

## Preface

Not so long ago, at a Master thesis fair, a Master student asked me if it is OK to do a Master thesis in computational fluid dynamics (CFD) even if it isn't your number one interest. He reasoned that, because I was doing a PhD in CFD, it must be *my* number one interest, *and* I must've always known that I wanted to do CFD, as if it had been my calling from birth. My answer was disappointing: no, CFD isn't my number one passion, I told him (more a means to a very noble end, but we'll come back to that throughout this book), and I hadn't always known I would want to do a PhD. What, then, sparked my interest in CFD and computational drug delivery? Which road brought me here? (He didn't end up asking me that, but I told him nonetheless.) Here is a short summary of what I said:

In 2018, in the first year of my Master in Biomedical Engineering, I took up an elective course at the Faculty of Pharmaceutical Sciences focusing on drug delivery, taught by professor Stefaan De Smedt. He taught me about using nanoparticles for targeted drug delivery, the enhanced permeation and retention effect, and the blood-brain barrier, among many other things. The topic fascinated me so much that, by the time I had to choose my own Master thesis topic, this interest led me to prof. Charlotte Debbaut, who had an active topic in the domain of targeted drug delivery (we would later re-name it to *locoregional drug delivery*, since it is probably a more apt name for the subject). Even though I was very stressed throughout and had to spend many weekends alone at Blok B, running my simulations, I thoroughly enjoyed my Master thesis research. More than CFD specifically (again, a means to an end), I thought the concept of using simulation for pre-operative planning was very cool, even though the full implications of that concept still eluded me (they probably still do). And so, when Charlotte asked me to stay on for a PhD, I was captivated. I went through the typical doubts that one has at the end of their studies, but eventually, in the summer of 2019, I decided to go for it. In September 2019, I joined the BioMMedA (although

it was capitalized differently at the time) lab and started my PhD. And I guess they say, the rest is history?

Of course, a PhD cannot be completed without the help of many, many people. And so I wanted to use this preface to thank all the people involved in the scientific side of the PhD. Of course, my main thank you in this preface has to go out to my promotor, Charlotte Debbaut and Geert Maleux. Without Charlotte, it should be clear from the story above that I would not be here. She introduced me to the subject, encouraged me to stay on, gave me all the freedom in the world to explore what I felt needed to be explored, and provided feedback to every single line of scientific text that I've written in the past five years. For that, I am incredibly grateful. At the side of UZ Leuven, Geert provided me with clinical insights that steered the direction of this project, gave us crucial data that made our research so novel, and supported and provided feedback throughout the multi-year process. Of course, to Geert, I am similarly grateful.

Luckily, I had the opportunity to collaborate with many different people on this topic, something that I don't take for granted, and something I will think back on fondly in the years to come. To my Dutch colleagues of the ULTIMO project (past and present), Jan van der Hoek, Romaine Kunst, Erik Groot Jebbink, Tristan Vlogman, Kartik Jain, Tess Snoeijs, Anne van den Brekel, Frank Nijssen: I'm glad we had the pleasure to exchange thoughts on a regular basis, visit each other's labs and that we could use your very relevant experimental data to validate our models. To Unai Lertxundi, my Basque counterpart: it's a shame your internship wasn't a bit earlier in my PhD process, as I would've had more time to help you (and your interesting ideas and work would have guided my own work, for sure). To Jorge Aramburu and Raúl Anton: your enthusiasm during the meeting we had during one of my first months led me to believe that I could actually do this, for which I'm very grateful. To my colleagues at UZ Gent and UZ Leuven, Elisabeth Dhondt, Laurens Hermie, Luc Defreyne, Peter Vanlangenhove, Lawrence Bonne, Chris Verslype (and again, Geert, of course): I'm indebted to you because of all your relevant insights, your help during data transfer, and your willingness to provide me with feedback despite your busy schedules. To Jurgen Deviche: your help with the experimental set-up was not only useful but crucial. To Saskia Claessens: thank you for all your necessary help with all things administration and my on-boarding. To Natalie Van den Ende from UZ Leuven, and Hélène De Naeyer, Lieselot Burggraave and other colleagues from HIRUZ: I could not have completed the administrative side of data transfer (and, by extension, my

