Unraveling proteoform complexity by native liquid chromatography-mass spectrometry

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Curriculum Vitae

Guusje van Schaick was born on the 6th of February 1995 in Amsterdam, Netherlands. After obtaining her VWO diploma from the St. Nicolaas lyceum in Amsterdam in 2013, she enrolled in the bachelor's program Pharmaceutical Sciences at Vrije Universiteit Amsterdam. During her studies, she focused on topics dealing with molecular toxicology and (bio)analytical chemistry. Her thesis was conducted at the department of molecular toxicology and aimed to characterize GST-mediated inactivation of drug reactive metabolites employing different bioactivation systems. After obtaining her bachelor's degree in 2016, she started her master's studies in Analytical Chemistry at the University of Amsterdam. She specialized in separation techniques and mass spectrometry for the analysis of biological samples. Her literature thesis reviewed the current status and future prospects of metaproteomics supervised by prof. dr. Chris de Koster. She performed her internship at the division of BioAnalytical Chemistry of the Vrije Universiteit Amsterdam under the supervision of dr. Andrea Gargano. During this internship, she focused on the characterization of glycoproteins using hydrophilic interaction liquid chromatography coupled to mass spectrometry, resulting in a first-author paper. Additionally, she contributed to a project in collaboration with DSM, where an industrial lipase was structurally characterized leading to a co-author publication. Besides these two research projects, she supervised students during practical courses for the Pharmaceutical Sciences and Chemistry bachelor's programs.

After graduating in 2018, Guusje started her PhD research at the Center for Proteomics and Metabolomics (CPM) at the Leiden University Medical Center under the supervision of dr. Elena Domínguez-Vega and prof. dr. Manfred Wuhrer. She is enrolled in the SATIN consortium, which was mainly focused on the separation and analysis of therapeutic and industrial proteins. Within this consortium, the project of Guusje dealt with the development of novel analytical strategies to characterize proteins using native separation technologies, mass spectrometric detection and functional assays. During her PhD project, she performed secondments at the University of Utrecht to gain experience on native MS and bottom-up analysis strategies and at DSM to learn about different activity assays to monitor enzyme function. To further expand her knowledge on protein conformation, she performed a 4-month secondment at the Laboratoire de Spectrométrie de Masse Bio Organique in Strasbourg, France. The project focused on the coupling of native separations with ion mobility - mass spectrometry for the analysis of therapeutic monoclonal antibodies under the supervision of dr. Oscar

Hernandez Alba and prof. dr. Sarah Cianferani. To conduct this research, she received a scholarship from the Leids Universitair Fonds. Throughout her PhD project, she presented her research at various national and international conferences both as poster and oral presentations. Her research has already led to four accepted and three submitted first-author manuscripts. After completing her thesis, Guusje will continue her research as a post-doctoral researcher at the CPM.

List of publications

1. **Studying protein structure and function by native separation-mass spectrometry**
   G. van Schaick, R. Haselberg, G. W. Somsen, M. Wuhrer, E. Domínguez-Vega
   Nature Reviews Chemistry, 2022, 6, 215-231 (Chapter 2)

2. **Dopant-Enriched Nitrogen Gas to Boost Nano-Electrospray Ionization of Glycoproteins Analyzed under Native Conditions**
   G. van Schaick, M. Wuhrer, E. Domínguez-Vega.
   Submitted (Chapter 3)

3. **Anion exchange chromatography – Mass spectrometry for monitoring multiple quality attributes of erythropoietin biopharmaceuticals**
   G. van Schaick ‡, C. Gstöttner ‡, A. Büttner, D. Reusch, M. Wuhrer, E. Domínguez-Vega.
   Analytica Chimica Acta, 2021, 1143, 166-172 (Chapter 4)

   ‡Authors contributed equally to this work

4. **Online collision-induced unfolding of therapeutic monoclonal antibody glyco-variants through direct hyphenation of cation exchange chromatography with native IM-MS**
   G. van Schaick, E. Domínguez-Vega, J. Castel, M. Wuhrer, O. Hernandez-Alba, S.Cianférani.
   Submitted (Chapter 5).

