Sophie COMBET

5000 € to buy **deuterated lipids**

Dystrophin: insertion into the muscle membrane?

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Dystrophinopathies (e.g. Duchenne muscular dystrophy) are caused by mutations in the gene that encodes **dystrophin** protein

AFMTÉLÉTHON
CURE THROUGH INNOVATION

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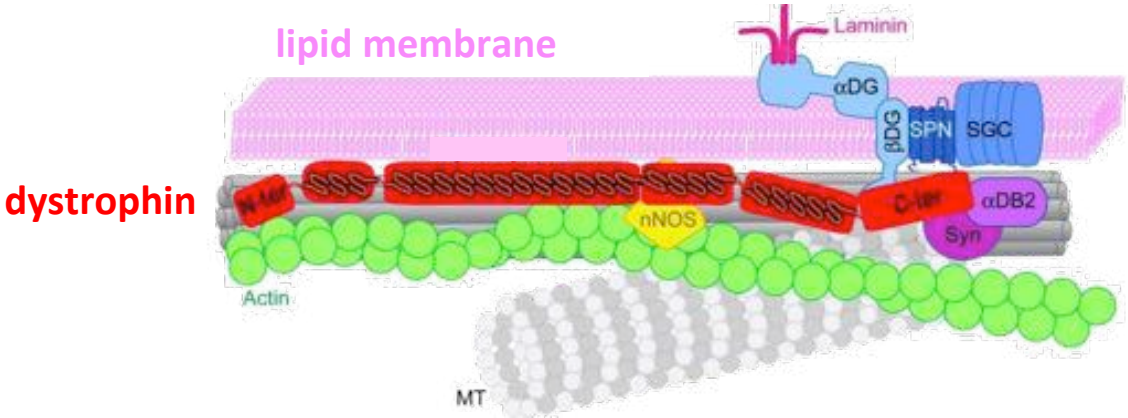
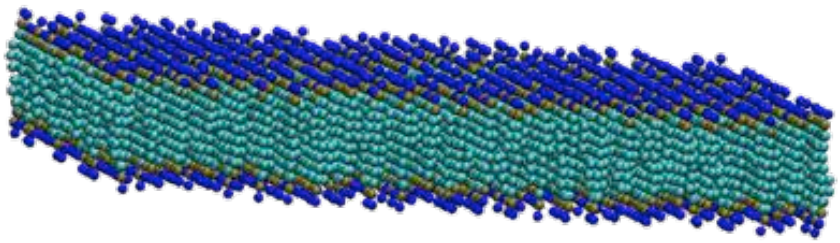
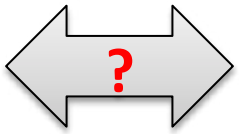
AFMTÉLÉTHON
CURE THROUGH INNOVATION

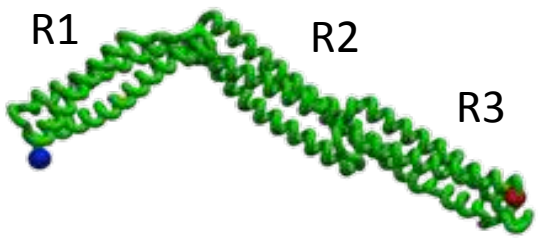


dystrophin is a peripheral membrane protein supporting the plasma **membrane** of muscle cells

Sophie Combet - LLB



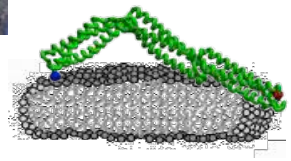




R1-3 dystrophin fragment

which conformation the dystrophin adopts in the presence of membrane lipids?

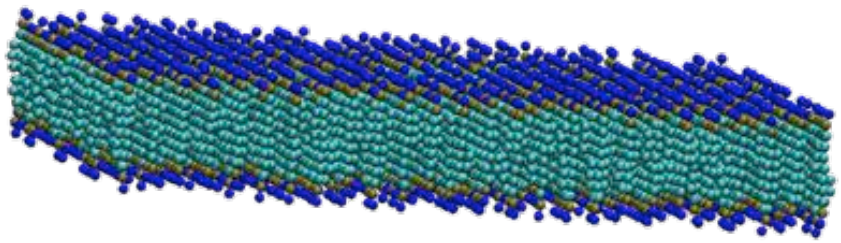
Raphael Dos Santos Morais
(PhD thesis 2014-2017)

