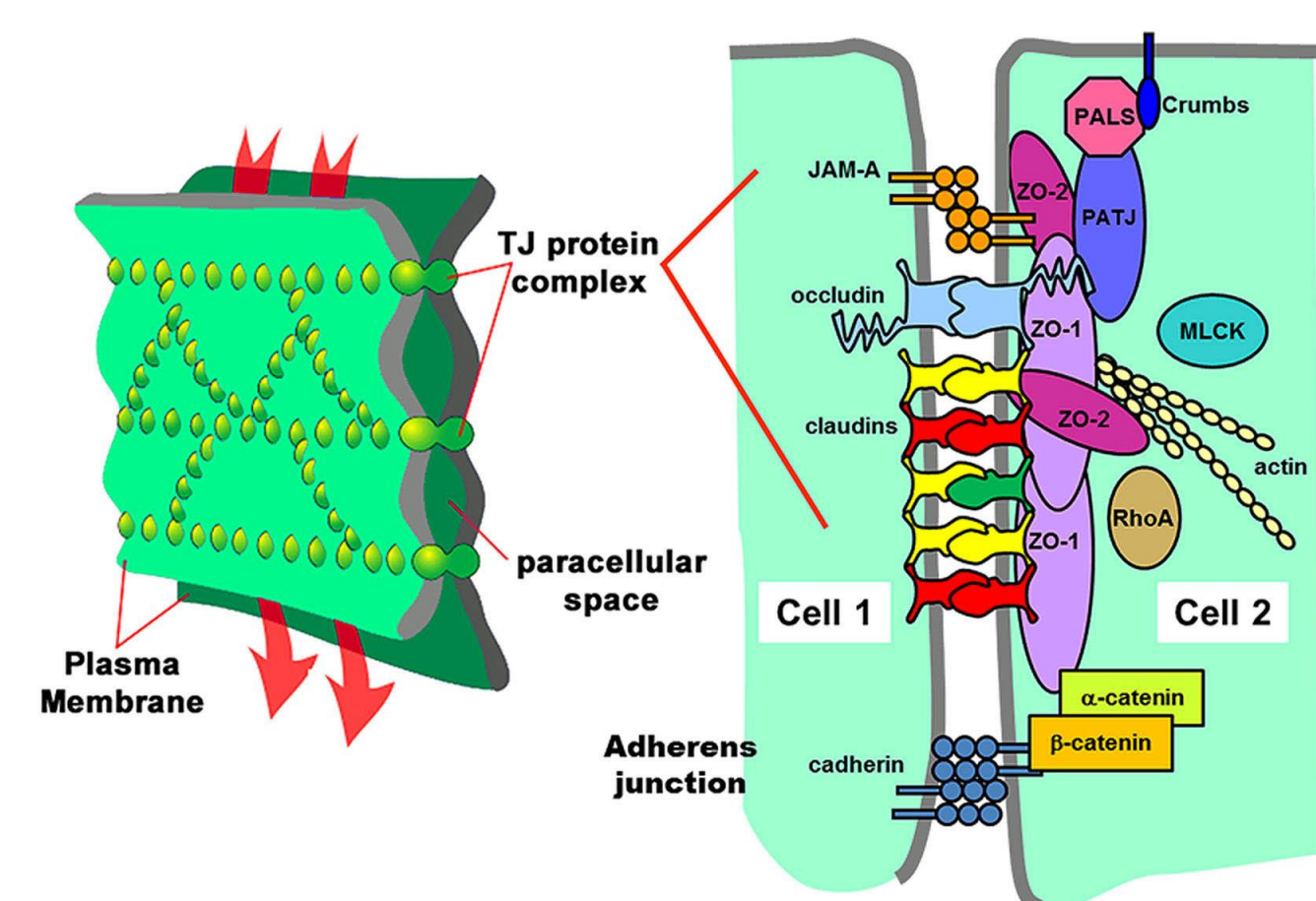


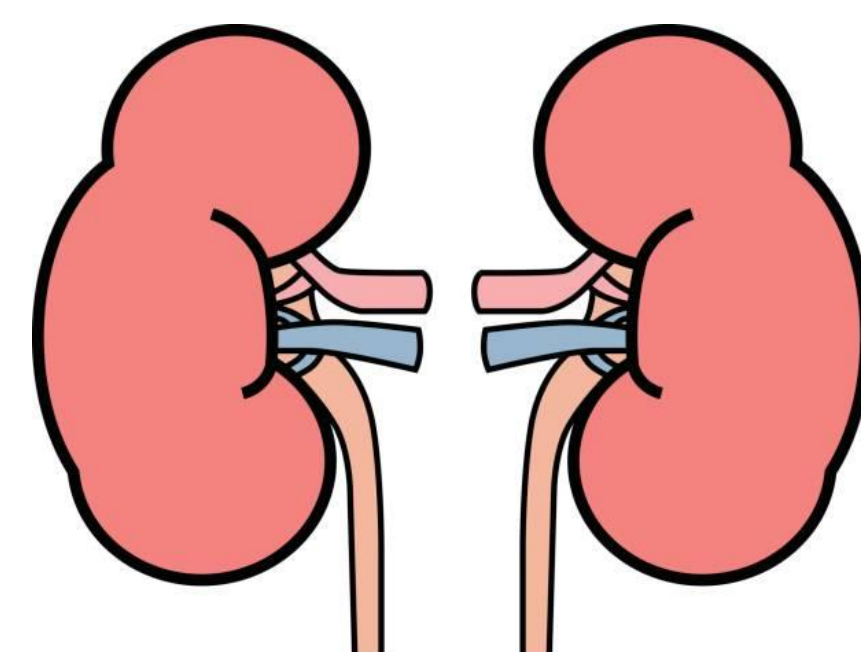
## Introduction

Claudin-6 is a member of the claudin family commonly expressed in tight junctions between cells found in the kidneys, liver, and other organ systems.

When palmitoylated, the protein attaches one or more fatty acid groups.



