

Carolina Tropini

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EDUCATION

Sept 08 -	PhD Biophysics, Stanford University, California, US. (GPA: 3.9/4.0) Stanford Graduate Fellow
Jun - Jul 11	Physiology Summer Course, Marine Biological Laboratory (MBL), Woods Hole, Massachusetts, US.
Jun 09-Jul 09	Summer Institute for Entrepreneurship, Stanford University, California, US.
Sep 03-Apr 08	Honors Biophysics, University of British Columbia (UBC), Vancouver, BC. (GPA: 3.8/4.0) Science One program – <i>interdisciplinary small-class first year program</i>
Sep 01 - Jun 03	Prince of Wales Secondary School, Vancouver, BC.
Sep 98 - Jul 01	Liceo Scientifico Giolitti, Bra, (CN) Italy.

AWARDS AND SCHOLARSHIPS

May 11 -	Bruce and Elizabeth Dunlevie Bio-X Stanford Interdisciplinary Graduate Fellowship	Stanford
Mar 08-Aug 11	Stanford Graduate Fellowship	Stanford
Jun - Jul 11	Physiology Summer Course Award	MBL
Mar 10, Jun 09	Bio-X Student Travel Fellowship award	Stanford
Jun 09	FEBS-EMBO lecture course travel award	
Apr 08	Science Service Award – <i>for contributions as the Biophysics students society president and for starting a research seminar series for undergraduates (AIS)</i>	UBC
Apr 08	Arthur Crooker Prize – <i>best experimental physics student 2008</i>	UBC
Dec 07	Thomas and Evelyn Hebb Memorial Scholarship - <i>academic excellence in physics</i>	UBC
Nov 07	Wesbrook Scholarship - <i>UBC's most prestigious designation awarded to senior students with outstanding academic performance, leadership, and involvement in community activities.</i>	UBC
Oct 07	Trek Excellence Scholarship – <i>top 5% of faculty of Science</i>	UBC
Sept 07	Charles and Jane Banks Scholarship	UBC
Sept 06-Apr 08	UBC Science Scholar for outstanding academic achievement	UBC

Summer 07	NSERC undergraduate scholarship research award	UBC
Winter 06-07	Dean of Science Scholarship	UBC
Sept 03-Apr 08	Dean's Honor List: Faculty of Science	UBC
May 04	British Columbia Government Scholarship	UBC
May 04	Larry Roberts Science One Memorial Scholarship	UBC

PUBLICATIONS

Peer Reviewed

C. Tropini and A. Marziali, "Multi-nanopore force spectroscopy for DNA analysis" Vol 92 1632-1637. March 2007, *Biophysical Journal*.

M. Wiggin, **C. Tropini**, V. Tabard-Cossa and A. Marziali, "Non-exponential kinetics of DNA escape from alpha-hemolysin nanopores" Vol 95 Number 11: 5317-5323. December 2008, *Biophysical Journal*.

Y. E. Chen*, **C. Tropini***, K. Jonas, C. G. Tsokos, K. C. Huang, M. T. Laub "Spatial gradient of protein phosphorylation underlies replicative asymmetry in a bacterium" Vol 108 no. 3 1052-1057. January 2011, *PNAS*. ***Co-first author**

K. Heyries, **C. Tropini**, M. VanInsberghe, O.I. Petriv, C. Hugesman, A. Singhal, K. Leung, C.L. Hansen. "Megapixel Digital PCR", doi:10.1038/nmeth.1640, July 2011, *Nature Methods*.

C. Tropini, E. A. Roth, M. Zanic, M. K. Gardner and Jonathon Howard. "Islands Made from Slowly Hydrolyzable GTP Analogs Promote Microtubule Rescues". Vol 7 (1) e30103, *Plos One*.

C. Tropini and KC Huang. "Modeling the effects of changes in protein localization and abundance on development in the bacterium *Caulobacter crescentus*". In review, *Plos Computational Biology*.

H. H. Tuson, G. K. Auer, L. D. Renner, M. Hasebe, **C. Tropini**, M. Salick, W. C. Crone, A. Gopinathan, K. C. Huang, and D. B. Weibel. "Measuring the stiffness of bacterial cells from growth rates in hydrogels of tunable elasticity". In review, *Molecular Microbiology*.

In Preparation

C. Tropini, Naveed Rabbani and KC Huang. "Formation of gradients in bacterial cells". In preparation, to be submitted to *Biophysical Journal*.

