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## **Unravelling the sugar-coating of prostate-specific antigen : method development and its application to prostate cancer research**

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# LIST OF PUBLICATIONS

1. **Kammeijer, G.S.M.**, Nouta, J., Rosette, de la J.J.M.C.H, Reijke, de T.M., Wuhrer, M. *An In-depth Glycosylation Assay for Urinary Prostate-Specific Antigen*. Analytical Chemistry, 2018, **90** (7), pp 4414-4421, DOI: 10.1021/acs.analchem.7b04281.
  
2. **Kammeijer, G.S.M.**, Jansen, B.C., Kohler, I., Heemskerk, A.A.M., Mayboroda, O.A., Hensbergen, P.J., Schappler, J., Wuhrer, M. *Sialic acid linkage differentiation of glycopeptides using capillary electrophoresis – electrospray ionization – mass spectrometry*. Scientific Reports, 2017 (7), 3733, DOI: 10.1038/s41598-017-03838-y.
  
3. **Kammeijer, G.S.M.**, Kohler, I., Jansen, B.C., Hensbergen, P.J., Mayboroda, O.A., Falck, D. Wuhrer, M. *Dopant Enriched Nitrogen Gas Combined with Sheathless Capillary Electrophoresis–Electrospray Ionization-Mass Spectrometry for Improved Sensitivity and Repeatability in Glycopeptide Analysis*. Analytical Chemistry, 2016, **88** (11), pp 5849-5856, DOI: 10.1021/acs.analchem.6b00479.
  
4. **Lageveen-Kammeijer, G.S.M.\***, Haan, de N.\*, Mohaupt, P., Wagt, A.P., Filius, M., Nouta, J., Falck, D., Wuhrer, M. *Highly sensitive CE-ESI-MS analysis of N-glycans from complex biological samples*. Manuscript Submitted.
  
5. **Kammeijer, G.S.M.**, Kohler, I., Jansen, B.C., Hensbergen, P.J., Mayboroda, O.A., Falck, D., Lock, S., Wuhrer, M. *Improved CESI-MS sensitivity and repeatability in Glycopeptide Analysis using a Dopant Enriched Nitrogen Gas*. Document nr: RUO-MKT-02-4920-A, 2016 (Technical Note).
  
6. **Kammeijer, G.S.M.**, Kohler, I., Jansen, B.C., Hensbergen, P.J., Mayboroda, O.A., Falck, D., Lock, S., Wuhrer, M. *Separation and detection of glycopeptide isomers with differentially linked sialic acids by CESI-MS. (Technical Note)*.
  
7. Sánchez López, E., **Kammeijer, G.S.M.**, Crego, A.L., Luisa Marina, M., Ramautar, R., Peters, D.J.M., Mayboroda, O.A., *Sheathless CE-MS based metabolic profiling of kidney tissue section samples from a mouse model of Polycystic Kidney Disease*. Scientific Reports, 2019 (9), 806, DOI: 10.1038/s41598-018-37512-8.
  
8. Clerc, F., Novokmet, M., Dotz, V., Reiding, K.R., Haan, de N., **Kammeijer, G.S.M.**, Dalebout, H., Bladergroen, M.R., Vukovic, F., Rapp, E. IBD-BIOM consortium, Targan, S.R., Barron, G., Manetti, N., Latiano, A., McGovern, D.P.B., Annesse, V., Lauc, G., Wuhrer, M. *Plasma N-glycan Signatures of Inflammatory Bowel Diseases*. Gastroenterology, 2018, **155** (3), pp 829-843, DOI: 10.1053/j.gastro.2018.05.030.



9. Plomp, R., Dekkers, G., Rombouts, Y., Visser, R., Koeleman, C.A.M., **Kammeijer, G.S.M.**, Jansen, B.C., Rispen, T., Hensbergen, P.J., Vidarsson, G., Wuhler, M. *Hinge-Region O-Glycosylation of Human Immunoglobulin G3 (IgG3)*. Molecular and Cellular Proteomics, 2015. **14** (5): p. 1373-1384, DOI: 10.1074/mcp.M114.047381.
  
10. Bondt, A., Nicolardi, S., Jansen, B.C., Stavenhagen, K., Blank, D., **Kammeijer, G.S.M.**, Kozak, R.P., Fernandes, D.L., Hensbergen, P.J., Hazes, J.M.W., van der Burgt, Y.E.M., Dolhain, R.J.E.M., Wuhler, M. *Longitudinal monitoring of immunoglobulin A glycosylation during pregnancy by simultaneous MALDI-FTICR-MS analysis of N- and O-glycopeptides*. Scientific Reports, 2016 (6), 27955, DOI: 10.1038/srep23296.
  