Tight junction

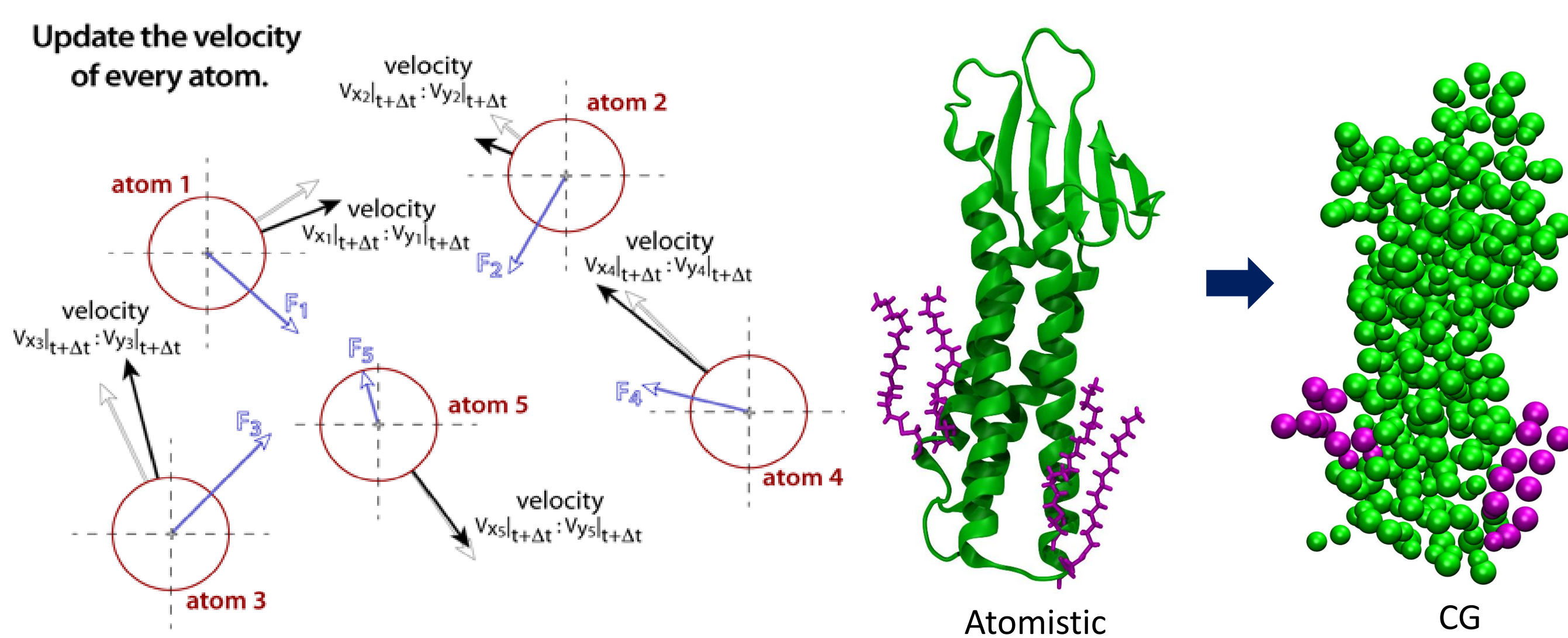


Kidneys – expression of CLD-6 may affect the glomerular filtration barrier permeability<sup>1</sup>

