BIOGRAPHICAL SKETCH

NAME:	Ellen Kuhl
eRA COMMONS USER NAME:	ELLEN.KUHL
POSITION TITLE:	Professor of Mechanical Engineering Bioengineering and Cardiothoracic Surgery

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Leibniz University of Hannover, Germany	M.Sc.	1995	Computational Engineering
University of Stuttgart, Germany	Ph.D.	2000	Civil Engineering
Delft University of Technology, The Netherlands	Post Doc	2000	Aerospace Engineering
Technical University of Kaiserslautern, Germany	Habilitation	2004	Biomedical Engineering

A. Personal Statement

I am a Professor of Mechanical Engineering, Bioengineering, and Cardiothoracic Surgery at Stanford University. My area of professional expertise is the computational simulation of cardiac electromechanics across multiple scales in space and time. My lab has pioneered algorithms for the simulation of excitation-contraction coupling and established computational tools to explore cardiac electrophysiology, dilated cardiomyopathy, hypertrophic cardiomyopathy, mitral regurgitation, and other phenomena of growth and remodeling in the living heart. Cardiac growth and remodeling can be induced naturally, e.g., through elevated pressure, stress, or strain, or interventionally, e.g., through prostheses or stents. We can potentially revert cardiac growth and remodeling by engineered tissue grafts or support devices. Combining theories of electrophysiology, photoelectrochemistry, biophysics, and continuum mechanics, my lab has specialized in predicting the behavior of the living heart using personalized custom-designed finite element models.

My long-term career goals are perfectly aligned with this research project to establish *A New Framework for Understanding the Mechanisms of Diastolic Dysfunction*. I have known Dr. Ennis for more than a decade an co-authored two papers with him during the short time that we both worked at Stanford together. For the past four years, we have closely collaborated through our current U01 on *Multi-Scale Laws of Myocardial Growth and Remodeling.* I am excited to further strengthen my collaboration with Dr. Ennis through this project on diastolic dysfunction now that he has returned to Stanford.

After my postdoctoral training, I received a Habilitation fellowship from the German National Science Foundation for my research on growth and remodeling of living systems. This work is documented in my habilitation thesis and in several journal articles on living systems. Motivated by this work, I have developed, established, and refined two new graduate courses on the Mechanics of the Cell and the Mechanics of Growth at Stanford University. Through these courses, I inspire, train, and recruit new graduate students into my lab to study physiology and pathology of the heart. Of my previous trainees, I have successfully mentored ten to pursue academic careers: One is now a full professor, one is an associate professor, eight are assistant professors. I have organized a conference on computational biomechanics, organized several minisymposia and workshops on cardiac modeling, and edited special journal issues on computational biomechanics, one with a special focus on simulating excitation-contraction coupling in the heart.

Throughout the past decade at Stanford, I have established numerous close and fruitful collaborations with clinical researchers and basic scientists in Cardiology, Cardiothoracic Surgery, Radiology, and in the Cardiovascular Institute. We jointly mentor graduate students and postdoctoral researchers. The proximity of the Stanford School of Engineering and the School of Medicine allows us to hold regular joint group meetings, discuss our research progress, and exchange future research directions. My research on the heart was acknowledged and supported by the NSF CAREER Award The Virtual Heart: Exploring the Structure-Function Relationship in Electroactive Cardiac Tissue. As part of this award, my lab has designed the first fully coupled electro-mechanical model for excitation-contraction coupling within a single, unified finite element framework. Our heart model has become a true success story: Since May 2013, I have worked with the largest finite element development company, Abaqus/Dassault Systemes, towards implementing our core algorithms into the Abaqus infrastructure. Together with the Living Heart team at Dassault Systemes, I have established the first four-chamber heart simulator for human heart function. The Living Heart project was officially launched in May 2014. Since then, our work has received broad media attention and was featured in a scientific publication, which I had submitted as lead senior author. To date, the Living Heart ecosystem has grown to 32 contributing member organizations, with more than 150 cardiovascular specialists from research, industry, and medicine, who have free access to our heart simulator to test and accelerate the development of the Living Heart via crowdsourcing. Ultimately, the Living Heart project will unite leading cardiovascular researchers, medical device manufacturers, regulatory agencies, and practicing cardiologists on the shared mission to develop and validate personalized digital human heart models and establish a unified foundation for in silico cardiovascular medicine.

