



Capsid stability and receptor mediated priming in calicivirus entry

Non-equilibrium Physics of Self-Assembly: from Viruses to Nano-containers

13th November 2023



Summary

- Introduction to the *caliciviridae*
- Receptor mediated priming for genome release
 - Feline Calicivirus
 - Entry kinetics as a determinant of virulence
- Conformational flexibility as a reproducibility challenge
 - Tulane virus

Introduction to the *caliciviridae*

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West Country NHS services hampered by norovirus cases

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Norovirus outbreaks have led to staff absences and partial ward closures

Cases of norovirus, the winter vomiting virus, are high and cases could have more than doubled in the past week in the West of England, figures say.

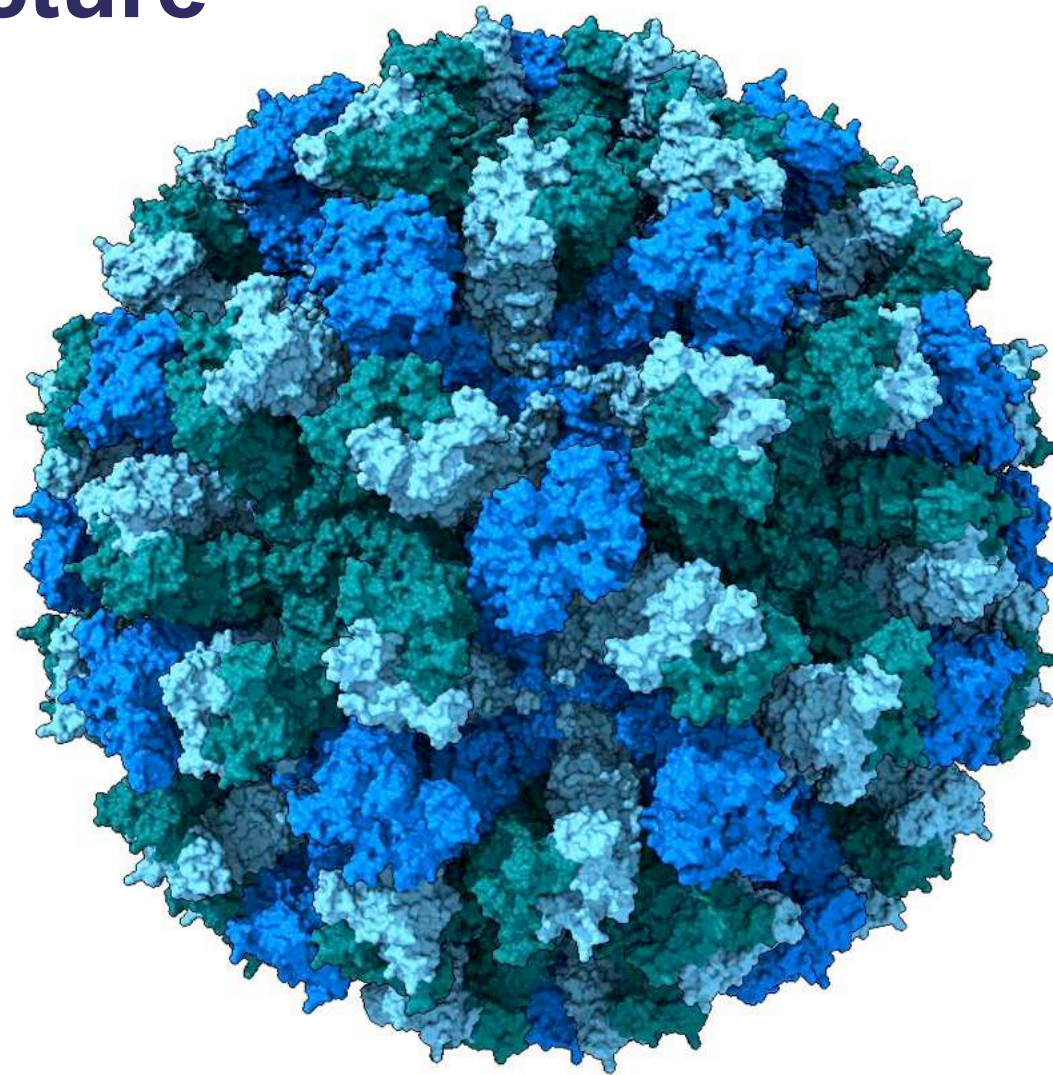
Symptoms include sudden, projectile vomiting and diarrhoea.

A growing number of people across Bath and North East Somerset, Swindon and Wiltshire are becoming unwell.

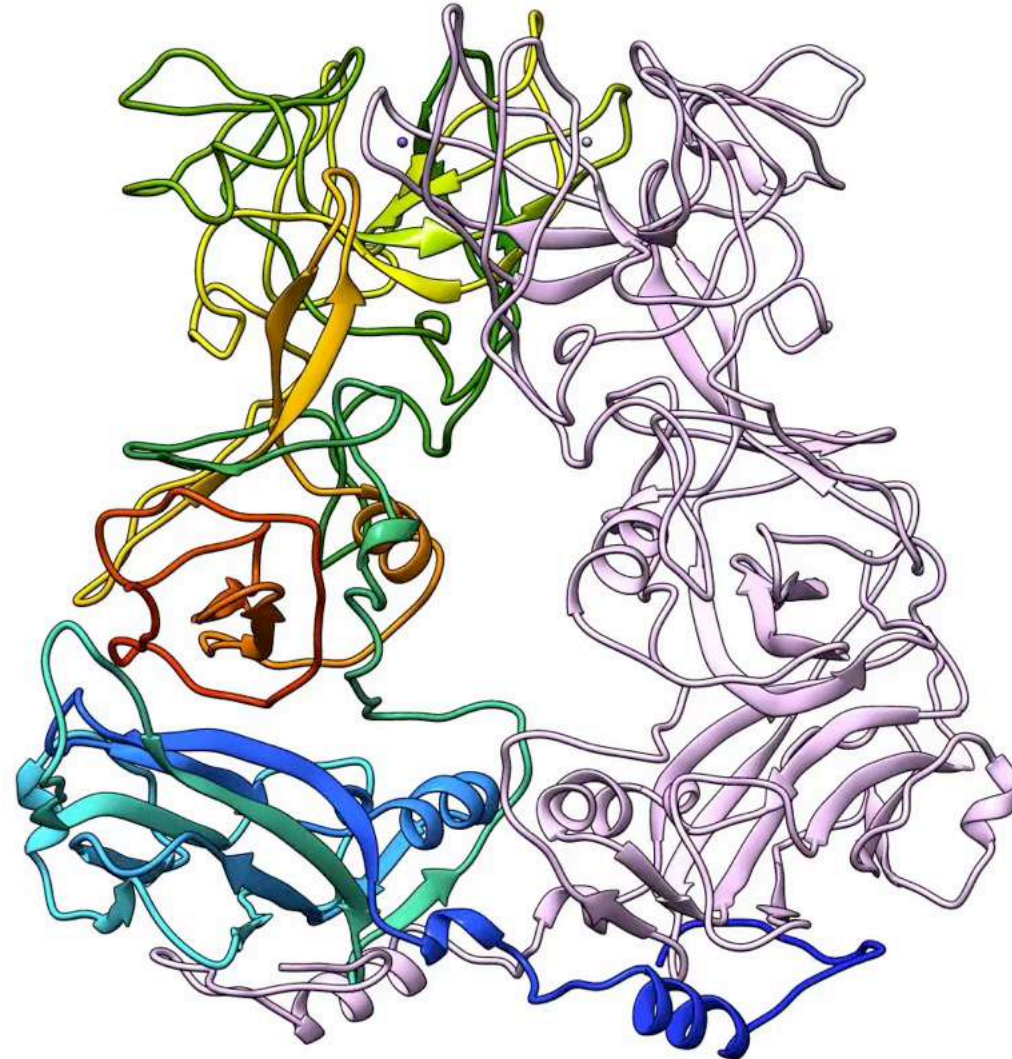
Health chiefs say the growing number of cases is putting added pressure on already very busy local NHS services, especially the region's hospitals.