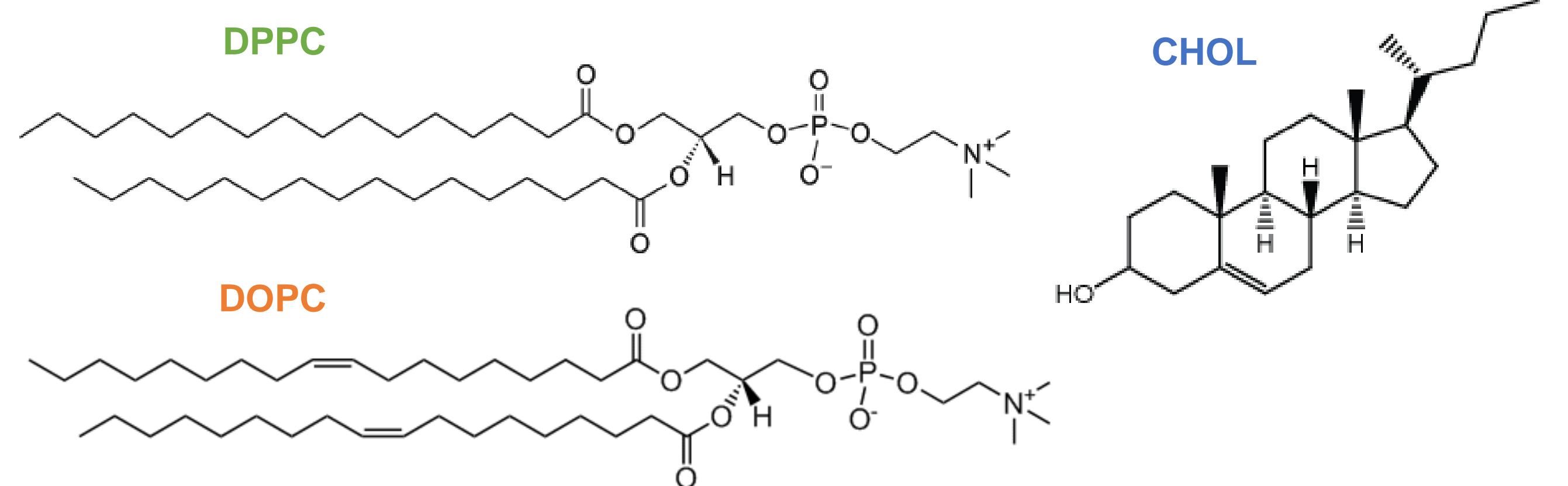
## Methods

Molecular dynamics simulations

Coarse grain resolution

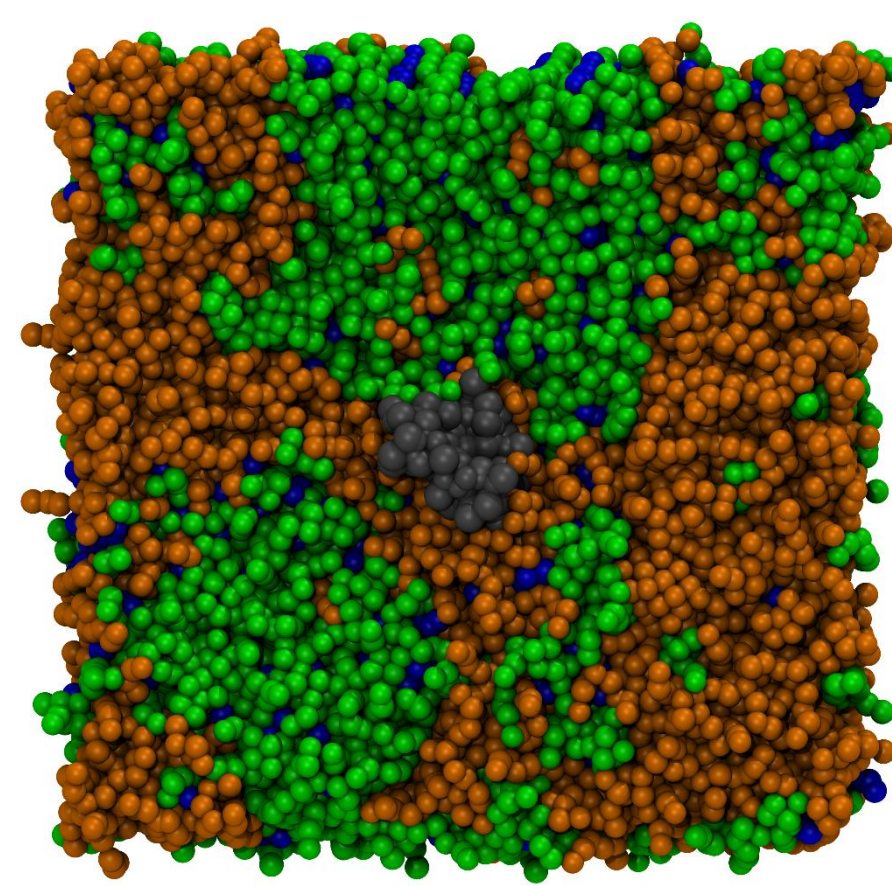


- Simulations were performed using GROMACS, a molecular dynamics engine
- Systems were maintained at constant  $T = 298$  K and  $P = 1.01$  bar
- Periodic boundary conditions were applied in all three directions
- Simulations were performed in triplicates

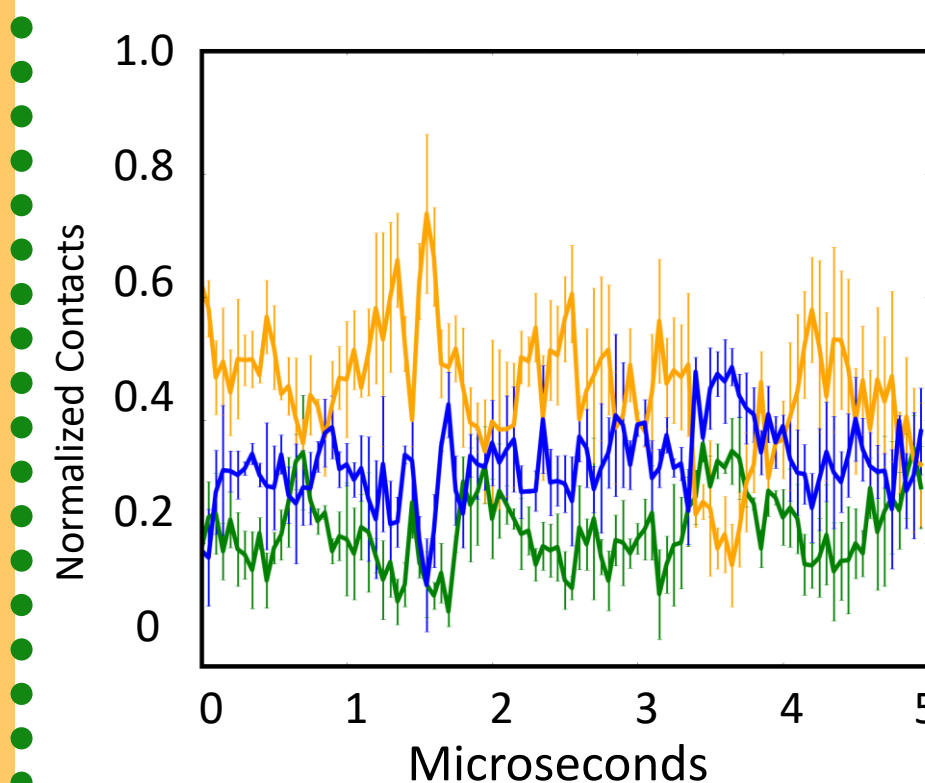


## Results

Comparison of membrane properties for claudin-6 in palmitoylated and nonpalmitoylated forms