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research) without your help. To my UGent-colleagues at TechTransfer, including but not limited to Alessandro Biondi, David Aubert and Katia Stevelinck: it was incredibly fascinating to experience the valorization side of research, so I want to specifically thank you for your relevant work. To my UGent-colleagues at IOF, Eline Soetens and Celine Vanhaverbeke: thank you for all your time and insights during my search for follow-up funding. To Klaus Bacher and Brent van der Heyden: thank you for your incredibly relevant input regarding the side of medical radiation physics (you made me realize I do not know enough about this). To Pascal Verdonck: thank you for lighting the spark in my 3rd Bachelor that eventually brought me to Biomedical Engineering. To my jury members, Jorge Aramburu, Annelies Coene, Liesbet Geris, Peter Vanlangenhove, and chair, Joris Degroote: thank you for spending your time to go through this work and for providing your insightful comments. To my fellow members of the Youngster National Committee on Biomedical Engineering, including (but not excluded to) Andrea Menichetti, Dries Hendrikx, Jonathan Dan, Virginie Otlet, and especially Alexandra Tits and Sophie Bekisz: thank you for your amazing efforts to make our National Days happen, and making me feel part of a team! Finally, to my own colleagues at BioMMedA and Medisip, who I feel each contributed to my research in their own way: Ghazal Adeli Koudehi, Amith Balasubramanya, Lise Gheysen, Mathias Peirlinck, Patrick Segers, Annette Caenen, Pieter van Mierlo, and my co-inventors Jolan Heyse and Saar Vermijs: thank you to each of you for providing pieces of the puzzle (in research, sometimes even the smallest of comments can lead to big, interesting detours). Of course, to my other colleagues, if you're looking for your name, you'll find that in the back!

Throughout the years, it was my absolute honor to be able to guide and supervise many Bachelor and Master students at both the Faculties of Engineering and Medicine as they navigated their own specific sub-topics within this broad topic. In fact, supervising them was by far my proudest work. My thank you to them is for their interest in the topic, their motivation and critical attitude, and their ability to come up with their own novel methods and insights, which steered my own research in new and exciting directions: Matthias, Heather, Marthe, Laura, Vic, Ekaterina, Danaë, Julie, Luca, Braïm, Gilles, Amaryllis, Charlotte C. and Rosario for your innovative experimental work; Thibault and Marius for your segmentation work; Rosario (again), Nathalie, Inten, Tibo, Casper, Gaël, Elien, Noah, Lucas, Charlot, Jana Z., Marthe (again), and Rune for your computational work. (Of course, the same goes for the students who did

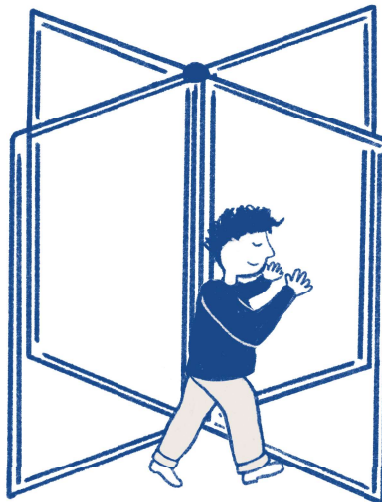
*not* work on the liver topic: Lieve, Laurens, Veerle, Jana P., Kenzo, Louise, Robbe, Elise, Kaat and Elke; you helped me broaden my horizons significantly beyond the domain of the liver.)

The work you will find below is not only the result of the thoughts I had and the person I became between 2019-2024, but also of the collaboration with all the people mentioned above, from student to professor and everything in-between; people who steered my research in both obvious and more subtle ways, giving critical remarks that led to further thinking, developing methods that I would not have developed on my own, cheering me on, inspiring me.

And so, thinking it over, I should've told that Master student: no, CFD isn't my number one passion - but working on a state-of-the-art project that, if successful, could help people around the world *and* doing that together with loads of interesting, smart people? Oh, there are worse things to be passionate about.

## Acknowledgements

If I'd have to compare doing a PhD to anything, I'd say it was eerily similar to a revolving door – a manual one, where you have to push the door ahead yourself. The moment you step in that door, the people who entered before you are already in the process of their own revolution. They might become a good friend, a mentor. The further you progress, the closer those people come to exiting the door – such is the nature of starting a project that is finite by nature. At the same time, new people start entering behind you. They might become your friend, you might become something resembling a mentor for them. As a result, doing a PhD feels like a constant symphony of goodbyes and welcomes. And as time goes on, you find everyone who is caught in the door together with you doing the same thing: doubting, wondering, trying, thinking, failing, repeating. And, most importantly: gently turning, in that door, pushing ahead.



