BIOGRAPHICAL SKETCH

NAME: Tambe, Dhananjay T.

eRA COMMONS USER NAME: dttambe

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
Pune University, India	B.E.	06/1999	Mechanical Engineering
Indian Institute of Technology, India	M.Tech.	05/2001	Mechanical Engineering
Brown University, Providence, RI	Sc.M.	05/2006	Applied Mathematics
Brown University, Providence, RI	Ph.D.	05/2008	Mechanics of Solids and Structures
Harvard University, Boston, MA	Postdoctoral	07/2014	Cellular and Tissue Mechanics

A. Personal Statement

An overarching goal of my research lab is to apply the principles of mechanics and material science to identify the physical rules that govern the function of cells, tissues, and organs. While seeking to identify the fundamental rules of life, we invest significant efforts in bringing automation technologies to build innovative products for life sciences researchers and healthcare providers.

As part of the Center for Lung Biology team, we primarily focus on the mechanobiology of lungs. Several of our ongoing projects involve identifying the physical laws that govern migration, deformation, division, detachment and death of lung endothelial cells. These projects are designed to (a) improve our understanding of the basic science of the endothelial cells, (b) identify novel mechanical modulators of lung pathologies including pulmonary hypertension, sepsis, and acute lung injury.

For a very long time, the advancement in mechanics and material science have not been translated in cell biology research. As a result, we have a remarkably detailed knowledge of the biochemical aspects of the cell, however, our knowledge of biomechanical aspects of the cell is frequently speculative. To overcome this major issue, we have now developed a unified experimental platform – *Integrative Cellular Signaling Toolkit* (iCST) – where any cell biologist with minimal training will be able to measure both biochemical and mechanical aspects of the cell in an automated and high-throughput way. iCST is designed to enable innovative experiments ranging from real-time assessment of the nature of mechanical interactions between neighboring cells to drug screening. We are currently designing a workshop aimed at facilitating the use and replication of iCST in cell biology labs across the University of South Alabama (USA) and beyond.

Besides lung mechanobiology, we are also working with an orthopedic surgeon from USA hospital to develop a smart drill that would reduce training duration, cost of surgery, and chances of infection and error, and lay the groundwork for robotic orthopedic surgery.

To expand and enhance interdisciplinary research across the university, we have teamed up with College of Education faculty members to design an experiential learning program called *Pick-up Engineering*™. Through this program, the students will use the inspiring and creative framework of pick-up games to engage in engineering problem-solving.

B. Positions and Services

Positions:

1999-2001 Teaching Assistant, Indian Institute of Technology, Madras, India.
2002-2007 Teaching Assistant, Brown University, Providence, RI.
2002-2008 Research Assistant, Brown University, Providence, RI.
2008-2011 Research Fellow, Harvard School of Public Health, Boston, MA.

2011-2014 Research Associate, Harvard School of Public Health, Boston, MA.
2014-present Assistant Professor, Department of Mechanical Engineering, University of South Alabama, Mobile, AL.
2014-present Member, Center for Lung Biology, University of South Alabama, Mobile, AL
2015-present Assistant Professor (joint), Department of Pharmacology, College of Medicine, University of South Alabama, Mobile, AL
2019-present Director, Cell Culture and Small Animal Core, Center for Lung Biology, College of Medicine, University of South Alabama, AL

Memberships / Affiliations:

- Materials Research Society
- Biomedical Engineering Society
- American Thoracic Society
- Biophysical Society
- American Society of Cell Biology
- American Physiological Society

Services to the Profession:

