



Aspirin Reorganizes the Lipid Membrane

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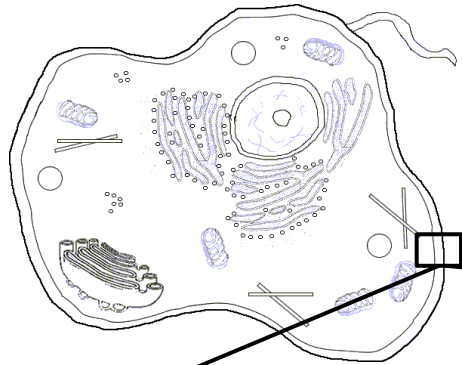
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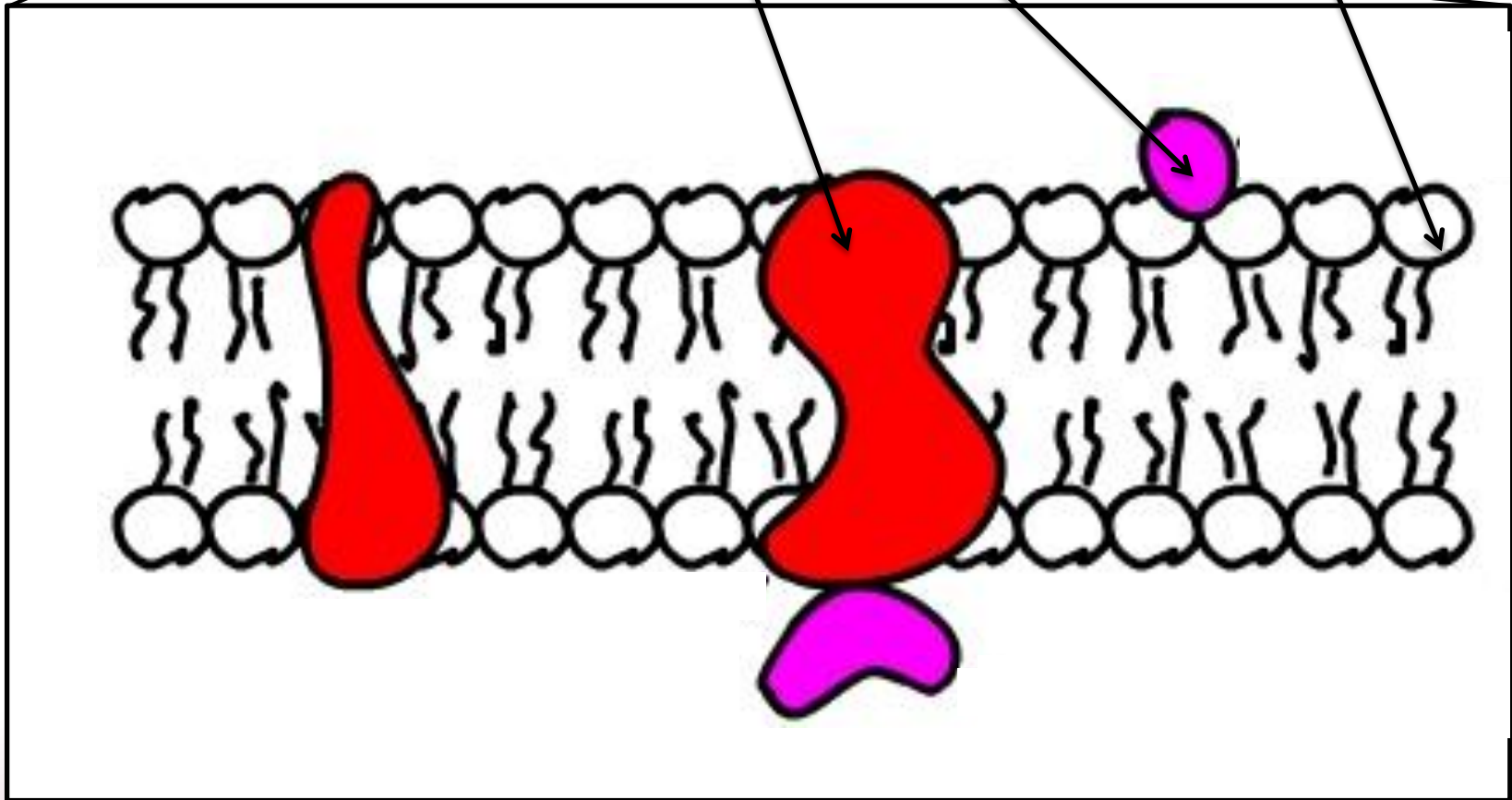


