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Therapeutic protein aggregation at material surfaces

Context

Proteins represent an important part in the development of today's therapeutics

Proteins are inherently unstable and tend to adsorb to surfaces and air interfaces

Protein adsorption at interfaces can lead to their aggregation

Understanding protein-interface interactions is of fundamental interest in the production and delivery of effective biotherapeutics

Objectives and strategy

Pharmaceutical industry
 production and formulation

Medical device industry
Hospitals

reconstitution and administration

Patient
 therapy

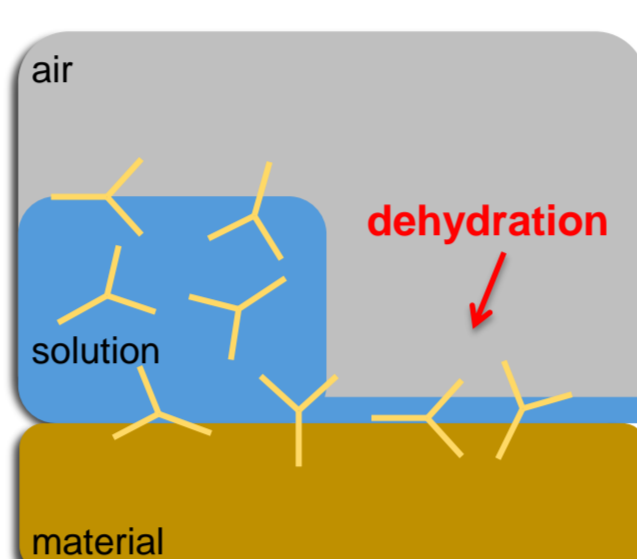
Study interfacial phenomena relevant to therapeutic protein stability

Develop industrial collaborations in the fields of production and delivery of biologics

Proteins at interfaces

Dehydration

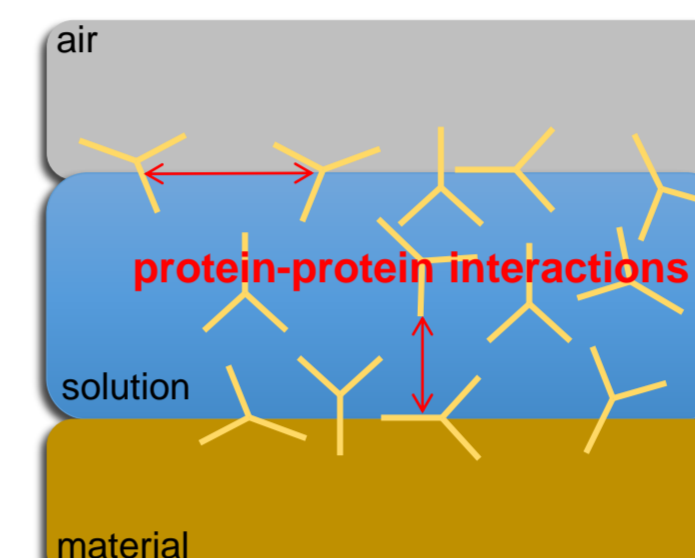
- material-adsorbed proteins can be exposed to air and become dehydrated
- repetitive dehydration during agitation or stirring destabilizes proteins



Study the effect of partial dehydration under controlled humidity
 Techniques: controlled hygrometry coupled with SPR, FTIR