1995-1999 *Balasaheb Vikhe Patil Scholarship* for the distinctive academic record (Pune University, India).
2001 *Dr. Anantharamakrishnan merit prize* for the best research project (IIT Madras, India).
2001 *Dr. Ramamohana Rao memorial prize* for the best academic record (IIT Madras, India).
2009-present Independent reviewer, Cellular and Molecular Bioengineering, Experimental Cell Research, Journal of Biological Physics, World Journal of Mechanics, Europhysics Letters, Soft Matter, Scientific Reports, Physical Review Letters and Journal of Applied Physiology.
2011 Chair of the session titled "*New Frontiers in Biomedical Engineering"* at the annual meeting of the Biomedical Engineering Society.
2014-present Member of the working group that bridges the gap between new investigators and organization leadership, *Respiratory Structure and Function*, American Thoracic Society.
2013-2014 Ruth L. Kirschstein NRSA Fellowship.
2015 Chair of the session titled "*Cardiovascular Biomechanics – II*" at the annual meeting of the Biomedical Engineering Society.
2015 Recognized as a "Professor of the year 2015" by the Epsilon chapter of the engineering honors society Tau Beta Pi.
2017 Organizer and chair of an early career training workshop on *How to start your independent research lab*, Annual American Thoracic Society meeting, San Diego, CA.
2017 Member of the organizing committee, 5th annual NanoBio Summit, Atmore, AL.

Services to the community:

2004-2006 Graduate student council representative for the Division of Engineering, Brown University, RI
2008-2013 Volunteer for the *North South Foundation* to conduct educational contests for kids in the USA to raise financial support for needy students in India.
2012 Organized a week-long educational workshop (in my hometown Nashik, India) that enabled about 150 high school students to seek motivation to take research as their career choice through interactions with 12 of the best scientists in India.
2012-2013 Served as a judge in children's science competitions at *Kennedy Academy Science Fair, Boston, MA* and at *Young Einstein's Science Club*, Acton, MA.
2015 At the University of South Alabama, Mobile AL, using Heron's fountain, demonstrated the principles of fluid mechanics to the high school students from 11 different Mobile County public high schools.
2015-2016 Chaired the interviews of the candidates from Alabama for admission to the undergraduate program at Brown University.
2018 Founded Spanish Fort CoderDojo at the Spanish Fort Public Library
2019 Summer Engineering Academy, College of Engineering, South Alabama, AL.

C. Contribution to Science

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/48764482/?sort=date&direction=descending

1. Invented Monolayer Stress Microscopy. Across an endothelial or epithelial tissue, spatial arrangement of the cells is not perfectly periodic, shape and size of the cells is not entirely identical, and signaling activities within the cells are not completely alike. However, the functional consequences of such heterogeneities remained largely hidden. To overcome this limitation, we developed the first *in vitro* assay (Monolayer Stress Microscopy (MSM)) that enabled quantitative visualization of the local physical forces that each cell within the tissue exerts on to its substrate and on its neighbors. Our approach is now implemented and reproduced in various research labs across the world including Harvard University, Northeastern University, University of Barcelona, and the University of Heidelberg. Building on the MSM platform, we recently established a novel force-based cellular platform for high-throughput drug discovery and identified several drug candidates for asthma and glaucoma.

1a. **Tambe DT**, Trepat X, Butler JP, Fredberg JJ, *Monolayer Stress Microscopy*, US Patent, 9,714,932.

1b. **Tambe DT**, Hardin CC, Angelini TE, Rajendran K, Park CY, Serra-Picamal X, Zhou E, Zaman MH, Butler JP, Weitz DA, Fredberg JJ, Trepat X, *Collective Cell Guidance by Cooperative Intercellular Forces*, Nature Materials, (2011). PMID: 21602808. PMCID: PMC3135682.
- Featured on Journal Cover, and News and Views – Gov N, *Cell mechanics: Moving under peer pressure*, Nature Materials, (2011). PMID: 21602874

1c. **Tambe DT**, Croutelle U, Trepat X, Park CY, Kim JH, Millet E, Butler JP, Fredberg JJ, *Monolayer Stress Microscopy: limitations, artifacts, and accuracy of recovered intercellular stresses*, PLoS One, (2013). PMID: 23468843. PMCID: PMC3585344.

