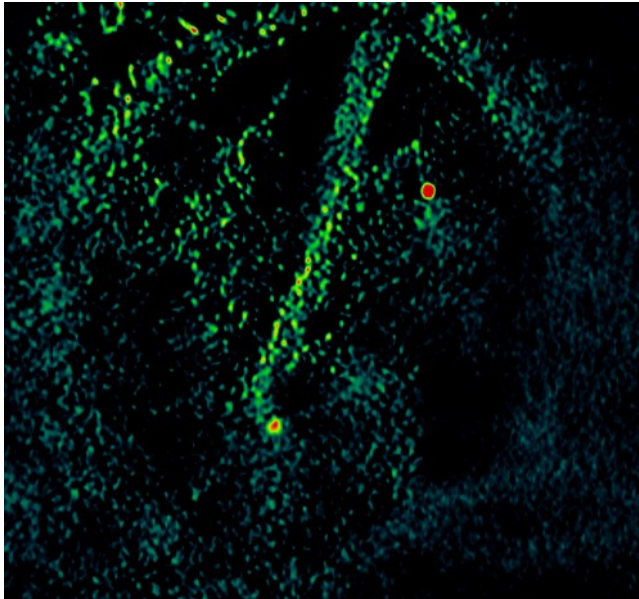
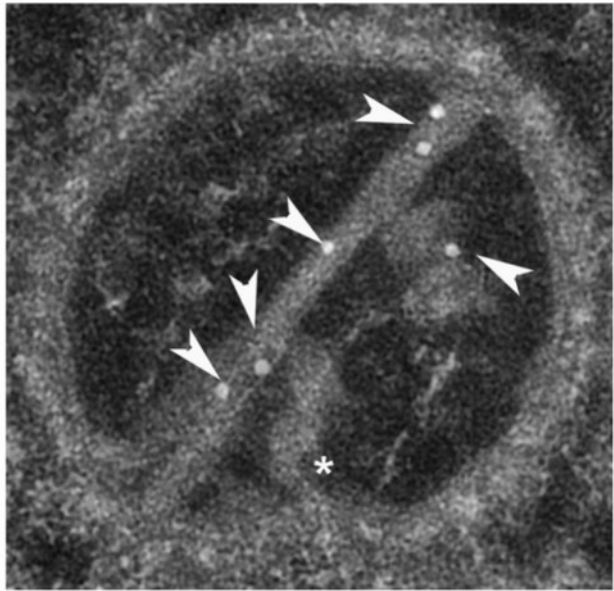
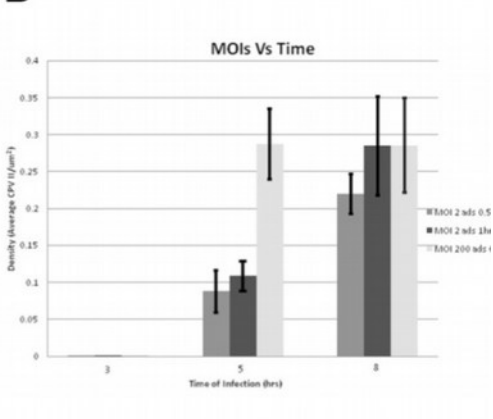
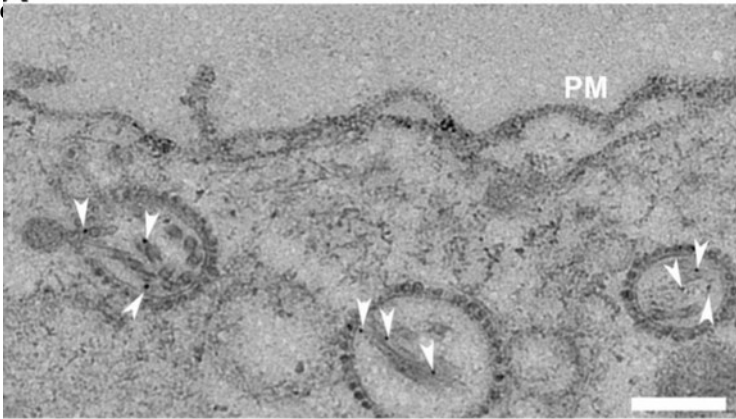


