

Ansys ADVANTAGE

POWERING INNOVATION THAT DRIVES HUMAN ADVANCEMENT

ISSUE 1 / 2024

SIMULATION TRANSFORMS HEALTHCARE

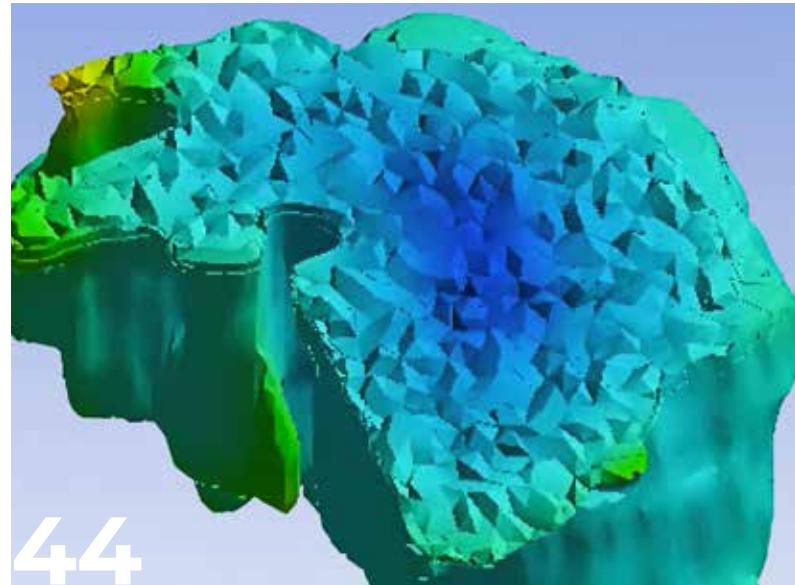


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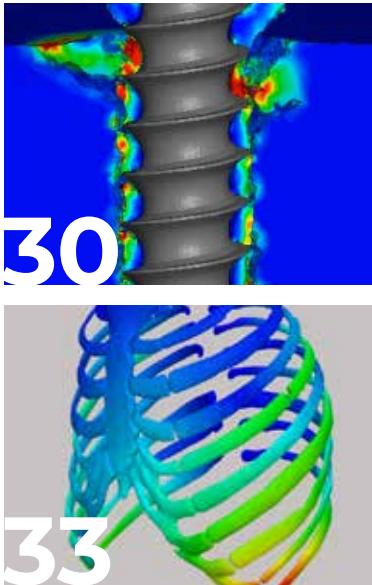
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Welcome to Ansys Advantage! We hope you enjoy this issue containing articles by Ansys customers, staff and partners.

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Powering Innovation That Drives Human Advancement

When visionary companies need to know how their world-changing ideas will perform, they close the gap between design and reality with Ansys simulation. For more than 50 years, Ansys software has enabled innovators across industries to push boundaries by using the predictive power of simulation. From sustainable transportation to advanced semiconductors, from satellite systems to life-saving medical devices, the next great leaps in human advancement will be powered by Ansys.

Ansys is the global leader in engineering simulation. We help the world's most innovative companies deliver radically better products to their customers. By offering the best and broadest portfolio of engineering simulation software, we help them solve the most complex design challenges and engineer products limited only by imagination.

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In Silico: A Healthcare Revolution

By **MARK PALMER**, Senior Chief Technologist for Healthcare, Ansys

Is a post-pandemic healthcare sector ready to join the Fourth Industrial Revolution? This period is characterized by a shift from valuing only what is manufactured to valuing the data and connectivity of the ecosystem in which it operates — and innovation in the human interaction with such ecosystems. Key enablers of the Fourth Industrial Revolution are digitalization, data, computer modeling, and artificial intelligence (AI). These technologies build on each other and multiply both capability and value. Healthcare systems are accelerating access to data, digitalization, analytics, and predictive modeling. The mindset is shifting from treating disease to preventing it, maintaining health, improving the quality of life, and achieving healthy longevity. These are indicators that the healthcare sector is indeed primed for transitioning to the Fourth Industrial Revolution.



