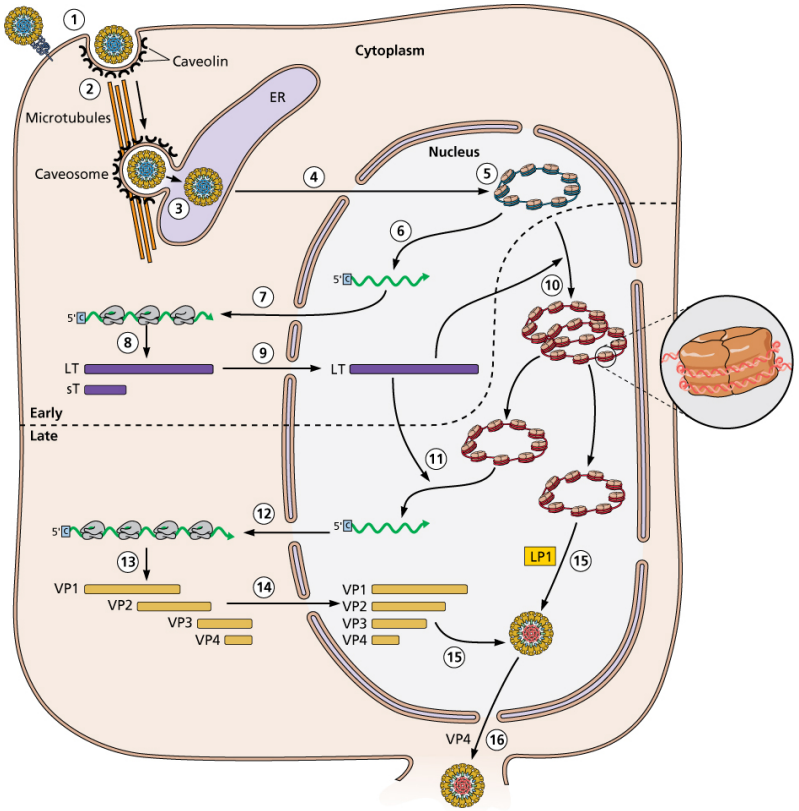
Attachment and Entry

Lecture 5
Biology 3310/4310
Virology
Spring 2017

Who hath deceived thee
so often as thyself?
--Benjamin Franklin

Viruses are obligate intracellular parasites



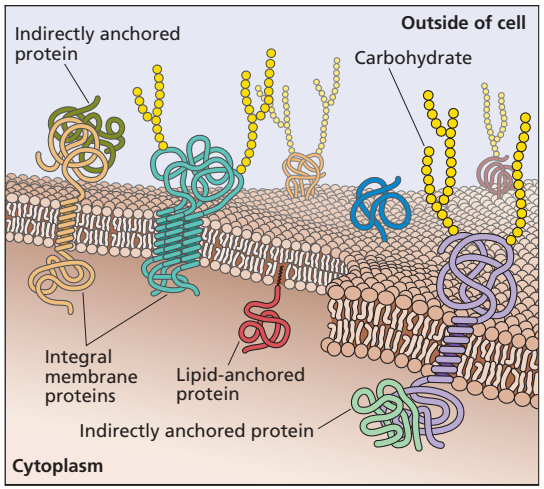
Virus particles are too large to diffuse across the plasma membrane

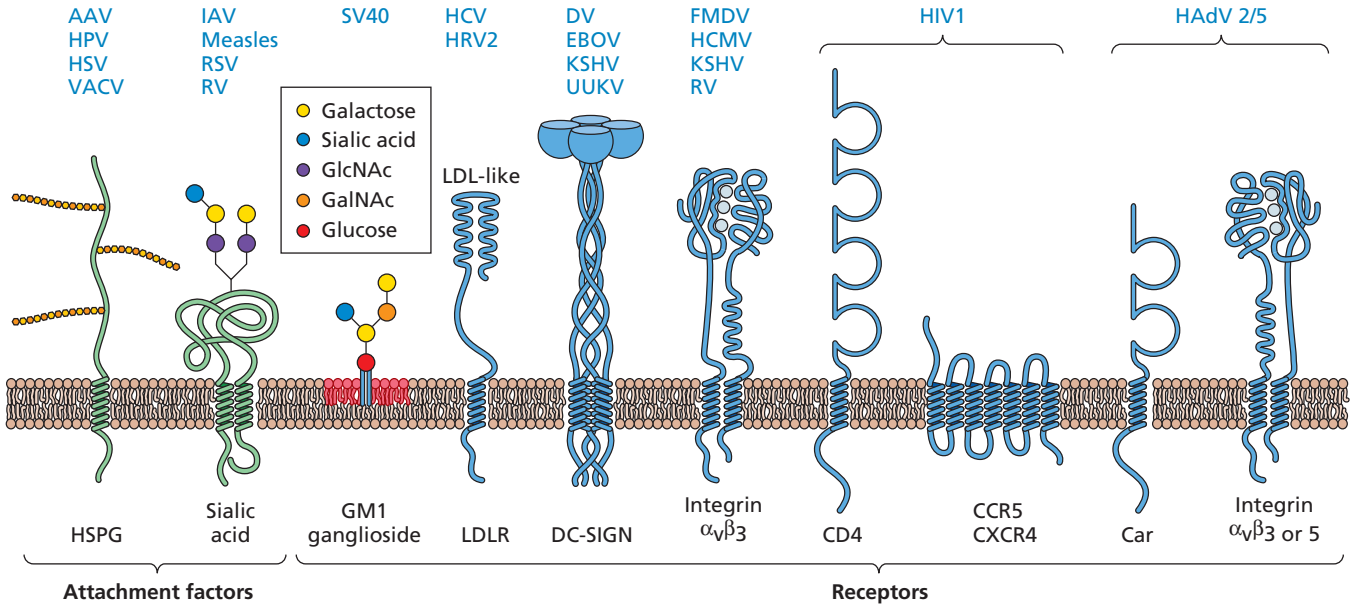
Finding the ‘right’ cell

- Step 1: adhere to cell surface (electrostatics)
  - No specificity
- Step 2: Attach to specific receptor molecules on cell surface
  - More than one receptor may be involved
- Step 3: Transfer genome inside the cell

Cellular receptors for viruses

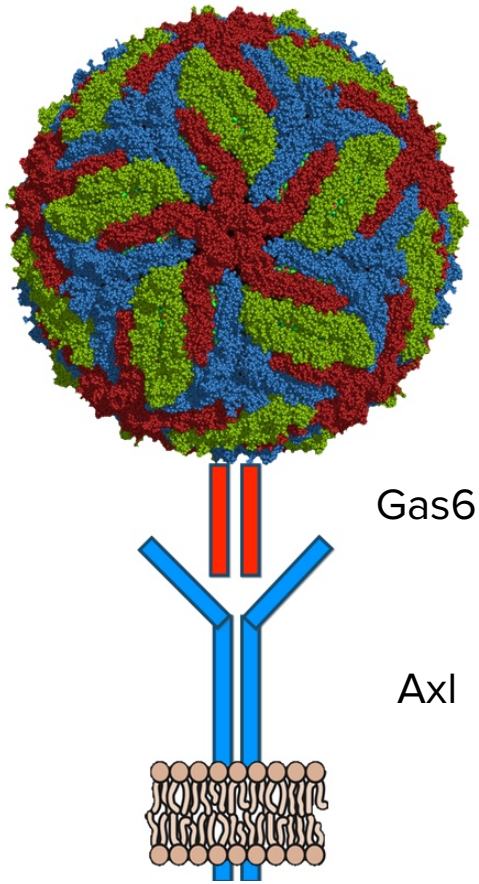
- Essential for all viruses except those of fungi (no extracellular phases) and plants (enter cells by mechanical damage)
- 1985: one receptor known, sialic acid for influenza virus



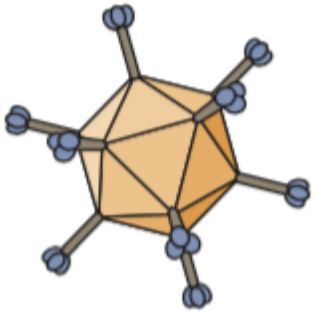


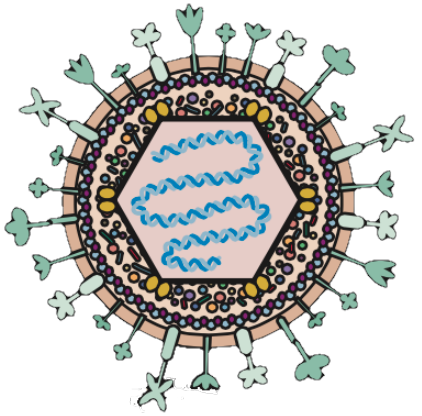
Cell functions!