11. Jansen, B.C., Bondt, A., Reiding, L., Londardi, E., Jong, de C.J., Falck, D., **Kammeijer, G.S.M.**, Dolhain, R.J.E.M., Rombouts, Y., Wuhler, M. *Pregnancy-associated serum N-glycome changes studied by high-throughput MALDI-TOF-MS*. Scientific Reports, 2016 (6), 23296, DOI: 10.1038/srep23296.
  
12. Clerc, F., Reiding, K.R., Jansen, B.C., **Kammeijer, G.S.M.**, Bondt, A., Wuhler, M. *Human plasma protein N-glycosylation*. Glycoconjugate journal, 2016, 33 (3), pp 309-343, DOI: 10.1007/s10719-015-9626-2.
  
13. Leoz, de M.L.A., ... Haan, de N., Falck, D., **Kammeijer, G.S.M.**, Wuhler, M., ... Stein, S.E. *NIST Interlaboratory Study on Glycosylation Analysis of Monoclonal Antibodies: Comparison of Analytical Methods*. Manuscript Submitted.



# CURRICULUM VITAE

Gerritje (Guinevere) Stevina Margaretha Lageveen - Kammeijer was born on July 6<sup>th</sup> 1989 in Sneek, the Netherlands. After Guinevere finished primary school and her higher general secondary education with the profile Nature & Health, she started the study Biotechnology with a special focus on Forensic Sciences at University of Applied Science van Hall Larenstein, Leeuwarden, the Netherlands. After she successfully finished her bachelor degree in 2011 she followed a Masters degree in Analytical Chemistry at the VU University, Amsterdam, the Netherlands. Her first encounter with capillary electrophoresis coupled to a mass spectrometer via electrospray ionization (CE-ESI-MS) was during her MSc program where she followed an internship in 2012 at the Center for Proteomics and Metabolomics at the Leiden University Medical Center, the Netherlands where she focused on small scale sample preparation with CE-ESI-MS/MS under supervision of Dr. Oleg. A. Mayboroda and Dr. Anthonius (Anton) A.M. Heemskerk.

After a fruitful internship, her interest in CE-ESI-MS was triggered and she started in June 2013 a PhD-project at the same Center for Proteomics and Metabolomics under the supervision of Prof. Dr. Manfred Wührer. Her main research involved the exploration of the well-known biomarker for prostate cancer, prostate-specific antigen (PSA) and its glycosylation. For this research, there was a special emphasis on the usage of CE-ESI-MS/MS for the analysis of glycopeptides, employing a porous nano-sprayer for MS coupling. In addition, she studied the possibilities for in-depth analysis of glycans and intact glycoproteins with the same analytical platform for biomarker discovery as well as for the characterization of biopharmaceuticals. During her PhD trajectory she had the opportunity to guide several MSc students as well as to be involved in projects of fellow PhD-students.

To expand her knowledge and horizon she visited the Chemistry and Chemical Biology Department at Barnett Institute at Northeastern University, Boston, MA in August 2017 and performed a 4-month project under supervision of Prof. Dr. Alexander Ivanov. During her short-stay in Boston, she focused on the development and evaluation of analytical approaches for the characterization of protein charge and proteoform heterogeneity using CE-ESI-MS.

Guinevere has been part in several organizational matters, such as the organization of a Masterclass on Prostate Cancer and Therapies held at the LUMC, Leiden, the Netherlands as well as the organization of a joint seminar between Japan and the Netherlands on glycoscience in 2016. Called: *Glycobiology in Health and Disease*. In addition, she was involved in the organization of several social activities at the CPM and is currently still part of the quality control group. Moreover, in 2017 she joined as a member of the organization committee from the Netherlands Area Biotech (NLab) Discussion group supported by CASSS. In 2019 she became a member of the scientific committee of the glycomics session and early career scientist at Mass Spectrometry Applications to the Clinical Lab EU.

Currently, Guinevere is employed as a post-doctoral researcher at the same department, within the group of Prof. Dr. Manfred Wührer she is proceeding with her research regarding the development of the PSA Glycosylation Assay and expanding this assay with her fellow colleagues.

Even though she is at the start of her career, her work seems to be of broad interest for the scientific community with already more than 25 international presentations since 2014, from which 13 on invitation. Furthermore, she received a total of 7 travel grants for several conferences and she received several fellowships in collaboration with the Urology department at the Amsterdam University Medical Centers, location AMC and Astellas to support her own research line.





