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POSITIONS/APPOINTMENTS

Associate Professor, July 2017 – Present
Undergraduate Departmental Representative, July 2019 - Present
Assistant Professor**,** September 2010-June 2017
Department of Chemical and Biological Engineering (CBE), Princeton University

- Associated Faculty, Department of Molecular Biology (MOL), Princeton University
- Affiliated Faculty, Graduate Program in Quantitative and Computational Biology (QCB), Lewis Sigler Institute for Integrative Genomics, Princeton University
- Affiliated Faculty, Global Health Program, Center for Health and Well Being, Woodrow Wilson School, Princeton University

Postdoctoral Research Associate, August 2008-August 2010
Howard Hughes Medical Institute
Department of Biomedical Engineering, Boston University

- Advisor: Professor James J. Collins

EDUCATION

Ph.D., Chemical Engineering, September 2008
University of California, Los Angeles (UCLA)

- Thesis: "Transcription network analysis with application to biofuel toxicity of *Escherichia coli*"
- Advisor: Professor James C. Liao

B.S., Chemical Engineering (Highest Honors), May 2002
Rutgers University, New Brunswick

- James J. Slade Scholar

HONORS AND AWARDS

- American Institute of Chemical Engineers, Division 15C Chair, 2020
- Princeton Engineering Council, Excellence in Teaching Award, 2016
- NSF CAREER Award, 2015-2020
- Howard B. Wentz, Jr. Junior Faculty Award, 2015
- UCLA Dissertation Year Fellowship, 2007-2008
- UCLA Quality of Graduate Education Stipend, 2006
- Arco Graduate Student Fellowship, 2006
- Merck Poster Award, Metabolic Engineering V: Genome to Product conference, 2004
- California NanoSystems Institute (CNSI) Graduate Student Fellowship, 2002-2003

RESEARCH INTERESTS

The overarching goal of my research group is to improve the performance of current antibiotics and identify targets for novel anti-infectives. My group seeks to accomplish this by using computational and experimental techniques in systems biology and metabolic engineering to develop novel, fundamental understanding of the molecular mechanisms and networks pathogens use to thwart immune antimicrobials and antibiotics. The phenomena we study are bacterial persistence and bacterial responses to the immune antimicrobials, $NO\cdot$ and H_2O_2.

PUBLICATIONS

57) Sivaloganathan DM, Wan X, **Brynildsen MP**. Quantifying nitric oxide flux distributions. *Methods in Molecular Biology*, 2020; 2088:161-188.

56) Mok WWK, **Brynildsen MP**. Nutrient depletion and bacterial persistence. *Persister cells and infectious disease*, 2019 Nov 14, pp 99-132.

55) Aedo SJ, Orman MA, **Brynildsen MP**. Stationary phase persister formation in *Escherichia coli* can be suppressed by piperacillin and PBP3 inhibition. *BMC Microbiology*, 2019 Jun 24; 19:140.

54) Adolfsen KJ, **Brynildsen MP**. Anti-virulence therapies through potentiating ROS in bacteria. *Bacterial Resistance to Antibiotics – from Molecules to Man*, 2019 Mar 14; 10:239-254.

53) Mok WWK, **Brynildsen MP**. Resistance and tolerance to aminoglycosides. *Bacterial Resistance to Antibiotics – from Molecules to Man*, 2019 Mar 14; 4:81-100.

52) Adolfsen KJ, Chou WK, **Brynildsen MP.** Transcriptional regulation contributes to prioritized detoxification of hydrogen peroxide over nitric oxide. *Journal of Bacteriology*, 2019 Jun 21;201(14).

51) Balaban NQ, Helaine S, Lewis K, Ackermann M, Aldridge B, Andersson DI, **Brynildsen MP**, Bumann D, Camilli A, Collins JJ, Dehio C, Fortune S, Ghigo JM, Hardt WD, Harms A, Heinemann M, Hung DT, Jenal U, Levin BR, Michiels J, Storz G, Tan MW, Tenson T, Van Melderen L, Zinkernagel A. Definitions and guidelines for research on antibiotic persistence. *Nature Reviews Microbiology*, 2019 Jul;17(7):441-448.

