Flow and rheology of complex fluids in microfluidic geometries: application to filling and injection processes of antibody solutions

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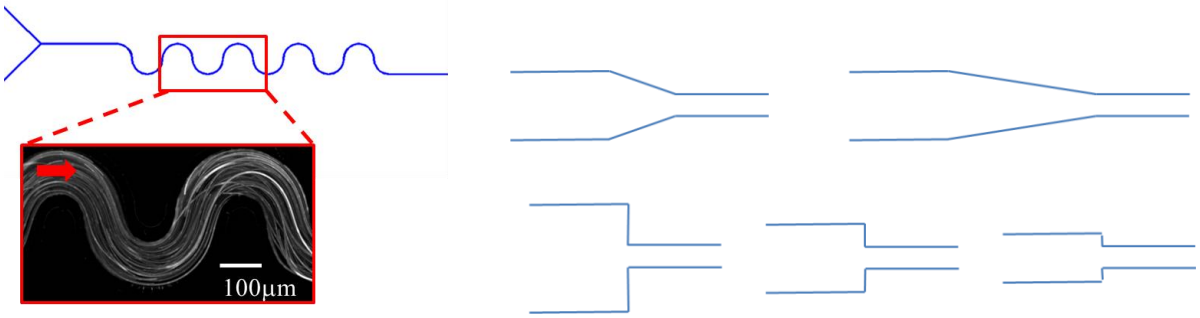
High antibody concentrations in aqueous compositions are becoming increasingly important in the pharmaceutical industry in order to deliver the required high dose in as small a volume as possible. However, higher concentrations lead to an increased viscosity, affecting both production processes (pumping, filling, and filtration) and the ability to deliver such compositions (through a syringe or auto-injector). The nature of the interactions of the monoclonal antibodies (proteins) at the origin of the observed viscosity, are not fully understood yet, making its control difficult.

Within this PhD project we plan to perform a careful characterization of the rheological behavior of solutions of representative monoclonal antibodies. These results will help to understand the microscopic mechanisms at play leading to the specific rheological response. In addition, the rheology of the solutions will be linked to their flow behavior in selected geometries. These results will help to understand the stability and injectability of these solutions in filling processes relevant for the application.



(Left) Microfluidic rheometer: serpentine channel for the measurement of viscoelastic properties [Zilz, Lab On Chip, 2013]. (Right) Microfluidic devices mimicking injection processes: (top) examples of cones of variable shapes and (bottom) abrupt restrictions. Typical channel widths vary between 20-600 microns. Typical channel heights between 20-100 microns.

We will use classical rheology in combination with new microfluidic devices to assess the properties of selected antibody solutions and chosen model fluids. Their flow will then be studied in microfluidic devices mimicking the flow geometries used in applications (continuous and abrupt restrictions, branched networks etc). Flow visualization (PIV techniques) will allow to measure the flow profiles, and to link them to the rheological properties. Pressure drop measurements will give information on the injectability of a given solution in the corresponding geometry. Protein aggregation will be assessed depending on the flow situation. Finally, optimized geometries will be suggested to improve injectability.

The PhD will be performed at the PMMH/ESPCI in close collaboration with researchers from Sanofi. No specific knowledge in pharmaceutics or antibody solutions is required, but a background in hydrodynamics, microfluidic or complex fluids is a plus.

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