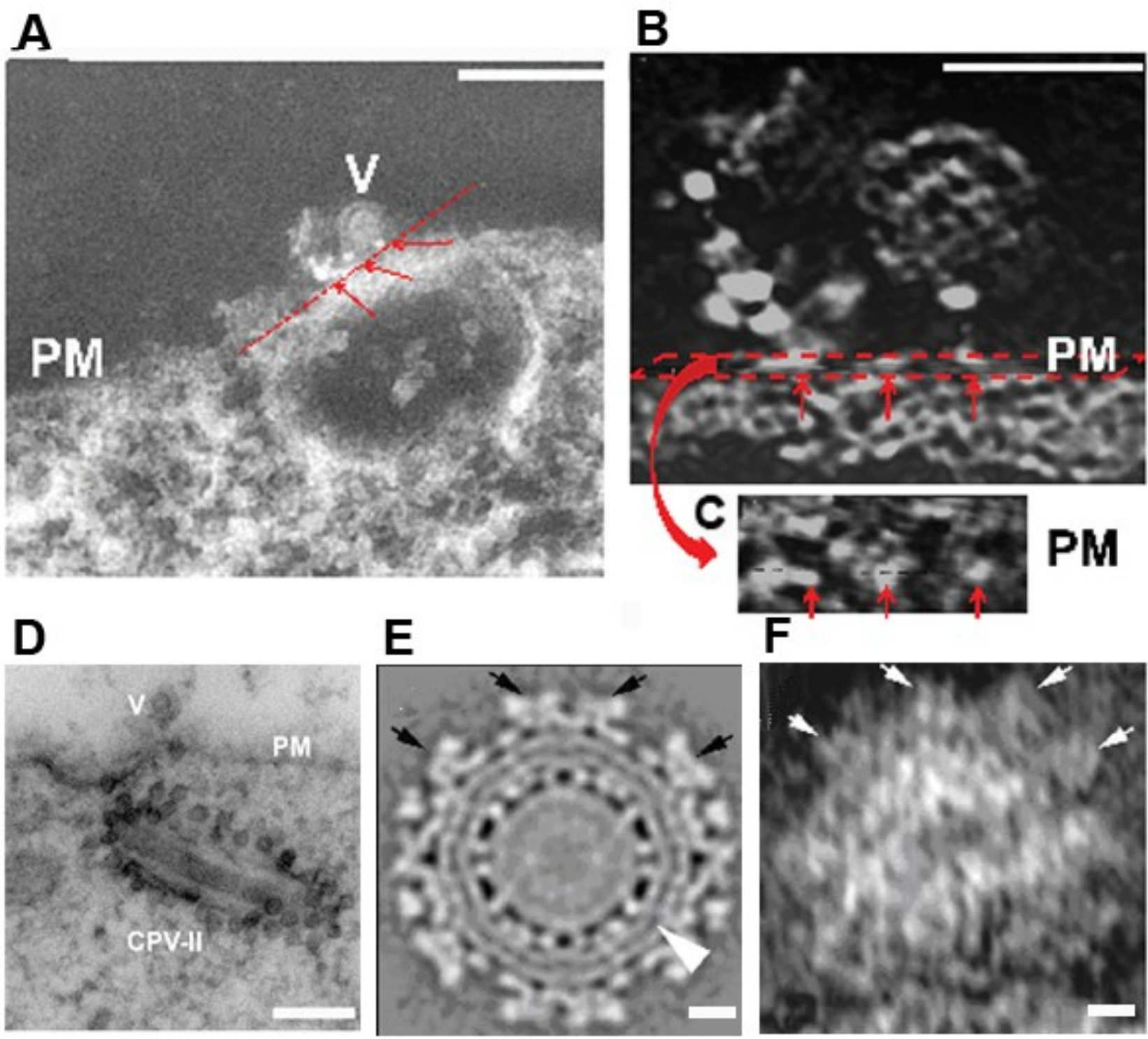
Microsc Microanal, 2001

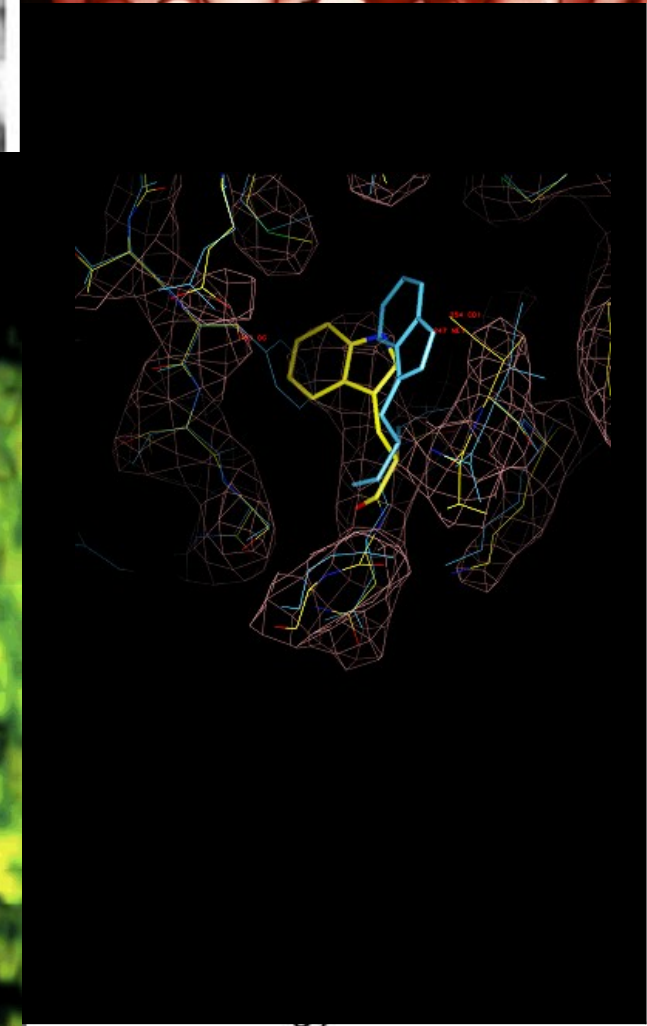
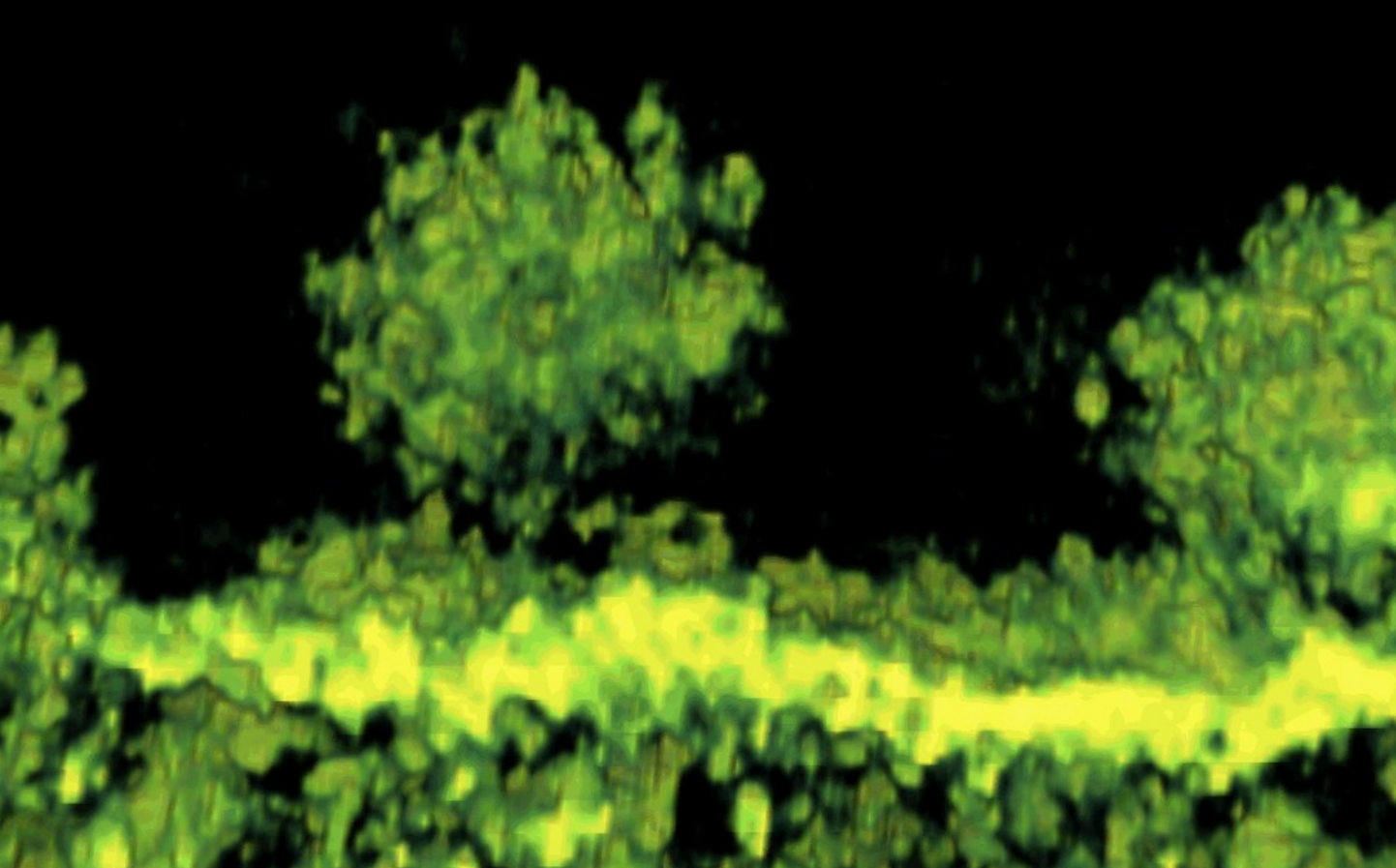
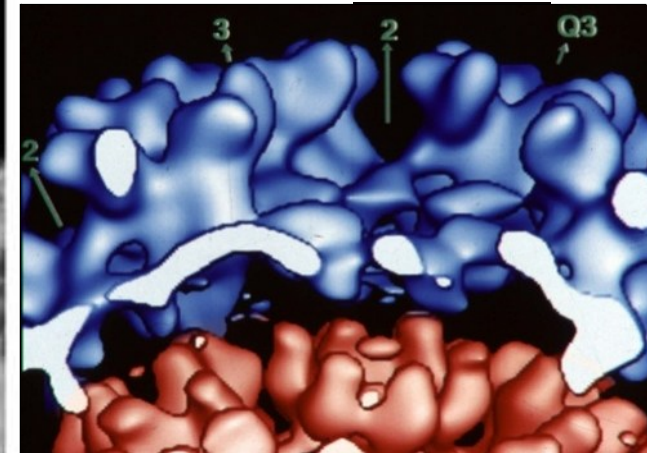
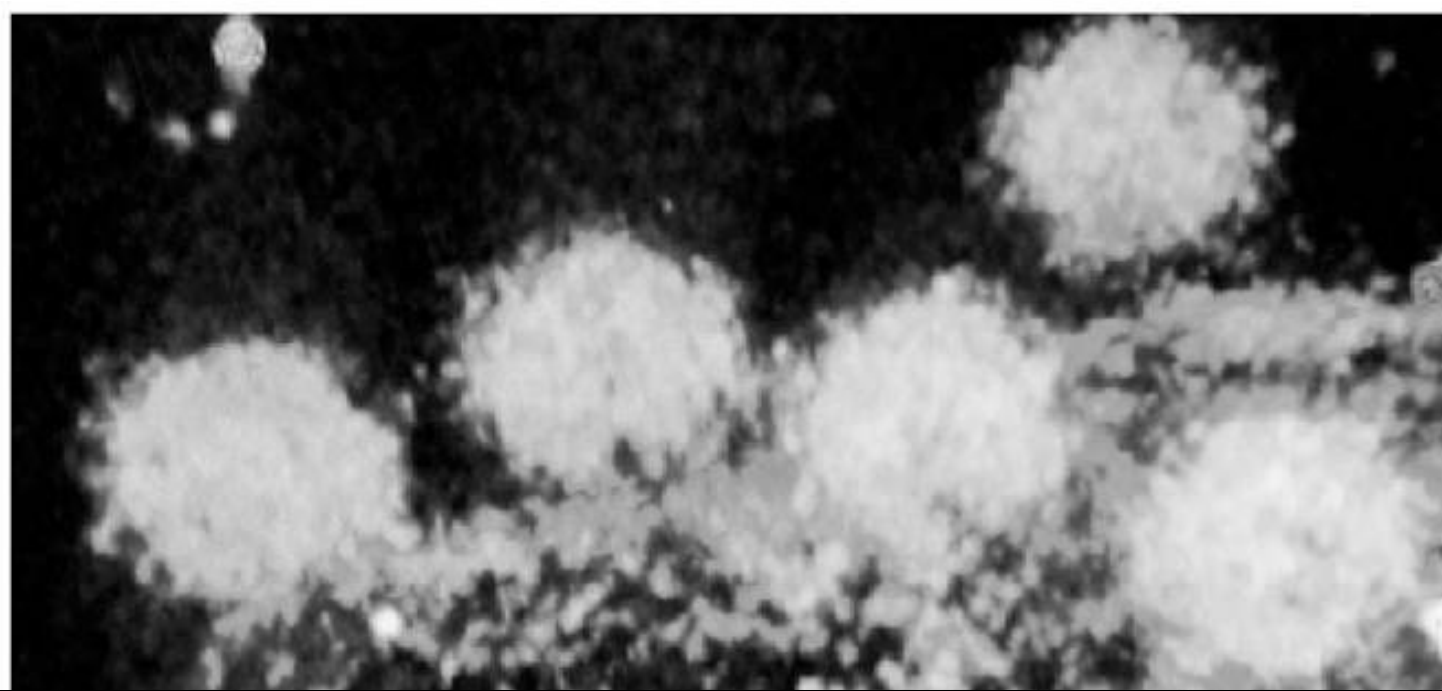


