JSS / NANO2, 2014

Nano Machinery & Imaging Towards Personalized Medicine

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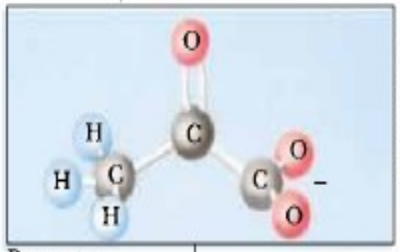
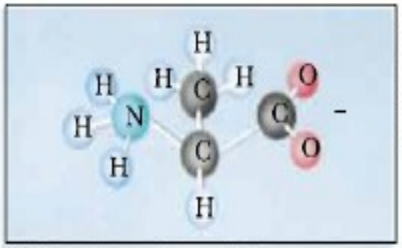
NIH Roadmap MHRP U.S. MILITARY HIV RESEARCH PROGRAM NOVARTIS

We walk through Biomolecular H[illegible]chy



Metabolites:
(50–250 daltons)
Pyruvate, Citrate, Succinate, Glyceraldehyde-3-phosphate, Fructose-1,6-bisphosphate, 3-Phosphoglyceric acid

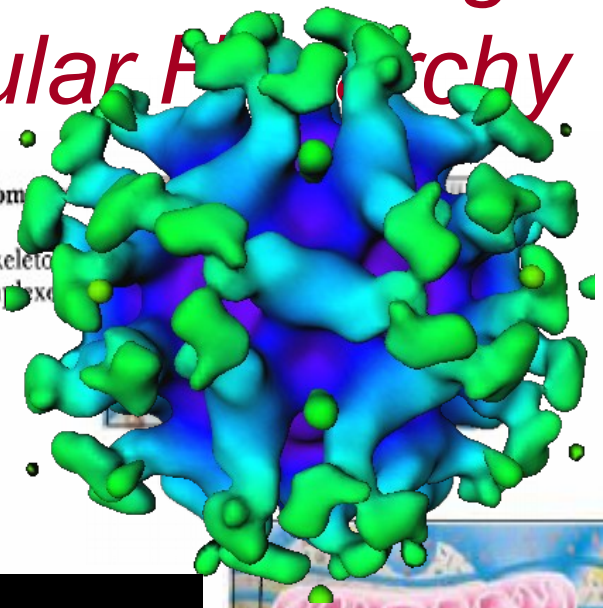
Pyruvate



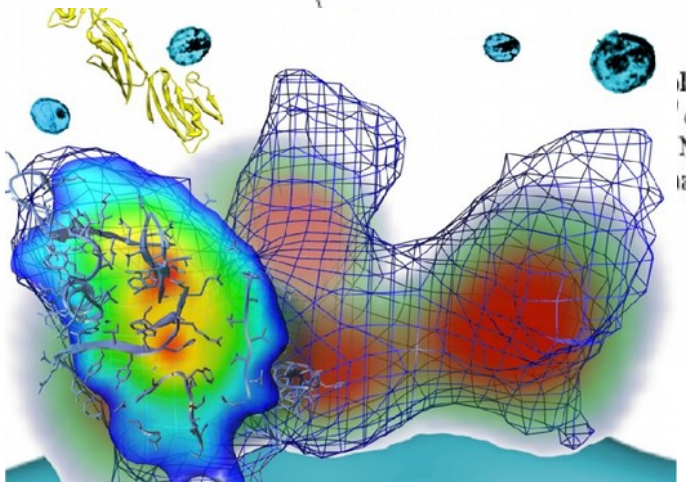
Building blocks:
(100–350 daltons)
Amino acids, Nucleotides, Monosaccharides, Fatty acids, Glycerol

Alanine (an amino acid)

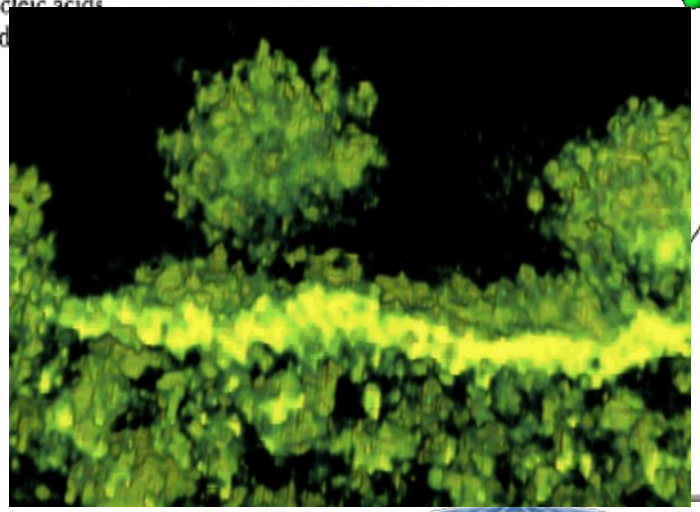
Supramolecular com[illegible]
(10^6–10^9 daltons)
Ribosomes, Cytoskelet[illegible]
Multi-enzyme com[illegible]



[illegible]lecules:
[illegible] daltons)
Nucleic acids
[illegible]arid



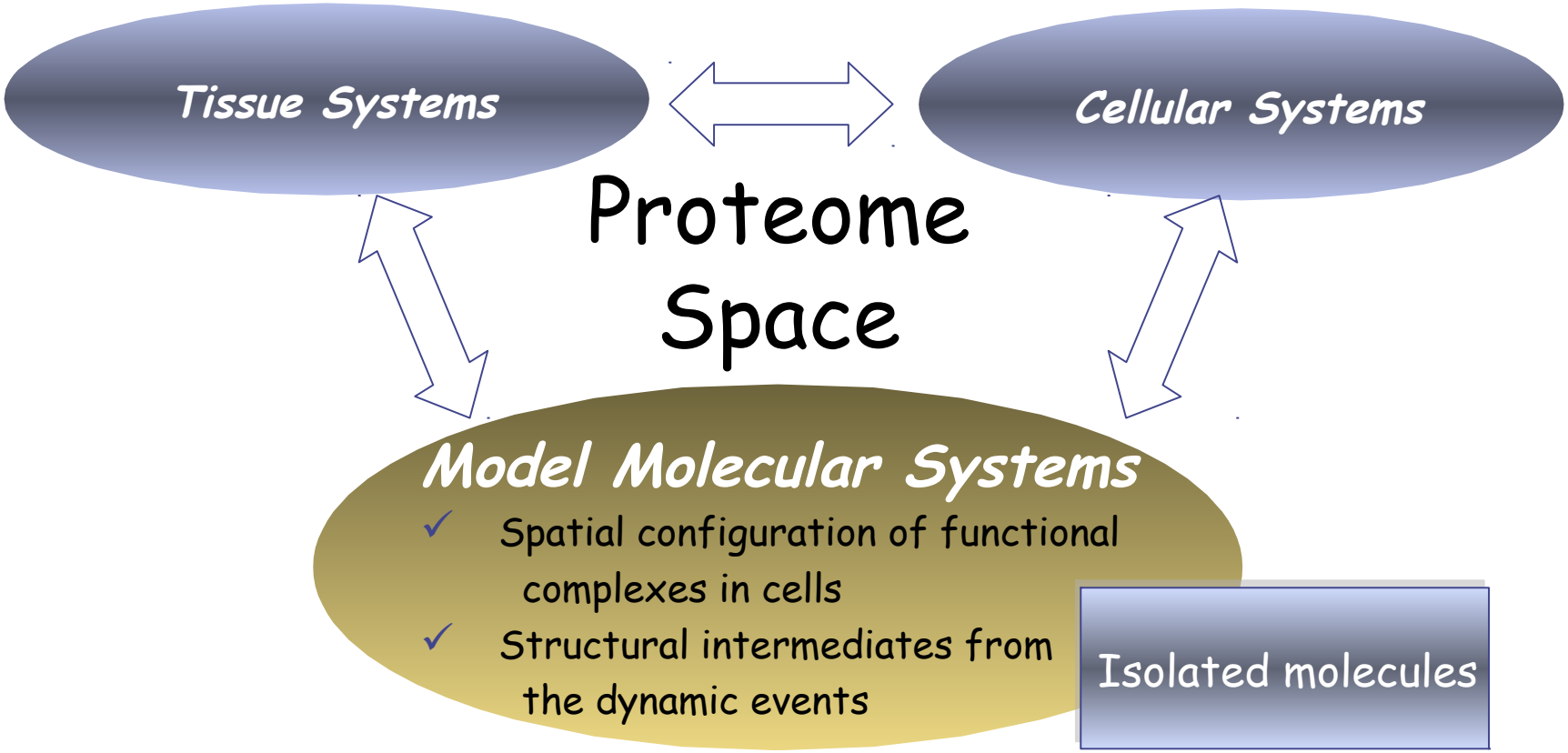
HIV Env protein



Organelles:
Nucleus, Mitochondria, Chloroplasts, Endoplasmic reticulum, Golgi apparatus, Vacuole

- *http://pioms.ucdavis.edu/*

Logic of biological phenomena reduced complexity



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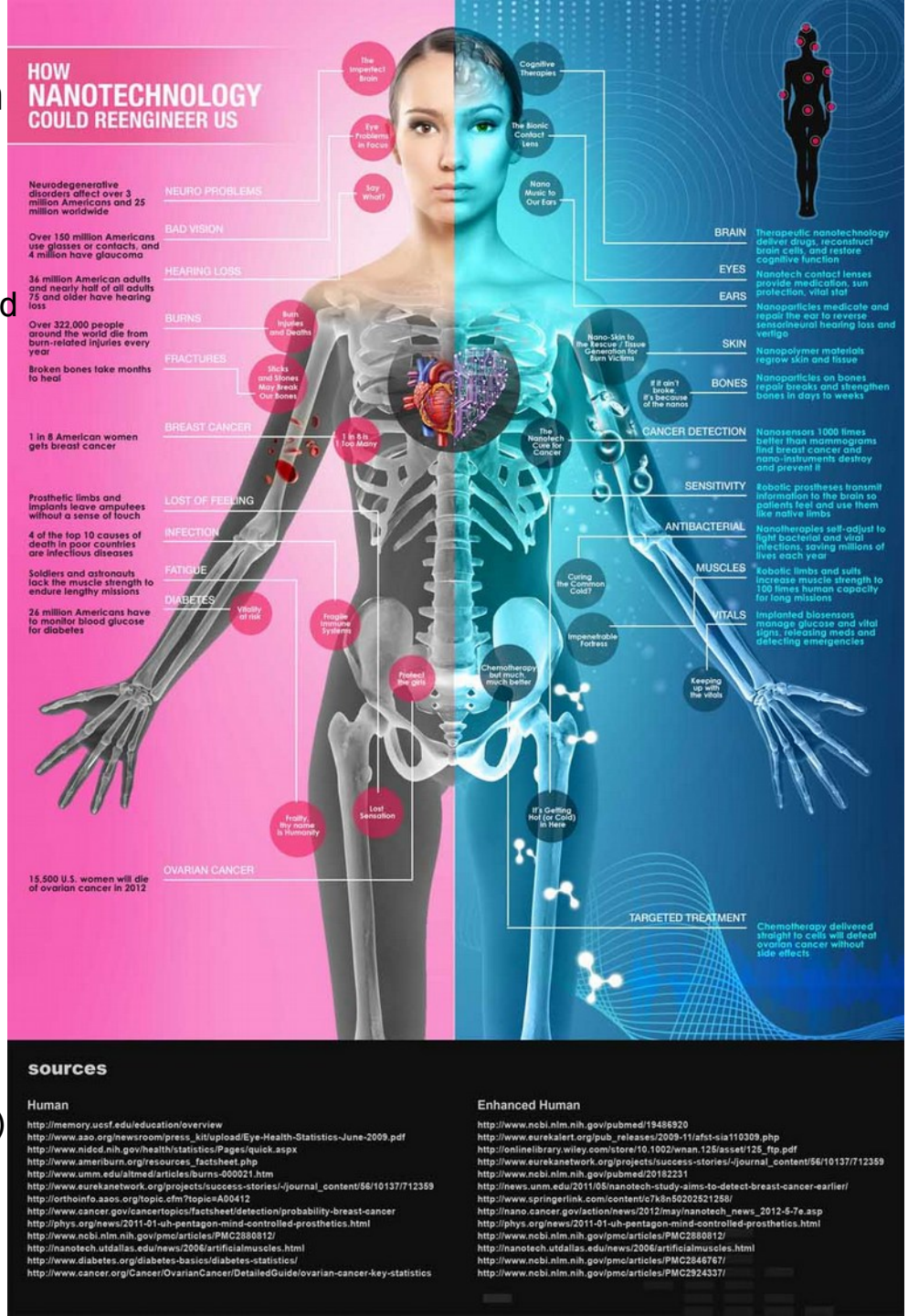
NANO phase 2 towards human health

Monday
12-13: Introduction (Dr. Varpu Marjomäki and FiDiPro Professor Holland R. Cheng)
13-17: **Nanoformulations** (Dr. Varpu Marjomäki and Dr. Silke Krol)

Tuesday
9-11: **Cell trafficking** (Dr. Varpu Marjomäki)
13-15: **Cell trafficking EM** (Dr. Varpu Marjomäki)
15-17: **BioImageXD** (Dr. Lassi Paavolainen)

Wednesday
9-11: **Algorithms for light microscopy quantification** (Dr. Lassi Paavolainen)
13-17: Algorithms for LM continues (Dr. Lassi Paavolainen)
15-17: **EM imaging and 3D structural analysis** (Mo Baikoghli)
Thursday
9-11: **Nano Machines and Electron tomography** (FiDiPro Professor Holland Cheng)
13-15: **Case Study and Nano Machines** (FiDiPro Professor Holland Cheng and Mo Baikoghli)
15-17: **Multiphoton imaging** (Johanna Laakkonen)
Friday
9-12: **Metabolic imaging** (Prof. Ulla Ruotsalainen)



"Nano": How small is that, really?

