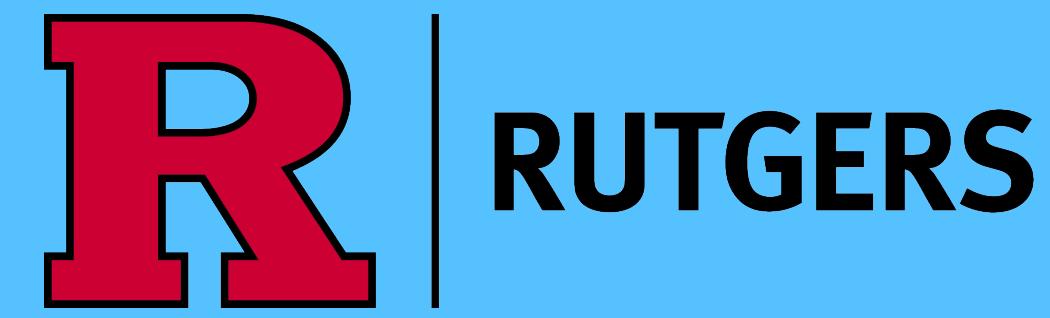
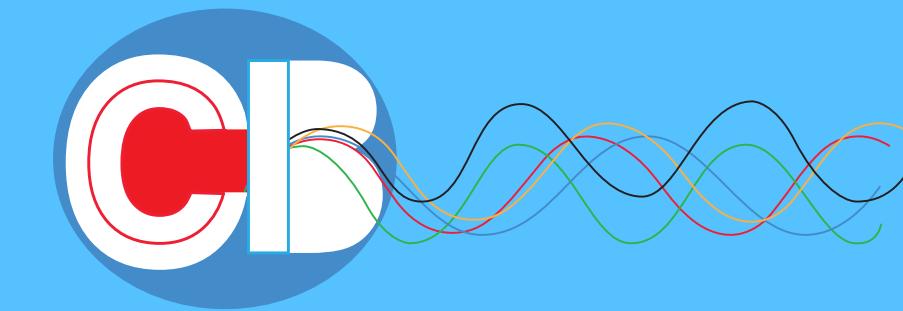


# The Effect of Lipid Length on Membrane Deformations Caused by the SARS-CoV-2 E Protein

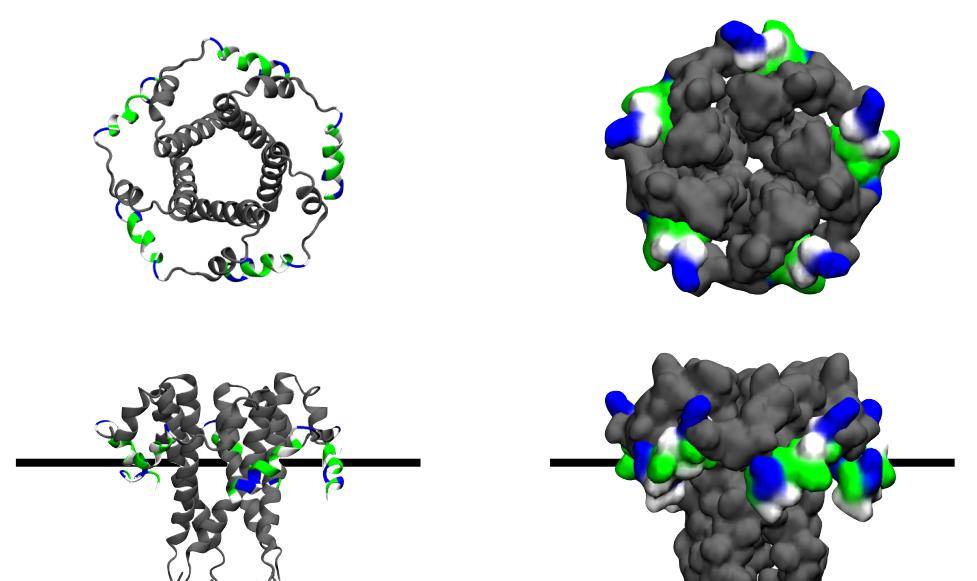


Jesse W Sandberg<sup>1</sup> and Grace Brannigan<sup>1,2</sup>

<sup>1</sup>Center for Computational & Integrative Biology, and <sup>2</sup>Dept. of Physics, Rutgers University, Camden



