BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Corey P. Neu	Donnelly Family Associate Professor of Mechanical Engineering
eRA COMMONS USER NAME COREYNEU	

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Brown University, Providence, RI	Sc.B.	1998	Mechanical Engineering
Brown University, Providence, RI	Sc.M.	1999	Biomedical Engineering
University of California, Davis, CA	Ph.D.	2004	Biomedical Engineering
UC Davis Medical Center, Sacramento, CA and University of California, Berkeley, CA	Postdoc	2007	Tissue Engineering / Cell Biology

A. Personal Statement

My research group studies multiscale biomechanics and mechanobiology of soft tissues, with a special emphasis on connective and cardiac tissues, making use of advanced magnetic resonance imaging and optical/atomic force microscopy-based techniques, to understand development, disease and regeneration in tissues and cells. We are greatly interested in translational research, and I have concentrated in the early part of my career on the creation of new dualMRI and hyperelastic imaging techniques to determine strain patterns and 3D mechanical cues in tissues and cells noninvasively, including articular cartilage, intervertebral disc, cell-laden hydrogels, and intra-nuclear regions of single cells. We most recently demonstrated *in vivo* intra-tissue strains patterns in the articular cartilage and intervertebral discs of human volunteers using dualMRI for the first time. For the past several years, we have become intensely involved with the creation of extracellular matrix-based mimetic biomaterials for use in cartilage repair, focusing most closely on native oligomeric collagens with tunable properties through magnetic alignment or densification of fibrils to attain near tissue-like structural properties. We have also focused our efforts on the effects of growth factors, cytokines, and enzymes on the mechanoregulation of zonal cartilage RNA and protein expression and surface tribology. Research activities in my lab have been supported by NIH, NSF, Alfred Mann Institute at Purdue, Spine Research Society, and Eli Lilly and Company. Key manuscripts include:

a. Chan D.D., Cai L., Butz K.D., Trippel S.B., Nauman E.A., **Neu C.P.** (2016). *In vivo* articular cartilage deformation: noninvasive quantification of intratissue strain during joint contact in the human knee. *Scientific Reports* 6:19220.
b. Chan D.D., Cai L., Butz K.D., Nauman E.A., Dickerson D.A., Jonkers I., **Neu C.P.** (2018). Functional MRI can detect changes in intratissue strains in a full thickness and critical sized ovine cartilage defect model. *Journal of Biomechanics* 66(3):18-25.
c. Novak T., Fites K., Xu X., Worke L., Ciesielski A., Breur G., **Neu C.P.**, (2016). *In vivo* cellular infiltration and remodeling in a decellularized ovine osteochondral allograft. *Tissue Engineering, Part A* 22(21-22):1274-1285
d. Griebel A., Trippel S.B., **Emery N.C.**, **Neu C.P.** (2013). Noninvasive assessment of human osteoarthritis severity by multicontrast magnetic resonance imaging. *Magnetic Resonance in Medicine* 71(2):807-14.

B. Positions and Honors

Positions and Employment

2004-2007 NIH NRSA Postdoctoral Fellow, University of California Medical Center, Sacramento, CA, and University of California, Berkeley, CA. Mentors: A.H. Reddi and K. Komvopoulos.
2007-2008 Assistant Professor (Orthopaedics), University of California, Davis, Sacramento, CA
2008-2014 Assistant Professor-tenure track (Biomedical Engineering), Purdue University, W. Lafayette, IN
2009-2014 Assistant Professor-adjunct (Orthopaedics), IU School of Medicine, Indianapolis, IN
2014-2015 Associate Professor (Biomedical Engineering), Purdue University, W. Lafayette, IN

2014-2015 Associate Professor-adjunct (Orthopaedics), IU School of Medicine, Indianapolis, IN
2015-2019 Associate Professor-adjunct (Biomedical Engineering), Purdue University, W. Lafayette, IN
2015-Present Donnelly Family Endowed Associate Professor (Mechanical Engineering), University of Colorado, Boulder, CO
2017-Present Member, BioFrontiers Institute