Concentration

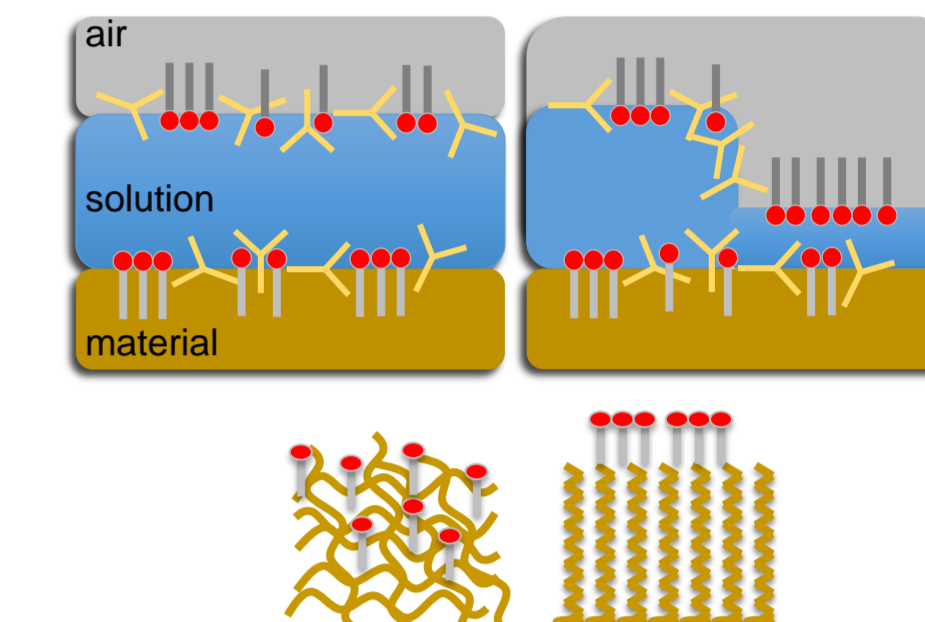
- therapeutic proteins are highly concentrated solutions
- protein-protein interactions affect interface phenomena



Investigate molecular cooperativity at interfaces
 Techniques: Labeling coupled with FRET, FRAP, TIRF

Surfactants

- surfactants are used to stabilize therapeutic proteins at interfaces
- this is attributed to kinetic competition at interfaces



Study surfactant stabilisation on different materials and their role during dehydration and at high protein concentration