# PHD PORTFOLIO



## ORAL PRESENTATIONS ON INVITATION

- 04-10-2017** Exploring CESI-MS for Isomer Separation of *N*-glycans and Glycopeptides - **CESI USER meeting**, SCIEX, Boston, MA, USA. <https://sciex.com/events/2017cesi>
- 01-02-2017** Using CE-ESI-MS for Glycoproteomic Research - Method Development & Biomarker Discovery, SCIEX, Brea, CA, USA
- 30-01-2017** Using CE-ESI-MS for Glycoproteomic Research - Method Development & Biomarker Discovery, Cedars Sinai Medical Center, Los Angeles, CA, USA
- 22-11-2016** A Different View on Prostate-Specific Antigen - towards an improved diagnosis of prostate cancer, Amsterdam Medical Center (AMC), Amsterdam, The Netherlands.
- 06-10-2016** Unravelling the Bitter Sweetness of Prostate-Specific Antigen, **CESI USER meeting** SCIEX, VU University, The Netherlands. <https://sciex.com/events/cesi-symposium>
- 22-09-2016** Center for Proteomics and Metabolomics (CPM) highlights, Leiden, The Netherlands
- 27-06-2016** Astellas NL ISR Expert meeting, Leiden, The Netherlands
- 15-06-2016** Glycomics and Glycoproteomics by CESI-MS for Biomarker Discovery and Biopharmaceutical Characterization, **WEBINAR**, SCIEX. <http://www.labroots.com/webinar/webinar-comparison-mass-spectrometric-techniques-glycomics-glycoproteomic-analysis-biopharmaceuticals>
- 06-06-2016** Glycomic and Glycoproteomic Analysis of Biopharmaceuticals Breakfast Seminar SCIEX, American Society for Mass Spectrometry (**ASMS**), San Antonio, TX, USA
- 16-03-2016** Glycan and Glycopeptide Analysis at Enhanced Sensitivity with CESI-MS(/MS), Analytical Technologies Europe (**ATE**) 2016, Vienna, Austria.
- 07-10-2015** Glycopeptide Analysis at Enhanced Sensitivity with CESI-MS(/MS), **The analytical Challenge** - CE user meeting, Utrecht, The Netherlands
- 30-09-2014** CESI-MS/MS as a Tool in Protein Glycosylation Analysis, **CESI User Meeting**, SCIEX, Strassbourg, France. <http://sciex.com/ce-esi-ms-ms-as-a-tool-in-protein-glycosylation-analysis>
- 29-04-2014** CESI-MS/MS as a Tool in Protein Glycosylation Analysis, MicroScale Bioseparations (**MSB**), SCIEX, Pecs, Hungary

## ORAL PRESENTATIONS

- 01-10-2018** High Throughput Glycomics And its application for clinical questions Mini-symposium Parasitology-CPM, Leiden, The Netherlands
- 12-09-2018** Development of MS-based Prostate-Specific Antigen Test with In-Depth Glycosylation Analysis Mass Spectrometry Applications to the Clinical Lab (**MSACL**), EU, Salzburg, Austria
- 29-05-2018** Exploring CE-ESI-MS for *N*-glycan Isomer Separation, Forum for Analytical Science and Technology (**FAST**), Veldhoven, The Netherlands
- 25-05-2018** The Bitter Sweetness of Prostate-Specific Antigen, Masterclass - On Prostate Cancer and Therapies, Leiden, The Netherlands
- 21-09-2017** Glycomic and Glycoproteomic Analysis of Biopharmaceuticals in a High Throughput and Highly Sensitive Manner, Practical Applications of Mass Spectrometry (**Mass Spec**), Boston, MA, USA



