BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Ateshian, Gerard A.

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

POSITION TITLE: Andrew Walz 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
Columbia University, New York, NY	B.S.	05/1986	Mechanical Engineering
Columbia University, New York, NY	M.S.	05/1987	Mechanical Engineering
Columbia University, New York, NY	M.Phil.	05/1990	Mechanical Engineering
Columbia University, New York, NY	Ph.D.	05/1991	Mechanical Engineering

A. Personal Statement

My primary research is in the field of soft tissue mechanics, with an emphasis on cartilage mechanics, lubrication, and tissue engineering, and the formulation of growth theories for biological tissues. In the field of cartilage contact mechanics and lubrication, our research demonstrated experimentally that the friction coefficient of cartilage is dependent on the pressurization of its interstitial fluid, resolving an open issue in the field of cartilage tribology and emphasizing that preserving the integrity of cartilage is critical to maintaining low friction. These studies followed earlier systematic experimental and theoretical analyses of cartilage interstitial fluid pressurization, which demonstrated that the large disparity between the tensile and compressive stiffnesses of articular cartilage plays a major role in promoting fluid pressurization, a mechanism not previously recognized. More recently we have shown that mechanical forces in the joint influence TGF-ß activation via synovial fluid shearing, leading to uptake of activated TGF-ß into the superficial zone where it can stimulate the synthesis of boundary lubricant molecules that can help reduce cartilage wear. These findings have provided critical insight into the structure-function relationship of articular cartilage, explaining how the collagen matrix, which contributes mostly to the tensile stiffness, plays a critical role in sustaining the compressive loads in diarthrodial joints by promoting interstitial fluid pressurization and reducing the friction coefficient. In collaboration with Clark Hung, we have translated our findings on cartilage mechanics to the field of functional cartilage tissue engineering. In 2000 we published the first study to demonstrate that dynamic loading significantly enhances cartilage construct mechanical properties. More recently, we have demonstrated from experiments that dynamic loading of cartilage can pump solutes into the tissue at concentrations that far exceed those achieved under passive diffusion. This highly novel outcome, which had first been suggested in our earlier theoretical studies, has major implications for our understanding of solute transport pathways in avascular adult cartilage, emphasizing a critical role for loading in nutrient transport. Together with Dr. Jeffrey Weiss at the University of Utah, we have developed open-source computational tools that facilitate the modeling of tissue mechanics, transport, and growth processes, which address many of our current research foci and allow us to better understand structure-function relationships and optimize the design of tissue engineering modalities. These computational tools accommodate neutral and charged solutes and solid-bound molecular species, as well as chemical reactions among these various constituents, allowing the examination of mechano-electrochemical phenomena in tissues and cells.

B. Positions and Honors

Positions and Employment

1991-1995 Assistant Professor of Mechanical Engineering, Columbia University

1991-2002 Associate in Orthopaedic Research, Columbia-Presbyterian Medical Center
1996-2002 Associate Professor of Mechanical Engineering, Columbia University
1996- Director, Musculoskeletal Biomechanics Laboratory, Columbia University
1998-2002 Associate Professor of Biomedical Engineering, Columbia University
1999-2002 Associate Director, Orthopaedic Research Laboratory, Columbia-Presbyterian Medical Center
1999-2002 Vice Chair, Department of Biomedical Engineering, Columbia University
2002-2013 Professor of Mechanical Engineering and Biomedical Engineering, Columbia University
2011-2014 Chair, Department of Mechanical Engineering, Columbia University
2013- Andrew Walz Professor of Mechanical Engineering, Columbia University