Biological Lipid Membranes



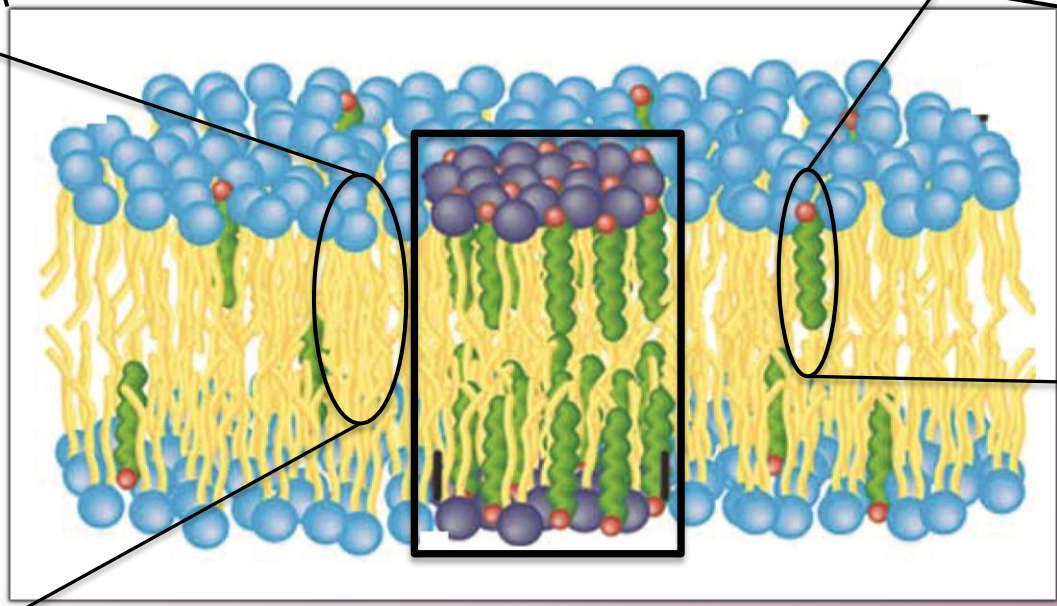
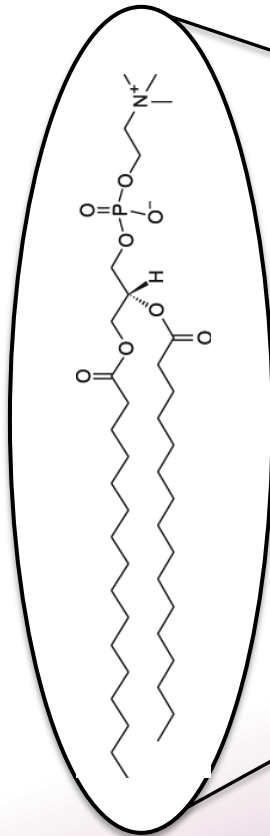
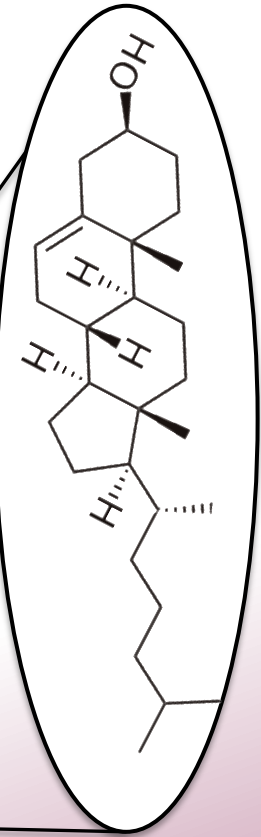
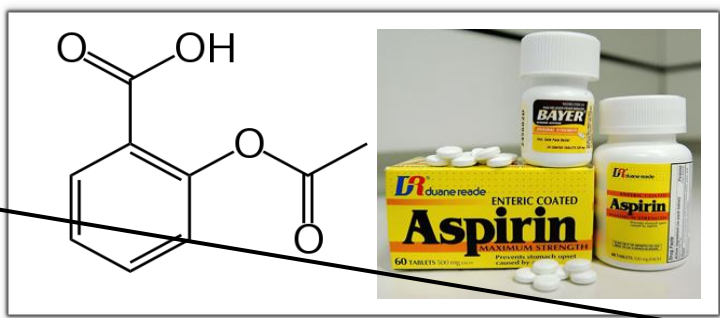
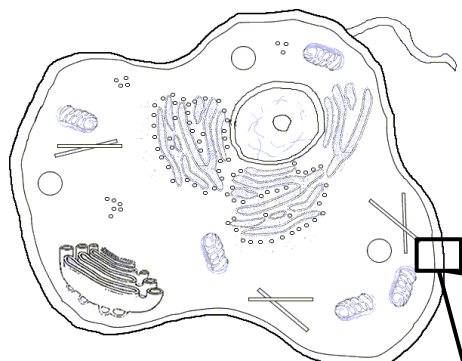
Proteins

Lipids



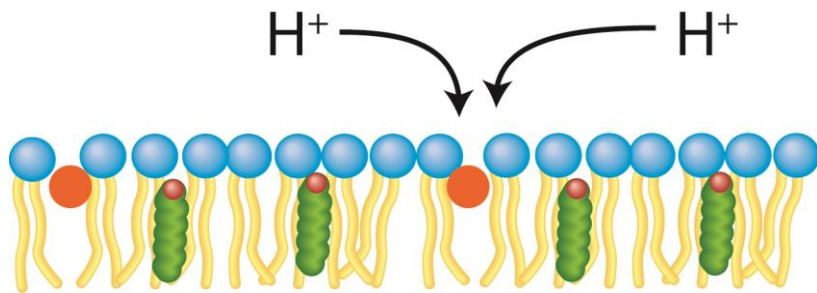


Membrane Domains



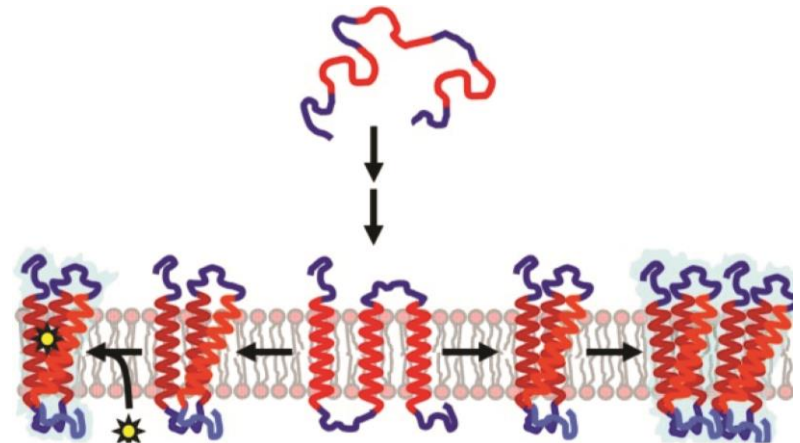


- Aspirin (acetylsalicylic acid, ASA) shows high affinity for lipids
- Aspirin interacts with mucosal membrane, leading to diffusion of stomach acid



Lichtenberger, L.M. *et al.* 2006
Lichtenberger, L.M. *et al.* 2013

- NSAID's can interrupt protein insertion and sorting within membranes

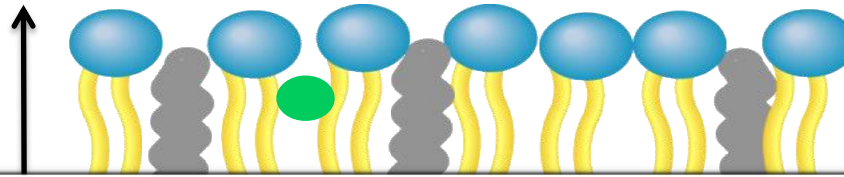


Zhou, Y *et al.* 2012
<http://www.bio.chemie.uni-mainz.de/46.php>

Specific changes in lipid organization due to NSAID's?