Nonpalmitoylated

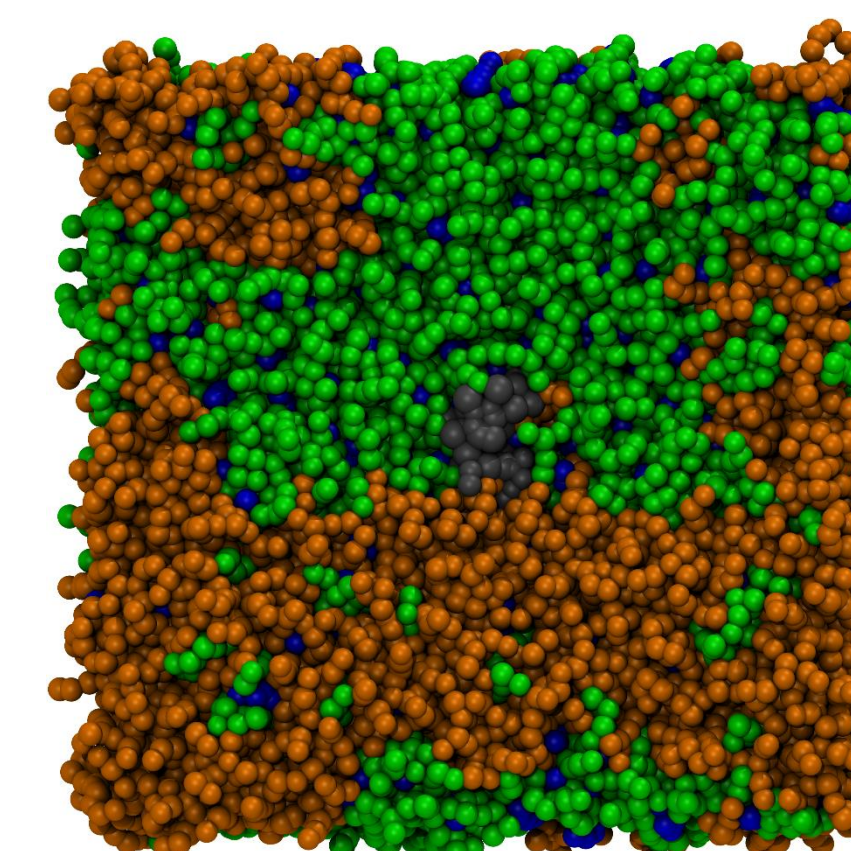


Protein embedded in lipid bilayer

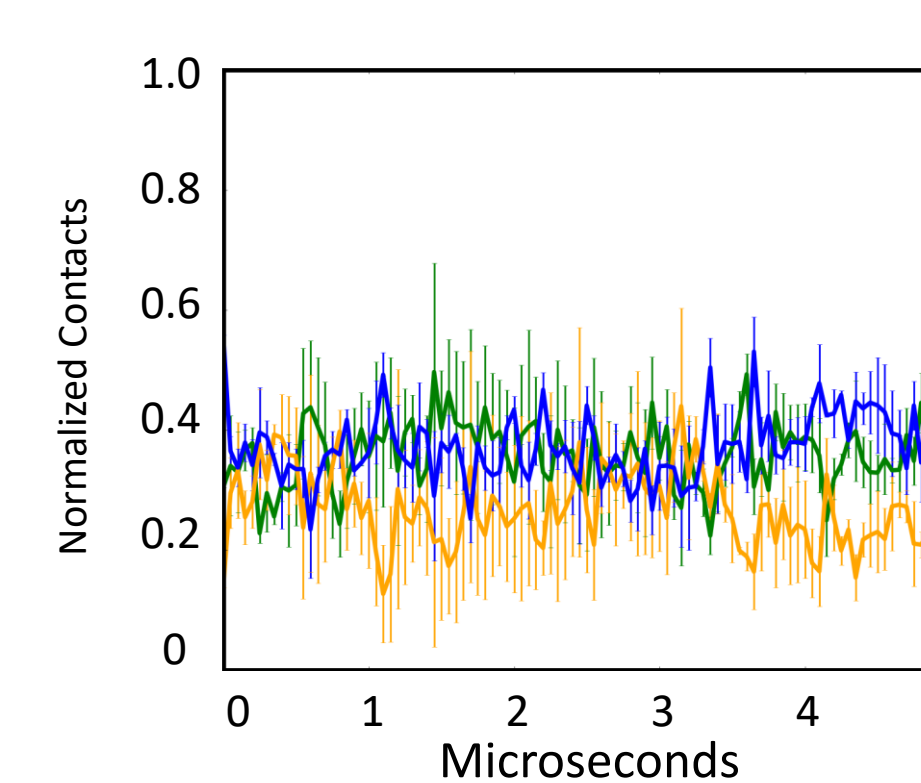
Saturated: Unsaturated: cholesterol

DPPC: DOPC: CHOL