A receptor and a soluble protein



Different viruses can bind the same receptor

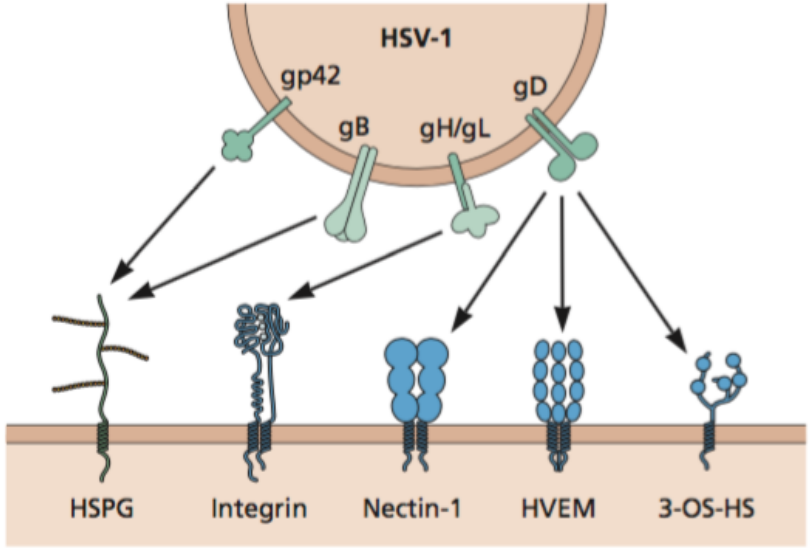


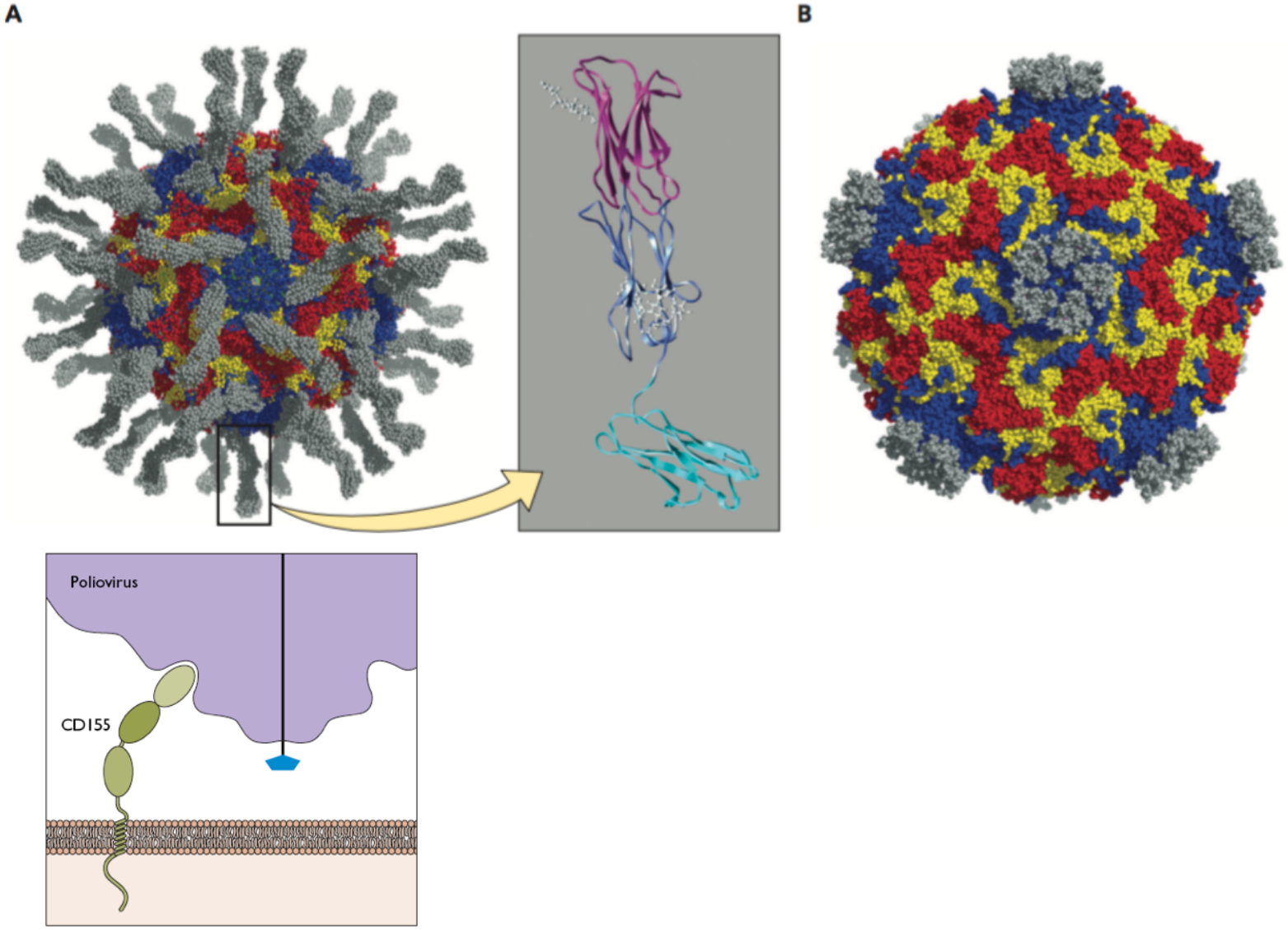


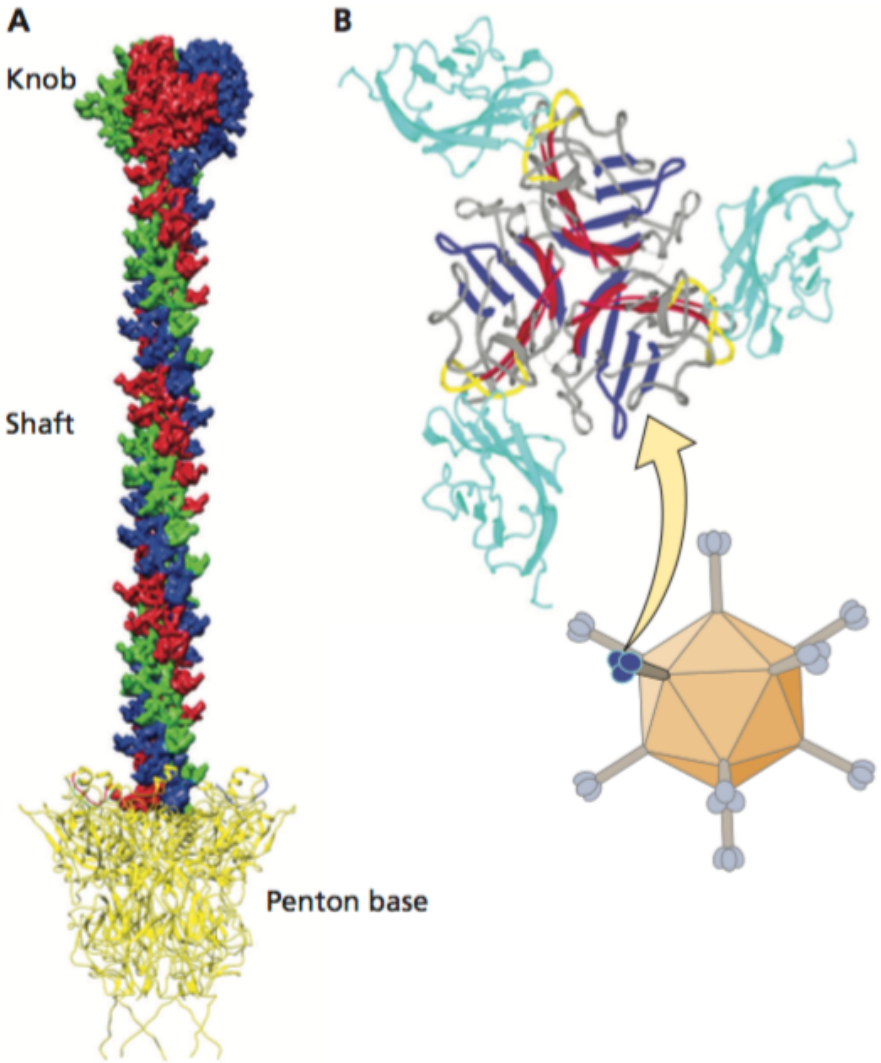
- Adenovirus and Coxsackievirus B3 have common primary receptor
- The swine herpesvirus, pseudorabies virus, binds same receptor as human poliovirus

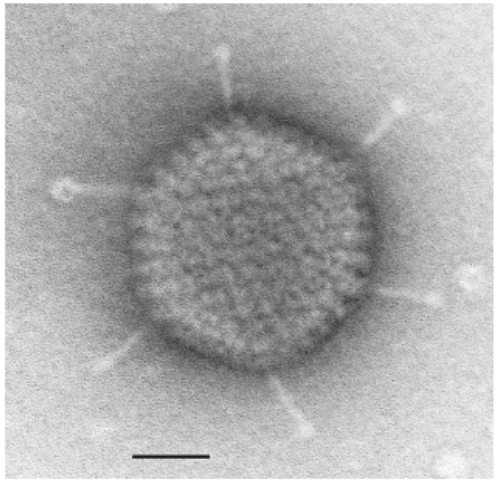
Viruses of the same family may bind different receptors

