# Experimental report

15/02/2021

**Proposal:** 8-03-912 **Council:** 4/2017

**Title:** Structural conformation of ApoE3 and ApoE4 in reconstituted HDL particles mapped by SANS and contrast variation

**Research area:** Biology

**This proposal is a new proposal**


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**Samples:**
ApoE3-PC reconstituted HDL
ApoE3 - PC+10%Chol+10% Trigl reconstituted HDL
ApoE4-PC reconstituted HDL
ApoE4 - PC+10%Chol+10% Trigl reconstituted HDL
ApoE3 - PC+10%Chol reconstituted HDL
ApoE4 - PC+10%Chol reconstituted HDL
ApoE4 - PC+20%Chol reconstituted HDL
ApoE3 - PC+20%Chol reconstituted HDL

| Instrument | Requested days | Allocated days | From | To |
|---|---|---|---|---|
| D11 | 2 | 2 | 21/03/2018 | 23/03/2018 |


**Abstract:**

In atherosclerosis lipids and fibrous elements accumulate in the blood vessels forming plaque that leads to the hardening of arteries and eventually to heart disease and stroke. This is the leading cause of death in the west and mortality rates double that of cancer. Different lipoprotein particles have been shown to play a role in the development and the progression of atherosclerosis and are currently used as biological markers, in addition to measurements of total lipid and cholesterol in the serum. Yet many people still develop the disease even when their blood lipid values fall within the healthy range. Better standards and methods for diagnostics of atherosclerosis are necessary for its prevention while a more comprehensive understanding of the mechanism of action behind the lipoprotein particles is crucial for the development of targeted therapies in the fight against cardiovascular disease. In this project, we are under way to understanding the lipid exchange dynamics and structure relationship for different lipoproteins to better understand initial plaque build-up at the onset of atherosclerosis

Experimental Report for experiment: **8-03-912**

Structural conformation of ApoE3 and ApoE4 in reconstituted HDL particles mapped by SANS and contrast variation

The aim of the experiment was to determine the structural conformation of ApoE3 and ApoE4 proteins in reconstituted HDL particles, using contrast variation.

During our beam time we measured ApoE3 and ApoE4 proteins alone to determine their structural conformations in 2 contrasts and SAXS with the allocated PSB BM29 time. This gave very interesting information about the aggregation states of the proteins and how they differ. ApoE3 was found to form random fractal aggregates, whereas ApoE4 was found to form more rigid rod-like shaped aggregates. Further in depth analysis is required for these datasets.

We also measured the rHDL in 3 contrasts each to determine their overall structure (Figure 1). This gave information about their size and allowed us to determine the composition of the discs in terms of number of proteins and lipids present, see table 1.

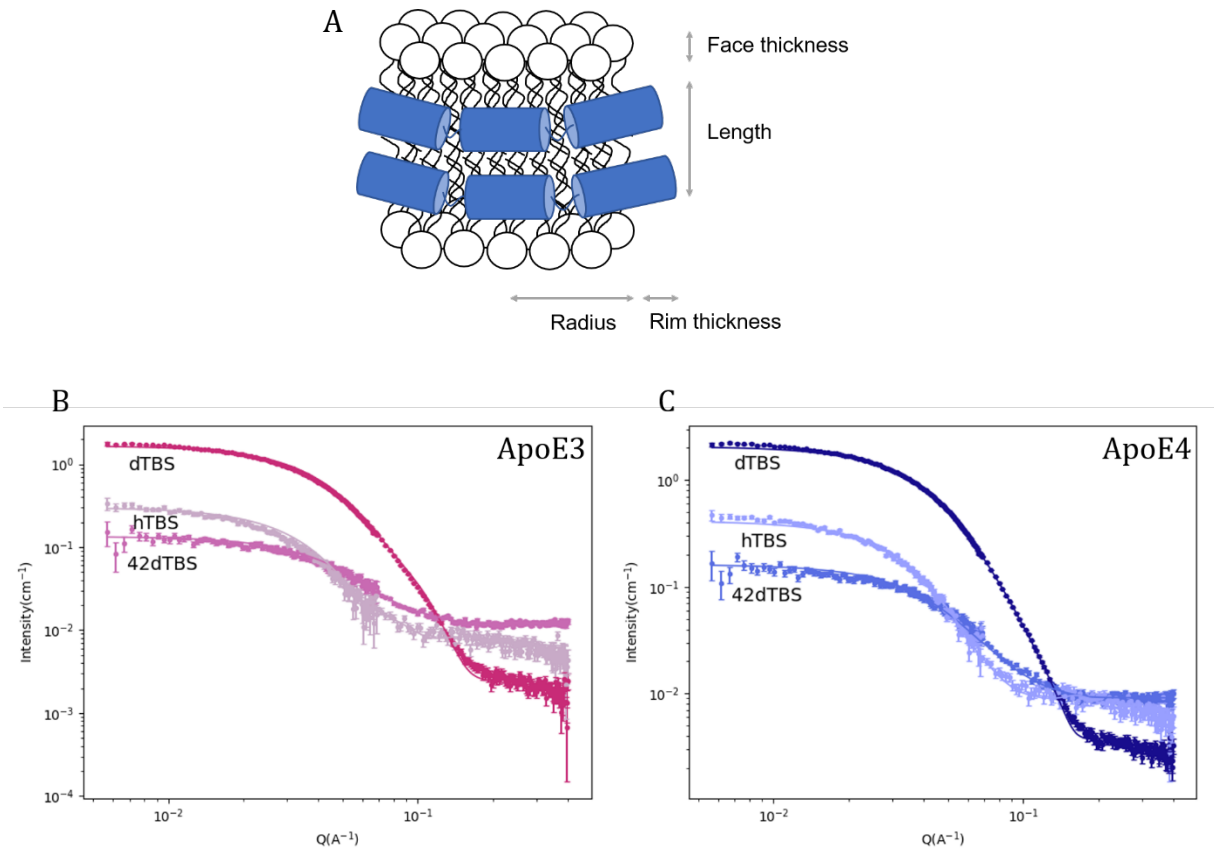


*Figure 1. Model used to fit SANS data (A) and SANS data in 3 contrasts for ApoE3- (B) and ApoE4-rHDL (C).*

*Table 1. Fitted and calculated parameters for the protein-DMPC particles.*

| Parameters | ApoE3 | ApoE4 |
|---|---|---|
| Radius* Å | 42.0 ± 0.4 | 38.1 ± 0.2 |
| Ellipticity ratio* | 1.4 | 1.7 |
| Protein rim thickness* Å | 11.0 ± 0.8 | 8.6 ± 0.3 |
| Lipid headgroup thickness* Å | 9.0 ± 0.1 | 9.0 ± 0.1 |
| Lipid core thickness*** Å | 28 | 28 |
| Short-long axis disc diameter** Å | 106-139.6 | 93.4-146.7 |
| Disc circumference** Å | 389 | 386 |
| No. amino acids** | 260 | 258 |
| Area per Lipid** $Å^2$ | 55.9 | 55.9 |
| No. lipids per leaflet** | 139 | 139 |
| No. proteins per disc** | 2 | 2 |

*Fitted values. ** Calculated values. *** Fixed value.

The data here has been submitted for publication.