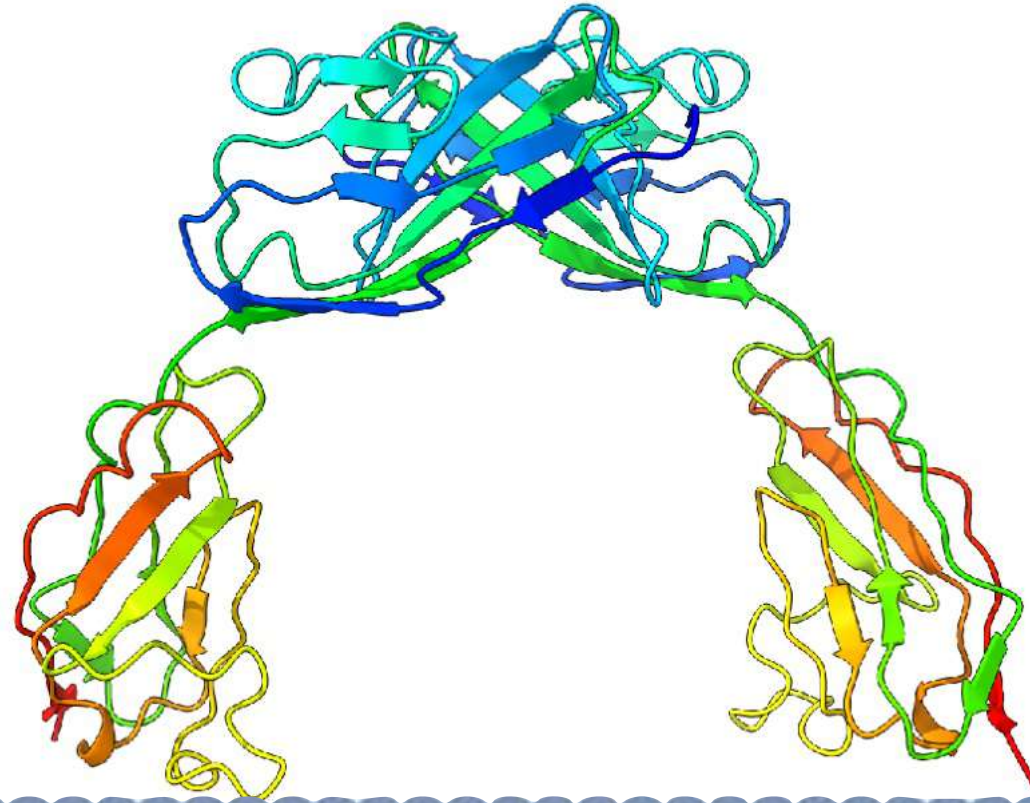
Capsid structure



Capsid structure

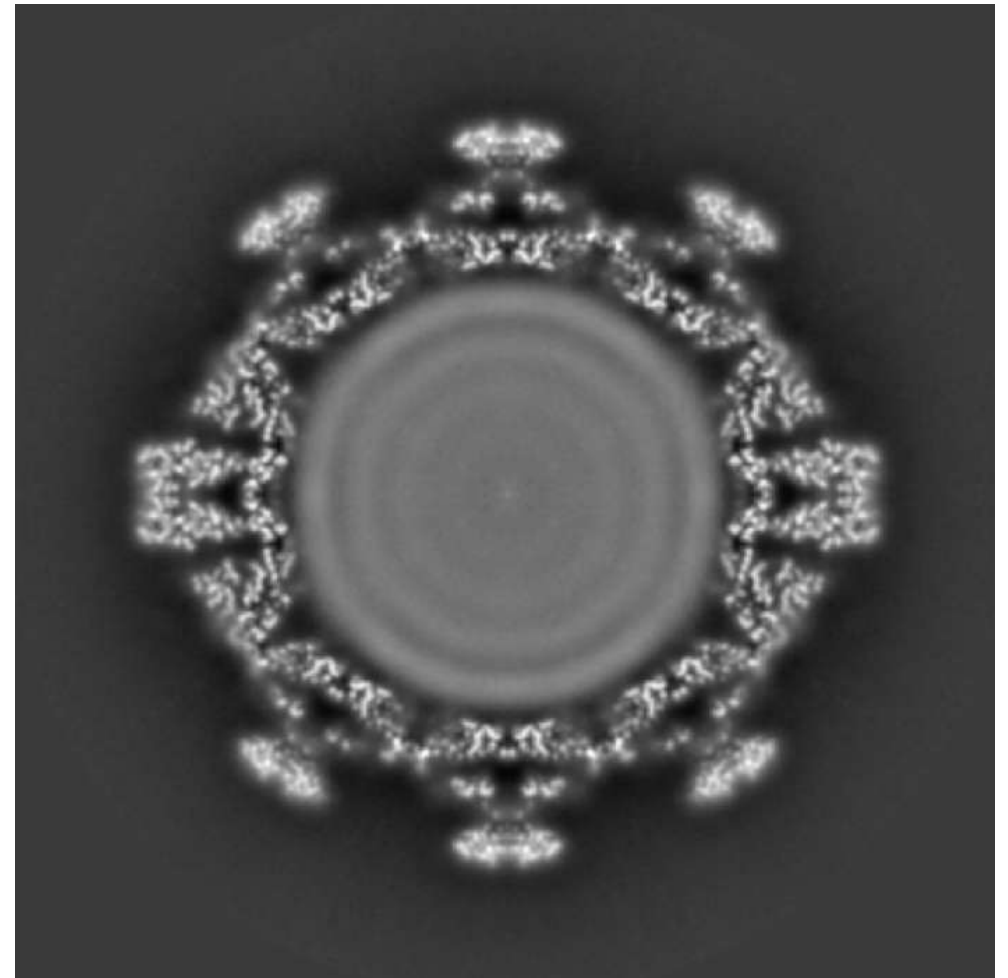
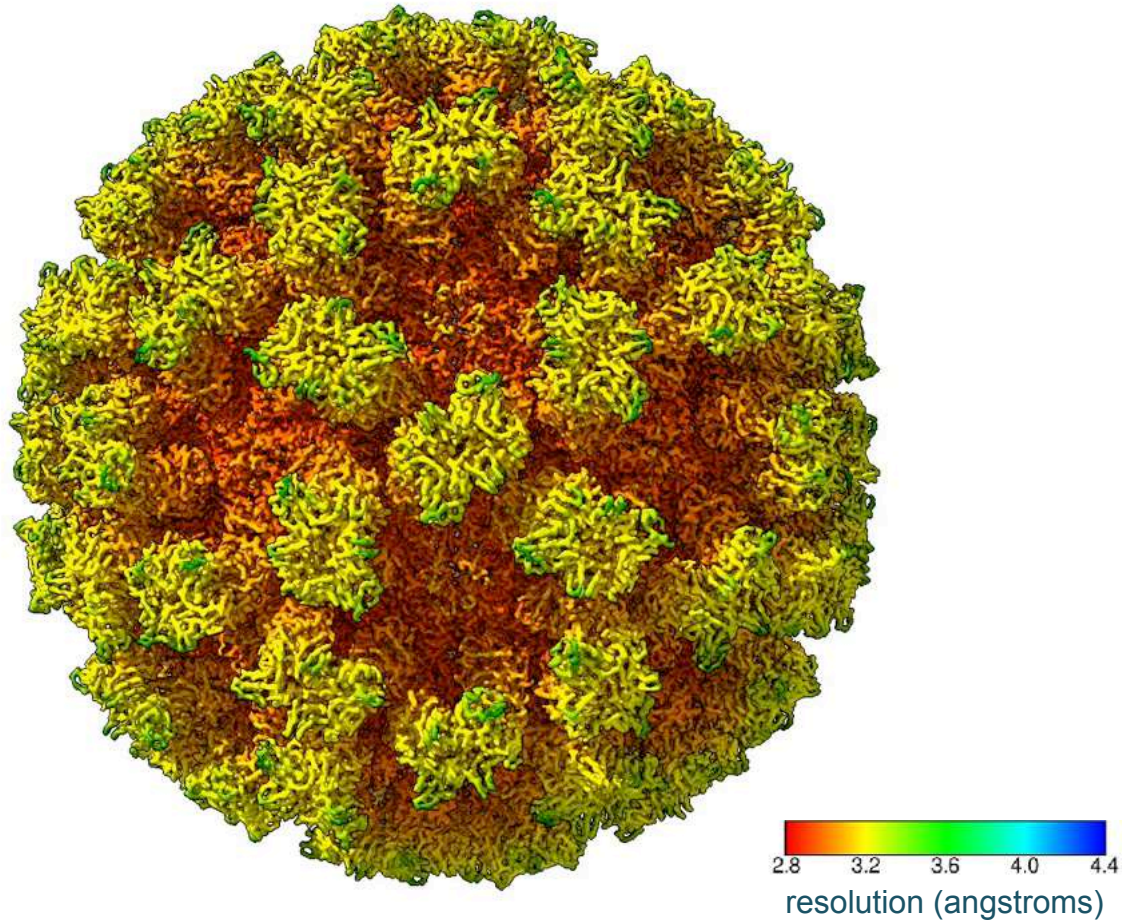


Junctional adhesion molecule A

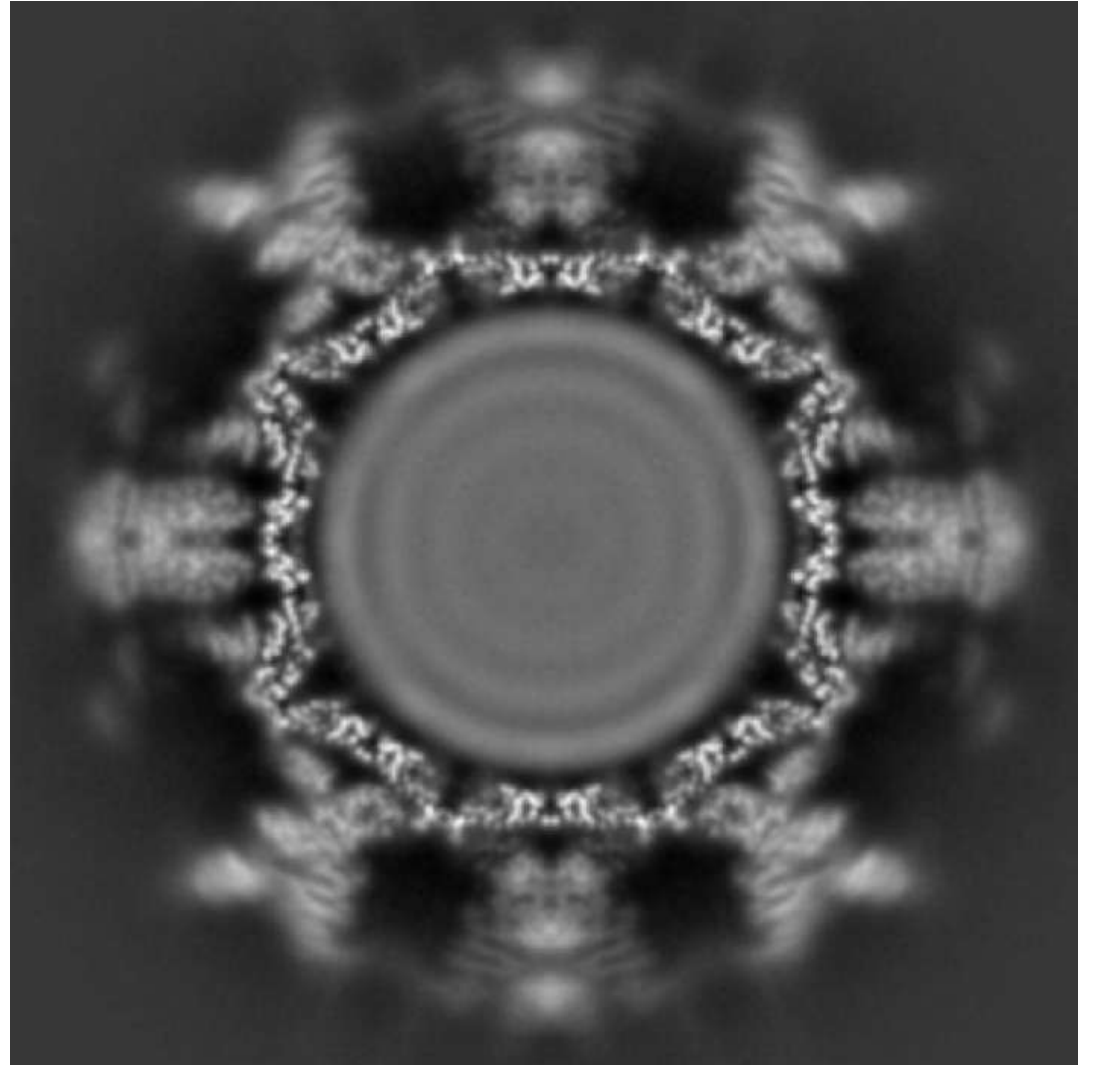
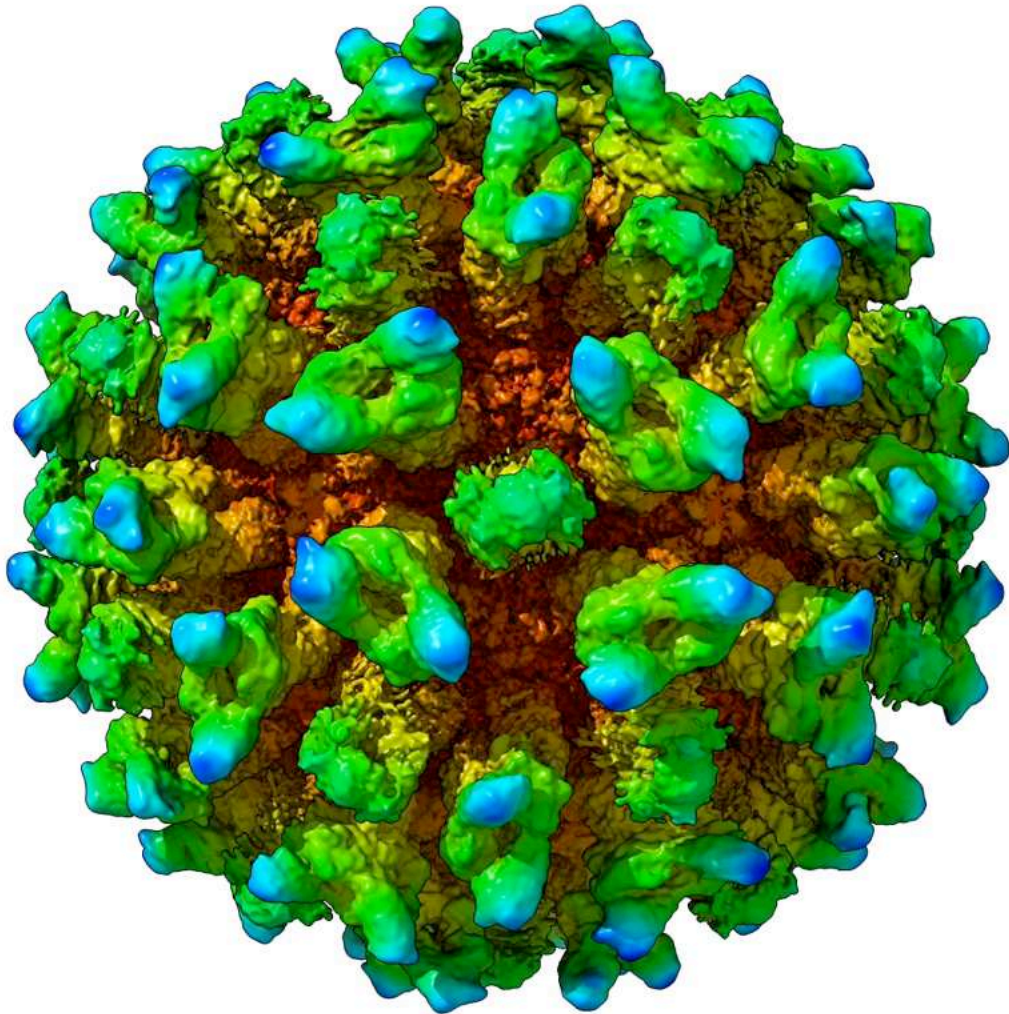