EMPLOYMENT

Sept 09 -

Huang Lab, Bioengineering Department, Stanford, Prof. KC Huang

As my graduate thesis project, I am investigating the establishment and function of dynamic spatial localization in the development of the bacterium *Caulobacter crescentus*. Using a combination of mathematical modeling and time-lapse microscopy, we demonstrated that asymmetry in chromosome replication is controlled by a spatial gradient of the master cell-cycle regulator CtrA. This work suggests a novel mechanism for

intracellular organization via gradients of protein activity, and we have systematically evaluated the efficacy of different gradient generation mechanisms and proposed experimental assays for evaluating gradient robustness. This work has led to two manuscripts, one of which I am co-first author and the other I am first author and will soon be submitted to PLoS Computational Biology. This work has also led to four talks (two of which were invited) and three poster presentations.

In parallel, I am elucidating mechanisms for cell shape control in Gram-negative bacteria by employing a combination of biophysical modeling, bioinformatics, genetic manipulation, and single-cell microscopy. The experiments involve systematic transplantation and genetic manipulation of cytoskeletal elements between related rod-shaped Gram-negative bacteria with different sizes. We have successfully generated strains of rod-shaped bacteria similar to *Caulobacter* with a range of sizes, which we will use to assay the phenotypic relevance of size control in bacteria. Our future aims revolve around developing technologies to control intracellular localization, which will allow us to experimentally test our theoretical predictions of shape determination mechanisms.

Sept 06 - July 08

Hansen Lab, UBC Proteomics, UBC, Prof. Carl Hansen

As my undergraduate thesis project, I applied microfabrication and soft lithography techniques to develop, construct and test a microfluidic device capable of a million parallel digital PCR reactions for non-invasive detection of fetal Down syndrome.

Digital polymerase chain reaction (digital PCR) allows for the measurement of absolute target sequence abundance by partitioning a sample into many sub-reactions at limiting dilution followed by PCR amplification and endpoint detection to determine the fraction of empty chambers. When compared to real-time quantitative PCR (RT-qPCR), digital PCR can provide dramatic improvements in sensitivity, specificity and precision, making it ideally suited to demanding diagnostic applications. Current technologies for digital PCR are limited by shortcomings including high technical error, low single-molecule detection efficiency, high cost, complexity in analysis, and limited numbers of reactions.

For non-invasive detection of fetal Down syndrome, our approach involves PCR amplification of single DNA molecules on chip to detect trisomy of fetal chromosome 21 by analysis of maternal rather than fetal blood samples. In addition to the direct medical implications on Down syndrome detection, we were the first to demonstrate the general capability of running millions of simultaneous PCR reactions in picoliter reactors. I also further optimized our microfluidic digital PCR device for detection of low copy number variants, and I tested the technology for numerous applications such as the detection of 1% increase in gene copy number, rare SNP analysis and gene co-localization (BCR-ABL leukemia).

I designed and performed the research above as well as analyzed the data. I also wrote a manuscript (submitted to Nature Methods) and gave four talks on this work (including an invited conference talk and an invited industry seminar) and one poster presentation. I am also co-inventor on a licensed patent based on this work.

May 06–Aug 06**Stanford Genome Technology Center, Stanford University, Prof. Ron Davis, Dr. Mostafa Ronaghi.**

Based on my nanopore work in the Marziali lab at UBC (see below), I was hired at the Genome Center to provide instruction on new tools for organic nanopore analysis. Based on their single-molecule detection capabilities, we envisioned developing a nanopore tool for electrical detection of ELISA assays, allowing for unprecedented single-molecule sensitivity. At the Genome Center, I designed and performed experiments employing synthetic nanopores for detection and real-time analysis of proteins and other metabolites. To determine their utility, I investigated nanopore surface properties upon protein binding and modification of the nanopore materials. Electrical detection of ELISA was accomplished by employing nanoporous membranes.

In addition, I concurrently developed a second project involving detection of epigenetic markers with nanopores. DNA methylation plays an important role in transcriptional control; recent studies suggest that changes in methylation patterns are correlated with cancer development. Atypical methylation of DNA is frequently found in tumorous cells and is linked both to chromosome instability and inactivation of tumor suppressor genes. Currently available techniques for methylation detection are based on bisulphate treatments, which irreversibly change the DNA tested. Although these techniques may give cues to the presence of methylation, they cannot easily reveal the patterns associated with it. The technique I developed is based on the kinetic behavior of a DNA strand exiting a biological nanopore, which is affected by the methylation state of the DNA molecule. I gave one invited talk at an international conference and one poster presentation based on this work.