CHALLENGES FOR ADOPTION

So what are the challenges or obstacles to the adoption of computational methods by the healthcare sector? In this sector, computational methods are referred to as computer modeling and simulation (CM&S) or *in silico* methods (ISMs). The "*in silico*" terminology is an extension of how experiments are performed in biology — namely "*in vitro*," which is Latin for "in the glass," and "*in vivo*," which is Latin for "in the living." *In silico* methods therefore mean "in the computer, computer modeling, or computer simulation." ISMs include simulations of bench tests, simulations of living systems, and simulations of clinical trials, also known as *in silico* clinical trials (ISCTs). According to surveys conducted by the Medical Device Innovation Consortium and InSilico UK across the medical device and pharmaceutical industries, the three most significant barriers to adoption of *in silico* methods are:

- 1. Uncertainty in regulatory acceptance.** Regulators in the different regulatory authorities vary in their experience and acceptance of modeling as evidence. Globally, geographies differ in their guidance documents, standards, and ability to

- 3. Insufficient skills and expertise in regulation and industry.** The healthcare sector requires a wide variety of expertise that comes together to deliver care, technology, and products to the sector. In this setting, computational modeling is relatively new and, compared with other industries, practitioners are 10 to 100 times less common.

MARKET FORCES DRIVING

DIGITALIZATION AND IN SILICO METHODS

This may imply that healthcare is indeed a slow adopter of technology, but that is not the case. When technology is presented to the sector in a way that can be easily adopted or significantly enhances the care of patients, industry is quick to act. This is seen in imaging technologies, as well as sensor and wellness technologies. However, significant market forces are driving the need for further adoption of computer modeling and simulation:

- Materials:** For medical devices and pharmaceuticals, there are increasing regulations to track, report, and minimize compounds that may harm patients. A rising number of regulations from the Environmental Protection Agency have significantly impacted sterilization methods and removed compounds from the supply chain. An additional environmental consideration is that in the United States, the healthcare sector generates 5 million tons of waste per year, according to a report from Arup and Health Care Without Harm titled "Health Care's Climate Footprint."
- Eroding profit margins and moats:** Over the past two years, there have been significant changes in the purchasing practices of different geographies. These resulted in a 36% drop in the per-unit price for a cardiac medication, an 80% to 90% drop in the price of certain cardiac stents, and an 80% drop in knee implant prices, depending on geography. Eroding moats come in the form of nontraditional players entering the healthcare space, including significant impact from consumer electronics. These players operate on significantly shorter product cycle times and have a longer history of simulation-driven design and digital methods. The trends affect traditional healthcare manufacturers by increasing the importance of internal efficiency, adoption of simulation-driven design, and digitalization of the product life cycle to remain competitive and maximize revenue.
- Competitive advantage:** Perhaps the most significant driver for computational methods is the ways in which computational modeling impacts competitive advantage. With the advances in simulation techniques and computational power, for each day that a company or product line delays adoption of modeling and simulation, a month of time is lost to a simulation-driven competitor. The first-to-market advantage can be substantial.

“With the advances in simulation techniques and computational power, for each day that a company or product line delays adoption of modeling and simulation, a month of time is lost to a simulation-driven competitor.”

WHERE IS THE HEALTHCARE SECTOR TODAY?

The healthcare sector is one of the largest and it has the most personal impact. Healthcare also has been criticized as one of the slowest sectors to adopt technology. The reason for that criticism is that compared with the rapid pace of software and consumer technologies, which are measured in fiscal quarters, the pharmaceutical and medical device industries measure their development cycles in years. For example, from the development of a new drug to approval for marketing often takes 10 to 15 years. Meanwhile, the average time from the concept for a new medical device to marketing is about six years. Clinicians have better, more seamless technologies in their lives as consumers than they do in their clinics and operating rooms.

accept modeling. This results in manufacturers often adopting the lowest common form of evidence that will be universally accepted.

2. Scientific maturity and model credibility. Human physiology and biology is a system in dynamic equilibrium with high variability. As a result, clinical studies require a large sample size to generate sufficient evidence to identify signal in the noise and achieve statistical significance. The ability to create large volumes of models has historically been a challenge due to the computational expense and the inability to convert clinical data into simulations. These challenges are being mitigated as we can mathematically capture more biological processes, gain the ability to process clinical data using AI and machine learning (ML) techniques, and witness the continued rapid growth of compute power.



ON THE COVER: Hans is a human body model from Ansys that includes bones, ligaments, tendons, organs, muscles, skin, and more. It can be used in many ways — from crash testing to modeling sports injuries.

In medical technologies, the economic benefit from being first to market usually results in market exclusivity for 2.8 to 3.8 years, and market dominance persists beyond five years.

THREE PILLARS OF HEALTHCARE

This issue of *Ansys Advantage* presents the role of Ansys' healthcare strategy in supporting and accelerating innovations in healthcare. We are excited to share our three pillars of healthcare:

1. Insights and personalization. The average patient does not exist. Therefore, our technologies focus on the ability to quickly generate a simulation of any patient from that patient's own data. These personal models then can be used to evaluate multiple interventions, drug combinations, or procedural approaches.