US20120301494 A1 (2012)
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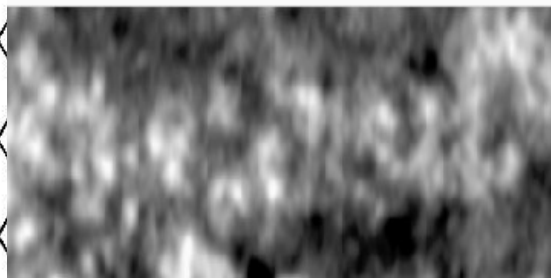
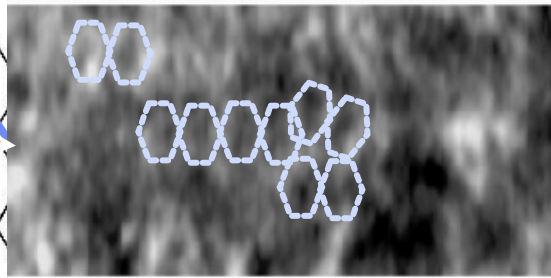
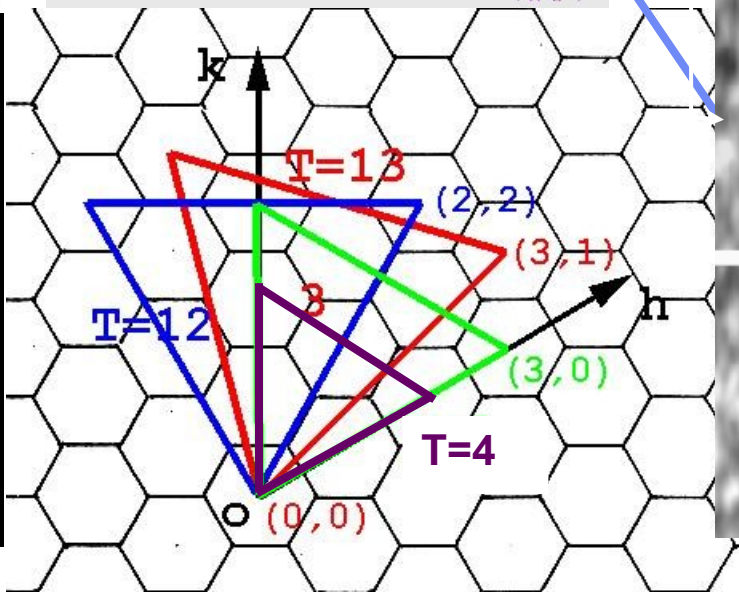
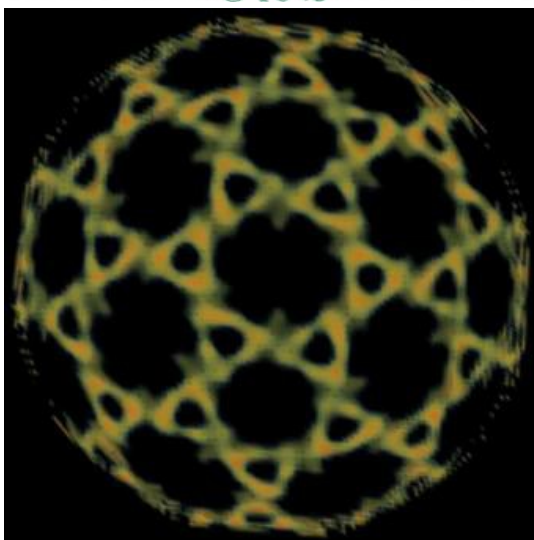
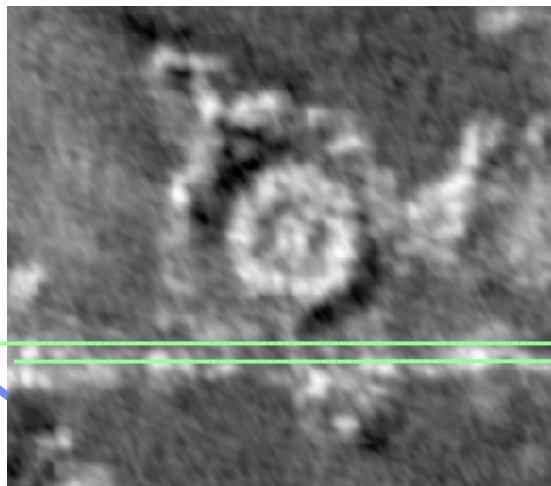
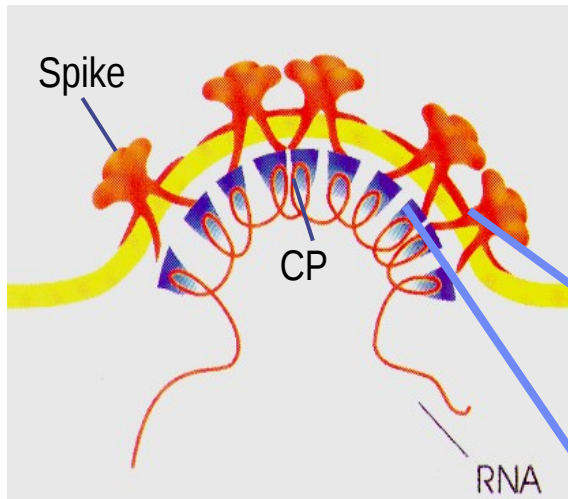
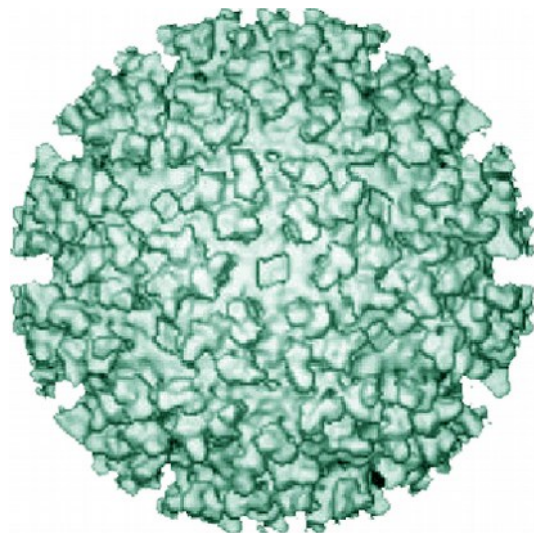
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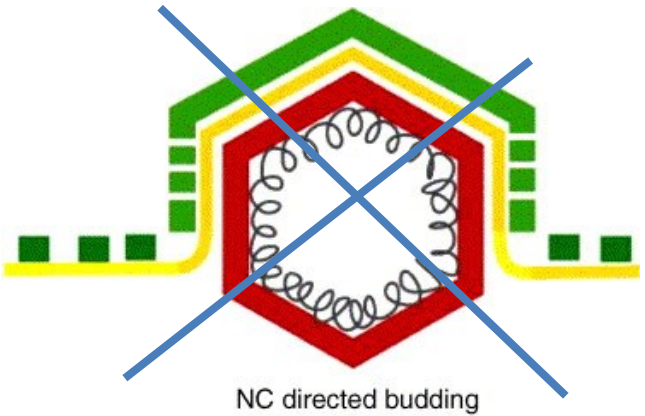
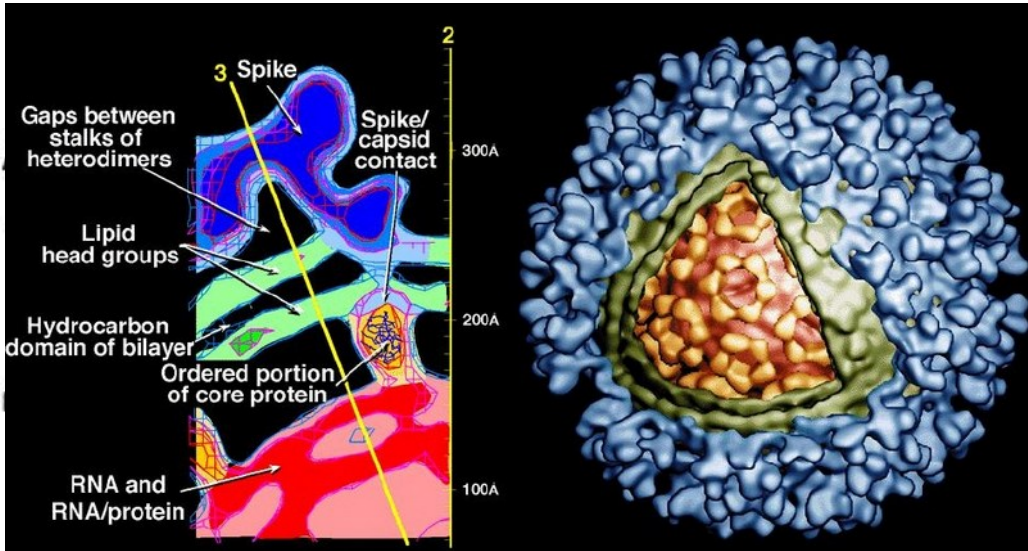


assembly along the cellular membrane

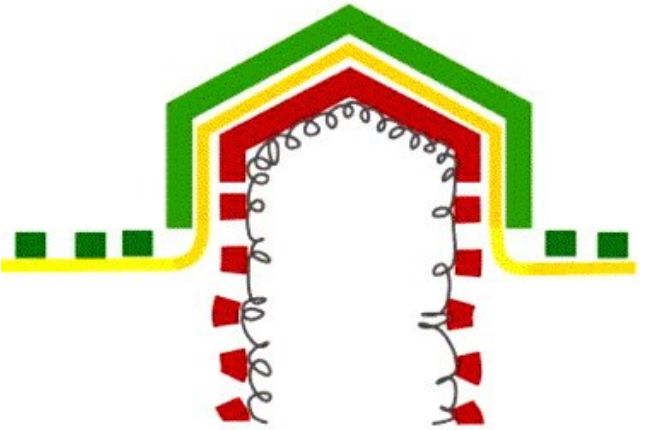
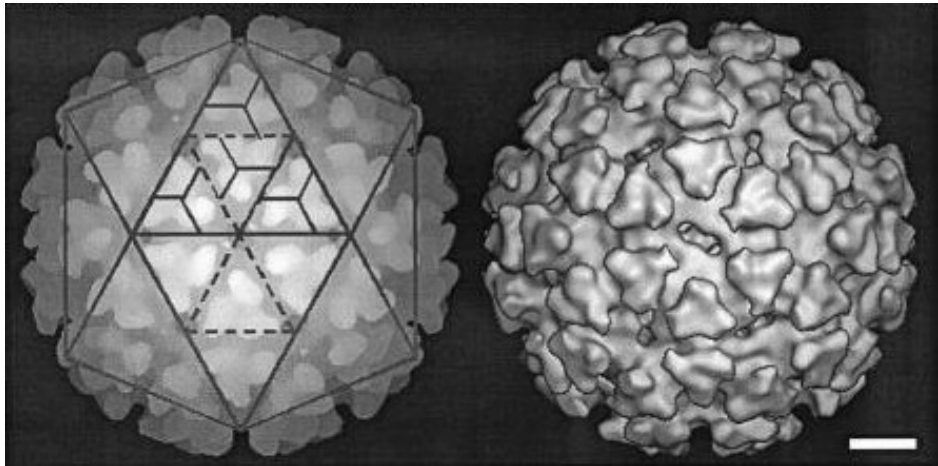