## Background



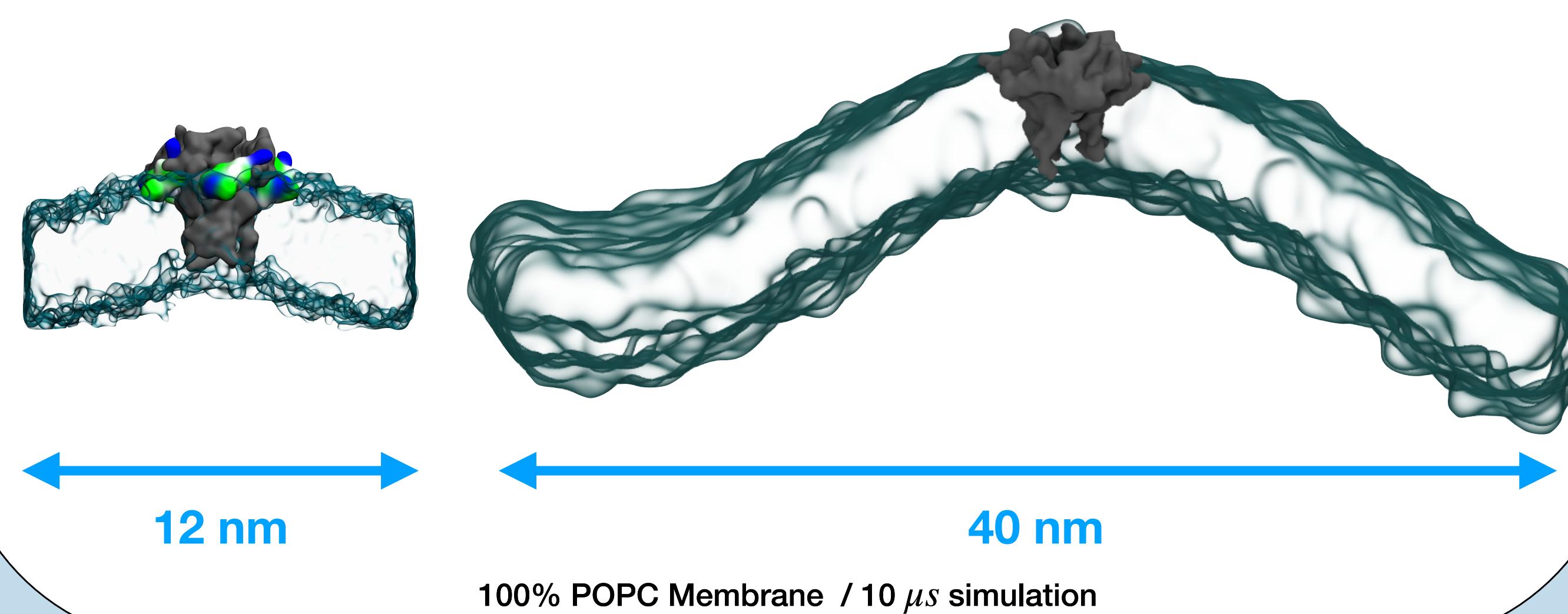
- Pentameric, weakly-selective ion channel
- Highly conserved across many coronaviruses, including SARS-CoV and SARS-CoV-2<sup>1</sup>
- Primarily found in the ER-Golgi Intermediate Complex (ERGIC) of infected host cells
- Known to induce membrane curvature, allowing a new virion to bud out and escape the host cell<sup>2</sup>
- Knock-out or mutation produces weakened virions that are unable to infect new cells<sup>3</sup>

Fig 1: The E protein of SARS-CoV (pdb id 5x29) shown in extracellular (top) and membrane/lateral (bottom) view. Black bars indicate approx. membrane position.