5. **Native structural and functional proteoform characterization of the prolyl-alanyl-specific endoprotease EndoPro from *Aspergillus niger***
   G. van Schaick, E. Domínguez-Vega, C. Gstöttner, J. van den Berg-Verleg, O. Schouten, M. Akeroyd, M.M.A. Olsthoorn, M. Wuhrer, A.J.R. Heck, N. Abello, V. Franc.
   Journal of Proteome Research, 2021, 20, 4875-4885 (Chapter 6).

6. **Native liquid chromatography and mass spectrometry to structurally and functionally characterize endo-xylanase proteoforms**
   G. van Schaick, N. el Hajjouti, S. Nicolardi, J. den Hartog, R. Jansen, R. van der Hoeven, W. Bijleveld, N. Abello, M. Wuhrer, M.M.A. Olsthoorn, E. Domínguez-Vega.
   International Journal of Molecular Sciences, 2022, 23, 1307(Chapter 7).

7. **Evaluating the effect of glycation on lipase activity using boronate affinity chromatography and mass spectrometry**
   G. van Schaick, S. Pot, O. Schouten, J. den Hartog, M. Akeroyd, R. van der Hoeven, W. Bijleveld, N. Abello, M. Wuhrer, M.M.A. Olsthoorn, E. Domínguez-Vega.
   Submitted (Chapter 8).

8. **Profiling of a high mannose-type N-glycosylated lipase using hydrophilic interaction chromatography-mass spectrometry**
A.F.G. Gargano, O. Schouten, G. van Schaick, L. Roca, J. H. van den Berg-Verleg, R. Haselberg, M. Akeroyd, N. Abello, G.W. Somsen.
Analytica Chimica Acta, 2020, 1109, 69-77.

9. **Computer-aided gradient optimization of hydrophilic interaction liquid chromatographic separations of intact proteins and protein glycoforms**
G. van Schaick, B.W.J. Pirok, R. Haselberg, G.W. Somsen, A.F.G. Gargano
Journal of Chromatography A, 2019, 1598, 67-76.

PhD Portfolio

Courses

Disciplinary courses

- Basiscursus Regelgeving en Organisatie voor Klinisch Onderzoekers (BROK®)
- Basic Methods and Reasoning in Biostatistics
- Advanced Biomolecular Mass Spectrometry Course
- Mass Spectrometry in Biotechnology and Medicine (MSBM)

Soft skill courses

- Effective Scientific Communication (presenting and writing)
- Legal requirements, industrial application and entrepreneurship
- Job orientation for PhDs

Grants

2021	Leids Universitair Fonds (LUF) scholarship to perform a 4-month secondment at University Strasbourg.

Secondments

2018	DSM	IEX of industrial enzymes
2019	DSM	Activity measurements of ENDO-I (Chapter 6)
	University Utrecht	Characterization of EndoPro (Chapter 5)
2021	University Strasbourg	CEX-CIU platform for mAbs (Chapter 3 and 4)

Supervision of students

2020	Gaetana Angelo	University of Pavia
2021	Nadi el Hajjouti	Inholland Hogeschool Amsterdam
2021	Sacha Boon	University of Amsterdam

Teaching

2018-2021	Designed and instructed “Science4U” (Stedelijk Gymnasium Leiden, the Netherlands)
2022	Organized and instructed “Young Science 4 a day” (Stedelijk Gymnasium Leiden, The Netherlands)

Scientific contributions to conferences

Oral presentations

- Native AEX Coupled to Mass Spectrometry for the Structural and Functional Characterization of Proteins. CHAINS 2020, Online, December 2020.
- Robust Native LC−MS Platform for In-depth Proteoform Characterization. HTC-17, Ghent, May 2022.
- Online Native CEX-IM(CIU)-MS to Monitor the Conformational Landscape of Therapeutic Monoclonal Antibody Proteoforms. AT Europe 2022, Lisbon, May 2022.
- Online Native CEX-IM(CIU)-MS Approaches to Decipher the Conformational Landscape of Therapeutic Monoclonal Antibodies Charge Variants. IMSC 2022, Maastricht, August 2022.