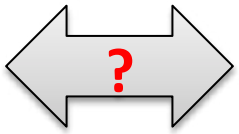


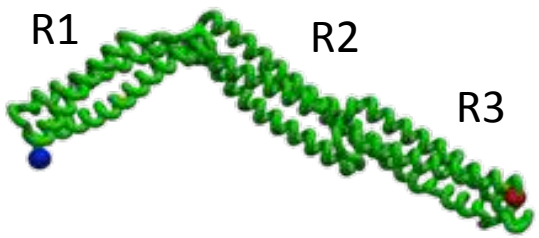
structural changes
upon binding to lipid membrane?

small-angle neutron scattering (SANS)

Sophie Combet - LLB







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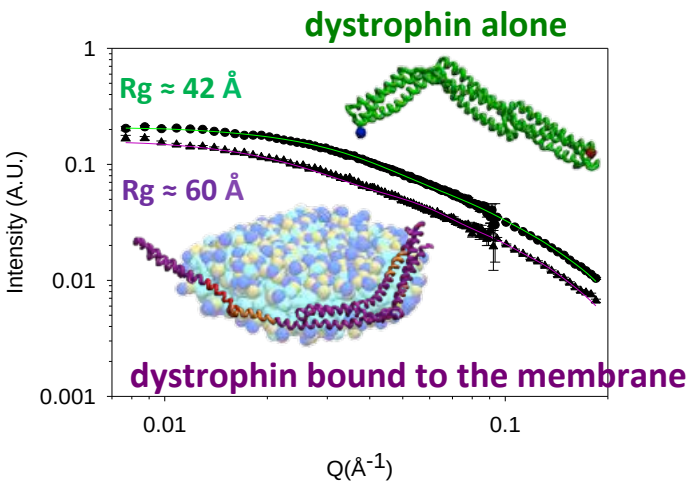
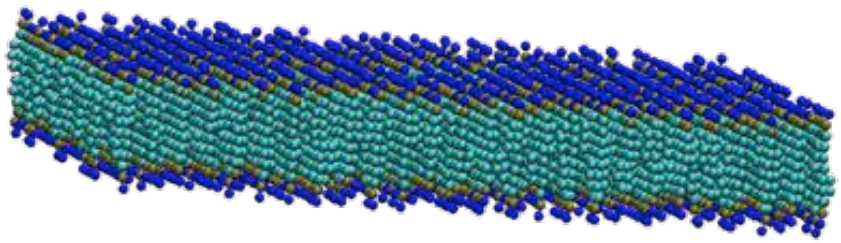
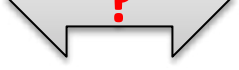
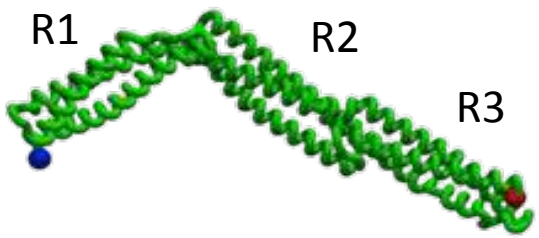


Dos Santos Morais R *et al.*, Langmuir 2017
Dos Santos Morais R *et al.*, Biophys J 2018

Sophie Combet - LLB







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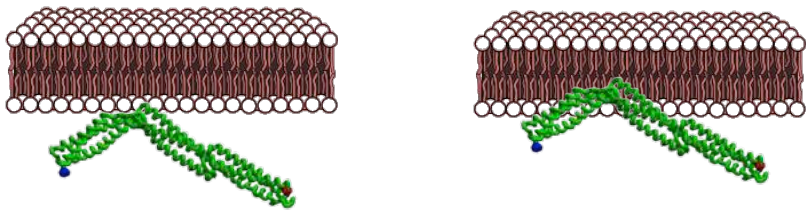
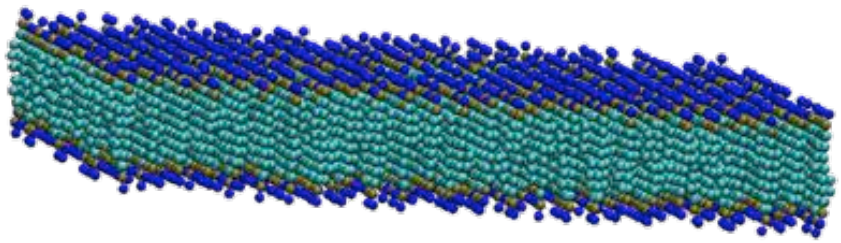
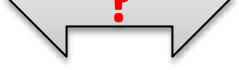