Human JAM-A
Prota et al. (2003) PNAS

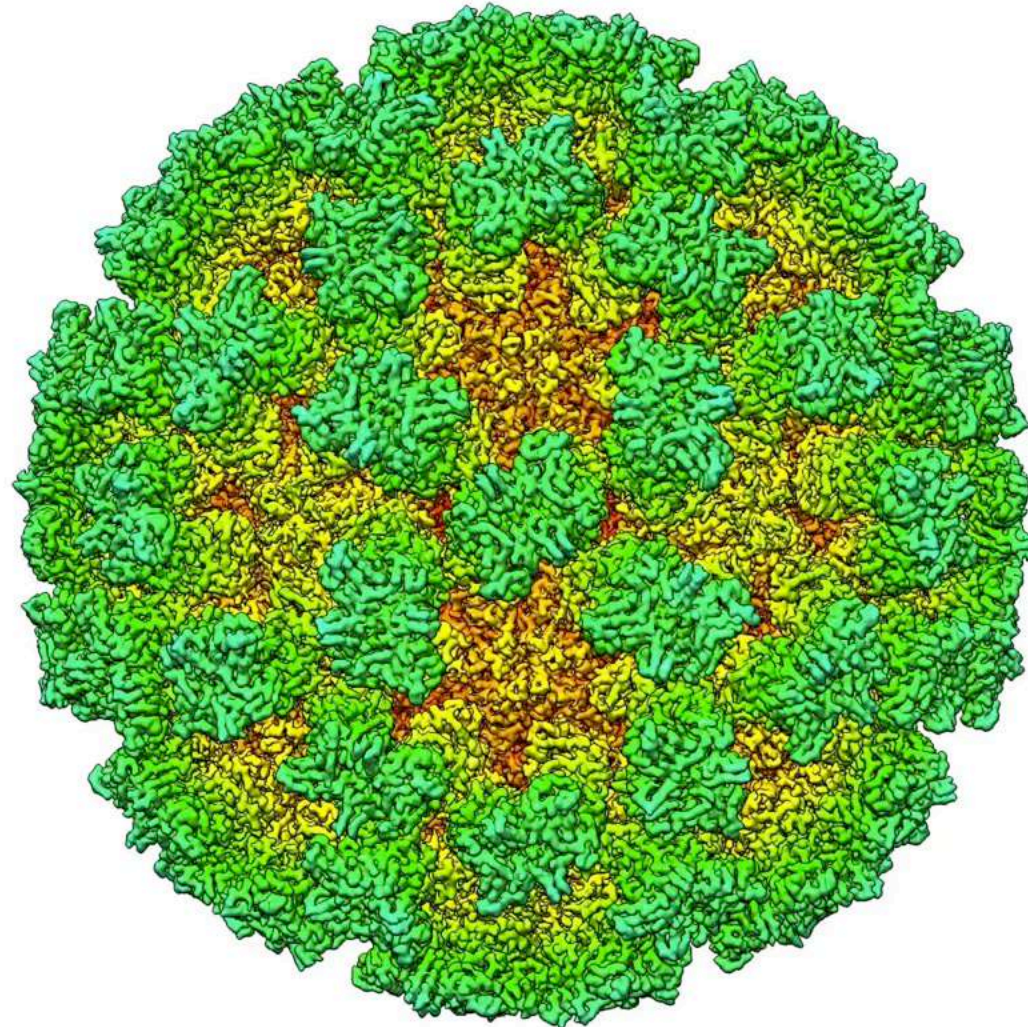
CryoEM structure of Feline Calicivirus F9



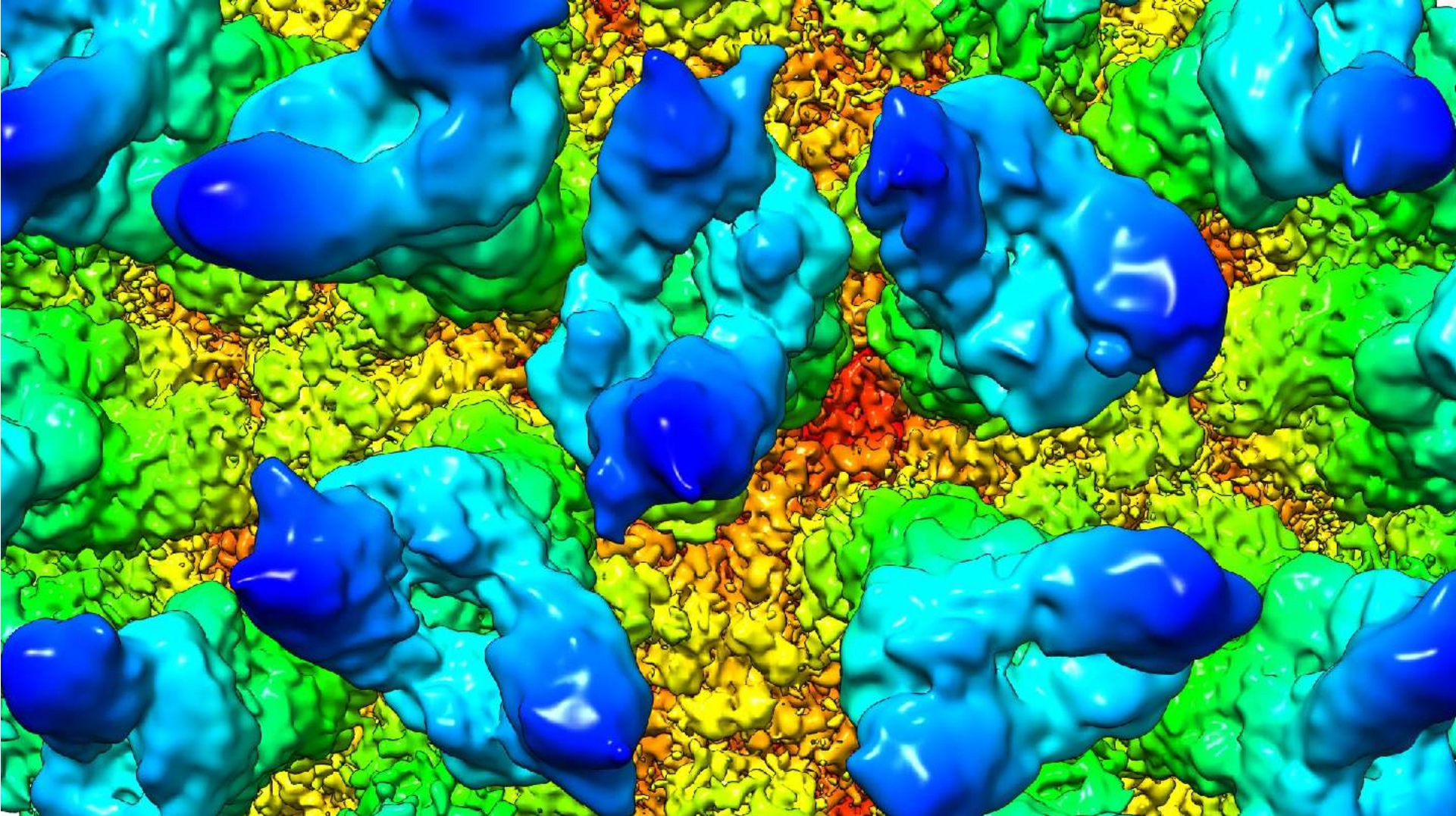
Feline calicivirus F9 bound to fJAM-A



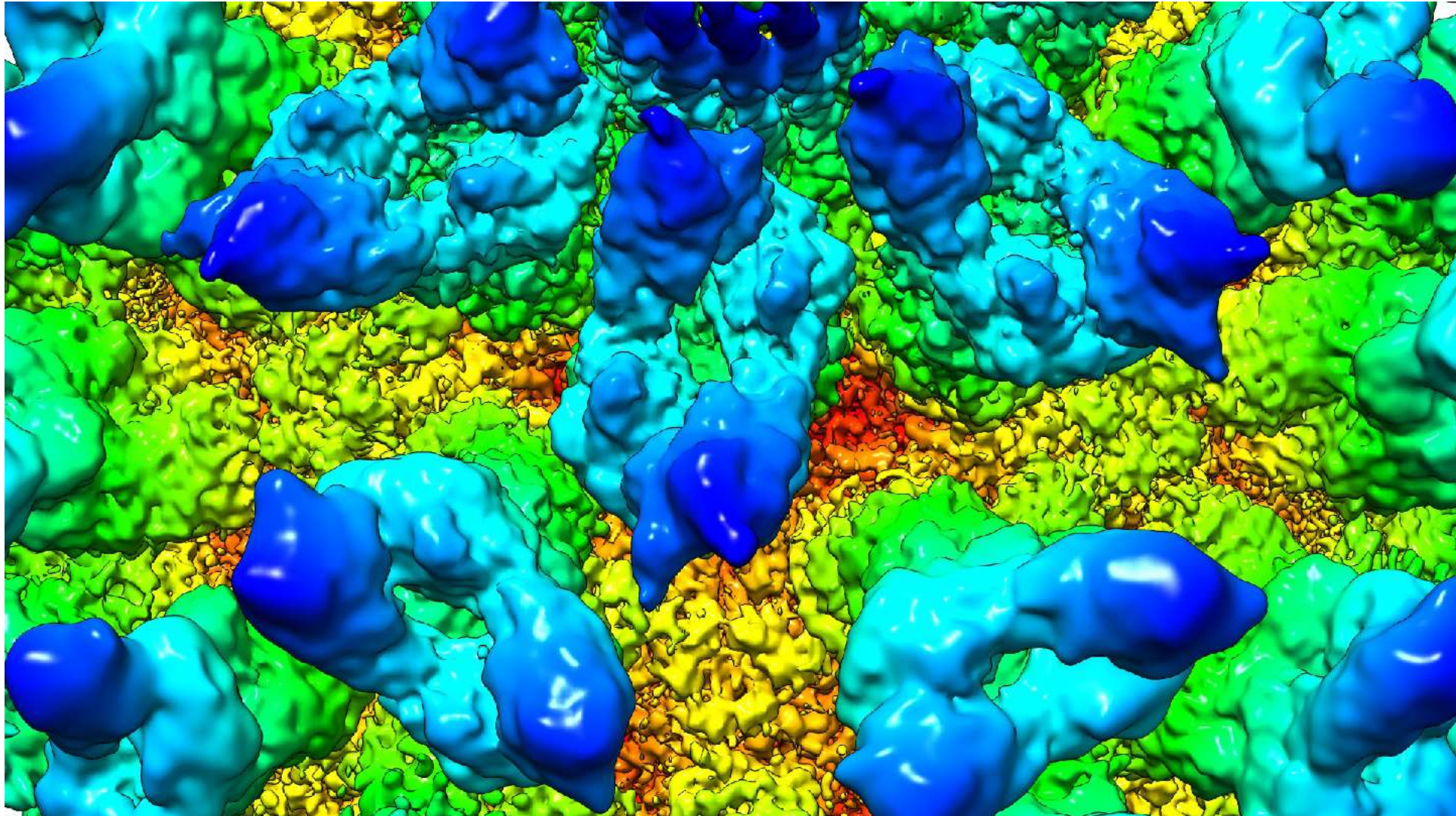
Focussed classification reveals P-domain mobility