May 05–April 06**Applied Biophysics Lab, UBC, Prof. Andre Marziali.**

The need for low-cost DNA sequence detection in clinical applications is driving development of new technologies. Nanopores represent an ideal candidate, providing single-molecule detection and analytical capabilities achieved by electrophoretically driving molecules in solution through the pore. In the highly confined space, single nucleic acid polymers can be analyzed directly without amplification or labeling. However, a challenge faced by this technique is the time required to obtain statistically significant data.

To overcome this obstacle, I developed a technology for parallel measurements of DNA oligomer hybridization using a lipid membrane with multiple nanopores, as a precursor for a multi-nanopore synthetic DNA sequencer. This method allows for detection of mutations in a DNA sequence purely by electronic means, without the need for fluorescent labeling. Through this work I reduced the time required to obtain statistically significant data by more than 100-fold. My work was the first to demonstrate multi-nanopore force spectroscopy measurements that could be used for single nucleotide polymorphism detection. This work led to one manuscript on which I am the first author, and I was invited to speak at an international conference based on this work.

During my time in the Marziali lab, I also developed a new organic single-molecule nanosensor for DNA analysis. To test its efficacy, I measured the kinetics of DNA escape from the sensor against an electrostatic energy barrier. I also designed LabVIEW software for data acquisition and analysis that is currently being used in the Marziali lab for similar

nanosensor measurements. This work led to one published manuscript on which I am a co-author, and I gave one invited talk and one poster presentation based on this work.

INTELLECTUAL PROPERTY

C. Hansen and **C. Tropini** "Microfluidic device and method of using same."
PCT/CA2008/001985. November 2008.

A. Marziali, D. Broemeling, J. Pel, J. Thompson, J. Perkins, T. Willis, H. Heyneker, D. Gray and **C. Tropini** "Systems and methods for enhanced Scoda." PCT/CA2009/001648.
November 2009.

TALK PRESENTATIONS

"Control of cell width in bacteria" Bioengineering retreat, Santa Cruz, CA, October 2011.

"Spatial gradient of protein phosphorylation underlies replicative asymmetry in a *Caulobacter crescentus*" American Society for Microbiology Meeting, New Orleans, LA.
Invited, May 2011.

"Spatial gradient of protein phosphorylation underlies replicative asymmetry in a bacterium". Microbiology Research Series, Stanford University, Stanford, CA. March 2011.

"Modeling and engineering intracellular organization", UBC, Vancouver, Canada.
Biophysics Seminar, **Invited**, May 2010.

"The role of spatial asymmetries in the development of the bacterium *Caulobacter crescentus*." American Physical Society Meeting, Portland, OR. March 2010.

"Tradeoff between localization and expression levels in flagellar pole development of the bacterium *Caulobacter crescentus*". Molecular Biophysics Seminar, Stanford University, Stanford, CA. November 2009.

"The Beginning of the Ends: Localization of Lipids to Bacterial Poles". EMBO biomembranes conference, Cargese, Corsica, France. **Invited**. June 2008.

"MegaPixel Digital PCR for Non-Invasive Detection of Fetal Down's Syndrome." IDSSG Conference, Vancouver, Canada, **Invited**. May 2008.

Valedictorian graduation speech, UBC, May 2008.

"Mega-Pixel Digital PCR with Application to Non-invasive Detection of Fetal Down Syndrome" Thesis Defense, UBC, Vancouver, Canada, April 2008.

"Mega-Pixel Digital PCR with Application to Non-invasive Detection of Fetal Down Syndrome" MURC Conference, UBC, Vancouver, Canada, March 2008.

"Mega-Pixel Digital PCR" Fluidigm (Company presentation), California, **Invited**, September 2007.

"Detection of Epigenetic Sequence and Base Mutations Using Organic Nanopores", Hangzhou Genomic Conference, Hangzhou, China, **Invited**, October 2006.

“Electronic Detection of Functional Biomolecules”, Frontiers in Biophysics Conference, Loon Lake, October 2006.

