



UPCOMING: FORCENET WEBINAR

with **Helene M. Langevin**

October 21st, 2 PM EST

MECHANICAL ASPECTS OF ACUPUNCTURE

Please join us on Monday, October 21st at 2pm EST for an exciting webinar with Dr. Helene M. Langevin, Director of the National Center for Complementary and Integrative Health (NCCIH) at the National Institutes of Health (NIH). Acupuncture needling involves the insertion and manipulation of acupuncture needles, which produce small but measurable stresses and strains within tissues. We are gradually becoming more aware of the importance of mechanically-generated signals in the body, as well as their modulation by the stiffness and viscosity of tissues. This talk will summarize what we know about the mechanical effects of acupuncture, current gaps in knowledge, and areas of research where an improved understanding of the mechanical aspects of acupuncture could contribute not only to a better understanding of acupuncture mechanisms, but also a broader understanding of mechanobiology.



Helene M. Langevin, M.D.
Director of NCCIH at NIH

Dr. Langevin, M.D., is director of the National Center for Complementary and Integrative Health (NCCIH) at the National Institutes of Health (NIH). As NCCIH director, Dr. Langevin oversees the U.S. Federal government's lead agency for research on the fundamental science, usefulness, and safety of complementary and integrative health approaches and their roles in improving health and health care. We are so excited to welcome her as a speaker for ForceNET - you won't want to miss it!

**Join us on October 21st at
2 PM EST!**

Zoom link: <https://duke.zoom.us/j/97377134739>

Meeting ID:
973 7713 4739

Join ForceNET
today via the QR
code!



SAVE THE DATE

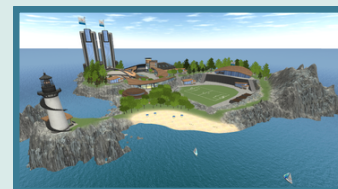
U24 Collaborative Virtual Symposium February 22nd, 2025

ForceNET is collaborating with SPINEWORK and NeuronS_MATTR to bring our membership communities an exciting event in February 2025!

We will be hosting our inaugural virtual scientific symposium through the Virbela platform. Members of ForceNET, SPINEWORK, and NeuronS_MATTR will be able to interact with colleagues in real-time, through Virbela's innovative, virtual reality (VR) technology that allows you to join in collaborative spaces from your personal computer (without a VR headset or any additional gear).

This event will feature 4 concurrent tracks for participants to attend that will feature presentations on topics such as imaging, force-based mechanisms for clinicians, and spinal modeling. You will also have the chance to interact with other attendees and present scientific posters of your research, just like an in-person symposium experience. We will share more information about registration and specific offerings with our collective communities as the date gets closer.

We are looking forward to get together as a Force-Based Manipulation community and are thrilled about the extended reach and flexibility that the Virbela will provide to our members across the globe. Mark your calendars and get excited!



**In the meantime, join ForceNET
and get connected!**

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SPRING/SUMMER 2024 WEBINAR RECAP

ForceNet hosted Steven George PT, PhD, FAPTA, for a webinar titled "Musculoskeletal Pain Phenotype Research -Team Building and Lessons Learned" on August 27th, 2024. The following are some highlights from this excellent and timely webinar.

Dr. George shared observations on team building, noting that meaningful clinical research is always done with a team because our current research questions require the need for different expertise. He described how he became interested in investigating how genetic and psychological factors interacted to impact experimental pain sensitivity and pain phenotypes. His phenotyping team has 8 types of team members, and currently consists of a physical therapist, psychologist, geneticist, statistician, orthopedic surgeon, exercise scientist, doctoral students and postdoctoral fellows. He then divided his presentation into 3 chapters of *Cautionary Tales and Lessons Learned*: (1) Lost in Translation, (2) House of Cards, and (3) Philosophical Differences.

Chapter 1: Lost in Translation.