## ACKNOWLEDGEMENTS

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Late September 2019, Patrick welcomed me at Blok B for the very first day of my research career. My first office constellation (in the now derogatorily used ‘old building’) consisted of Annette, Federico and Matthias (give or take a couple of Cubans who were really into Bohemian Rhapsody). **Federico**, I remember your Italian-ness and your kindness most of all, making sure to explicitly invite me to lunch on my first day (the new kids wouldn’t understand this, but back then there was no crazy person yelling ‘LUNCH!’ in the hallway to gather everyone). You also gave crucial information from ‘ground zero’ (Italy in March 2020), correctly predicting that we would all be working from home ‘soon’. It’s a shame the panini hit us around that time, because you’re one of the people I feel like I didn’t get to spend enough time with during our short period together. **Matthias**, my big bear, you would continue to sit with me in that office for years to come, my stable beacon in the most turbulent times. I remember the thing we bonded over initially was The National at my Starter’s Party. While it took both of us some time to let each other in, I see you now as one of my dearest friends. I’m very happy that, even after you left the office, we remained neighbors (more or less) and can still share the occasional espresso martino. Hope we can talk more soon about your school and that I can give you many, many more dilemma’s to overthink. **Annette** (emphasizing the final ‘e’ here in text, because I never remember to do it in real life, for which I can only apologize), with time you would become my go-to mentor, and I’m incredibly grateful for all the times you let me pop in to your office for some ‘quick advice’ (which typically turned into at least 1-hour conversations). I know you were always incredibly busy, but I’ve cherished your advice like holy scripture throughout the years. Notably, you’re also just a very nice person to hang out with, a strong leadership figure and an incredible scientist! (I know this, not only from my own judgement, but from the way the people who work with you talk about you!)

In those early days, I remember being intimidated by quite a lot of people, especially the people who were in the office before me (even only by a couple of weeks). One of those people was **Amith**. You dazzled me with Fluent knowledge, always ready to give your advice; the definition of an academic older-brother-figure. We bonded over Liverpool/Arsenal and Indiana Jones, while also teaching quite a lot together. Next to being just a straight-up great guy, I honestly don’t think the lab would have functioned at all without you: both me and Sarah desperately needed you at times, and without your wits

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my PhD would've gone a lot less smooth. We did not have many postdocs at the lab, but you were a true 'postdoc' in spirit. **Lise**, I also look up to/was intimidated by you, as you were always extremely well-prepared and insightful, and displayed a level of professionalism I strived to for years (but never quite reached). I thoroughly enjoyed our lunch BBB sessions (after they were done) and watching you speed by in the swimming pool. Undoubtedly, my favorite moments were with you and Sarah during Ingenieursproject. Every company or school to hire you will be lucky to have an exemplary figure as yourself among their ranks. I also sincerely want to thank **Ghazal**, my OG thesis supervisor, for helping me with the transition of student to PhD. All three of you were important role models for me during those early moments, and I would not be where I am today without your guidance.

Next to these role models, there were also a lot of Starters starting their own trajectories alongside of me. **Sarah**, I wholeheartedly apologize for 'putting you on the rooster' every lunch. It was a pleasure hosting Ingenieursproject and heart dissections with you. You are an intelligent person with your heart in the right place, both attributes that you will get you very far during your adventure abroad. I wish you all the best for what lies ahead! **Jens**, fellow Starter, I also apologize to you, mainly for all the hugs you were involved in that you probably didn't want to be involved in. You were always someone who I felt connection to because our journeys were so similar with respect to timing and future prospects, and I'm really grateful to have shared that with you. You're a very nice and kind person and I'm very happy for you that you have a great imaging team to work with at Medisip! **Gert**, I'm glad that, while I'm writing this, I can congratulate you with your PhD and the work that you did - it really is impressive. We didn't see you that often but it was always a pleasure having you around. **Ashkan**, another fellow Starter, I'm not sure whether we can actually be considered colleagues because I still don't know why you were actually located on our floor, but you're probably the most hard-working, driven person that I know, and the trajectory you've been on with Exoligamentz is truly inspiring. In addition to that, the bond you have with your family is beautiful, and you never forgot to pass by my office when you were around, which I really appreciated. Bro, I hope that we keep running into, and fist bumping, each other for the foreseeable future.