Mountain
1 km
1000 m

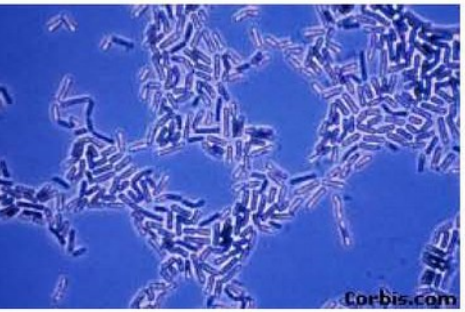
0.001 km = 1 m

Child
1 m

Ant
1 mm
0.001 m

1,000 mm = 1 m

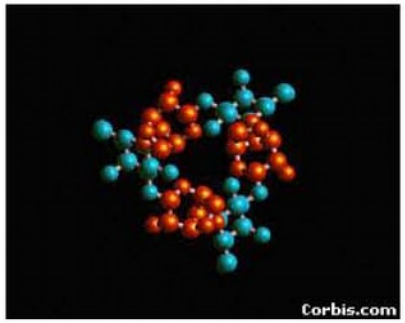
Or
1,000,000 nm



Bacteria
1 μm
0.000001 m

1,000,000 μm = 1 m

Or 1,000 nm



Sugar Molecule
1 nm
0.000000001 m

1,000,000,000 nm = 1 m

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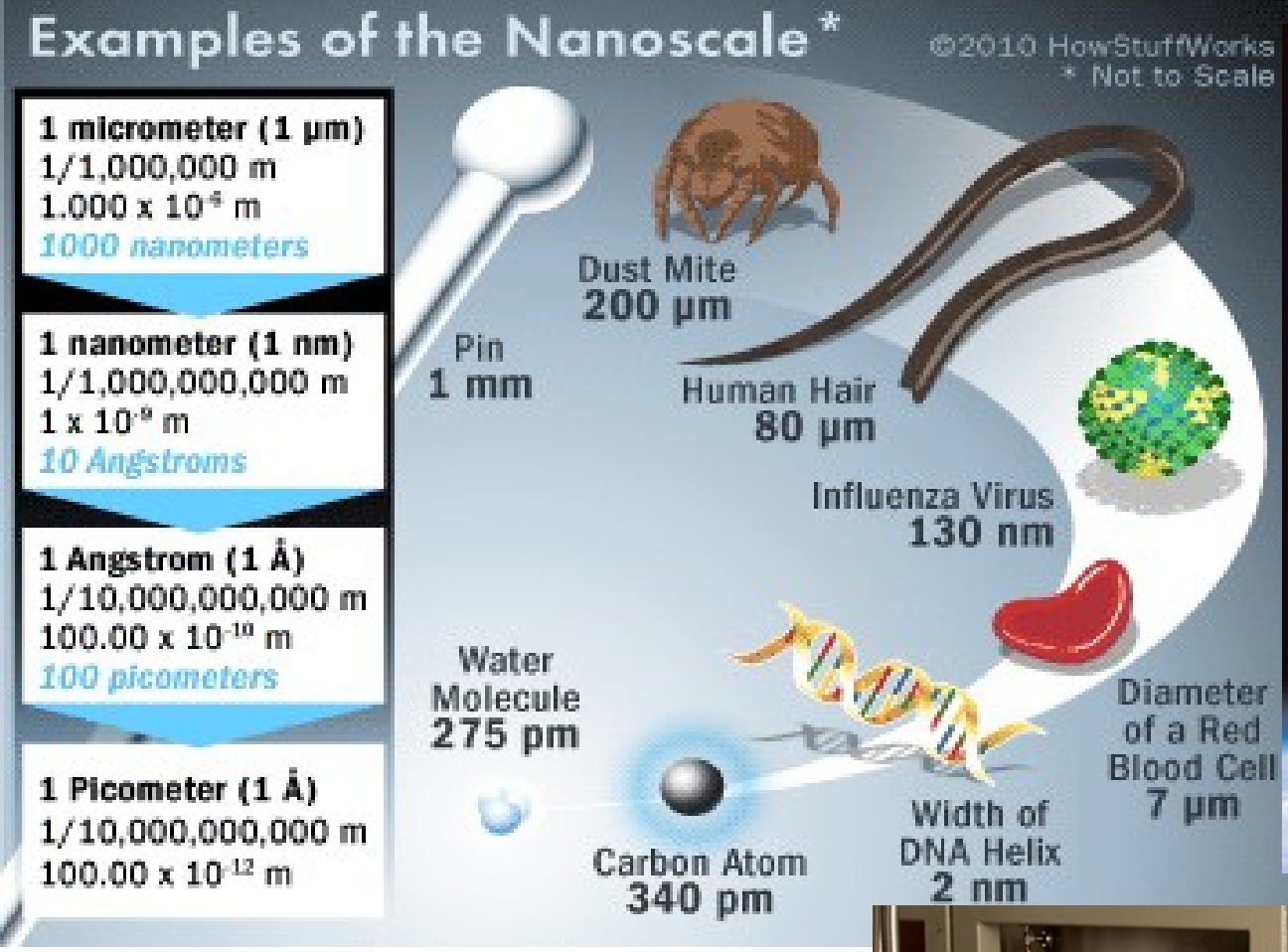

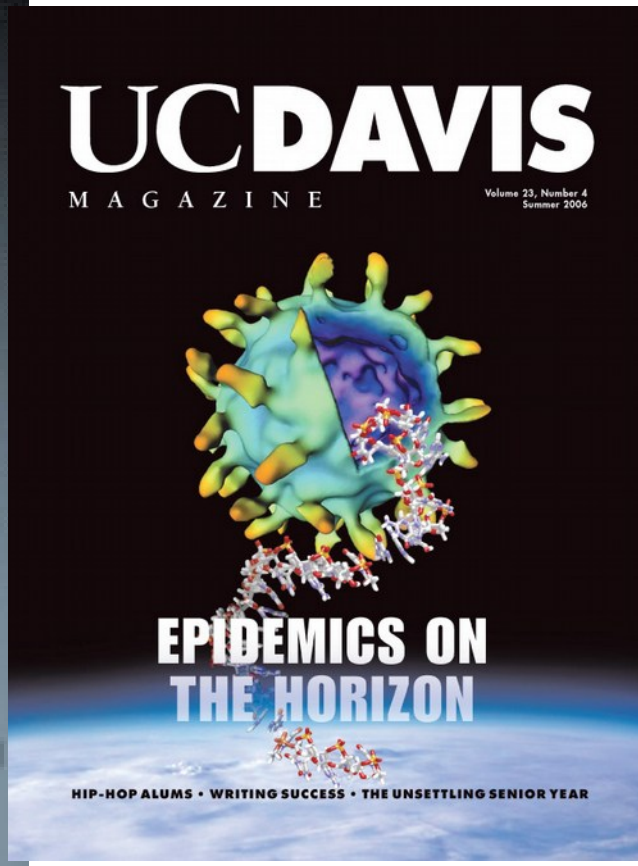

form.function

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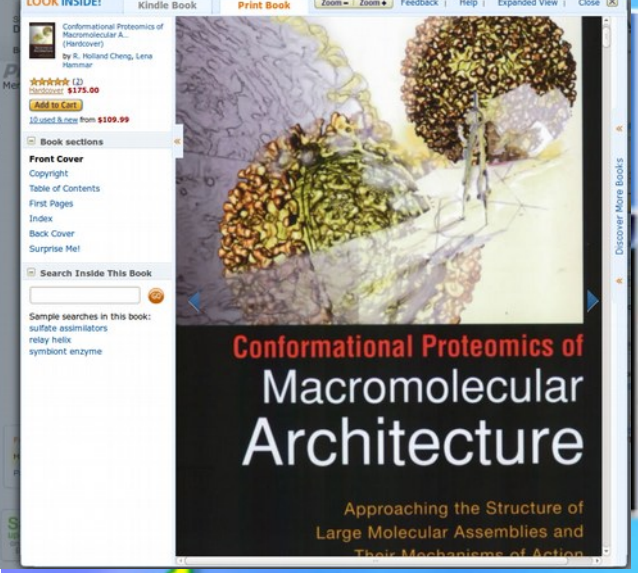
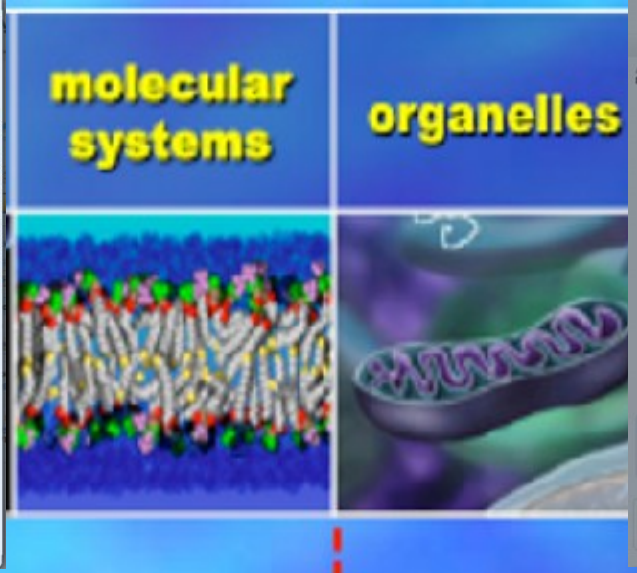
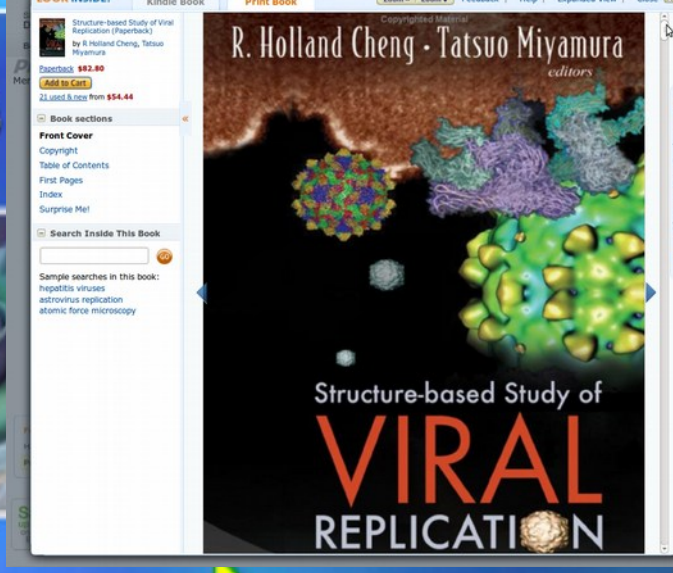
UCDAVIS HEALTH SYSTEM