2: 2: 1



Palmitoylated



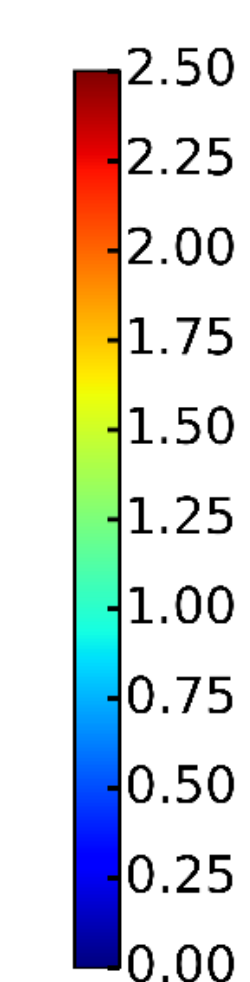
Lipid mixing

DPPC

DOPC

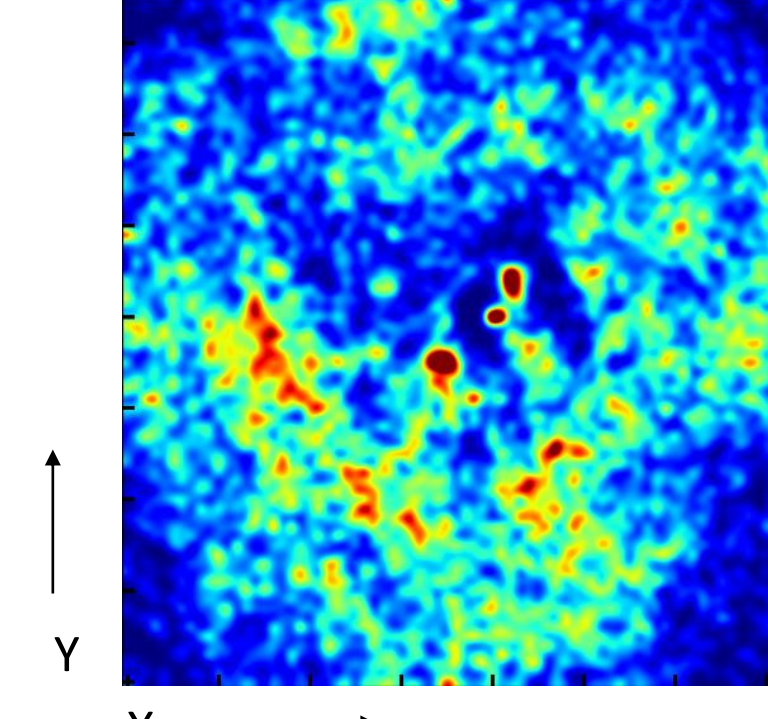
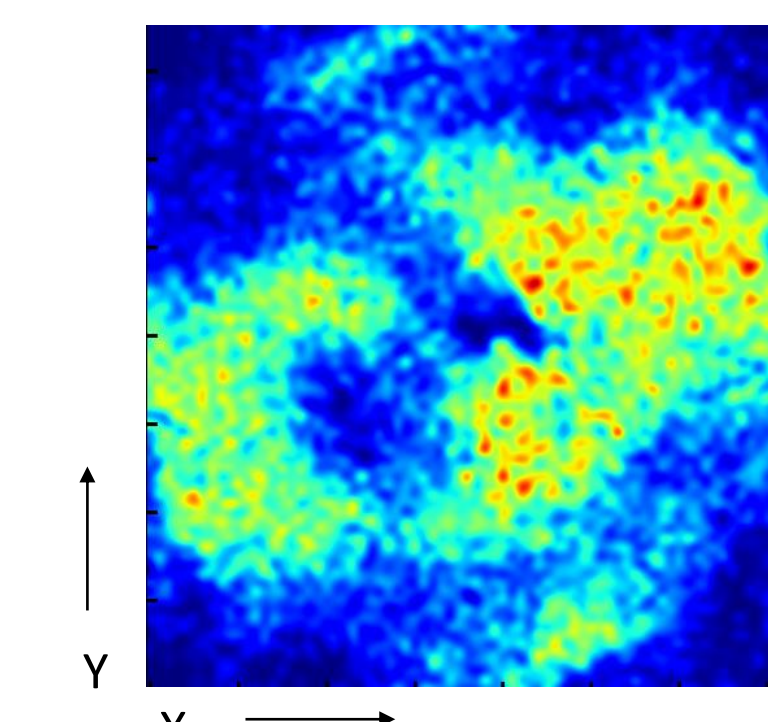