**Milan, Gerlinde, Charlotte T., Mariele, Emma C.**, you are all people who were at the lab way before me, and just as I said with

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Federico, I would've liked to spend more time together, but I feel like we didn't get to do that because of the panini. You made feel very comfortable during those early-day lunch conversations, for which I am very grateful! Other OGs, **Mohammad** (the first colleague I went to a conference with) and **Hooman**, I feel like we would've seen even less of you if you wouldn't have come to steal our water once every day, but it was always nice to talk to you and I really appreciated the discussion we had about future plans. Next to being nice guys you also give solid career advice! **Mathias**, prof. Peirlinck, it was an honor to inherit your seat in Blok B; I sincerely want to thank you for the help that you offered regarding the first draft of 'De Medische Revolutie' and my FWO application. I am also sure that you didn't actually need my help for your PhD Cup write-up but I'm very grateful that I could still give you some pointers, because that was definitely a confidence booster!

As hinted above, we only spent a couple of months together before a Chinese bat started to wreak havoc. It was March 2020 and I had just handed in my FWO application when we received the news that we would have to work from home for 'a couple of weeks'. This marked the end of the first phase of my PhD life, and brought us into an entirely new era.

We would spend the next year-and-a-half mostly indoors, holding virtual coffee breaks and experiencing the highs and (mostly) lows of Microsoft Teams. I consider the Covid period until early 2023 the second phase of my PhD because I formed some key friendships there, even if they were stalled a bit by the circumstances. It was during the panini that I first started to go on walks with **Jolan**. Despite your small hands, I consider you one of my best friends (top 4?), and the partnership we formed during lunch conversations was absolutely horrifying for everyone but us. Those walks were also around the time you bought a canoe, which is not super relevant here, but I just think it's funny you bought a canoe. Your YOLO sunk-cost attitude to finances would become a theme in the next years, and my favorite most unnecessary expense of yours is definitely that Christmas troll (the second XL Christmas tree being a close second). Next to being incredibly caring, you're one of the smartest persons that I know (even though you will never admit that, you silly goose!). Of course, another topic that (regrettably) came up often during walks and talks was your turbulent love life, which seamlessly brings me to my next point.



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In the second part of 2020, **Saar** joined the lab. We taught quite some courses together, including Ingenieursproject and CBFM (to a lot of future colleagues), which gave rise to some all-time quotes ('sebietjes', 'ke me vant weekend eki gesmeten ip die pomp'). The first of many races we ran together was the Blaarmeersen Trail Run in late 2021; in the next years, many Exploots, a 10 Miles and a 20 km van Brussel, and of course many, many training sessions, would follow. In you, I found a partner in crime, and having you around was a life-saver for my mental health. Maybe not even my mental health alone, since you apparently diagnose long-term illnesses better than most doctors. That being said, you would also throw me in front of rabid dogs to save yourself if you had the chance so I guess that more or less evens out. Regrettably, a topic that also came up often during our many runs was also your love life, which peaked from the Starters Party 2023 onwards. Highlights for the three of us definitely include the Dune tri-costume cosplay at Saar's Starters Party and the after-running Kantien sessions.

Not so long after Saar, **Emma** also joined the lab. Emma, the words-per-minute ratio increased significantly after you joined our lives; your office (or oven) would become a crucial office-hang-out spot; and I look back very fondly to our Christmas raclettes and brunches. You are one of the most resilient persons that I know, and I hope that you can find some rest in the years to come. From Bordeaux, London to Sicily, the four of us made quite some unforgettable trips together. Other highlights I have to include is our White Lotus binge and Big Lebowski team-up at the Personeelskampioenschap Bowlen.

Another lab legend **Simeon**, who also joined the Ingenieursproject team (who didn't actually?). I can only thank you sincerely, Simeon, for your additions to the office lore. From FMK Office to top-3s (or top 10 arrows?) to 'least woke moment of the weekend', from Draakklaps to Bourgondiëklaps, you were the heart and soul of many, many social events. You're the kind of guy who's always got a weekend story in store, a fact to share or a joke to tell - if I could take anyone to my next office, it would definitely be you. When you are done building walls, I hope you and those carotid signals finally work it out, because I think what you can have together is beautiful. Ar-te-ry!