- Rhinoviruses (3), retroviruses (16)
- One virus may bind multiple receptors

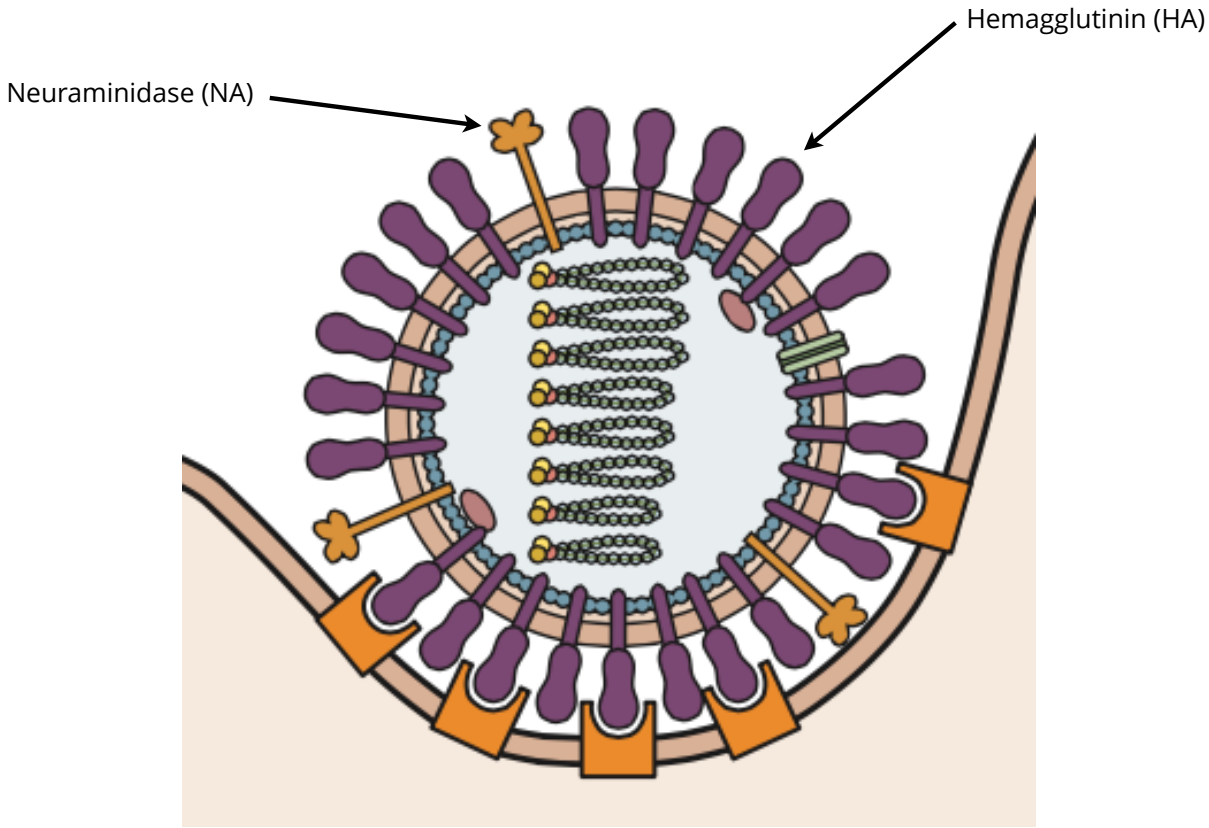




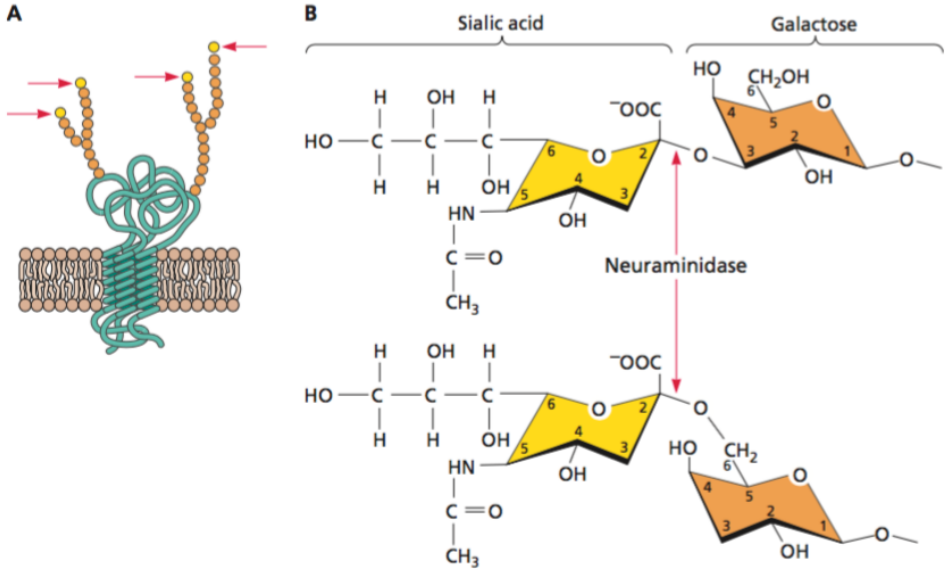




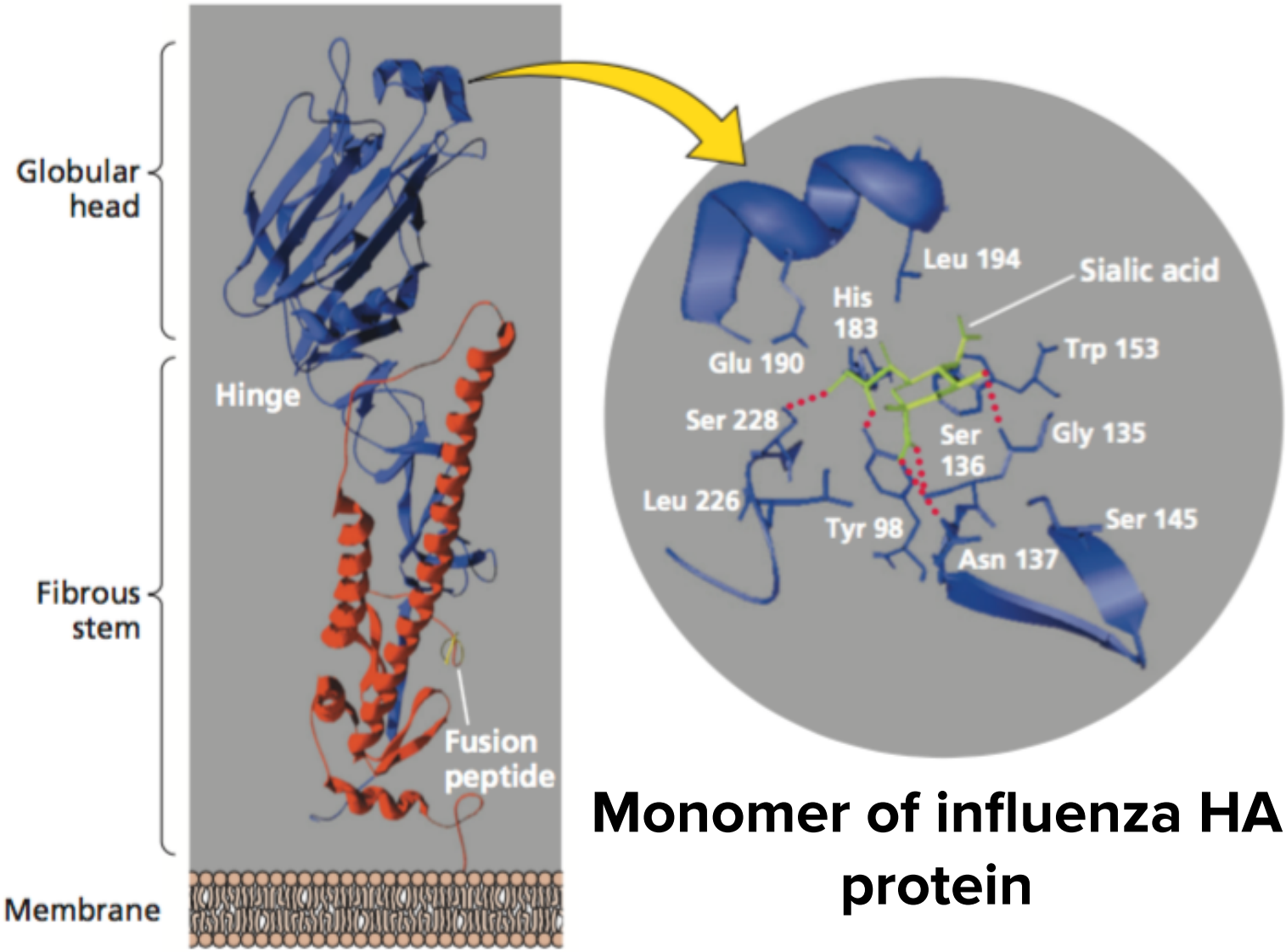
Influenza virus attachment to cells



Sialic acid: receptor for influenza viruses

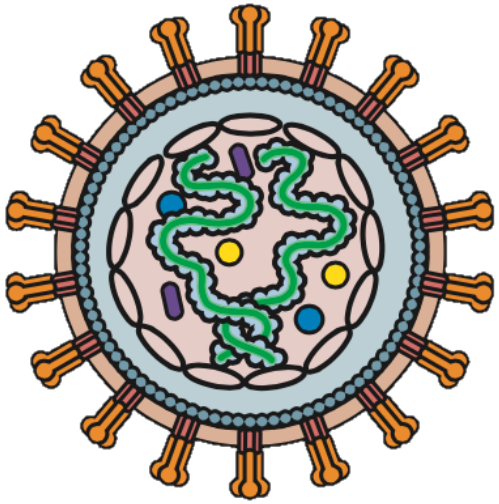


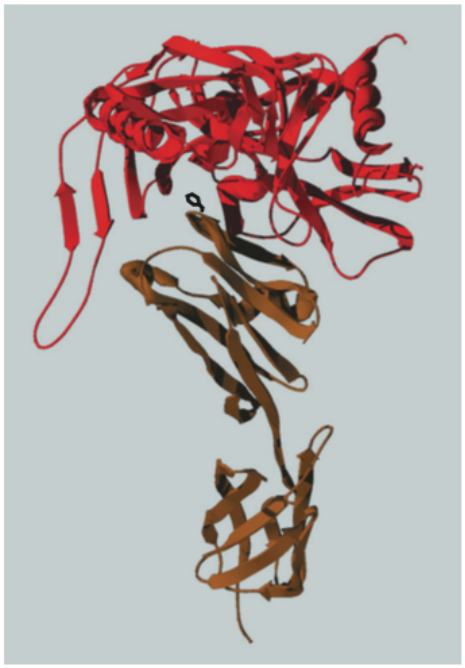
- Sialic acids: N-acetylneuraminic acid (A,B); 9-O-acetyl-N-neuraminic acid (C)
- α(2,6) preferentially bound by human strains, α(2,3) by avian

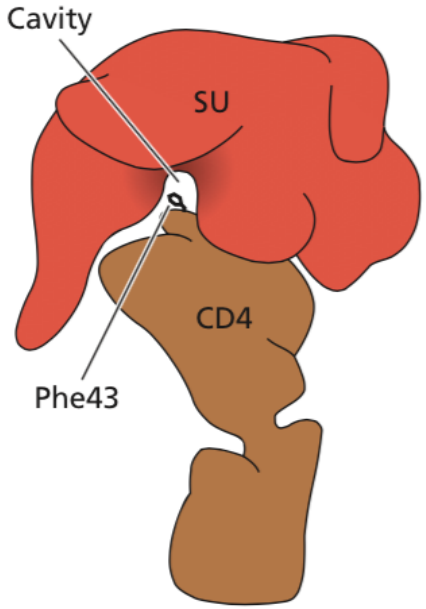


Monomer of influenza HA protein

HIV-1 attachment







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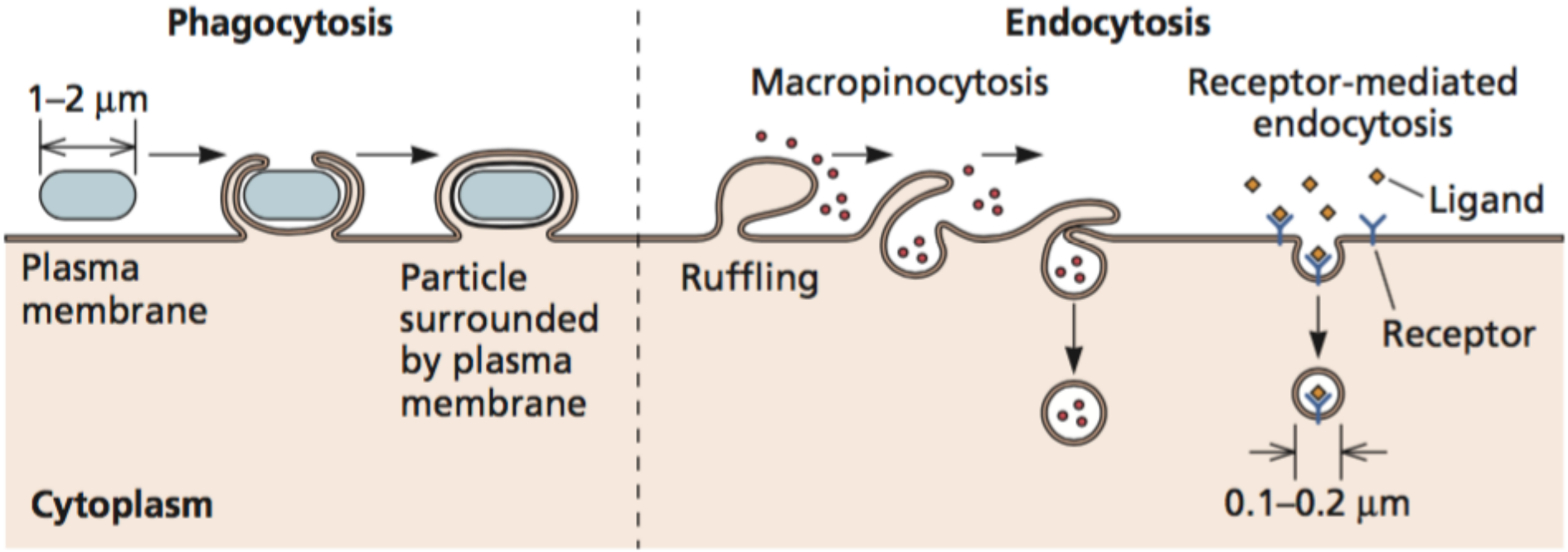
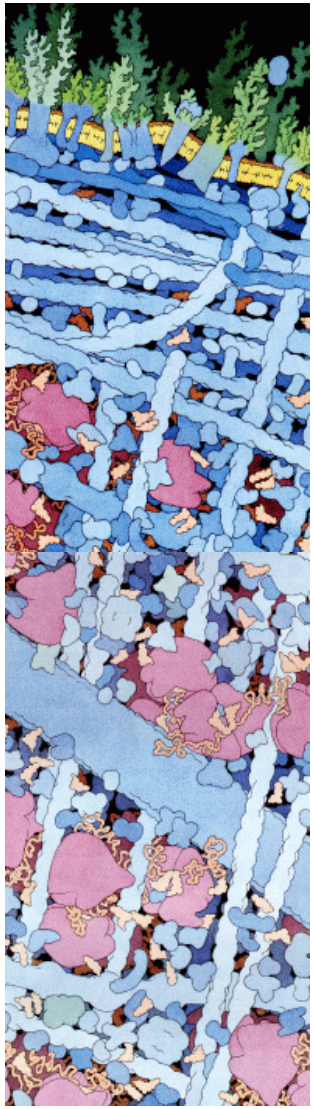
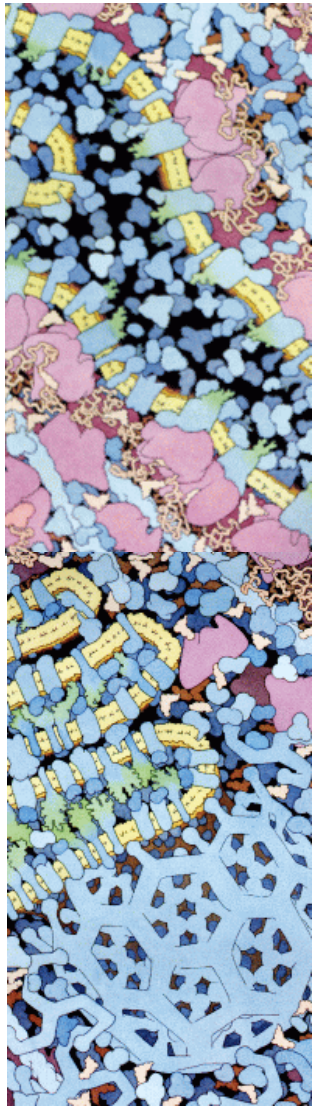
Viral receptors on the cell surface:

