

## Analysis of clinical metabolomics data with routine analysis of patients suspected of having an inborn error of metabolism.

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**Type of thesis:** Computational

**Required competences:** Basic statistics, Basic knowledge of R and/or Matlab and Python

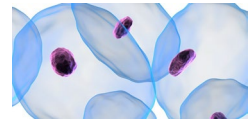
**Acquired competences:** Network analysis, Multivariate statistics, analysis of metabolomics data, phenotyping of human metabolism

**Date start of the project:** Open

### Description

With unprecedented pace, the number of known inborn errors of metabolism (IEM) is expanding. It is a challenge to diagnose this diverse spectrum of diseases in a timely manner. Thus, there is an emerging need for a comprehensive test to acquire a complete view of metabolite status of an individual. To meet this need, metabolomics—the comprehensive determination of thousands of small-molecule metabolites in a biofluid (blood, urine, cerebrospinal fluid, etc...)—is regarded as the way forward. Using metabolomics, all intermediates and final products of metabolic pathways in the body can potentially be measured.

Within the Wilhelmina Children's Hospital at UMC Utrecht, patient-derived material such as blood, urine and cerebrospinal fluid is analysed for biochemical aberrations to assess whether the patient suffers from an IEM. The metabolites measured depend on the clinical presentation and subsequent differential diagnosis of the patient. In parallel to these



routine diagnostic procedures, untargeted metabolomics using direct-infusion high-resolution mass spectrometry (DI-HRMS) is explored to assess to what extent it may improve and replace current diagnostic practice.

The scope of the thesis is to integrate results from DI-HRMS with data from routine standard diagnostic procedures obtained on blood and urine samples from patients and assess to what extent untargeted metabolomics may replace current procedures.

In this project you will deploy an array a statistical and machine learning tools in combination with the reconstruction of biological networks and analysis to highlight key components related to inborn error of metabolism.

At the end of this project the student will have gain knowledge in clinical metabolomics, mass spectroscopy, analysis of large metabolomics data sets and inborn errors of metabolism.

This thesis project is a collaboration between the Laboratory of Systems and Synthetic Biology (Dr. Cristina Furlan and Edoardo Saccenti) and the section Metabolic diagnostics at the Wilhelmina Childrens Hospital in Utrecht (Dr. Judith Jans).

## References

Direct Infusion Based Metabolomics Identifies Metabolic Disease in Patients' Dried Blood Spots and Plasma. Haijes HA, Willemsen M, Van der Ham M, Gerrits J, Pras-Raves ML, Prinsen HCMT, Van Hasselt PM, De Sain-van der Velden MGM, Verhoeven-Duif NM, Jans JJM. *Metabolites*. 2019 Jan 11;9(1):12.

Cross-Omics: Integrating Genomics with Metabolomics in Clinical Diagnostics. Kerkhofs MHPM, Haijes HA, Willemsen AM, van Gassen KLI, van der Ham M, Gerrits J, de Sain-van der Velden MGM, Prinsen HCMT, van Deutekom HWM, van Hasselt PM, Verhoeven-Duif NM, Jans JJM. *Metabolites*. 2020 May 18;10(5):206