1d. Park CY, Zhou EH, **Tambe DT**, Chen B, Lavoie T, Dowell M, Simeonov A, Maloney DJ, Marinkovic A, Tschumperlin DJ, Burger S, Frykenberg M, Butler JP, Stamer WD, Johnson M, Solway J, Fredberg JJ, Krishnan R., *High-throughput screening for modulators of cellular contractile force,* Integrative Biology (2015). PMID: 25953078. PMCID: PMC4657543.

2. Discovered plithotaxis, kenotaxis, and forceful propagation of EMT. In collective cell migration, the role of local physical forces that each cell applies to its neighbor was largely based on theories and remained controversial. MSM enabled visualization of such local forces and lead to a series of discoveries on the nature of these forces across the cellular monolayer and how cells respond to such forces. In a monolayer, the intercellular forces exhibit remarkable spatial fluctuations. Superposed on these fluctuations is cooperative action of cellular units of about 15-20 cells; across such units, the intercellular forces tend to build-up and align. Within this rugged force landscape, however, local cellular motion tends to be guided along the local maximum tension orientation; we called this migration tendency as *plithotaxis*. An independent lab followed this finding and established that the *plithotaxis* is strongly associated with normal function of the tumor suppressor gene *Merlin* [Das T. et al, Nature Cell Biology (2015) PMID: 25706233]. At the beginning of wound healing and symmetry breaking, epithelium transitions from quiescent apical-basal polarity to motile planar polarity. We found that this epithelial-to-mesenchymal transition propagates through the monolayer in a manner similar to the propagation of mechanical waves. These waves are, however, appear to be supported entirely by cellular ability to generate and transmit forces across the cell sheet. Using human umbilical vein endothelial cells (HUVECs), we found that the well-known tendency of HUVECs to align the cellular morphology with the orientation of flow appears to be steered by the intercellular forces.

2a. **Tambe DT**, Hardin CC, Angelini TE, Rajendran K, Park CY, Serra-Picamal X, Zhou E, Zaman MH, Butler JP, Weitz DA, Fredberg JJ, Trepat X, *Collective Cell Guidance by Cooperative Intercellular Forces*, Nature Materials, (2011). PMID: 21602808. PMCID: PMC3135682.
- Featured on Journal Cover, and News and Views – Gov N, *Cell mechanics: Moving under peer pressure*, Nature Materials, (2011). PMID: 21602874

2b. Serra-Picamal X, Conte V, Vincent R, Anon E, **Tambe DT**, Bazellieres E, Butler JP, Fredberg JJ, Trepat X, *Mechanical waves during tissue expansion*, Nature Physics, 8, 628 (2012).
- Featured on Journal Cover, and News and Views, Manuel Théry, *Cell mechanics: Wave of migration*, Nature Physics, 8, 583 (2012).

2c. Kim JH, Serra-Picamal X, **Tambe DT**, Zhou E, Park CY, Sadati M, Park JA, Krishnan R, Gweon B, Millet E, Butler JP, Trepat X, Fredberg JJ, *Propulsion and navigation within the advancing monolayer sheet*, Nature Materials, (2013). PMID: 23793160. PMCID: PMC3750079.
- Featured on Journal Cover, and News and Views, Dufresne ER, Schwartz MA *Cell migration: Towards the void*, Nature Materials (2013). PMID: 23966050

2d. Park J-A, Kim JH, …, **Tambe DT**, …, Fredberg JJ, *Unjamming and cell shape in the asthmatic airway epithelium*, Nature Materials, (2015). PMID: 26237129. PMCID: PMC4666305.

2e. Hardin CC, Chattoraj J, Manomohan G, Colombo J, Nguyen T, **Tambe DT**, Fredberg JJ, Birukov K, Butler JP, Del Gado E, Krishnan R, *Long-range stress transmission guides endothelial gap formation*, Biochem Biophys Res Commun (2018). PMID: 29137986, PMCID: PMC5761675.