2. Democratization of simulation. Healthcare consists of a variety of experts working together. Similarly, accurate simulation of the human body must bring together many technologies and broad technical expertise. Our goal is to provide an ecosystem for creating modeling and simulation solutions tailored to each expert in the product life cycle, from design and innovation to interventional planning and clinical application.

3. Digital evidence for regulatory approval. Modeling individuals and making those models easy to use by different experts enables the creation of patient populations for clinical studies without putting individuals at risk. Therefore, we are accelerating our core solver technologies, as well as increasing model prep automation, including statistical variation as an input, automating data extraction, and providing ecosystem knowledge management.

We hope that the examples of innovation we are sharing in this issue of *Ansys Advantage* capture your imagination and inspire collaboration for the use of modeling and simulation to improve health and wellness around the world. ▲



In Silico Clinical Trials: Changing Minds To Save Lives

Billions of people around the world are waiting for a new pharmaceutical drug or medical device to improve their quality of life — or maybe even to save them.

Unfortunately, some will die waiting, and it doesn't have to be this way.

A technology shift to an *in silico* clinical trial (ISCT) approach — which uses virtual human patients based on a blend of realistic anatomical data, physiological information, and computational modeling and simulation (CM&S) techniques — can supplement (or even replace) human participants in traditional clinical trials. This would greatly reduce the time and cost to develop new drugs and obtain regulatory approvals. But this would require the acceptance of simulated clinical results by global health authorities. So far, only the U.S. Food and Drug Administration has formally taken this step.

Ansys has been instrumental in promoting the ISCT approach to U.S. Congress members and to parliament members in the EU and other regions of the world. For more than a decade, the company has encouraged Ansys employees Marc Horner and Thierry Marchal in their tireless efforts to share their perspectives and insights regarding ISCT to the healthcare community, including regulators, policy makers, and standards organizations. With the help of their *in silico* colleagues from industry and academia, they are successfully converting the equations of engineering simulation into new legislation and standards.



Avicenna Alliance
Association for Predictive Medicine

“We can test hundreds, thousands, and even millions of virtual patients relatively quickly using *in silico* methods. It’s just a question of computational time and energy.”

— THIERRY MARCHAL

Chief Technologist Healthcare for EMEA, CTO Office, Ansys

STARTING BY JOINING FORCES

The Avicenna Alliance, founded in part by Ansys, is devoting time and effort to convince politicians, policymakers, and regulatory agencies around the world that ISCTs are the future. Founded in 2016 at the request of the European Commission, the Avicenna Alliance advocates for the regulation and deployment of *in silico* medicine. It comprises leading pharmaceutical and medical device companies — both established market leaders and startup companies — and has partnerships with many regulatory and standards agencies. Additionally, 50% of its members are from academia, ensuring that the advances of basic research are both well represented and implemented.

“By joining together in the Avicenna Alliance, we are not speaking in the name of Ansys or any other single company,” says Thierry Marchal, Secretary General of the Avicenna Alliance for the past eight years and Chief Technologist Healthcare for EMEA, CTO Office, Ansys. “We are speaking in the name of all these organizations who are willing to accelerate care to the patient. So this is changing things completely in that people are willing to listen.”

Marchal, who has spoken about ISCTs to the European Commission, members of the U.S. Congress, the Brazilian Parliament, U.K. leaders, regulators in Australia, and many other government organizations worldwide, is quick to point out that Alliance members are there not only to talk but also to listen.

“We are not there to tell them ‘Here is what you need to do,’ he says. “All these organizations have the same motivation as us — bringing the latest and most advanced therapies to the patient as quickly and safely as possible. We tell them that there is a very good technology — *in silico* technology — that is accepted by the FDA, and you should learn about it. And we are asking the question, ‘What do you need in order to be convinced that this is valuable?’”

Beyond high-level parliamentary discussions, Ansys is also involved in pushing ISCTs forward on the regulatory side. Marc Horner, Distinguished Engineer at Ansys and Vice Chair



Ansys' Thierry Marchal (third from left) in front of the United States Capitol building.

of the ASME VVUQ (verification, validation, and uncertainty quantification) 40 subcommittee, works to develop standards that support VVUQ for medical device industry applications. One output of this subcommittee is the ASME V&V 40 standard, which defines a risk-based framework for establishing model credibility. This standard was used as the basis for the Medical Device Innovation Consortium's Virtual Patient project, where Horner was part of a team that demonstrated how an ISCT could be used as part of a regulatory submissions to the FDA.

