



Universiteit  
Leiden  
The Netherlands

## Engineering a metabolomics workflow to capture single-cell diversity in 3D models

Hetzel, L.A.

### Citation

Hetzel, L. A. (2026, September 9). *Engineering a metabolomics workflow to capture single-cell diversity in 3D models*. Retrieved from <https://hdl.handle.net/1887/4309354>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/4309354>

**Note:** To cite this publication please use the final published version (if applicable).

---

## Curriculum vitae

Laura earned a Bachelor of Science degree in Material Science and Engineering from the Illinois Institute of Technology in Chicago, USA. During undergraduate studies, she participated in a hands-on project based class (IPRO) engineering prosthetic fingers for developing countries.

Laura was a metallurgical engineer at Finkl Steel in Chicago, USA for approximately five years following graduation. In this role she performed failure analysis and collaborated with multiple departments to improve the quality of the steel. During this time, Laura assisted in leading the IPRO class under the guidance of Dr. Kevin Meade.

Laura earned a Master of Science degree in Biomedical Engineering from the Illinois Institute of Technology in Chicago, USA after following a cell and tissue engineering track. Her thesis, titled “Ultrasensitive Protein Quantification Using Rolling Circle Amplification”, was supported by lab work using microfluidics and fluorescence to tag, pseudo-amplify, and subsequently quantify C-peptide and was carried out under the guidance of Dr. Abhinav Bhushan. The workflow could be easily adapted to quantify a multitude of other proteins.

Laura then pursued a doctoral degree in analytical biosciences at Leiden University, NL. Under the guidance of Dr. Ahmed Ali, Laura worked to optimize and develop workflows for applications of single-cell metabolomics with complex 3D models. She developed the R package MeDUSA to be the modular data analysis base for single-cell metabolomics. Additionally, she developed a single-organoid sampling workflow to isolate and capture single organoids for mass spectrometry. To elevate the analytical techniques needed to analyze complex models, Laura developed the single-cell untargeted FAIMS methodology. The FAIMS platform was then optimized for targeted metabolites in drug gradient study carried out in a microfluidic organ-on-chip device.

## List of publications

### *Publications related to this thesis*

1. **Hetzel, L.A.**, Hetzel, E., Ali, A. Staring down direct infusion metabolomics datasets with MeDUSA. JOSS (2026)
2. **Castaneda, L.**, Hetzel, E., Gul, F. From mythology to methodology: Untargeted single-cell metabolomics in R with MeDUSA. Journal of the American Society for Mass Spectrometry (2026)
3. **Castaneda, L.**, Gül, F., Aerts, D., Ali, A. Hankemeier, T. FAIMS-Enhanced single-cell metabolomics expands metabolic coverage in the low-abundance regime. Analytical Chemistry (2025) [In review]
4. Verschoor, V., **Castaneda, L.**, Nicholas, A., Trietsch, B., Ali, A., Hankemeier, T. Resolving drug uptake heterogeneity in 3D organ on chip models via live single-cell microsampling and ion mobility spectrometry. Analytica Chimica Acta (2025) [In review]
5. **Hetzel, L. A.**, Ali, A., Corbo, V. & Hankemeier, T. Microfluidics and Organoids, the Power Couple of Developmental Biology and Oncology Studies. IJMS 24, 10882 (2023).

### *Other publications*

6. Pandian, K. Aguiar, L., **Hetzel, L.**, Zwier, R., van Veldhuizen, P., Schubert, C., Karuppusamy, J., Harms, A., Ali, A., Hankemeier, T. Enabling high-sensitivity live single-cell mass spectrometry using an integrated electrical lysis and nano electrospray ionization interface. Analytica Chimica Acta 1324, 343068 (2024).
7. Wevers, D., Koldenhof, L., **Castaneda, L.**, van der Zeeuw, A., Fass, H., Hankemeier, T., Clark, C., Ali, A. An m/z- and intensity-based HRMS clustering algorithm targeted towards single-cell metabolomics. Analytical Chemistry (2025) [In review]
8. Zhang, C., Xiang, Y., Simon, D., **Castaneda, L.**, Hankemeier, T., Ali, A., Takats, Z. Single-cell metabolic differentiation in triple negative breast cancer cell cycle phases using REIMS [In preparation]