Industrial collaborations

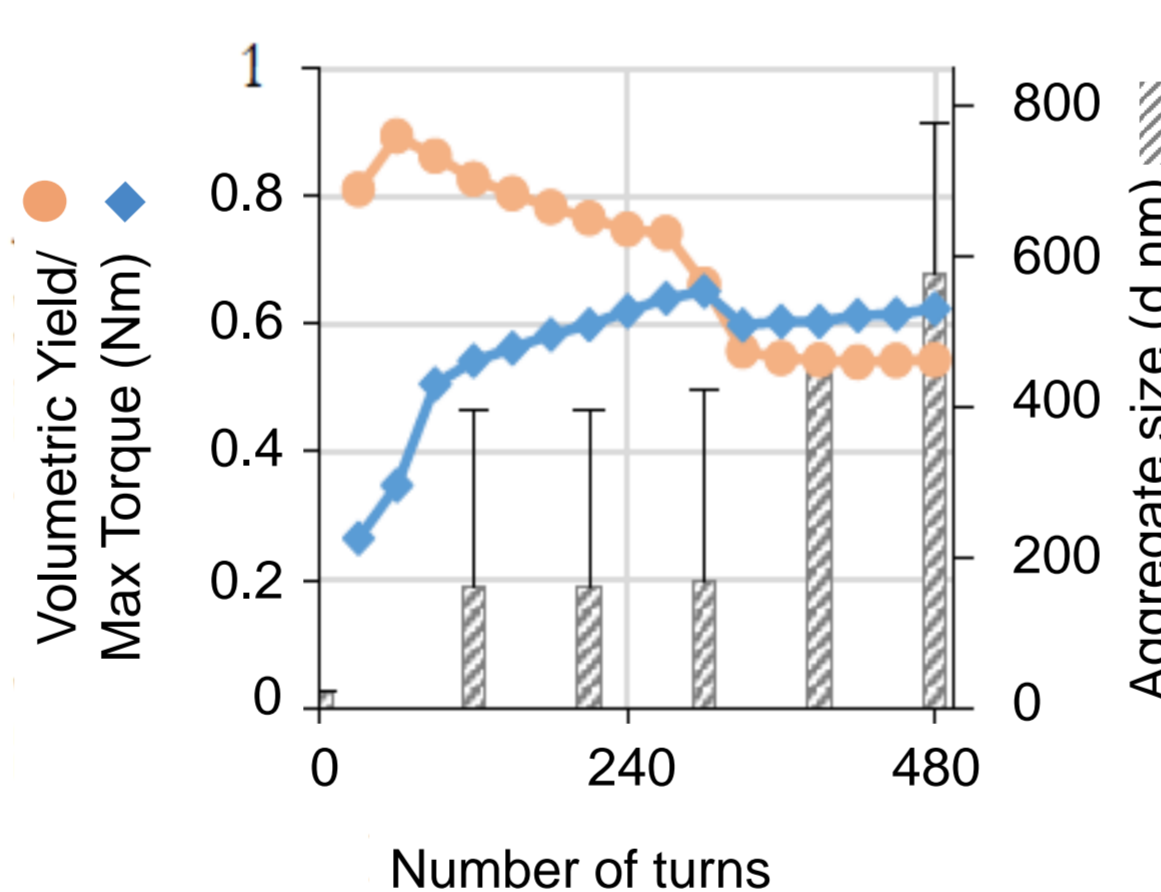


LabCom LMGP-Eveon

Optimize components and reconstitution protocols for therapeutic protein stability



Protein stability and related pump parameters



References:
 Nault L et al. (2013) Acta Biomaterialia 9, 5070-5079
 Nault L et al. (2013) FEBS Letters, 587, 1281-1286
 Chouchane K et al. (2015) J Phys Chem B 119, 10543-10553