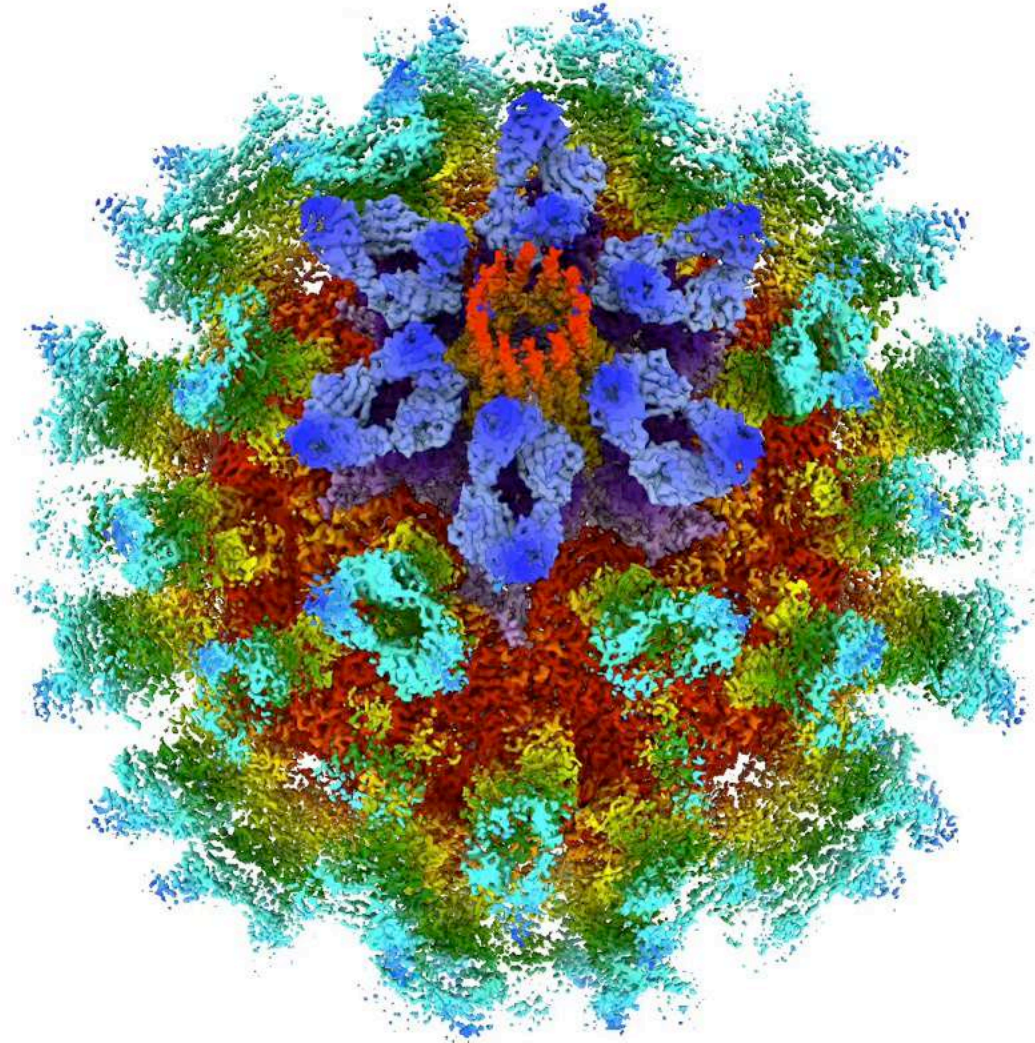
Focussed classification reveals P-domain mobility



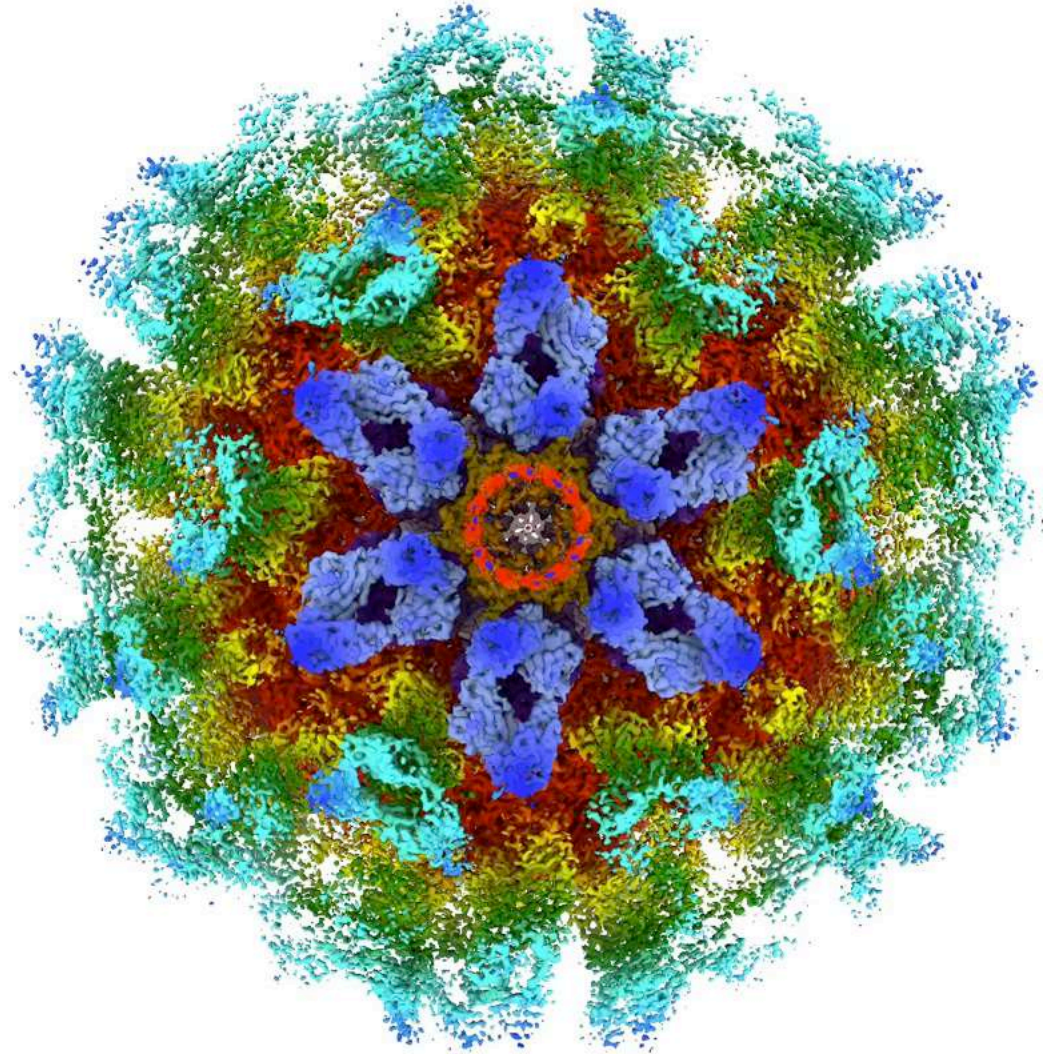
A novel feature at the 3-fold axis



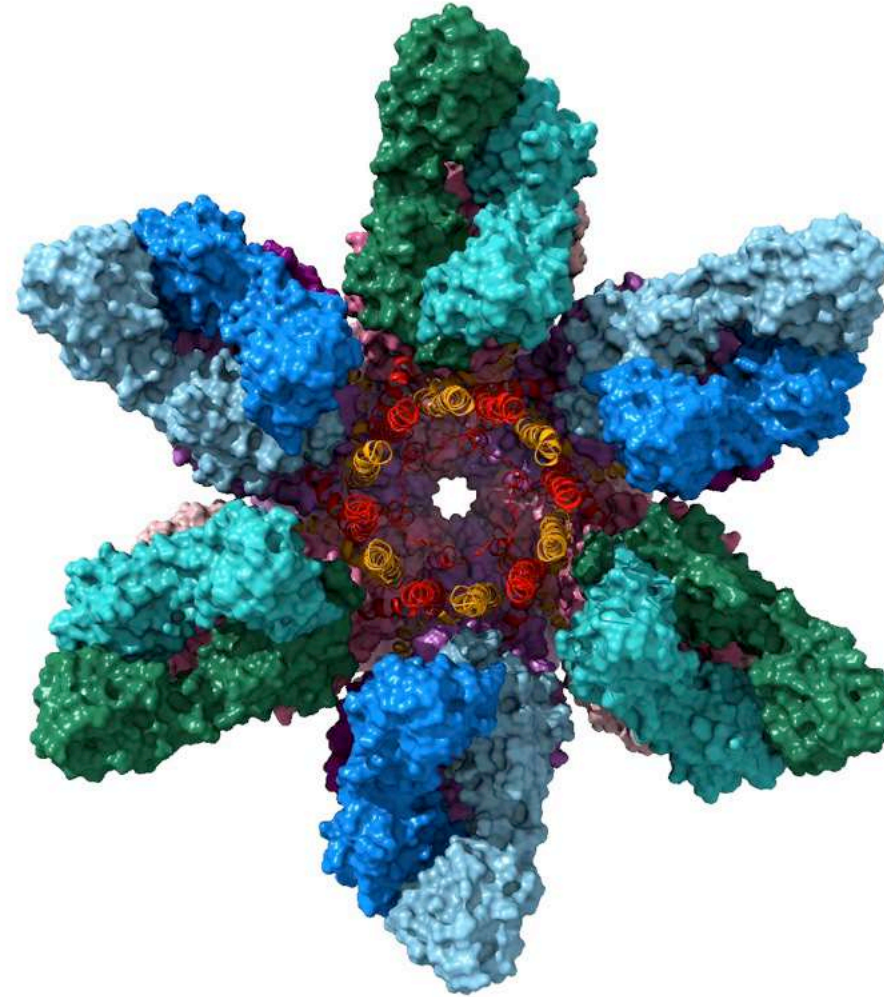
A portal for genome delivery?



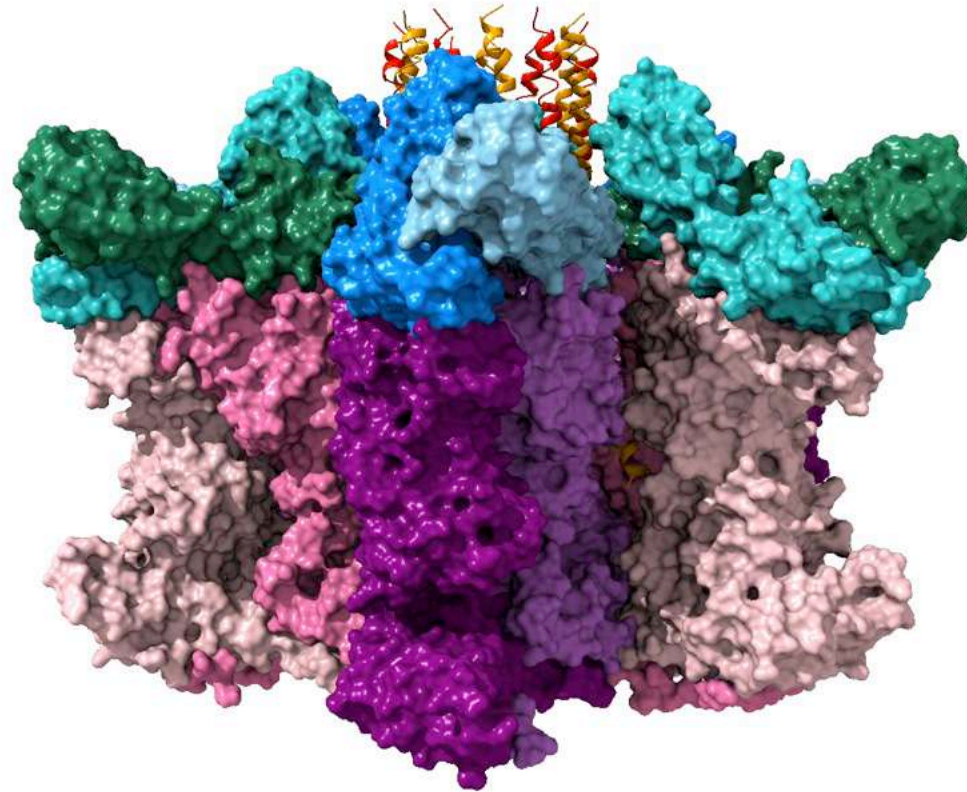
A portal for genome delivery?