Conformational changes in viral assembly



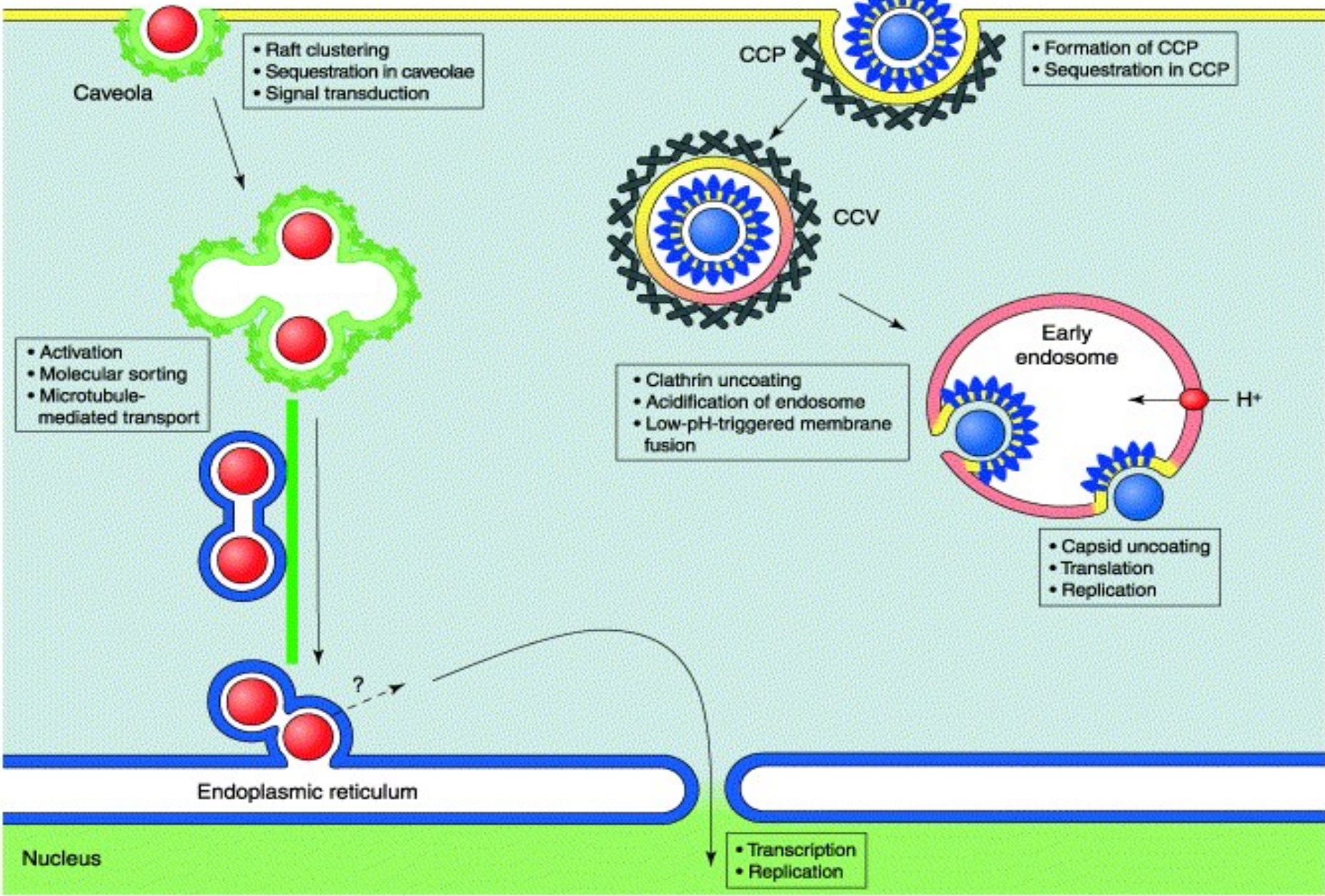
NC directed budding



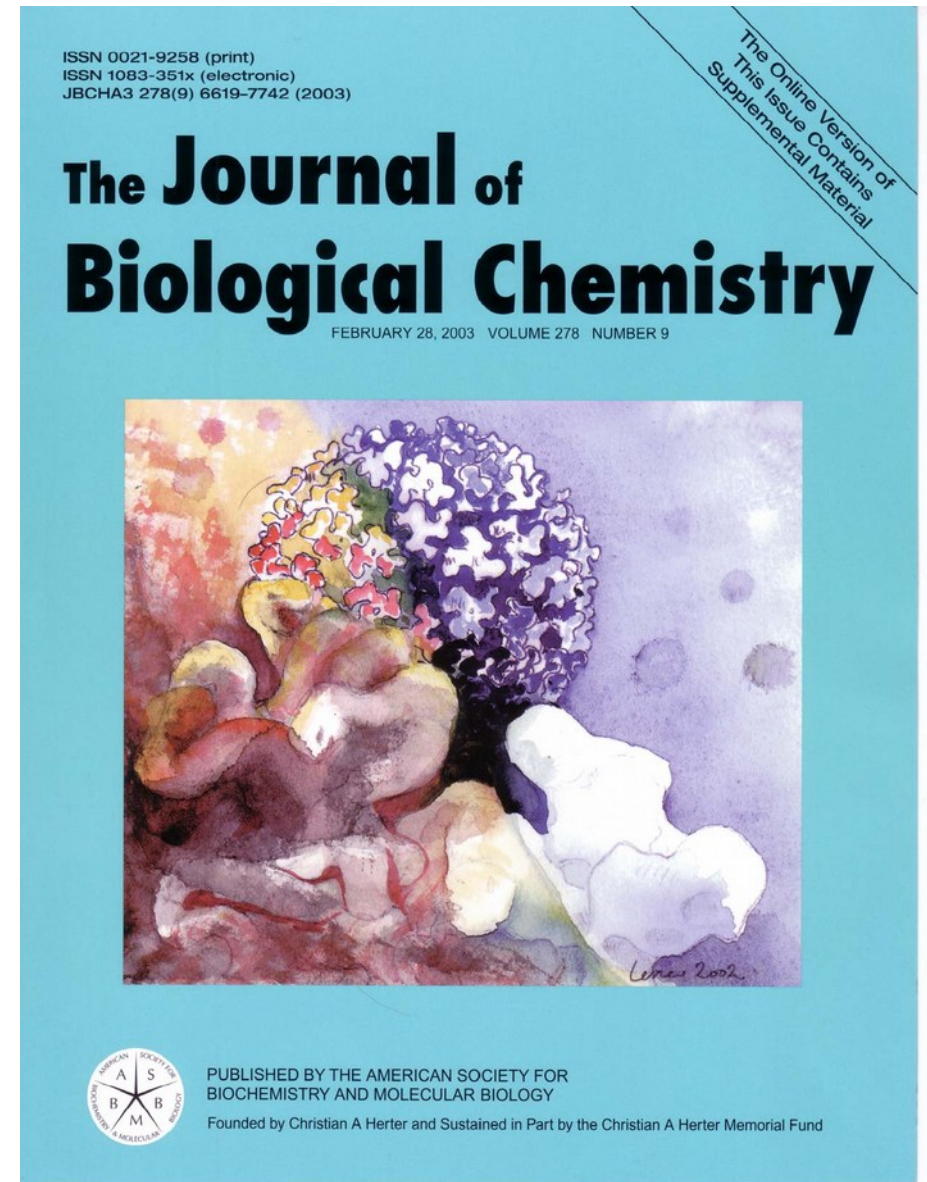
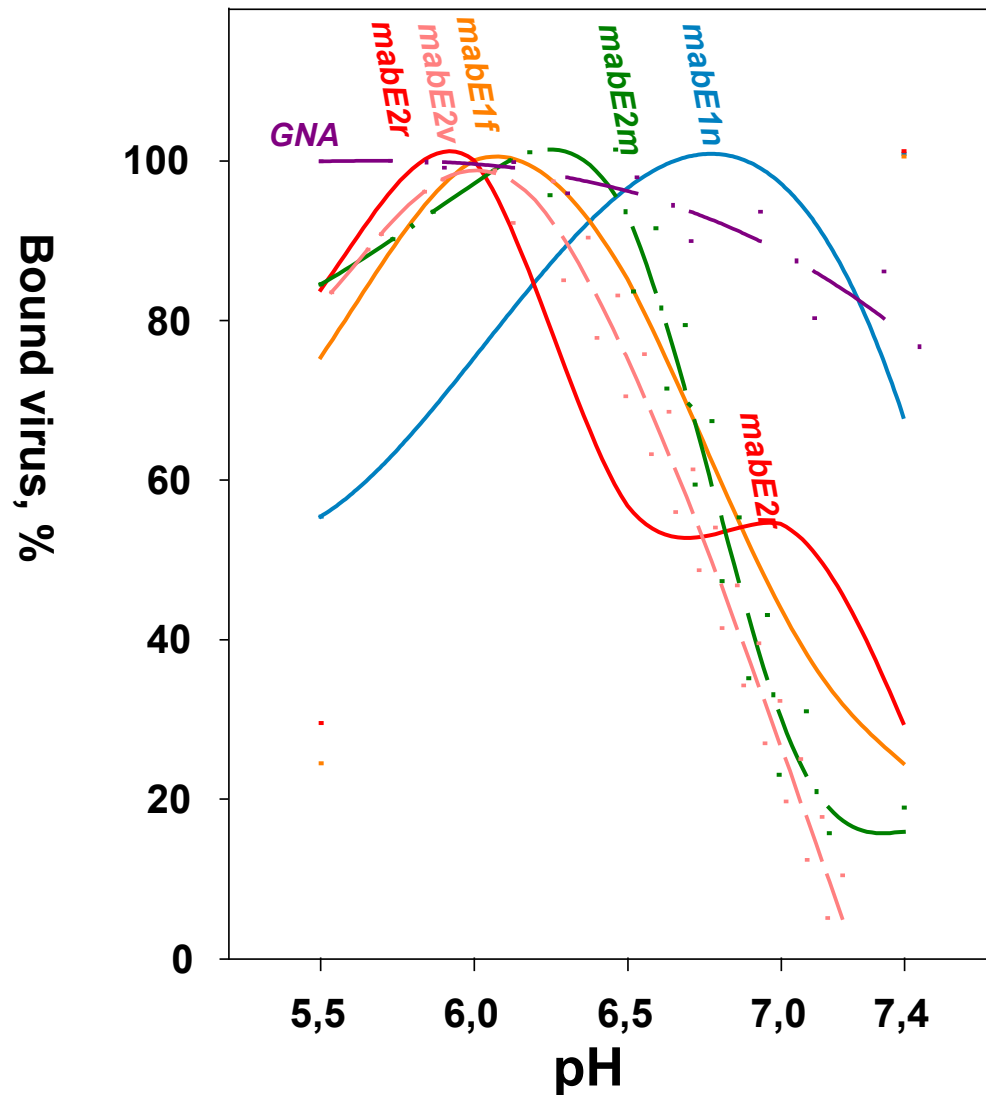
Glycoprotein directed budding