- 18-09-2017** Isomer Separation of Positively Labelled *N*-glycans by CE-ESI-MS, CE in the biotechnology & pharmaceutical industries (**CE pharm**), Boston, MA, USA
- 26-03-2017** Glycosylation Analysis of Prostate-Specific Antigen - Towards Improved Diagnosis of Prostate Cancer, Microscale Separations and Bioanalysis (**MSB**), Noordwijkerhout, The Netherlands
- 26-01-2017** Prostate-Specific Antigen Glycomics Assay as a More Specific Tool for Early Diagnosis of Prostate Cancer, Mass Spectrometry Applications to the Clinical Lab (**MSACL**), Palm Springs, CA, USA
- 09-06-2016** Dopant Enriched Nitrogen Gas Enhances Sensitivity and Repeatability, Opening New Possibilities for Glyco(proteo)mics Analysis with Sheathless CE-ESI-MS, American Society for Mass Spectrometry (**ASMS**), San Antonio, TX, USA
- 04-04-2016** CE-ESI-MS as a Tool for Glycomic and Glycoproteomic Analysis of Biopharmaceuticals- Microscale Separations and Bioanalysis (**MSB**), Niagara-on-the-Lake, ON, Canada
- 18-04-2016** Dopant Enriched Nitrogen Gas Enhances Sensitivity and Repeatability of Glycopeptide Analysis with Sheathless CE-ESI-MS - **NVMS** spring meeting 2016, Kerkrade, The Netherlands
- 11-09-2015** CESI-MS as a Tool for Glycosylation Analysis of PSA and Improved Ionization Efficiency with Acetonitrile-enriched Nebulizer Gas, Mass Spectrometry Applications to the Clinical Lab (**MSACL**), EU, Salzburg, Austria. [https://www.msaccl.org/index.php?header=Learning\\_Center&tab=Video\\_Management&subtab=Video\\_Request&id=31&conference=2015\\_EU&type=podium](https://www.msaccl.org/index.php?header=Learning_Center&tab=Video_Management&subtab=Video_Request&id=31&conference=2015_EU&type=podium)
- 28-04-2015** Increasing Sensitivity of Glycopeptide Analysis with CESI-MS, MicroScale Bioseparations (**MSB**), Pudong Shanghai, China
- 25-08-2014** CESI-MS/MS as a Tool in Protein Glycosylation Analysis, International Mass Spectrometry Conference (**IMSC**), Geneva, Switzerland
- 29-04-2014** Sialic Acid Linkage Analysis on Glycopeptides using CE-ESI-MS/MS, MicroScale Bioseparations (**MSB**), Pecs, Hungary

## GRANTS AND FELLOWSHIPS

- 2018** Young Investigator Travel Grant, Mass Spectrometry Applications to the Clinical Lab (MSACL), EU, Salzburg, Austria
- 2017** Fellowship of Cure for Cancer to further support the following research: *“High-resolution glycosylation profiling of prostate-specific antigen for early diagnosis of prostate cancer”* collaboration of the Urology department of Amsterdam Medical Center and the Center for Proteomics and Metabolomics at the Leiden University Medical Center.
- 2017** CASSS Student Travel Grant, Practical Applications of Mass Spectrometry (Mass Spec). Boston, MA, USA
- 2017** Young Investigator Travel Grant, Mass Spectrometry Applications to the Clinical Lab (MSACL), Palm Springs, CA, USA
- 2015** Fellowship of Astellas Pharma B.V to support the following research: *“High-resolution glycosylation profiling of prostate-specific antigen for early diagnosis of prostate cancer”* collaboration of the Urology department of Amsterdam Medical Center and the Center for Proteomics and Metabolomics at the Leiden University Medical Center.

- 2015** Young Investigator Travel Grant, Mass Spectrometry Applications to the Clinical Lab (MSACL), EU, Salzburg, Austria
- 2015** NVMS conference attendance fund, MicroScale Bioseparations (MSB), Pudong Shanghai, China
- 2015** CASSS Student Travel Grant, MicroScale Bioseparations (MSB), Pudong Shanghai, China
- 2014** CASSS Student Travel Grant, MicroScale Bioseparations (MSB), Pecs, Hungary

## EXPERIENCE IN LOCAL ORGANIZATION:

- 2019 - present** Scientific Committee Member of the Glycomics Session and Early Career Scientist at Mass Spectrometry Applications to the Clinical Lab EU
- 2017 - present** Member of the Organization Committee of The Netherlands Area Biotech (NLab) Discussion Group
- 10 & 11-10-2018** Global CESI-MS Symposium - SCIEX, Leiden, The Netherlands
- 25-05-2018** Masterclass - On Prostate Cancer and Therapies, Leiden, The Netherlands
- 19 till 22-04-2016** Glycoscience Japan - The Netherlands Joint Seminar 2016, Glycobiology in Health and Disease, Leiden, The Netherlands