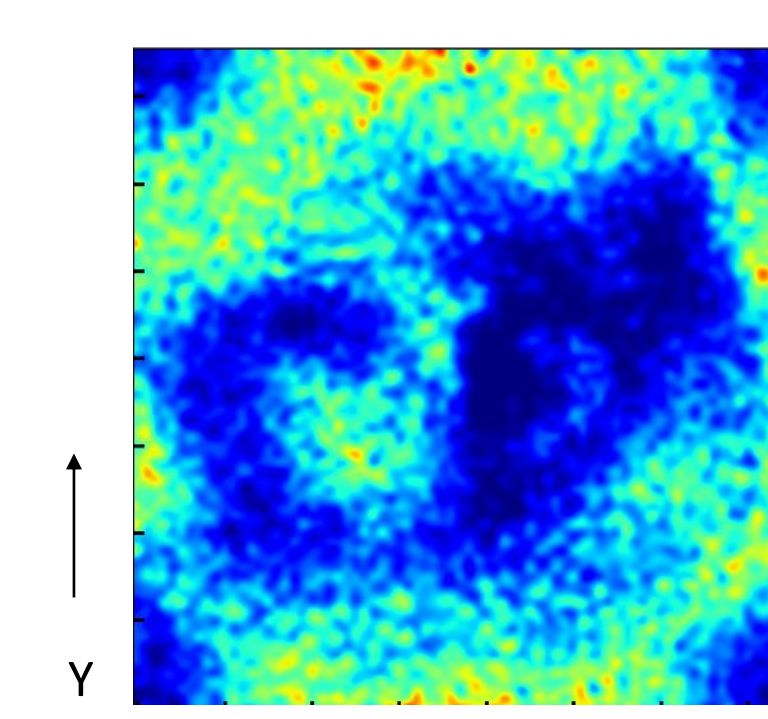
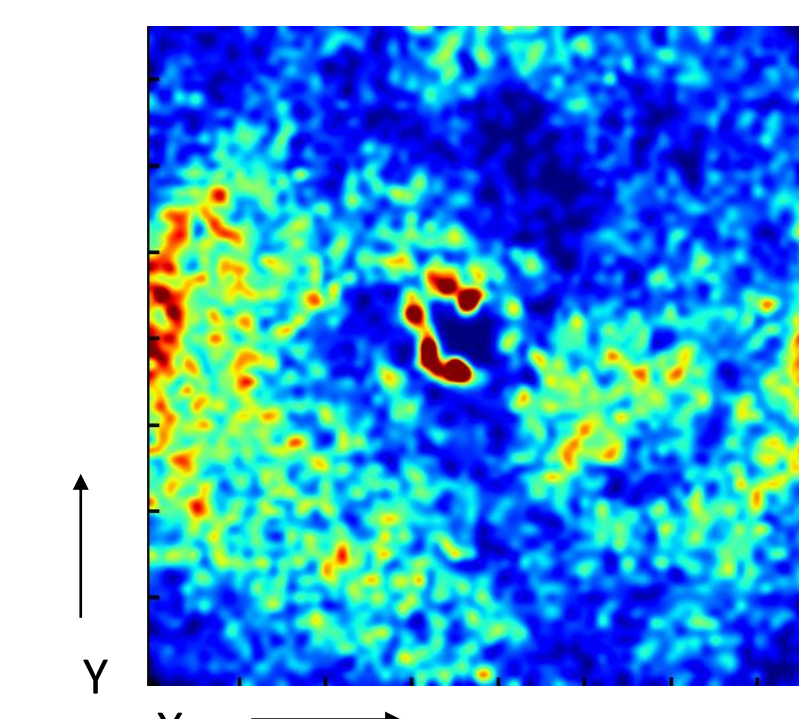
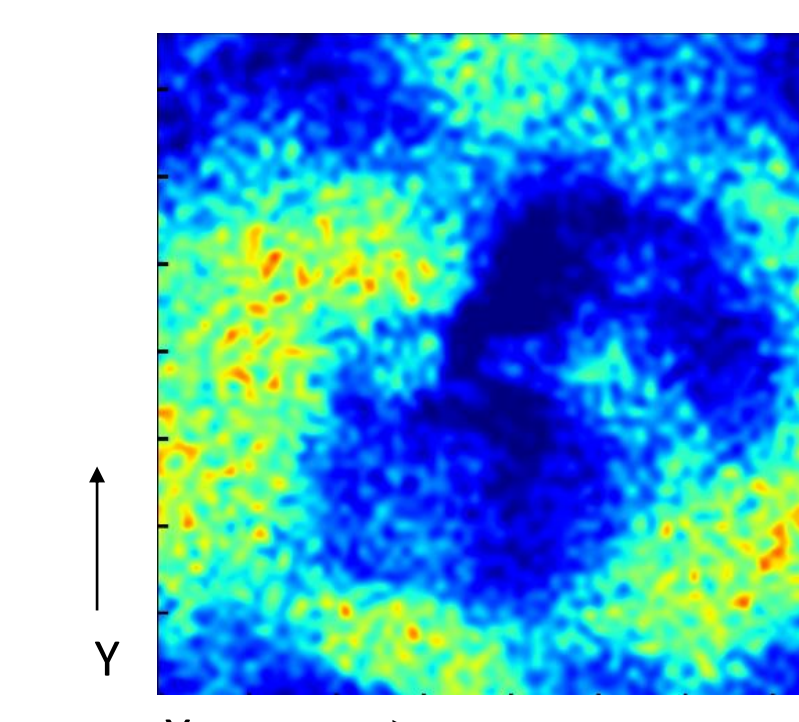
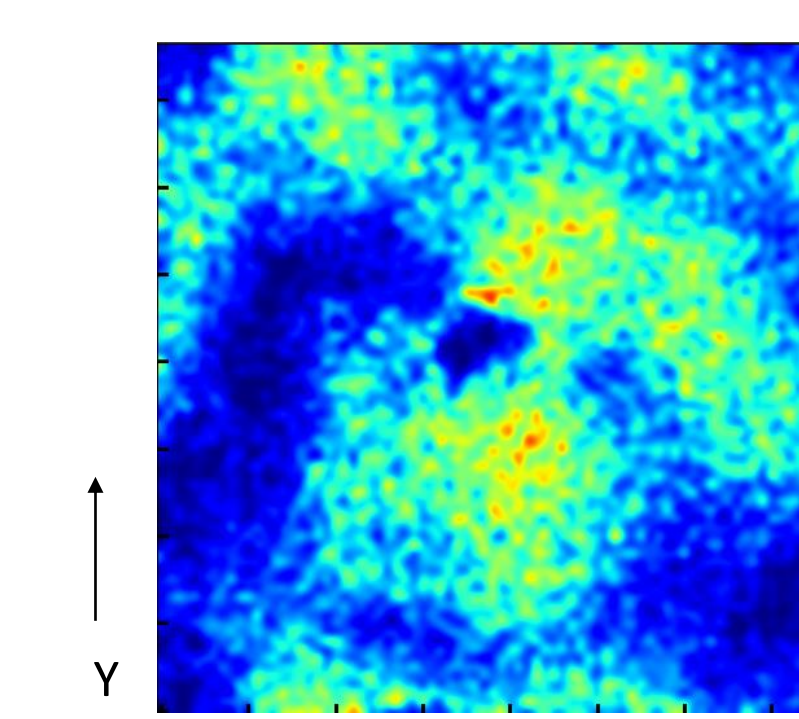
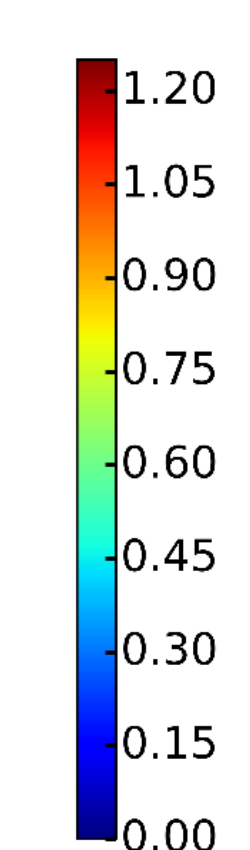
CHOL