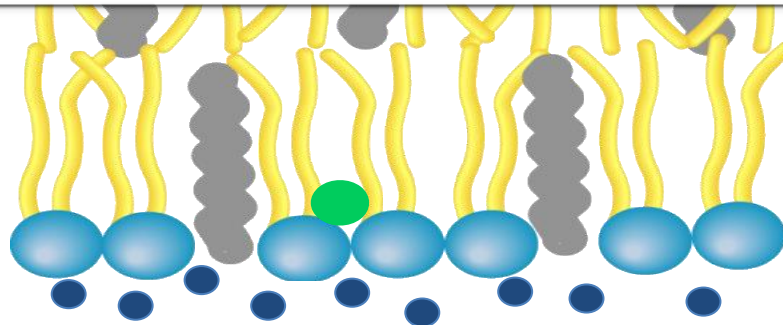


Stacked Membrane System



Does ASA participate in the bilayer?
(X-ray reflectivity)

Structure of membranes with ASA different from those with lipid and cholesterol?
(In-plane diffraction)

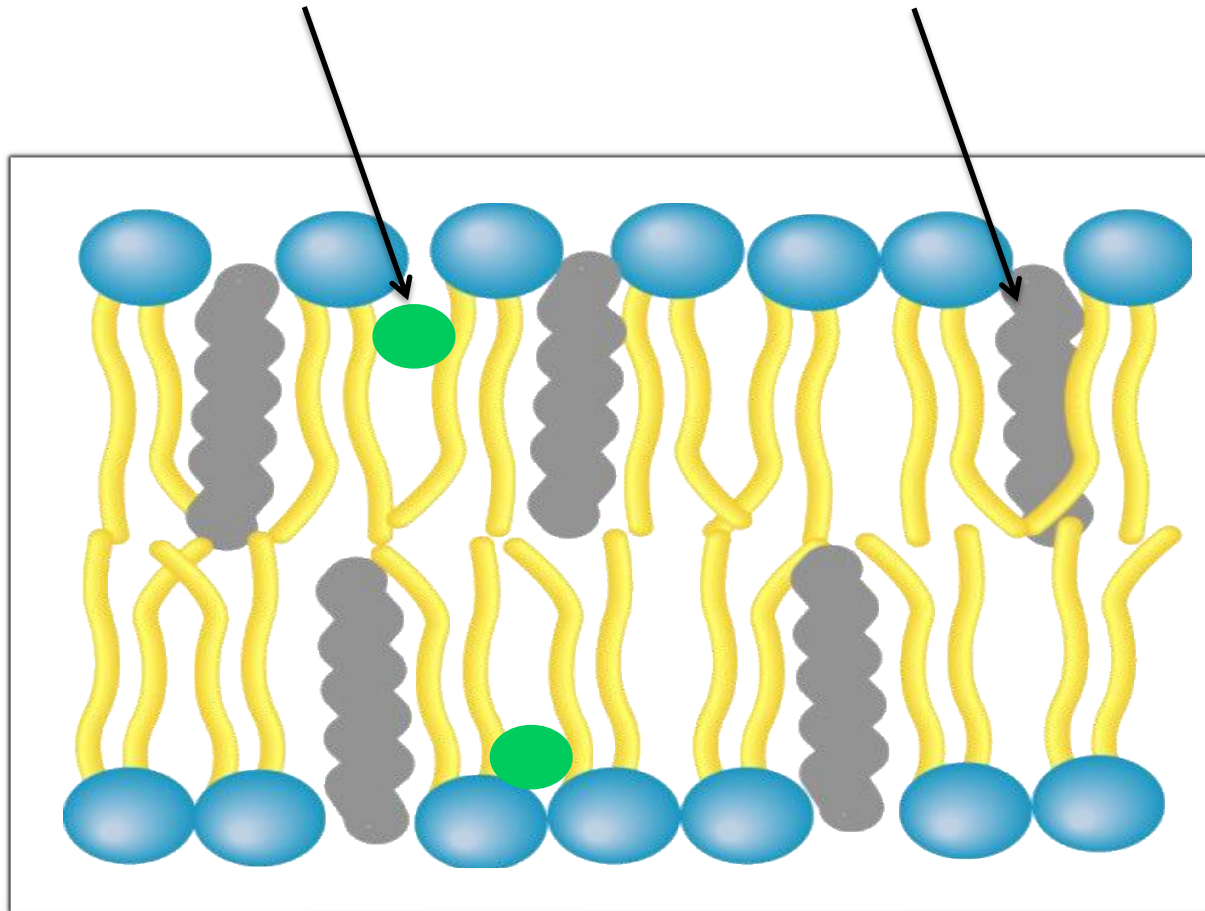




Partitioning of Molecules

Aspirin participates in the
headgroups

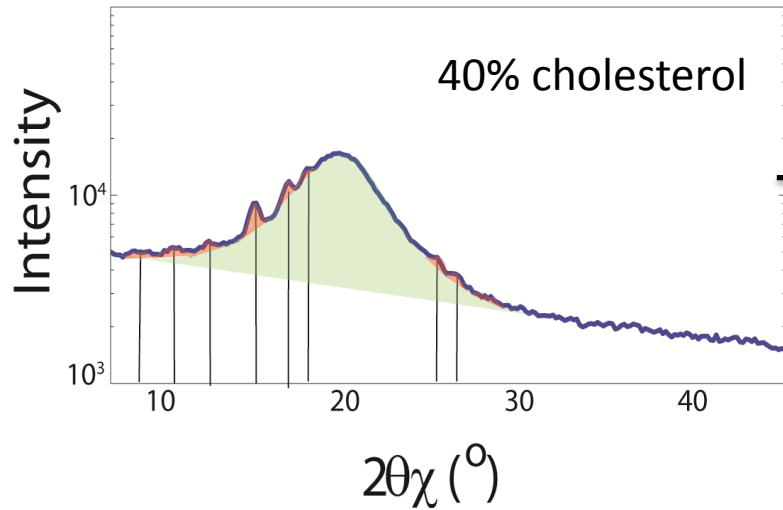
Cholesterol interacts with
The tails



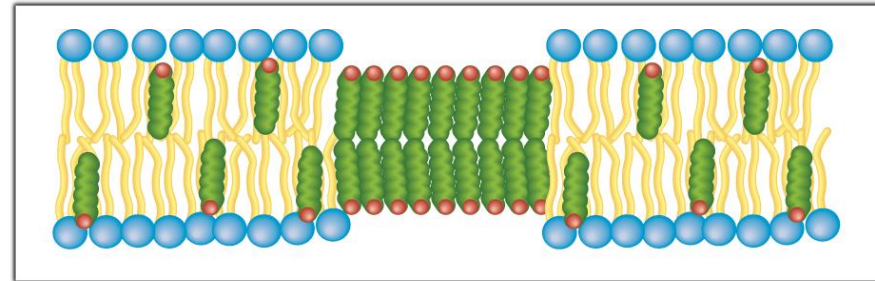