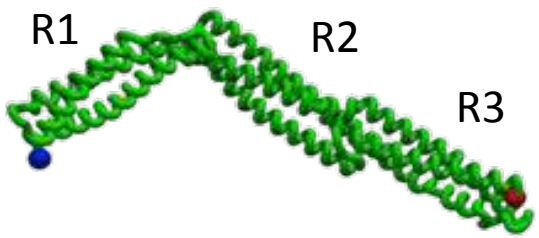
degree of insertion
into the lipid membrane?

specular neutron reflectivity (SNR)

Sophie Combet - LLB







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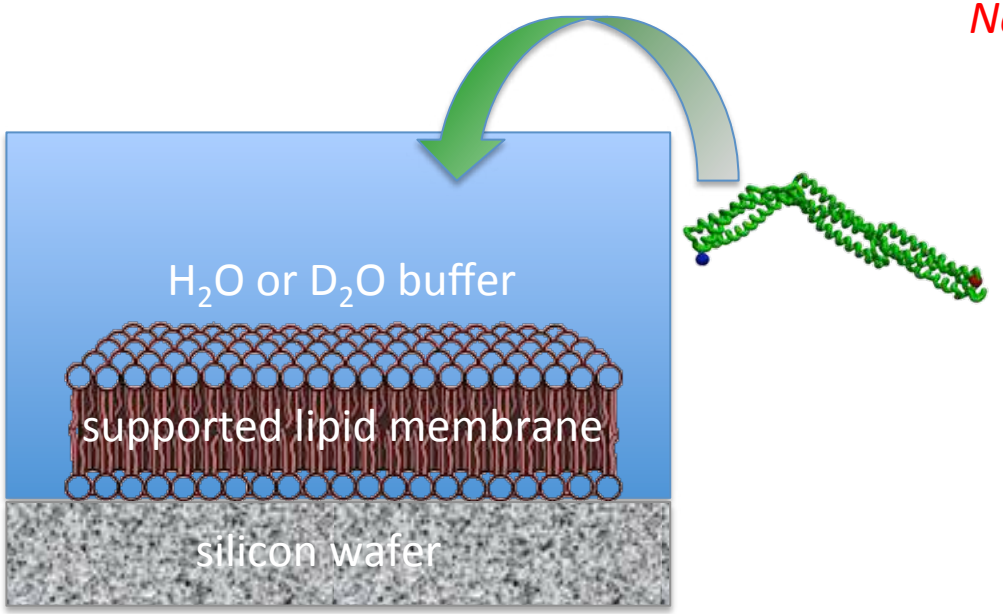
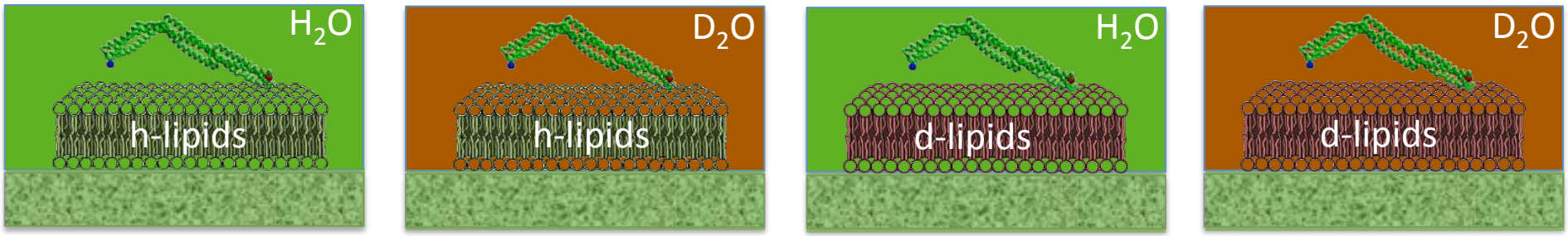
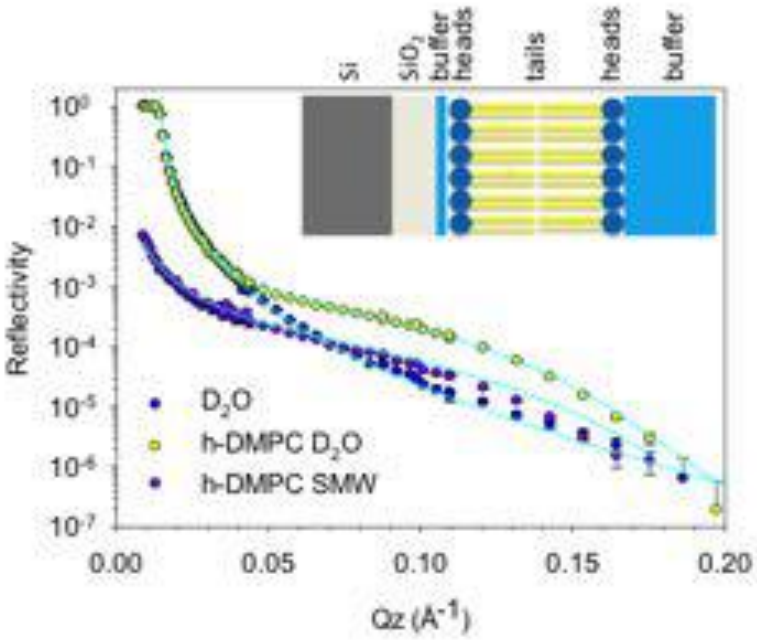
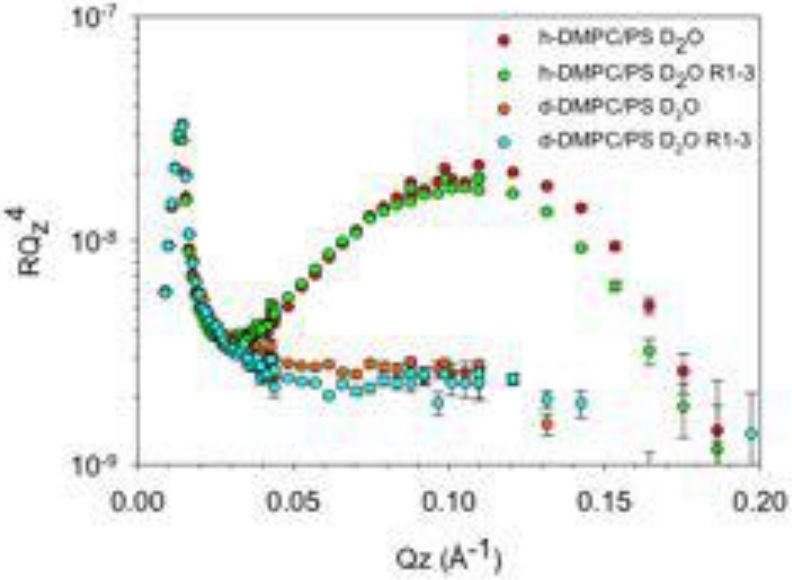


