Medical Xpress

Another step forward in the fight against lower back pain: Integrating experiments and computational methods

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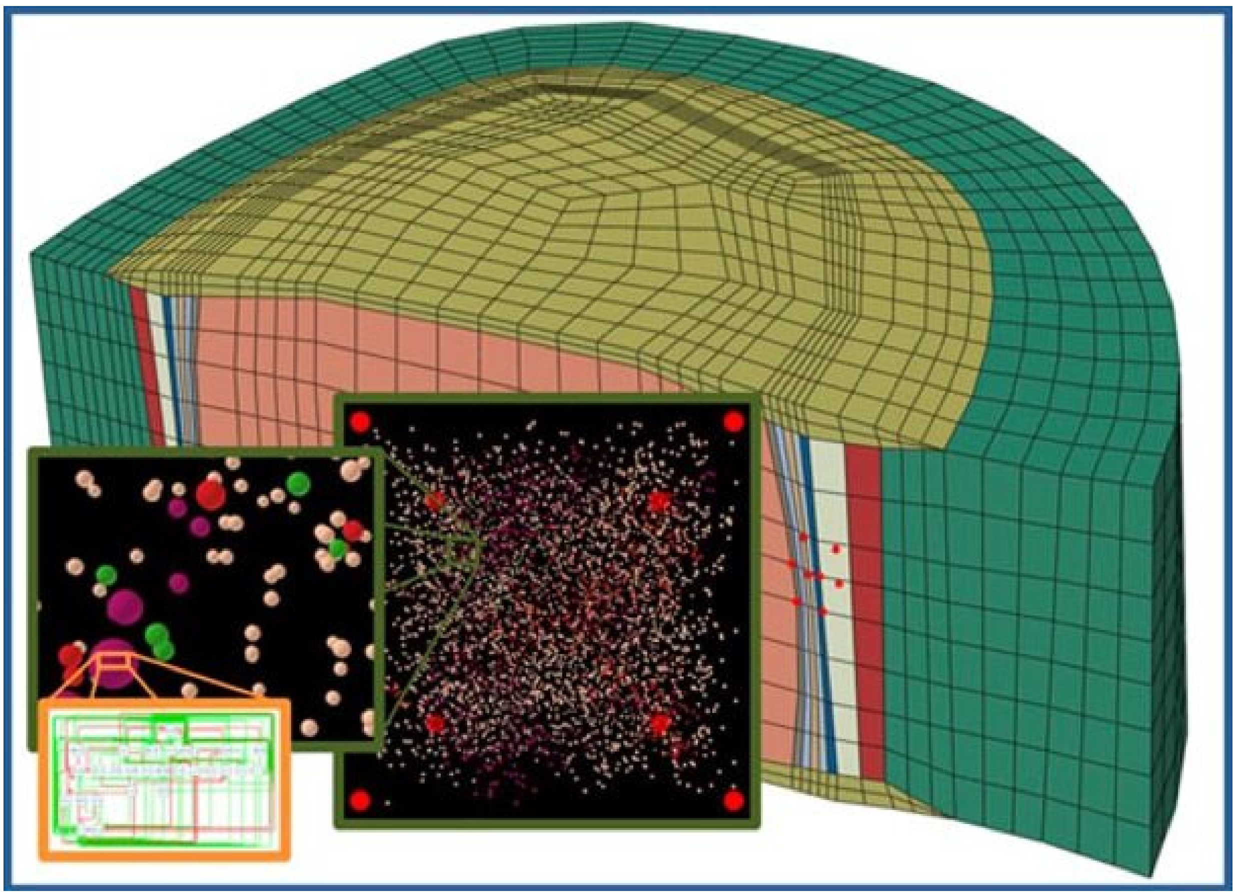

Scheme of representation of the intervertebral disc in which the vision of the organ is integrated up to the subcellular levels. Credit: UPF

Lower back pain is the most widespread musculoskeletal problem in the population, with a huge economic and social impact. According to data for 2017, years of living with disability due to lower back pain have increased by more than 50% since 1990, especially in low- and middle-income countries. In addition, it is the main cause of employee absenteeism, and the difficulty of establishing a clear diagnosis limits treatment options, which usually focus on the pain treatment, without being able to propose possibilities for curing the problem. As a result, people suffering with chronic low back pain are often greatly misunderstood. The difficulty for health professionals is that there are many causes of low back pain and they are difficult to identify. Degeneration of the lumbar intervertebral discs usually causes more than a third of low back pain. While a better understanding of this degeneration can bring great benefits to the treatment and management of the disease, the degeneration of the lumbar intervertebral discs is highly multifactorial and the mechanisms are poorly understood, despite advances in experimental and clinical research.