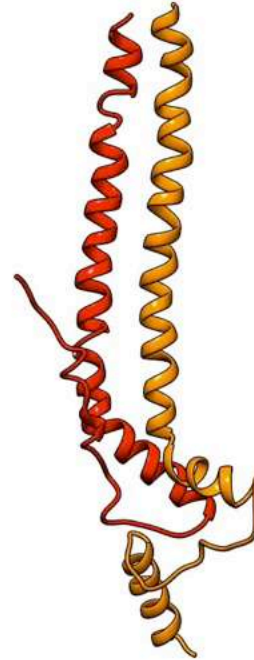
An atomic model of the portal vertex



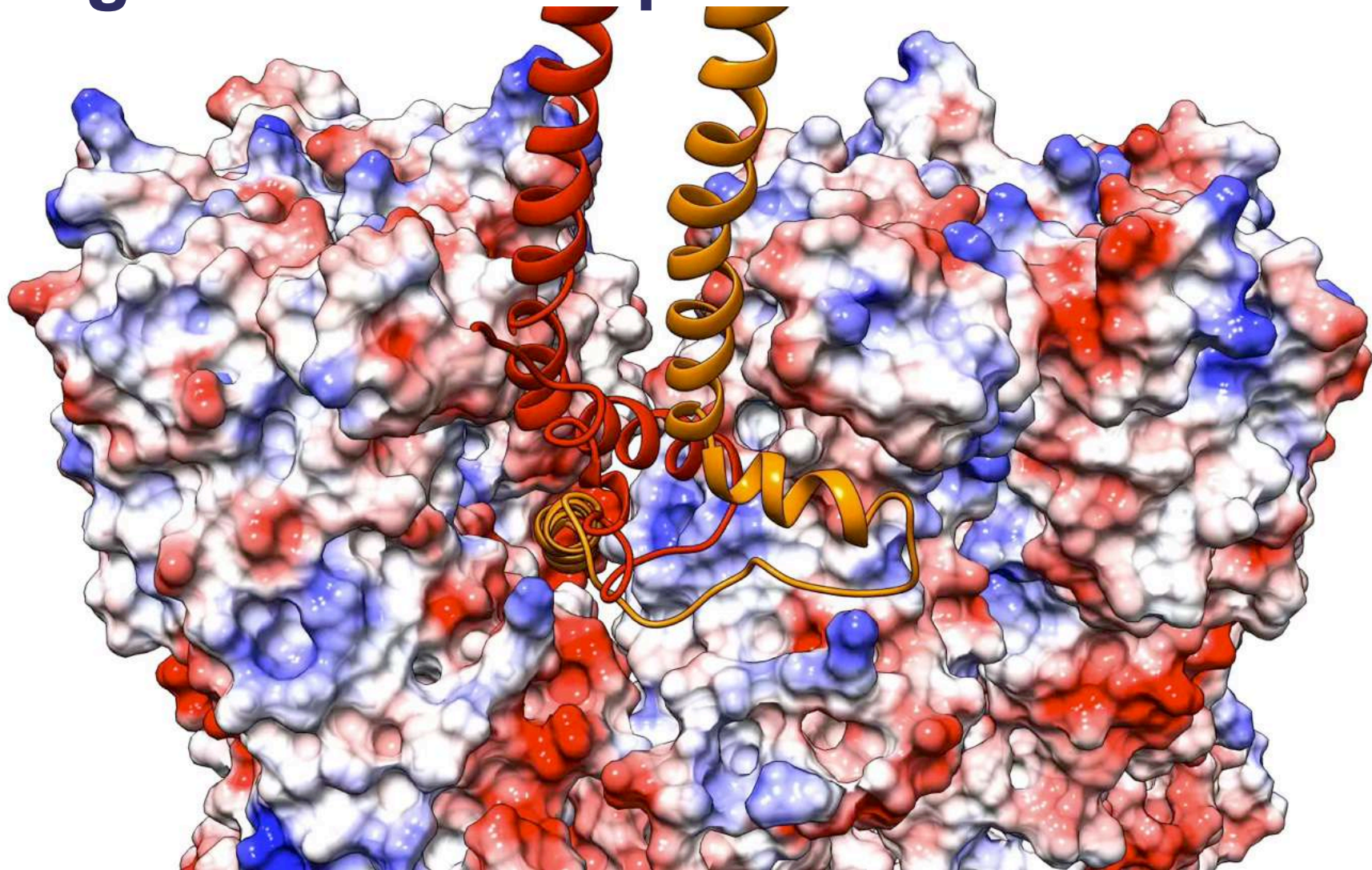
An atomic model of the portal vertex



Anchoring VP2 to the capsid surface

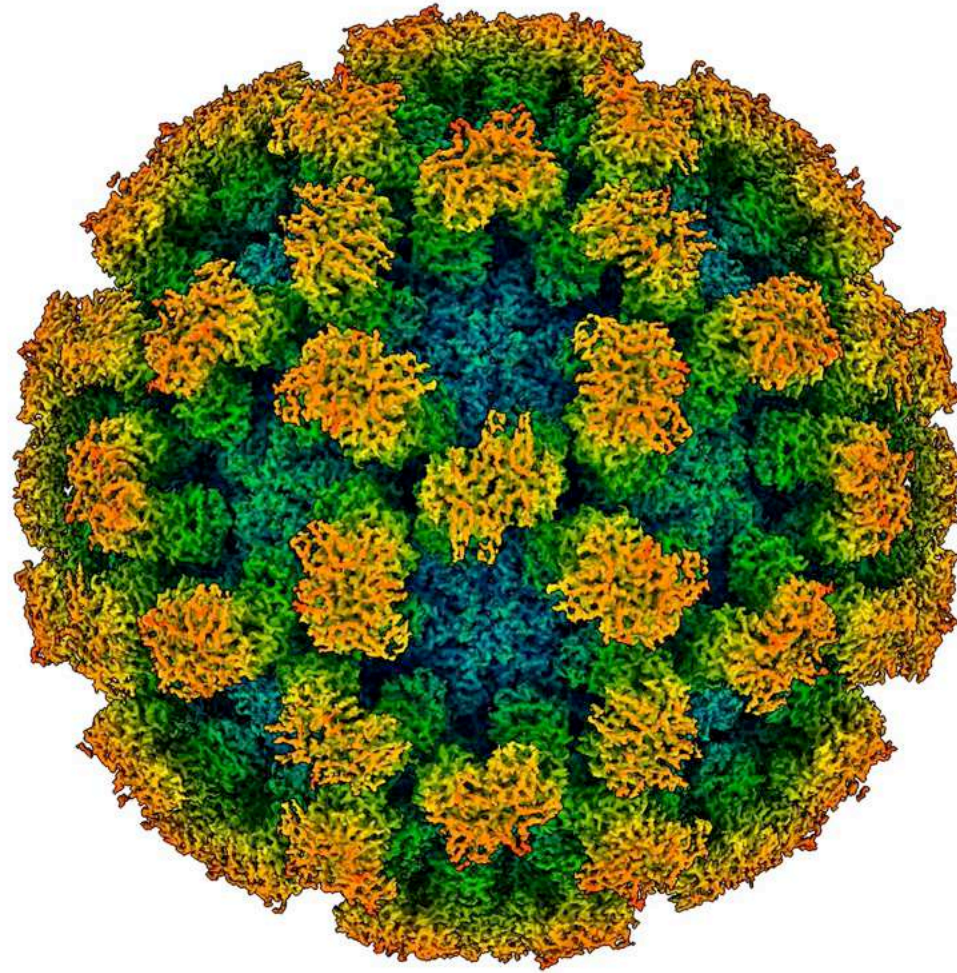


Anchoring VP2 to the capsid surface

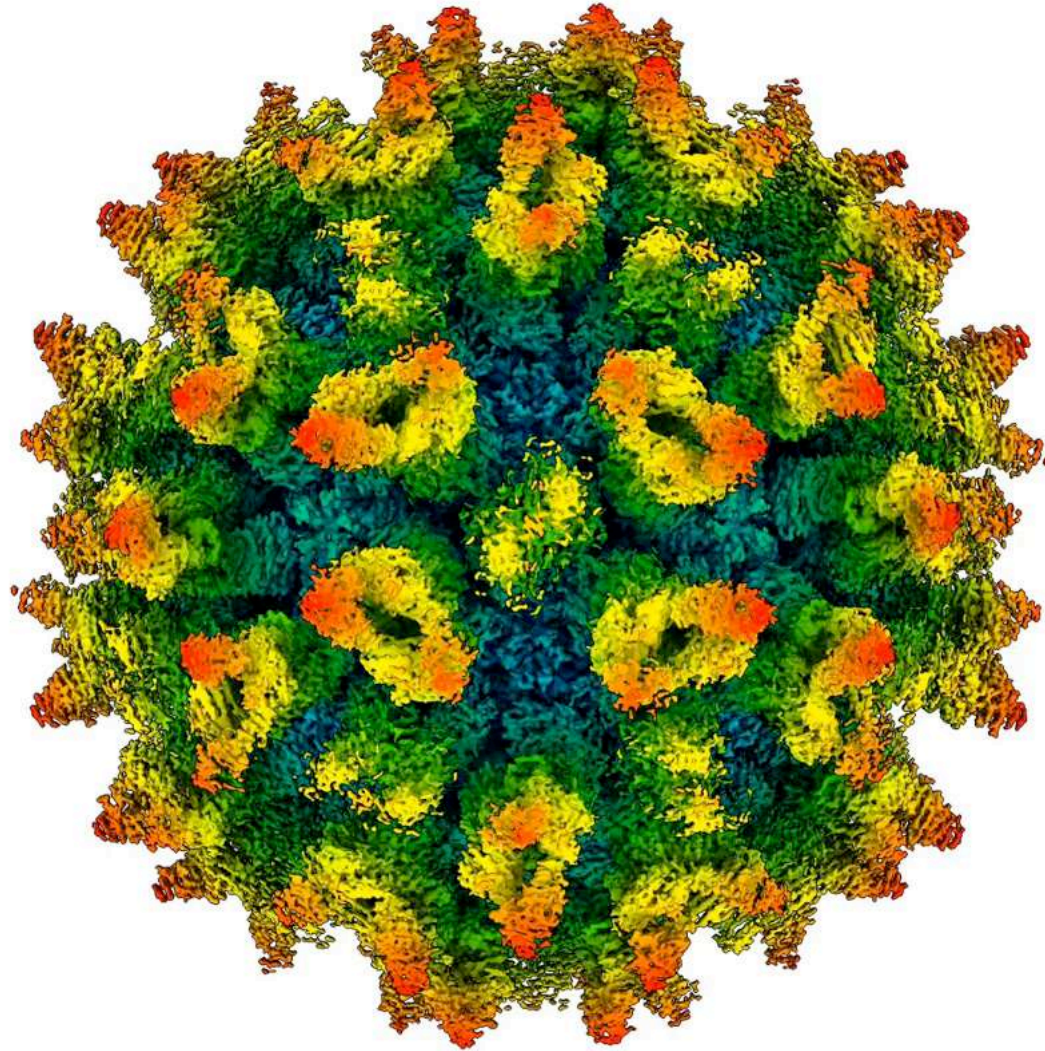


Entry kinetics as a determinant of virulence?