Other Experience and Professional Memberships

2002-Present Member, International Society for Magnetic Resonance in Medicine
2005-Present Member, Orthopaedic Research Society
2007-Present Journal Reviewer: *ACS Nano, Acta Biomaterialia, Advanced Functional Materials, Applied Physics Letters, Biophysical Journal, Magnetic Resonance in Medicine, Nature Protocols, Osteoarthritis and Cartilage, PNAS, Tissue Engineering, Parts A-C, Journal of Biological Chemistry, Journal of Biomechanics, Journal of Orthopaedic Research, Tissue Engineering, Science Translational Medicine, Science Translational Medicine, Scientific Reports*
2009-Present Member, American Society of Mechanical Engineers
2013-Present Member, Biomedical Engineering Society
2015-2018 American Society for Mechanical Engineering Summer Bioengineering Conference: Musculoskeletal Tissue Mechanics Theme Chair, Solid Mechanics Committee
2015-2019 Member, NIH Musculoskeletal Tissue Engineering (MTE) Study Section
2019-Present Founder and CEO, TissueForm, Inc.

Honors

2004-07 National Institutes of Health Ruth L. Kirschstein National Research Service Award
2005 Zuhair A. Munir Best Dissertation Award
2011-12 Fellow, Entrepreneurial Leadership Academy (Burton D. Morgan Center / Kauffman Foundation)
2014 BMES-CMBE Rising Star Award
2014 National Science Foundation CAREER Award
2015 Donnelly Family Endowed Professorship

C. Contribution to Science

1. Noninvasive Imaging Methods to Characterize the Mechanics of Musculoskeletal Tissues. For nearly a decade, we have been developing noninvasive imaging methods to assess multiscale biophysics and biomechanics of soft tissues. Our main goals in this area of research are to provide tools that measure functional mechanical quantities as imaging biomarkers of disease and repair, and to enable fundamental studies of small-scale motion in response to physical stimuli and cellular changes. We developed dualMRI (displacements under applied loading by magnetic resonance imaging), a versatile and noninvasive technique that measures internal material strains with high spatiotemporal resolution. dualMRI is able to measure the mechanics of connective and cardiac tissues, and short T2 biomaterials, including ligament and meniscus, that are traditionally difficult to image by MRI. We are able to determine the mechanics of diverse biomaterials, including cartilage, intervertebral disc, and cell-laden hydrogels and collagen-rich tissue constructs. We found significant correlations between dualMRI and histological-based assessments osteoarthritis severity, indicating a promising clinical and diagnostic utility for the technique *in vivo* in the detection of the early disease state. We have imaged explanted and intact joint tissues. Most recently, we acquired internal strains in both tibiofemoral cartilage and cervical intervertebral discs of human volunteers *in vivo* for the first time, as represented in the selected publications below:

a. Pastrama M.I., Ortiz A.C., Zevenbergen L., Famaey N., Gsell W., **Neu C.P.**, Himmelreich U., Jonkers I. (2019). Combined enzymatic degradation of proteoglycans and collagen significantly alters intratissue strains in articular cartilage during cyclic compression. *Journal of the Mechanical Behavior of Biomedical Materials* (*in press*) https://doi.org/10.1016/j.jmbbm.2019.05.040.
b. Zevenbergen L., Gsell W., Chan D.D., Vander Sloten J., Himmelreich U., **Neu C.P.**, Jonkers I. (2018). Functional assessment of strains around a full-thickness and critical sized articular cartilage defect under compressive loading using MRI. *Osteoarthritis & Cartilage*. 26(12):1710-1721.
c. Luetkemeyer C.M., Cai L., **Neu C.P.**, Arruda E. (2018). Full-volume displacement mapping of anterior cruciate ligament bundles with dualMRI. *Extreme Mechanics Letters.* 19:7-14

d. **Neu C.P.** (2014). Functional Imaging in OA: Role of Imaging in the Evaluation of Tissue Biomechanics. *Osteoarthritis & Cartilage* 22(10):1349-1359.