- MARIA reflectometer (MLZ, Germany): supported lipid bilayers on silicon wafers
- 4 different contrasts: h-lipids (H_2O), h-lipids (D_2O), **d-lipids** (H_2O), **d-lipids** (D_2O)

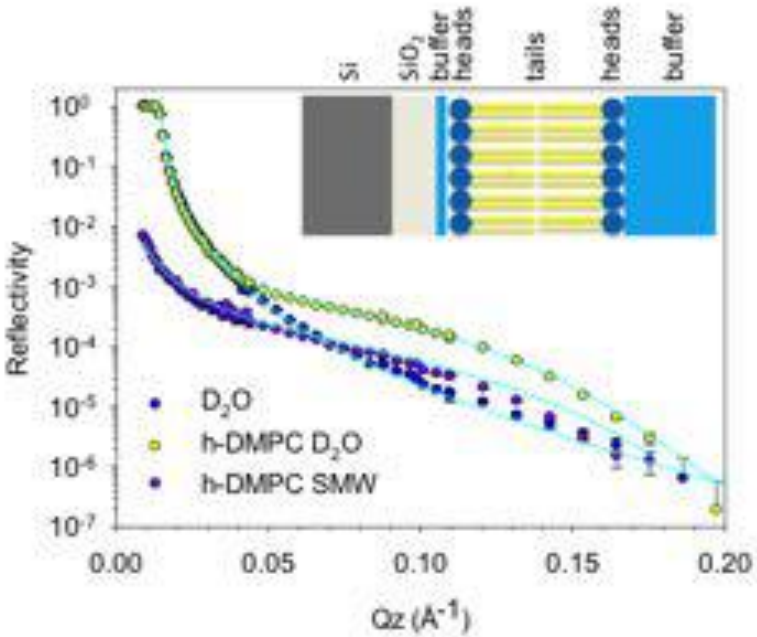


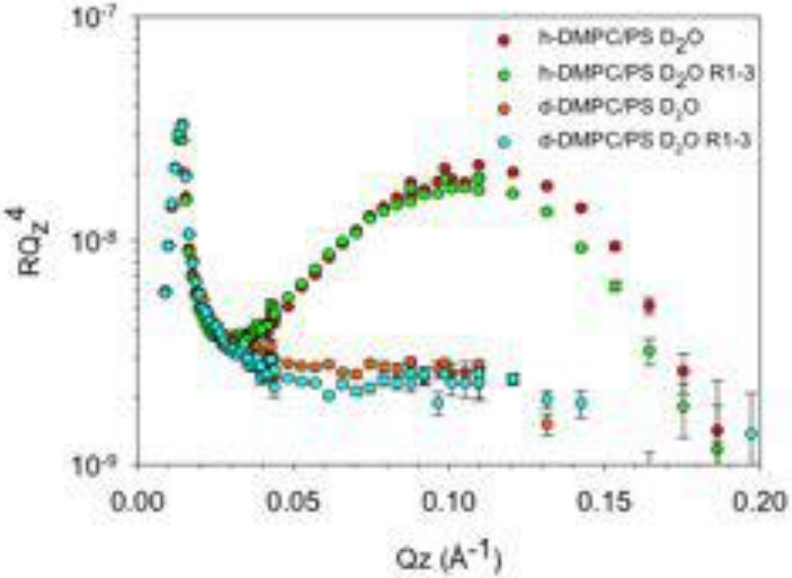




- Supported lipid bilayers with the expected dimensions (≈ 40 Å thickness)

- Preliminary results show that **the protein adsorbs at the surface of the lipid bilayer** (or into the hydrophilic heads), **without insertion into the hydrophobic part of the membrane**





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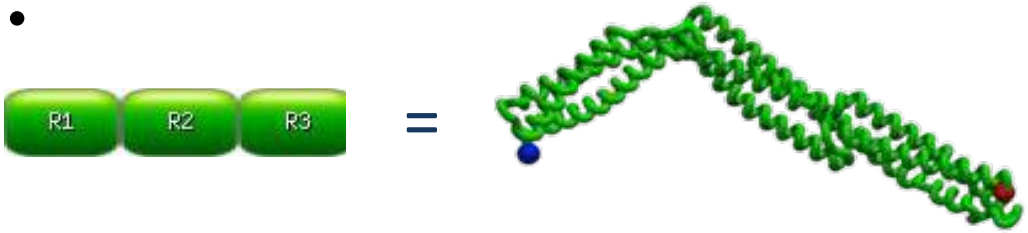