## SUPERVISION

Valeriia Kuzyk	PhD-student	<i>October 2016 - present</i>
Alan Moran	PhD-student	<i>April 2017 - present</i>
Wei Wang	PhD-student	<i>October 2017 - present</i>
Wenjun Wang	PhD-student	<i>May 2018 - present</i>
Katarina Madunic	PhD student	<i>May 2018 - present</i>
Di Wang	PhD student	<i>September 2018 - present</i>
Anna Kaluža	Visiting PhD-student	<i>May 2018 - September 2018</i>
Laura Pont Villanueva	Visiting PhD-student	<i>April 2016 - June 2016</i>
Sander Wagt	MSc student	<i>August 2016 - June 2017</i>
<i>(Received a poster prize for his poster presented at MSB 2017)</i>		
Tamás Pongrácz	MSc student	<i>January 2017 - April 2017</i>
Sarah Azaabal	MSc student	<i>November 2015 - November 2016</i>
Alexander Jansma	MSc student	<i>June 2015 -August 2015</i>



## TEACHING EXPERIENCE

**Frontiers of Science Course** - Parasitology, Leiden University Medical Center

January 2019

*Course about glyco(proteo)mics for BSc students*

**Bio-Pharmaceutical Sciences** - Leiden Academic Centre for Drug Research

January 2019/January 2018

*Course about glyco(proteo)mics for MSc students*

**Frontiers of Science Course** - Center for Proteomics and Metabolomics, Leiden University Medical Center

October 2018

*Course about glyco(proteo)mics for BSc students*

## COAST ASTP course

March/November 2018, March/October 2016, September 2014

*Course about glyco(proteo)mics (and CE-ESI-MS) for HLO students*

**Practical course at Hogeschool Leiden** (Applied University Leiden)

March 2018 - June 2018

*Second year bachelor students Analytical chemistry*

## ORGANIZATIONAL EXPERIENCE

Borrel committee CPM	2013-2017
Quality Control CPM	2015-present
Christmas dinner CPM	2013 & 2015
Labouting CPM	2015
Labouting CPM/VU	2015

## COURSES FOLLOWED

Introduction to Cytoscape	<i>Completed April 2017</i>
BROK	<i>Completed December 2016</i>
Developing Medical Tests that improves patient outcomes	<i>Completed November 2016</i>
Biostatistics course	<i>Completed Sept. 2016</i>
Documentbeheer iProva voor beginners	<i>Completed July 2016</i>
ASMS Short Course on ION mobility mass spectrometry	<i>Completed June 2016</i>
Breaking up with Excel - R course	<i>Completed September 2015</i>
Advanced Genetic & Omics Data analysis 2	<i>Completed October 2014</i>
MedGenCentre course - Technology facility	<i>Completed October 2013</i>
Using R in Data Analysis	<i>Completed November 2012</i>



# ACKNOWLEDGMENTS

A PhD can be a real rollercoaster with ups and downs but, to be able to survive it, the most essential part is the support from your colleagues, friends and family. Therefore I am forever grateful for those who were involved in one way or another in establishing this thesis.

First of all I would like to thank Prof. Dr. Manfred Wührer for his trust in me and CE-ESI-MS, due to this we were able to expand the available analytical platforms for the analysis of glycopeptides and glycans within our group. I have great respect for your supervision, passion, fast responses and your availability for a discussion.

Around half-way through my PhD trajectory my research deviated from inflammatory bowel disease towards prostate cancer and, during this time, I met Dr. Theo de Reijke. Thanks to your faith in our project we could bring this research further than I could ever dream off, by applying our developed platform on patient samples and thereby truly perform biomarker discovery.

During the last few years I got the opportunity to expand my horizon and I am looking forward on further expanding my knowledge and the research about cancer glycomics until we will find a more specific biomarker for prostate cancer.

Furthermore, I also would like to thank Dr. Oleg Mayboroda and Dr. Anton Heemskerk, thanks to the two of you I was able to start my scientific career and find my way into the field of CE. During the start of my PhD, Dr. Paul Hensbergen was of valuable help and therefore I would like to thank you, Paul, for guiding me whenever I needed some steering towards the right direction. In addition, Dr. Isabelle Kohler, Isa, I would like to thank you for your time, advice and endless support on helping me to get my papers published. Hans, Rico and Bart, you guys were of great help whenever I ran into instrument issues, thank you for everything.

Bram and Frank, my paranymphs, I could not have imagined a better team than the three of us. You guys were always there when I needed a good conversation, support or advice and I am forever grateful for our friendship. In addition, with our shared joy for boxing you ensured that I also stayed physically in shape. Therefore some final words for you: BOKS!