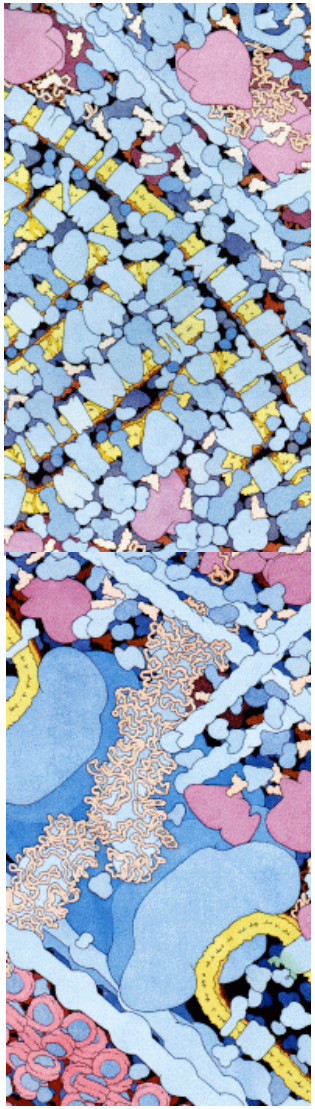
A. Can bind directly to icosahedral virus capsid proteins
B. Interact with glycoproteins of enveloped viruses
C. Can be carbohydrate or protein molecules
D. Have cellular functions
E. All of the above

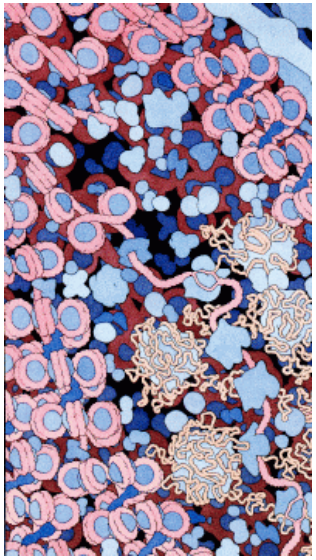
Entry into cells





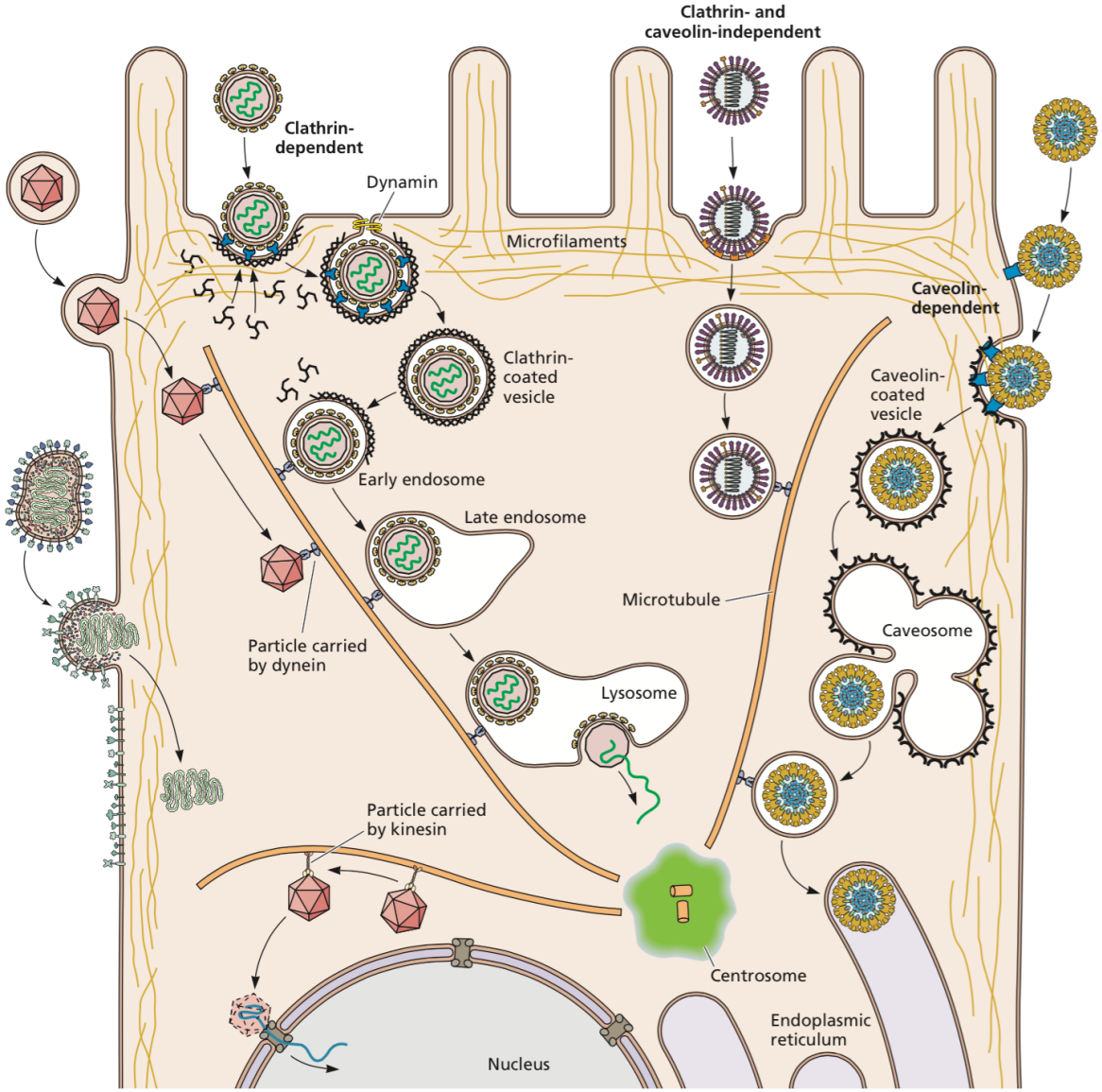




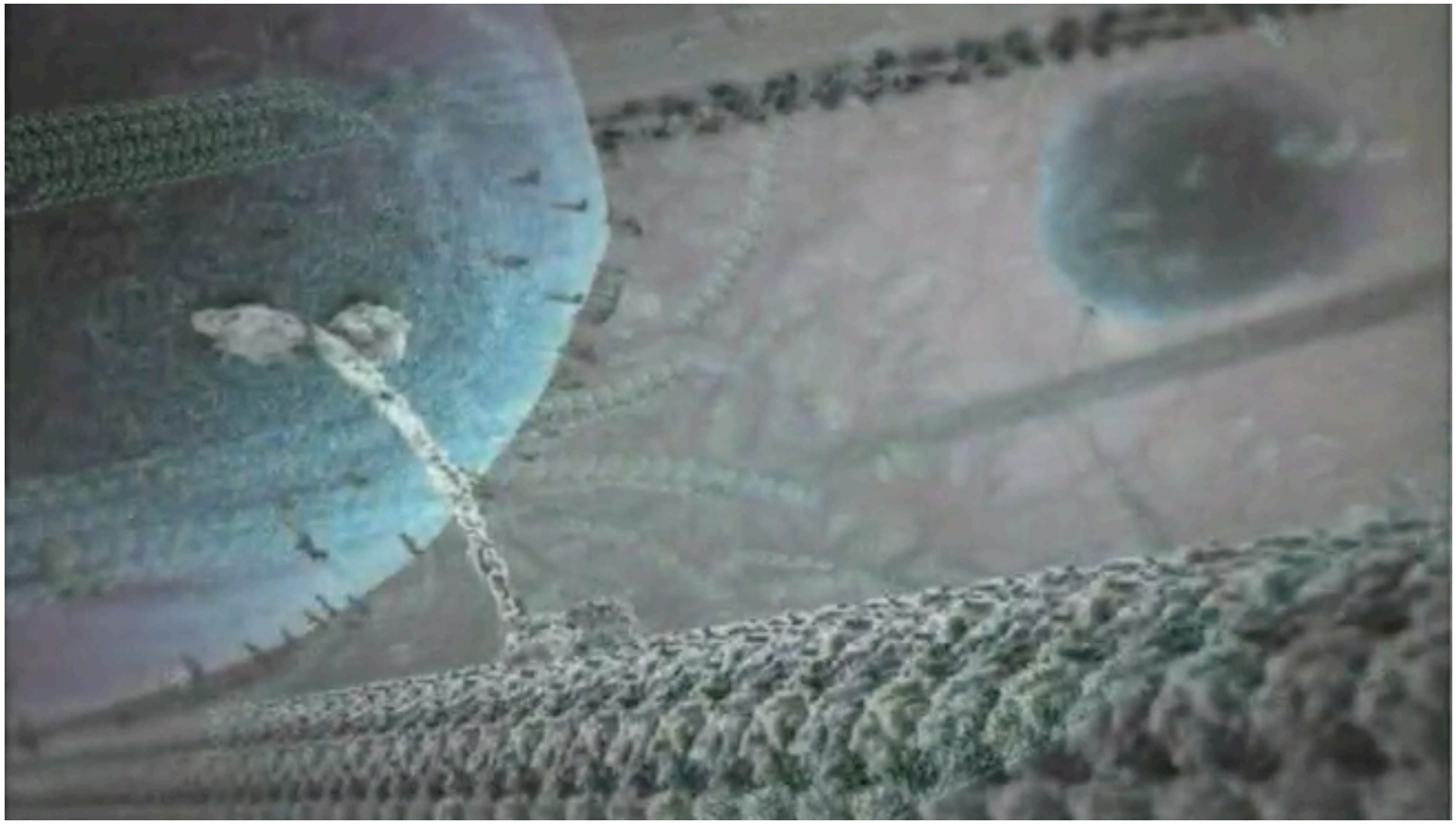


The cytoplasm is crowded!

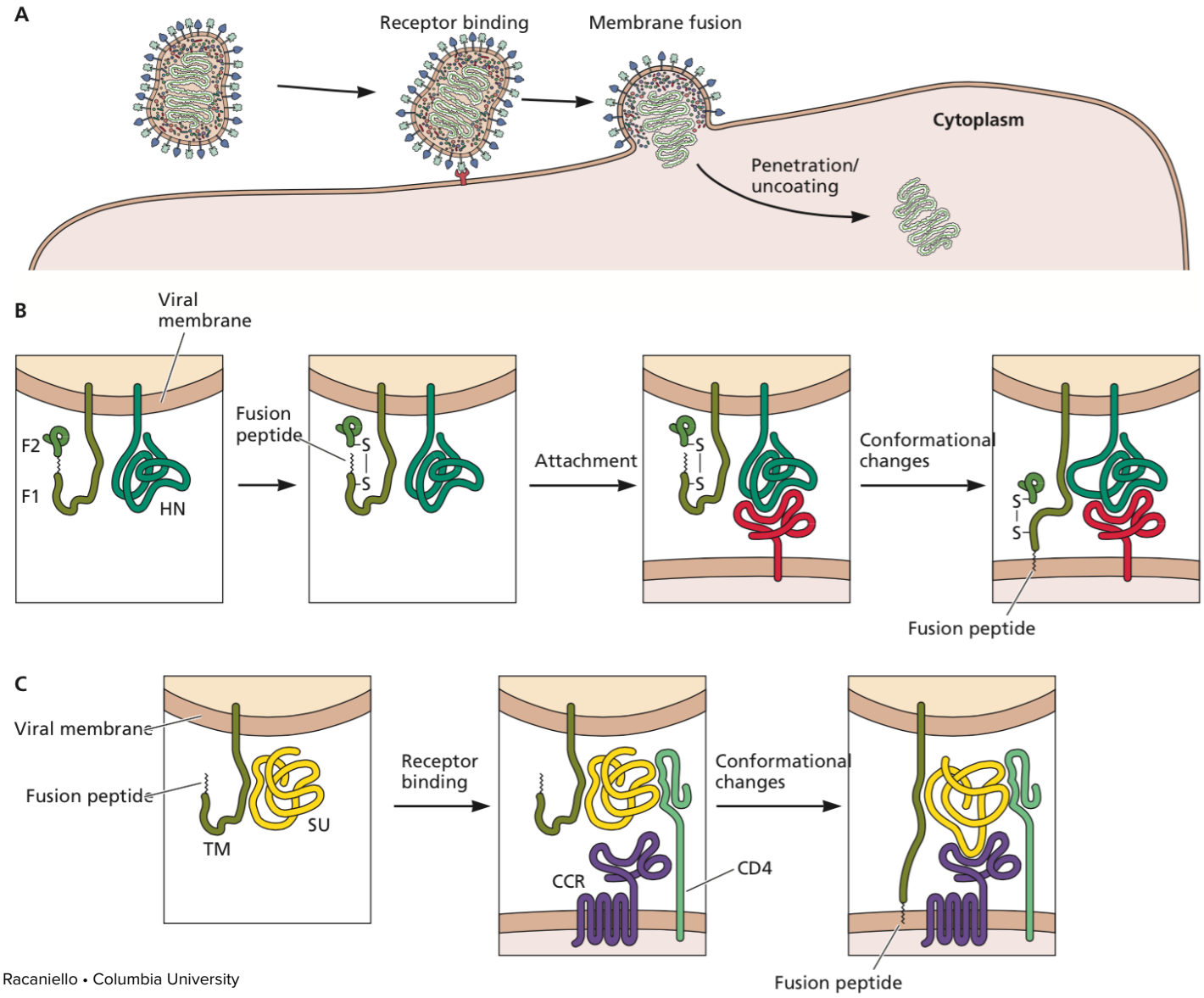
Movement of large protein complexes will not occur by diffusion!