The panini was not without its academic highlights (my first publication, receiving funding for four years by the FWO), but I was more than eager to return to the office whenever we were given the chance.

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The string of office parties and Baracita Fridays that followed the end of the panini (or was it?) was undoubtedly the one of the wildest office life streaks we had. By that time, the office had changed quite a bit, with Federico graduating, Annette moving offices, and Bhawna and Yousof moving in. **Bhawna**, your taste in music is great and I still listen to our shared playlist now and then! I look back very fondly on the fun times we had together (Baracita especially!). **Yousof**, since I don't have peripheral vision, it was extra scary sharing an office with you for so many years because I never knew where you were standing exactly. That being said, you brought an energy and enthusiasm to the office that was unmatched, and office life would have looked entirely different without you. Another legend to spice up office life was **Samaneh**; while it took some time for you to warm up to our ways (and the other way around), I'm so glad you were part of our lab because it was so much fun going out with you (the policeman is a core memory). Additionally, **Wouter**, your Morty impressions will haunt me until the day I die, and your Word of the Day scheme enriched my life to the point that I am now aware of the importance of carcinization.



Over the years, we also welcomed a lot of interns to the office. **Melissa**, you broke the mold of what an intern could be; it still amazes me to this day how you charmed everyone and formed such great bonds over such a short period. From the moment you left, I knew you were destined to join us again, and I'm very happy that we could be colleagues for all those extra years. I also want to shout out **Vlada**, broad-shouldered **Nino**, Parisian chef **Solene** who prepared

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a four-course meal on her goodbye party, Swiss **Paula** who made an unexpected but very welcome return, Portugal 1 and 2 **David** and **Maria**, the kindest OG Portugal **Goncalo**, and Master student **Robin**. During your periods, you formed an integral part of lunch conversations, afterworks and the social tapestry of office life.

The third and final phase started halfway 2023, with a tumultuous move out of Blok B and many ex-students joining the lab as colleagues. **Jessie**, it was already clear when I was teaching CBFM to you, but now that we're colleagues I'm 100% sure you're one of the smartest people I know. Together with Ashkan, I would also consider you the most driven person that I know and you're also very fun to hang around and sit on a Flibco bus with (even if your social battery is running low). However, your navigation skills are questionable, and I just hope you never get the death penalty because your final meal would be the most saddening final meal ever. I promise I will make you chili con carne once and you will like it! **Jellis**, I can only say it's been an extreme honor being colleagues with someone who will either become the first president of Belgium or go to jail for a failed secession - whatever it will be, best of luck! And even though we have a different vibe politically, we agreed on many other things, such as the amount of alcohol that should be consumed in-flight during a professional trip. **Ariana**, honestly, when I look at you (academically), I see much of my younger self. That being said, you also have a lot of good qualities: you're very smart, motivated, sportive and very nice to talk to! I see in you a natural successor to our top-3 shenanigans, but you will have some competition for the leader role (see below). In you, I found a great swimming partner; I will miss our weekly outings! **Beatrice**, grawzie millee for showing us around Taormina and giving us the full Sicilian-American experience, you're one of the most fun persons I have ever met! I'm glad that we could overcome our initial teacher-student relationship and I hope you never have to ignore me on a plane to Milan again. Cala cala cala! For all four of you, I'm absolutely sure your PhD stories will be a success, but next to that, I also hope you enjoy and relax during your time here.

Of course, there were also some additional new faces who I never taught. **Elias**, Bambino, Pilsken, even though you're a bit scared of me, I thoroughly enjoyed having you around (and sharing a bed with you of course); you have a great career ahead of you and I'm sure you will make Flemish Charleroi proud. If you would spend a little bit less time scrolling through Instagram Reels and a little bit

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more time taking over the lunch conversations, you would already be a group leader! **Nicole**, not everyone was always sure who you were during meetings, and it was only in Edinburgh that I really got to know you as well, but our discussions about the top 5 pop girlies and your IAESTE stories were definitely the highlight of that conference. **Sina**, I have no idea what you're actually working on, but you're a very nice guy and you gave us an all-time scientific bio moment when you taught us how to uncook an egg! It was probably the only time we discussed something during an scientific bio that was useful in practice.

