

# The Role of Transport Phenomena in Whispering Gallery Mode Optical Biosensor Performance

Thesis by

Jason Gamba

In Partial Fulfillment of the Requirements

for the Degree of

Doctor of Philosophy



California Institute of Technology

Pasadena, California

2012

(Defended June 3, 2011)

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For Ashley, my wife and friend. Everything changed when I met you.

# Acknowledgements

The fact that a single name appears on the title page of a dissertation can be quite misleading. Neither this document, nor the research behind it, could have been completed without the help of a great number of people.

I would first like to thank my advisor, Professor Rick Flagan, who has given me the opportunity to work on a project I truly enjoy. I came to him at the end of my third year of graduate school seeking help from the Executive Officer of Chemical Engineering with finding a new research home on campus. I was looking for a project in a research lab that could support me while I completely rebooted my graduate career, and hoped Professor Flagan could advise me on how to go about my search. After listening to me describe my situation for nearly an hour, he politely asked if I would be interested in hearing about a project available in his own group involving an extraordinary optical biosensor. Within days I was a Flagan Lab member, eager to return to my roots as a chemical engineer by applying the field's core disciplines to the analysis of what was essentially a physicist's toy. Professor Flagan has taught me a great deal about instrument development and validation, and working in his lab has been an excellent education as a researcher.

I am also very grateful to Professor Andrea Armani, who has been a valuable mentor and friend to me since we began working together in 2008. It was her work as a Clare Boothe Luce Postdoctoral Fellow that began the collaboration between the Flagan, Vahala, and Fraser laboratories at Caltech, of which I have been a part. I was fortunate enough to learn this field from her, and benefit from the extraordinary care and patience she put into developing the procedures she used for her experiments. Even after Professor Armani accepted her faculty position at the University of Southern California, she continued to offer her time to answer my (seemingly endless) questions. I cannot express how helpful this was for a researcher trying to

learn a field outside his expertise. Working with her and getting to know her has truly been one of the most rewarding pieces of my graduate career.

I would like to thank Professors Scott Fraser and Mark Davis as well for all of their helpful suggestions and guidance as members of my thesis committee. Of course, my work would not have been possible at all if not for the much-appreciated funding from the Jacobs Institute for Molecular Engineering for Medicine at the California Institute of Technology.

I have also been fortunate to work alongside a wonderful group of researchers in the Flagan/Seinfeld Laboratory. The person who has most affected my own research is Xerxes Lopez-Yglesias. He is a resource of incalculable value to the group, with nearly everyone relying on his broad expertise at one point or another during their tenure. He and I conducted a thorough analysis of the physics involved in sensing a single biomolecule with a whispering gallery mode sensor, debating the value of previous methods and the interpretation of reference texts for hours on end. This intense academic endeavor led us to two main conclusions: (i) that theoretical modeling comes entirely down to how you justify the shortcuts you took in order to preserve your sanity, and (ii) that the selection of Pasadena dining establishments open at 3 am is sadly limited.

Andy Downard is another fine groupmate to whom I am indebted. In addition to being a good friend, Andy was of particular help with my efforts to model the fluid flow around sensors. He contributed even more to the daily operations of the lab by generously providing organizational advice and encouraging a multidisciplinary spirit that is too often absent in research environments. Our research group often posed unique challenges, as everyone must quickly develop a broad range of abilities in order to make any progress. I am grateful, however, to *all* the members of the Flagan and Seinfeld groups for creating a cooperative and friendly atmosphere, which should never be taken for granted. You all conduct your research (and yourselves) with class in the face of overwhelming pressure to succeed at any cost.

I would also like to thank two outstanding collaborators, Jacob Sendowski and Naresh Satyan, for their friendship, help, and patience during our work to integrate a tunable laser source of their creation into the nascent sensor apparatus described in the chapters that follow here. Along with the help of other members

of the Yariv Laboratory in Applied Physics and Electrical Engineering, especially Scott Steger and Arseny Vasilyev, we began what I hope is a long and productive research partnership for our groups. From the many, many hours I spent working with Jacob and Naresh, I can say that both represent the finest that Caltech has to offer. They are excellent scientists and just truly fun people to be around, both of which only made the grueling frustration of troubleshooting a relatively untested experimental setup that much more pleasant.

Though they get too little credit for the impact they have on student life and graduate research, the various staff at Caltech also deserve a great deal of gratitude. Chemical Engineering administrative assistants like Kathy Bubash, Laura King, Anne Hormann, Marcy Fowler, Martha Hepworth, Karen Baumgartner, and Yvette Grant play a huge role in making sure students have access to their advisors and that the academic machinery continues to run smoothly for everyone. Additionally, a great systems administrator like Suresh Gupta is pivotal in a research environment like Caltech where computation and data storage/transfer are so important. Technical staff, including machinists like Mike Roy, Steve Olsen, and Mike Vondrus as well as glassblowers like Rick Gerhart, are also valuable resources that allow students to push the envelope of their field by creating new equipment and techniques. It also helps that they are all so friendly, welcoming, and generous with their time. I would like to thank all of these fine Caltech staff members for all of the tasks, large and small, they have helped me with since I started here. I would especially like to thank Mike Roy for teaching me so much about machining and for being such a great friend to me through all of my frustrations. He is a bright and inquisitive man who perfectly embodies the spirit of Caltech's ingenuity and curiosity.