Unsaturated lipid density



Saturated lipid density

Cholesterol density



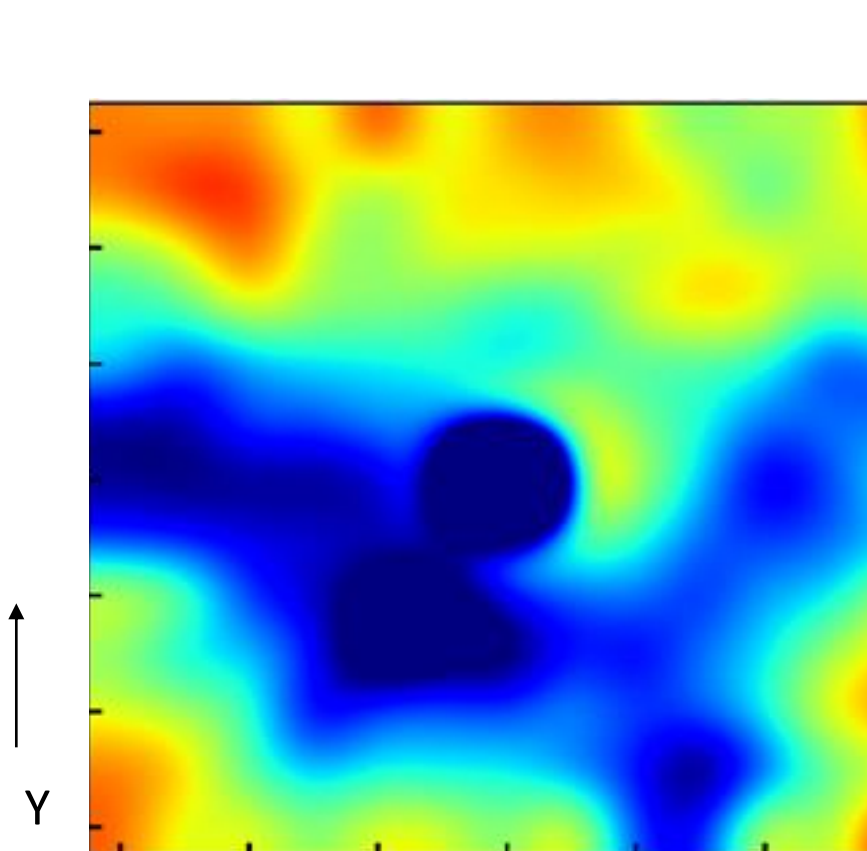
## Conclusions

CLD6 prefers to engage with saturated lipids more often when palmitoylated.

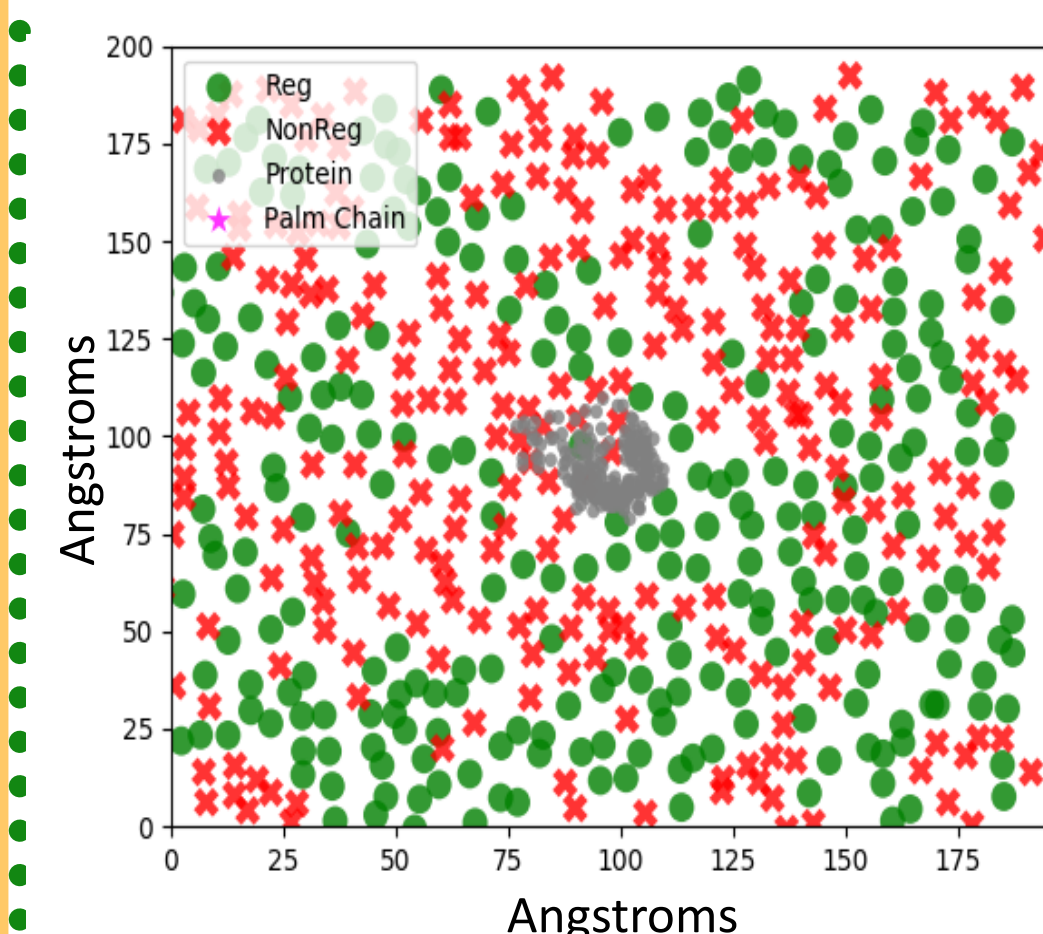
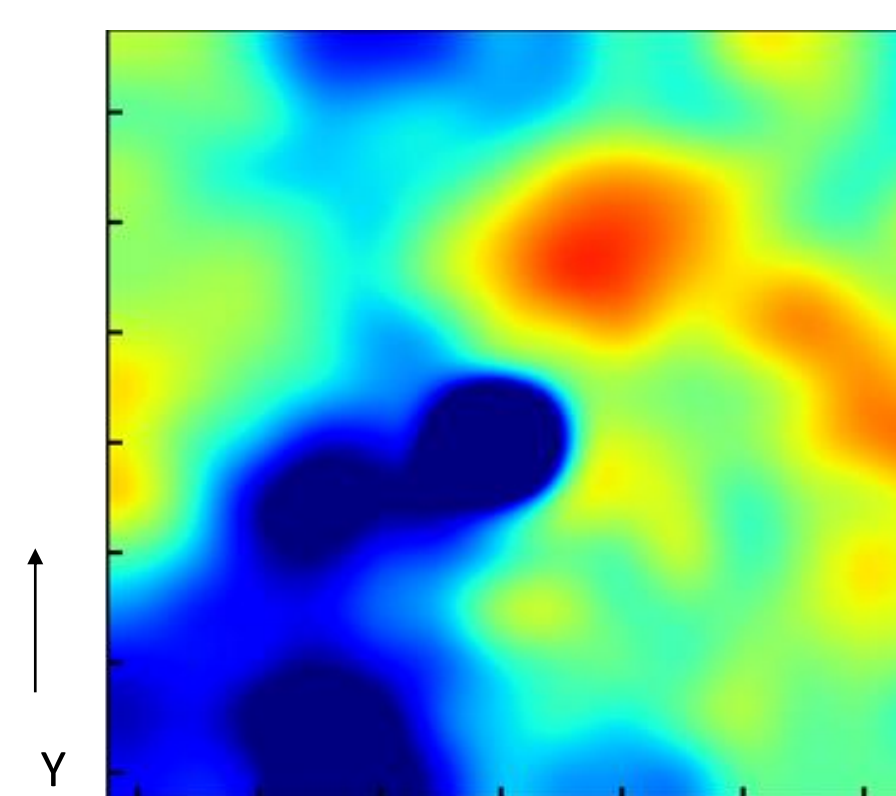
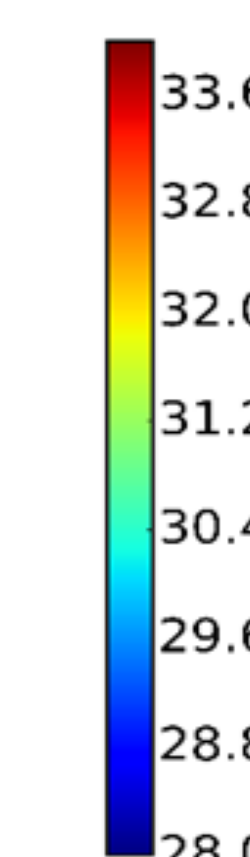
Any degree of palmitoylation alters the environment.

