SUMMARY

Microbiome research has become a vibrant and popular research field over the course of the last decade. Modern molecular techniques and technological innovations, such as next generation sequencing (NGS), have contributed to the emergence of this fascinating scientific field, revealing the invisible world of uncultivated bacteria, which evidently dominate our intestines. While the role of the microbiome in health and disease has been extensively explored, and its clinical potential as a non-invasive diagnostic approach well established, there are hitherto no diagnostic tools available in practice. This is because, firstly, diagnostic microbiology laboratories have yet to adapt to prepare, process and handle NGS samples in their clinical routine, and, secondly, standardization challenges and high costs have prevented NGS from being implemented in microbial diagnostic applications.

The IS-pro technique was designed specifically to meet the challenges associated with the implementation of microbiota analysis in a clinical environment, and to serve as a universal, inexpensive and swift bacterial detection technique that could be applied in any microbiology laboratory. This thesis investigates how the IS-pro technique can be used to both analyze gut microbiota data and to develop a microbiota-based diagnostic test. It comprises both descriptive studies, in which gut microbiota data was analyzed to demonstrate the effects of either diet or antibiotic treatment, and predictive studies, which aimed to diagnose inflammatory bowel disease patients based on their gut microbial signature. It includes gut microbiota analysis from in vitro studies, and clinical trials with infant and adult populations.

This thesis also has significant methodological implications for the development of a diagnostic test based on IS-pro gut microbiota data. Reproducibility between laboratories and analysis machines was investigated, and a robust predictive algorithm was established. Finally, this thesis addresses the “black-box” problem of machine learning classifiers, proposing an interpretive method that would allow clinicians to understand a microbiota-based diagnosis.