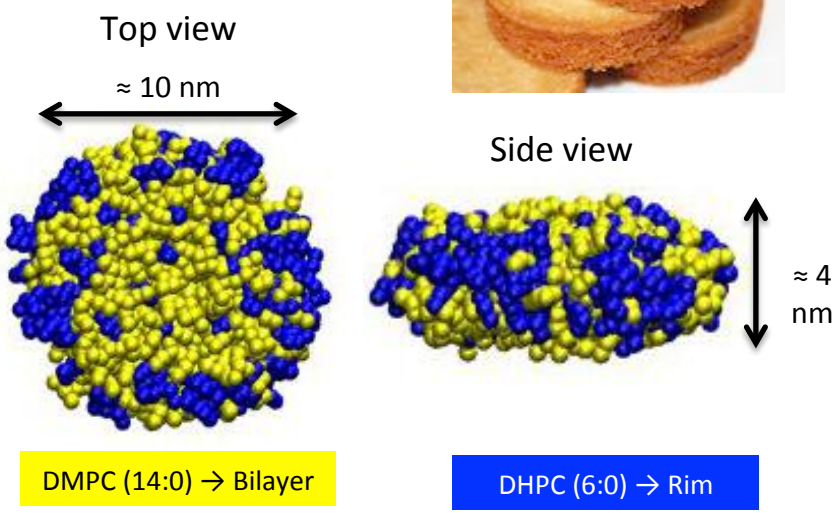
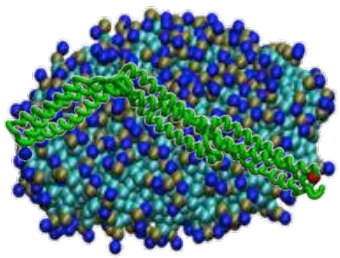


R1-3 dystrophin fragment
lipid binding protein



- Bio-mimetic objects: **bicelles** = disk-shaped objects made of long- (DMPC/DMPS) and short- (DHPC) chain of phospholipids

- "**Ghost**" (contrast-matched) deuterated **bicelles** (in 100% D_2O buffer) by SANS



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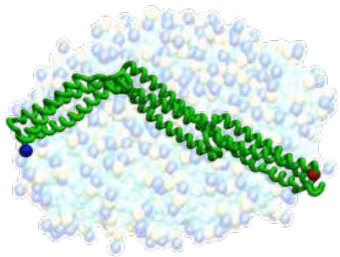

R1-3/bicelle complex

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Dos Santos Morais R *et* al., Langmuir 33: 6572-6580, 2017