50) Barrett TC, Mok WWK, Murawski AM, **Brynildsen MP**. Enhanced antibiotic resistance development from fluoroquinolone persisters after a single exposure to antibiotic. *Nature Communications*, 2019 Mar 12;10(1):1177.

49) Aedo SJ, Ma HR, **Brynildsen MP**. Checks and balances with use of the Keio collection for phenotype testing. *Methods in Molecular Biology*, 2019; 1927:125-138.

48) Chou WK, **Brynildsen MP**. Loss of DksA leads to multi-faceted impairment of nitric oxide detoxification by *Escherichia coli*. *Free Radical Biology and Medicine,* 2019 Jan;130:288-296..

47) **Brynildsen MP.** Nitric oxide stress as a metabolic flux. *Advances in Microbial Physiology*, 2018;73:63-76.

46) Mok WWK, **Brynildsen MP**. Timing of DNA damage responses impacts persistence to fluoroquinolones. *Proc Natl Acad Sci U S A*, 2018 Jul 3;115(27):E6301-E6309.

45) Aedo SJ, Gelderman G, **Brynildsen MP**. Tackling host-circuit give and take. *Nature Microbiology,* 2017 Dec;2(12):1584-1585.

44) Sacco SA, Adolfsen KJ, **Brynildsen MP**. An integrated network analysis identifies how ArcAB enables metabolic oscillations in the nitric oxide detoxification network of *Escherichia coli*. *Biotechnology Journal*, 2017 Aug;12(8).

43) Barrett TC, Mok WWK, **Brynildsen MP**. Biased inheritance protects older bacteria from harm. *Science*, 2017 April 21;356(6335):247-248.

42) Robinson JL, Jaslove JM, Murawski AM, Fazen CH, **Brynildsen MP**. An integrated network analysis reveals that nitric oxide reductase prevents metabolic cycling of nitric oxide by *Pseudomonas aeruginosa*. *Metabolic Engineering*, 2017 Mar 29;41:67-81.

41) Mok WWK, **Brynildsen MP**. An orphan riboswitch unveils guanidine regulation in bacteria. *Molecular Cell*, 2017 Jan 19;65(2):205-206.

40) Chou WK, **Brynildsen MP**. A biochemical engineering view of the quest for immune-potentiating anti-infectives. *Current Opinion in Chemical Engineering*, 2016 Nov; 14, 82-92.

39) Robinson JL, **Brynildsen MP**. Ensemble modeling enables quantitative exploration of bacterial nitric oxide stress networks. *Stress and Environmental Regulation of Gene Expression and Adaptation in Bacteria*, 2016 Aug 12;17.6:1009-1014.

38) Amato SM, **Brynildsen MP**. Mechanisms of stress-activated persister formation in *Escherichia coli*. *Stress and Environmental Regulation of Gene Expression and Adaptation in Bacteria*, 2016 Aug 12;6.3:446-453.

37) Gowers GF, Robinson JL, **Brynildsen MP**. Starved *Escherichia coli* preserve reducing power under nitric oxide stress. *Biochem Biophys Res Commun.,* 2016 Jul 15;476(1):29-34.

36) Henry TC, **Brynildsen MP**. Development of PersisterFACSeq: a method to massively parallelize quantification of persister physiology and its heterogeneity. *Scientific Reports*, 2016 May 4;6:25100.

35) Henry TC, **Brynildsen MP**. Quantifying current events identifies a novel endurance regulator. *Trends in Microbiology*, 2016 May;24(5):324-6.

34) Robinson JL, **Brynildsen MP**. Discovery and dissection of metabolic oscillations in the nitric oxide response network of *Escherichia coli*. *Proc Natl Acad Sci U S A*, 2016 Mar 22;113(12):E1757-66.

33) Robinson JL, **Brynildsen MP**. Construction and experimental validation of a quantitative kinetic model of nitric oxide stress in enterohemorrhagic *Escherichia coli* O157:H7. *Bioengineering,* 2016 Feb 6, 3(1),9.

