Causes and Consequences of Gene Expression Noise

Thesis by

Chiraj K. Dalal

In Partial Fulfillment of the Requirements for the degree of

Doctor of Philosophy

CALIFORNIA INSTITUTE OF TECHNOLOGY

Pasadena, California

2010

(Defended July 21, 2009)

© 2010

Chiraj K. Dalal

All Rights Reserved

ACKNOWLEDGEMENTS

One of the things I have never understood about life as a graduate student was the graduation itself. You're supposed to stand at a podium and present your results, defending that the work you have done is worthy of a degree. The part I don't understand is the practice of a single person presenting their own results. I haven't been doing lab work very long, but as far as I can tell, it is very rare for a single person to generate their own results. Scientific ideas are the result of interaction, discussion and inspiration, usually divided up into several small conversations with a wide variety of people including oneself. Experiments are usually done after someone has shown you how to do bench work, how to use equipment, and how to analyze data. The process is not easy and it takes a lot of time, but more importantly, it takes a lot of help. The most important ingredient then, of course, is to work in an environment which is conducive to discussion and education.

I was incredibly lucky to work in a lab where such an environment was fostered and I think all the credit for that must go to my advisor, Michael Elowitz, and my labmates throughout the years for their innumerable implicit contributions to this work. I want to start by thanking what I refer to as the 1st generation labowitzers, Jonathan Young, Sidney Cox and Gurol Suel for helping to set the tone and culture of the laboratory. Ensuing members of the lab, David Sprinzak, Avigdor Eldar, Joe Levine, Shaunak Sen, Randall Wald, Michelle Fontes & Georg Seelig, added diversity to the lab, slowly making it more multilingual and multicellular. As the lab grew, so did our competence in several biological systems, and having members such as Fred Tan, Lauren LeBon, John Yong, Leah Santat, Julia Tischler, Long Cai, James Locke, Rajan Kulkarni, Murat Acar and Amit Lakhanpal to bounce ideas off of was incredibly useful. In addition to the educational and open environment, the lab was also a hub of fun and time-wasting activities. I think a special note should be made to Joe Levine and Jon Young for propagating such activities. In a similar vein, I think it's only fair to thank our neighboring labs, especially the Pierce lab for their patience and tolerance.

Additionally, I would also like to specifically thank members of other labs and facilities at Caltech for all their help in helping me get certain projects started. Most notably, I would like to thank Rochelle Diamond of the flow cytometry facility for teaching me flow cytometry, Robert Oania of the Deshaies lab for helping getting started with yeast genetics, Allison Ross for making sure all my paperwork was up to date and Ernesto Mercado, for nourishment. Of course, I would also like to thank my thesis committee, Professors Scott Fraser, Paul Sternberg and Barbara Wold, for generously spending time with me, and giving me constructive criticism about both science and graduate school itself.

Of course, most of the work described was part of a collaboration. Dr. David Sprinzak helped quite a bit with the analytic model described in chapter 1. Dr. Long Cai was my partner in crime for the works described in Chapters 3 and 4. Kasra Rahbar, a SURF student, also helped with the work described in Chapter 4 and Appendix C. It is absolutely critical for me to thank all of them for their hard work that contributed towards the described work.

Yet, despite having a strong support system in lab, on campus and amongst collaborators, graduate school is still hard because no matter how many experiments you do, it is virtually guaranteed that 73% of them will utterly fail. In this case, it is nice to have a support system outside of the lab which enables sanity. For that, I have to thanks my family, especially my parents and sister Radha, all of whom are local, as well as various friends, including Ming Gu, Steven Kuntz, Michael Krout, Ryan Zeidan, and Habib Ahmad, for their helps in keeping me engaged in other disciplines, especially in sports, where I was a member of two IM sports teams on campus, Playmakers, in football, and How we Roll, in basketball. Both activities were absolutely vital in getting me out of the lab, a critical ingredient to getting me to this stage.

Finally, I'd like to thank Pa Ra Ma, a nickname for someone who is incredibly dear and important to me, for whom I have no words to describe, to whom I owe everything.