MA Barrett, S Zheng, G Roshankar, **R Alsop** *et al.* PLoS ONE (2012)



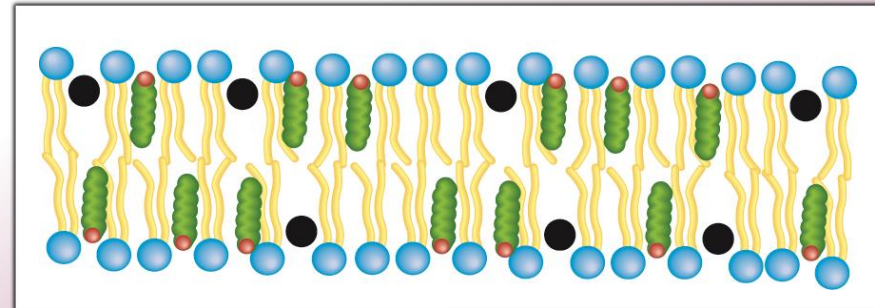
X-ray diffraction



Not rafts,
plaques



MA Barrett, S Zheng, L Topozini, RJ
Alsop, *et al.* *Soft Matter* (2013)



RJ **Alsop** *et al* *Soft Matter* (2014)

Transient Domains?



Coherence Length

Disordered Membrane

Fluctuating or ordered
Membrane structure

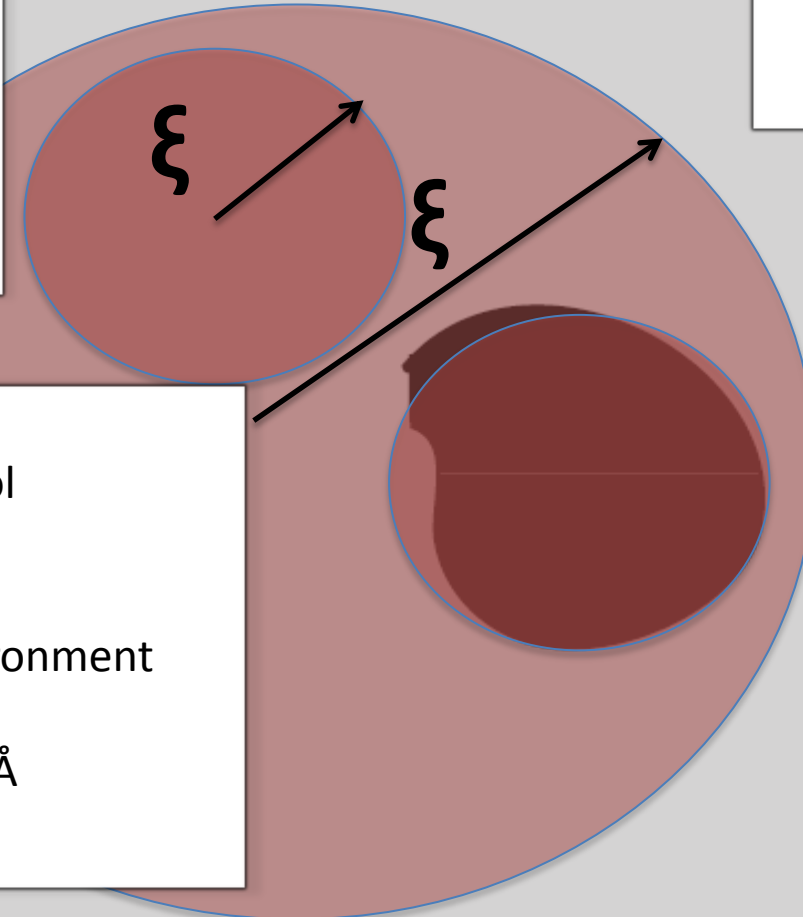
CL Armstrong *et al* Soft
Matter (2012)

CL Armstrong *et al* PLoS
ONE (2013)