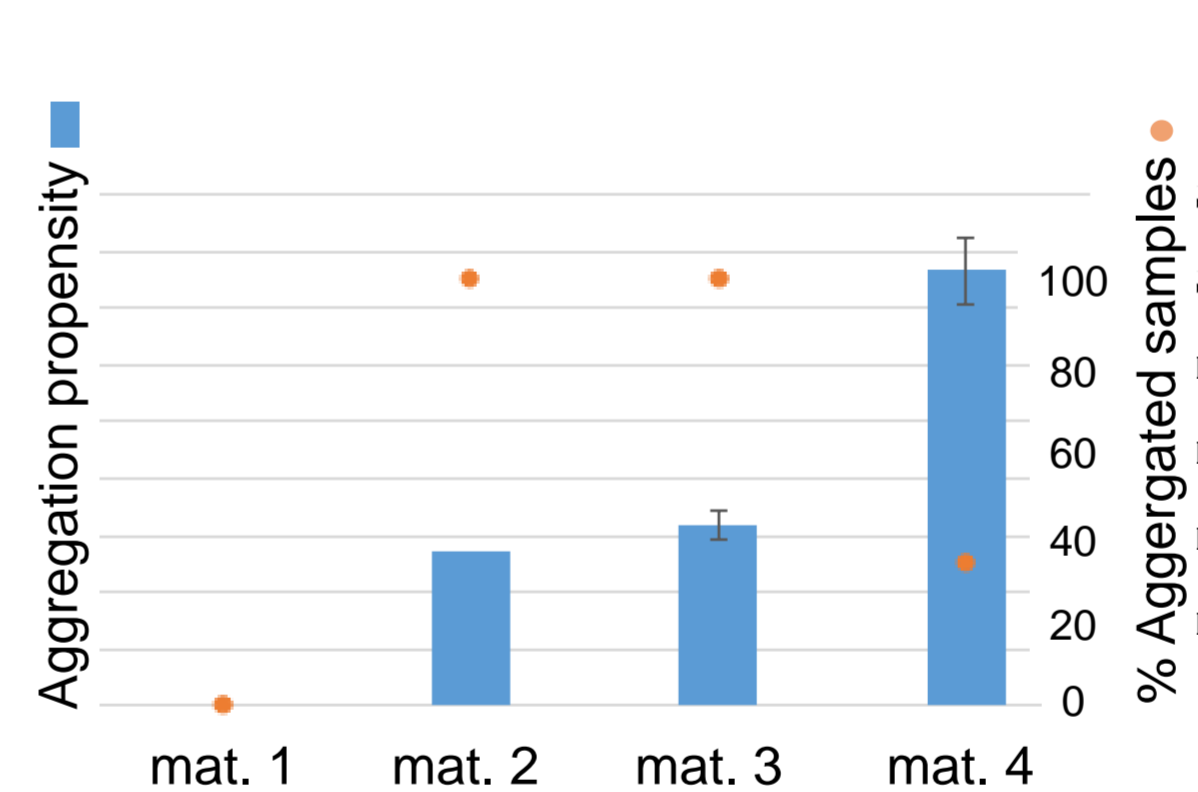


Cifre PhD & Research collaboration

Interactions of therapeutics with materials for medical use



Protein stability on different materials



Frachon T et al. (2016) Langmuir 32, 13009-13019
 Chouchane K et al. (2018) J Photochem Photobiol B181, 89-97

