**Computational Approaches for Mass**

**Spectrometry-based Characterization**

**of Antibody Repertoires**

Laymans summary

Antibodies are key proteins in our immune system, that assist in fighting pathogen and as such combat diseases. There is nowadays a strong interest on creating antibody-based drugs for use as therapeutics. To better understand the functional roles of antibodies, scientists are continuously seeking for more and new ways to study them.

To investigate and identify antibodies, it’s important to know their protein sequence: which building blocks are used, and in what order. Traditionally, scientists would look at the genetic code for the sequence analysis of antibodies. More recently, methods are developed aiming to sequence them more directly at the level of the protein. This would enable to directly analyze antibodies in our body originating from different localization and different physiological situations. Mass spectrometry is a tool that is often used to analyze proteins directly. However, in particular studying antibodies is challenging because there are trillions of distinct antibodies, all with very alike sequences.

In this thesis, I describe computational methods I developed to analyze and identify antibodies in our bodies. By tracking individual antibodies over time, we can observe how our immune system responds to vaccines or pathogens. We were able to detect and quantify the unique antibodies in human blood and milk. We found that our immune system relies on a surprisingly low number of hundreds to thousands of antibodies, despite the trillions of possibilities.

We also developed a way to directly sequence endogenous antibodies, by combining several MS approaches. This brings us closer to automatic antibody analysis, which may be useful in the longer term to find potential new therapies.

*These methods help to study our antibody responses and identify functionally relevant antibodies in serum. By sequencing these antibodies, they can potentially be developed further into biotherapeutics.*

*We show that mass spectrometry can be used to study antibody responses. By understanding how our antibodies respond to different situations, we can potentially simplify and speed up drug development and combat pathogens more effectively.*