At long last, an important shout-out to my Corelleagues, **Sarah**, **Rosalie**, **Winter** and **Simon** (among others). Leaving Blok B for The Core was one of the best work-related changes that happened during the PhD, and the many kitchen conversations and Corefter-works were true highlights. Coref wiedersehen?

Of course, a huge shout-out my colleagues from Medisip. **Zoé**, I hope you stay strong and never succumb to peer pressure! I'm already looking forward to some new klaps that we can do. **Rabia**, the 8 minutes I had to lie down in your scanner when you were doing tests were the only 8 peaceful minutes of my PhD; I am forever indebted to you for that. **Maya**, I enjoyed looking forward to and then critically analysing the Taylor Swift Eras Tour with you. I hope you never get over your chips addiction because chips are awesome. Mr. **Amir**, you truly are a ray of sunshine that lit up our office, please never change. And say hi to your daughter from me! But enough breaks now, let's get to work, OK? To Jolan and Amir! **Boris**, your Norwegian cheesecake is life-altering, and it's because of that that I forgive you for always eavesdropping every time we talk about you. It's just not very polite! You're also my secret style king, always wearing something that makes me want to copy your fits. **Florence**, Romance, I am still waiting for the invite to your Restarters Party! Why do you keep going to the US and coming back? Don't you like us? **Meysam**, I will never forget the look of instant regret on your face when you were joking that I was late one morning and I replied that I just came back from my psychologist. It's OK, king! I will miss your kind spirit!

From the end of 2023 onwards, I stopped most of my analyses and start working on writing this little book here. I completed the first version in March 2024 and saved the acknowledgments for the end, as a little treat for myself. I knew that I would enjoy looking back

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on all these memories and people throughout the years. You were not only colleagues but companions, in easy and hard times; all of us working toward similar goals, wondering, trying, thinking, failing, starting over. All of you were instrumental in making my time here a core memory.

Of course, I also want to thank all of my friends and family for their unwavering support. Your enthusiastic response to things I told you about my PhD often helped me to see my own project again through different, often less analytic eyes, which can really help if you've been stuck in the grind. I've made a non-exhaustive list here: **Katrien, Marc, Silke, Frieda, Daniël, Liesbet, Steven, Jasper, Hannelore, Willy, Leen, Dina, Fien, Eline, Céline.** Additionally, I want to thank the many students I encountered (also the ones I didn't name in the preface) because teaching you was by far my favorite part of the job. A special thank you also has to go out to Eline Van Herreweghen for providing me with these beautiful illustrations. Finally, I want to thank the team at AZ Maria Middelaers for taking care of me and always being available.

My other main thank you can only go out to my constant companion, **Nele.** I'd like to think I'm good with words, but still then it's difficult to express in words the impact you have had on my life (the few words I do have for that I'm saving for a different occasion, so I'm not wasting them here). You have been so intertwined with this process from its very beginning: In the summer of 2019, we were discussing whether I should pursue a PhD or not while walking along the cliffs in sunny Spain. In the winter of 2022, when we came back from celebrating Christmas, we were discussing everything that I think was going wrong in my PhD. We celebrated the highs and dealt with the lows and now we'll be celebrating this milestone together for many times, I'm sure! In the six-and-counting years that we have been together, you've helped me grow as a person, and the book I put down here is a result of that. From the moment this book is printed, the lines I've written on all of these pages will belong to everyone, but everything that's between the lines will belong to us, and us alone.

And so, you might ask, after all this: How does someone think back on a PhD? For me, it's mainly all of the people I've listed here. This book is a product of its circumstances, and it would be impossible to think about my PhD without thinking about all of you. And yes, sometimes it was hard. There were times that I had to push

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the door, push hard, to keep things moving. On the one hand, you want to keep things moving for yourself, because you really want to finish that paper, that presentation, that class. On the other hand, sometimes you push when you feel there's lots of work to do around you, so others don't have to push as hard. Because when you push, you can make space for others to get in behind you. And that's where the magic kicks in - keep things moving long enough, and you'll find that those revolving doors might not even need you that much. Years fly by; and after a while, with enough critical mass inside, you can start to let your grip off the handle, softly at first. You notice that the door keeps turning, one person after another, one generation after another, everyone pushing at their own rhythm and writing their own stories, and you feel that you can finally let go. And the beauty of that? It goes on turning, round and round again.

