BIOGRAPHICAL SKETCH

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NAME: Mayalu, Michaëlle Ntala

eRA COMMONS USER NAME (credential, e.g., agency login): MAYALUM

POSITION TITLE: Assistant Professor of Mechanical Engineering

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology	B.S	06/2010	Mechanical Engineering
Massachusetts Institute of Technology	M.S	06/2012	Mechanical Engineering
Massachusetts Institute of Technology	Ph.D.	06/2017	Mechanical Engineering
California Institute of Technology	Postdoctoral	03/2022	Computing and Mathematical Sciences

A. Personal Statement

My group's research focuses on model-based analysis, design, and control of biological function at the molecular, cellular, and organismal levels to optimize therapeutic intervention. We are an interdisciplinary group of engineers interested in the advancement of healthcare treatment technologies using mathematical models to elucidate useful latent trends and/or principles that might underlie relevant biological phenomena. In particular, developing more accurate and efficient modeling frameworks that incorporate computation, dynamical systems, and control theory may become more widespread and impactful in the design of electro-mechanical and/or biological therapeutic machines. The crossover between control theoretic, biological and healthcare viewpoints is the fundamental strength of our projects.

My postdoctoral training involved collaborations between the Elowitz (Caltech), Pierce(Caltech), Doyle(Caltech) and Murray(Caltech) labs on robust multi-layer control systems for cooperative cellular behaviors. I published several papers based on this research including a co-authored paper with the Elowitz lab that was published in the journal Cell. In an additional collaboration with the Hsiao (UCLA), Doyle, Ismagilov(Caltech), Murray, Liberles(HMS), and Chervonsky(UChicago) I conceived a systems level mathematical framework of the microbiome-gut-brain axis to increase conceptual understanding of how gut, vagus nerve, immune and vascular subsystems contribute to optimal cognitive performance. These were great experiences on how to collaborate with biologists to bridge theory with implementation.

Now as a faculty member in the department of Mechanical Engineering at Stanford University, I am continuing to pursue my research goals of understanding, controlling, and predicting response of biological systems with respect to healthcare while teaching and mentoring the next generation of scientists and engineers. My training in both experimental and computational methods along with my expertise in identifying control theoretical principles of biological processes drives the my group's mission to investigate open questions in the design and implementation of engineered cell, bio-mechanical and bio-electrical healthcare treatment technologies. Specific goals include synthetic bacterial "microrobots" for preemptive and targeted therapeutic intervention, and multi-scale modeling of gut-associated skin disorders.

Relevant publications:

- Huang, Y. and **Mayalu, M.N.** (2023). Biomolecular Control Circuit With Inherent Bi-Stability Is Applicable for Automatic Detection of Gut Infection. IEEE Control Systems Letters 7, 2251–2256. 10.1109/LCSYS.2023.3285766.
- Ma, Y., Budde, M.W., **Mayalu, M.N.**, Zhu, J., Lu, A.C., Murray, R.M., and Elowitz, M.B. (2022). Synthetic mammalian signaling circuits for robust cell population control. Cell 185, 967-979.e12. 10.1016/j.cell.2022.01.026.
- **Mayalu, M.N.**, Sarma, A., Xiao, F., Doyle, J.C., and Murray, R.M. (2021). Systems Level Model of Dietary Effects on Cognition via the Microbiome-Gut-Brain Axis. In 2021 European Control Conference (ECC), pp. 312–318. 10.23919/ECC54610.2021.9655216.
- **Mayalu, M.N.**, Mehta, H., and Murray, R.M. (2019). Model of Paradoxical Signaling Regulated T-Cell Population Control for Design of Synthetic Circuits. In 2019 18th European Control Conference (ECC), pp. 2152–2158. 10.23919/ECC.2019.8795764.
- **Mayalu, M.N.**, Kim, M.-C., and Asada, H.H. (2019). Multi-Cell ECM compaction is predictable via superposition of nonlinear cell dynamics linearized in augmented state space. PLoS computational biology 15, e1006798.

B. Positions, Scientific Appointments, and Honors

Employment

2022 -	*Assistant Professor of Mechanical Engineering*, Stanford University, Stanford, CA
2018	*Adjunct Assistant Professor (Nontenure track)*, Engineering Department, Harvey Mudd College, Claremont, CA
2017-2022	*Postdoctoral Scholar*, Department of Computing & Mathematical Sciences, California Institute of Technology, Pasadena, CA
2012-2017	*Graduate Teaching Assistant*, Mechanical Engineering Department, Massachusetts Institute of Technology, Cambridge, MA
2010-2017	*Graduate Research Assistant*, d'Arbeloff Laboratory, Massachusetts Institute of Technology, Cambridge, MA