In spite of these successes, one roadblock is that ASME standards are not formally recognized globally, therefore other countries are understandably hesitant to adopt them. To address this, “ASME, Avicenna, and others are currently seeking approval to develop an IEC standard that recognizes ASME V&V 40,” Horner says. “The new standard would recognize that there is a continuum of models, ranging from knowledge-based to data-based, which all require credibility assessment. This standard would hopefully address the issue of global acceptance without re-inventing the wheel.”

HOW ISCT CAN OVERCOME THE CHALLENGES OF CLINICAL TRIALS

Unlike consumer products, medical solutions require regulatory approval before they can be

“We’ve got the same goals, but we need to learn to speak each other’s language. ... This means we have to provide training, to inform the non-expert about *in silico*, and we have to go beyond the modeling to provide information about regulatory best practices.”

— MARC HORNER, Distinguished Engineer, Ansys



Ansys' Thierry Marchal (third from left), representing the Avicenna Alliance at the European Parliament

released to the public to ensure they are safe and effective, and this takes a lot of time. For example, regulatory approval of a novel medical device takes between five and six years, and typically costs up to \$100 million. For a new pharmaceutical, these numbers can increase to 10 to 15 years and \$2.5 billion.

The long lead times and high expenses are mostly due to multiple levels of clinical trials required for approval. Initial lab testing (known as *in vitro*, or in glass testing) using no living subjects is followed by a round of testing on laboratory animals (*in vivo*, or involving living creatures), and finally, human trials. Finding 5,000 to 10,000 people who agree to participate in human trials is a challenge in and of itself. And if the medical solution is designed to address a rare disease, then getting significant numbers of participants to yield statistically relevant results is even more difficult.

ISCTs can help in a number of ways. The most obvious is by creating simulated human models

to add to the clinical testing pool. If you need people with conditions x, y, and z in your testing pool, but do not have any human volunteers with these conditions, you can create virtual humans that reflect these requirements. In addition, *in silico* technology can be used to:

- Reduce the overall number of participants or trial duration
- Refine the trial to minimize suffering or improve its relevance to humans
- Replace the trial with *in silico* testing

“We can test hundreds, thousands, and even millions of virtual patients relatively quickly using *in silico* methods,” Marchal says. “It’s just a question of computational time and energy.”

DEVELOPING A COMMON LANGUAGE TO PROMOTE TRUST

Marchal and Horner have been traveling the world in recent years to talk to lawyers, politicians, policymakers, and regulators to convince them that ISCTs are the correct path

forward. They are also meeting with other important stakeholders within medical device and drug companies, such as R&D leaders, quality assurance, and regulatory affairs professionals who can advocate for *in silico* approaches internally at their organizations.

“We need to talk to all the people,” Marchal says. “None of them are opposed to what we are proposing. But before making a decision, before changing the law or transforming development processes, they need to be convinced that what we are proposing is a good thing.”

Marchal and Horner believe that it’s only natural that they should have questions, because what they are proposing is not intuitive.

“The key argument is that we can replace clinical testing of humans with computer models,” Marchal says. “Really? Are the computer models good enough? Are the colorful pictures we are showing of fluid flow in the heart and the lungs accurate and valuable? Are they fully validated? And can you define what ‘validated’ means?”

These are just some of the questions that Marchal and Horner have been answering in their ISCT efforts. The fact that the questions are coming from people of varying backgrounds increases the challenge.

“We’ve got the same goals, but we need to learn to speak each other’s language,” Horner says. “We believe that it is up to us to learn to speak the language of the regulator, the politician, and even the clinician in some cases, and they are doing their best to understand our language. If you are speaking to someone who is not an engineer, you’re not going to convince them by showing them convergence plots from simulations. The results have to be translated into a language or outcome that is meaningful to them.”

Even in places where decision makers are convinced of the necessity of using *in silico* methods, sometimes it is difficult to find anyone besides the regulatory authority who has the knowledge to review this kind of computer model.

“This means we have to provide training, to inform the non-expert about *in silico*, and we have to go beyond the modeling to provide information about regulatory best practices,” Horner says.

THE RACE IS ON

Many global medical device and pharmaceutical companies are already using engineering simulation to develop new products, but few are invested in using simulations for regulatory approval, mainly because the regulators in



Marc Horner (fourth from left) joining colleagues from Edwards Lifesciences and VPhi at ANVISA, the Brazilian Health Regulatory Agency.

their countries have not yet provided a formal framework for the acceptance of *in silico* data.

