LMGP
Laboratoire des matériaux et du génie physique
une vision des matériaux

2015-2016

Internship proposal (Master 2 or final internship) at the LMGP

Probing Protein Stability at Interfaces

Context

One of the prime objectives in the development of protein therapeutics, like monoclonal antibodies, is to ensure their stability. During the expression, purification, storage and administration, therapeutic proteins are exposed to varying material surfaces and interfaces, all of which can potentially lead to protein adsorption and sometimes entail aggregation. Several studies point out that interfaces between air and liquid or air-liquid and material surface are involved in protein aggregation: Rudiuk et al.[1] have demonstrated that antibody (polyclonal and monoclonal) aggregation occurs at the air-liquid interface and that mechanical stress releases aggregates in solution. Our team has recently demonstrated, using a wetting-dewetting experiment in a microchannel, that insulin aggregates form at the border of droplets remaining on the surface during dry phases, where the triple air-liquid-solid interface is not stable in time[2].

Using our experience in biophysical measurements at the triple interface, we propose to study the aggregation of monoclonal antibodies in a combined approach using surface plasmon resonance imaging (SPRi) and Sarfus imaging[3] coupled to fluorescence microscopy.

Project

Adsorption and aggregation kinetics of different antibody preparations will be studied at different air-liquid-solid interfaces.

Using SPRi, antibody adsorption and desorption kinetics on material surfaces will be studied in liquid conditions. The effect of antibody concentration, temperature and different material surface hydrophobicities will be investigated.

Sarfus and fluorescence microscopy allow studying antibody adsorption at the triple air-liquid-solid interface and on the dried surface. "Surf" surfaces[4], which consist of engineered glass surfaces that allow to precisely control the reflection properties and therefore optimize interference microscopy, are used to image adsorbed antibodies and antibody aggregates on material surfaces, both in wet and dry conditions. Different surface chemistries and the addition of surfactants can be studied. Using fluorescently labeled probes (anti-IgG markers), visualization of antibody aggregates on material surfaces after drying will be achieved.

The combination of the proposed techniques will provide a comprehensive view on how antibodies adsorb and possibly aggregate at different air-liquid-solid interfaces. The expected results will strengthen our knowledge on protein behavior at interfaces. Controlling this behavior governs protein stability, which is crucial in the elaboration and delivery practices of therapeutic preparations.

Competences

The student should have an educational background in physics or physical instrumentation and some basic knowledge in biomolecules. Good oral and written English is an asset.

Time and place

Feb-July 2016 at the LMGP in Grenoble, France. Web site of the lab: http://www.lmgp.grenoble-inp.fr/

PhD possible : Yes, provided that funding can be recruited

Internship stipend : 554€ per month

Contact

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References

[1] Rudiuk S, Cohen-Tannoudji L, Huille S and Tribet C. Importance of the dynamics of adsorption and of a transient interfacial stress on the formation of aggregates of IgG antibodies. 2012, Soft Matter **8**, 2651

[2] Frachon T, Weidenhaupt M, LeMasne Q and Bruckert F. Fast insulin amyloid aggregation at the air-liquid-solid triple interface. 2015, Poster communication at Colloque Adebiotech Stabilité et formulation des protéines et des peptides, Romainville Sept 23-24. Manuscript in preparation

[3] for a quick overview: https://en.wikipedia.org/wiki/Sarfus; see also:

Souplet V, Desmet R and Melnyk O. Imaging of protein layers with an optical microscope for the characterization of peptide microarrays. 2007, J Peptide Science **13**, 451

Pauliac-Vaujour E, Stannard A, Martin CP, Blunt MO, Notingher I and Moriaty PJ. Fingering Instabilities in Dewetting Nanofluids. 2008, Phys Rev Letters **100**, 176102

[4] http://www.nano-lane.com/products/seec-sensors/transparent-seec-sensors-for-inverted-optical-stations/t-sio2-surfs