Dr. George's research team desired to identify phenotypes and develop precision medicine approaches that limited the development of chronic shoulder pain after shoulder surgery. They named this project the "Biopsychosocial Influence on Shoulder Pain (BISP) project, which consisted of Phase I and II components. Phase I identified several candidates for genetic and psychological factors with one particular combination being predictive of outcomes in two independent cohorts (experimentally induced shoulder pain and shoulder pain arthroscopy at 12 months). Individuals with this particular risk phenotype had about twice the likelihood of developing chronic shoulder pain. Phase II dealt with a more tailored approach of

testing treatments involving 4 subgroups that were matched to the risk phenotype. While there was about a 63% recovery rate for those that had both the genetic and psychological phenotypic trait, this was only about 4% greater than the other subgroups, which wasn't likely to be clinically relevant. Despite the failure, Dr. George noted that these types of translational approaches have been fantastic for improving our understanding of pain biology and processing of nociception. So the question becomes, "Is pain lost in translation?" The results of these Phase I & II projects led Dr. George to think that: A) phenotypes formed with nociception in mind may not be relevant for the pain experienced, and B) phenotypes formed with the pain experience in mind may not be relevant for reducing pain impact.

Chapter 2: House of Cards.

The question then becomes, is it important to differentiate structure from pain in order to develop pain phenotypes, or do we need to differentiate phenotyping based on structure and phenotyping based on pain? Dr. George went on to discuss the work by his colleague Adam Goode (PMID: 35991624, 36804589) on osteoarthritis and lumbar phenotypes. One take home message from this work was that pain biomarkers that looked good in cross-section, may not look nearly as good when investigated longitudinally - especially with regard to phenotypic pain. He also noted the large variability in the data of relevant studies. The summary of Chapter 2 was that structural and pain phenotypes will differ if you are looking only at structural changes subgroups, but these structural subgroups may not relate to clinical pain outcomes. Structural change phenotypes are easier to identify, but the idea that these structural phenotypes will relate to pain phenotypes has been easily dispelled in the current research literature.

Chapter 3: Philosophical Differences.

Dr. George referenced quotes by E.M. Forster saying "it is one thing to postulate a goal, but quite another to say that science is capable of achieving that goal," and W. Savage saying "a pin for example - may cause someone to feel pain, but to feel the pin is not to feel the pain. It is not the ability to feel pins we wish to measure here but the ability to feel pains." He noted that there is a recent push for objective measures of pain; however, this often shows a lack of understanding of these philosophical issues at hand. He noted that there are long-standing philosophical tensions with "objectification" of pain and phenotyping that we need to remain ever mindful of, and that if you desire to change pain impact, you need to think in terms of your pain phenotype being local, and not starting at nociception. Dr. George concluded the webinar by answering several questions from the virtual audience.

We would like to thank Dr. George for sharing his insights and research with ForceNET! We encourage you to view the recorded webinar in its entirety [here](#).



Steven George, PT, PhD, FAPTA
Duke University

SPRING/SUMMER 2024 WEBINAR RECAP

ForceNet hosted Dr. Neil Theise, MD, of the NYU Grossman School of Medicine for a webinar titled "The Human Interstitium as a Body-Wide Communication Network" on April 23rd, 2024. The following is a summary of this fascinating presentation.

Dr. Theise opened his presentation by saying that he thinks of the interstitium as more of a system and not an organ, despite earlier publicity around the finding of a "new organ." He notes that we have known of the interstitium for centuries, but what he and his colleagues discovered was an unrecognized interstitium. The two levels of scale that had been described to date are the intercellular interstitium (the space between cells such as squamous cells) and a perivascular interstitium (or pericapillary space), which is the space where nutrition crosses into tissues and wastes out of the tissues into the bloodstream. He reminded us that the interstitium regulates fluid flow, cell nourishment, permeability and movement of cells, liquids, solutes, mechanical properties (resistance to compression), and is a source of lymph.

Dr. Theise related the story of what he originally thought were "empty space" artifacts created during histological tissue processing of the bile duct tissue, but upon closer examination, surprisingly found that these "empty spaces" in the collagen were not regular vascular endothelial cells - and that the circumference of these spaces were not completely lined with cells. This was unusual, because it was universally accepted

that whenever you have an extracellular matrix in the body, you have a cell interposed between the extracellular matrix and any fluid that is going by.