$$X = \frac{l^2}{D/}$$

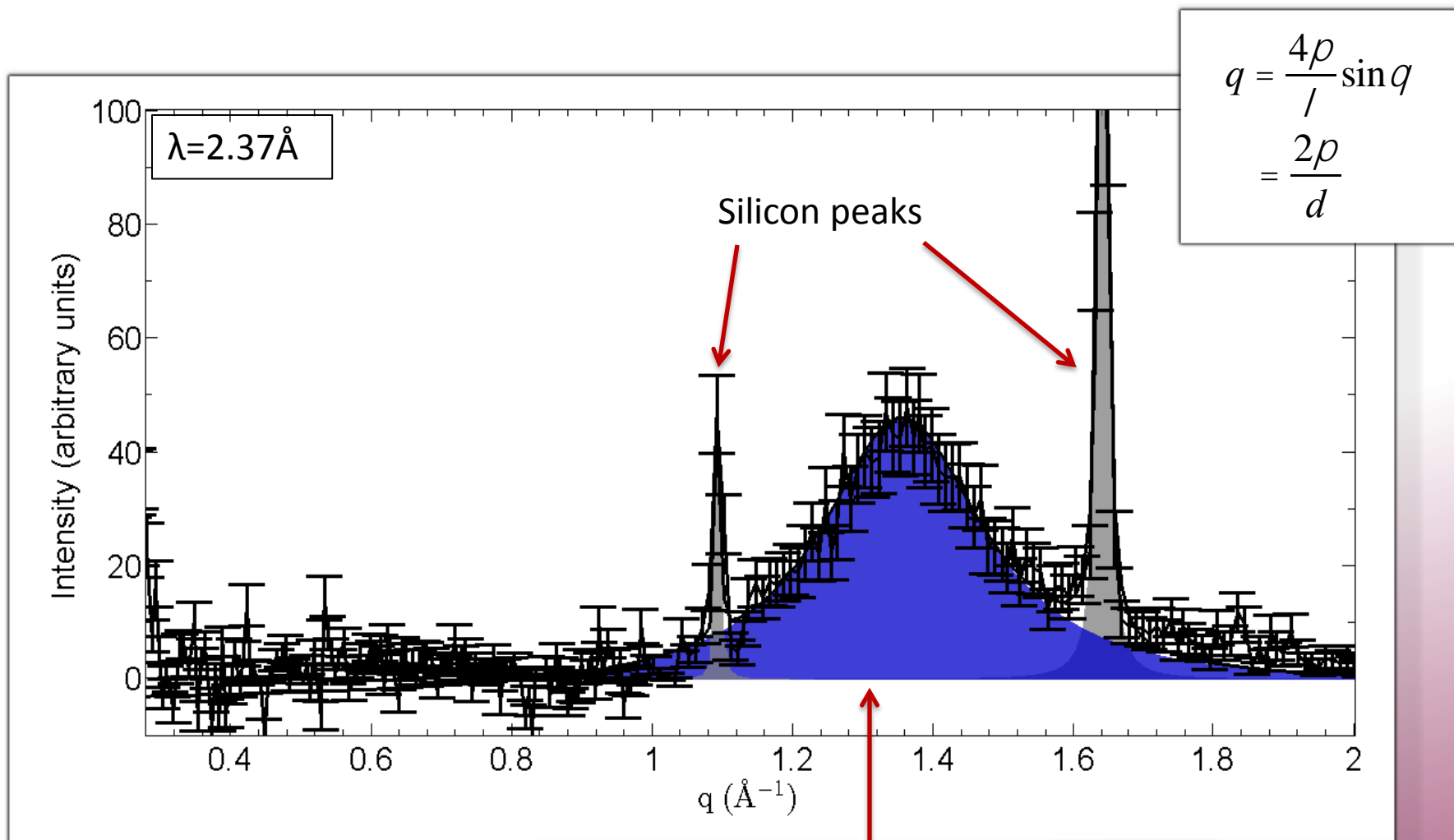
New Sample

- DPPC-d62 with 29mol% chol
- 10% ASA
- 50°C
- Heavy water hydrated environment
- Two experiments:
 - Typical setup: $\lambda = 2.37\text{\AA}$
 - High res: $\lambda = 1.49\text{\AA}$

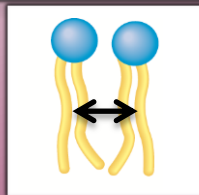




High Coherence length

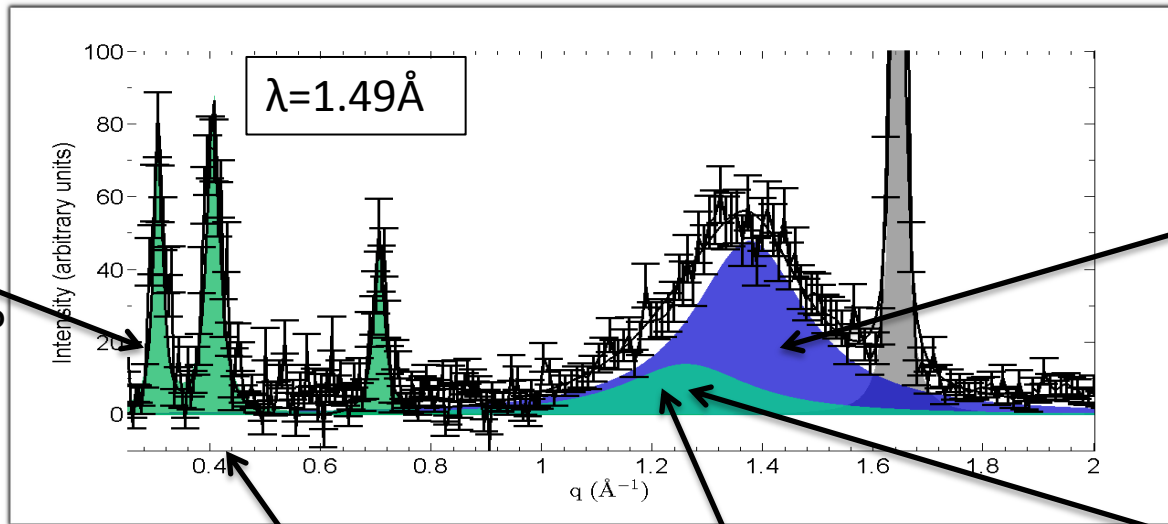


Chain correlation peak

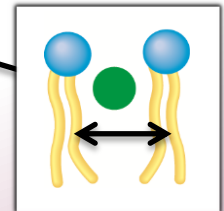
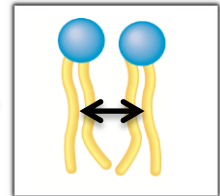




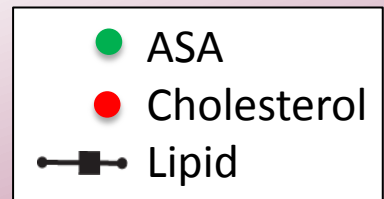
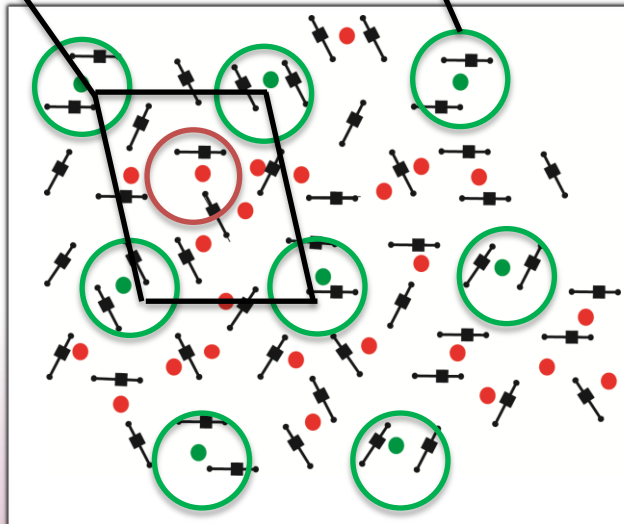
Low Coherence Length



Peak from an 'ASA Superstructure'?