With more than 20 years of experience in continuum mechanics, mathematical modeling of biological systems, and finite element simulation, both through research and education, I have the expertise, leadership, and motivation to contribute to this research project on Understanding the Mechanisms of Diastolic Dysfunction. I have a successful track record of productive research projects in the area of cardiovascular modeling and in the computational mechanics of whole heart systems. My experience has prepared me to successfully oversee, mentor, and guide the research as part of this project.

a. Rausch MK, Zollner AM, Genet M, Baillargeon B, Bothe W, **Kuhl E**. A virtual sizing tool for mitral valve annuloplasty. Int J Num Meth Biomed Eng. 2017;33:e02788. PMCID: PMC5289896
b. Baillargeon B, Rebelo N, Fox DD, Taylor RL, **Kuhl E**. The Living Heart Project: A robust and integrative simulator for human heart function. Eur J Mech A/Solids. 2014;48:38-47. PMCID: PMC4175454
c. Rausch MK, Famaey N, O'Brien Shultz T, Bothe W, Miller DC, **Kuhl E**. Mechanics of the mitral valve. Biomech Mod Mechanobio. 2013;12:1053-1071. PMID: 23263365
d. Goktepe S, **Kuhl E**. Computational modeling of electrophysiology: A novel finite element approach. Int J Num Meth Eng. 2009; 79:156-178.

B. Positions and Honors.

Positions and Employment

2002-2006	Assistant Professor	Department of Mechanical Engineering, TU Kaiserslautern, Germany
2007-2009	Assistant Professor	Departments of Mechanical Engineering and Bioengineering (affiliation), Stanford University
2010-2016	Associate Professor	Departments of Mechanical Engineering, Bioengineering (courtesy), and Cardiothoracic Surgery (courtesy), Stanford University
2011	Professor	Department of Mechanical Engineering, ETH Zurich
2016-	Professor	Departments of Mechanical Engineering, Bioengineering (courtesy), and Cardiothoracic Surgery (courtesy), Stanford University

Honors and Awards

1996 - 1999	Graduate Research Fellowship, German Science Foundation (DFG)
2001 - 2004	Habilitation Research Fellowship, German Science Foundation (DFG)
2009	Hellman Faculty Scholar
2010 - 2014	CAREER Award, National Science Foundation (NSF)
2014	Midwest Mechanics Seminar Speaker
2014	American Institute for Medical and Biological Engineering (AIMBE) Fellow
2016	American Society of Mechanical Engineers (ASME) Fellow
2016	Alexander von Humboldt Research Award (Alexander von Humboldt Foundation)
2013	Annals of Biomedical Engineering Editor's Choice Award, Manuel K. Rausch et al.
2013	Taylor & Francis Best Podium Presentation (CMBBE), Ellen Kuhl
2013	Taylor & Francis 3rd Place Student Podium Presentation (CMBBE) Manuel K. Rausch
2013	Taylor & Francis Best Poster Presentation (CMBBE) Daniel E. Hurtado
2017	HPC Wire Editor's Choice Award for Best Use of High Performance Computing in the Cloud
2017	Hyperion Innovation Excellence Award for Simulating Drug Interactions Across the Heart