Proteome Imaging

XRF

SRM

Optical microscopy

Coherent X-ray diffraction imaging and microscopy

Electron/ X-ray tomography

Fluorescence

White light / transmission

Electron microscopy

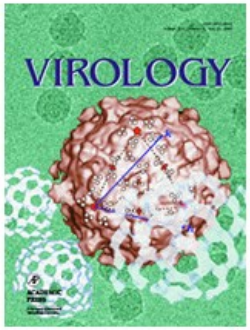
←[Diffraction limit of optical resolution ~ 250nm]

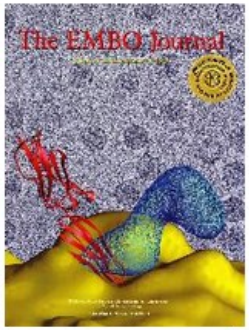
Angstroms	nanometers	< 250 nm	0.25 - 1 μm	microns	millimeters

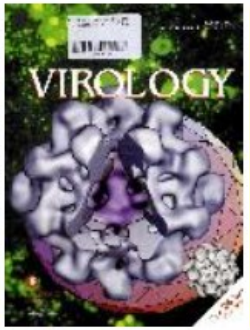
PIOMS

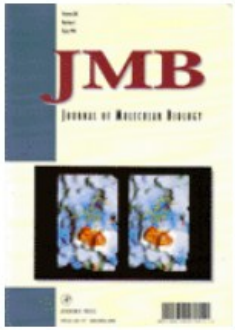
Form Function

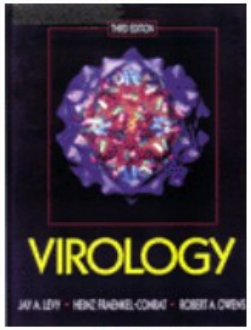
Home | Lab Introduction | Our Research | Group Members | Publications | Lab Resource | Useful Links | Contact us

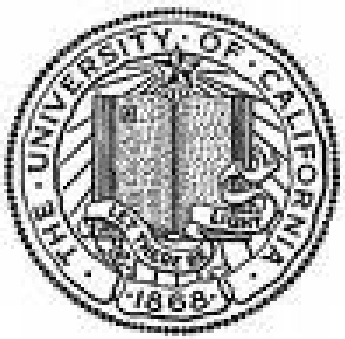


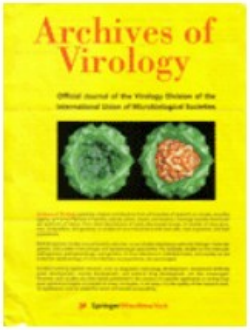


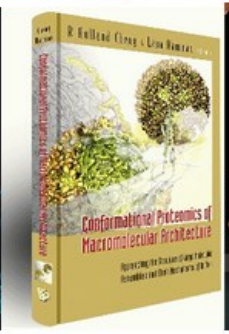


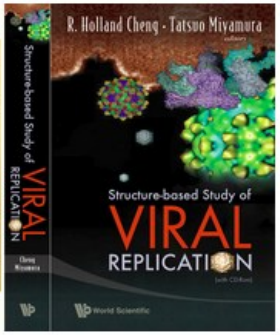


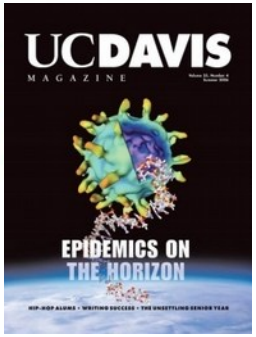






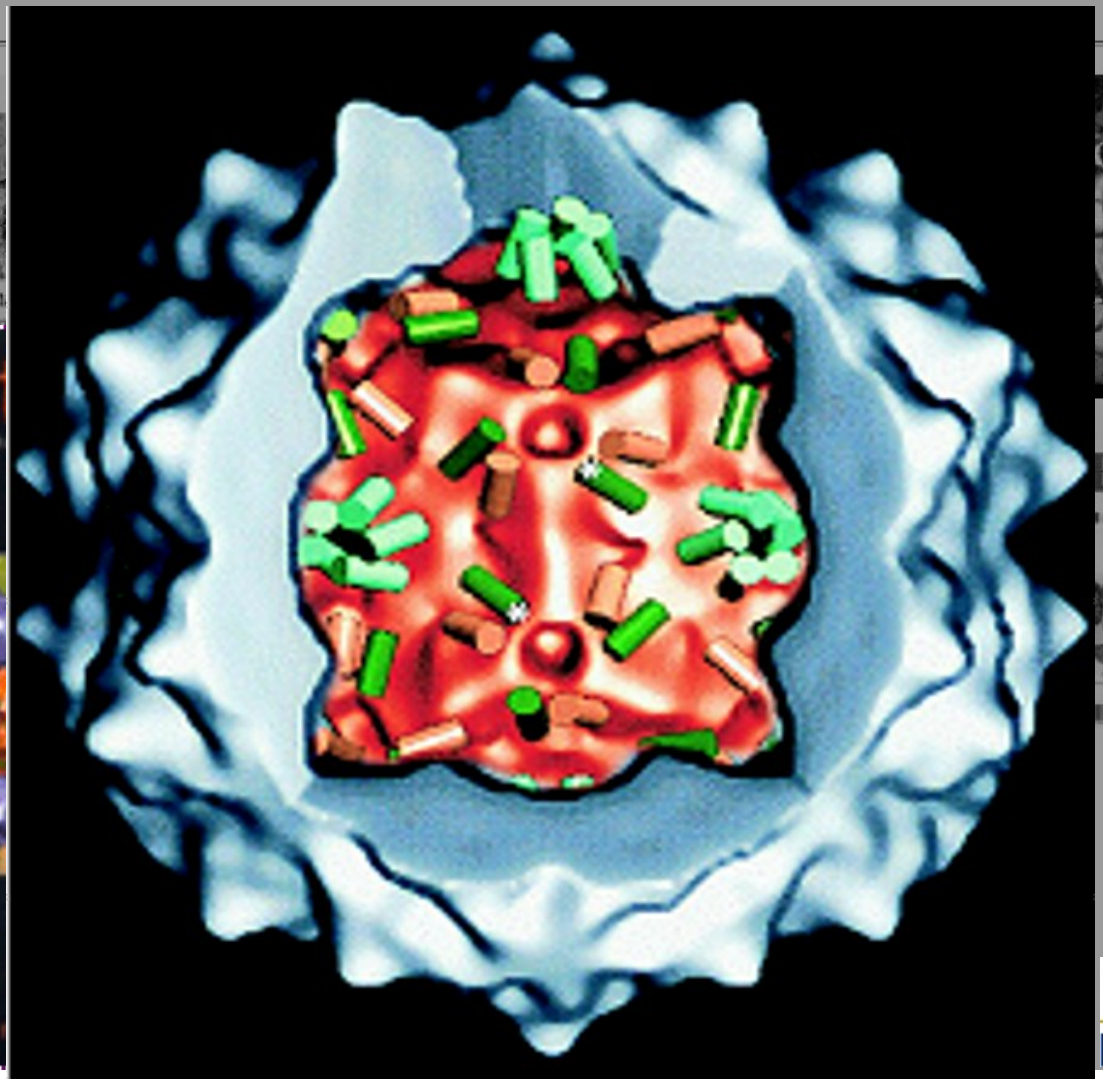


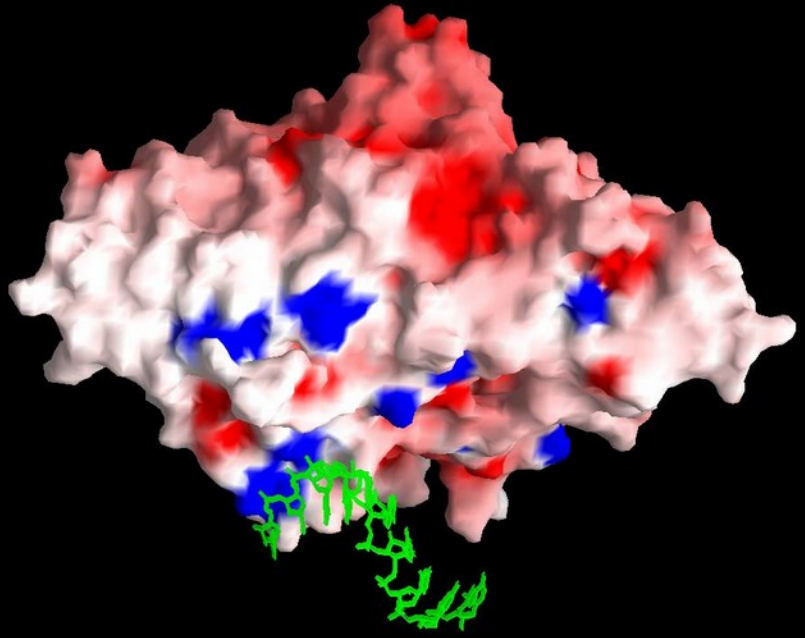




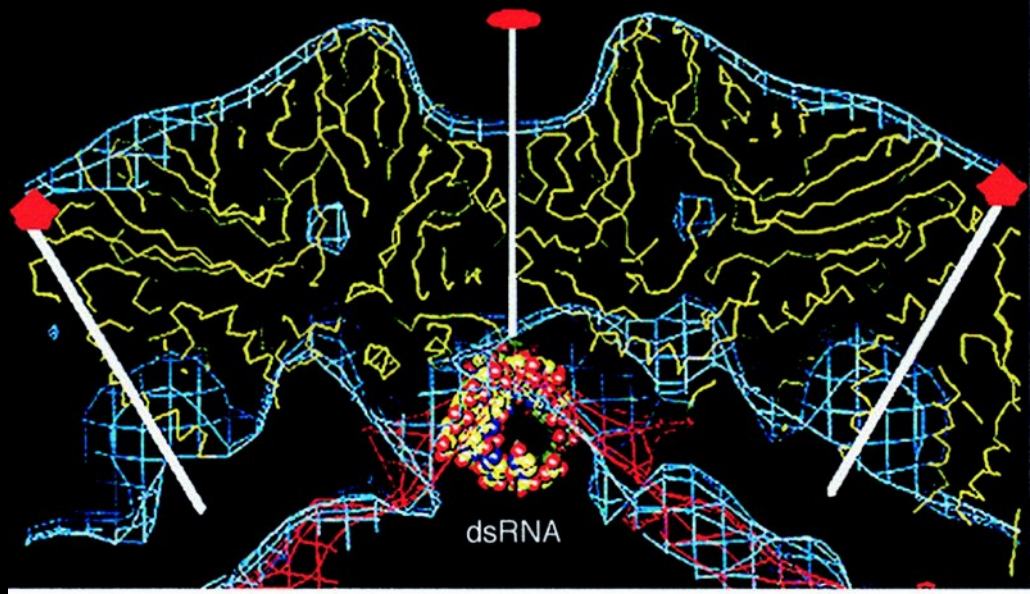
Cheng et al. Structure (1994)