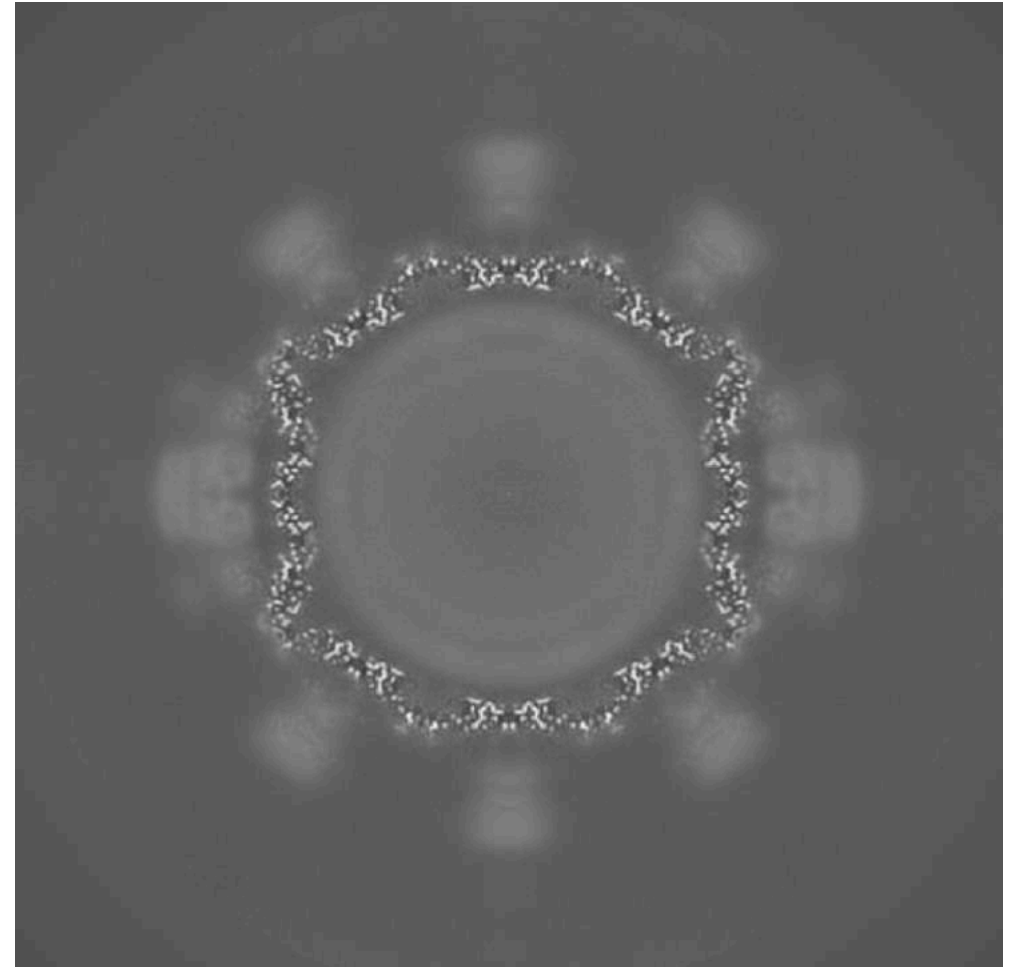
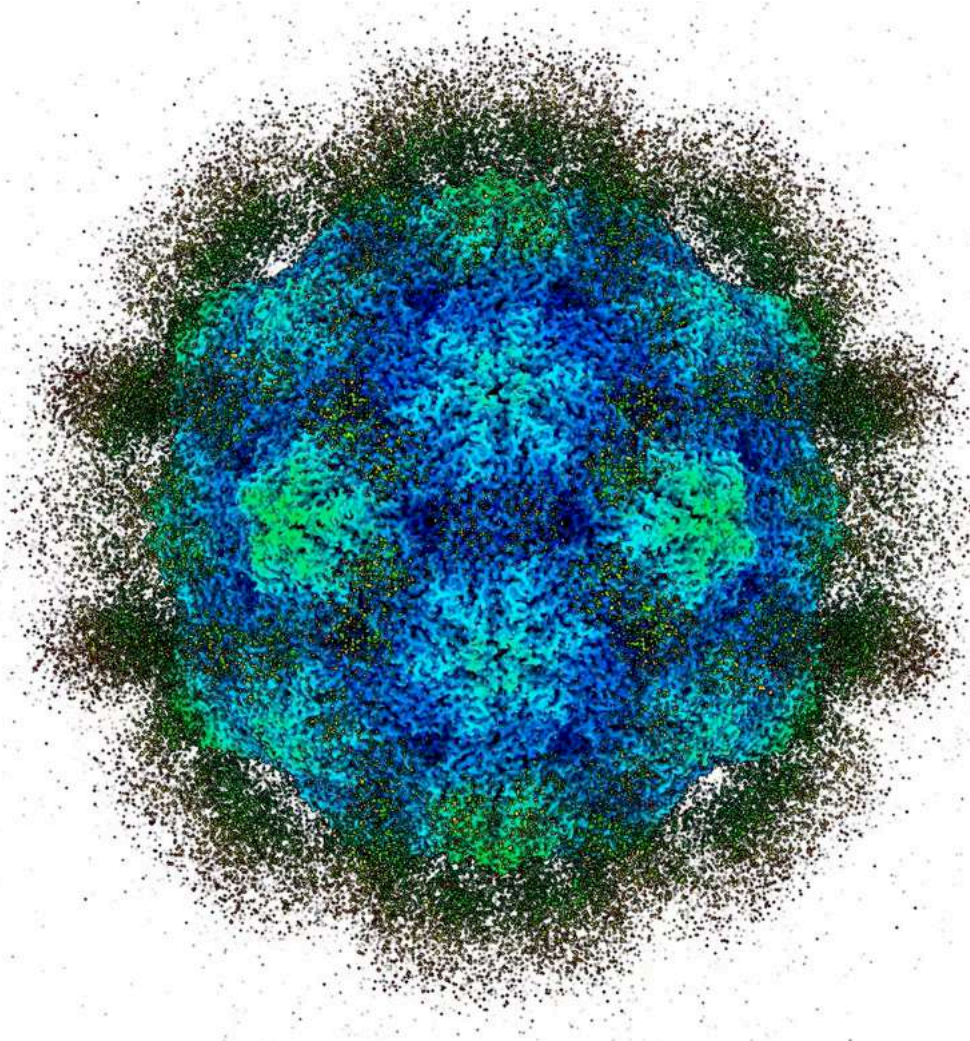
Structure of a respiratory clinical isolate



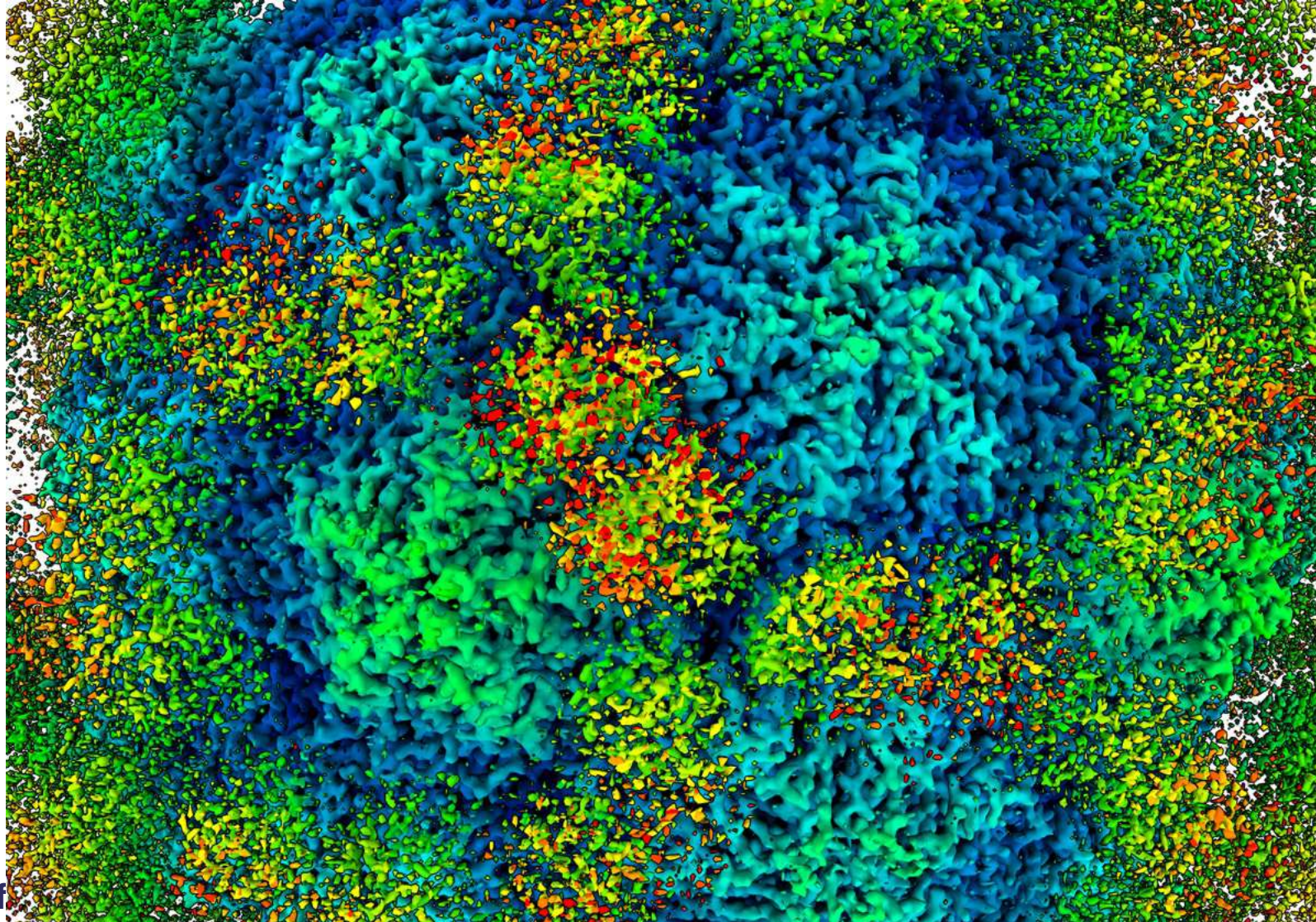
Structure of a respiratory clinical isolate



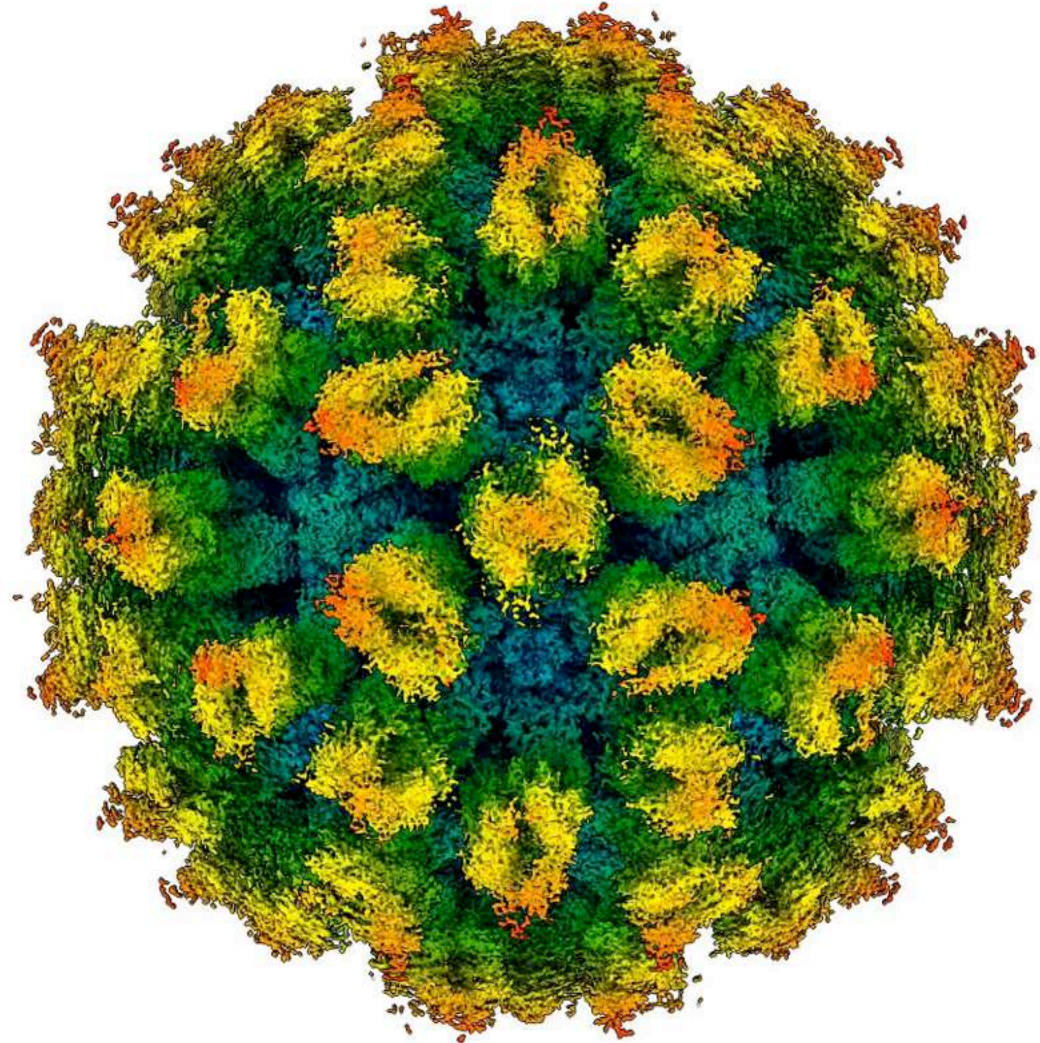
Structure of a virulent systemic clinical isolate