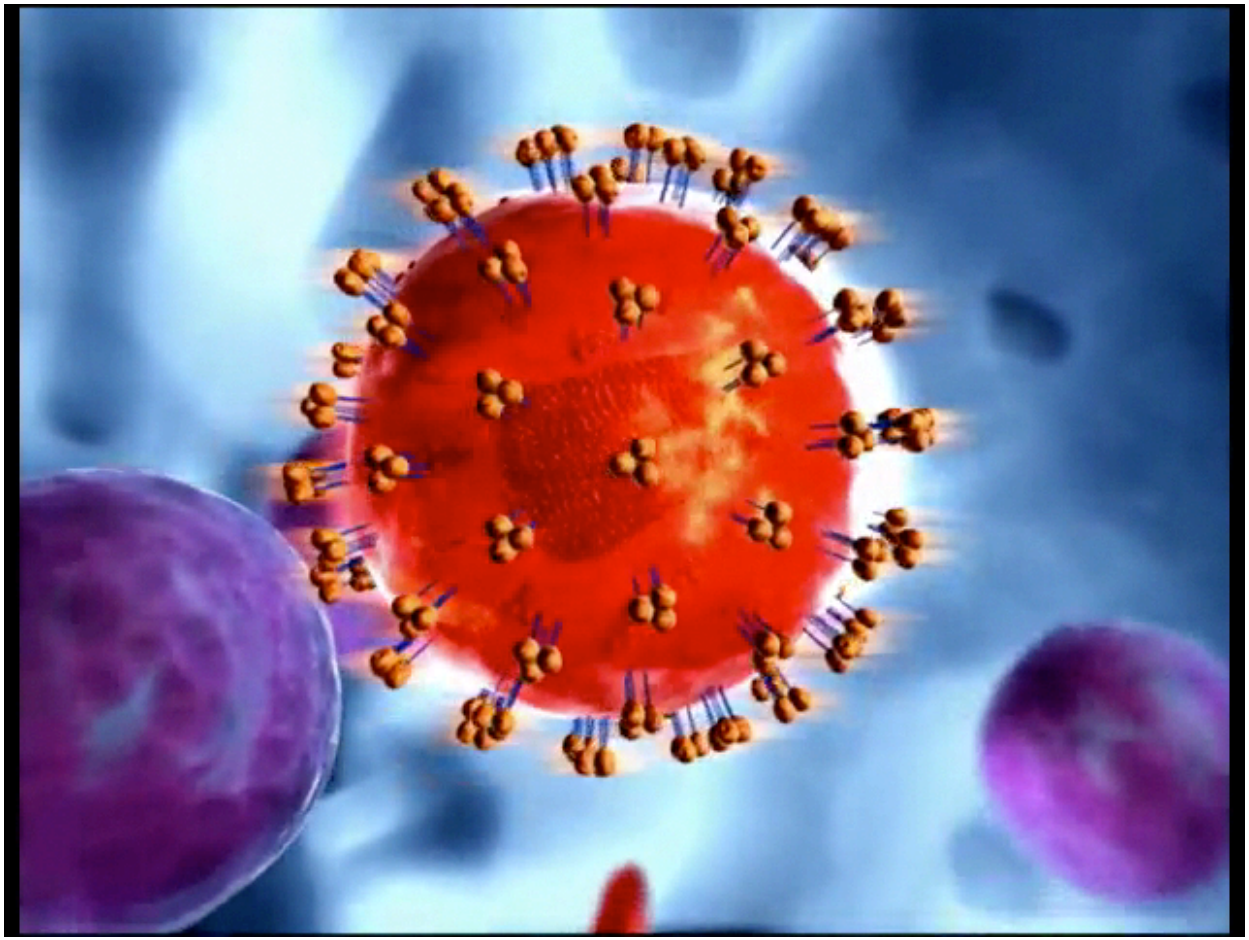


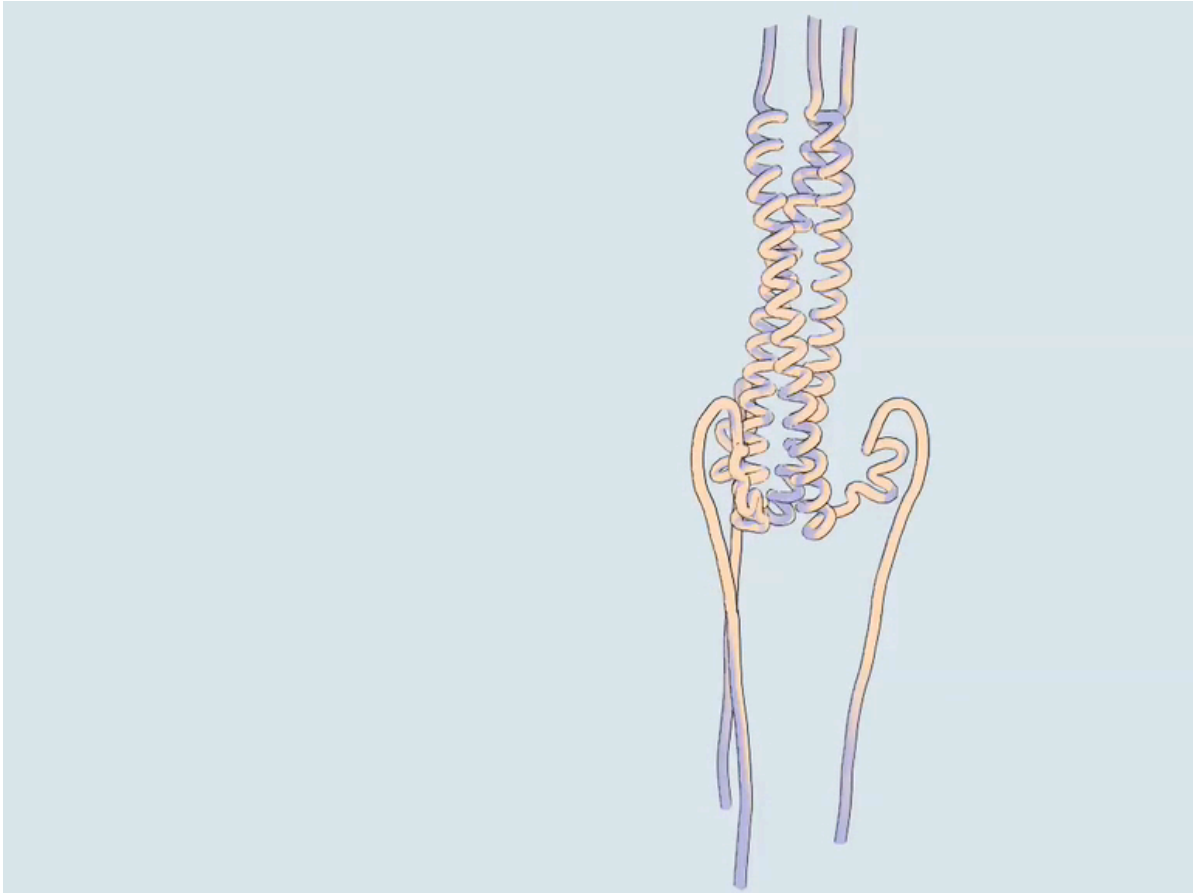
Movement of endosomes



XVIVO Scientific Animation http://www.xvivo.net/







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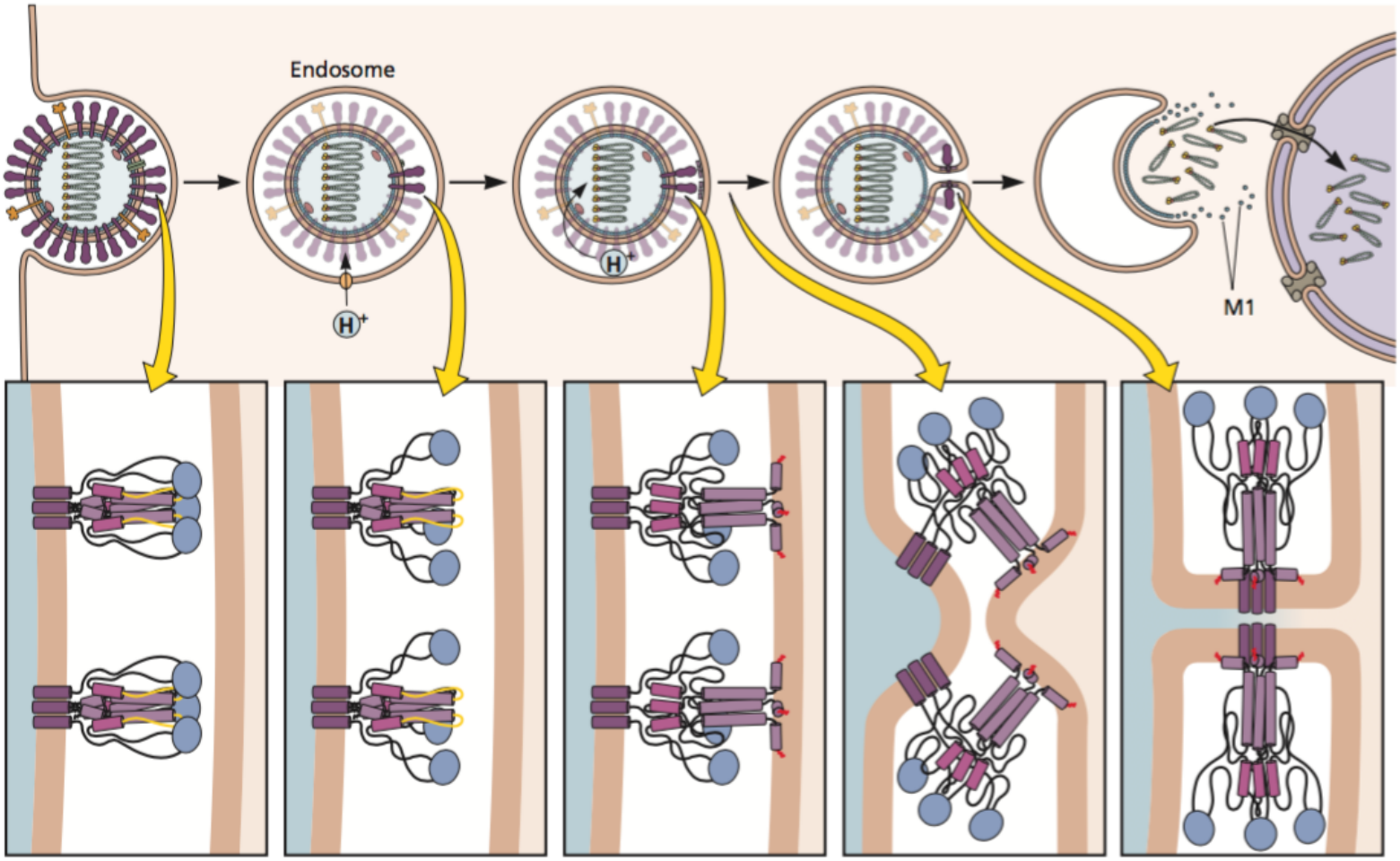
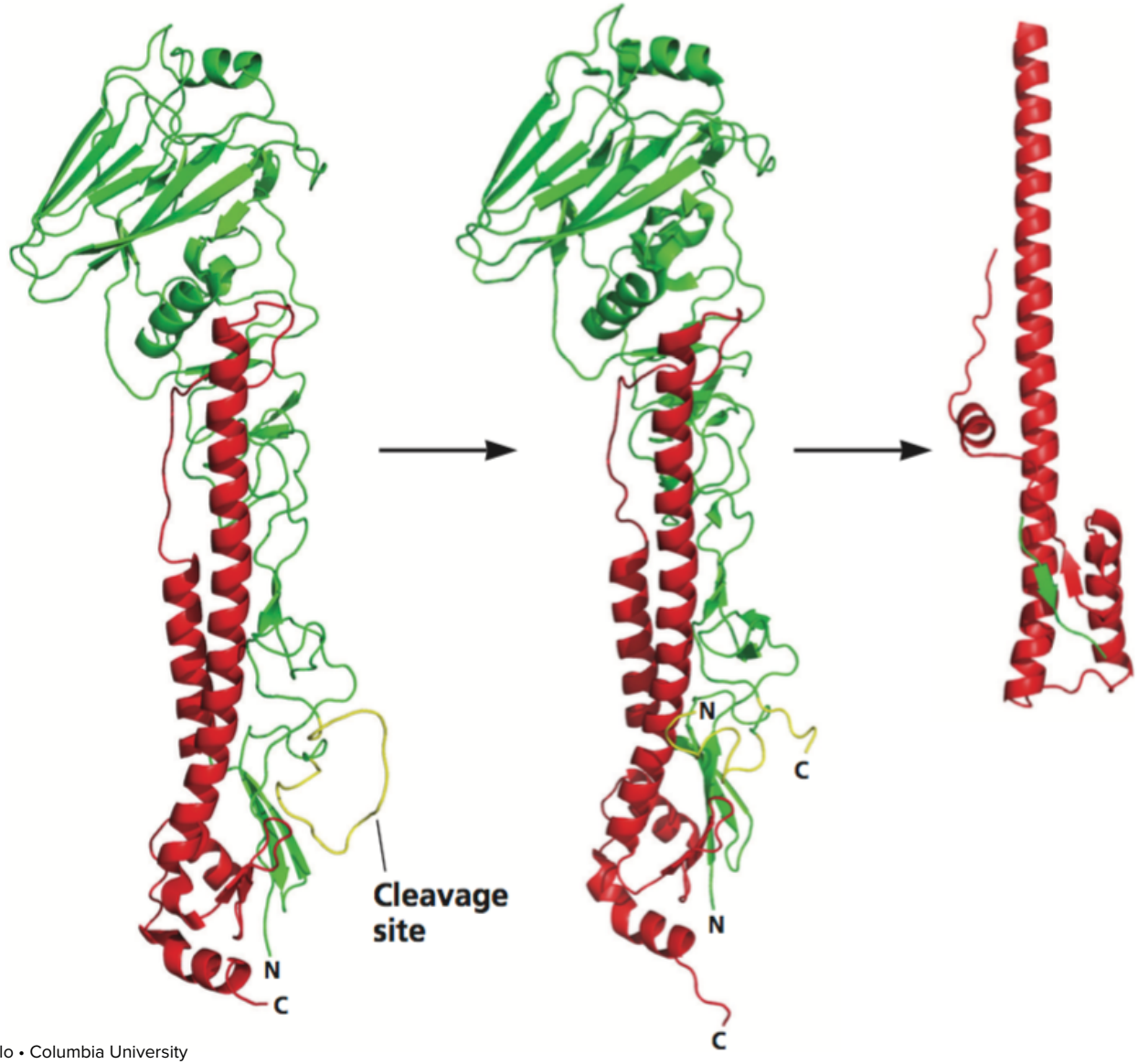
Which of the following does not play a role in virus entry:

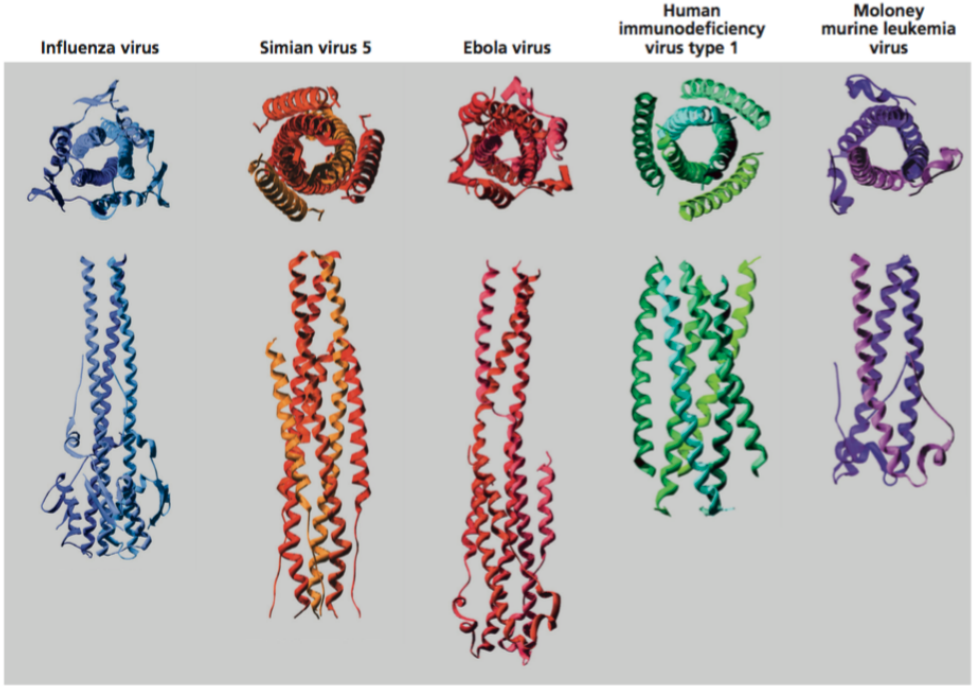
A. Clathrin-mediated endocytosis
B. Fusion of viral and plasma membranes
C. Diffusion of virus particles in the cytoplasm
D. Microtubule-mediated transport
E. Lysosomes





Class I fusion proteins

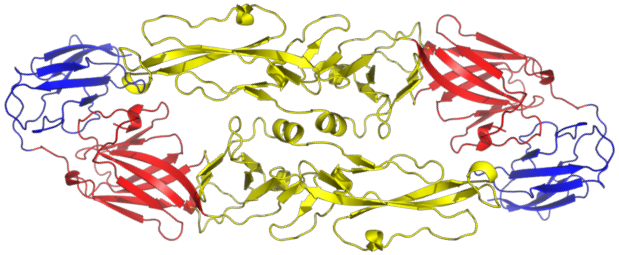
- Perpendicular to membrane - spikes
- Mostly α-helical
- Form trimers