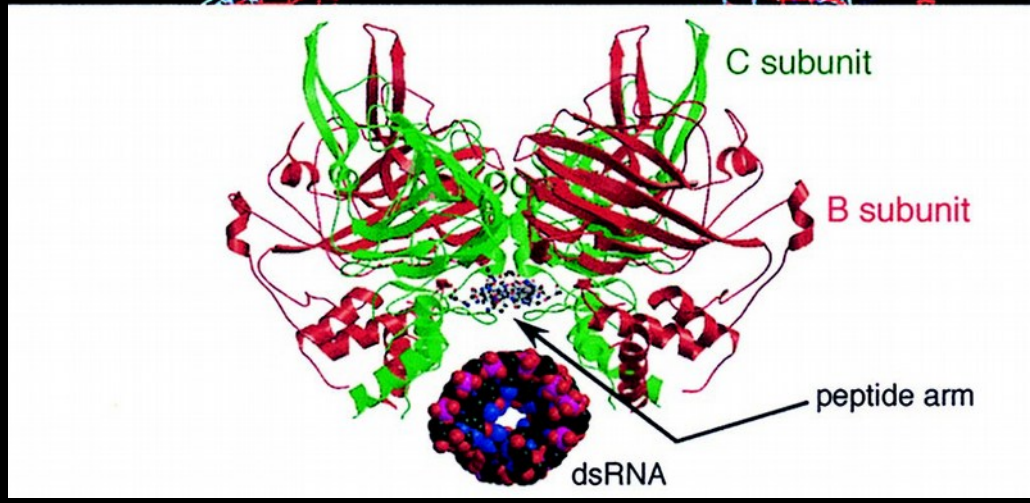
Genome In/Out via a 30nm particle





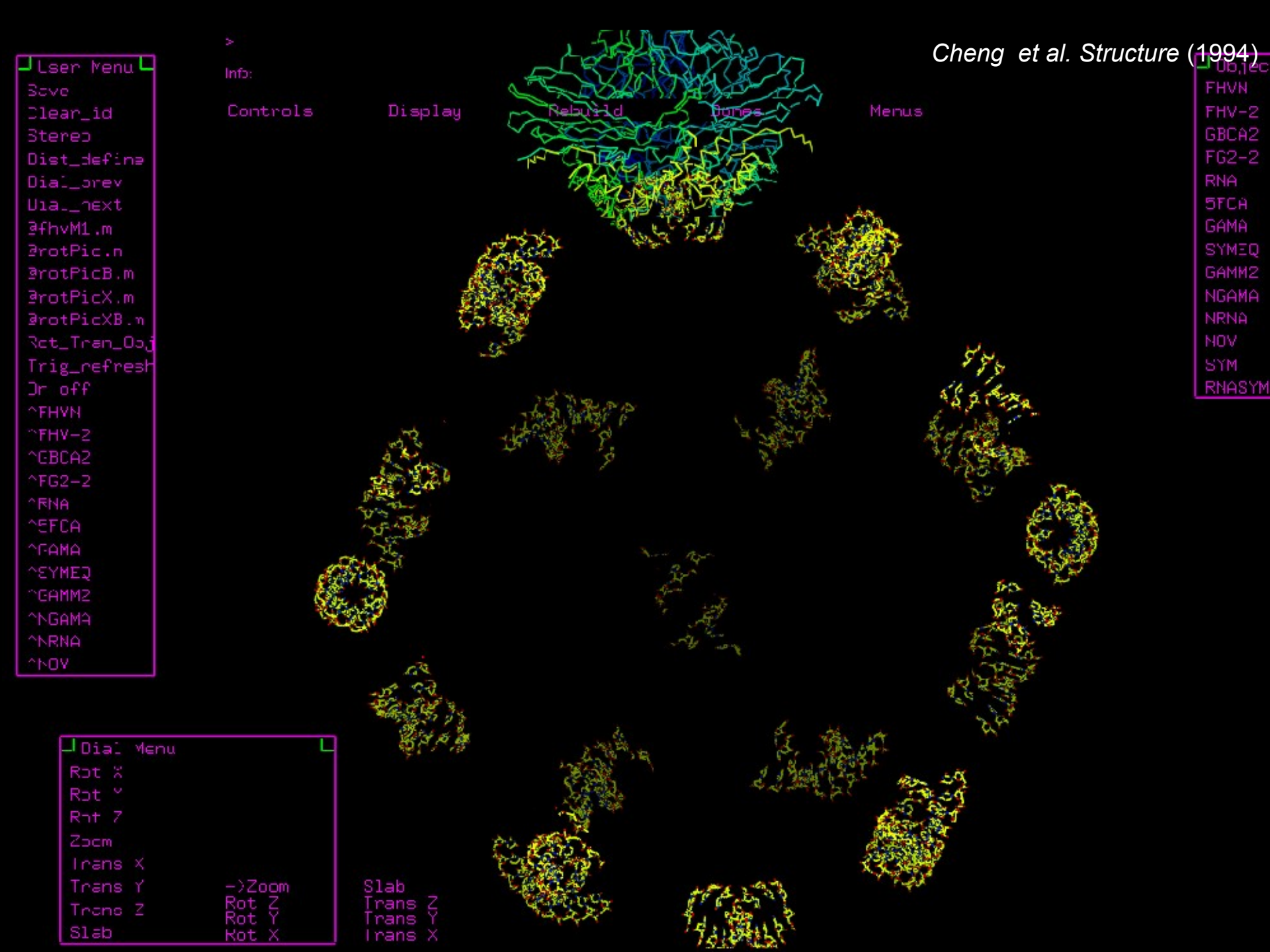
Cheng et al. Structure (1994)