Other Experience and Professional Memberships

- Committees: US National Committee on Biomechanics, Chair (since 2018); US Association for Computational Mechanics, Executive Council Member (since 2016), US Association for Computational Mechanics, Chair of TTA Biological Systems (since 2015); Stanford Department of Mechanical Engineering, Chair of Graduate Curriculum (2017-2018); US National Committee on Biomechanics, Vice Chair (2016-2018); Stanford University, Fellow (2015-2017); Mechanical Engineering Faculty Search Committee, Chair (2015-2016); US National Committee on Biomechanics, Secretary (2014-2016); Stanford Mechanics and Computation Group, Chair (2014-2016); Stanford Department of Mechanical Engineering, Chair of Graduate Admission (2012-2014)
- Memberships: American Heart Association (AHA), American Physical Society (APS), American Society of Engineering Education (ASEE), American Society of Mechanical Engineers (ASME), Biomedical Engineering Society (BMES), Biophysical Society (BPS), European Society of Biomechanics (ESB), European Mechanics Society (EUROMECH), German Association for Applied Mathematics and Mechanics (GAMM), International Association for Computational Mechanics (IACM), US Association for Computational Mechanics (USACM)
- Associate Editor: Annals of Biomedical Engineering (since 2015), Journal of the Mechanics and Physics of Solids (since 2015)
- Editorial Board: Acta Mechanica Sinica (since 2011), Applied Mechanics Reviews (since 2012), Biomechanics and Modeling in Mechanobiology (since 2015), Computer Methods in Biomechanics and Biomedical Engineering (since 2011), International Journal for Numerical Methods in Biomedical Engineering (since 2011), Journal of Computational Surgery (since 2012), Journal of the Mechanics and Physics of Solids (2013-2015)
- Reviewer: Acta Biomaterialia, American Journal of Physiology Heart and Circulatory Physiology, Annals of Biomedical Engineering, Archive of Applied Mechanics, Biomechanics and Modeling in Mechanobiology, Cardiovascular Engineering and Technology, Computational Materials Science, Computational Mechanics, Computer Methods in Applied Mechanics and Engineering, Computer Methods in Biomechanics and Biomedical Engineering, Computer Methods and Programs in Biomedicine, Computers and Concrete, Continuum Mechanics and Thermodynamics, Encyclopedia of Computational Mechanics, Engineering and Computational Mechanics, Engineering Computations, Engineering with Computers, European Journal of Mechanics, Experimental Biology and Medicine, Frontiers in Computational Physiology and Medicine, International Journal for Numerical and Analytical Methods in Geomechanics, International Journal for Numerical Methods in Biomedical Engineering, International Journal for Numerical Methods in Engineering, International Journal of Engineering Science, International Journal of Mechanics of Materials and Structures, International Journal of Non-Linear Mechanics, International Journal of Solids and Structures, International Journal of Applied Mathematics and Mechanics, Journal of Applied Mechanics, Journal of Biological Dynamics, Journal of Biomechanics, Journal of Computational Physics, Journal of Elasticity, Journal of Engineering Mechanics, Journal of Mechanics of Materials and Structures, Journal of Multiscale Computational Engineering, Journal of the Royal Society Interface, Journal of Structural Changes in Solids, Journal of the Mechanical Behavior of Biomedical Materials, Journal of the Mechanics and Physics of Solids, Journal of Theoretical Biology, Nature Materials, Nature Physics, Mechanics Research Communications, Medical Engineering and Physics, PLoS Computational Biology, PLoS ONE, Proceedings of the National Academy of Sciences PNAS, Proceedings in Applied Mathematics and Mechanics, Proceedings of the Royal Society London, Philosophical Magazine
- Scientific Reviewer: NIH Study Section Modeling and Analysis of Biological Systems (2014-2018), National Institutes of Health (NIH), National Science Foundation (NSF), American Heart Association (AHA), German Science Foundation (DFG), Israel Science Foundation (ISF), Swiss National Science Foundation (SFN)
- Guest Editor: Computational Mechanics of Biological Systems, Computer Methods in Applied Mechanics and Engineering, in progress, 2015; Frontiers in Finite-Deformation Electromechanics, European Journal of Mechanics, Vol 48, 2014; Growing Matter, Journal of the Mechanical Behavior of Biomedical Materials, Vol 29, 2014; Recent Advances in the Biomechanics of Growth and Remodeling, Mechanics Research Communications, Vol 42, 2012; Active Tissue Modeling: From Single Muscle Cells to Muscular Contraction, International Journal of Multiscale Computational Engineering, Vol 10, 2012; Mechanics in Biology: Cells and Tissues, Philosophical Transactions of the Royal Society London, Vol 369, 2009; Computer Simulations of Mechanobiology, Computer Methods in Biomechanics and Biomedical Engineering, Vol 11, 2008.