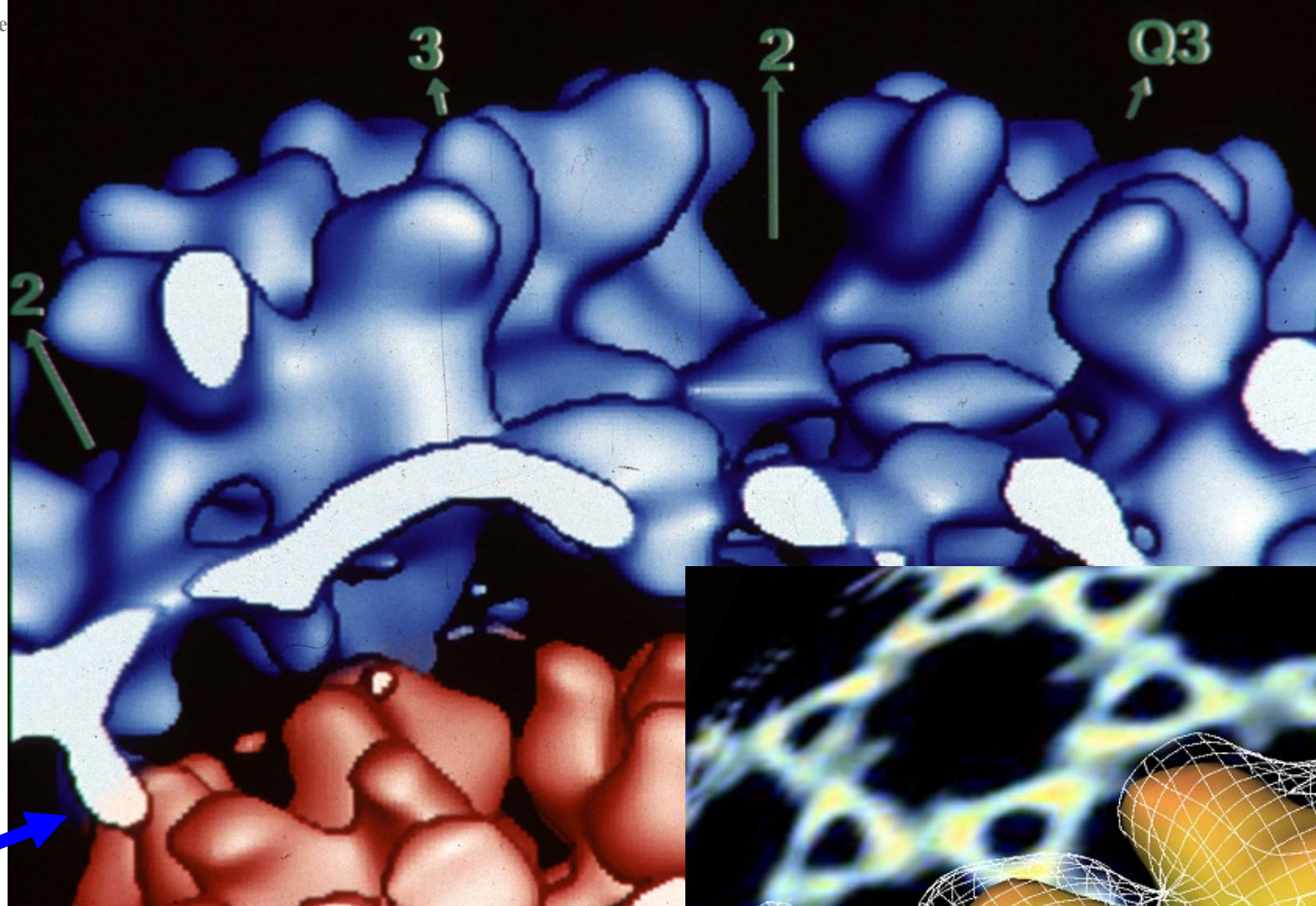
Echovirus 1

SFV

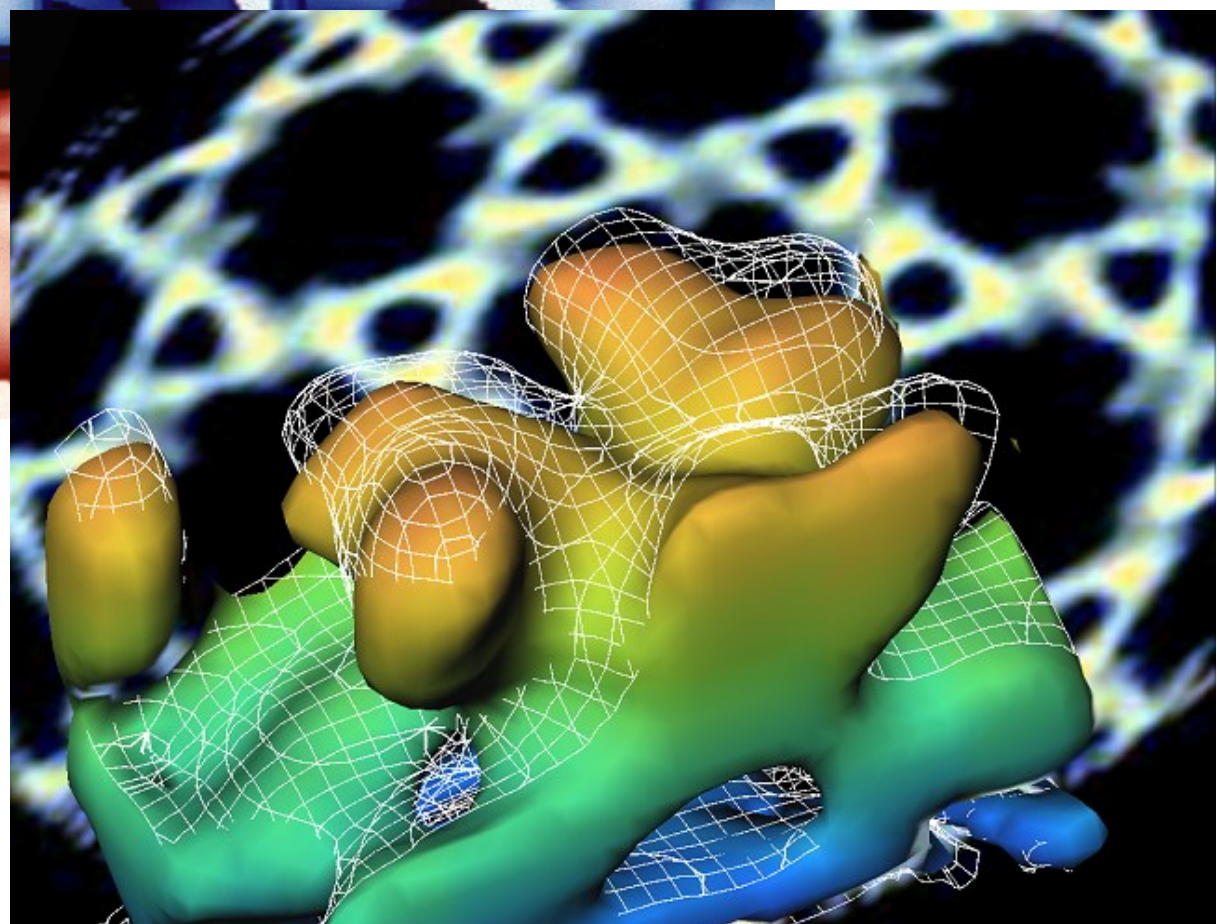


Biacore and antibody detect the pH dependence of fusion peptide

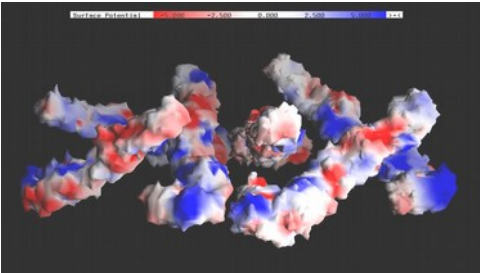
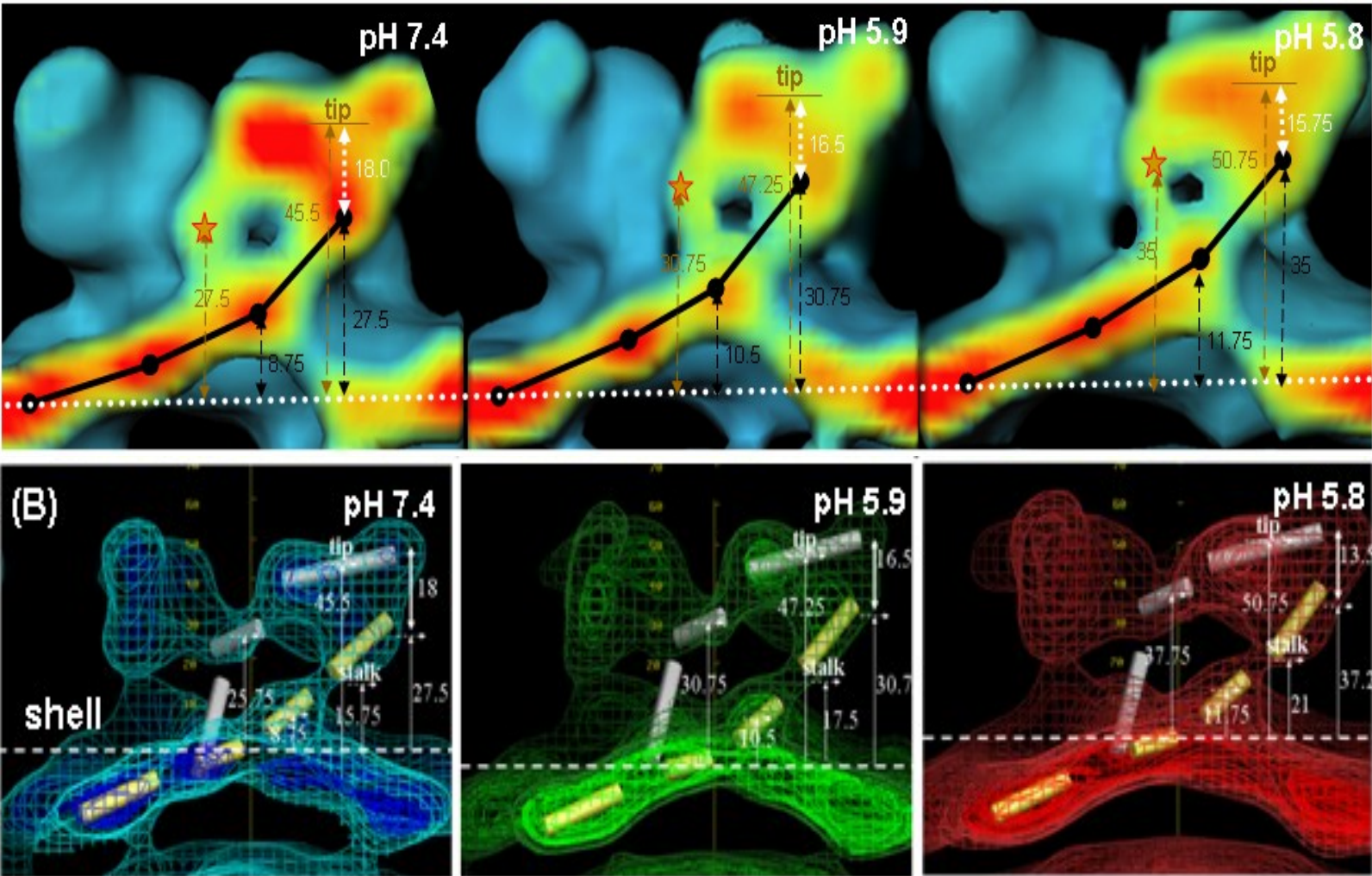