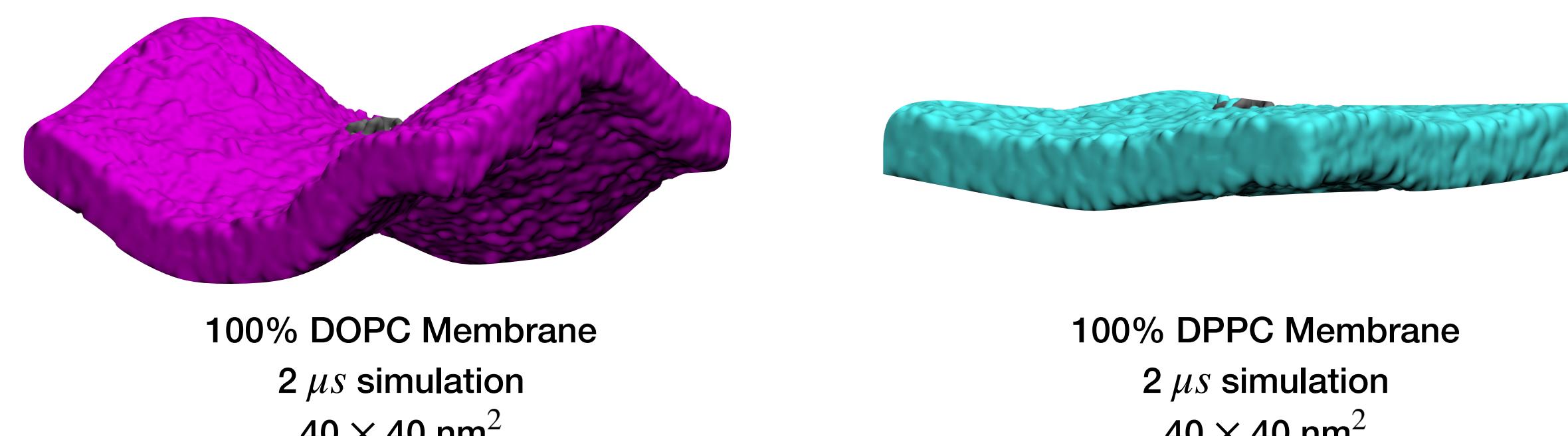
## Approach

- Simulate with GROMACS 2021 and MARTINI 2.2
- Vary lipid length and flexibility
- Measure membrane shape with nougat
- Perform Monte Carlo continuum simulation to compare MD results with elastic theory