- Workshops, Symposia, and Session Organization: New Challenges in the Physics of the Brain, Ecole de Physique des Houches, Les Houches, France, 2016; Miniworkshop on the Mathematics of Differential Growth and Morphogenesis, Oberwolfach, Germany, 2015; 7th World Congress of Biomechanics, Track-Co-Chair, Boston, MA, 2014; IUTAM Symposium on Computer Methods in Biomechanics: From Nano to Macro, Stanford, CA, 2011; Minisymposium on Computational Modeling of Electro-Active Materials, WCCM IX, Adelaide, Australia, 2010; Minisymposium on Active Tissue Modeling from Single Muscle Cells to Muscular Contraction, USNCCM X, Columbus, OH, 2009, IUTAM Symposium on Cellular, Molecular and Tissue Mechanics, Woods Hole, MA, 2008; Miniworkshop on the Mathematics of Growth and Remodeling of Soft Biological Tissues, Oberwolfach, Germany, 2008; Minisymposium on Growth and Remodeling, USNCCM IX, San Francisco, CA, 2007; Minisymposium on Multiscale Modeling of Materials, USNCCM IX, San Francisco, CA, 2007; Biomechanics, GAMM Annual Meeting, Berlin, 2006.

C. Contribution to Science underlined: Kuhl's students and postdocs

1. Our heart is not only our most vital, but also our most complex organ: Precisely controlled by the interplay of electrical and mechanical fields, it consists of four chambers and four valves, which act in concert to regulate its filling, ejection, and overall pump function. While numerous computational models exist to study either the electrical or the mechanical response of its individual chambers, the integrative electro-mechanical response of the whole heart remains poorly understood. My lab has designed the first fully coupled electro-mechanical model for excitation-contraction coupling within a single, unified finite element framework. Since May 2013, I have worked with the largest commercial finite element company, Abaqus/Dassault Systemes, towards implementing our core algorithms into the Abaqus infrastructure. Together with the Living Heart team at Dassault Systemes, we have established the first four-chamber heart simulator for human heart function. The Living Heart project was officially launched in May 2014. Since then, the Living Heart ecosystem has grown to 40 contributing member organizations, with more than 150 cardiovascular specialists from research, industry, and medicine. Ultimately, the Living Heart project will unite leading cardiovascular researchers, medical device manufacturers, regulatory agencies, and practicing cardiologists on the shared mission to develop and validate personalized digital human heart models and establish a unified foundation for in silico cardiovascular medicine. Our computational models, which form the core of these efforts are documented in more than 40 peer-reviewed journal publications.
   a. Sahli Costabal F, Concha FA, Hurtado DE, **Kuhl E**. The importance of mechano-electrical feedback in cardiac electromechanics. Comp Meth Appl Mech Eng, 2017;320:352-368. PMID:29056782
   b. Genet M, Lee LC, Baillargeon B, Guccione JM, **Kuhl E**. Modeling pathologies of systolic and diastolic heart failure. Ann Biomed Eng. 2016;44:112-127. PMCID: PMC4670609
   c. Sahli Costabal F, Hurtado DE, **Kuhl E**. Generating Purkinje networks in the human heart. J Biomech, 2016;49:2455-2465. PMID:26748729
   d. Abilez OJ, Wong J, Prakash R, Deisseroth K, Zarins CK, **Kuhl E**. Multiscale computational models for optogenetic control of cardiac function. Biophys J, 2011;101:1326-1334. PMCID: PMC3177076

2. Growth and remodeling are fundamental hallmarks of all living things. In the heart, growth and remodeling can occur under physiological and pathological conditions. While there is general agreement on the importance of growth and remodeling, both phenomena remain poorly characterized, mainly because we lack the fundamental theories that describe living systems. Our lab has pioneered mathematical models and computational tools to model, simulate, and predict growth and remodeling of numerous living systems with a particular focus on the human heart. We have calibrated and validated our growth models in ovine models of mechanical overload and, more recently, in porcine models of concentric and eccentric growth and remodeling induced by pressure and volume overload. Our mathematical models for growth and remodeling have been widely adopted by various labs worldwide. Our tools have been generalized to many other biological systems including skeletal muscle, skin, the eye, the lung, and the brain. Throughout the past decade, our work on growth and remodeling has inspired more than 40 peer-reviewed journal articles.
   a. Menzel A, **Kuhl E**. Frontiers in growth and remodeling. Mech Res Comm, 2012;42,1-14. PMID: 22919118
   b. Rausch MK, Dam A, Göktepe S, Abilez OJ, **Kuhl E**. Computational modeling of growth: Systemic and pulmonary hypertension in the heart. Biomech Mod Mechanobio, 2011;10:799-811. PMID: 21188611