Other Experience and Professional Memberships

1995 USNCB Delegate to the Fourth China-Japan-USA-Singapore meeting, Taiyuan, China
1998 USNCB Delegate to the Fifth Japan-USA-Singapore-China meeting, Sendai, Japan
1999-2004 Editorial Consultant, Journal of Biomechanics
2000-2006 Associate Editor, ASME Journal of Biomechanical Engineering
2001-2008 Executive Committee Member, ASME Bioengineering Division
2001- Editorial Board Member, Biomechanics and Modeling in Mechanobiology
2004-2009 Survey Editor, Journal of Biomechanics
2005-2008 Member of Board of Directors, Biomedical Engineering Society
2006-2007 Chair of Bioengineering Division of the American Society of Mechanical Engineers
2006-2008 Associate Editor, Journal of Osteoarthritis and Cartilage
2008-2010 Executive Committee Member, Biomedical Engineering Society
2009- Editorial Advisory Board Member, Journal of Biomechanics
2011- Executive Committee Member (Chair, 2016-2018), U.S. National Committee on Biomechanics
2014- Associate Editor, Computational Methods in Biomechanics and Biomedical Engineering

Honors

1985-1986 President, Pi tau Sigma, Mechanical Engineering Honor Society, Columbia University chapter
1985 Tau Beta Pi, Engineering Honor Society
1986 William A. Hadley Award in Mechanical Engineering, Columbia University
1986-1987 Fellowship Award, Department of Mechanical Engineering, Columbia University
1987-1991 Frank E. Stinchfield Fellowship, Orthopaedic Research Lab, New York Orthopaedic Hospital
1991 Sigma Xi, Honor Society
1995-2000 First Independent Research Support and Transition Award (FIRST), National Institutes of Health
1997 Y.C. Fung Young Investigator Award, American Society of Mechanical Engineers
2002 Great Teacher Award, Society of Columbia Graduates
2003 Fellow, American Institute of Medical and Biological Engineers
2003 Best Paper Award, Stapp Car Crash Journal, 47:1-13.
2006 Fellow of the American Society of Mechanical Engineers
2010 Fellow of the Biomedical Engineering Society
2012 Columbia Engineering Alumni Association Distinguished Faculty Teaching Award
2013 Basic Science Award, Osteoarthritis Research Society International
2013 Andrew Walz Professorship in Mechanical Engineering, Columbia University
2017 H.R. Lissner Medal, American Society of Mechanical Engineers
2019 ASME Journal of Biomechanical Engineering Editor's Choice award, 140(8):081013, 2018.

C. Contributions to Science

1. Early in my career, I focused on the application of geometric modeling and computer aided design for reconstructing the three-dimensional topography of the articular layers of diarthrodial joints. Our 1991 paper (paper a) described the application of stereophotogrammetry for reconstructing the geometry of the articular layers of the human knee joint, including their thickness maps. These maps provided the first extensive characterization of the articular layers of this joint, thanks to the computerized methodologies developed during this relatively early period in the field of computer-aided geometric modeling and design. We were similarly at the forefront of applying magnetic resonance imaging (MRI) to characterize the geometry of articular layers, using non-invasive techniques applicable to in vivo studies in patients. Our 1999 study (paper b) was the first to establish the accuracy of MRI measurements of cartilage topography,

using stereophotogrammetry as the gold standard. We also conducted many experimental studies investigating the contact mechanics of thumb, shoulder and knee joints, since excessive contact stresses had been implicated as pathomechanical factors in the early onset of osteoarthritis. Examining the contact mechanics of diarthrodial joints required a thorough understanding of the theoretical foundations for contact mechanics of deformable porous-hydrated biphasic materials. In 1994, we proposed the first analytical solution for the contact of spherical biphasic layers, representative of diarthrodial joint contact mechanics, using asymptotic expansions for the dependent variables appearing in the partial differential equations governing this problem (paper c). This study was the first to formulate the correct set of boundary conditions at the interface of contacting biphasic materials. It also demonstrated that the interstitial fluid within cartilage pressurizes considerably upon contact loading, supporting up to 94% of the total contact load in the early time response. A companion study published in 1995 (paper d) employed Fourier transform methods to overcome some of the restrictions imposed by asymptotic expansion methods.

