Experimental report

27/05/2020

Proposal: 9-10-1572 **Council:** 10/2018

Title: Understanding the role of the morphology of nanogels and nature of interaction with Blood–Brain Barrier (BBB)

Research area: Chemistry

This proposal is a new proposal

Main proposer: **Ali ZARBAKHSH**

Experimental team: Ali ZARBAKHSH
Federico TRALDI

Local contacts: Armando MAESTRO

Samples: NIPAM
NPAM

Instrument	Requested days	Allocated days	From	To
FIGARO	2	2	06/07/2019	08/07/2019

Abstract:

The main aim of this proposal is to investigate the intermolecular interaction between nanogels and lipids on a molecular length scale. The objectives are to examine how the related interfacial structure varies with different nanogels structure as a function of concentration and to understand the nature of their interaction morphology. This contributes to in-depth understanding of diffusion mechanisms of drug delivery across the biological barriers.

1 PRINCIPAL INVESTIGATOR

Name and institution of the Principal Investigator

Dr A Zarbakhsh
Department of Chemistry
Queen Mary University of London
UNITED KINGDOM

2 EXPERIMENT DETAILS

Experiment: 9-10-1572

Title: Understanding the role of the morphology of nanogels and nature of interaction with Blood Brain Barrier (BBB)

Instrument: FIGARO

Dates scheduled: 6th July 2019 to 8th July 2019	No. Days allocated: 3

Date of experimental report: 26 May 2020

3 EXPERIMENT OBJECTIVES

There are multiple mechanisms that allow permeation of the blood brain barrier (BBB), including diffusion or tagging with peptides or molecules, such as transferrin, which use already existing receptors. The development of any system for the delivery of therapeutics to the central nervous system requires an in-depth understanding of the nature of interaction mechanisms of these at the BBB interface. Understanding how to overcome this biological barrier is an important area of science.

Our group has a track recording in the research of nanogels, which are commonly defined as organic spherical cross-linked polymers with a 3D internal network structure. They are prepared by high dilution radical polymerization using a combination of functional monomers and cross-linkers in varying proportions. Important characteristics of these type of materials include high surface to volume ratio, low viscosity and polydispersity and tunable chemical structure, obtained by changing the cross-linker and chemical structure of the monomer. This makes these materials very attractive candidates for drug delivery vehicles.

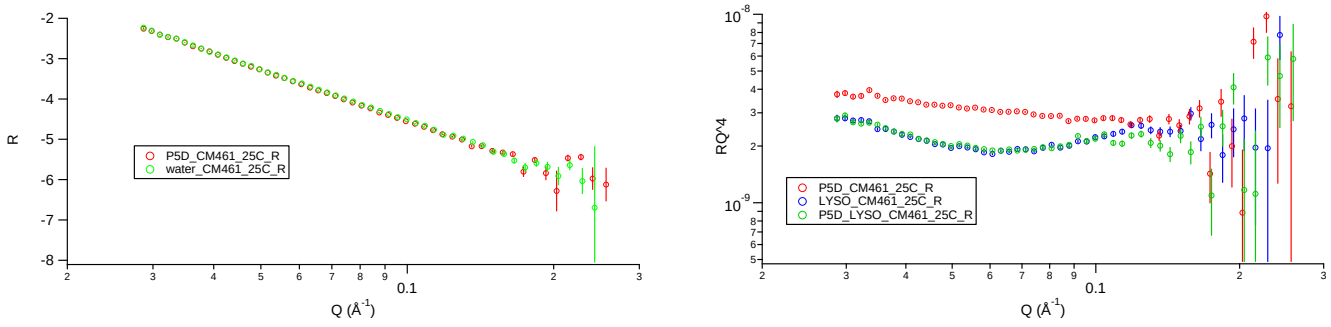
The BBB morphology is very complex. Therefore, we firstly simplify the system by studying the interaction of nanogels with proteins. The level of complexity then will increase in future experiments one step at the time. The main aim of this proposal is to investigate the intermolecular interaction between nanogels and proteins on a molecular length scale. The principle objectives here are to use to measure the structural changes and composition of protein-nanogel complexes at the air-water interface on an Ångström-nanometre scale and to examine how the related interfacial structure varies with different nanogels structure.