With collaboration from other undergraduates, other claudins studied also exhibit this behavior.

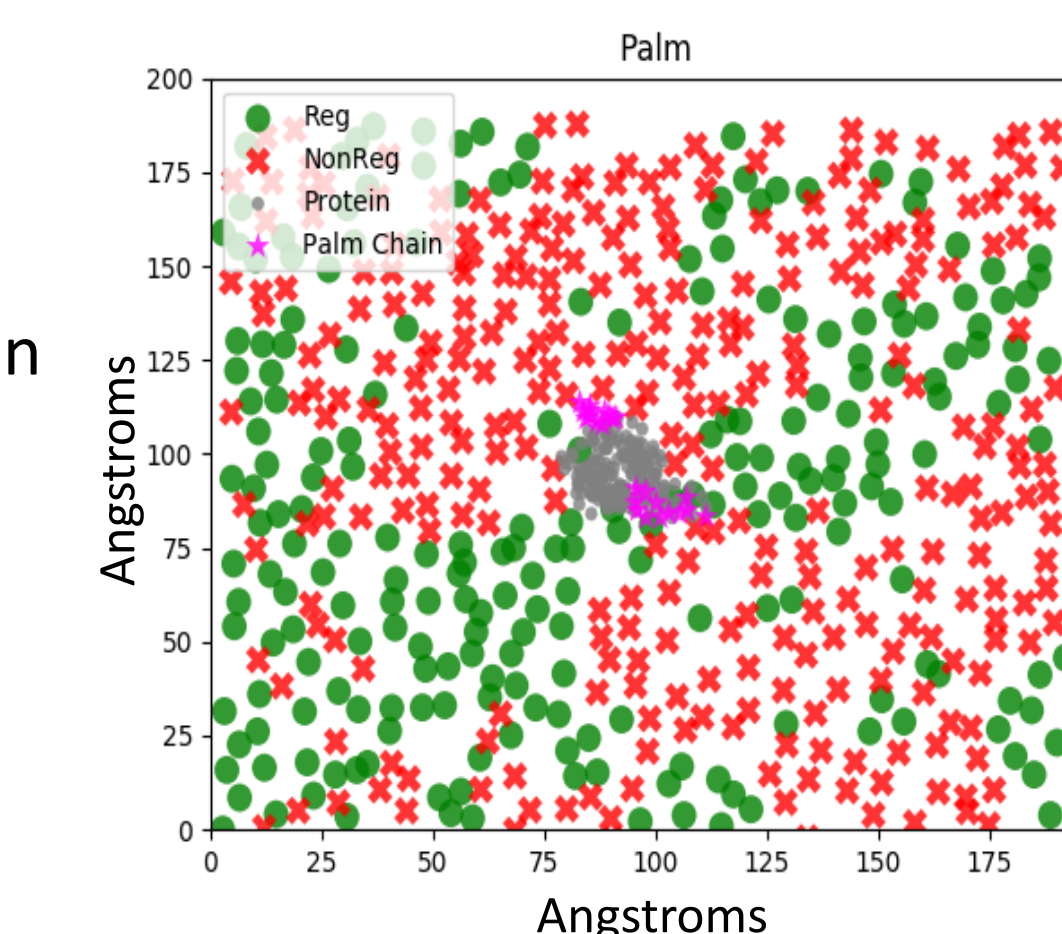
This research will help lay foundation for disease research with more claudins and more membranes in a single tested system.



Hydrophobic thickness



Lipid registration



## Acknowledgments

This work is supported by the CAREER CBET-1453312 grant from National Science Foundation. Computational resources were provided by Information and Technology Services at Syracuse University (Eric Sedore, Larne Pekowsky, and Michael R. Brady).



## References

1. Tight junction claudins and the kidney in sickness and in health. Balkovetz, D. F. (2008, July 16). Retrieved August 5, 2019, from <https://www.sciencedirect.com/science/article/pii/S0005273608002101>
2. Palmitoylation of Claudin-5 Proteins Influences Their Lipid Domain Affinity and Tight Junction Assembly at the Blood–Brain Barrier Interface Nandhini Rajagopal, Flaviyan Jerome Irudayanathan, and Shikha Nangia, The Journal of Physical Chemistry B 2019 123, 983-993 DOI: 10.1021/acs.jpbc.8b09535
3. Tight junction & Gap junction! Blogshaala, B. (2016, September 21). Retrieved from <https://ruia.bioanalyticalsciences.wordpress.com/2016/09/20/tight-junction-gap-junction/>