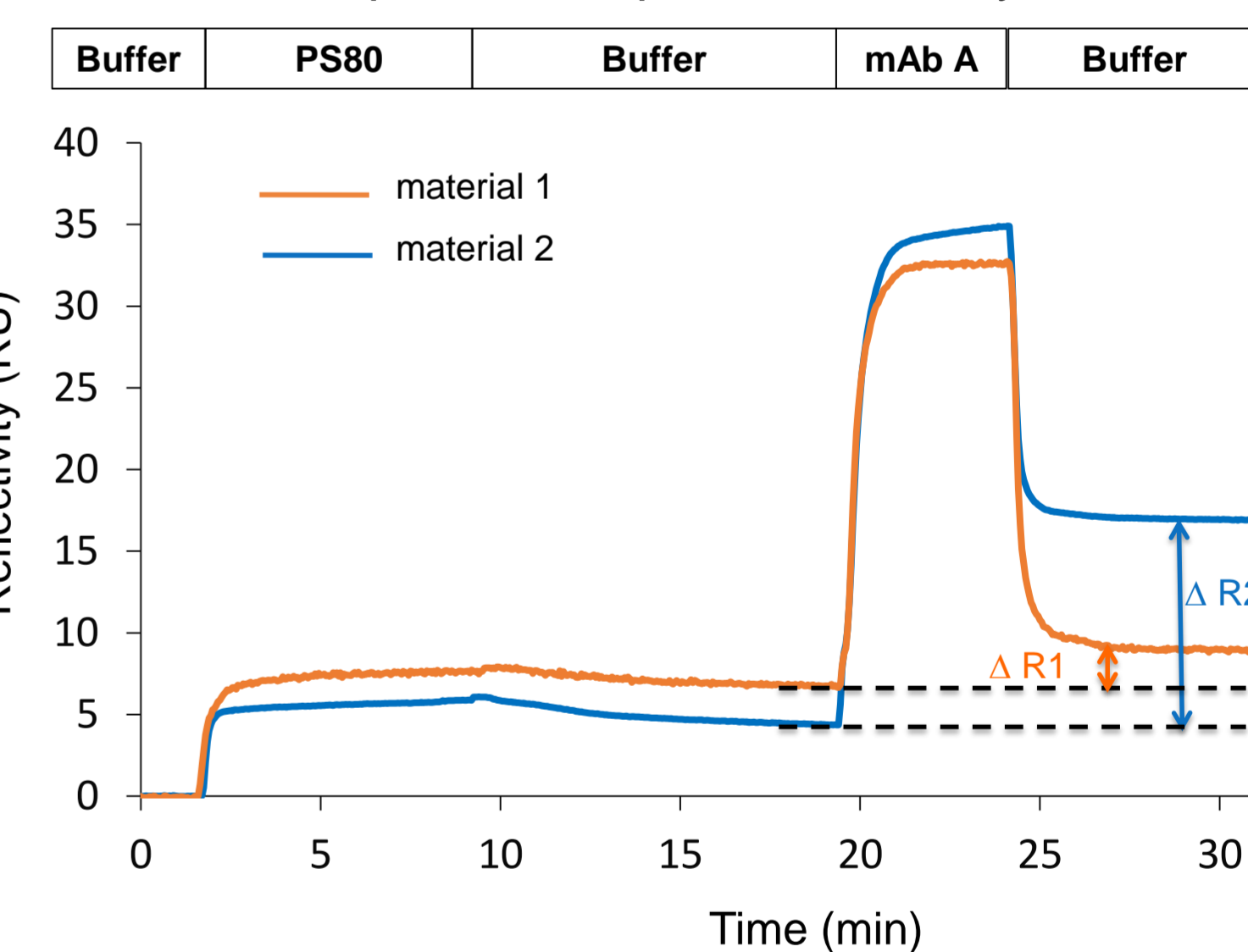


Cifre PhD

Formulation optimisation: Role of surfactants at the liquid-solid interface



Material dependency of surfactant stabilisation
 Adsorption/desorption kinetics by SPRi



Adsorption and aggregation of proteins at material surfaces

Context

Spider silks and barnacle cement are made of self-assembled proteins that stick to materials in air or water
 Adhesive proteins contain repetitive sequences that are involved in self-assembly

Objectives and strategy

Use repetitive sequences from natural adhesive proteins to study their adsorption and aggregation properties on materials

Develop a bioglue based on combinations of repetitive sequences



Natural adhesive proteins

Selection of repetitive peptide sequences from natural adhesive proteins : self-assembly and adsorption studies

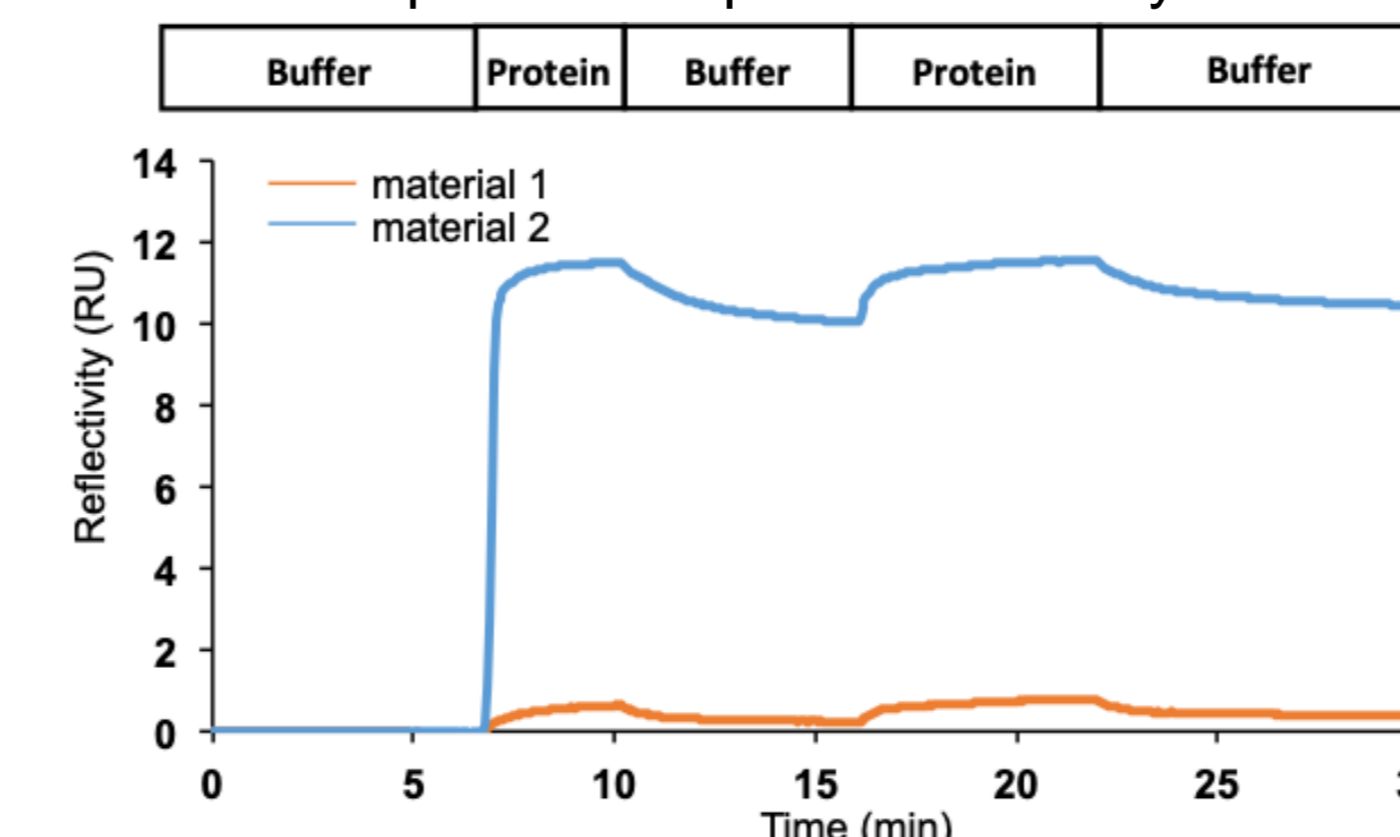
Production and purification of proteins with repeat modules