3. Findings on which novel component of the microenvironment influence cellular behavior, and how. The response of a human airway smooth muscle (HASM) cell to periodic stretches lacked consensus. We found that when the stretch is inhomogeneous, signaling pathways trigger cellular reinforcement. But when the stretch is homogeneous, independent of the signaling pathway, actin depolymerization causes cellular fluidization. For HASM cell, physical properties such as stiffness, prestress, and remodeling rate were known for the entire cell but not locally within the cell. We quantified these physical properties locally within the cell and found novel uniqueness amongst geometric features such as edge, center, and corner. A single isolated cell senses thickness (t) of its substrate, but length scales relevant to this mechanosensing remained unclear. We showed that around an isolated point force, mechanosensing is influenced greatly by intrinsic stiffness of the substrate; but over the size of the cell (r), when $r \geq t$ the mechanosensing is influenced by the thickness, rather than intrinsic stiffness, of the substrate. Using human lung microvascular endothelial cells (HLMVECs), we found that barrier-disruptive agents (thrombin, histamine, and H_2O_2) increase average intercellular force and that barrier-protective agents (Y27632, S1P, and HGF) decrease average intercellular force. In addition, we found that increased intercellular force appears to attenuate associated spatial fluctuations and decrease in intercellular force appears to enhance associated spatial fluctuations.

3a. Park CY, **Tambe DT**, Alencar AM, Trepat X, Zhou E, Millet E, Butler JP, Fredberg JJ, *Mapping the cytoskeletal prestress*, Am J Physiol Cell Physiol, (2010). PMID: 20164383. PMCID: PMC4116352.

3b. Lin YC, **Tambe DT**, Park CY, Wasserman MR, Trepat X, Krishnan R, Lenormand G, Fredberg JJ, Butler JP, *Mechanosensing of substrate thickness*, Phys Rev E, (2010). PMID: 21230324. PMCID: PMC3641827.

3c. Chen C, **Tambe DT**, Deng L, Yang L, *Biomechanical properties and mechanobiology of the articular chondrocyte*, Am J Physiol Cell Physiol, (2013) PMID: 24067919

3d. Zareian R, Susilo ME, Paten JA, McLean JP, Hollmann J, Karamichos D, Messer CS, **Tambe DT**, Saeidi N, Zieske JD, Ruberti JW. *Human Corneal Fibroblast Pattern Evolution and Matrix Synthesis on Mechanically Biased Substrates*, Tissue Engineering Part A, (2016). PMID: 27600605. PMCID: PMC5073220.

4. Discovered the mechanics of actin-based propulsion of Listeria and spheres. Actin polymerization propels pathogenic bacterium, *Listeria monocytogenes*, to exhibit migration patterns that were considered to be random. We identified a remarkably simple model that explained all of the observed trajectories and established that the patterns, instead of being random, were in fact deterministic. This model provided a simple robust approach to differentiate between a wild-type and a mutant bacterium. Random migration pattern was a far more widely accepted notion associated with actin-based propulsion reconstituted using a spherical bead. Considering the differences in geometric constraints that the actin-network would impose on the ellipsoidal object like Listeria and symmetric object like a spherical bead, we developed another model that predicted long-term migration patterns for the spherical bead. Contrary to the existing notion, our theory suggested that the motion of spherical beads would be deterministic. Moreover, we made a very specific prediction that while the migration patterns of Listeria have zero mean curvature, the migration patterns of a spherical bead would have non-zero mean curvature. Subsequent experiments found that these predictions were, in fact, correct [Kang H et al., Biophysical Journal, (2010). PMID: 21044576].

4a. Shenoy VB, **Tambe DT**, Prasad A, Theriot JA, *A kinematic description of the trajectories of Listeria Monocytogenes propelled by actin comet tails,* Proceedings of the National Academy of Sciences, USA, (2007). PMID: 17485664. PMCID: PMC1895934.