Developing an international (ISO or IEC) standard would go a long way in overcoming this barrier, and that is what the Avicenna Alliance is now pushing for. Meanwhile, patients in countries that have longer regulatory approval processes might suffer.

“I’m trying to convey this feeling to the different authorities that we are in a race,” Marchal says. “The only winners of this race will be the patients. If you do not allow a new medical product to be validated with the *in silico* method, it could take a long time to get validated and approved, and during this time your local citizens cannot access this technology while the same technology might be saving lives in the U.S., but not yet in Europe. This is kind of a punishment for the local citizen.”

Through the Avicenna Alliance, governments, politicians, clinicians, engineers, academics, and software providers are working as a community to ensure that every country and every citizen will be winners in this race. If we can adopt international regulatory standards for faster approval of medical procedures, treatments, and devices using simulated clinical trial results, we can save lives worldwide instead of just in small areas of the globe. If you are not already involved in this effort, we encourage you to join us today. ▲

LEARN MORE

Join the Avicenna Alliance
avicenna-alliance.com



Get to the Heart of the Matter

By **Michel Rochette**, Senior Director of Research, Ansys, and
Martijn Hoeijmakers, Senior R&D Engineer, Ansys

Ansys' dedicated Healthcare Research team is helping to revolutionize the treatment of cardiovascular disease with their innovative heart-modeling methods.

Engineering simulation has made critical contributions to healthcare research since it was first introduced more than 50 years ago. But most customers don't realize that Ansys has a dedicated group, the Ansys Healthcare Research team, that increases the impact and scale of those contributions by pioneering innovative new modeling techniques for medical applications.

This team, primarily based in Europe, includes highly qualified, doctorate-level engineers and students who focus on a range of healthcare topics including brain studies, orthopedic models, and respiratory system simulations. Some members are embedded in leading hospitals to facilitate collaboration and real-world validation of the team's biological models.

By perfecting a new set of best practices and disseminating them to Ansys customers, the Ansys Healthcare Research team is helping translate advanced simulation theory to practical real-world applications. One of its primary goals is to democratize advanced simulation methods by making them more accessible to non-simulation experts, then putting them in the hands of a range of academic, clinical, and industrial partners.

These collaborators can leverage advanced modeling practices to design new healthcare devices, diagnostic methods, and treatment plans — and, ultimately, develop personalized models that reflect the (patho)physiological state of actual human patients, i.e., personal digital avatars. Eventually, the hope is that medical innovators can use these models for two purposes:

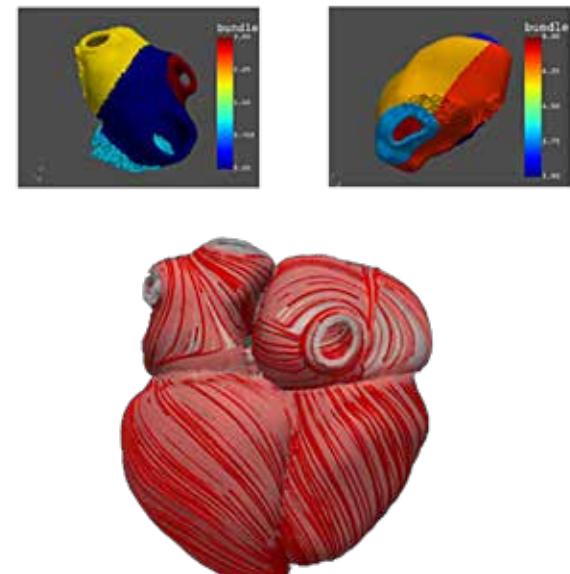
1. Test new treatments on a specific patient's "digital twin" before implementing them.
2. Create virtual cohorts of large numbers of patients to provide evidence that treatments are safe and effective.

A NEW, NONINVASIVE VIEW OF CARDIOVASCULAR DISEASE

Since 2019, the Ansys Healthcare Research team has been addressing some of the most urgent challenges in healthcare. One of those challenges is improving the detection and treatment of cardiovascular diseases, the leading cause of death worldwide. According to the World Health Organization, cardiovascular disease causes nearly a third of all deaths globally — a statistic that's on the rise despite modern medicine and research efforts.

The world's academic institutions, hospitals, and private companies are heavily investing in efforts to understand the fundamental mechanisms of cardiovascular disease. But a clear obstacle is an inability to measure the clinically unmeasurable inside the heart through *in vivo*, or even *ex vivo*, studies.