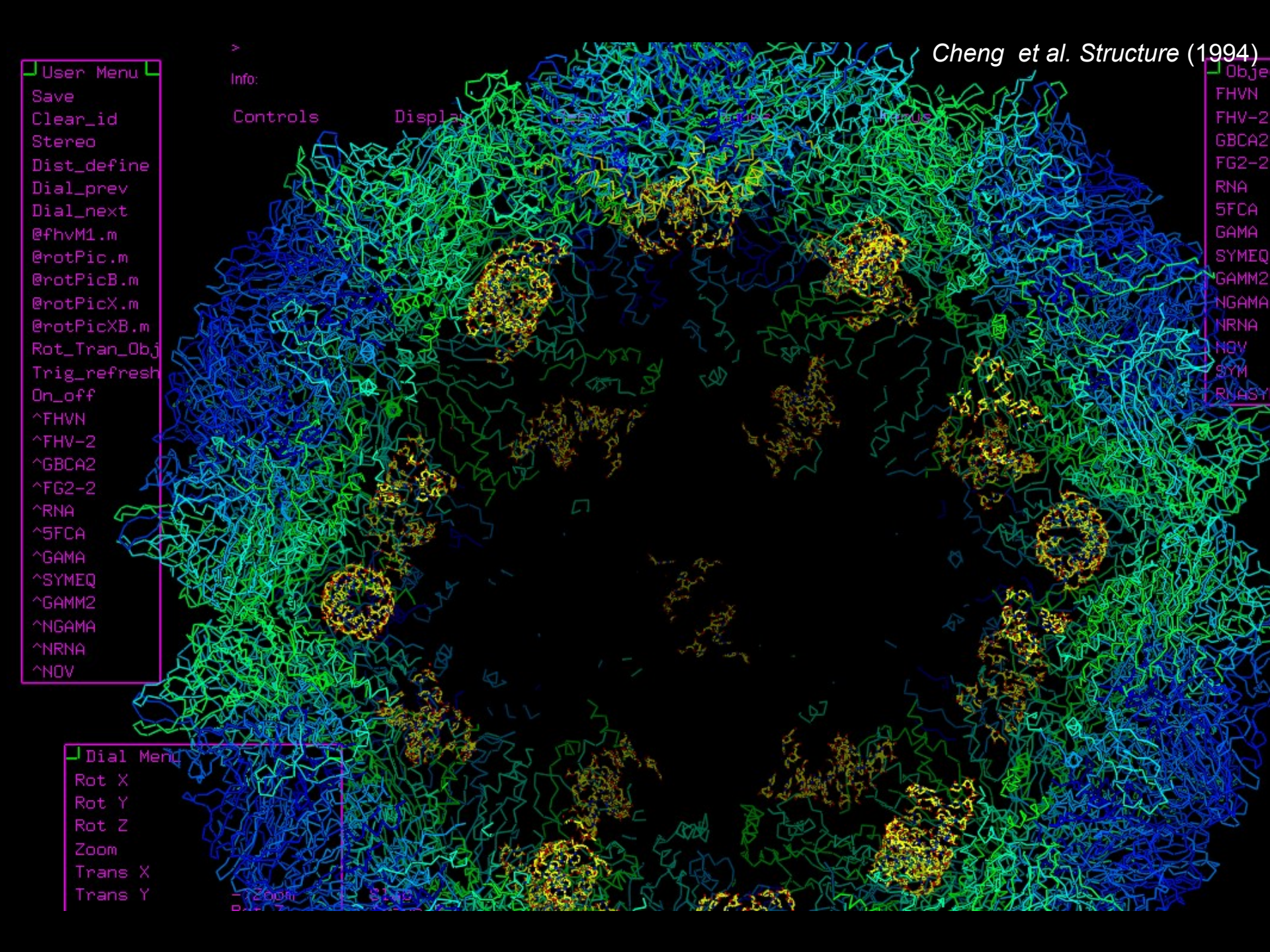




Genome brings 180 protein subunits into a mega-capsid cage

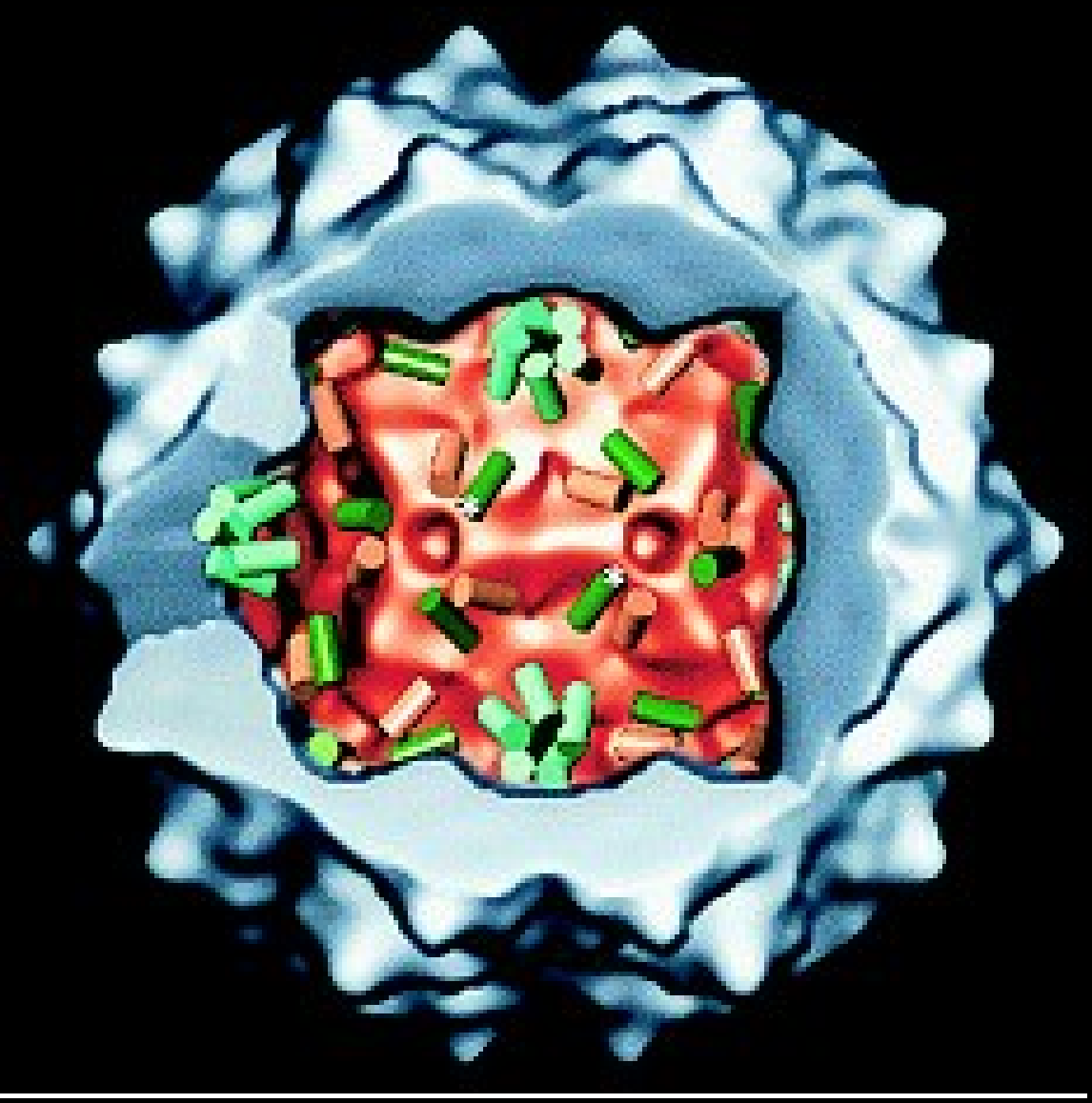
1F8V.PDB

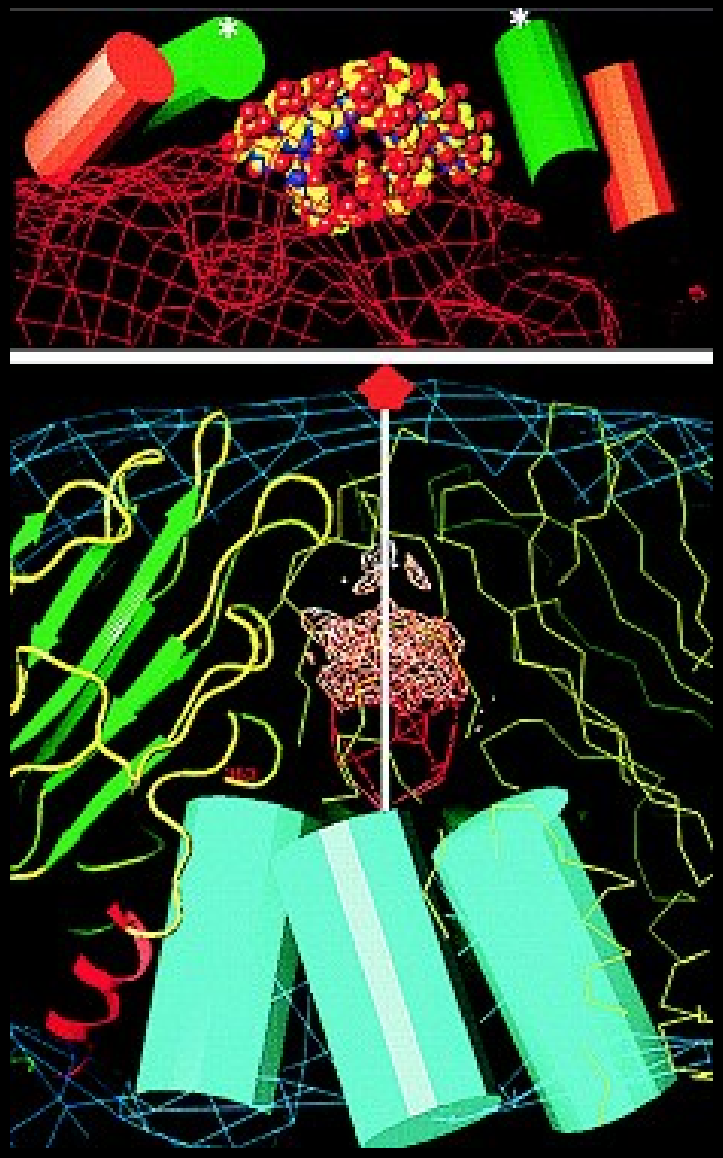

Cheng et al. Structure (1994)
Controls
Display
Rebuild
Menus
FHVN
FHV-2
GBCA2
FG2-2
RNA
SFCA
GAMA
SYMEQ
GAMM2
NGAMA
NRNA
NOV
SYM
RNASYM
Slab
Trans Z
Trans Y
Trans X



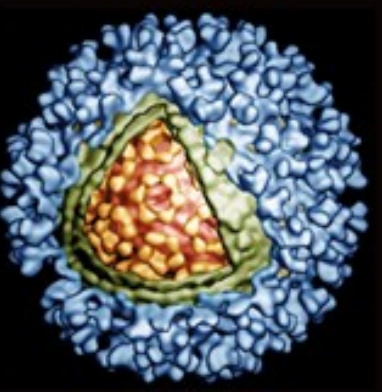
Cheng et al. Structure (1994)

Cheng et al. Structure (1994)