Other Experience and Professional Memberships

2023	*Member*, Institute of Electrical and Electronics Engineers (IEEE)
2023	*Member*, Control Systems Society (CSS)
2022	*Co-Chair*, Student Activities Committee for 7th IEEE Conference on Control Technology and Applications 2023, Bridgetown, Barbados
2021	*Co-chair*, Session at IEEE European Control Conference, June 29 - July 2, Virtual
2019	*Member*, Computing Advisory Committee, California Institute of Technology, Pasadena, CA
2017	*Co-chair*, for Session at IEEE American Control Conference, May 24-26,Seattle, WA
2012-2017	*Member*, EBICS Student Leadership Council, Massachusetts Institute of Technology, Cambridge, MA
2006-2017	*Member*, National Society of Black Engineers, Massachusetts Institute of Technology, Cambridge, MA
2006-2017	*Member*, Society of Women Engineers, Massachusetts Institute of Technology, Cambridge, MA
2006-2010	*Member*, Sigma Xi, Massachusetts Institute of Technology, Cambridge, MA
2006-2010	*Member*, Pi Tau Sigma, Massachusetts Institute of Technology, Cambridge, MA

Honors

2022	Gabilan Faculty Fellow
2022	Terman Faculty Fellow
2022	Burroughs Wellcome Fund PDEP Transition to Faculty Award
2019	Burroughs Wellcome Fund Postdoctoral Enrichment Program Award
2017	California Alliance Postdoctoral Fellowship, California Institute of Technology, Pasadena, CA
2010	John C. and Elizabeth J. Chato Award for Excellence in Bioengineering, Massachusetts Institute of Technology, Cambridge, MA
2010	Karl H. Otte Fellowship, Massachusetts Institute of Technology, Cambridge, MA

C. Contribution to Science

1. **Graduate Career: Integrated Mechanistic-Empirical Modeling of Cellular Response Based on Intracellular Signaling.** Earlier in my graduate career I constructed integrated mechanistic-empirical models that accurately represented response of single cells to extracellular cues. The key construct in my approach was the treatment of a cell's internal biochemical network as a nonlinear dynamic mapping of extracellular input cues into a higher dimensional, and more informative, input space. Consequently, upstream signaling mechanisms (close to the cell membrane) were first simulated stochastically to generate a large number of internal variables (forming a high-dimensional, augmented input space) and then empirically correlated to the experimental data of the downstream response using Partial Least Squares Regression. The result was a lower-order, nonlinear, mechanistic-empirical model that accurately represented the process being studied. I successfully applied this method to a T-Cell immuno-response problem through collaboration with Professor Melissa Kemp at Georgia Tech.

    - **Mayalu, M. N.**, and Asada, H.H. (2014). An information-theoretic approach to integrated mechanistic-empirical modeling of cellular response based on intracellular signaling dynamics. In American Control Conference (ACC), 2014 (IEEE), pp. 1755–1760.
    - **Mayalu, M. N.**, and Asada, H.H. (2013). Integrated Mechanistic-Empirical Modeling of Cellular Response Based on Intracellular Signaling Dynamics. In ASME 2013 Dynamic Systems and Control Conference (American Society of Mechanical Engineers), p. V003T43A002-V003T43A002.

2. **Graduate Career: Reduced Order Modeling Using Dual-Faceted Linearization for Predicting Behaviors of Multi-Cellular Systems.** For my thesis work, I recognized the need for more tractable computations of biomechanical mechanisms underlying cell-ECM interactions to predict emergent multicell-ECM behaviors. I had the novel idea to redefine the prediction of emergent multicell-ECM behaviors from nonlinear stochastic interactions to high dimensional linear relationships between latent variables. I created a linearized augmented state equations using my understanding of the biophysical principles involved. The linearized system, although higher order than the original nonlinear system, could be reduced rigorously and effectively. Furthermore, once linearized, single cell dynamics could be superimposed to predict emergent behaviors of multiple cells interacting through the ECM. The Koopman operator theory and others have proven that nonlinear systems can be expressed with linear dynamic equations. My theory and techniques are along the same line as those theories in spirit, but outperform the prior methods in two major points. One is that, unlike Koopman, I obtained an accurate linear representation with much fewer auxiliary variables. The other is that I superimposed linearized models of individual cells to predict emergent behaviors of multiple cells interacting with each other. This opened up the possibility of computing nonlinear behaviors of a large population of cellular systems through linear superposition. Therefore, the primary computational and control theoretical contribution of this work was the development of a reduced order systems framework that exploited linear superposition of individual agents to study the dynamics of their nonlinear interaction. The primary biomedical contribution of this work was increased understanding of how contractile cells induce emergent mechanical changes leading to matrix compaction important for pathological situations such as wound healing.

    - **Mayalu, M.N.**, Kim, M.-C., and Asada, H.H. (2019). Multi-Cell ECM compaction is predictable via superposition of nonlinear cell dynamics linearized in augmented state space. PLoS computational

biology 15, e1006798.