a. Ateshian GA, Soslowsky LJ, Mow VC. Quantitation of articular surface topography and cartilage thickness in knee joints using stereophotogrammetry. J Biomech 1991; 24: 761-776
b. Cohen ZA, McCarthy DM, Kwak SD, Legrand P, Fogarasi F, Ciaccio EJ, Ateshian GA. Knee cartilage topography, thickness, and contact areas from MRI: in-vitro calibration and in-vivo measurements. Osteoarthritis Cartilage 1999; 7: 95-109
c. Ateshian GA, Lai WM, Zhu WB, Mow VC. An asymptotic solution for the contact of two biphasic cartilage layers. J Biomech 1994; 27: 1347-1360
d. Ateshian GA, Wang H. A theoretical solution for the frictionless rolling contact of cylindrical biphasic articular cartilage layers. J Biomech 1995; 28: 1341-1355

2. We validated these theoretical studies with a series of experimental measurements of interstitial fluid pressurization. Capitalizing on the emergence of cheap micro-electromechanical fluid pressure sensors (MEMS), we demonstrated that the theoretical predictions of interstitial fluid pressure using the biphasic theory agreed remarkably well with experimental measurements (paper a). These findings represented an important turning point since they established unequivocally that the biphasic nature of cartilage was essential to the function of this tissue, whereas classical elasticity models of cartilage could not provide insights into this fluid pressurization mechanism. Based on these theoretical and experimental results, we proposed a primary functional role for this interstitial fluid pressurization, whereby elevated fluid pressure would reduce the friction coefficient of articular cartilage by shifting the contact load away from the porous collagen matrix. Using fundamental principles of mass, momentum and energy conservation across the contact interface of porous deformable media, we formulated a novel framework describing the dependence of the friction coefficient on the ratio of interstitial fluid pressure to total contact stress, as well as on the porosity of the contacting surfaces (paper b). To validate these theoretical predictions from experiments conducted on cylindrical cartilage plugs loaded under unconfined configuration, we first demonstrated that the standard biphasic model for cartilage, when extended theoretically to account for the well-known large disparity between its tensile and compressive moduli, could predict a much higher magnitude of interstitial fluid pressurization, consistent with experimental findings (paper c). Using MEMS transducers, we then showed that the experimental frictional response of cartilage depended on the measured interstitial fluid pressurization exactly as predicted from our model (paper d).

a. Soltz MA, Ateshian GA. Experimental verification and theoretical prediction of cartilage interstitial fluid pressurization at an impermeable contact interface in confined compression. J Biomech 1998; 31:927-934
b. Ateshian GA, Wang H, Lai WM. The role of interstitial fluid pressurization and surface porosities on the boundary friction of articular cartilage. Trans. ASME, J. Tribol. (USA) 1998; 120: 241-251
c. Soltz MA, Ateshian GA. A Conewise Linear Elasticity mixture model for the analysis of tension-compression nonlinearity in articular cartilage. J Biomech Eng 2000; 122: 576-586 PMCID: 2854000.
d. Krishnan R, Kopacz M, Ateshian GA. Experimental verification of the role of interstitial fluid pressurization in cartilage lubrication. J Orthop Res 2004; 22: 565-570 PMCID: 2842190.

3. In 1996, I teamed up with Prof. Clark Hung to apply my cartilage mechanics expertise to the emerging field of cartilage functional tissue engineering. Whereas the majority of investigators in this field approached this challenge from the perspective of identifying a suitable scaffold biomaterial, culture environment, or cell sources, we investigated the role of mechanics in the growth process. In 2000, we published a study which was the first to demonstrate that dynamic mechanical loading of engineered cartilage constructs elaborated

far better mechanical properties than unloaded controls (paper a). We have since made considerable progress in our efforts to engineer large cartilage constructs using theoretical and computational tools to optimize nutrient supply (paper b), maximize matrix synthesis by increasing cell seeding density (paper c) and translate our animal cell models to human cartilage constructs (d).

