**Computational Approaches for Mass**

**Spectrometry-based Characterization**

**of Antibody Repertoires**

Laymans summary

Antibodies are key proteins in our immune system, that help fight pathogens that cause diseases. There is nowadays a strong interest on creating antibody-based drugs for use as therapeutics. To better understand antibody functioning, scientists are continuously seeking new ways to study them.

To investigate antibodies, it’s important to know their protein sequence: which building blocks are used, and in what order. Traditionally, scientists derived antibody sequences from genetic code. More recently, methods for directly sequencing the protein are being developed, using mass spectrometry. This would enable directly analyzing antibodies in our body originating from different physiological localizations and situations. However, studying antibodies is challenging because there are trillions of distinct but highly similar antibodies.

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, several hundred, 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, may help find potential new therapies.

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.