## E Protein causes membrane bending that increases with system size in CG-MD simulations



## Unsaturated membranes bend Saturated membranes do not bend



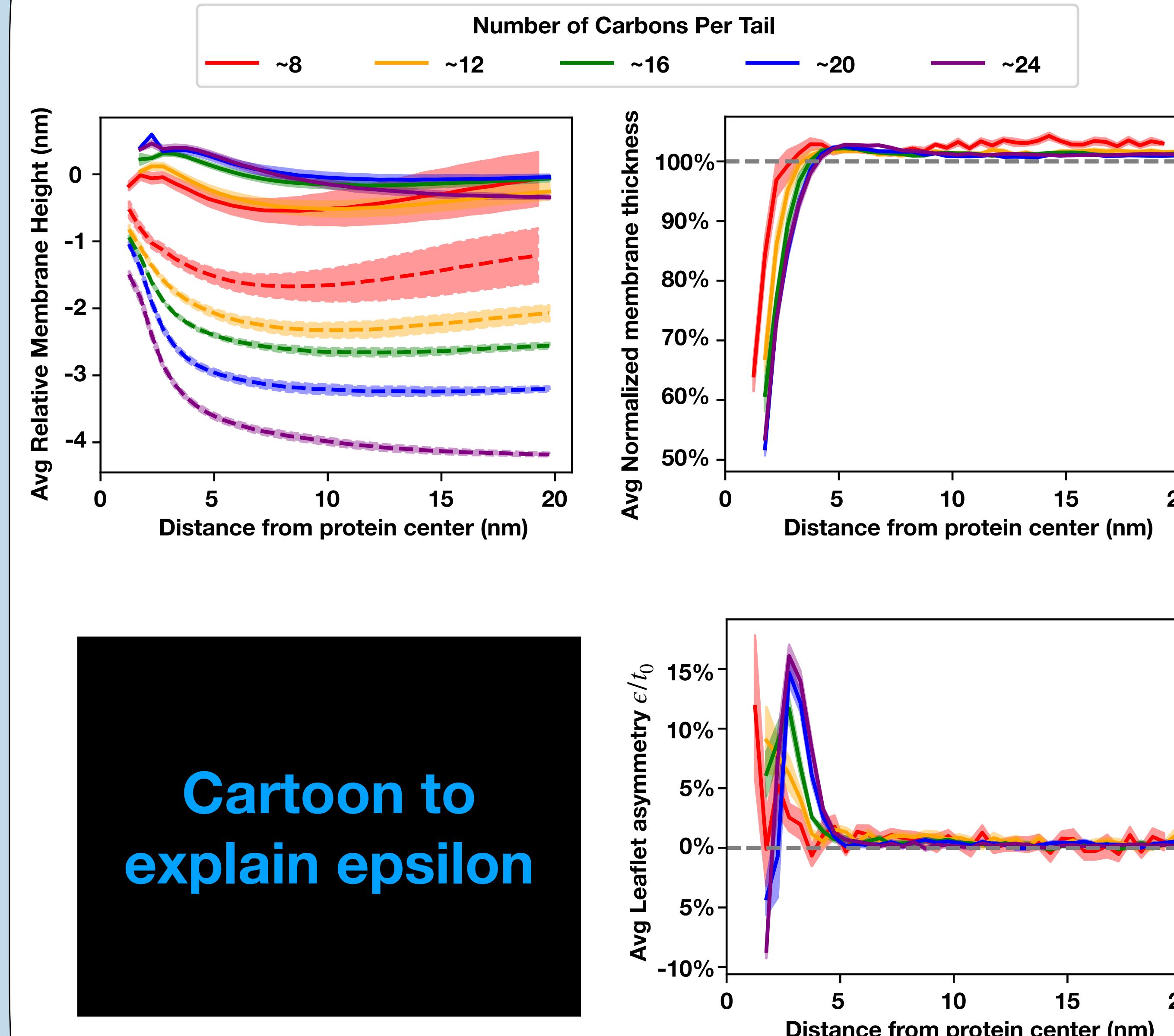
## Acknowledgments & Funding

NRT Award: NSF DGE 2152059

ACCESS (formerly XSEDE): BIO220103

Rutgers Office of Advanced Research Computing (OARC)