a. Mauck RL, Soltz MA, Wang CC, Wong DD, Chao PH, Valhmu WB, Hung CT, Ateshian GA. Functional tissue engineering of articular cartilage through dynamic loading of chondrocyte-seeded agarose gels. J Biomech Eng 2000; 122: 252-260
b. Nims, R.J., Cigan, A.D., Albro, M.B., Vunjak-Novakovic, G., Hung, C.T., and Ateshian, G.A., 2015. Matrix Production in Large Engineered Cartilage Constructs Is Enhanced by Nutrient Channels and Excess Media Supply. *Tissue Eng Part C Methods* **21**(7)**,** 747-757 PMCID: 4499772
c. Nims, R.J., Durney, K.M., Cigan, A.D., Dusseaux, A., Hung, C.T., and Ateshian, G.A., 2016. Continuum theory of fibrous tissue damage mechanics using bond kinetics: application to cartilage tissue engineering. *Interface Focus* **6**(1)**,** 20150063 PMCID: 4686240
d. Cigan, A.D., Roach, B.L., Nims, R.J., Tan, A.R., Albro, M.B., Stoker, A.M., Cook, J.L., Vunjak-Novakovic, G., Hung, C.T., and Ateshian, G.A., 2016. High seeding density of human chondrocytes in agarose produces tissue-engineered cartilage approaching native mechanical and biochemical properties. *J Biomech* **49**(9)**,** 1909-1917, PMCID: 4920373

4. These experimental findings motivated us to formulate a novel theoretical framework for describing solute transport (such as nutrients) in deformable porous media subjected to dynamic loading, using the framework of mixture theory. By carefully accounting for the frictional interactions of solutes with the porous solid matrix, this theoretical framework predicted that the solute could be pumped from the culture bath into the tissue construct under dynamic loading, at concentrations far exceeding those achieved under passive diffusion (paper a). Since this type of response had never been reported experimentally, several experimental studies were performed which confirmed these theoretical findings unequivocally, under a variety of conditions (papers b & c). More recently, a more direct mechanobiological pathway was discovered in our lab, whereby the latent form of TGF-ß present in synovial fluid was observed to be activated by shearing of the fluid, a natural physiological process in normal joint motion (paper d). The active form of TGF-ß increases the synthesis of lubricin, reducing friction and wear at the articular surfaces.
   a. Mauck RL, Hung CT, Ateshian GA. Modeling of neutral solute transport in a dynamically loaded porous permeable gel: implications for articular cartilage biosynthesis and tissue engineering. J Biomech Eng 2003; 125: 602-614 PMCID: 2854001.
   b. Albro MB, Chahine NO, Li R, Yeager K, Hung CT, Ateshian GA. Dynamic loading of deformable porous media can induce active solute transport. J Biomech 2008; 41: 3152-3157 PMCID: 2633098.
   c. Albro MB, Li R, Banerjee RE, Hung CT, Ateshian GA. Validation of theoretical framework explaining active solute uptake in dynamically loaded porous media. J Biomech 2010; 43: 2267-2273 PMCID: 2993250.
   d. Albro MB, Cigan AD, Nims RJ, Yeroushalmi KJ, Oungoulian SR, Hung CT, Ateshian GA. Shearing of synovial fluid activates latent TGF-beta. Osteoarthritis Cartilage 2012; 20: 1374-1382 PMCID: 3448789.

5. Since 2007, my work has focused significantly on the theoretical foundations for growth mechanics, formulating the foundations for coupling chemical reactions with equations of elasticity, fluid, and solute transport in mixture models representative of biological tissues and cells. This research focus extends the traditional framework of continuum mechanics to encompass phenomena relevant to biological processes, especially in relation to mechanobiology and tissue engineering. To help disseminate these advances to a broader audience of end-users, I teamed up with Jeffrey Weiss at the University of Utah to implement these mixture models of biphasic and multiphasic materials into an open-source finite element code called FEBio (www.febio.org). FEBio, whose development is partly funded by the National Institutes of Health, has now been adopted by a significant segment of the biomechanics community. As of February 2019 the finite element software has over 10,000 registered users. Since 2012 it has been cited in more than 411 journal articles. We have used this growth framework to optimize the culture conditions of large engineered articular layer constructs for the purpose of replacing entire joints with tissue grown in vitro.
   a. Maas SA, Ellis BJ, Ateshian GA, Weiss JA. FEBio: finite elements for biomechanics. J Biomech Eng 2012; 134: 011005 PMCID: 3705975.
   b. Ateshian GA, Maas S, Weiss JA. Multiphasic finite element framework for modeling hydrated mixtures with multiple neutral and charged solutes. J Biomech Eng 2013; 135: 111001 PMCID: 3792408.