## Acknowledgements

First and foremost, I want to thank my supervisors, Prof. Thomas Hankemeier and Dr. Ahmed Ali. Prof. Hankemeier, thank you for building a laboratory that felt like a scientific playground. You surrounded us with incredible technology and then trusted us to explore it. It was an incredible place to learn, experiment, and occasionally fail spectacularly before figuring things out. Looking back, I appreciate even more the freedom you gave me, especially during the second half of my PhD, to chase ideas that were sometimes unconventional, occasionally ambitious, and, thankfully, often successful. That freedom helped me become not only a better scientist but a more confident one. Thank you for every opportunity along the way.

Dr. Ali, after working together for more than four years, I'm not sure a single page could cover everything I learned from you. Thank you for your patience, your guidance, and for somehow always knowing when I needed a challenge and when I needed reassurance. As I grew, you adjusted your mentorship in ways I didn't fully appreciate at the time but certainly do now. Thank you for sharing your knowledge, your opportunities, your spotlight, and, perhaps most importantly, your confidence in me until I found my own.

Some people provided the foundation for success. I want to thank my family. Mom and Dad, your unwavering support, encouragement, and the values you taught me are the foundation on which this work was built. Every lesson, pep talk, and reality check eventually found its way into this thesis somehow.

Anthony, Haley, Evelyn, and Harrison, thank you for reminding me that there is a world outside of experiments, deadlines, and reviewer comments. The adventures, video calls, random texts, and laughs were exactly what I needed, often before I even realized it.

## Appendix

---

Rosa, your gentle acceptance and warm hugs helped me through the dark and rainy Dutch winters, even though you always made me go on walks. Thank you for listening to me practice every presentation and going on long walks, bike rides, and runs with me. You are the real hero of this journey.

Eric, thank you for believing in me during the moments when I was convinced I had absolutely no idea what I was doing. You had enough confidence for both of us, and I borrowed quite a bit of it along the way.

Stacey and Ashley, at this point, "friends" feels like an understatement, you've become family. Thank you for cheering me on through every milestone, listening to every rant, and for the late-night crafting sessions that became the perfect antidote to scientific frustration. I honestly don't think this thesis would exist without your encouragement (or the occasional reminder to step away from my laptop).

There are also many people who entered my life because of this adventure and left it infinitely better than they found it.

To my students, Moenisha, Demi, and Fercan, thank you for making supervision one of the most rewarding surprises of my PhD. You each brought your own perspectives, ideas, and personalities to the lab, and I learned just as much from working with you as I hope you learned from me.

To my collaborators, Prof. Melanie Bailey, Prof. Zoltan Takats, Dr. Vincenzo Corbo, and everyone in your groups, thank you for welcoming me into your labs, teaching me new techniques, answering endless questions, and always being willing to entertain new ideas. I am a better scientist because you opened your doors and trusted me enough to let me learn alongside you.

To my colleagues who became lifelong friends along the way, Ahmed, Vincent, Toni, Isa, Annemiek, and Leylana, thank you for making even the hardest days enjoyable. Whether we were celebrating successes, commiserating over failed experiments, or simply sharing a beer, your

---

friendship made this journey one that I will always remember with a smile. The science was important, but the people made the experience.

Finally, to the people I met during the side quests of this adventure, Cait, Sarah, and Stephan, thank you for giving me somewhere to put my energy that wasn't the lab. You reminded me to have hobbies, go outside, and occasionally talk about something other than metabolomics. You brought balance to a chapter of life that often felt wonderfully chaotic, and I couldn't be more grateful that our paths crossed.

To everyone who played a part in this journey, whether you taught me something, challenged me, supported me, distracted me, or simply made me laugh when I needed it most, thank you. This thesis may have one name on the cover, but it carries pieces of all of you. As every good experiment reminds us, the final result is rarely the product of a single variable. This thesis is no exception.