Structural characterization of self-assembled inspired myelin sheath complexes: biophysical perspective on adrenoleukodystrophy

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Introduction and Motivation

Neuronal axons are enwrapped in myelin sheaths. The myelin sheaths act as an electrical insulator, forming a capacitor surrounding the axons.

We wish to correlate change in **lamellar spacing and phase transition as a result of alterations in the lipid`s hydrocarbon chain lengths** as reported for adrenoleukodystrophy [1].
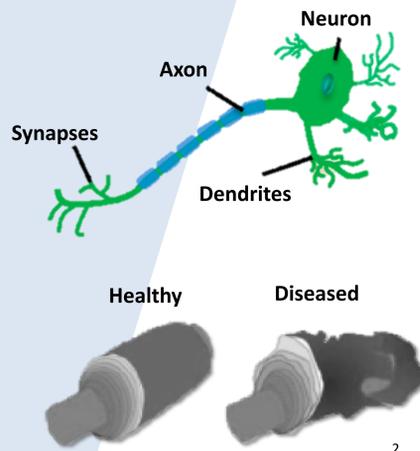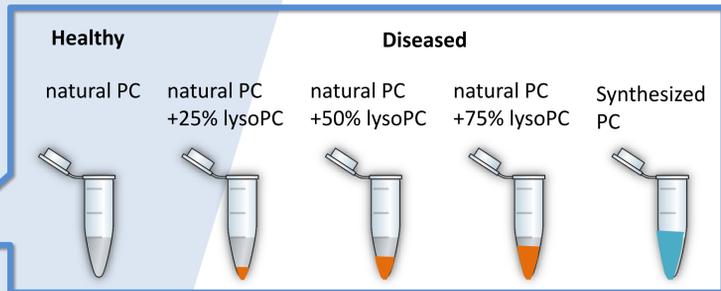
[1] Wilson R & Sargent J (1993) Lipid and fatty acid composition of brain tissue from adrenoleukodystrophy patients. *J. Neurochem* **61**, 290–297
[2] Shaharabani R, Ram-On M, Avinery R, Aharoni R, Arnon R, Talmon Y & Beck R (2016) Structural Transition in Myelin Membrane as Initiator of Multiple Sclerosis. J. Am. Chem. Soc.
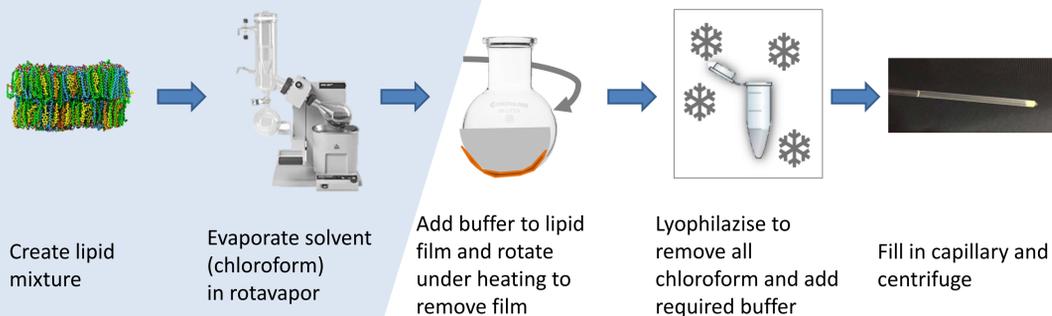
Model System & methods

- Samples prepared with native composition and alterations in lipid's chain length
- Change in chain length of Phosphatidylcholine (PC) distribution by replacing parts of natural PC with a very long chain fatty acid (VLCFA): 24:0 lysoPC (24 hydrocarbons) or synthesized PC (14:0, 18:0, 18:1, 22:6)

Lipid	Mol%
PS	7.0
SM	6.2
PE	29.0
PC	**25.9**
Chol	31.6

Healthy: natural PC

Diseased: natural PC +25% lysoPC, natural PC +50% lysoPC, natural PC +75% lysoPC, Synthesized PC