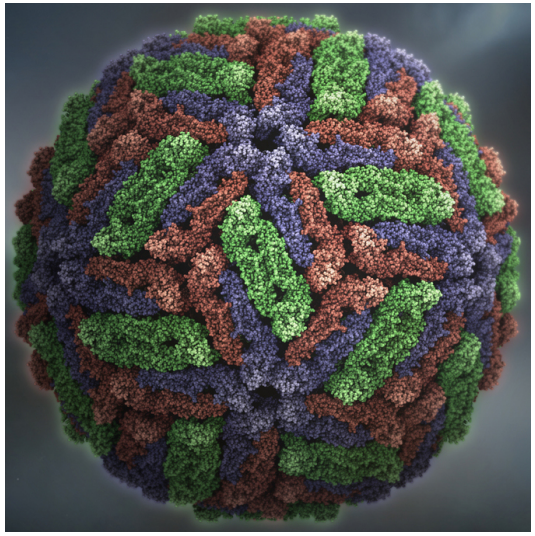


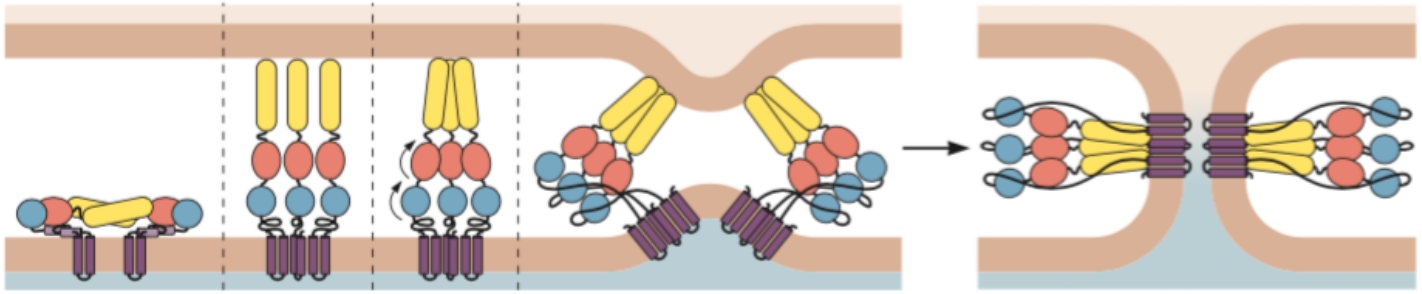
Influenza virus entry

Class II fusion proteins

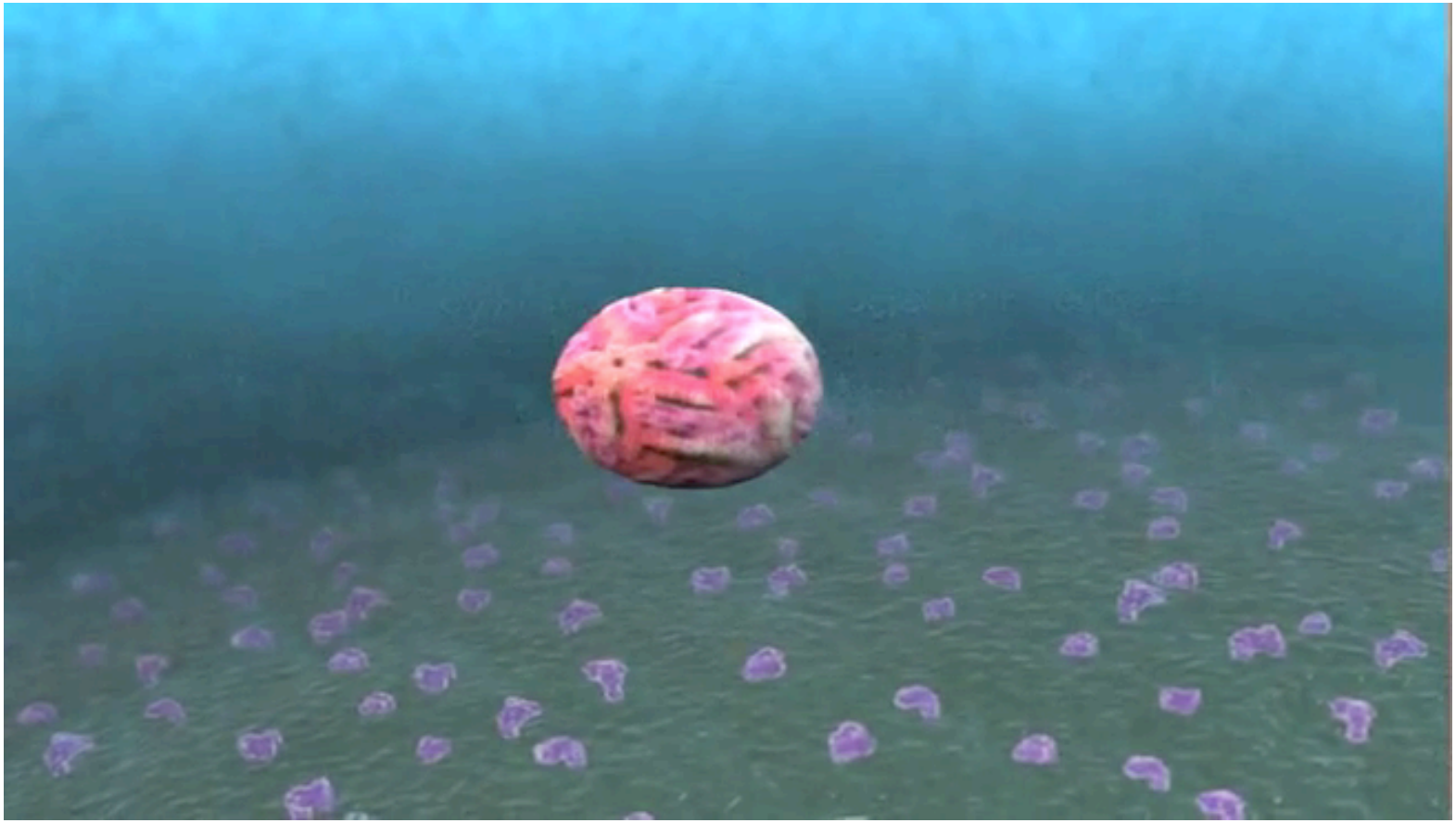
- Mostly β-sheet
- Form dimers
- Parallel to the membrane



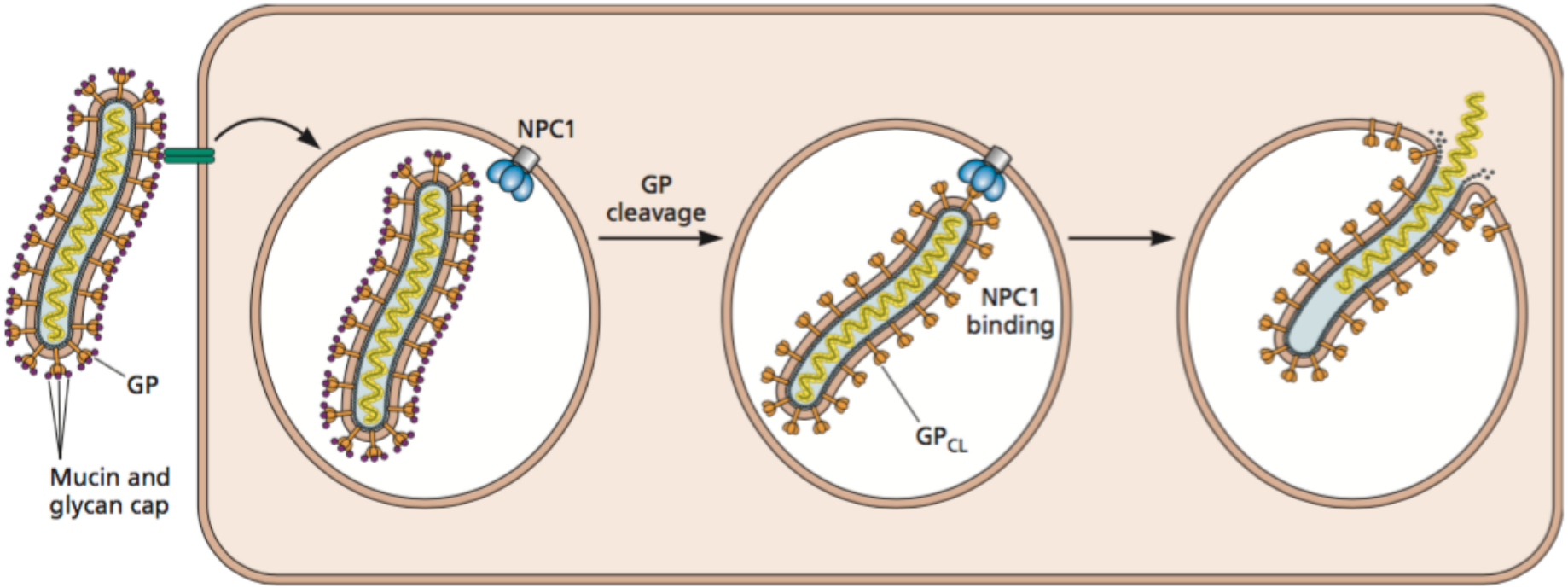




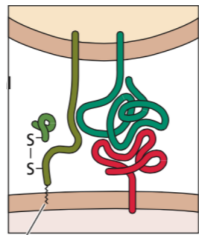
Dengue virus entry



Ebolavirus entry



Fusion is regulated



- Must not occur in the wrong location
- Neutral pH (plasma membrane):
  - Second protein receptor interaction