32) Orman MA, **Brynildsen MP**. Persister formation in *Escherichia coli* can be inhibited by treatment with nitric oxide. *Free Radical Biology and Medicine*, 2016 Feb 2;93:145-154.

31) Orman MA, Henry TC, DeCoste CJ, **Brynildsen MP**. Analyzing persister physiology with fluorescence activated cell sorting. *Methods in Molecular Biology*, 2016;1333:83-100.

30) Sandvik EL, Fazen CH, Henry TC, Mok WWK, **Brynildsen MP**. Non-monotonic survival of *Staphylococcus aureus* with respect to ciprofloxacin concentration arises from prophage-dependent killing of persisters. *Pharmaceuticals*, 2015 Nov 17, 8, 778-792.

29) Mok WWK, Park JO, Rabinowitz JD, **Brynildsen MP**. RNA futile cycling in model persisters derived from MazF accumulation. *mBio*, 2015 Nov 17, 6(6):e01588-15.

28) Adolfsen KJ, **Brynildsen MP**. A kinetic platform to determine the fate of hydrogen peroxide in *Escherichia coli*. *PLoS Comput. Biol.*, 2015 Nov 6;11(11):e1004562.

27) Volzing KG, **Brynildsen MP**. Stationary-phase persisters to ofloxacin sustain DNA damage and require repair systems only during recovery. *mBio*, 2015 Sep 1;6(5).

26) Amato SM, **Brynildsen MP**. Persister heterogeneity arising from a single metabolic stress. *Current Biology*, 2015 Aug 17;25(16):2090-8.

25) Orman MA, **Brynildsen MP**. Inhibition of stationary phase respiration impairs persister formation in *E. coli*. *Nature Communications*, 2015 Aug 6;6:7983.

24) Robinson JL, **Brynildsen MP**. An ensemble-guided approach identifies ClpP as a major regulator of transcript levels in nitric oxide-stressed *Escherichia coli*. *Metabolic Engineering,* 2015 Sep;31:22-34.

23) Mok WWK, Orman MA, **Brynildsen MP**. Impacts of global transcriptional regulators on persister metabolism. *Antimicrob Agents Chemother.*, 2015 May;59(5):2713-9.

22) Adolfsen KJ, **Brynildsen MP**. Futile cycling increases sensitivity toward oxidative stress in *Escherichia coli*. *Metabolic Engineering,* 2015 May;29:26-35.

21) Orman MA, Mok WWK, **Brynildsen MP**. Aminoglycoside-enabled elucidation of bacterial persister metabolism. *Curr. Protoc. Microbiol.* 2015 Feb; 36:17.9.1-17.9.14.

20) Robinson JL, Miller RV, **Brynildsen MP**. Model-driven identification of dosing regimens that maximize the antimicrobial activity of nitric oxide. *Metabolic Engineering Comm.,* 2014 Dec; 1:12-18.

19) Robinson JL, Adolfsen KJ, **Brynildsen MP**. Deciphering nitric oxide stress in bacteria with quantitative modeling. *Curr Opin Microbiol.,* 2014 Jun; 19C:16-24.

18) Amato SM, **Brynildsen MP**. Nutrient transitions are a source of persisters in *Escherichia coli* biofilms. *PLoS One*, 2014 Mar 25;9(3):e93110.

17) Amato SM, Fazen CH, Henry T, Mok WWK, Orman MA, Sandvik EL, Volzing KG, **Brynildsen MP**. The role of metabolism in bacterial persistence. *Frontiers in Microbiology*, 2014 Mar 3;5:70.

16) Orman MA, **Brynildsen MP**. Establishment of a method to rapidly assay bacterial persister metabolism. *Antimicrob Agents Chemother.,* 2013 Sep;57(9):4398-409.

15) Orman MA, **Brynildsen MP**. Dormancy is not necessary or sufficient for bacterial persistence. *Antimicrob Agents Chemother.,* 2013 Jul;57(7):3230-9.

14) Robinson JL, **Brynildsen MP**. A kinetic platform to determine the fate of nitric oxide in *Escherichia coli*. *PLoS Comput Biol.,* 2013 May;9(5):e1003049.