c. Ateshian GA, Nims RJ, Maas S, Weiss JA. Computational modeling of chemical reactions and interstitial growth and remodeling involving charged solutes and solid-bound molecules. Biomech Model Mechanobiol 2014; 13: 1105-1120 PMCID: 4141041.
d. Ateshian GA, Shim JJ, Maas SA, Weiss JA. Finite Element Framework for Computational Fluid Dynamics in FEBio. J Biomech Eng 2018; 140 PMCID: 5816258.

Complete List of Published Work in MyBibliography
http://www.ncbi.nlm.nih.gov/sites/myncbi/gerard.ateshian.1/bibliography/40390663/public/?sort=date&direction=ascending

D. Research Support

Ongoing Support

NIH R01 GM083925 Weiss JA (Utah), Ateshian GA (PIs) 09/01/2016- 08/31/2020
"FEBio - Finite Elements for Biomechanics and Biophysics"
This application extends the public-domain finite element program FEBio to model the biomechanics and biophysics of living tissues using fluid-solid interactions with optimized pre-conditioners and solvers, adaptive mesh refinements, new pre- and post-processing features, and dissemination.

NIH R01 AR068133 Hung CT (PI) 05/16/2016-04/30/2021
"Incorporation of Dexamethasone Delivery within Engineered Cartilage"
This application examines the hypothesis that incorporation of polymer microspheres that release dex from within cell-seeded hydrogel constructs will protect constructs from the deleterious effects of cytokine exposure and improve cartilage repair in an inflammatory environment.

Honda Motor Company Morrison B (PI) 01/08/2018-03/31/2019
"Edema Simulations with FEBio"
This project examines brain swelling in traumatic brain injuries caused by the impact of a car with a pedestrian. Brain swelling is simulated using the FEBio finite element software, based on the multiphasic framework for predicting Donnan osmotic pressure.

DoD GRANT12507452 Ateshian GA (PI) 09/01/2018-08/31/2021
"Adaptively Conforming Osteochondral Allografts for Joint Replacements"
The driving hypothesis of this application is that transplanted osteochondral allografts that conform better to the opposing articular surface result in better clinical outcomes than allografts that have only been size-matched for the host site. This project develops a practical methodology for adaptively bending osteochondral allografts during transplantation surgery, such that their articular surface conforms to the anatomy of the recipient's joint.

NIH R01 AR073289 Ateshian GA, Vukelic S (PIs) 01/01/2019-12/31/2022
"Laser Treatment Modality for Strengthening Osteoarthritic Cartilage"
This application develops a novel laser treatment modality to crosslink osteoarthritic cartilage, rendering it stiffer and more resistant to wear.

Completed Support During Last 3 Years

NIH R01 AR060361 Ateshian GA, Hung CT (PIs) 09/20/10-08/31/16
"Optimizing Nutrient Supply in Large Engineered Cartilage Tissue Constructs"
An engineering solution is proposed for the technical challenge of supplying plentiful nutrients for large engineered cartilage constructs by optimizing the number and spacing of narrow channels through the full thickness of construct layers, to recapitulate conditions provided by cartilage canals in early development.

NIH T32 AR059038 Ateshian GA (PI) 09/01/11-08/31/16
"Multidisciplinary Engineering Training in Musculoskeletal Research"
This program provides predoctoral trainees with a superb foundation in the biomedical engineering sciences and technologies that are a critical component of musculoskeletal research, while also teaching them the language of communication and collaboration with clinician and biomedical scientists in this broad field.