## Local asymmetric thickness deformations in saturated membranes

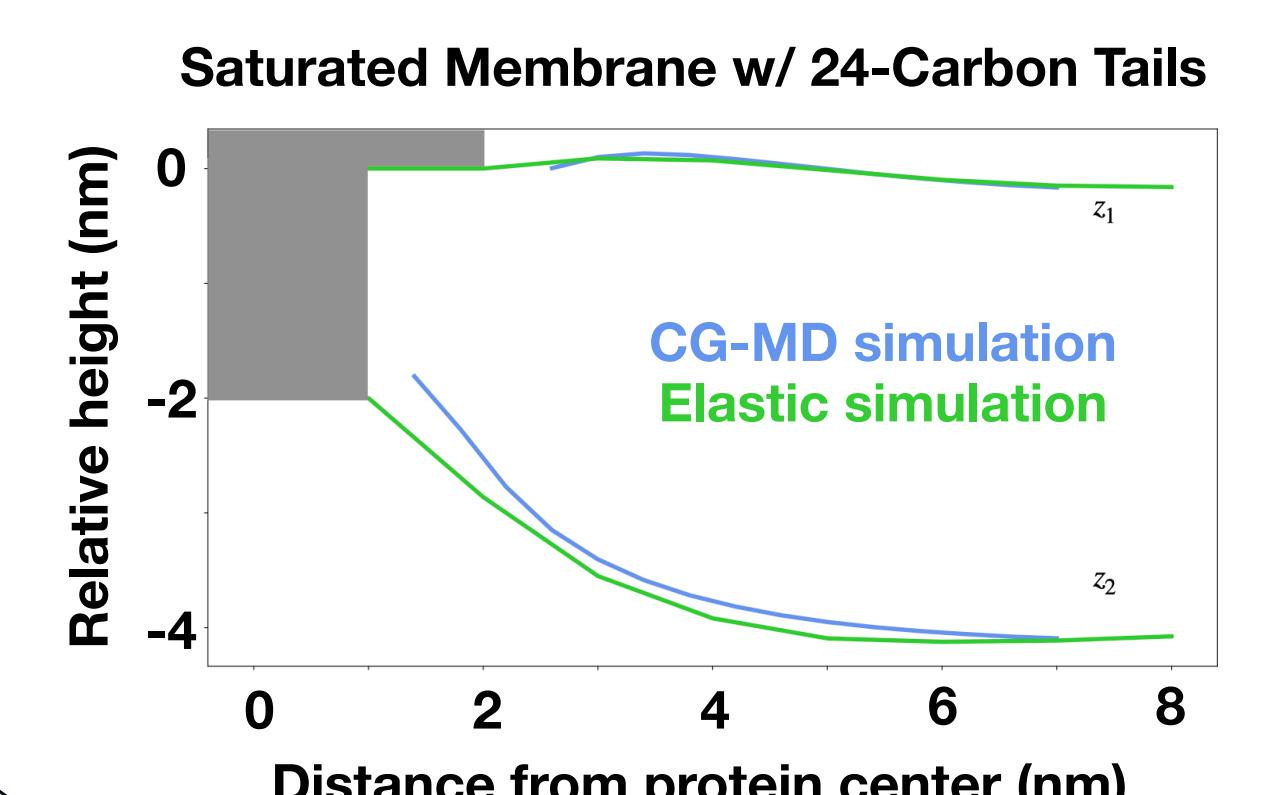


## Cartoon to explain epsilon

## Continuum free energy expression only describes local (saturated) deformations

$$f_z = \frac{1}{2} K_C (H^-)^2 + 2K_C c_0 H^- + \frac{2K_C \zeta z^- H^-}{t_0} + \frac{K_A (z^-)^2}{2t_0^2} + \frac{1}{2} K_C (H^+)^2 + \frac{2K_C \epsilon \zeta H^+}{t_0} + \frac{K_A \epsilon^2}{2t_0^2}$$

To account for the asymmetric thickness deviations close to the protein, we revised an earlier expression [4] for the bending energy of the membrane to allow for local leaflet asymmetry  $\epsilon$ .



Cannot replicate large-scale bending seen in mono-unsaturated membrane series using this expression!

## References

1. Rahman, et al. Gene Reports, 2021
2. Schoeman & Fielding, Virology, 2019

3. Fischer, et al. Journal of Virology, 1998
4. Brannigan & Brown, Biophysical Journal, 2006

## BUG REPORT!

"refcoord\_scaling all" in GROMACS

Things are broken #1

Things are broken #2

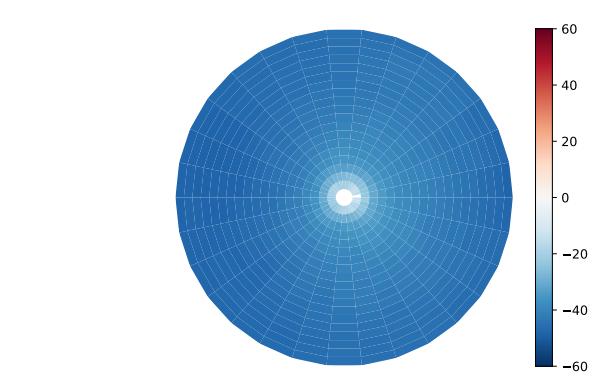
## Saturated membrane results unaffected by this bug

Prettier version of APL graph

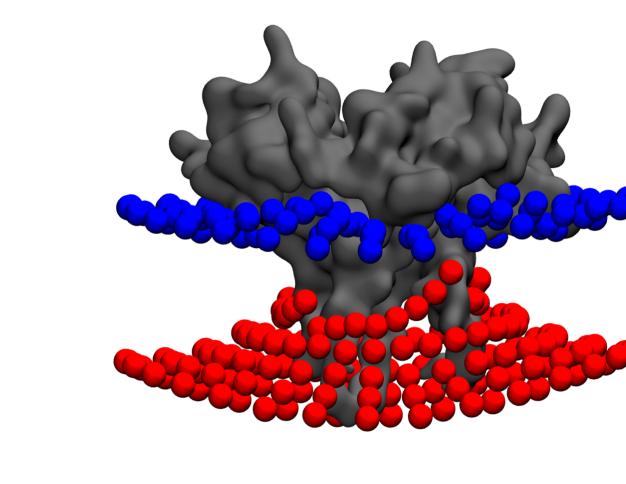
## Conclusions

- The E protein induces local, asymmetric thickness deformations in saturated membranes
- These deformations are well-described by continuum-level free energy expressions, provided leaflets are allowed to fluctuate independently of one another
- refcoord\_scaling all is not behaving as expected in GROMACS

## Try nougat!



Heat maps in polar and cartesian coordinates



Average surface pdb file generated for direct visualization in VMD



github.com/BranniganLab/nougat