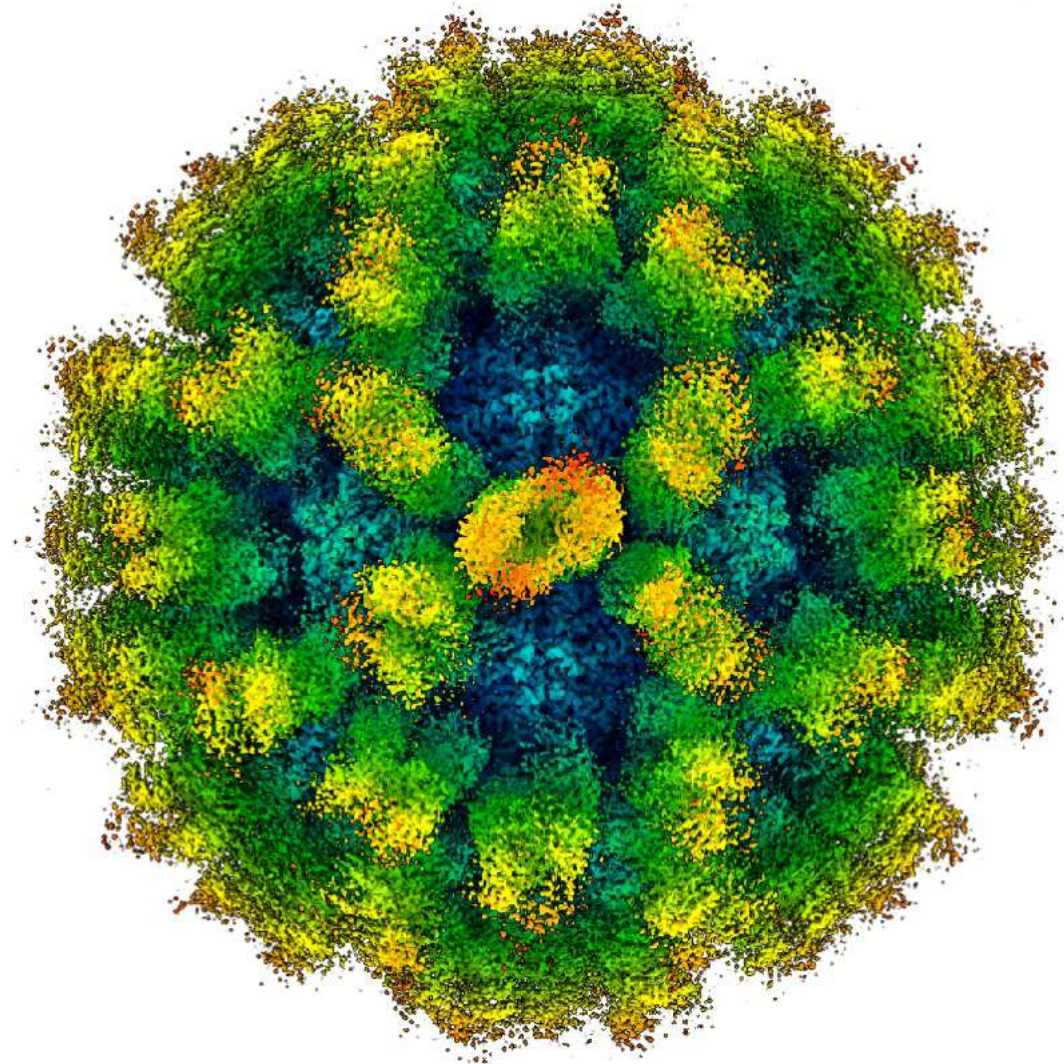
Raised and resting poses



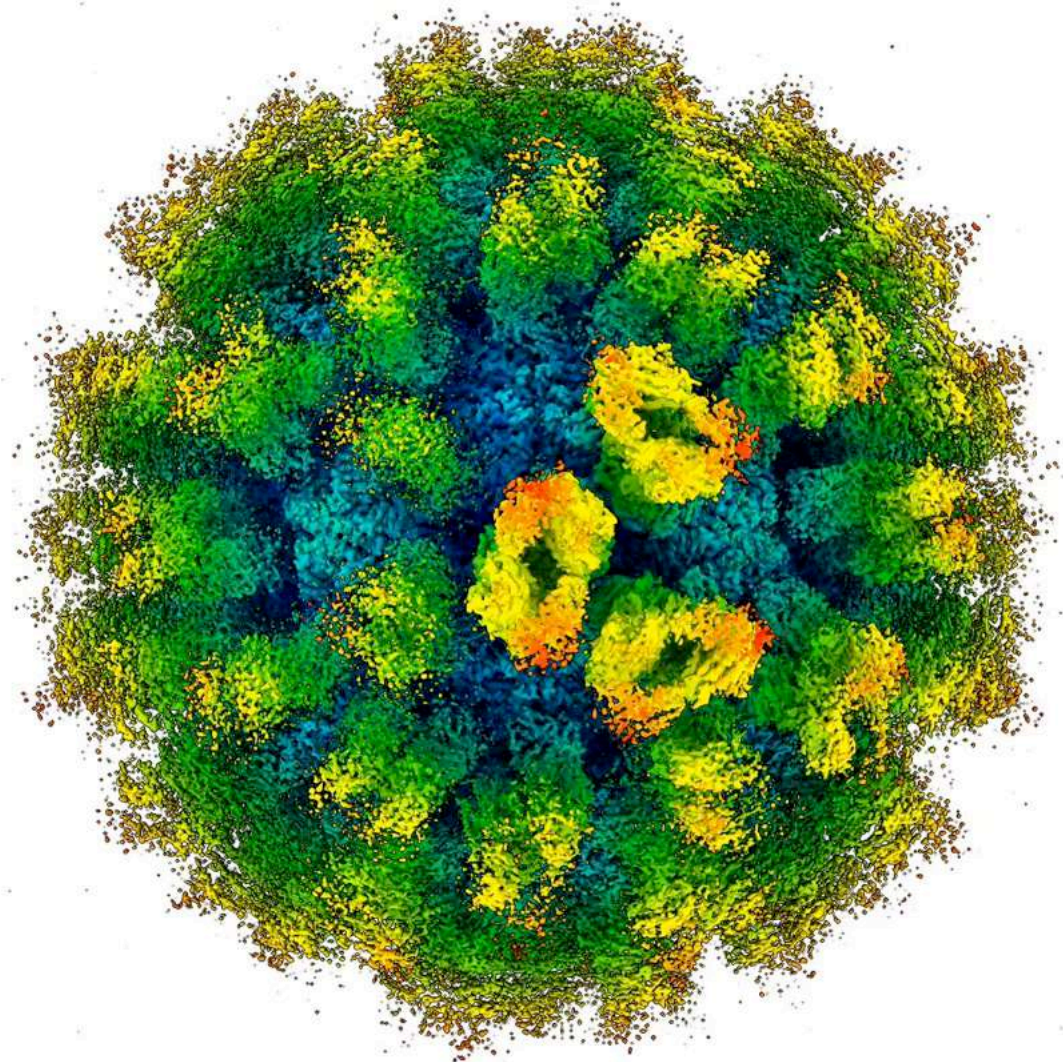
Receptor engagement



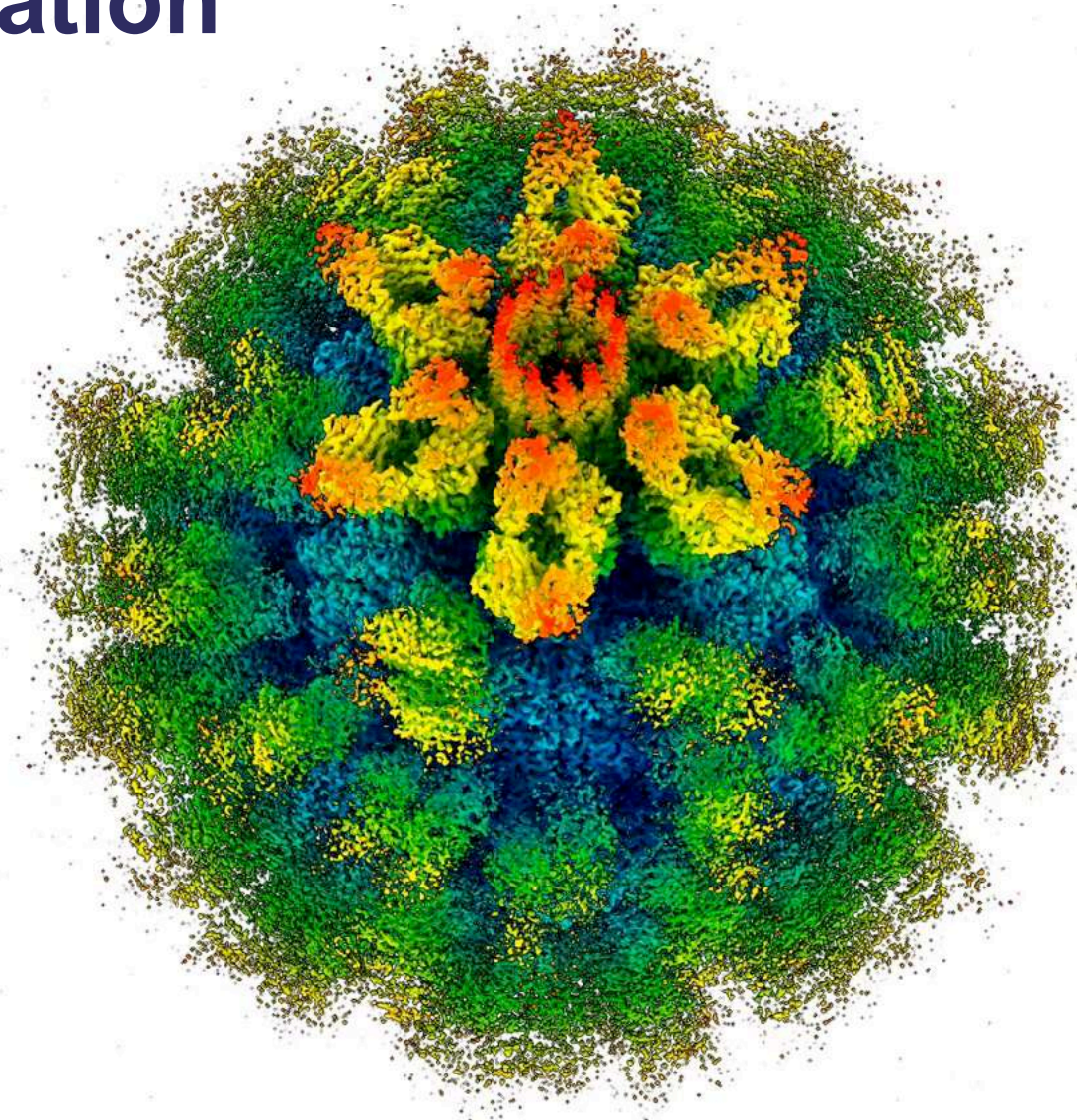
CC-domain mobility



CC-domain mobility



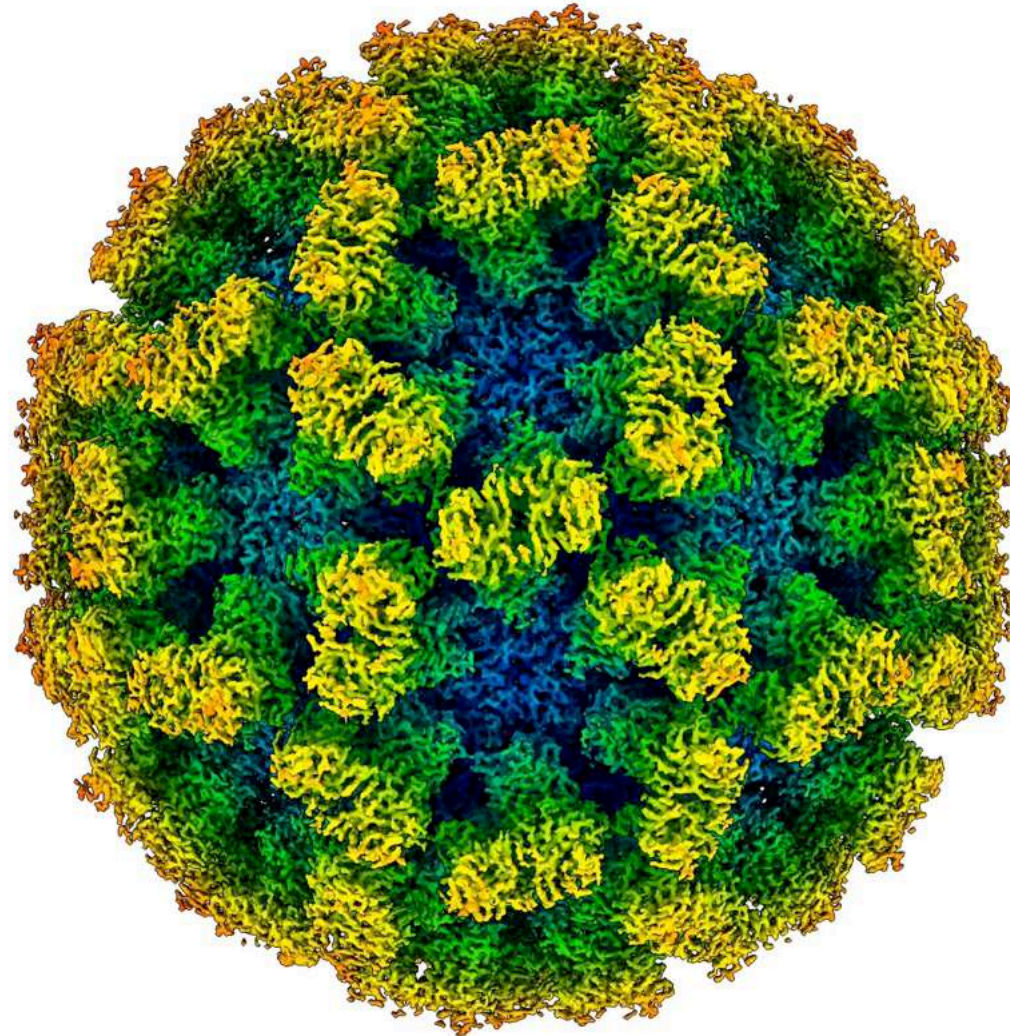
Portal formation



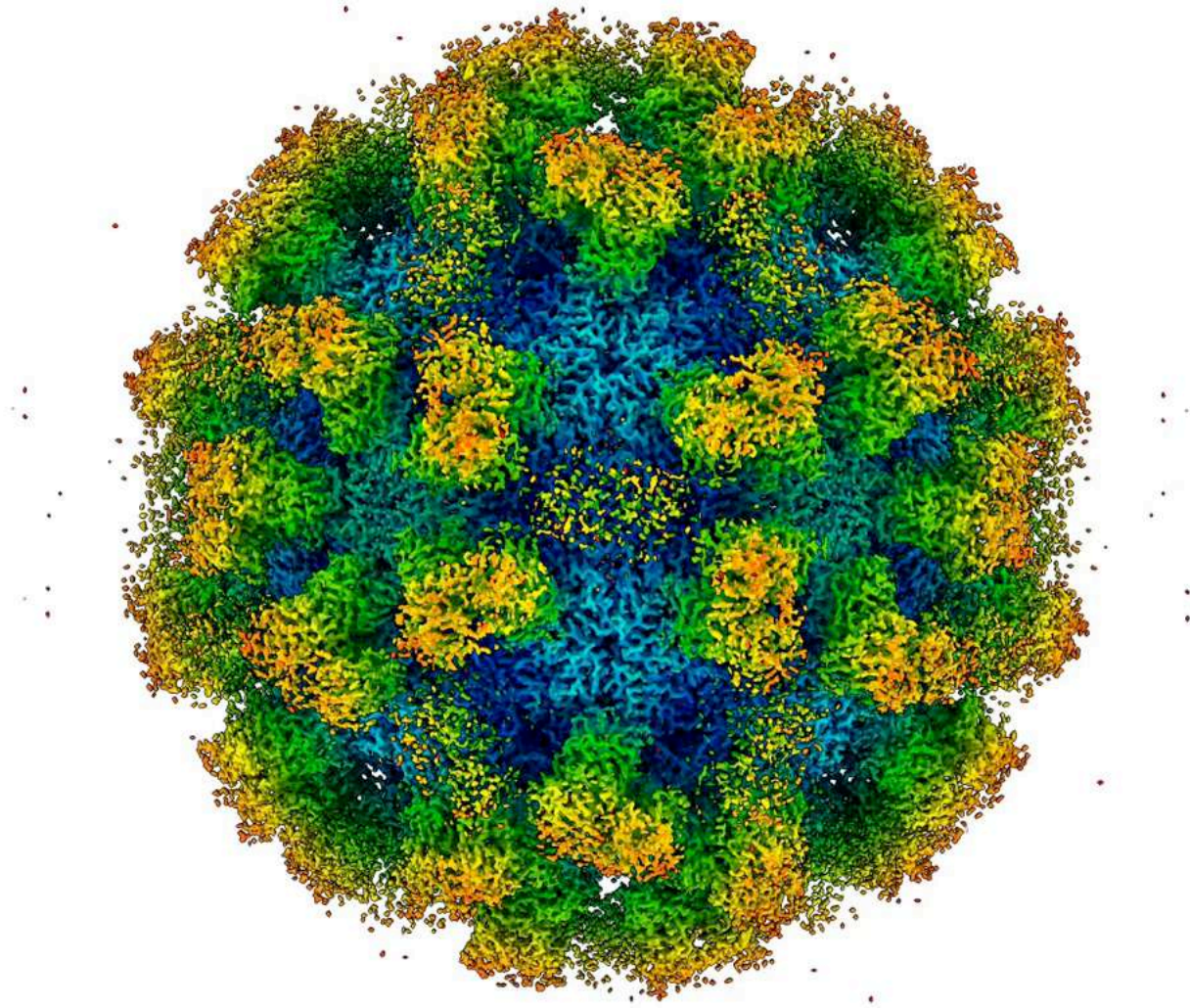
Calicivirus capsid dynamics

A reproducibility challenge?

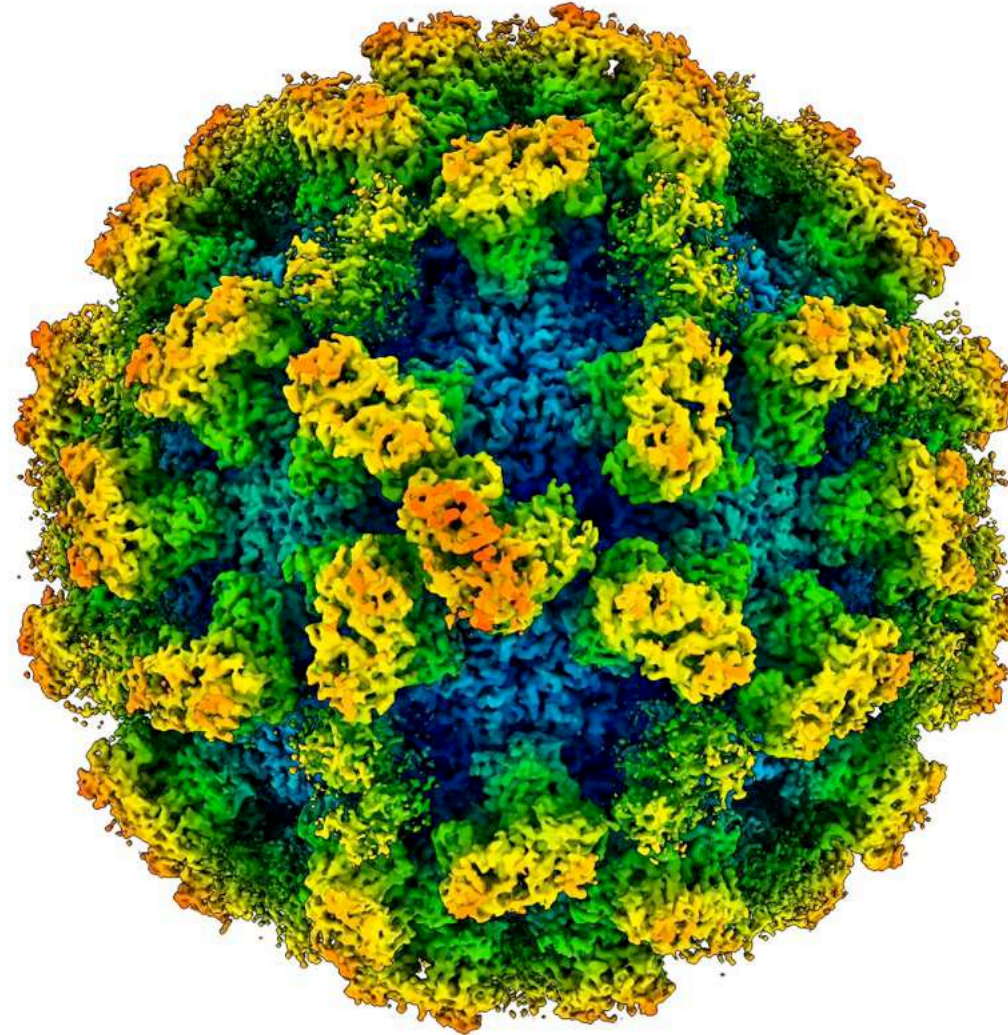
Tulane virus structure



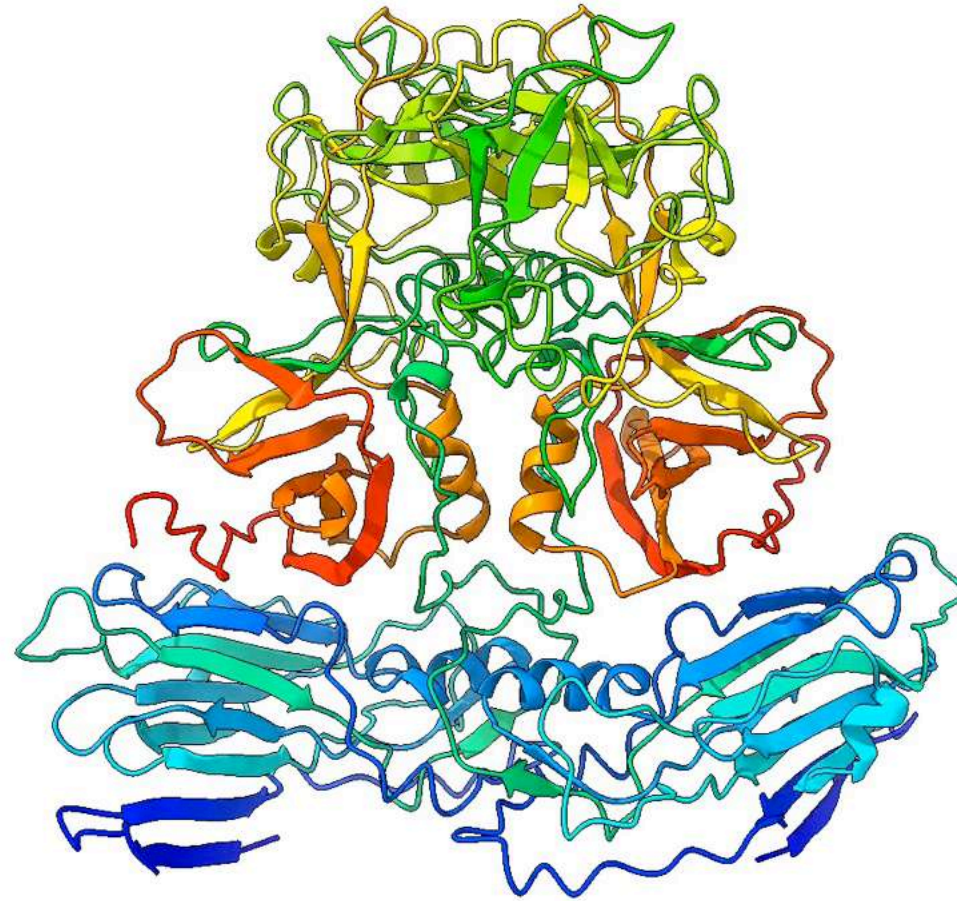
Another Tulane virus structure



Focussed classification (CC) reveals P-domain mobility



Morph of CC-dimer tilting



Questions and implications for virion assembly

- What are the environmental cues that trigger P-domain mobility?
- Does VP2 form a portal for genome delivery across the endosomal membrane?
- What further factors drive genome release and how does it proceed?
- Is the site of egress determined at the time of virion assembly?
- Does VP2 directly engage with the genome?

Acknowledgements



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