**NC + glycoprotein conform
viral particles
Maturation requires
membrane budding based on
1:1 glycoprotein-capsid
interactions**

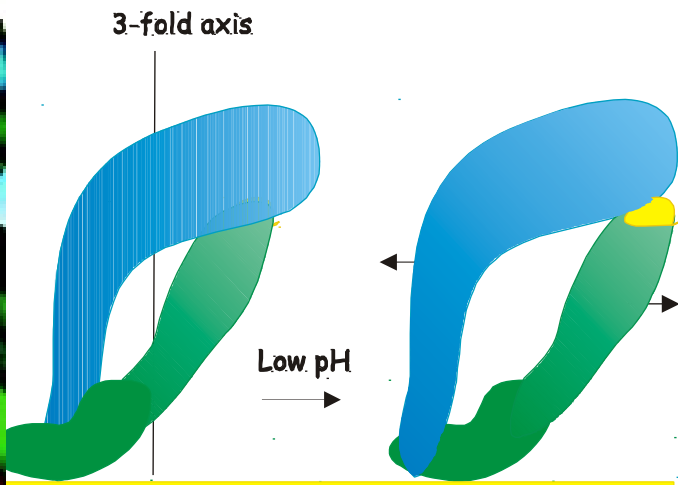
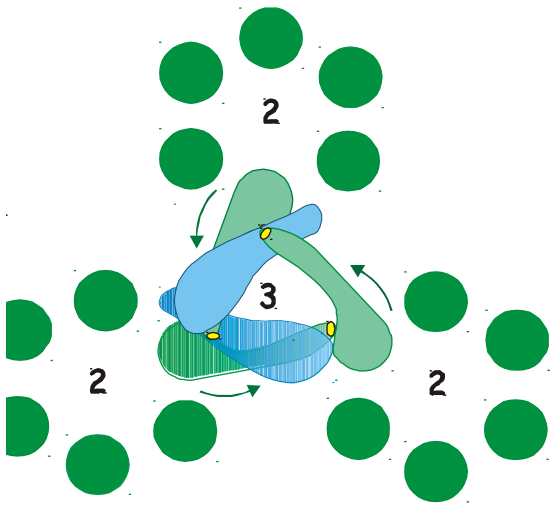
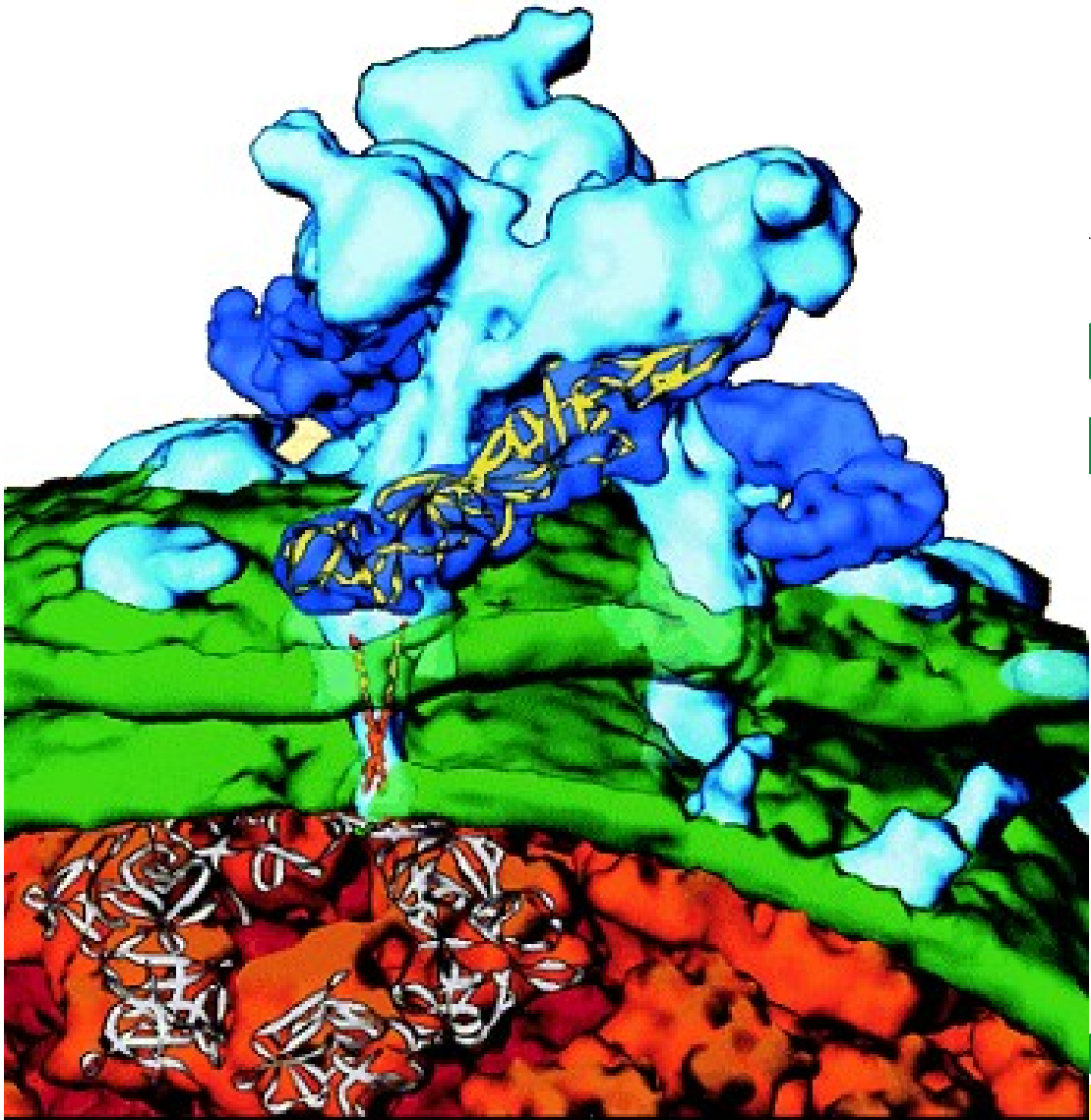