Computer simulation offers a low-risk, noninvasive, increasingly realistic alternative. Simulation can provide additional, otherwise unmeasurable but relevant metrics, and consequently improve clinicians' understanding of the diseases. While it will never replace *in-vivo* studies entirely, the *in-silico* modeling approach enables much faster, more efficient, and cost-effective studies of the human body, including the cardiovascular system, than *in vivo* human



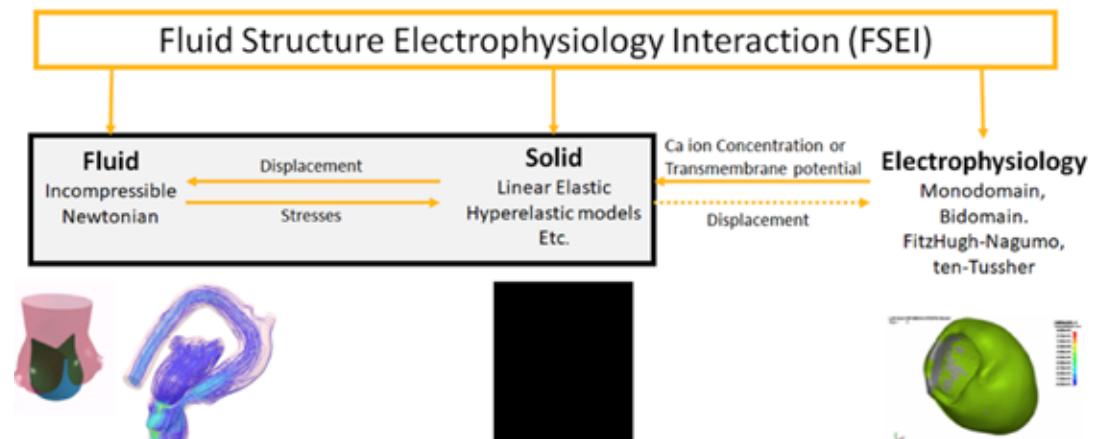
The geometry and orientation of the heart's muscle fibers play a critical role in both structural strength and electrical excitation. PyAnsys Heart enables researchers to compute, visualize, and use these fibers in subsequent simulations.

studies and trials — with absolutely no risk to human patients. Furthermore, these models help researchers better understand the fundamental mechanisms of human physiology and how it develops certain pathologies.

To make rapid progress in developing the right tools to understand, diagnose, and treat cardiovascular disease, the Ansys Healthcare Research team has devoted significant resources to a project it calls "PyAnsys-Heart." For four years and counting, the members of the Healthcare Research team have used Ansys LS-DYNA to model blood flow, tissue mechanics, and the electrophysiological behavior of the heart. These models allow for detailed studies of the real-world fluid structure electrophysiology interaction (FSEI) that characterizes a patient-specific beating human heart.

These detailed FSEI models replicate complex, otherwise hard-to-measure features of the heart in a noninvasive way, including structural stresses, electrical excitation, and muscle fiber orientation. These models also account for the pericardium — the double-layered, fluid-filled sack that surrounds the heart — and they also consider the heart's valves and atria as boundary conditions.

Due to its multiscale and multiphysics nature, heart modeling is numerically and financially costly. In addition, it requires both



- Three physics, all coupled
- Numerically challenging and costly

- Application determines required level of detail
- Simplify physics where possible
- No one-size-fits-all solution