He and his colleagues discovered that these "empty spaces," previously dismissed as artifacts, were not just located in the bile duct and bladder tissues, but instead were present all throughout the gastrointestinal tract, skin and other body tissues. These mystery "empty spaces" were not vascular, venous, or sinusoidal spaces, but were pre-lymphatic spaces. Therefore, these spaces are, by definition, an interstitium with fibroconnective tissue and a source of lymph. It turns out that these "empty spaces" were actually filled with hyaluronic acid - and when stained, allowed the continuity of these interstitial spaces to be seen. Certain cancer cells on histological tissue sections appear to line themselves up in single file - it turns out that these single file cancer cells were moving through these interstitial spaces prior to entering a lymph node. Dr. Theise concluded his presentation with a summary for future directions. He noted that:

- Fibroconnective tissue is a body-wide network comprised of layers that are more stiff than collagen (what most people know as fascia) and less stiff than the interstitium (mostly hyaluronic acid);
- The interface between these two domains allows for modulation of shear stress at microscopic and macroscopic scales;

- Hyaluronic acid containing domains are water-holding and allow for free flow of water and small molecules;
- Resident cell populations of the interstitium include a complex of mesenchymal cells, as well as macrophages and mast cells. Other inflammatory cells (e.g. lymphocytes) traverse the interstitium in the setting of tissue injury or disease. The interstitium serves as conduits for trafficking of malignant cells and infectious organisms.

ForceNET would like to thank Dr. Theise for sharing the story of this exciting discovery with our members. We encourage you to watch the entirety of his presentation, which you can find [here](#).



Neil Theise, MD
NYU Grossman School of Medicine

We extend our thanks and appreciation to our esteemed speakers that dedicated their time to the ForceNET community! In case you missed any, you can access recordings of these and past events on our website or YouTube page. If you have any requests for future topics, please reach out to the ForceNET team. We'd love to hear from you!

ForceNET Member Spotlight: Dr. Medha

Pathak

We are excited to announce a new member of the ForceNET core team, Dr. Medha Pathak, PhD.

Dr. Pathak is an associate professor of physiology and biophysics at the University of California, Irvine School of Medicine and heads the Pathak Lab where she investigates how mechanical forces shape neural processes and develops novel approaches to study complex biological processes. Dr. Pathak has joined ForceNET leadership as a co-investigator, and we are excited for her contributions!



Medha Pathak, PhD
University of California, Irvine

What drew you to become involved with ForceNET?

As a researcher studying how mechanical forces shape cellular- and tissue-scale processes, I'm naturally curious about the mechanisms by which these modalities work. As someone with hyper-mobile Ehlers Danlos Syndrome, I have benefited greatly, as a patient, from hands-on therapies that involve force-based manipulations (FBMs). ForceNET's mission to bridge the knowledge gap between clinical outcomes and mechanisms underlying FBMs is thus one close to my heart as both a researcher and a patient. I was especially drawn by their dual mission to support research, as well as outreach, across diverse fields both of which are crucial to advancing this inter-disciplinary field.

What are you most looking forward to contributing to ForceNET in your new role?

I am excited to strengthen the interactions between basic scientists like myself, who think of cellular force transduction at the molecular and cellular levels, and clinicians and researchers who employ forces at the tissue and organism scale

for therapeutic outcomes. Breaking down the silos between these groups is essential to understanding how force-based manipulations work and to improving their efficacy and outcomes in the clinic.

What inspired you to pursue a career in your field?

My fifth grade science teacher in India encouraged me to ask why, and never tired of my questions. She introduced me to the fascinating world of science and the joy of figuring out how things work. My parents, an engineer and a child psychologist, taught me to think independently and gave me the freedom to follow my passions. I grew up surrounded by books and lively discussions with three inquisitive siblings. By age 11, I knew I wanted to be a scientist and I'm fortunate that I was able to pursue that dream.

Can you share a memorable moment or experience that shaped your professional journey?

As a Master's student in India, I presented a paper from Udi Isacoff's lab for a journal club, which described a novel genetically-

encoded sensor for membrane voltage. I was drawn to this paper for its creative approach! Looking back now, it was a landmark paper that ushered in a new generation of voltage sensors that revolutionized neuroscience.

When I started applying for grad schools, Udi's lab was my top choice. As luck should have it, I was accepted into the Biophysics Graduate Program at UC Berkeley, and I ended up doing my PhD with Udi. This was a truly wonderful experience! Udi's lab was as creative and fun a place as the journal club paper suggested, and I learnt so much about how to do science from him and my lab mates. Udi was also an incredibly fun and supportive mentor who challenged me to go beyond what I thought I was capable of.