Sample preparation

Create lipid mixture → Evaporate solvent (chloroform) in rotavapor → Add buffer to lipid film and rotate under heating to remove film → Lyophilaze to remove all chloroform and add required buffer → Fill in capillary and centrifuge
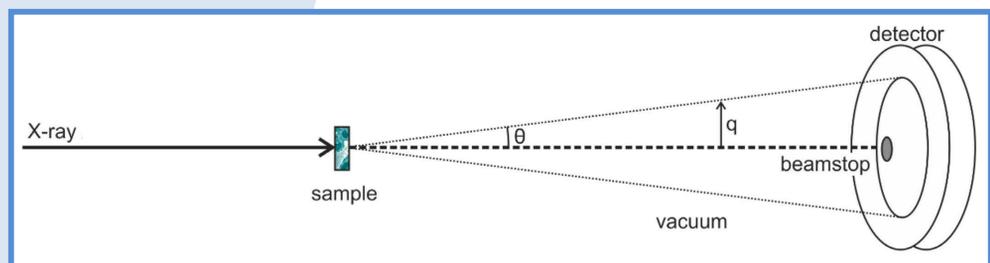
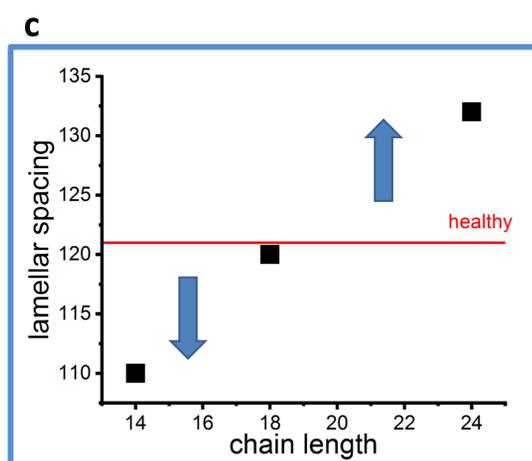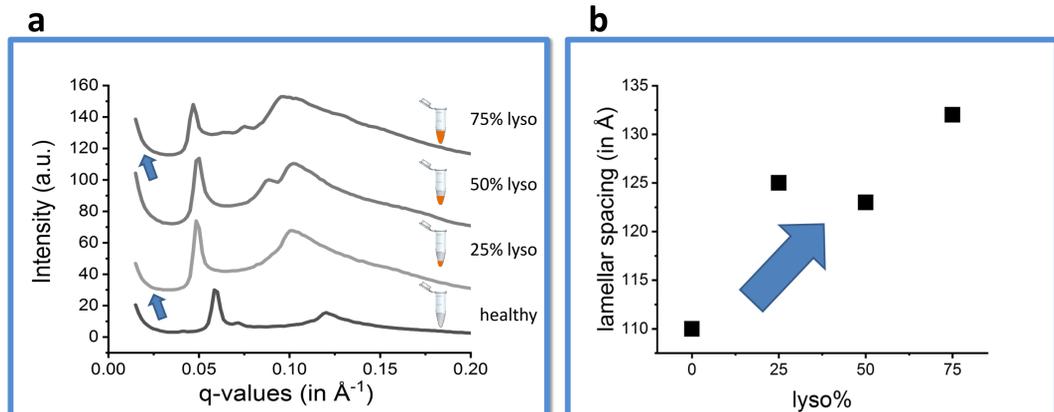## Small and wide angle x-ray scattering

Bilayer repeat distance d appears in SAXS profile as a distinct peak $d = 2\pi/q$

X-ray Scattering

a — 75% lyso, 50% lyso, 25% lyso, healthy

b

c — healthy

a. X-ray scattering data lysoPC 25, 50 and 75 (mol%) compared with healthy myelin
b. Lamellar spacing as a function of lysoPC mol%. Increasing the percentage of VLCFA increases the spacing
c. Lamellar spacing as a function of chain length of synthesized PC. Increasing chain length of PC increases the spacing.

d

Temperature	20	30	40	50	60	70
Healthy	lamellar	lamellar	lamellar	lamellar	lamellar	hexagonal
14:0 PC	lamellar	lamellar	hexagonal	hexagonal	hexagonal	hexagonal
18:0 PC	lamellar	lamellar	hexagonal	hexagonal	hexagonal	hexagonal
18:1 PC	undefined	undefined	hexagonal	hexagonal	hexagonal	hexagonal
22:6 PC	undefined	undefined	undefined	undefined	undefined	hexagonal
18:0 SM	lamellar	lamellar	lamellar	lamellar	lamellar	hexagonal
24:0 SM	lamellar	lamellar	lamellar	hexagonal	hex.+cubic	hex.+cubic
24:1 SM	lamellar	lamellar	lamellar	hexagonal	hex.+cubic	hex.+cubic

d. Different effects of Temperature for phase transitions for the different compositions

Further Investigations

? Validation of current results at synchroton

? Establish myelin model with synthesized lipids

Synchrotron measurements done at

ESRF — The European Synchrotron
PAUL SCHERRER INSTITUT — PSI
SOLEIL SYNCHROTRON

Tel Aviv University