- **Mayalu, M.N.**, Kim, M.-C., and Asada, H. (2018). Modeling of Collective Cell Behaviors Interacting With Extracellular Matrix Using Dual Faceted Linearization. In Dynamic Systems and Control Conference (American Society of Mechanical Engineers), p. V001T14A005.
- **M. N. Mayalu**, H. H. Asada, and Min-Cheol Kim (2017). Latent space superposition of multiple solutions to predict emergent behaviors of nonlinear cellular systems. In 2017 American Control Conference (ACC), pp. 2146–2151. 10.23919/ACC.2017.7963270.
- M. Kim, **M. N. Mayalu**, and H. H. Asada (2016). Dynamic modeling of collective cell migration on an elastic substrate of extracellular matrix fiber network. In 2016 American Control Conference (ACC), pp. 6911–6916. 10.1109/ACC.2016.7526761.

3. **Postdoctoral Career: Modeling and Theory of Synthetic Paradoxical Signaling Circuit.** One of the main focuses of my postdoctoral work was a collaboration with the Elowitz lab where I created several mechanistic models surrounding cooperative control of population homeostasis via paradoxical signaling in mammalian cells. A paradoxical feedback signal provides both cell proliferation and death in different regimes. As a consequence, the relationship between feedback signal concentration and net growth rate (cell proliferation minus death rates) can be non-monotonic. This relationship is a condition for robustness to certain cell mutational overgrowths and allows for increased stability in the presence of environmental perturbations. In order explore intracellular mechanisms that naturally exhibit this behavior, I created a model of IL-2 regulated intracellular pathways leading to the paradoxical feedback control in T-Cells. This analysis elucidated basic design principles for paradoxical signaling control systems that informed a synthetic implementation in mammalian cells. Additionally, I developed a model of the synthetic paradoxical feedback circuit being implemented in mammalian cells. The model contained experimentally identifiable and accessible parameters and could make verifiable and appropriate predictions. Successful *in silico* and *in vitro* implementations of genetically engineered mammalian cells containing paradoxical signaling components sparked interest in development of analogous synthetic systems. Consequently, I developed a mathematical model representing the behavior of a synthetic paradoxical circuit design in *E. coli*.

   My representation of the aforementioned synthetic and natural paradoxical feedback systems was distinct from previous works since I took a “ground up” approach by developing detailed differential equations of significant reactions and then simplified them using singular perturbation techniques. Furthermore, the theoretical analysis of these multiple systems revealed common design principles may exist among paradoxical feedback circuit implementations. This suggests prospective control theoretical contributions in the development of a theory to identify underlying basic design principles for paradoxical signaling control systems. And prospective biomedical contributions include facilitated design of synthetic paradoxical signaling circuits *in vitro*.

   - **Mayalu, M.N.**, and Murray, R.M. (2020). Theoretical Design of Paradoxical Signaling-Based Synthetic Population Control Circuit in E. coli. bioRxiv, 2020.01.27.921734. 10.1101/2020.01.27.921734.
   - **Mayalu, M.N.**, Mehta, H., and Murray, R.M. (2019). Model of Paradoxical Signaling Regulated T-Cell Population Control for Design of Synthetic Circuits. In 2019 18th European Control Conference (ECC), pp. 2152–2158. 10.23919/ECC.2019.8795764.
   - Ma, Y., Budde, M.W., **Mayalu, M.N.**, Zhu, J., Lu, A.C., Murray, R.M., and Elowitz, M.B. (2022). Synthetic mammalian signaling circuits for robust cell population control. Cell 185, 967-979.e12. 10.1016/j.cell.202

4. **Postdoctoral Career: Systems Level Model of Dietary Effects on Cognition via the Microbiome-Gut-Brain Axis.** During my postdoc, I also conceived a systems level mathematical framework of the microbiome-gut-brain axis to increase conceptual understanding of how gut, vagus nerve, immune and vascular subsystems contribute to optimal cognitive performance. Based on data from collaborators, I structure the framework as an interconnection of organ-level dynamical subsystems which capture important underlying mechanisms. I treated the microbiome-gut-brain axis as a control system within the mathematical framework to further characterize possible modes of regulation. This treatment also facilitates the analysis

of component level changes on systems level response. Contributions of this work include the identification of systems-level trade-offs and trends occurring within the microbiome-gut-brain axis to complement experimental data and further drive hypotheses and experiments.

- **Mayalu, M.N.**, Sarma, A., Xiao, F., Doyle, J.C., and Murray, R.M. (2021). Systems Level Model of Dietary Effects on Cognition via the Microbiome-Gut-Brain Axis. In 2021 European Control Conference (ECC), pp. 312–318. 10.23919/ECC54610.2021.9655216.

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1t_Ifqs7YkA5CJ/bibliography/public/