“DNA, nanopores and the art of genome sequencing”, MURC Conference, UBC, Vancouver, Canada, March 2006.

“Escape Kinetics of DNA through an alpha-hemolysin nanopore”, UBC, Vancouver, Canada. Biophysics Seminar, *Invited*, December 2005.

POSTER PRESENTATIONS

C. Tropini, A. Stewart, D. Swem, M. Hidestrand, S. Sinha, Z. Gitai and K.C. Huang, “Exploring mechanisms for cell width control in Gram-negative bacteria with PALM and digital PCR”. Single Molecules Meet Systems Biology Conference, Janelia Farm Research Campus, Ashburn, VA. October 2011.

C. Tropini, Y. E. Chen, K. Jonas, C. G. Tsokos, M. T. Laub, K. C. Huang, “Spatial gradient of protein phosphorylation underlies replicative asymmetry in a bacterium”. BioX Symposium, Stanford, CA. March 2011 and September 2011.

C. Tropini, S. Sciochetti, A. Newton, KC Huang. “Tradeoff between localization and expression levels in flagellar pole development of the bacterium *Caulobacter crescentus*”. Physics2Life conference, Weizmann Institute, Rehovot Israel. May 2010.

C. Tropini, S. Sciochetti, A. Newton, KC Huang. “Tradeoff between localization and expression levels in flagellar pole development of the bacterium *Caulobacter crescentus*”. Biophysical Society Conference, San Francisco, CA. February 2010.

C. Tropini, KC Huang. “The Beginning of the Ends: Localization of Lipids to Bacterial Poles”. EMBO biomembranes conference, Cargese, Corsica, France. Poster selected for oral presentation. June 2008.

C. Tropini, J. Dueber, D. Endy. “State Output for Genetic Memory: Early Insights and Foundations.” SynBerc Conference, Berkeley, California, February 2009.

C. Tropini, C. Hansen. “MegaPixel Digital PCR for Non-Invasive Detection of Fetal Down's Syndrome.” ISPD Conference, Vancouver, British Columbia. June 2008.

C. Tropini, M. Wiggin, V. Tabard-Cossa, A. Atalasaz, M. Ronaghi and A. Marziali. “Detection of Epigenetic sequence mutation with organic nanopores”, Biophysical Society Meeting, Baltimore, March 2007.

C. Tropini, M. Wiggin, D. Trivedi and A. Marziali. “Anomalous Kinetics of DNA interaction with an organic nanopore”, AGBT Conference, Marco Island. February 2006.

M. Wiggin, **C. Tropini**, D. Trivedi, N. Jetha, D. Broemeling, and A. Marziali, "Kinetic Studies of DNA Escape from Nanopores", NHGRI grantee meeting, Marco Island, Florida, Feb 2006.

OTHER EXPERIENCE

Jan 11-May 11 **BMECS Conference organizer: fundraising and publicity coordinator.**

Jan 10-Mar 10 **Teaching assistant for undergraduate class “Physical biology of the cell”.**
Development of class material, class and tutorial teaching, grading.

- Sept 08 – Jan 09** **High School Tutor - EPATT.**
Volunteer tutor.
- April 09** **SPLASH - High school instructor.**
Designed and taught a high school course on molecular motors.
- May 08-July 08** **Dance Instructor, Dance 4 U.**
Ballroom dancing teacher – Intermediate level.
- April 07-April 08** **Biophysics Student Society President, UBC.**
Organizer and Creator of “Adventures in Science” seminar series.
Coordinator of UBC biophysics events and student society.
- Feb 07-Feb 08** **Welcome Women to Physics event coordinator, UBC.**
Organizer for the outreach event towards women in physics.
Group leader, laboratory tour guide.
- Jan-Mar 07** **Physics and Astronomy Outreach event, UBC.**
Volunteer for the Physics high school recruitment yearly event.
Laboratory tour guide.
- Mar 03-Jul 05** **Dunbar Community Centre, Vancouver, BC.**
Volleyball coach, activity organizer.

LANGUAGES

Italian, Intermediate French, Intermediate Spanish.

INTERESTS

Volleyball (Rated AA in the California Beach Volleyball Association, ranked 368th in California)
 Rock Climbing, Bouldering
 Ballroom Dancing (UBC, Silver Level) Ballet, Flamenco
 Tennis
 Golf
 Downhill skiing
 Horseback riding

REFERENCES

Available Upon Request.