internal feature of viral glycoprotein molecules



Modular consequences in fusion activation

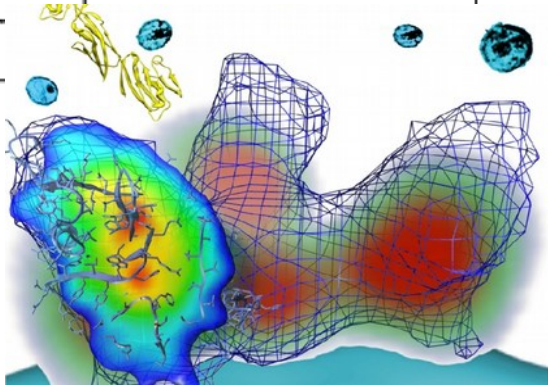
membrane fusion — type II



1995	2000	2005	2010

VaxGen Trial
(Protein only- AIDS VAX)
Clade B gp120 (MN)
Clade AE gp120 (A244)


Failed to induce protection



HIV Env protein

Step Trial
(Vector only)
Ad5 (gag, pol, nef)

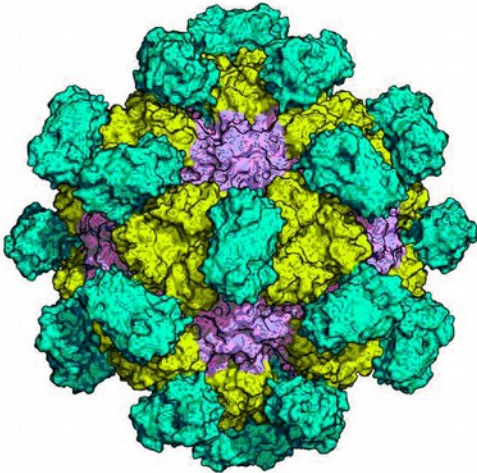


RV144 Trial, & further RV217
(prime-boost: ALVAC, protein+ ALVAC)
ALVAC= env, gag, pro
Protein= AIDS VAX

transiently increased the rate of acquisition of HIV
in uncircumcised Ad 5 seropositive MSM


31% efficacy, limited duration

HVTN 505
(prime-boost: DNA, Ad5)
DNA= env, pol, nef
Ad5= env, pol, gag




Failed to induce protection

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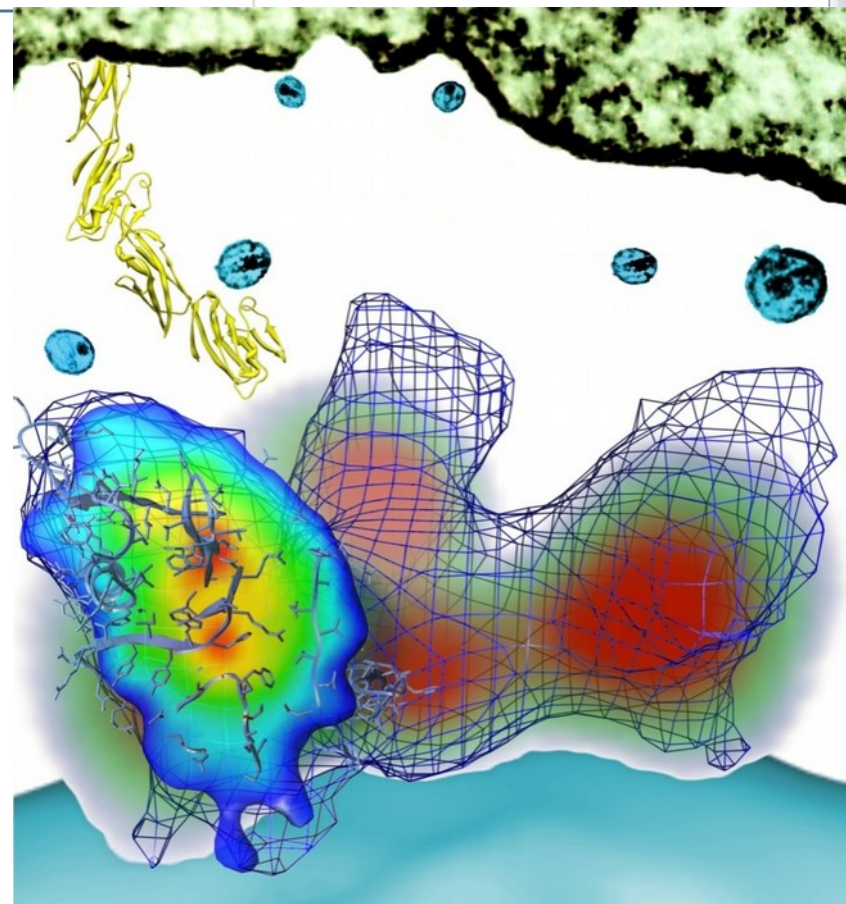
HIV protein unveils vaccine target

March 30, 2011. Tags: [AIDS/HIV](#), [Vaccines](#)

UC Davis scientist heads international study.

An international study headed by a UC Davis scientist describes how a component of a potential HIV vaccine opens like a flower, undergoing one of the most dramatic protein rearrangements yet observed in nature. The finding could reveal new targets for vaccines to prevent HIV infection and AIDS. A paper describing the work was published online this week in the journal *Proceedings of the National Academy of Sciences*.

In the new study, researchers from the U.S., Sweden and France explored the structure and behavior of the HIV envelope protein complex, which could potentially serve as a component of a vaccine aimed at eliciting