Adsorption and adhesion studies of modular proteins on different materials

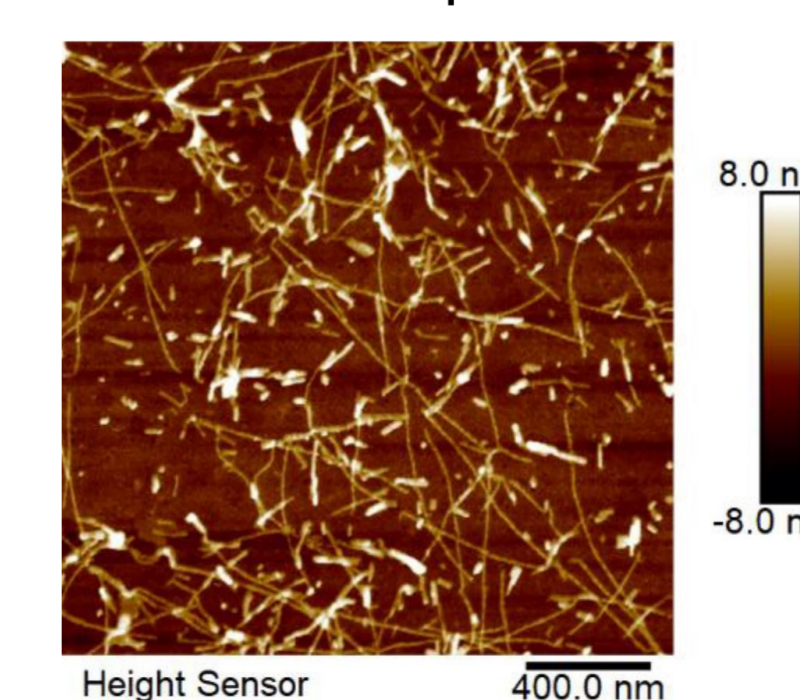
Self-assembly of repetitive peptides

pH	2.5	4.0	5.5	7.4	8.0
Peptide 1	+	+	+	+	++
Peptide 2	++	++	++	+	++
Peptide 3	-	-	+	-	++
Peptide 4	-	-	-	-	-
Peptide 5	-	-	-	-	-

Adsorption/desorption kinetics by SPRi



Self-assembly of recombinant modular protein



Collaboration

