2023-2024 Internship proposal at LMGP Lab.

Investigating antibody-surfactant competition on medical surfaces using FTIR

Abstract

Numerous therapeutics are based on proteins (hormones, antibodies, growth factors) because their exquisite molecular specificity allows targeted treatments without major side effects. Insulin and monoclonal antibodies (mAbs) are among the most produced therapeutic proteins.

Therapeutic antibody solutions are administered through injection during which the therapeutic solution is in contact with different plastic materials constituting the administration device (e.g intravenous bags).

The amphiphilic nature of proteins makes them particularly prone to material surface adsorption, which can lead to protein loss in solution but also induce protein aggregation. In order to minimize protein adsorption, surfactants are commonly added to therapeutic protein formulations because they can efficiently compete for adsorption on material surfaces and hence limit mAb adsorption (Fig.1).

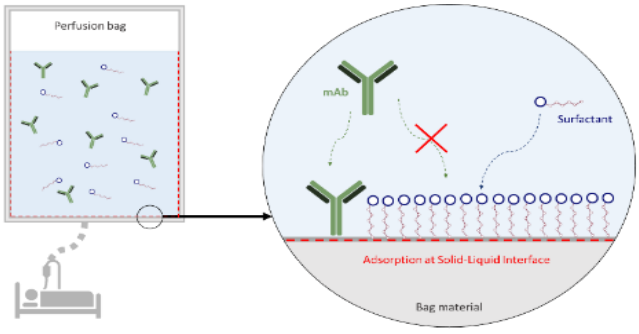

Fig.1 Competition between mAbs (green) and surfactants (blue on hydrophobic material surfaces (red)

We have developed different biochemical and biophysical protocols to quantify mAb and surfactant adsorption on model surfaces (Lefebvre et al 2021) and also on real medical device materials. Beyond quantitative results, a general understanding of how mAb and surfactants are organized on a given surface is still lacking.

Project description

In this project, we would like to simultaneously analyse the concentration and possibly orientation of mAbs and surfactants on material surfaces using Attenuated Total-Reflection Fourier Transform InfraRed (ATR-FTIR) spectroscopy (Fig.2), taking advantage of the specific peaks of these molecules in the "fingerprint "region. The project objectives are the following:

1- Learn the principles of infrared spectroscopy and its use to detect molecules in solution, materials and material-liquid interfaces. Get acquainted with the different tools available for FTIR and ATR-FTIR, using model molecules
2- Using ATR-FTIR, determine the amount of mAbs or surfactants adsorbed on model surfaces, when pure solutions are used.
3- Using polarized IR light, study the orientation of the molecules adsorbed on the surface
4- Using ATR-FTIR, determine the amount of mAbs and surfactants adsorbed on model surfaces, when mixtures of mAbs and surfactants are used.
5- Using ATR-FTIR,) study the displacement kinetics of mAbs by surfactants.

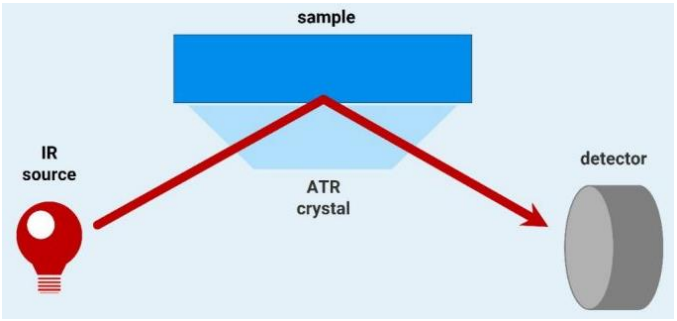

Fig.2 Principle of ATR-FTIR (from Bruker website)

Scientific environment

The candidate will work within the LMGP, Materials and Physical Engineering Laboratory, in the IMBM team in collaboration with a Sanofi PhD student (Rosa Alvarez Palencia Jimenez). Located in the heart of an exceptional scientific environment, the LMGP offers the applicant a rewarding place to work. LMGP Web Site: http://www.lmgp.grenoble-inp.fr/

Profile & requested skills

We look for a highly motivated student with a strong background in biophysics or physical chemistry, with clear interest with protein biochemistry. Basic practical lab skills in spectroscopy and protein biochemistry are required. The student should be able to work in a team, have excellent writing skills (reports, presentations…) and a good knowledge of spoken and written English.

Subject could be continued with a PhD thesis: POSSIBLE

Allowance: Internship allowance will be provided

Contact : To apply, please send a CV and motivation letter to Marianne Weidenhaupt , Associate Prof, team leader IMBM (marianne.weidenhaupt@grenoble-inp.fr), Franz Bruckert (franz.bruckert@grenoble-inp.fr) and to Rosa Alvarez-Palencia Jimenez, PhD student (Rosa.ALVAREZ-PALENCIA-JIMENEZ@sanofi.com).

Reference: Lefebvre et al (2021) Surfactant Protection Efficacy at Surfaces Varies with the Nature of Hydrophobic *Materials. Pharm Res 38, 2157-66.*