- a. *A pathogens movements are fairly loopy and quite formulaic*, New York Times, (May 22, 2007)
- b. *Math formula describes pathogen movements*, Washington Times, (May 16, 2007)

4b. **Tambe DT**, *Topics in the mechanics of self-organizing systems,* Ph. D. thesis, Brown University https://repository.library.brown.edu/studio/item/bdr:97/ (2008).

5. Discovered the forces that drive self-organization of quantum dot nanostructures. Next generation data processing chips are expected to rely heavily on the ability to form highly periodic patterns of stable semiconductor quantum dot nanostructures. The process is, however, controlled by self-organization where forces intrinsic to the system govern the pattern formation and the structural stability. Using computational tools including quantum mechanical calculations, molecular statics calculations, finite element calculations, kinetic Monte Carlo techniques, we focused on developing theoretical and conceptual foundations of such self-

organization observed in a variety of technologically important experimental situations. For example, on Silicon (113) surface widely separated steps repelled each other whereas closely spaced steps attracted each other. We found that the attraction was driven by a reduction in surface energy by the annihilation of monopoles when the steps become bunched. At the growth and operating temperatures of the quantum dots, the morphology of the quantum dots can change by surface diffusion-based mass transport. We discovered that, if the diffusing atom spends large time in detaching from the surface steps (ADL kinetics), then flattening of the quantum dot is surprisingly accompanied by an increase in the flattening rate. Around the quantum dots, there emerges a trench whose depth is linearly related to the base-width of the island. We showed that this relationship is determined by the competition between the reduction in strain energy and the increase in surface energy. During the early stages of the growth of quantum dots, numerous systematic patterns emerge surprisingly from just two types of linear atomic structures. We derived analytic equations that explain this surprising observation and it led to the discovery of the law that governed elastic interaction between those two linear structures.

5a. **Tambe DT**, Shenoy VB, *On the energetic origin of self-limiting trenches formed around Ge/Si quantum dots*, Applied Phys Lett (2004) 85 (9), 1586-1588.

5b. Shenoy VB, Ramasubramaniam A, Ramanarayan H, **Tambe DT**, Chan WL, Chason E., *Influence of step-edge barriers on the morphological relaxation of nanoscale ripples on crystal surfaces*, Phys Rev Lett, (2004), PMID: 15245035

5c. Ciobanu CV, **Tambe DT**, and Shenoy VB, *Comparative study of dimer-vacancies and dimer-vacancy lines on Si(001) and Ge(001)*, Surface Science, 556, 171 (2004)

5d. **Tambe DT**, Ciobanu CV, and Shenoy VB, *Self-assembly of steps and vacancy lines during the early stages of Ge/Si(001) heteroepitaxy*, Applied Physics Letters, 87, 251908 (2005)

D. Research Support

Ongoing Research Support

P01 HL66299 (Stevens) 05/15/2018-04/30/2023
NIH/NHLBI
Lung endothelial cell phenotypes
This Program Project Grant is founded on the hypothesis that endothelium lining the lung's extra-alveolar and alveolar blood vessels is phenotypically distinct, and that the unique behavior(s) of cells from these different vascular locations is necessary for them to fulfill their site-specific function(s).
Role: Leader of Core B (Cell Culture and Small Animal Core)

Intramural Grant (Tambe) 04/01/2018-12/31/2019
University of South Alabama
Research and Scholarly Development Grant Program
Mechanical behavior of pulmonary endothelial cells
Assess the mechanical behavior of an heterogeneous interface between the endothelial cells pulmonary artery and endothelial cells from pulmonary microvessels.
Role: Principal Investigator

Completed Research Support

Intramural Grant (Tambe)
University of South Alabama 07/20/2015-11/30/2017
Abraham A. Mitchell Cancer Research Fund
Role of heterogeneities in UV-induced injury and silver nanoparticle-induced chemoprevention in HaCaT Cells
Role: Principal Investigator