PCL vaccine, engineering packaging cell lines

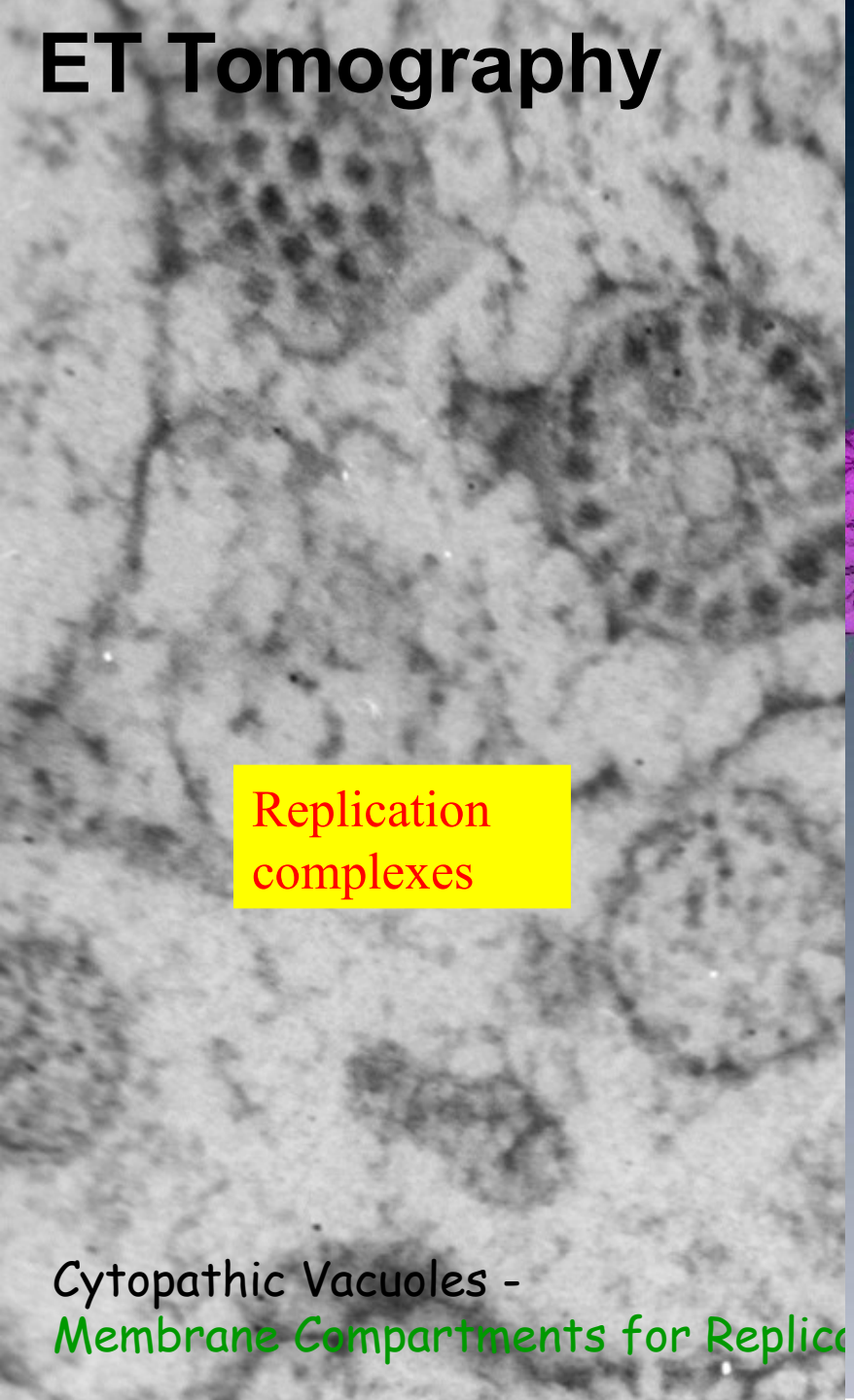


Transcription efficiency

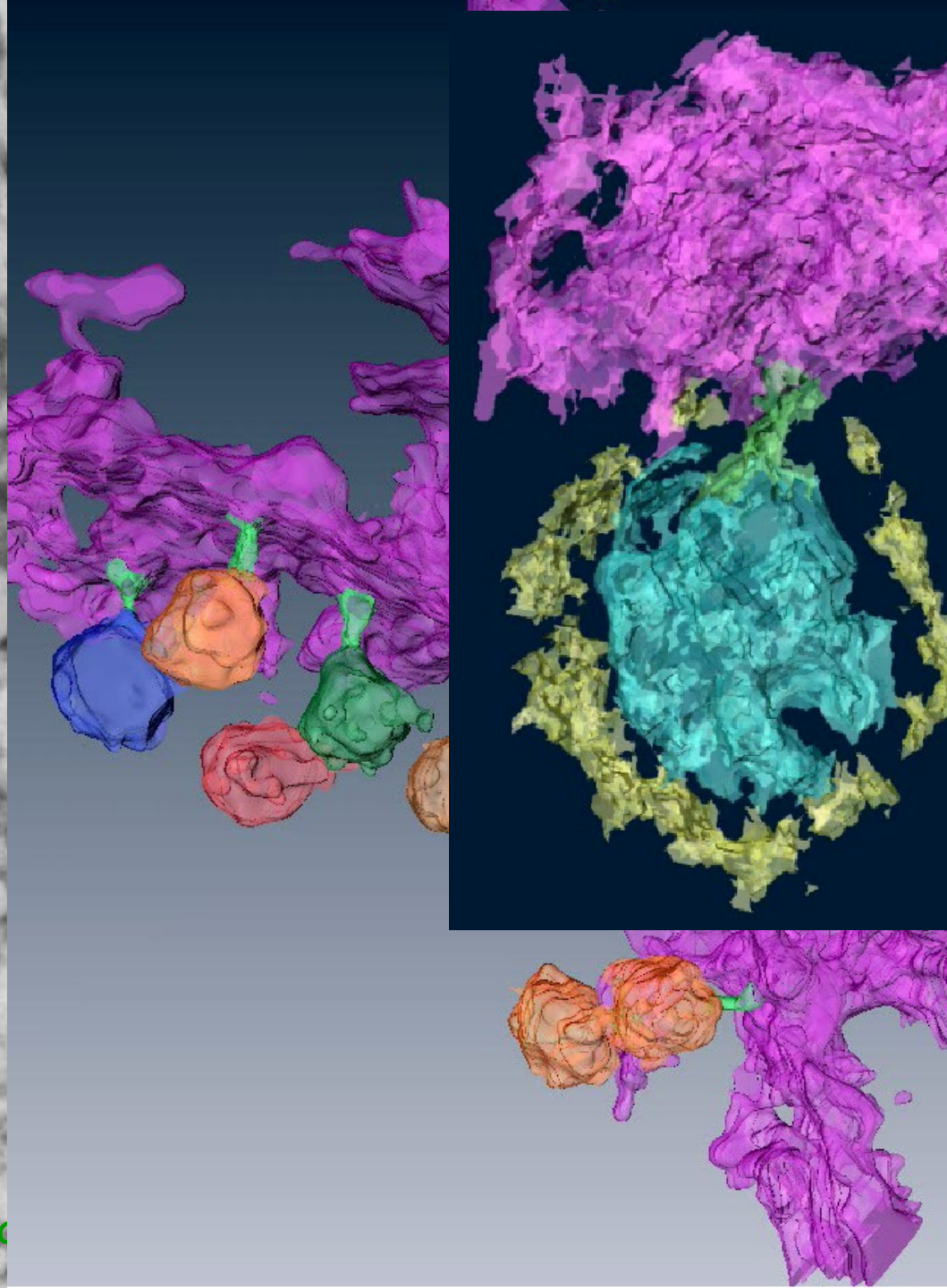
RNA stability

Replication complexes

ET Tomography

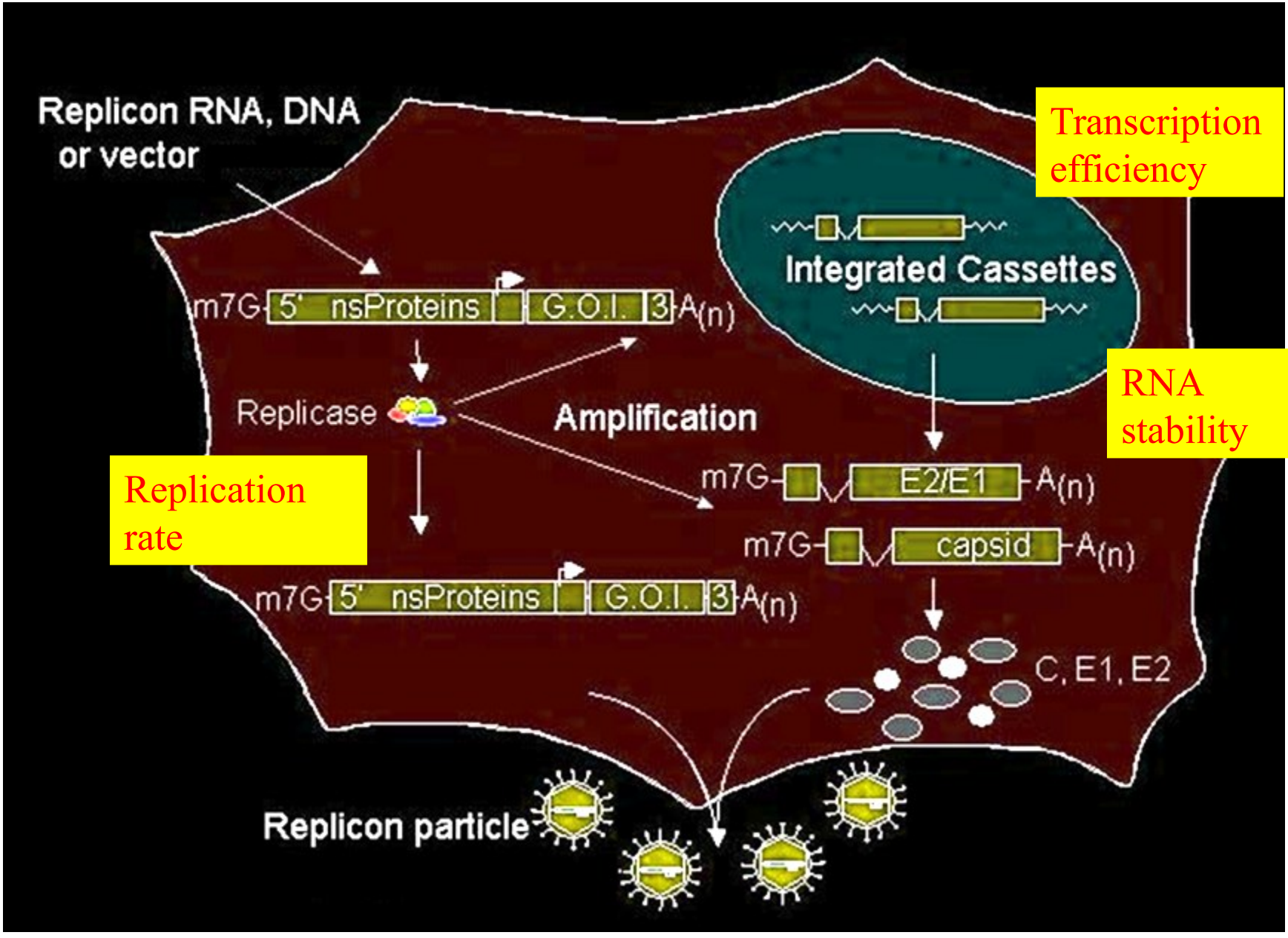


Replication complexes



Cytopathic Vacuoles -
Membrane Compartments for Replica

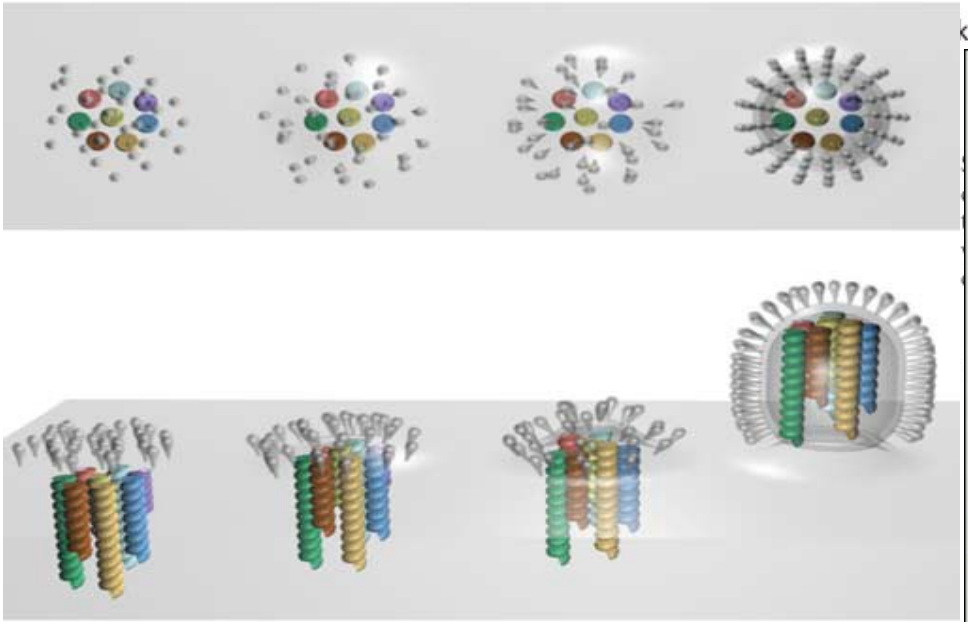
PCL - RNA packaging



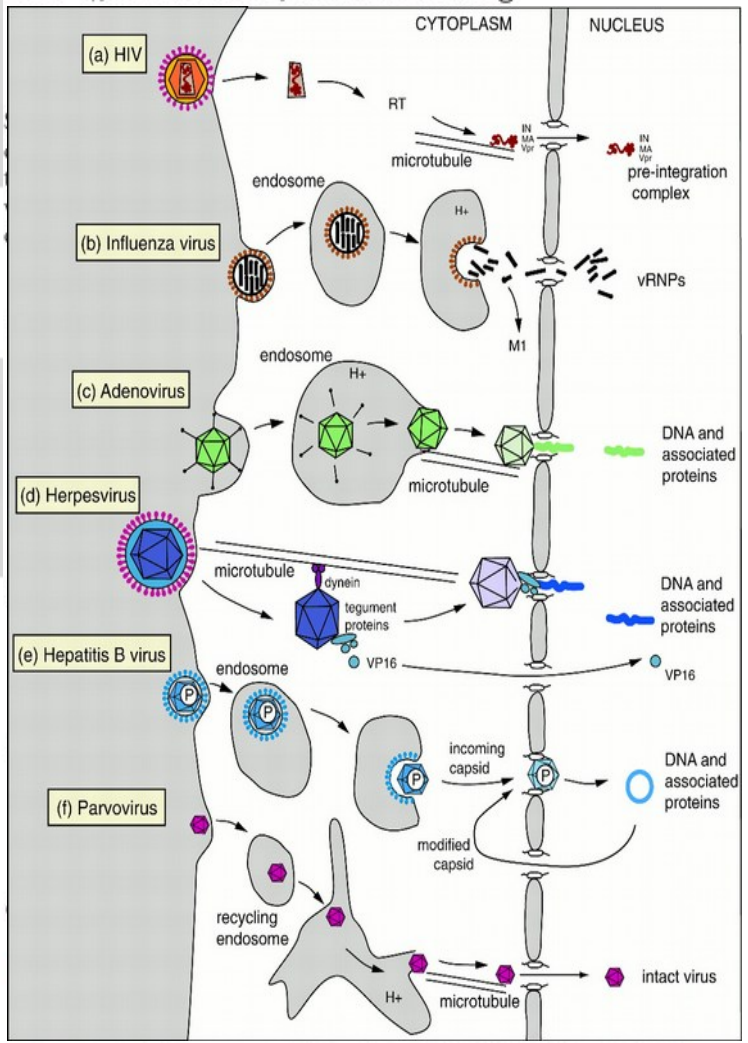
LETTERS

Protein-RNA interaction in flu virus
Noda et al. Nature 2006

Architecture of ribonucleoprotein complexes in influenza A virus particles



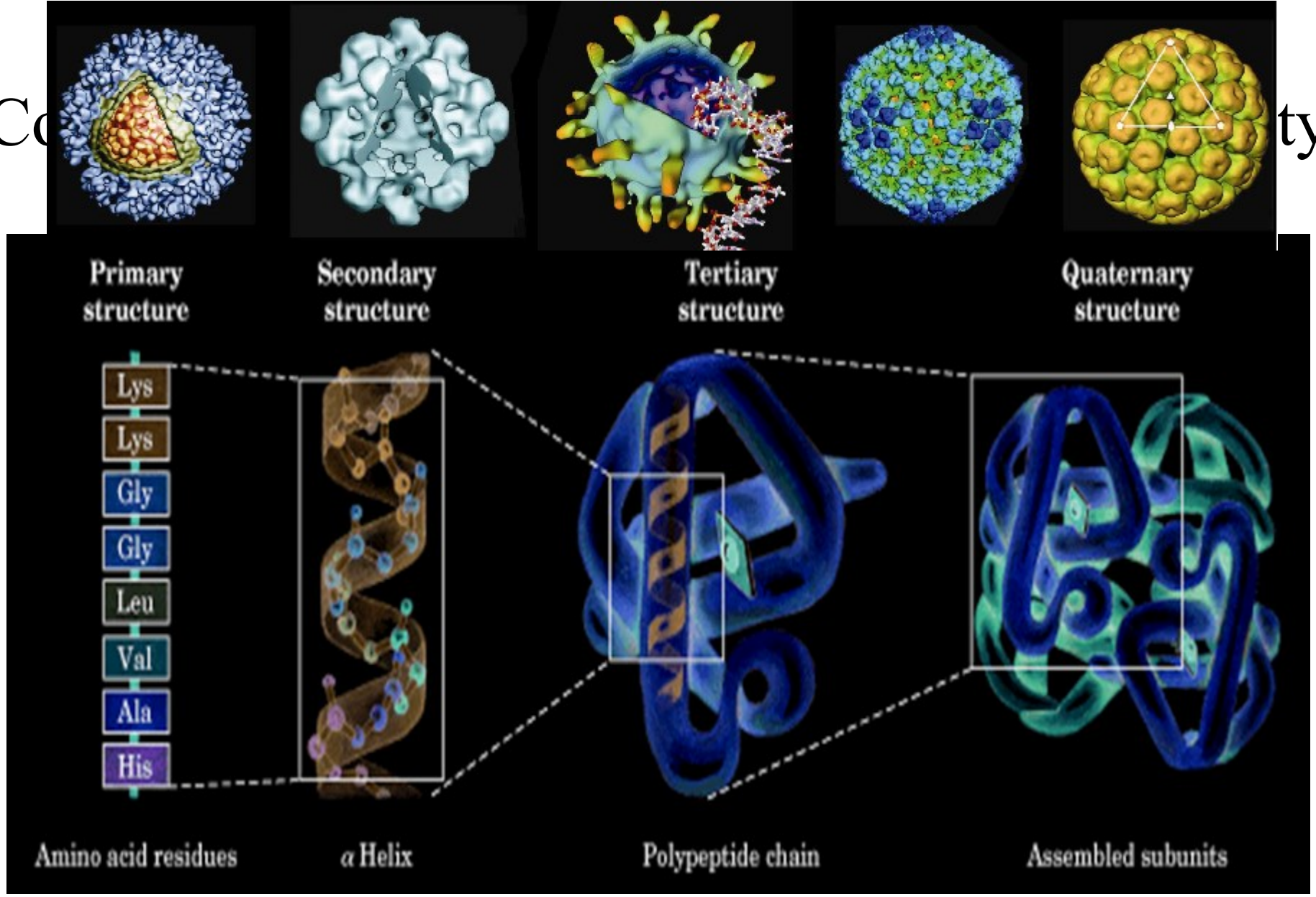
kada[3,6]†, Hiroshi Kida[2], R. Holland Cheng[5,7]