2. Fabrication Processes to Create Unique Scaffold Architectures. Our group has explored the regeneration of soft biological tissues through cell-extracellular matrix interactions, with a focus on particulated tissues, collagen-rich environments, and fibrosis. We have developed a new scaffold fabrication technology, termed *Cartilage Clay*, to nondestructively combine decellularized and micron-scale cartilage particles in a chondrogenic resin material. We also demonstrated tissue-like properties using molecular packing of collagen to both densify and align fibrils, while also maintaining viable and encapsulated cells and other molecules (e.g. proteogylcans) that are critical to native tissue function. We showed preclinically that recellularized osteochondral scaffolds *in vivo* demonstrate excellent healing and lateral integration with surrounding tissues. Representative publications include:

a. Worke L., Barthold J.E., Seelbinder B., Novak T., Main R.P., Harbin S.L., **Neu C.P.** (2017). Densification of type I collagen matrices as a model for cardiac fibrosis. *Advanced Healthcare Materials*. 6(22). DOI: 10.1002/adhm.201700114.
b. Novak T., Seelbinder B., Twitchell C.M., Voytik-Harbin S.L., **Neu C.P.** (2016). Dissociated and reconstituted cartilage microparticles in densified collagen induce local hMSC differentiation. *Advanced Functional Materials* 26(30):5427-5436.
c. Novak T., Seelbinder B., Twitchell C.M., van Donkelaar C.C., Voytik-Harbin S.L., **Neu C.P.** (2016). Mechanisms and microenvironment investigation of cellularized high density gradient collagen matrices via densification. *Advanced Functional Materials* 26(16):2617-2628.
d. Novak T., Voytik-Harbin S.L., **Neu C.P.** (2015). Cell encapsulation in a magnetically aligned collagen-GAG copolymer microenvironment. *Acta Biomaterialia* 11:274-82.

3. Microscopy Techniques for Biomechanics and Mechanobiology of Single Cells. In recent years we have focused on the small-scale measurement of mechanics and biology in single cells. We designed a novel hybrid method that uses optical microscopy and hyperelastic warping to directly link intranuclear strain patterns to RNA expression. Our data suggest that strain is transferred over spatial scales from the tissue surface to nucleus interior, and directly contributes to patterns of gene expression through spatially-dependent nuclear deformation. Moreover, we have recently shown that substrate stretching and osmotic loading of single cells influences both the traction force experienced at the cell surface, and the transfer of strain to the nuclear interior, as represented in the selected publications below:

a. Ghosh S., Seelbinder B., Henderson J., Watts R., Scott A.K., Veress A.I., **Neu C.P.** (2019). Deformation microscopy for dynamic intracellular and intranuclear mapping of mechanics with high spatiotemporal resolution. *Cell Reports* 27(5):1607-1620
b. Xu X., Li X., Cai L., Calve S., **Neu C.P.** (2016). Mapping the nonreciprocal micromechanics of individual cells and the surrounding matrix within living tissues. *Scientific Reports* 6:24727.
c. Calve S., Ready A., Huppenbauer C., Main R., **Neu C.P.** (2015). Optical clearing in dense connective tissues to visualize cellular connectivity in situ. *PLoS ONE*. Jan 12;10(1):e0116662. PMID: 25581165.
d. Mousoulis C., Maleki T., Ziaie B., **Neu C.P.** (2013). Atomic force microscopy-coupled microcoils for cellular-scale nuclear magnetic resonance spectroscopy. *Applied Physics Letters* 102, 143702.

4. Tribology and Viscosupplements for Articular Cartilage Repair. In addition to our imaging work, we have been interested in the basic biology and tribology of articular cartilage. We have identified the role of growth factors (e.g. TGFbeta) and cytokines in the mechanotransduction of cartilage lubrication. We have also designed novel tissue constructs to better study cartilage using defined model systems, and explored new optical clearing methods for dense collagen- and proteoglycan-rich tissues, as represented by the selected publications below:

a. Lawrence A., Xu X., Bible M.D., Calve S., **Neu C.P.**, Panitch A. (2015). Synthesis and characterization of a lubricin mimic (mLub) to reduce friction and adhesion on the articular cartilage surface. *Biomaterials* 73:42-50. PMID 26398308.
b. Chan S.M.T., **Neu C.P.**, DuRaine G.D., Komvopoulos K., Reddi A.H. (2010). Atomic force microscope investigation of the boundary-lubricant layer in articular cartilage. *Osteoarthritis and Cartilage* 18(7):956-63.