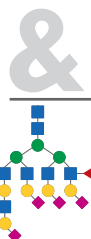
While glycosylation was a whole new world for me 5 years ago, there was, luckily, a powerful group which I could consult whenever that was needed. Therefore, I would like to thank Agnes, Albert, Bas, Carolien, Cees, Karli, Maurice, Rosina and Stephi for their patience whenever I got lost in the way you can get lost in studying glycosylation. Next to performing research, an essential part is to now and then relax, thanks to Anton, Bart, Benjamin, Bram, Clara, Dana, DP, Frank, Hulda, Isabelle, Kate, Linda, Ricardo, Robert, Ruben and Tugçe, I managed to find some time for a wine or two as well as to have some epic weekends away!

As usual I also switched some offices during my PhD, and thanks to that I had the chance to interact with many of you and filter my complaints when a system was not performing, or when it was though with research in general. So I would like to thank Anna, Alan, Bas, Christoph, Dana, Elena D, Elena S, Hans, Florent, Gerda, Jan, Laura, Leria, Linda, Tamás, Sander, Sarah, Steffen, Wei and Wenjun for their support whenever it was needed! Moreover, I would like to thank Noortje, Bas and Karli for their contribution to solving my data-analysis problems as well as for the good interaction on many scientific topics.

Even though I started rather lonely working on the CE-ESI-MS platform, I am happy to see that the group has expanded! By far most I need to thank Jan for his invaluable work on the PSA project, I enjoyed working with you and I am happy that we will still be working together in the future to make sure that we can bring the assay to the next level! The group was even further expanded with the addition of Alan, Christoph, Elena D., Leria, Steffen, Wei and Wenjun, all of you added essential pieces, with your own expertise and interests, to further improve the CE-ESI-MS platform and its available applications.

I also would like to thank my students Alan, Di, Katarina, Leria, Sander, Sarah, Tamás, Wei, Wenjun and Alexander J. as all of you have contributed to this thesis and to the scientist I am today. I have learned so much from all of you and I hope that I can be of help for your own start as a scientist.

This thesis would not have existed without great collaborations and I need to thank many people in this context. I would like to thank Julie, Elena S., Alexander I., Laura, Anna and Rawi for their contribution to my thesis and some small side projects. It was a pleasure working with all of you. In addition, I would like to thank the team at the AMC (especially Alice!) for their help in collecting all the patient samples as well as everybody at Ludger for providing reagents whenever needed. Manu, thank you for your endless patience and help. You ensured my thesis and manuscripts were of the highest quality possible. Additionally, I need to give a great thanks to the huge SCIEX team that I have





been working with in the last few years, Aad, András, Bryan, Chitra, Christopher, Edna, Esme, Jeff, Jim, Manfred, Marcia, Mark, Mike and Steve thanks to you we were able to push limits and go beyond the general usage of the CESI instrument and I am forever thankful for your knowledge, patience and interest in my research. I am looking forward to working together in the near future.

Moreover, I would like to express my gratitude to the volunteers and patients for providing urine samples and the grant partners (Cure for Cancer & Astellas): Without them this research would not have been possible.

I would also like to thank my dear friends for their patience when I was not able to attend events, when I was too tired to have a proper conversation or when I was not able to play my best volleyball match. I promise after this defense I will make up for it and I will try to be there at housewarmings/birthdays/baby visits and anything else! Special thanks for your support and comforts that often resulted in some wining and dining.

I would not have come this far without the endless support of my parents and family. Pap en mam bedankt voor jullie oneindige steun en vertrouwen, zonder jullie had ik nooit zover kunnen komen! En pap ontzettend bedankt voor jouw creatieve visie omtrent mijn cover, zonder jou had het niet zo mooi kunnen worden. Tarquin en Tristan (& Henny en Anastassia) bedankt voor jullie steun wanneer jullie kleine zusje het nodig had. Also my cats were the best medicine you can have while writing your thesis, they always made sure that I would have a break from writing by their selfless actions of making sure I at least petted them every 5 minutes.

Last but not least, my husband, Henk, you are my everything and you have supported me in uncountable ways and there is no way imaginable how I can thank you for this. You were there whenever I got lost and whenever I was desperate and hopeless because my experiments kept on failing. Also you were my go-to person whenever I needed to practice my presentations, and there were a lot of them! You (almost) never complained when I decided to go back to the lab late in the evenings or during the weekends, you always understood how important this was and still is for me and undoubtedly you are the best husband a (scientific) girl can wish for! I hope that you will always be by my side while I keep on exploring my scientific career.

*Guinevere*