c. Goktepe S, Abilez OJ, Parker KK, **Kuhl E**. A multiscale model for eccentric and concentric cardiac growth through sarcomerogenesis. J Theor Bio, 2010;265:433-442. PMID: 20447409
d. **Kuhl E**, Maas R, Himpel G, Menzel A. Computational modeling of arterial wall growth. Biomech Mod Mechanobio. 2007;6:321-331. PMID: 17119902

3. The developing human brain remains one of the few unsolved mysteries of science. Advancements in developmental biology, neuroscience, and medical imaging have brought us closer than ever to understanding brain development in health and disease. However, the precise role of mechanics throughout this process remains under appreciated and poorly understood. My lab has recently shown that mechanical stretch plays a crucial role in brain development. Using the nonlinear field theories of mechanics, supplemented by the theory of finite growth, we have modeled the human brain as a living system with a morphogenetically growing gray matter surface and a growing white matter core. To characterize the stiffness of gray and white matter tissue, we have designed new protocols for indentation testing. Our combined experimental and computational approach suggests that anisotropic white matter growth, as an emergent property from chronic axon elongation, intrinsically induces symmetry breaking, and predicts surface morphologies in agreement with magnetic resonance images from very preterm neonates. Our models predict that deviations in cortical thickness, elasticity, and growth induce morphological abnormalities, which agree with the classical pathologies of lissencephaly and polymicrogyria. Understanding the mechanisms of human brain development has direct implications for the diagnostics and treatment of neurological disorders, including epilepsy, schizophrenia, and autism.

a. **Kuhl E**. Biophysics: Unfolding the brain. Nature Physics. 2016;12:533-534.
b. Budday S, Steinmann P, **Kuhl E**. Physical biology of human brain development. Front Cell Neurosci. 2015;9:257. PMID: 26217183
c. Budday S, Nay R, de Rooij R, Steinmann P, Wyrobek T, Ovaert TC, **Kuhl E**. Mechanical properties of gray and white matter brain tissue by indentation. J Mech Behavior Biomed Mat. 2015;46:318-330. PMCID: PMC4395547
d. Budday S, Raybaud C, **Kuhl E**. A mechanical model predicts morphological abnormalities in the developing human brain. Sci Rep. 2014;4:5644. PMCID: PMC4090617

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/48255284/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

- NIH U01 HL119578, PIs Guccione, Kassab, Kuhl $2,500,000 07/01/14-06/30/19
  Title: Multi-scale laws of myocardial growth and remodeling.
  Goal: This study will provide functional insight into cardiac growth and remodeling using animal models.
- NSF CMMI 1727268, PI Kuhl $400,000 09/01/17-08/31/20
  Title: Understanding neurodegeneration across the scales.
  Goal: This project focuses on multiscale modeling of neurodegeneration and brain damage.
- BIO-X IIP 7, PI Kuhl $200,000 10/01/16-09/30/18
  Title: Molecular mechanisms of chronic traumatic encephalopathy.
  Goal: This research provides a multiscale computational model of brain damage in response to impact.

Completed Research Support

- NSF INSPIRE 1233054, PI Kuhl 08/15/12-08/14/16
  Title: Optogenetic control of the human heart – Turning light into force.
  Goal: This project focuses on creating a biological pacemaker from genetically engineered heart cells.
- NSF CAREER 0952021, PI Kuhl 02/01/10-01/31/15
  Title: The Virtual Heart – Exploring the structure-function relationship in electroactive cardiac tissue.
  Goal: This study provides a multiscale computational toolbox to simulate excitation-contraction coupling.
- NSF EFRI-CBE 0735551, PI Pruitt, co-PIs Heilshorn, Kuhl, Wu, Zarins 09/01/07-08/31/12
  Title: Engineering of cardiovascular cellular interfaces and tissue constructs.
  Goal: This project is targeted at designing tissue-engineered grafts for cardiac repair after infarction.