- Fluctuating superlattice formed by ASA
- **Cholesterol driven domains frustrated beyond a few molecules**





Conclusions and Next

- Aspirin frustrates domain structures when incorporated in model lipid membrane
- dependent on...
- What are the...

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Self-medicators, beware the Aspirin myth

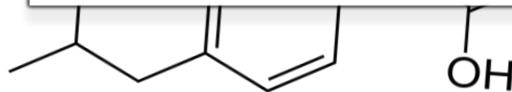
ANDRÉ PICARD
The Globe and Mail
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0 comments

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Earlier this month, the U.S. Food and Drug Administration rejected a decade-old request from Bayer HealthCare LLC, the maker of Aspirin, to label the popular drug as an effective way of preventing heart attacks and strokes.

This comes as a bit of a surprise because, since the late 1980s, cardiologists and family doctors have been recommending that many patients take Aspirin every day as a way to prevent cardiovascular events.



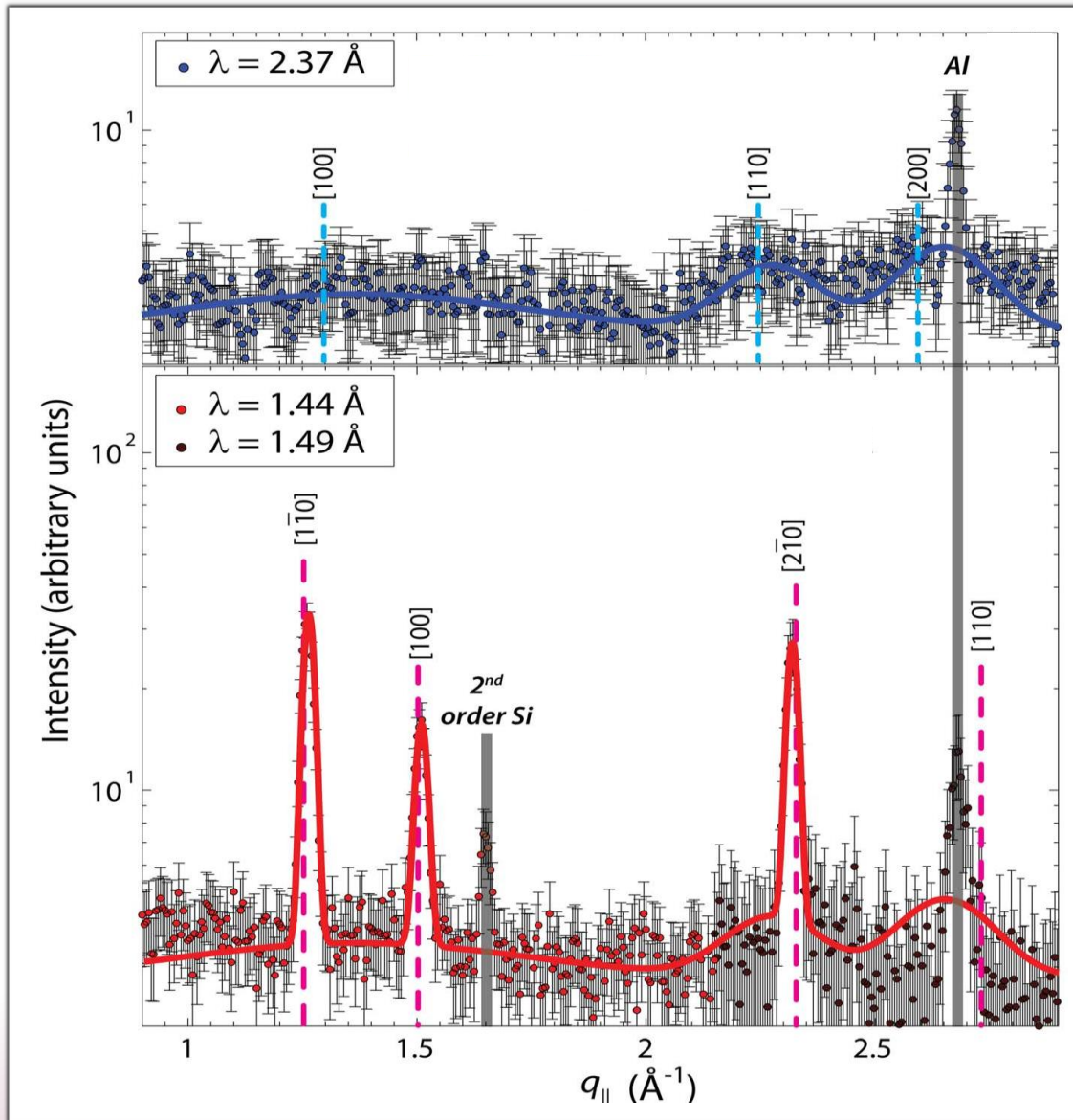
Acknowledgements

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- Laboratory for Membrane and Protein Dynamics