c. **Neu C.P.**, Komvopoulos K., Reddi A.H., Schmid T.M., Di Cesare, P.A. (2010). Friction Coefficient and Superficial Zone Protein are Increased in Patients with Advanced Osteoarthritis. *Arthritis and Rheumatism* 62(9):2680-7. PMID: 20499384.
d. **Neu C.P.**, Khalafi A., Komvopoulos K., Schmid T.M., Reddi A.H. (2007). Mechanotransduction of superficial zone protein by TGF-β signaling. *Arthritis and Rheumatism* 56(11):3706-3714.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1nK45KHEjhGQw/bibliograpahy/48864777/public/?sort=date&direction=descending

D. Research Support

There is no overlap with any of the currently funded research.

Active Research Support

NIH 2 R01 AR063712-07 / Probing Osteoarthritis Pathogenesis by Noninvasive Imaging of Cartilage Strain
PI: Neu 4/2019–3/2024
Goal: To utilize novel noninvasive imaging methods of measuring articular cartilage biomechanics to predict osteoarthritis (OA) pathogenesis *in vivo* following anterior cruciate ligament transection.

NIH R01 AR071359 / Biomechanical Influence of ECM Remodeling on the Developing Enthesis
CoI: Neu; PI: Calve 9/2017–8/2022
Goal: To quantify protein dynamics in the developing enthesis using ncAAs and mass spectrometry, map architectural changes in ECM organization during enthesis formation, and measure the influence of growth and embryonic motility on developing enthesis mechanics.

NSF (CMMI) 1349735 / CAREER: Direct Measurement of Intranuclear Strain and Gene Expression in Single Cells *In Vivo* (+ Equipment Supplement)
PI: Neu 7/2014 – 6/2020 (NCE)
Goal: To simultaneously measure *in vivo* mechanisms of strain transfer that influence intranuclear strain and RNA synthesis in the nuclei of single cells.

NSF (CMMI) 1662429 / Biomechanical Simulations of Progressing Osteoarthritis to Advance Understanding and Therapies
CoI: Neu; PI Pierce 9/2017–8/2020
Goal: To establish a new class of computational tools that allows, for the first time, patient-specific modeling of OA progression considering the biomechanics and kinetics of cell and extracellular matrix turnover.

Lab Venture Challenge / Next-generation dermal fillers
PI: Neu 12/2018 – 11/2020
Goal: To test the safety and efficacy of transplantable matrices for dermal filling, including *in vitro* endotoxin measures and *in vivo* murine (subcutaneous) studies.

Completed Research Support (within the last three years)

NIH R01 AR063712 / Probing Osteoarthritis Pathogenesis by Noninvasive Imaging of Cartilage Strain
PI: Neu 9/2013–3/2019
Goal: To apply new displacements under applied loading MRI (dualMRI) technology to noninvasively identify the earliest disease stages using three established OA models.

NIH R21 AR066665 / Intervertebral Disc Mechanics Measured by dualMRI *In Vivo*
PI: Neu 6/2016–5/2019 (NCE)
Goal: Noninvasively measure in humans intervertebral disc mechanics using displacements under applied loading by MRI, and correlate measures to quantitative MRI values.

NIH R01 AR065398 / Investigation of Proteoglycan Mimetics as Treatments for Osteoarthritis
CoI: Neu; PI: Panitch 4/2014–3/2019
Goal: To apply new mimetics of several key proteoglycans in the joint for the treatment of osteoarthritis, especially at the early stage

NIH R21 AR066230 / Biomechanics of Human Articular Cartilage Measured *In Vivo*
PI: Neu 4/2014–3/2018
Goal: Implement displacements under applied loading by MRI for the measurement of articular cartilage mechanics, and correlation to quantitative MRI values

OVPR Emerging Research Incentive Grant Program / Next-Generation Orthobiologics for Joint Repair
PI: Neu 9/1/13 – 8/31/16
Goal: To fabricate and functionally test a new cell-free material for the repair of joint tissues.