13) Amato SM, Orman MA, **Brynildsen MP**. Metabolic control of persister formation in *Escherichia coli*. *Molecular Cell,* 2013 May 23;50(4):475-87.

12) **Brynildsen MP**, Winkler JA, Spina K, MacDonald IC, Collins JJ. Potentiating antibacterial activity by predictably enhancing endogenous microbial ROS production. *Nature Biotechnology*, 2013 Feb; 31(2):160-5.

11) Allison KR, **Brynildsen MP**, Collins JJ. Heterogeneous bacterial persisters and engineering approaches to eliminate them. *Curr Opin Microbiol.,* 2011 Oct;14(5):593-8.

10) Allison KR, **Brynildsen MP**, Collins JJ. Metabolite-enabled eradication of bacterial persisters by aminoglycosides. *Nature*, 2011 May 12; 473(7346):216-20.

9) **Brynildsen MP**, Liao JC. An integrated network approach identifies the isobutanol response network of *Escherichia coli*. *Molecular Systems Biology*, 2009; 5:277.

8) **Brynildsen MP**, Collins JJ. Systems biology makes it personal. *Molecular Cell*, 2009 Apr 24;34(2):137-8.

7) Atsumi S, Cann AF, Connor MR, Shen CR, Smith KM, **Brynildsen MP**, Chou KJ, Hanai T, Liao JC. Metabolic engineering of *Escherichia coli* for 1-butanol production. *Metabolic Engineering*, 2008 Nov;10(6):305-11.

6) **Brynildsen MP**, Wu TY, Jang SS, Liao JC. Biological network mapping and source signal deduction. *Bioinformatics*, 2007 Jul 15;23(14):1783-91.

5) **Brynildsen MP**, Tran LM, Liao JC. A Gibbs sampler for the identification of gene expression and network connectivity consistency. *Bioinformatics,* 2006 Dec 15;22(24):3040-6.

4) **Brynildsen MP**, Tran LM, Liao JC. Versatility and connectivity efficiency of bipartite transcription networks. *Biophys J*, 2006 Oct 15;91(8):2749-59.

3) **Brynildsen MP**, Wong WW, Liao JC. Transcriptional regulation and metabolism. *Biochem Soc Trans*, 2005 Dec;33(Pt 6):1423-6.

2) Yang YL, Suen J, **Brynildsen MP**, Galbraith S, Liao JC. Inferring yeast cell cycle regulators and interactions using transcription factor activities. *BMC Genomics*, 2005 Jun 10;6(1):90.

1) Tran LM, **Brynildsen MP**, Kao KC, Suen JK, Liao JC. gNCA: A framework for determining transcription factor activity based on transcriptome: Identifiability and numerical implementation. *Metabolic Engineering*, 2005 Mar;7(2):128-41.

INVITED TALKS

40) Allen Institute, Paul G. Allen Frontiers Group Symposium on Modeling of Biological Systems: "Toward next-generation antibiotics: Systems-level dissection of bacterial responses to phagosomal stressors", July 2019, Seattle, WA.

39) Princeton University, Office of Undergraduate Research, Summer Research Colloquium: Mentoring Workshop, July 2019, Princeton, NJ.

38) Weill Cornell Medical College, Weill Family Foundation Global Health Research Laboratories Symposium on Microbial Systems Biology: "Toward next-generation antibiotics: Systems-level dissection of bacterial nitric oxide stress networks", May 2018, New York, NY.

37) Rutgers University, Department of Chemical and Biochemical Engineering: Graduate Student Organization Career Event: Careers in Academia, March 2018, New Brunswick, NJ.

36) Dartmouth College, Department of Microbiology and Immunology at Geisel School of Medicine: "Toward knowing thy enemy: investigations of bacterial persister physiology", March 2018, Hanover, NH.

35) University of Pittsburgh, Department of Chemical and Petroleum Engineering: "Toward next-generation antibiotics: Systems-level dissection of bacterial nitric oxide stress networks", February 2018, Pittsburgh, PA.