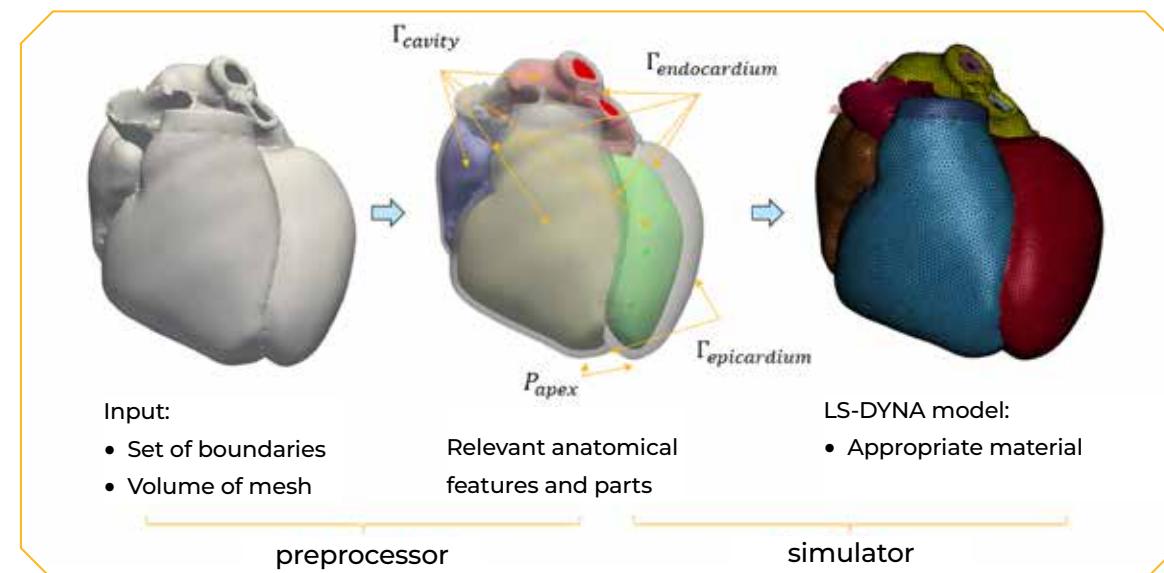
Developing a realistic human heart model means bringing together three separate, tightly coupled physics to study fluid structure electrophysiology interaction (FSEI). This poses a significant challenge for even the most advanced healthcare research teams.

theoretical knowledge and hands-on simulation expertise. That's why the Ansys Healthcare Research team is working closely with clinical and academic partners to generate and provide these models to the world's cardiovascular research teams.

The team's PyAnsys-Heart Python library, enables users to generate both partial and full-heart anatomies and simulation models, and will soon be available to Ansys customers to facilitate their own heart modeling efforts.

AN OPEN PLATFORM TO DRIVE BROAD ADOPTION

Because a key goal is to make the team's models available to a wide range of users with a spectrum of research interests, PyAnsys-Heart models are based on the open-source Python programming language and feature an intuitive, user-friendly interface. They are fully compatible with other elements of the Python ecosystem. Even nonexperts can easily walk through the basic steps of preprocessing,



PyAnsys-Heart models that have been developed by the Ansys Healthcare Research team provide a visual, graphical way to better understand and study the complexities of a blood-filled, beating human heart.

simulation, and post-processing for the PyAnsys-Heart models.

PyAnsys-Heart models from Ansys enable users to reduce computational complexity, streamline workflows, and save time, labor, and other resources by focusing on components of the heart relevant to their own specific application. Researchers can conduct full, system-level simulations or only model fluid flows, tissue mechanics, or electrophysiological activity. The multiphysics capabilities of LS-DYNA software include computational fluid dynamics (CFD) solvers, finite element analysis (FEA) solvers, and electromagnetic (EM) solvers in a single environment, making it ideal for capturing the physical complexities of the human heart.

The first version of the PyAnsys-Heart modeling library has been tested on multiple publicly available heart geometries from actual human patients with heart failure. In the future, the Ansys Healthcare Research team hopes to enable users to create large cohorts of customized, patient-specific models as simulation capabilities advance.

By providing medical device manufacturers, university research teams, and clinicians with these building blocks, Ansys can support and help accelerate the development and adoption of innovative new devices, detection methods, and treatments. The open-source nature of PyAnsys means that it can easily be combined with researchers' own internal efforts. Users can build on top of existing features in

PyAnsys-Heart to build their own simulation workflows or models, and conduct simulations tailored to their own requirements.

Ansys is making a significant investment in the PyAnsys-Heart project, as it expects to see an enormous return in terms of improved patient outcomes — and, over the long term, play a significant role in the fight against cardiovascular diseases. This will also lead to a wider adoption of simulation tools throughout the healthcare industry.

TAKING HEALTHCARE INNOVATION TO HEART

The PyAnsys-Heart project is just one way Ansys is committed to democratizing simulation to create social benefits.

The reality is that, while simulation can drive incredible healthcare research results, many academic, clinical, and industrial development teams simply can't afford to invest in hiring experienced engineers who are already trained in computational modeling solutions and methods. And there have traditionally been long delays associated with getting new users of simulation software up to speed when faced with the demands and challenges of multiphysics, multiscale biological modeling.