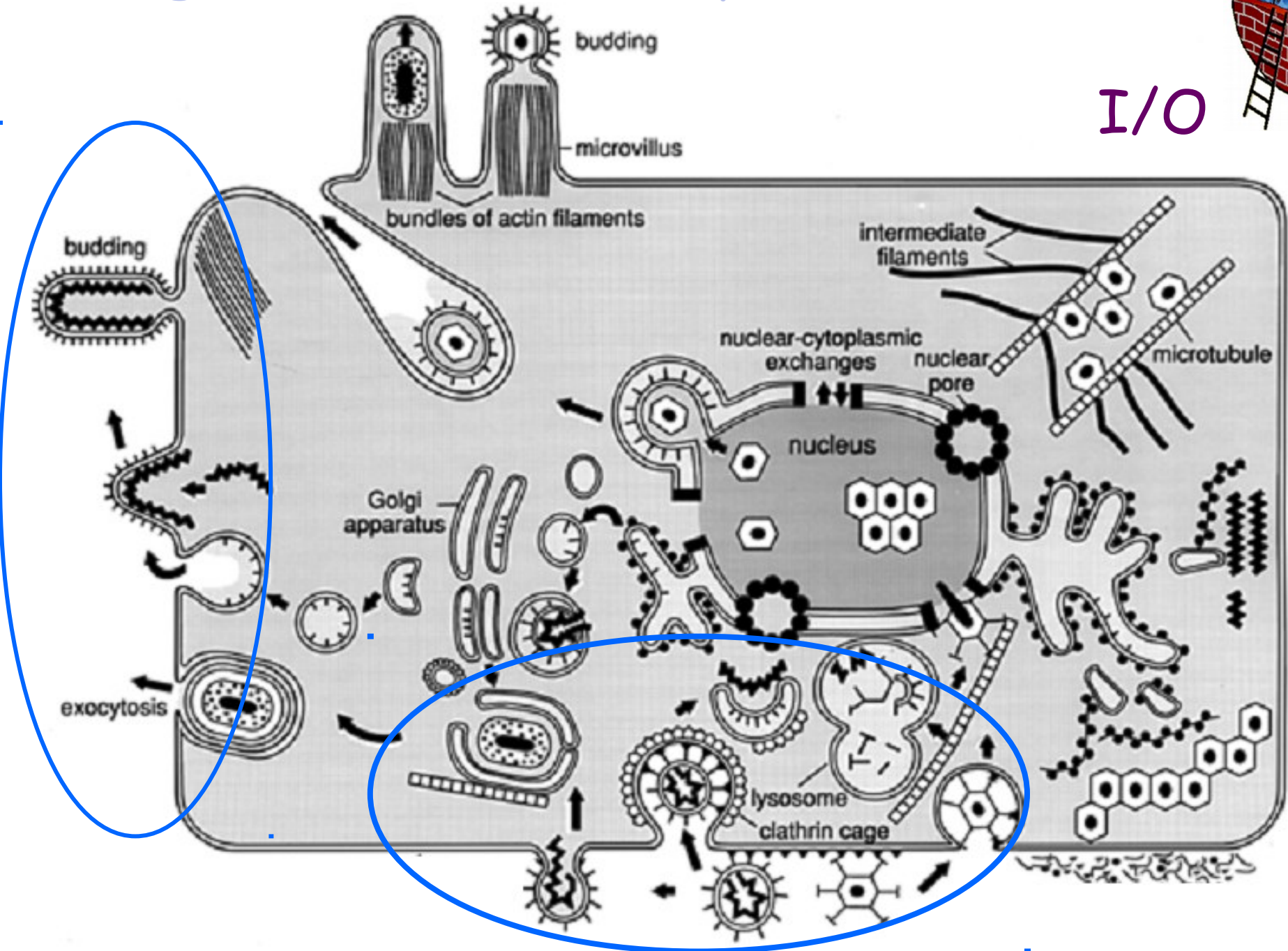


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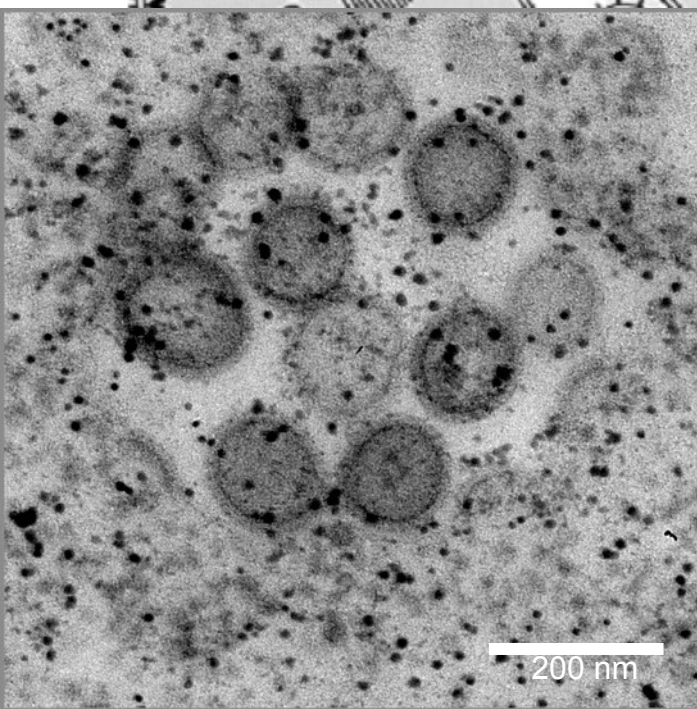
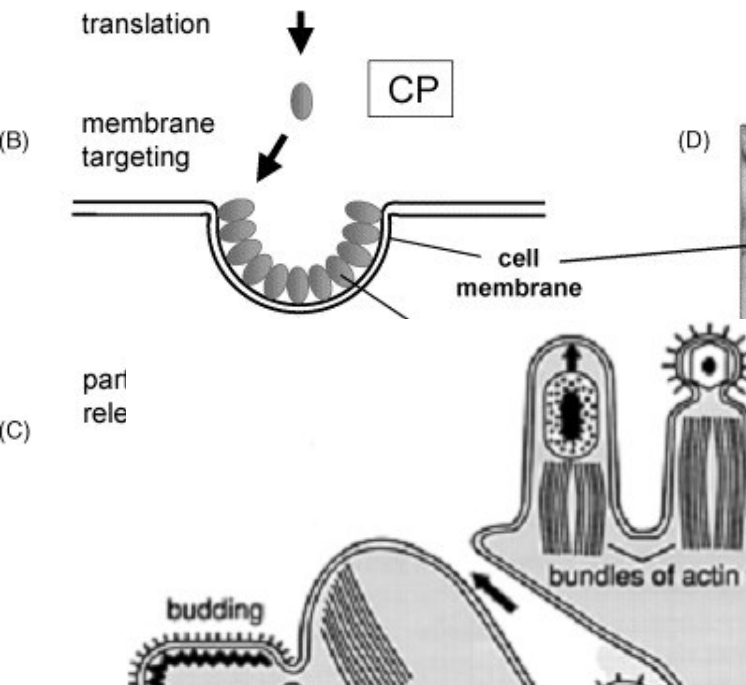
insights of cellular compartments



I/O

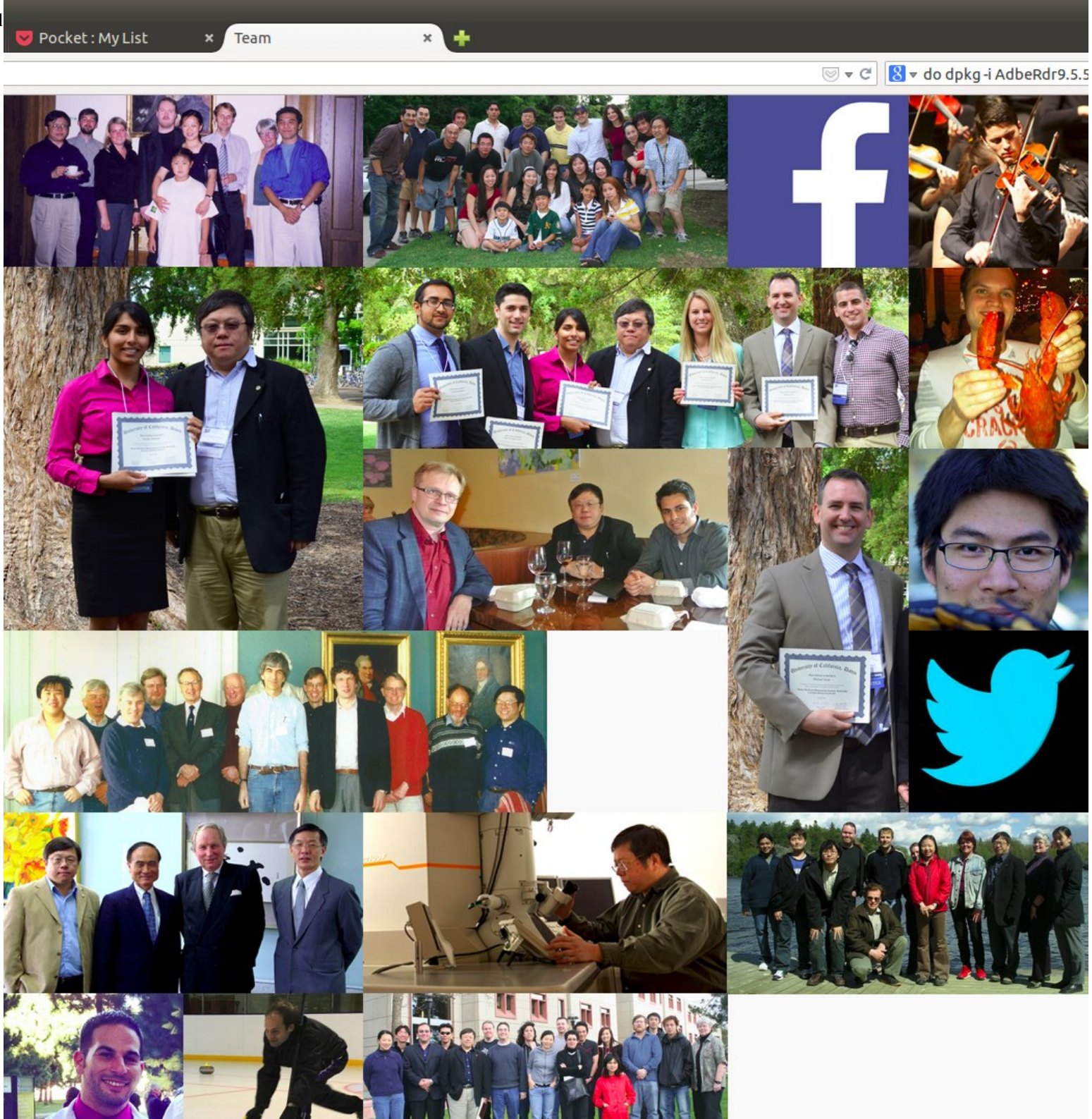
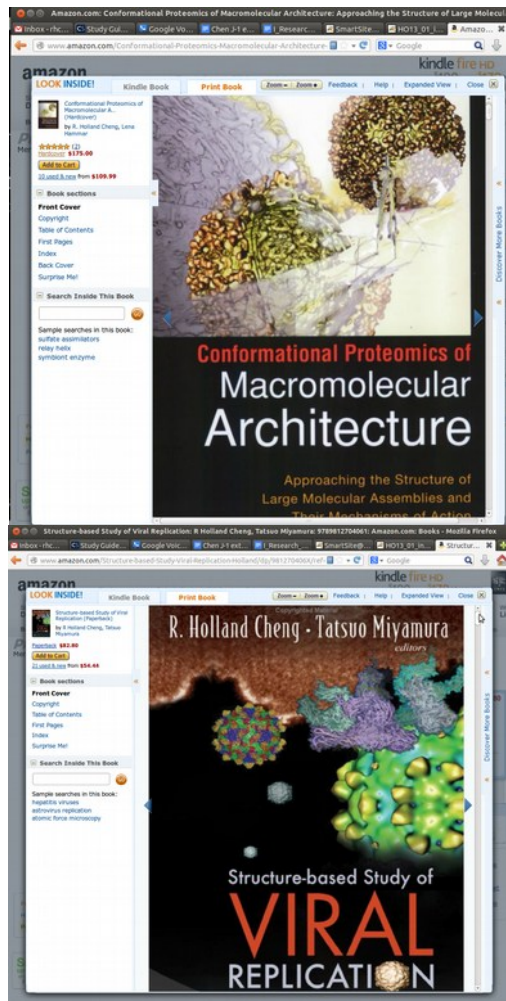


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UC Davis has 33,000 students, 2,500 faculty and 21,000 staff, an annual research budget of \$750M, a comprehensive health system. The university offers interdisciplinary graduate study and 100 undergraduate majors in four colleges & six professional schools