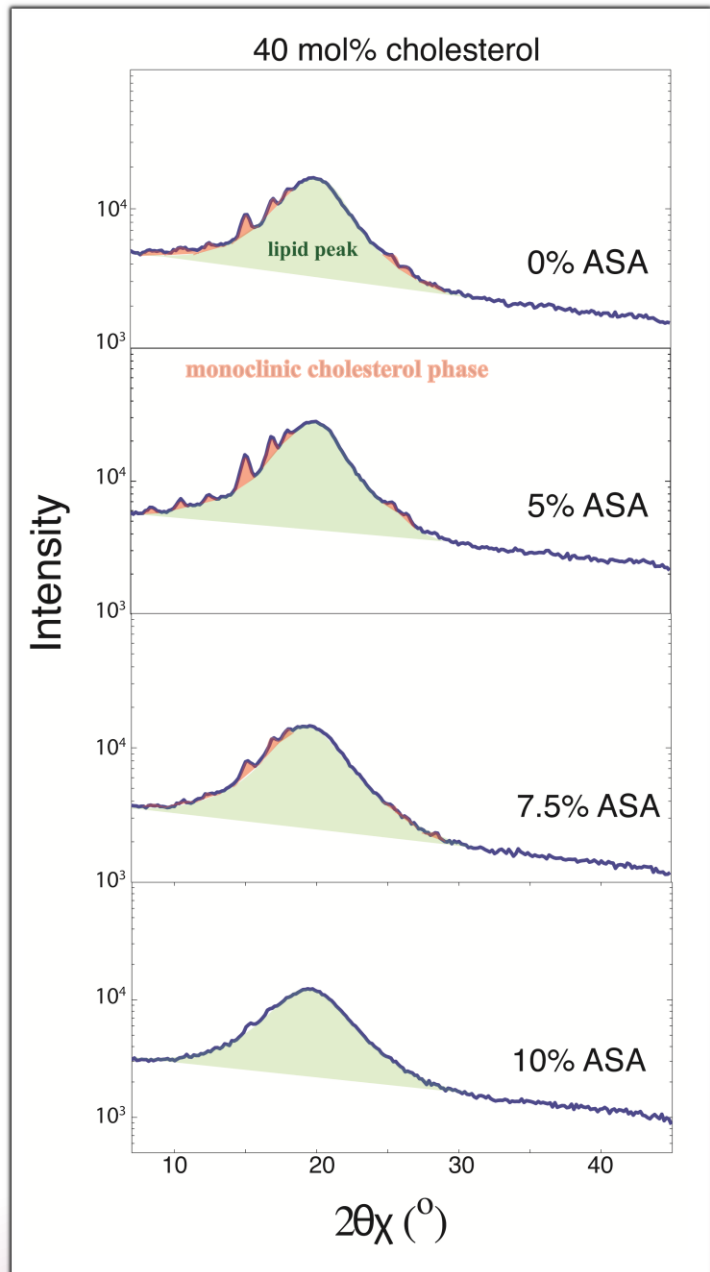


C.L.
Armstrong *et al.* PLoS ONE
2013

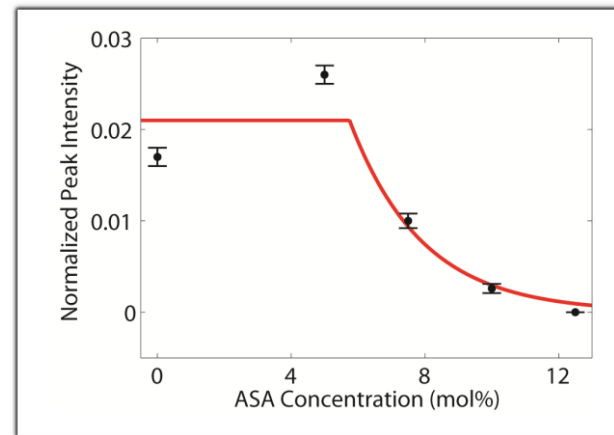




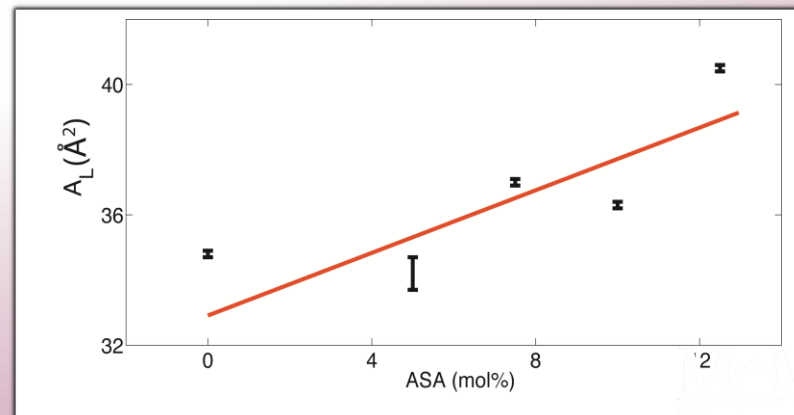
Aspirin and Cholesterol Plaques



Volume Fraction Decrease