Poster presentations

- Computer-Aided Method Optimization of the Separation Proteins and Glycoforms of Glycoproteins in HILIC. CHAINS 2018, Veldhoven, December 2018.
- Characterization of Industrial Enzymes by Native LC Coupled to MS. NVMS-BSMS conference 2019, Rolduc, March 2019.
- Characterization of Industrial Enzymes using Native separations and Mass Spectrometry. CHAINS 2019, Veldhoven, December 2019.

Acknowledgments

This is it, the end of my PhD thesis. I hope you enjoyed reading it and that you learned (a great deal) about the wonderful world of proteins. The fascinating research in this thesis would not have been possible without the motivated and amazing group of people around me and I am truly thankful for their support during the last four years.

First, I would like to thank my promotor, Manfred, for the opportunity to conduct my PhD research at the Center for Proteomics and Metabolomics (CPM). You supported me at every (small) step of the way and never let a moment pass to encourage me to further develop myself. Elena, my co-promotor, I am so grateful that you were my supervisor. You gave me the freedom to conduct my own research, challenged me to think outside of the box and provided me with confidence when I needed it.

A special thanks to my paranymphs, Christoph and Marlien. Christoph, thank you for being a great colleague and friend the past years. It is "wunderbärchen" how much fun we had in the lab and office but also outside of the department. Marlien, jij bent naast mijn paranymph ook de degene met wie ik lief en leed kon delen tijdens deze intense tijd. Jij was er in elk dal maar ook op elke piek en daar ik ben je ongelofelijk dankbaar voor. Ook ben ik trots dat wij samen al zo ver gekomen zijn en ik kan niet wachten tot ik jouw thesis in mijn handen heb!

To all CPM colleagues, thank you for helping me when things were not going smoothly and also for making my time at the CPM a lot of fun! Specifically, I want to thank the people that spend time in our (sometimes messy) office, thanks Constantin, Sanne, and Steffen. A big thanks for the (instrumental/technical) support, Agnes, Carolien, Jan and Simone. Di and Wei, it has been great to learn more about the Chinese culture (and food). Moreover, I want to thank the students I supervised for their hard work, Tania, Nadi and Sacha. Thank you, Yuri, for always being willing to read and correct my Dutch texts. The "Scientist 4 a day" team (Bart, Suzanne, Rick, and Rosalie), thanks for your enthusiasm and innovative thinking, we turned it into a great success (even though covid did not make our lives easy).

The research in this thesis would not have existed without the great collaborations within the SATIN consortium. First of all, I would like to thank DSM for supplying industrial enzymes that kept surprising me but also for the fruitful discussions and support to solve the difficult challenges we faced. Thank you, Maurien, Michiel, Nicolas, Olaf, Rob, and Wim. Also thanks to Dietmar and

Markus from Roche for their help with the projects. The collaboration with the University of Utrecht was very valuable, thank you, Albert and Vojtech. Finally, I want to thank the other consortium partner FrieslandCampina and my fellow PhD students, Inge and Dario, for their input during the meetings.

Furthermore, I would like to thank Sarah and Oscar for the opportunity to perform experiments in their lab and the support during my stay in Strasbourg. Also thanks to my colleagues Rania, Marie, Jérôme, Corentin and Evolène for showing me around Strasbourg and teaching me all about the French (and Alsacian) culture.

Lieve vrienden, jullie zijn geweldig! Zo fijn dat ik altijd bij jullie terecht kon om stoom af te blazen of om gewoon zorgeloos van het leven te genieten. Oma Thea, ik waardeer het enorm dat jij altijd klaar stond met motiverende en opbeurende wijsheden. Daarnaast ben ik je ook dankbaar voor de financiële bijdrage om boekje te laten drukken. Lieve Thomas, jouw oneindige zee aan geduld, vertrouwen en humor heeft de laatste periode van mijn PhD zoveel fijner en gezelliger gemaakt, dankjewel.

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