34) Google X: "Toward next-generation antibiotics: Systems-level dissection of bacterial nitric oxide stress networks", January 2018, Mountain View, CA.

33) Colorado State University, Department of Chemical and Biological Engineering: "Toward next-generation antibiotics: Systems-level dissection of bacterial nitric oxide stress networks", October 2017, Fort Collins, CO.

32) Rutgers New Jersey Medical School, Molecular Biology, Genetics and Cancer Program: "Toward knowing thy enemy: investigations of bacterial persister physiology", September 2017, Newark, NJ.

31) Department of Defense and NASA Joint Biology Workshop: "Investigating the metabolic mechanisms of bacterial persistence", August 2017, Mountain View, CA.

30) Federation of European Microbiological Societies, 7th Congress: "Toward knowing thy enemy: investigations of bacterial persister physiology", to be presented in July 2017, Valencia, Spain.

29) Tufts University, Department of Chemical and Biological Engineering: "Looking to metabolism in order to revitalize our antibiotic medicine cabinet", to be presented in April 2017, Medford, MA.

28) University of Michigan School of Medicine, Department of Biological Chemistry: "Looking to metabolism in order to revitalize our antibiotic medicine cabinet", to be presented in March 2017, Ann Arbor, MI.

27) Dartmouth College, a course entitled Microbial Physiology and Metabolic Engineering: "A Health Application of Metabolic Engineering", February 2017, a webinar.

26) University of Virginia, Department of Chemical Engineering: "Toward next-generation antibiotics: Model-guided dissection of bacterial nitric oxide stress networks", December 2016, Charlottesville, VA.

25) University of Colorado, Boulder, Department of Chemical and Biological Engineering: "Toward next-generation antibiotics: Model-guided dissection of bacterial nitric oxide stress networks", November 2016, Boulder, CO.

24) University of Delaware, Center of Computation Biology and Bioinformatics: "Looking to metabolism in order to revitalize our antibiotic medicine cabinet", October 2016, Newark, DE.

23) Princeton University, Department of Chemical and Biological Engineering: "Looking to metabolism in order to revitalize our antibiotic medicine cabinet", September 2016, Princeton, NJ.

22) Institut Pasteur, Department of Microbiology: "Toward knowing thy enemy: investigations of bacterial persister physiology", September 2016, Paris, France.

21) Université libre de Bruxelles, Institute of Molecular Biology and Medicine: "Toward knowing thy enemy: investigations of bacterial persister physiology", September 2016, Brussels, Belgium.

20) Stanford University School of Medicine, Frontiers in Quantitative Biology Seminar Series: "Metabolic engineering to potentiate immunity and discover new antivirulence targets", April 2016, Palo Alto, CA.

19) Villanova University, Department of Biology: "Toward knowing thy enemy: investigations of bacterial persister physiology", December 2015, Villanova, PA.

18) Merck Research Laboratories: "Metabolic mechanisms of antibacterial failure", December 2015, Kenilworth, NJ.

17) American Institute of Chemical Engineering Annual Meeting: "An engineering approach to discover novel antivirulence strategies," November 2015, Salt Lake City, UT.

16) KU Leuven, Department of Microbial and Molecular Systems: "Toward knowing thy enemy: investigations of bacterial persister physiology," November 2015, Leuven, Belgium.

15) University of Maryland, College Park, Department of Cell Biology and Molecular Genetics: "Metabolic mechanisms of antibacterial failure", October 2015, College Park, MD.

14) University of Texas, Austin, Department of Chemical Engineering: "Metabolic engineering to discover novel antivirulence strategies", August 2015, Austin, TX.

13) Biochemical and Molecular Engineering XIX Conference (ECI): "An engineering approach to identify antivirulence strategies", July 2015, Puerto Vallarta, Mexico.

12) University of Pennsylvania, Center for Targeted Therapeutics and Translational Nanomedicine: "An engineering approach to identify antivirulence strategies", April 2015, Philadelphia, PA.

11) Stevens Institute of Technology, Department of Chemical Engineering and Material Science: "An engineering approach to identify antivirulence strategies", February 2015, Hoboken, NJ.