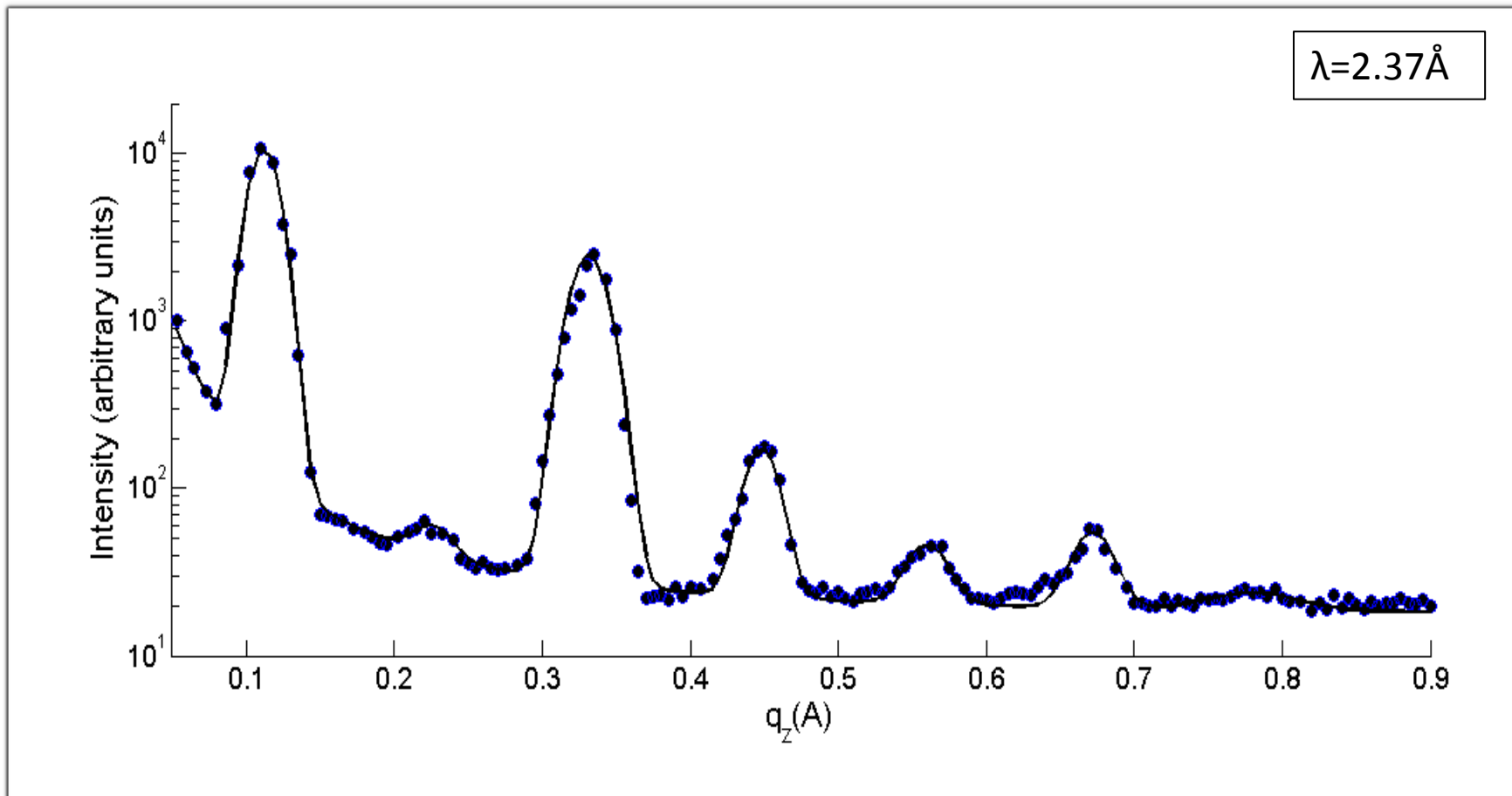


Area Per Lipid Increase



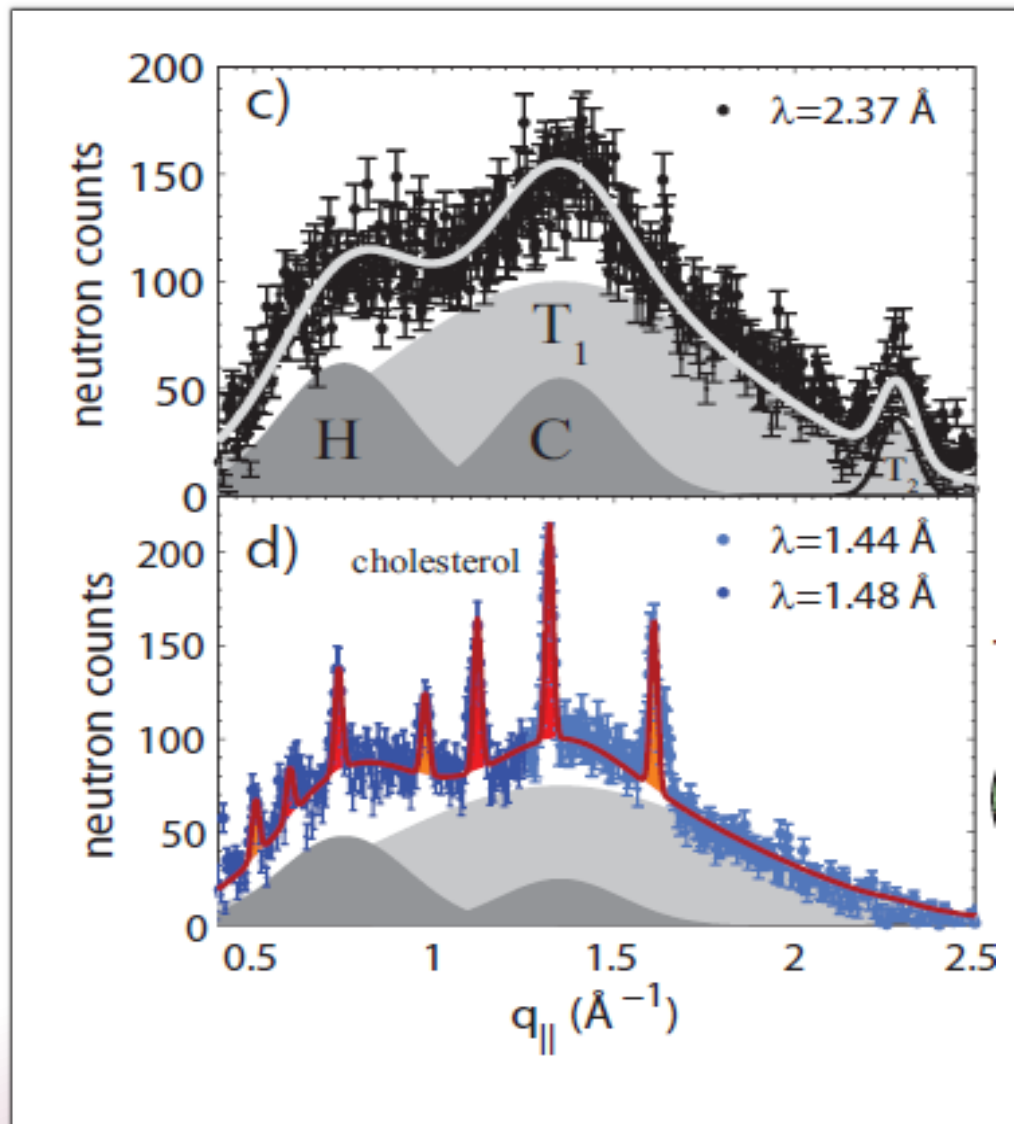


Out-of-Plane Result





Deuterated Cholesterol





MA Barrett, S Zheng, G Roshankar, **R Alsop** *et al.* PLoS ONE (2012)