The six years I spent living in Berkeley, with all its charming quirks and cultural diversity, shaped my outlook both as a person and a scientist, and gave me lifelong friends from all over the world. That journal club presentation years ago led me to the best launching pad I could have ever imagined for an academic career!

What is the best part of your job?

My two favorite parts of my job are experiencing the thrill of discovery and the joys of mentoring. That magical moment when you figure something out is so exhilarating -- the heady feeling that it gives you! Watching my trainees grow and succeed is another special feeling, especially when they begin to come up with their own ideas or to challenge mine, and we transition to discussing as colleagues rather than teacher and student.

...Continue to the next page to read more from our Spotlight interview!

ForceNET Member Spotlight with Dr. Pathak: Continued

Why are you interested in force-based manual therapy?

I have experienced the enormous therapeutic benefits of force-based manual therapies such as physical therapy, massage, and acupuncture. As a scientist, I want to understand the mechanisms underlying their efficacy and figure out ways to make them even more effective.

What gaps do you see in force-based manipulation research?

There is such a gulf between the practice of these therapies and the understanding of the underlying physiological mechanisms. Lack of information regarding how these therapies work is holding back progress in achieving greater clinical efficacy.

In which direction should research progress?

Research into FBMs needs to have an interdisciplinary approach, with teams comprising clinical practitioners and basic scientists. We need a combination of pre-clinical animal models and human subjects research to uncover fundamental physiological mechanisms. Insights from such mechanistic studies will fuel improvements in clinical practice, which will need to be tested through rigorous clinical trials.

How do you envision the future of healthcare?

My hope for the future of healthcare is an approach individualized for the person, with a focus on optimizing health and preventing disease. The proliferation of personal wearable devices, data science approaches to track health metrics, and low-cost genomic analysis gives us an unprecedented opportunity to make this a reality. Done right, this can bring down healthcare costs and make it more accessible to everyone.

Do you have a personal motto?

Do what you love and love what you do.

Share your most cherished project.

My favorite project is typically the one that I'm currently focused on! My lab studies the Piezo ion channels - whose discovery was recognized with a Nobel Prize to Ardem Patapoutian in 2021. Piezos have emerged as critically important mechanosensors in a number of physiological processes, and they could well be important players in FBMs. These days, my lab is really excited about a new hiPSC-based molecular platform we have developed to visualize the spatial and temporal dynamics of endogenous Piezo1 in native cellular conditions in a variety of human cells and organoids. We believe this approach will help us understand how Piezo1 can mediate a number of different outcomes based on mechanical and physiological context.

What motivates you to get up in the morning?

To explore the world, whether it is by traveling, sampling new cuisine, or peering through the microscope to spy on cells. And to interact with fun, curious, and playful people, both in my large and international circle of friends and family, and the wide network of collaborators that I'm lucky to work with.

Which virtue do you find overrated or underrated?

Honesty is an "old-fashioned" and underrated virtue these days, but one that I feel is foundational for strong science, society, and relationships.

What is one thing you couldn't live without?

My hat and sunglasses!

Which words or phrases do you overuse?

"Have fun with it" - life is too short to not be doing what we enjoy and enjoying what we do!

Favorite neurotransmitter?

Serotonin, 95% of which is found outside the brain. I have been introduced to its many roles thanks to my husband, who has studied serotonin receptors for over 30 years.

Comfort food of choice?

Khichdi with kadhi - an Indian dish made with split moong daal lentil and rice, seasoned with ginger, turmeric, green chilies, cumin, served steaming hot with a bowl of mildly spicy yogurt soup.

Share your favorite guilty pleasure.

A bowl of Alphonso mango ice cream!

Where would you like to live?

I love traveling and experiencing new places. I'd be happy to live in many places, and I have been lucky to experience the rich diversity of growing up multilingual in India and then living in three different parts of the US. I have very much enjoyed my time in California, which offers such a breathtaking variety of landscapes, climates, cultures, flora and fauna.

Any favorite podcasts?

Ground Truths by Dr. Eric Topol; Bendy Bodies by Dr. Linda Bluestein.

What advice would you give your younger self?

It will all work out; enjoy the journey!

Special thanks to Dr. Pathak for featuring in the ForceNET Member Spotlight! We are so excited to welcome you to the team.



Medha, with her dog, Elsa (named after Elsa the Lioness from *Born Free*)