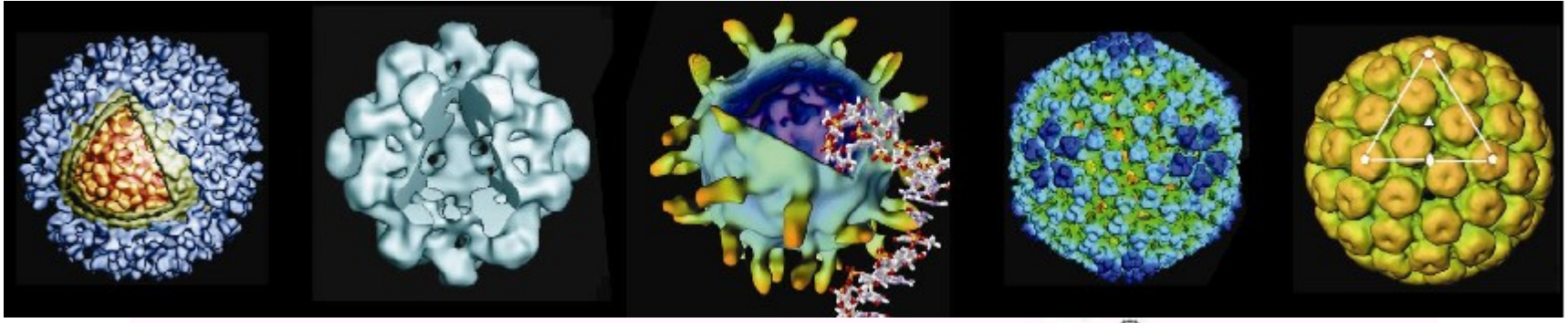


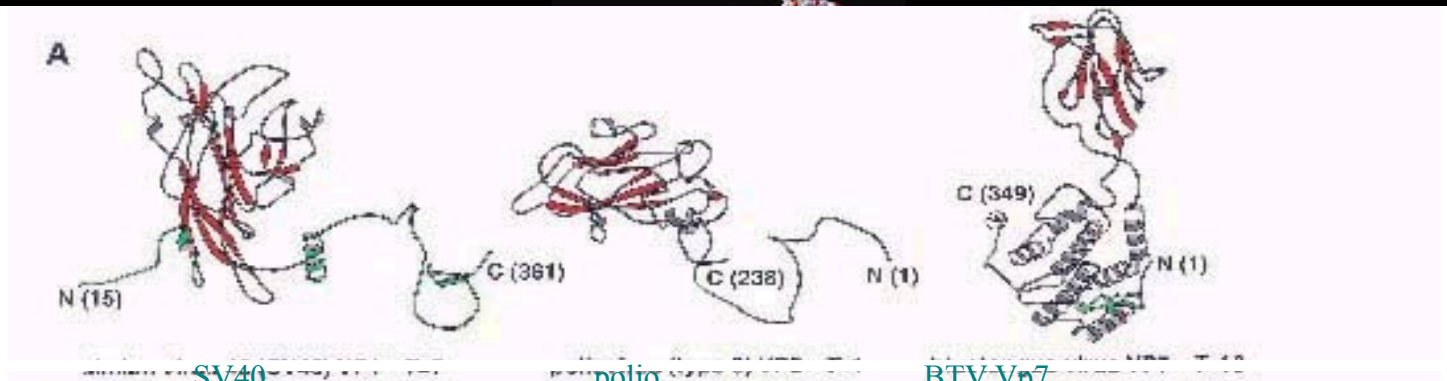
and are oriented perpendicular to the budding tip. This finding argues against random incorporation of RNPs into virions[5], supporting instead a model in which each segment contains specific incorporation signals that enable the RNPs to be recruited and packaged as a complete set[6–12]. A selective mechanism of RNP incorporation into virions and the unique organization of the eight RNP segments may be crucial to maintaining the integrity of the viral genome during repeated cycles of replication.

To elucidate the architecture of the virion interior, we longitudinally and transversely sectioned A/WSN/33 (H1N1) virions budding from Madin–Darby canine kidney (MDCK) cells at 10 h after infection. Although A/WSN/33 virions released into culture medium are spherical in shape[13], the budding virions in longitudinal sections were elongated and contained rod-like structures that were associ-

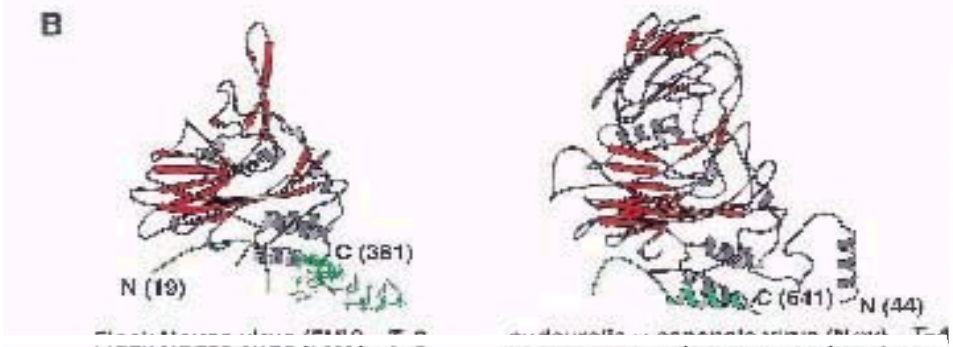
Co ty


Primary structure
Secondary structure
Tertiary structure
Quaternary structure
Lys
Lys
Gly
Gly
Leu
Val
Ala
His
Amino acid residues
α Helix
Polypeptide chain
Assembled subunits