10) Massachusetts Institute of Technology, Department of Chemical Engineering: "An engineering approach to identify antivirulence strategies", November 2014, Cambridge, MA.

9) Metabolic Engineering X Conference (iMES): "Metabolic strategies to enhance the toxicity of nitric oxide in pathogens", June 2014, Vancouver, Canada.

8) Ribosome and Antibiotics Conference (University of Tartu): "Bacterial persistence: a metabolically stimulated state", June 2014, Tartu, Estonia.

7) Syracuse University, Department of Biomedical and Chemical Engineering: "Metabolism and its role in bacterial persistence", April 2014, Syracuse, NY.

6) Harvard University, Center for Systems Biology: "Engineering approaches to discover next generation antibiotics", March 2014, Cambridge, MA.

5) University of Nebraska Medical Center, Basic Science Seminar Series: "Metabolism and its role in bacterial persistence", February 2014, Omaha, NE.

4) Interscience Conference on Antimicrobial Agents and Chemotherapy (ASM): "Antivirulence therapies from emergent systems properties", September 2013, Denver, CO.

3) Rutgers University, New Brunswick, Biomedical Engineering Society: "Combating antibiotic failure: Engineering approaches to develop next generation antimicrobials", April 2012, New Brunswick, NJ.

2) Rutgers University, New Brunswick, Department of Chemical and Biochemical Engineering: "Combating antibiotic failure: Engineering approaches to develop next generation antimicrobials", December 2011, New Brunswick, NJ.

1) Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Controls in Synthetic Biology Symposium: "Metabolic engineering to potentiate immunity", September 2011, Boston, MA.

CONTRIBUTED PRESENTATIONS

10) American Chemical Society National Meeting: "Prioritized detoxification of toxic metabolites by *Escherichia coli*," to be delivered March 2020, Philadelphia, PA. (talk)

9) Gordon Research Conference on Phagocytes: "Prioritized detoxification of immune antimicrobials by *Escherichia coli*," June 2019, Waterville Valley, NH. (poster)

8) International Conference on Biomolecular Engineering: "A metabolic engineering approach to realize nitric oxide-potentiating anti-infectives," January 2017, San Diego, CA. (talk)

7) American Institute of Chemical Engineering Annual Meeting: "Quantitative dissection of bacterial nitric oxide stress networks", November 2016, San Francisco, CA. (talk)

6) European Symposium on Biochemical Engineering Sciences: "A metabolic engineering approach to discover next-generation antibiotics", September 2016, Dublin, Ireland. (talk)

5) Metabolic Engineering XI Conference (iMES): "Toward next-generation antibiotics: Model-guided dissection of bacterial nitric oxide stress networks", June 2016, Kobe, Japan. (talk)

4) American Chemical Society National Meeting: "Discovery and deconstruction of oscillations in the nitric oxide stress network of *Escherichia coli*", March 2016, San Diego, CA. (talk)

3) International Conference on Biomolecular Engineering: "Ensemble modeling identifies how ClpP impacts NO• defenses in *E. coli*", January 2015, Lost Pines, TX. (poster)

2) Gordon Research Conference on Microbial Stress Response: "Metabolic control of persister formation", July 2012, South Hadley, MA. (poster)

1) Biochemical and Biomolecular Engineering XVII (ECI): "Metabolic engineering to potentiate immunity", June 2011, Seattle, WA. (poster)

PATENTS

3) *Compositions and methods to boost endogenous ROS production from bacteria*, Collins JJ, **Brynildsen MP**, Winkler JA, Spina C. US Patent Application 20150071904.

2) *Proton-motive force stimulation to potentiate aminoglycoside antibiotics against persistent bacteria*, Collins JJ, Allison KR, **Brynildsen MP**. US Patent Application 20150366889.

1) *Butanol production by recombinant microorganisms*, Liao JC, Atsumi S, **Brynildsen MP,** Cann AF, Chou KJ, Shen CR, Smith KM, Hanai T, Connor MR. US Patent Application 20090111154.