I also want to point out the contributions that another staff member, Dr. Mike Vicic, has made to my graduate career. He is a truly gifted educator who cares deeply about helping his students learn *and remember* as much of the mountain of information that the Chemical Engineering curriculum presents to them as possible. I TAed courses administered by Mike three times, and I may have learned more TAing his undergraduate courses than I did during my own undergraduate career. I want to thank him for all of the conversations and guidance he has given me as my friend and unofficial mentor. I cannot overstate his value to the Chemistry and Chemical Engineering Division, or to the many students that get the chance to

interact with him.

One of the most important reasons I chose to come to Caltech for graduate school was the altogether wonderful people that I would get to study with in Chemical Engineering. Though the majority of them graduated (well) before me, I consider myself fortunate to have worked with such a fine group as them. I am truly lucky to have met and learned from people like Brendan Mack, Nick Brunelli, Yoshie Narui, Chris Alabi, Jim Van Deventer, Chase Beisel, and John McKeen. Thank you all for making Caltech such a wonderful place to be and learn.

These and many other friends enriched my life and helped me make it through the more difficult times in graduate school. Matt Jacob-Mitos and I left Rensselaer Polytechnic Institute as best friends, which is probably why he followed me out to the West Coast for school (albeit to a different university). I shudder to put this in writing lest he never let me live it down, but he is one of the brightest people I have ever met and he makes things fun. I owe him a great deal for supporting and continually encouraging my pursuit of a Ph.D. Additionally, Charlotte Mack has been a constant source of fun since I met her many years ago. She is a voice of comfort and inspiration, and her love of life and learning is contagious. I am so very grateful to her and her husband, Brendan, for all of their support through graduate school, my ongoing job search, and life in general. Other brilliant and wonderful friends like Sara Broadhead, Rick Tabor, Chris and Jessica Hansen, and Jackie Kopcsak have all helped me keep a healthy perspective by letting me think and talk about something other than science during all of the fun times we have gotten to spend together. To all of these great friends I give my love, admiration, and thanks.

I want to thank my wonderful family for their extraordinary support. My parents, David and Eileen, have always fostered my curiosity and joy for learning, but their love and encouragement has meant a great deal to me. They have worked so hard to make sure every possible educational opportunity was available to their children, from pre-kindergarten to this day. They have always given me the freedom to pursue my interests, even when that carried me 3000 miles away for graduate school. I am truly fortunate to have such caring and giving parents. I could not have accomplished any of this without their sacrifice and love. I want to thank them for all of this, and for raising me a Red Sox fan.

My entire family has helped me get to this point in my life. I want to thank, in particular, all of my grandparents for being such wonderful examples of how people should treat each other and approach their lives and their work. They are and were passionate individuals, and I love them very much.

Thank you, also, to my brother, David, for always backing me up and helping me to persevere through his encouragement and love. You are the best big brother and friend anybody could have.

Finally, I want to thank my wonderful wife, Ashley. Everything in my life improved when I met you. There is no way I can thank you enough for the sacrifices you have made or the lengths to which you have gone to help me on this (regrettably) long road to graduation. You are an extraordinary woman who volunteered to live the lavish life of a graduate student's wife. I still do not understand what saintly feat I must have accomplished to deserve you, but I am grateful everyday because chance sat me next to you on that airplane. Thank you so very much.



# Abstract

Whispering gallery mode (WGM) optical resonator sensors have emerged as promising tools for label-free detection of biomolecules in solution. These devices have even demonstrated single-molecule limits of detection in complex biological fluids. This extraordinary sensitivity makes them ideal for low-concentration analytical and diagnostic measurements, but a great deal of work must be done toward understanding and optimizing their performance before they are capable of reliable quantitative measurements. The present work explores the physical processes behind this extreme sensitivity and how to best take advantage of them for practical applications of this technology.

I begin by examining the nature of the interaction between the intense electromagnetic fields that build up in the optical biosensor and the biomolecules that bind to its surface. This work addresses the need for a coherent and thorough physical model that can be used to predict sensor behavior for a range of experimental parameters. While this knowledge will prove critical for the development of this technology, it has also shone a light on nonlinear thermo-optical and optical phenomena that these devices are uniquely suited to probing.

The surprisingly rapid transient response of toroidal WGM biosensors despite sub-femtomolar analyte concentrations is also addressed. The development of asymmetric boundary layers around these devices under flow is revealed to enhance the capture rate of proteins from solution compared to the spherical sensors used previously. These lessons will guide the design of flow systems to minimize measurement time and consumption of precious sample, a key factor in any medically relevant assay.

Finally, experimental results suggesting that WGM biosensors could be used to improve the quantitative detection of small-molecule biomarkers in exhaled breath condensate demonstrate how their exceptional sensitivity and transient response can enable the use of this noninvasive method to probe respiratory distress.

WGM biosensors are unlike any other analytical tool, and the work presented here focuses on answering engineering questions surrounding their performance and potential.

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