4 EXPERIMENT REPORT

Due to the commissioning of the new 8-adsorption-trough for our experiments, the first angle of the NR data was wrong. Here we present some preliminary data only at the second angle.

We have investigated the interaction of lysozyme with both non-surface active nanogel (80%AAm-20%MBA) and charged nanogel (60%NIPAM-20%AMPS-20%MBA) at the air/water interface at 25°C. Detailed data analysis is still ongoing. Exemplary NR profiles of 80%AAm-20%MBA nanogel and solvent (water, SLD=4.61 $\times 10^{-6}$ $Å^{-2}$) are presented (Fig 1a) The data are overlapping with each other, suggesting that this AAm based nanogel is not surface active at all. In Fig 1b, however, the NR profile of the lysozyme-nanogel mixture is overlapping the lysozyme solution on its own, which indicates that there was not interaction of this non-surface active nanogel with

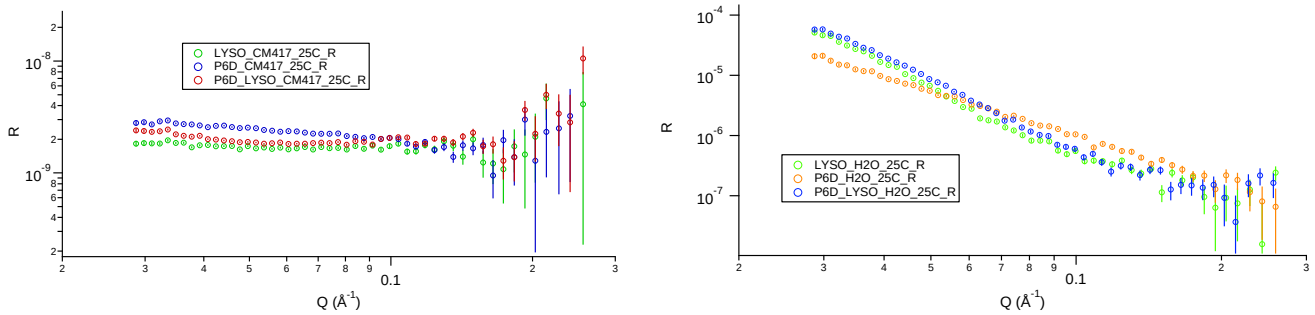
the protein in water.



(a) (b)

Fig. 1. NR profiles for 80%AAm-20%MBA nanogels (a) on its own and (b) with lysozyme at the air/water interface at 25°C. The subphase was contrast matched to SLD=4.61 ×10 $^{-6}$ Å^{-2}. The concentration of nanogel and lysozyme are 0.1 and 4 mg ml^{-1}, respectively.

We have also explored the AMPS charged nanogels with lysozyme in both H_2O and contrast matched to DLS=4.17×10 $^{-6}$ Å^{-2} water and the exemplary NR profiles are shown in Fig 2. It can be seen clearly that the charged nanogels had different surface activities compared to lysozyme on its own. More importantly, the NR profiles of the mixture located in between the nanogel and lysozyme on their owns. This confirms the complexation of this charged nanogels with lysozyme. Therefore, electrostatic interaction may play an important role in the nanogel-protein complexation.



(a) (b)

Fig. 2. NR profiles for 60%NIPAM-20%AMPS-20%MBA nanogels with lysozyme at the air/water interface at 25°C. The subphases were (a) contrast matched to SLD=4.61 ×10 $^{-6}$ Å^{-2} and (b) H_2O.The concentration of nanogel and lysozyme are 0.1 and 4 mg ml^{-1}, respectively.

5 LIKELY OUTCOMEs FROM EXPERIMENT *Please indicate what the experiment is likely to lead to by putting an 'x' next to one or more of the possible outcomes below.*	
Likely outcome	
Journal publication	*x*
Data for thesis	*x*
Follow-up experiment at ILL	-
Follow-up experiment at another facility	*x*
Other	*x*
No outcome anticipated	-

6 SUGGESTIONS FOR IMPROVEMENTS TO YOUR EXPERIMENT, EQUIPMENT OR THE FACILITY
NA