TEACHING STUDENTS AND CLINICIANS ABOUT APPLYING SIMULATION TO MEDICINE

The Insigneo Institute for in silico Medicine helps pave the way for the use of simulation in both education and clinical practice

The Insigneo Institute for in silico Medicine at the University of Sheffield, UK, is transforming how engineering is being used in medicine, with support from Dassault Systèmes. "This transformation is perhaps the most far-reaching ever to benefit medical practice, as computational technologies begin to alter the ways in which clinical decisions are made," says Prof. Damien Lacroix, Research Director of Insigneo. "These computer-driven processes are enabling clinicians for the first time to combine exquisitely detailed 3D mathematical models of their patients with finite element (FE) solution systems to see into their patients' futures."

Employing in silico medicine in this way allows doctors to consider different treatment options in the safety of computer models, Lacroix points out. "FE solutions present clinical teams with new 'biomarkers'—previously unavailable computed measures of physiological status—that lend strong support to their decisions. Clinicians are learning to cope with complexity by introducing computational simulation."

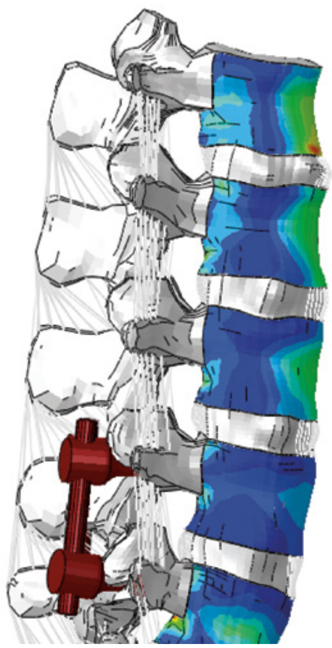

Figure 1: Finite element model of the lumbar spine where a fixation system is inserted to simulate the effect of fusion on the biomechanics of the spine. Copyright: Insigneo, University of Sheffield.

Various applications have been developed within Insigneo, though they are at different Technology Readiness Levels (TRL)—some being close to the clinics and others still at the stage of basic science. Below are three examples:

CLINICAL DECISION-MAKING FOR TREATMENT OF LOWER BACK PAIN

To improve upon the existing clinical approaches to the diagnosis and treatment of spinal conditions, in silico techniques were developed through an EC-funded project, MySpine, led by Lacroix, to help clinicians select the treatment that promises the greatest long-term success for each patient. Applying this approach on a patient-specific basis is a great example of how this transformative process will impact medicine (See Figure 1).

TISSUE ENGINEERING SCAFFOLD FOR REGENERATIVE MEDICINE

All soft tissues are made of interstitial fluid and a solid matrix usually composed of collagen. Thus many scaffolds that are developed for regenerative medicine are made of collagen gel that will interact with cells seeded within the scaffold. A poro-hyperelastic finite element model of such a gel was developed using Abaqus by Dr. Andre Castro from Insigneo. He calculated the solid and fluid mechanical stimuli acting on the cells when the scaffold is deformed in a bioreactor or in situ in the body. This will help experimentalists to better design their scaffolds and bioreactors for the optimization of tissue regeneration (See Figure 2).

MECHANOTRANSDUCTION IN CELL REGULATION

The glycocalyx layer in the membrane of many cells is believed to be essential for sensing mechanical stimuli that can activate functions such as migration, proliferation and differentiation. Lacroix developed a single-cell FE model using Abaqus which was later coupled by Insigneo's Stefania Marcotti into a fluid-structure interaction simulation (See Figure 3). These models allow for quantitative measurement of properties affecting human cells in physiological and pathological environments. This quantitative data can provide insight into important cell properties, but is often challenging to acquire in experimental settings. The simulations produce useful information on cell mechanics and mechanotransduction that allows for further understanding of these complex biological questions.

VIRTUAL REALITY IN THE CLASSROOM

Insigneo's efforts to integrate in silico medicine into real-world, clinical applications have continued alongside the development of one of the most advanced technologies of our

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time: virtual reality (VR). With grant funding by La Fondation of Dassault Systèmes, the group plans to bring two brand new VR laboratories—including a virtual reality "cave"— to the M.Eng. and M.Sc. candidates at Sheffield. Students from different backgrounds (mechanical and bioengineering, science, or medicine) will be offered the opportunity to take courses that use VR technology in the lab to study, interact with, and create biomechanical models based on real human geometry.