- Low pH fusion
  - Proteolytic cleavage activates the fusion protein for cleavage (class I)
  - Cleavage of a second protein (class II) activates the fusion protein
  - Endosome fusion receptor

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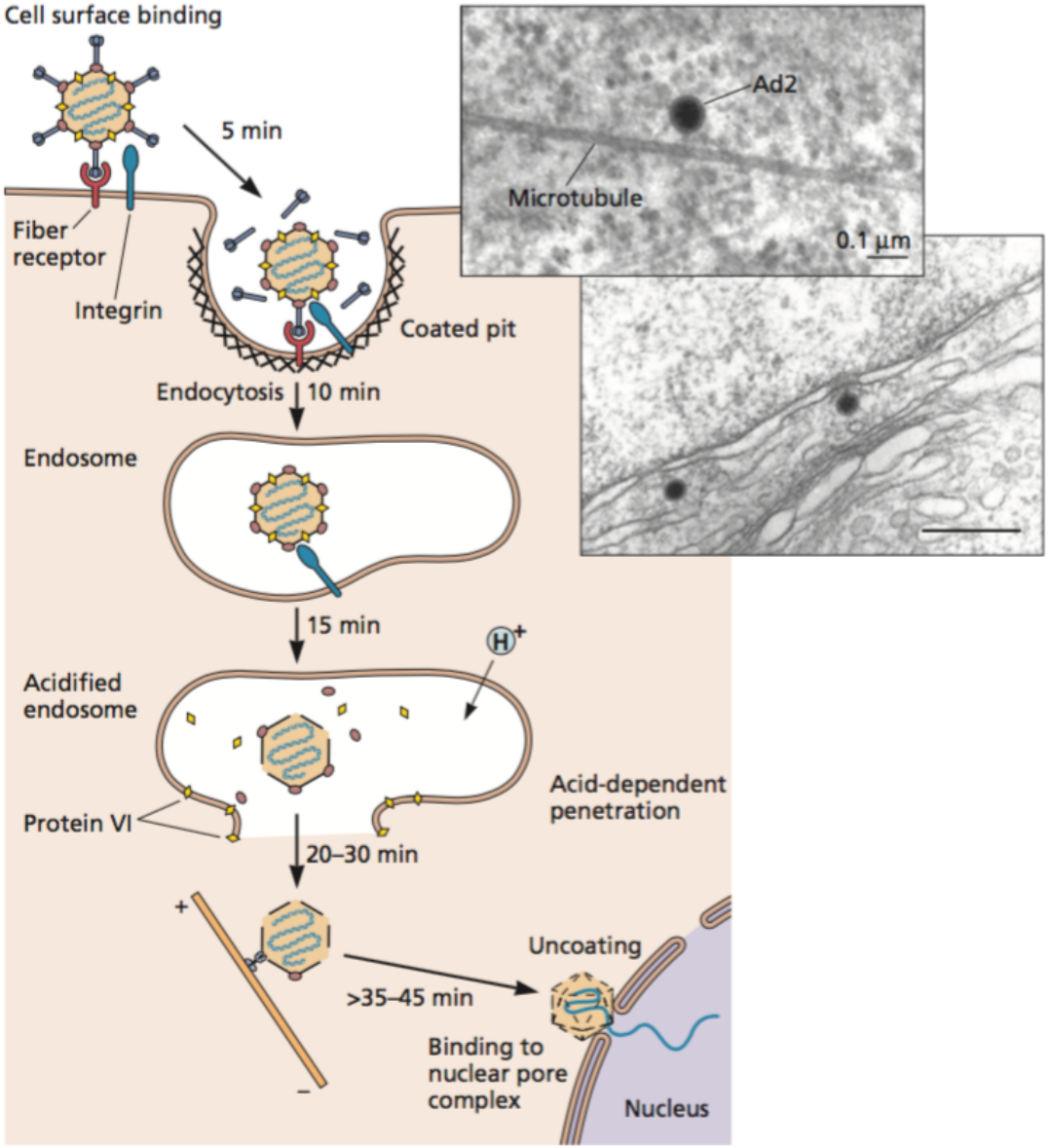
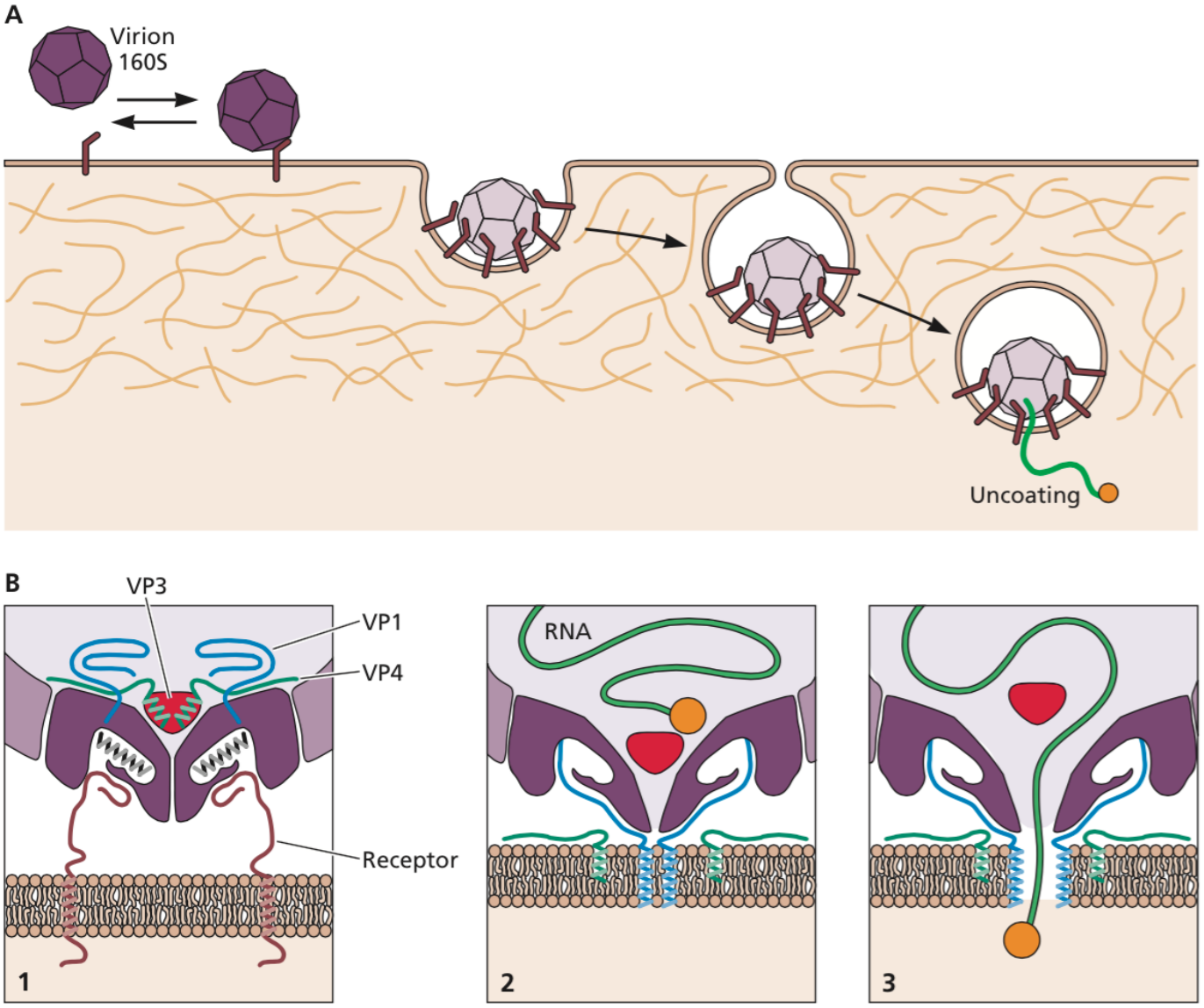
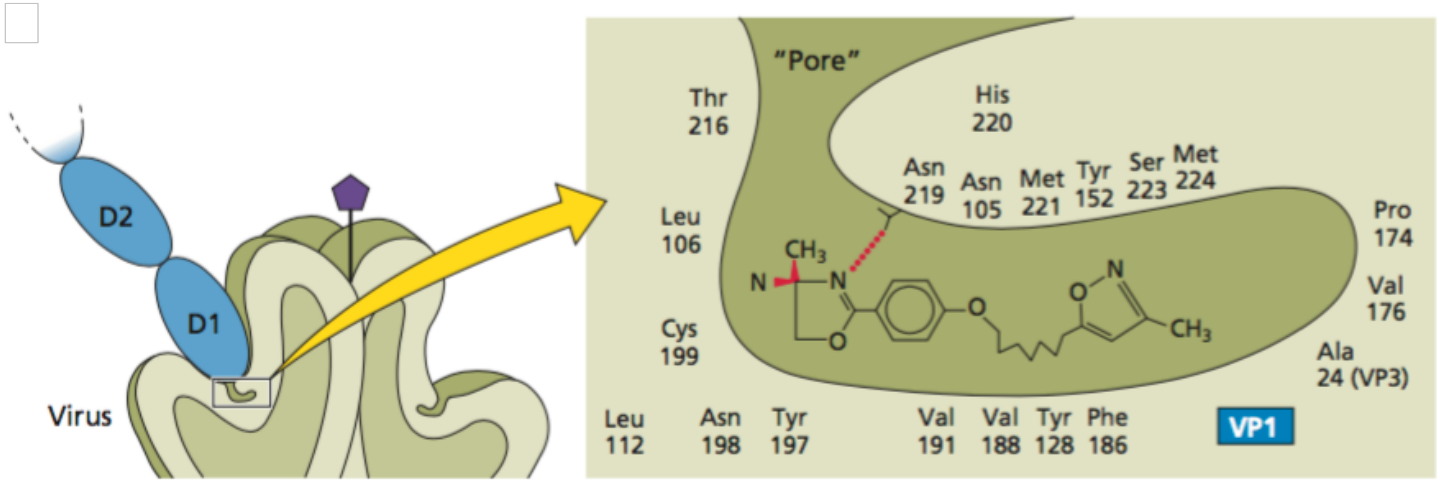
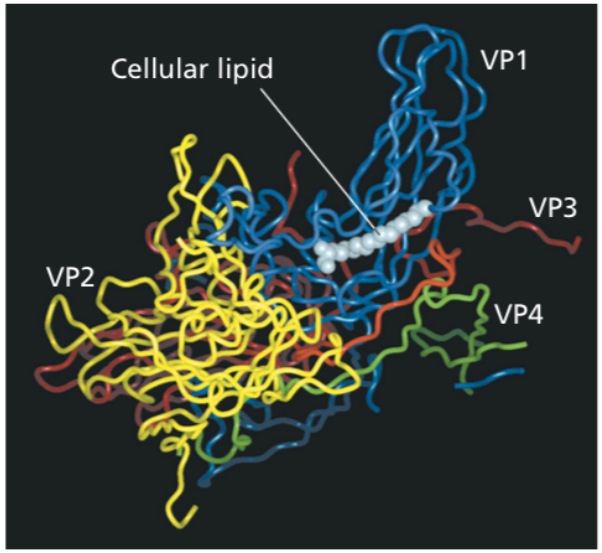
Viral fusion peptides are exposed for insertion into the host cell membrane when:

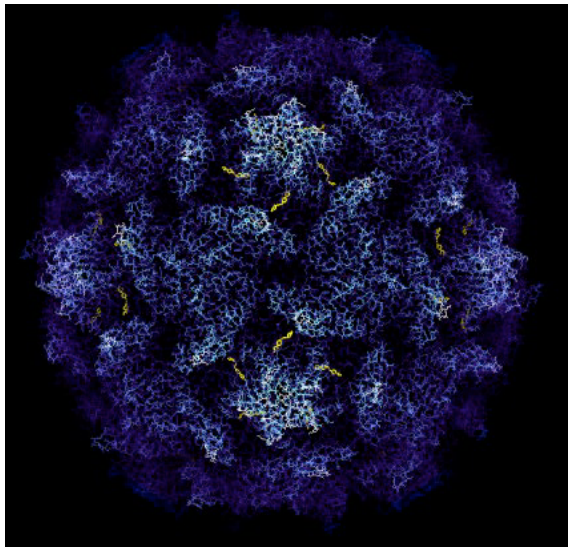
A. The virus particle is near a cell
B. The virus particle is in the cytoplasm
C. Trimers of the fusion peptides form
D. The endosome becomes acidified
E. The virus is docked on the nuclear pore





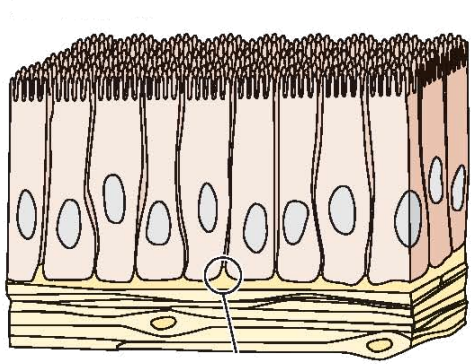


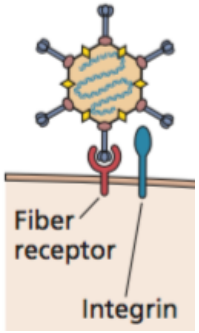


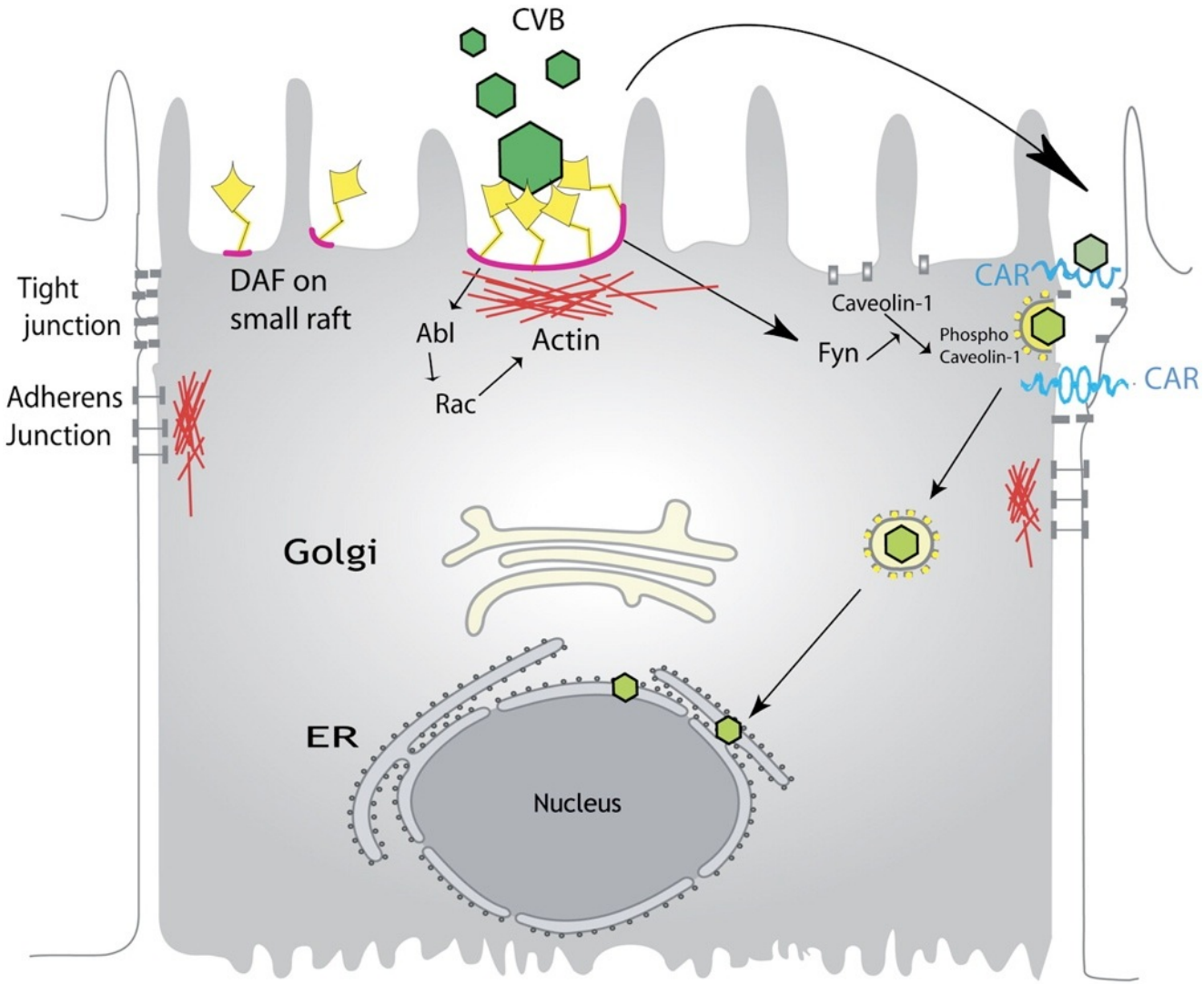


Role of a co-receptor in viral infection

- Entry of Coxsackievirus group B viruses requires two receptors: decay-accelerating factor (DAF), and CAR (coxsackievirus-adenovirus receptor)
- These viruses initiate infection at the epithelial surface
- CAR is a component of tight junctions, not accessible to viruses on the apical surface






CVB
Tight
junction
Adherens
Junction
DAF on
small raft
Abl
Actin
Rac
Caveolin-1
Fyn
Phospho
Caveolin-1
CAR
CAR
Golgi
ER
Nucleus