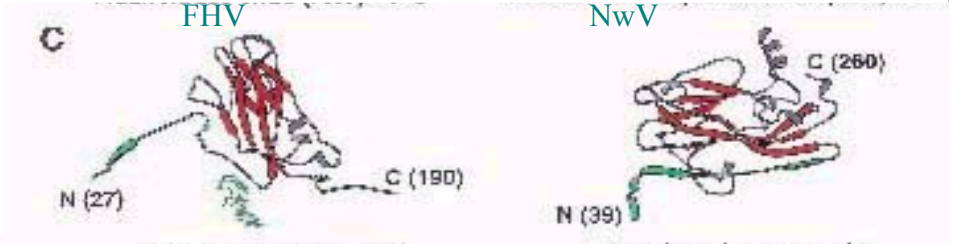




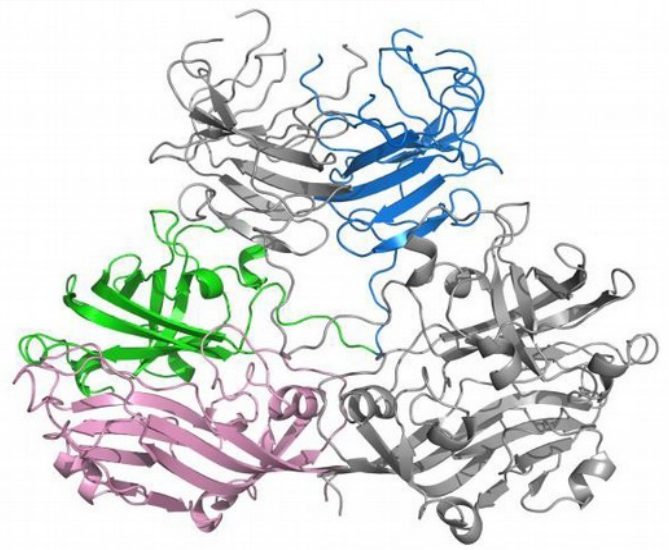
SV40 polio BTV Vp7

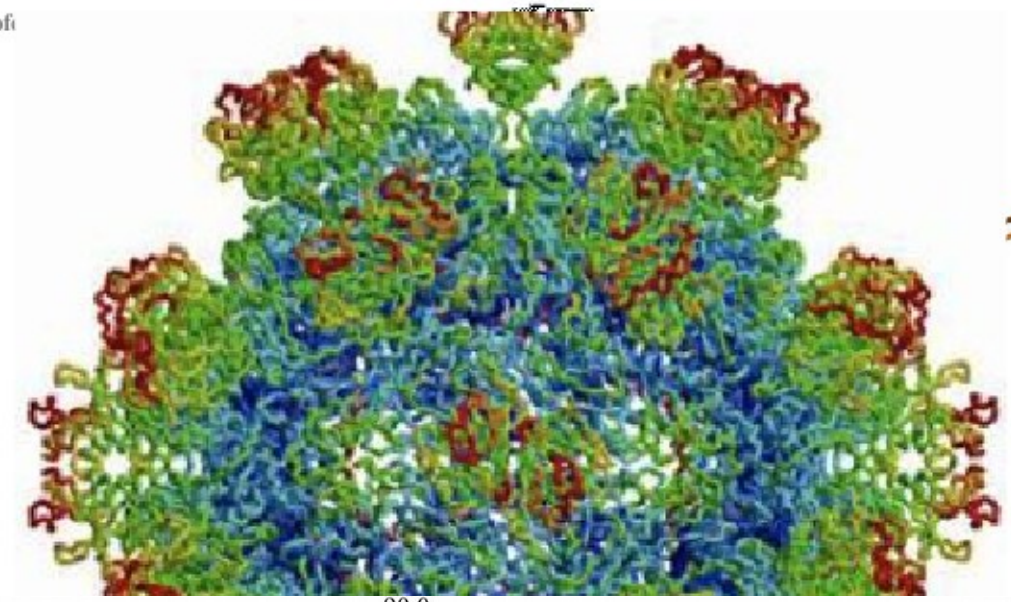


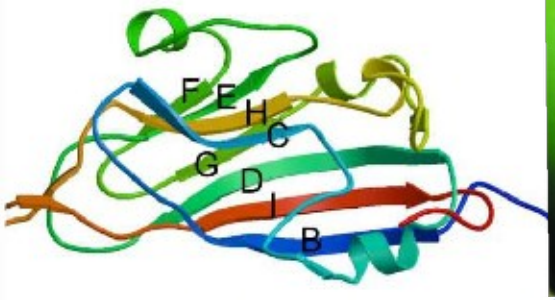
FHV NwV



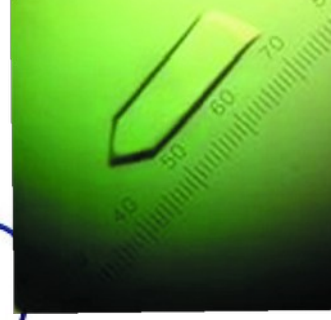
CCMV SBMV



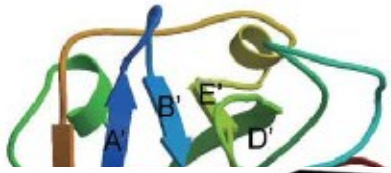


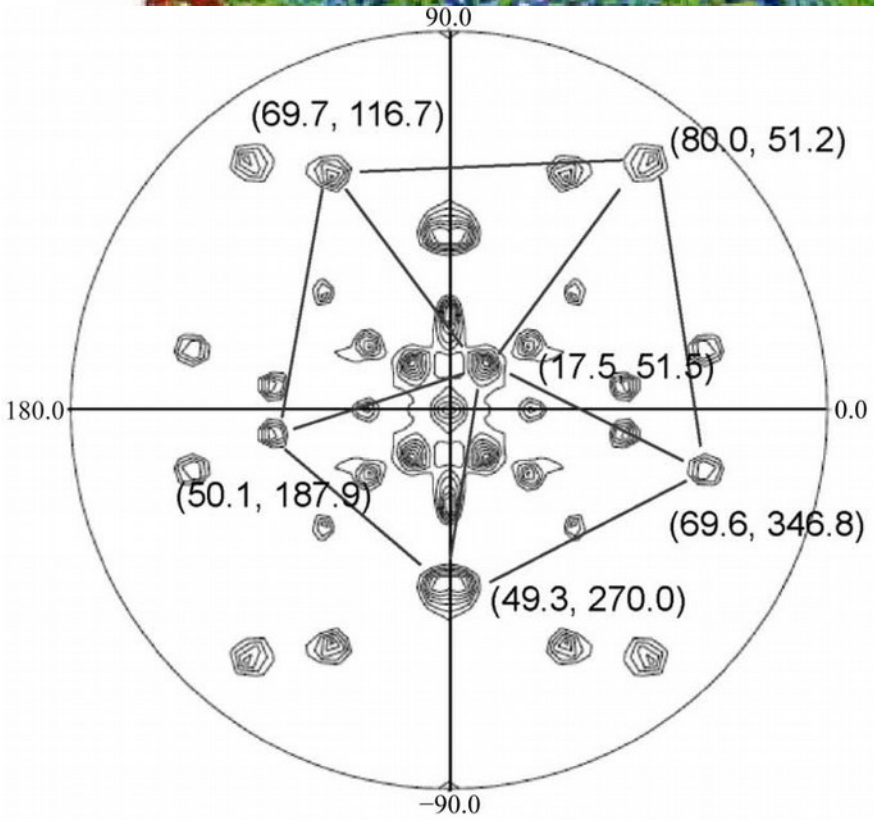


S1 domain

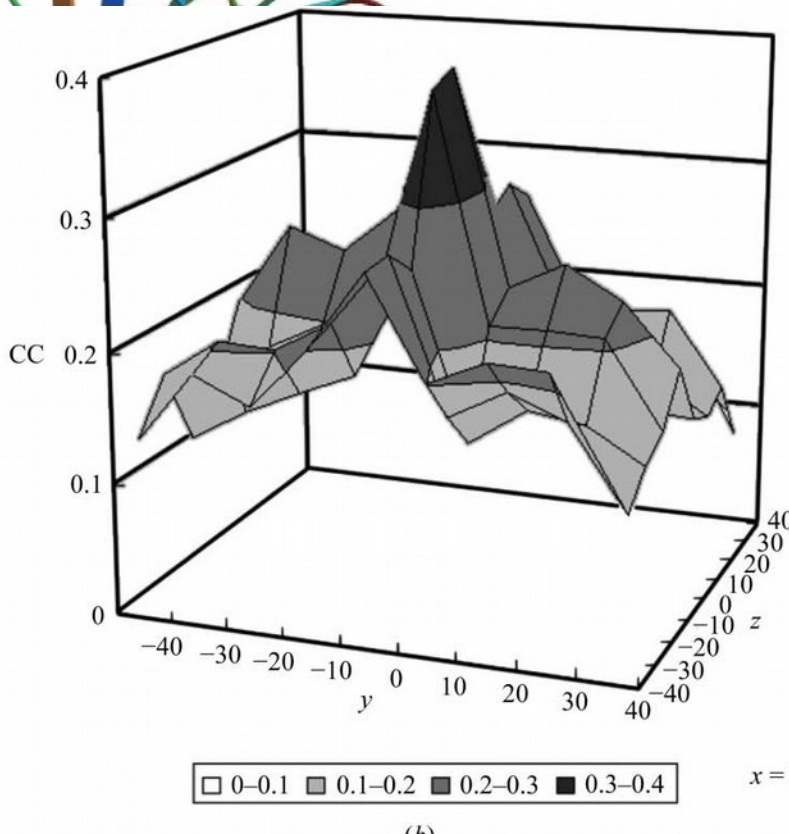


Acta Cryst. (2008). F64, 318–322





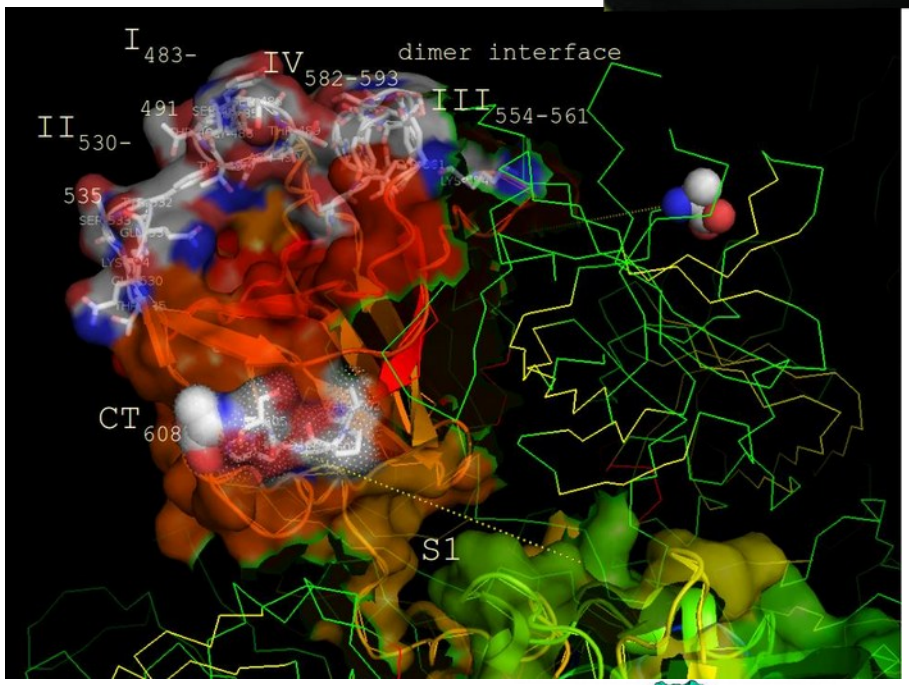
(a)

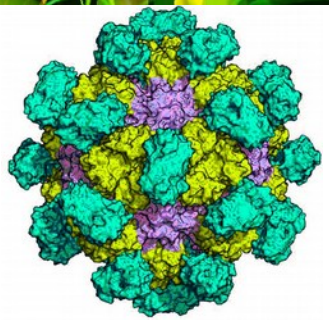


(b)

HEV β-strand jellyroll core

- The sheets in the core of a globular protein are typically constant and conserved in sequence and structure
- Much of the surface is composed of loops and tight turns that connect the helices and sheets of the core
- The surface is a complex landscape of different structural elements
- These surface elements can be engineered to redirect the interactions with other proteins





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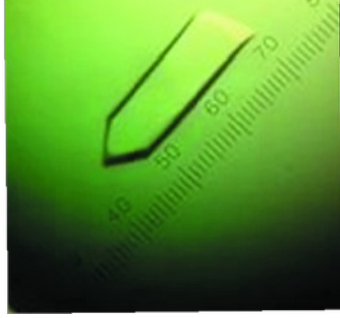
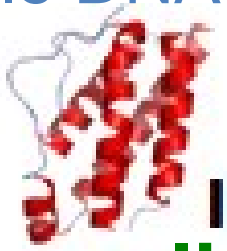
Beyond a simple DNA vehicle



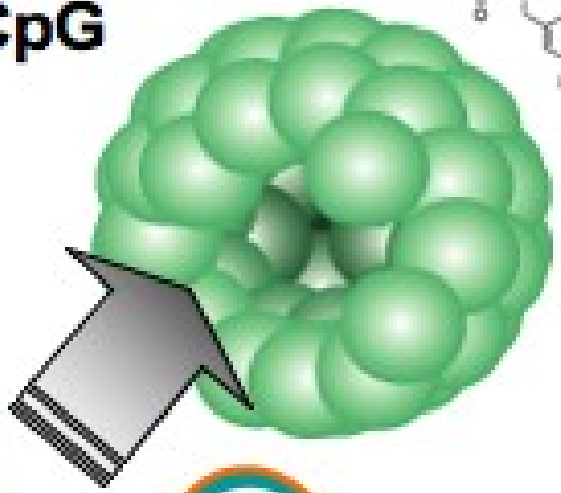


LXY3

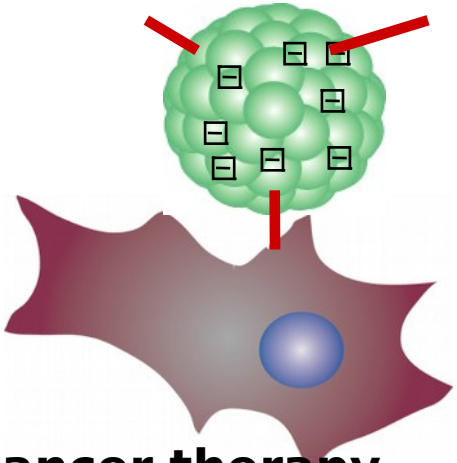
IL-2

ligation

CpG



EGF



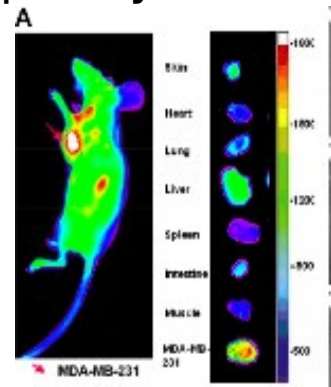
Therapeutic packaging

GFP yCD

Gold

Ferrite

hyperthermo cancer therapy on magnetic field frequency triggers



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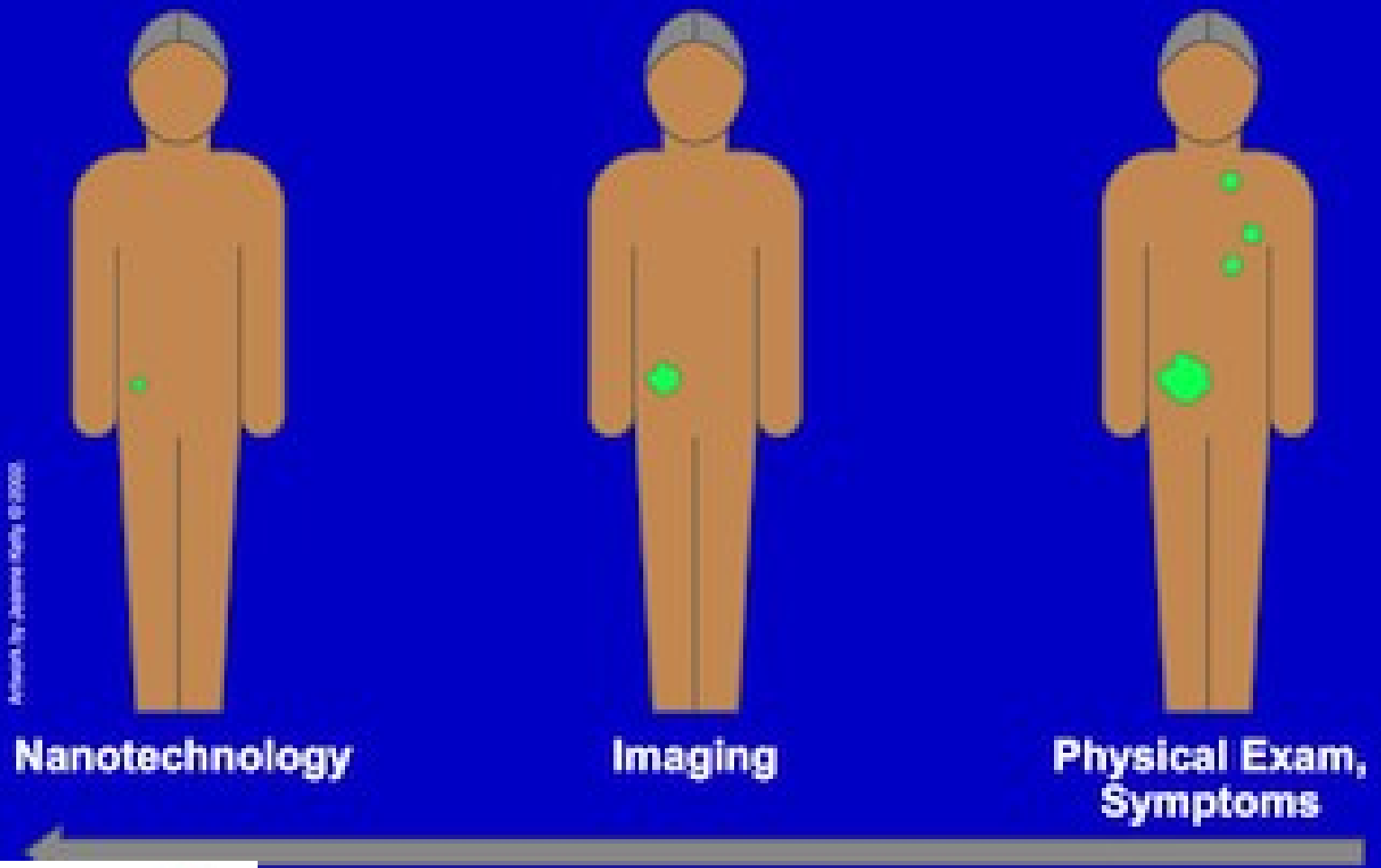
UCDAVIS HEALTH SYSTEM

Nanodevices Can Improve Cancer Detection and Diagnosis



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