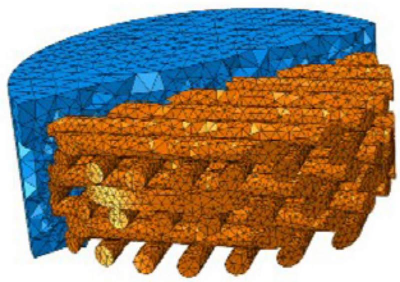

Fig 2: Finite element model of a scaffold for tissue engineering showing the cross section of a hydrogel (blue) embedded within an additive manufacturing scaffold (orange). Copyright: Insigneo, University of Sheffield

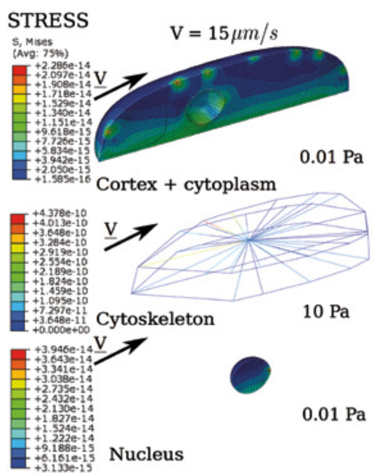

Fig 3: Fluid-structure interaction of fluid flow passing over a cell to calculate stresses within the cytoplasm, cortex and nucleus in order to elucidate the intracellular mechanotransduction pathways. Copyright: Insigneo, University of Sheffield

"We are trying to develop a VR lab where students will be able to visualize computational simulations," says Lacroix. "The labs that are being proposed focus on the spine and the cardiovascular system. In each of these, we want to have the students interact with some imaging data from a patient and be able to build personalized models that represent the geometry and physiological properties of the individual. From there we will be able to predict stresses and strains on the body as well as investigate particular diseases—and find the best treatments for a specific person."

After dedicating the last four years of the development of in silico medicine to research, Insigneo has recognized the need for new types of researchers and engineers who can master the novel technologies related to simulation. Accordingly, they have created a new degree in Mechanical Engineering with Biomechanics, which includes course work in computational medicine as well as the two VR labs. "By training with all this new technology, students at Sheffield will be the ones who will bring it forward into the real world and find applications in which to use it," says Lacroix.

CLINICIANS TO BENEFIT AS WELL AS STUDENTS

Abaqus is one of Insigneo's main simulation tools, but the institute plans on expanding to other SIMULIA software as well—including obtaining a licence for the **3D**EXPERIENCE® platform this year. "We have received a lot of interest from clinicians who want to implement enhanced visualization into their practices," says Lacroix. "We would like to develop a portal where doctors of all backgrounds will be able to upload imaging data from their patients. We then would use that information in a workflow—integrated within the **3D**EXPERIENCE platform—in which we would be able to preserve the images, develop patient-specific models, and eventually provide the clinicians with predictions about the outcome of any given treatment."

Lacroix and the rest of the team at Insigneo understand the power of simulation, as well as the savings that can result from adopting simulation tools like Abaqus. "It's important to look at the total cost of care when deciding on whether or not to integrate simulation into medical practice," he explains. "It can save you money while also leading to better quality care for patients. With the introduction of these tools, clinicians will be able to work towards disease prevention—reducing the number of people who get sick—and better treatment, which in turn minimizes patient complications."

Lacroix also believes that the use of in silico technology within clinical trials has the potential to massively cut costs for clinicians. "There are three phases to clinical testing and Phase III is by far the most expensive," he says. "More often than not, it is during Phase III (testing on several thousand people) that new drugs or medical devices fail. A high number of patient tests are needed for statistical reliability, but if we used a mechanical model instead, we could account for the specificity of each person and run large trials on a computer."

Performing in silico trials in this way could significantly cut costs, reduce time-to-market, and make medicine more accessible to patients around the world, Lacroix feels. The FDA is already aware of this potential and is accepting simulation data for appropriate applications.

It will be interesting to see what other technological developments will play a role in the future of medicine, how Insigneo will incorporate them into student curriculums at Sheffield, and how current and future clinicians will put them to good use on behalf of patients. Insigneo and Dassault Systèmes' SIMULIA have recently signed a Memorandum of Understanding that ensures their activities continue to develop in parallel.

For More Information

http://insigneo.org