Researchers in the area of Biomechanics and Mechanobiology (BMMB) at the UPF Biomedical Engineering Research Unit BCN MedTech directed by Jerôme Noailly have been working for more than ten years on the development of computer models that can reflect the mechanisms associated with intervertebral disc degeneration. These models combine mechanics and biology. They allow generating information that is not directly measurable, to discover levers that can slow down or deactivate the degenerative processes that take place in addition to the effects of natural aging in some people. In recent years they have been inspired by the modeling used in systems biology to create a computer model to understand the complex cellular interactions that take place inside the intervertebral discs. The results have been published in the journal *Frontiers in Bioengineering and Biotechnology* and are part of the doctoral thesis of the researcher Laura Baumgartner.

Intervertebral discs are large gelatinous sacs largely composed of water, up to 80% of the volume in the central area. Like sponges, if they lose water they are crushed by the pressure exerted by the body. Dehydration of the discs is common in cases of degeneration and there is currently no treatment to rehydrate the affected tissues. UPF researchers are trying to understand the reasons and dynamics for this dehydration and degeneration.

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"The goal of our models is to see what activity there is in cells in different regions of the central tissue of the intervertebral disc, the nucleus pulposus, where degenerative processes are assumed to begin", Baumgartner explains. "We aim to integrate the combined effect of various stimuli into cellular activity and see what effects they have".

Intervertebral disc cells respond to a large number of stimuli. These stimuli are largely regulated by the mechanical load caused by a person's physical activity. On the one hand, the cell feels this load on the surface, and on the other hand, these loads also affect the concentrations of biochemical stimuli in the cellular environment, such as the inflammatory environment, the nutritional environment, etc.

"The integrated study of all stimuli on an experimental level is very complicated and involves a very high financial cost", Baumgartner continues, "but the combination with computational research enables approximations of individual cell responses in a complex environment".

The researchers have developed a truly interdisciplinary methodology, which they hope to see increasingly replicated, and consists of the integrated management of experimental work with in vitro samples, and modeling work with mathematical and computational methods (in silico).

To perform the in vitro experiments, Baumgartner spent four months in the Laboratory for Orthopaedic Technology at ETH Zurich University. She examined cellular behavior under different variables, such as various levels of glucose concentration, and measured the production of inflammatory factors, the gene expression of the structural proteins that make up the tissues of the intervertebral disc, that of enzymes that are responsible for degrading these structural proteins and, finally, cell viability (the number of living cells that exist).

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The integration of data from these in vitro experiments was crucial to refine the computational model. "By optimally combining two research disciplines, we are able to achieve an efficient methodology for understanding very complex regulations in a tissue, which ultimately increases our understanding of degenerative processes", Baumgartner affirms.

The next step for the researcher is to add more different types of stimuli, including the impact of mechanical stimuli. Noailly's laboratory has been developing computer models of different tissues of the human body for years. In relation to the model in question, the goal is to integrate the cellular response to mechanical loads experienced in our day to day, such as sleeping, walking, driving a car or walking with a heavy backpack. "The result of Laura's research is an excellent example of a proof of concept of the new methodology that we have developed and allows us to transfer experimental information into suitable parameters for computational models. It is crucial to be able to move from the lab to the clinic, but it is also a big challenge. In the future, contour data that we will give to the model will be much more refined using information specific to each patient and thus, perhaps, achieve a personalized model for each one", concludes Professor Noailly, principal investigator of this research laboratory and co-author of the publication.

More information: L. Baumgartner et al, Evidence-Based Network Modelling to Simulate Nucleus Pulposus Multicellular Activity in Different Nutritional and Pro-Inflammatory Environments, *Frontiers in Bioengineering and Biotechnology* (2021). DOI: 10.3389/fbioe.2021.734258

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