By forming a dedicated Healthcare Research team closely interacting with worldwide colleagues engaged with healthcare and making its PyAnsys Heart models available to customers, Ansys is doing its part to drive transformative innovations that can help in the fight against cardiovascular disease. ▲

GO FROM 4D SCAN TO SIMULATION IN 20 MINUTES

Many companies and hospitals have their own imaging database of patient specific hearts. For them, the PyAnsys-Heart approach is an excellent way to use this valuable data. Some might be willing to create a general-purpose model of the heart that could be customized to different simulations; for this, they may need to use more general purpose, off-the-shelf tools.

Despite the excellence of available segmentation software, the general process to go from imaging to simulation can be time consuming, resource intensive, and may lead to unexpected challenges. A collaboration between healthcare experts Peggy Huang and Christoph Maurath of Ansys, and George Hyde-Linaker and Chris Goddard of Synopsys led to a polished workflow using AI driven AS Cardio from Synopsys to smoothly generate heart meshes from clinical imaging for import to Ansys LS-DYNA.

Using this approach, relying on off-the-shelf tools, it is possible to go from the 4D scan of a patient to simulating the transient blood flow of a patient-specific heart in LS-DYNA in less than 20 minutes. Once a fine and robust mesh is available in LS-DYNA, standard general purpose modeling including fluid, structure, electrophysiology, and a combination of these physics can be performed by the user. The workflow has been tested on several hearts. However, the goal is to further refine and automate the process to enable scaling thousands of patient-specific cardiac images.

SIMULATION:

The Heart and Soul of Preoperative Planning

Congenital heart defects (CHDs) are the most common types of birth defects. Thankfully, nearly all children with simple defects survive into adulthood and lead normal lives. But about 1 in 4 of those children have more complex CHDs that require surgical intervention. There are many kinds of CHDs with many anatomical variations, meaning the surgical plan is different for nearly every patient. Understanding the intricacies of every individual patient's heart is essential for positive outcomes.

By Aliyah Mallak, Senior Marketing Communications Writer, Ansys

Cardiac surgeons usually use imaging tools such as echocardiograms, cardiac computed tomography (CT) scans, and magnetic resonance imaging (MRI) for preoperative planning. While great diagnostic tools, they have limited three-dimensional visualization capabilities. Surgeons only see the 3D, or in fact 4D, details of the heart when the patient is on the operating table, leaving little time to plan a perfect reconstruction.

The Boston Children's Hospital Cardiovascular 3D Modeling and Simulation Program, co-directed by Dr. David Hoganson and Dr. Peter Hammer, has created and institutionalized preoperative planning using 3D simulation tools. Their team of engineers and doctors create patient-specific 3D models of the heart and blood vessels for preoperative planning and intraoperative guidance.

"Making the best treatment decision really comes down to that individual patient and their specific anatomy and physiology," says Hoganson. "We put together a team to use modeling and simulation in congenital heart disease to better understand and predict what operations and treatments would be best for individual children."

A-TEAM MERGES ENGINEERING AND SURGERY
As a double board-certified cardio-thoracic surgeon, Hoganson's clinical focus is on newborns and children with congenital heart disease. But he started his educational journey with engineering. "My degree is in electrical engineering, and I developed devices for interventional cardiology and cardiac surgery," he says. "During my surgical residency, I did three years of full-time research at Massachusetts General Hospital and did a fair bit computational dynamics there."



After completing his education and training, he joined Boston Children's Hospital, where he and Hammer created the modeling and simulation program in 2018. Hammer is a mechanical engineer with over two decades of experience in cardiovascular modeling. "Initially, we focused on computational fluid dynamics (CFD) in children with congenital heart disease and now also plan things like patches or new vessels that are created during these repairs," he says.

The program has grown tremendously, in part because other clinicians are interested in using 3D models to help plan and conduct operations. For example, it is now a standard of care at the Benderson Family Heart Center to create patient-specific 3D models. Their team of 12 includes engineers who focus on CFD using Ansys Fluent and patient-specific 3D models using different simulation tools, including Ansys Discovery.

HELPING 1,000 CHILDREN, ONE AT A TIME
Hoganson and his team have created over 1,000 patient-specific 3D models of hearts with a CHD.

"Any time you do simulation, it's essential that you validate the work and confirm the simulation matched the clinical outcome," says Hoganson. "So, for all our patients who have done CFD, we've done MRIs three to six months after surgery, so we know exactly how well the CFD model matches the outcome. This gives us great confidence that these simulations really tell the story of how the blood flow distributes, what the energy loss is going to be, and all these different important parameters."

To ensure the models account for the different parameters as accurately as possible, Hoganson places particular importance on fine tuning boundary conditions that match individual patient

"We've done well over 20 clinical CFD patients. ... One hundred percent of the time we have changed the operation based on the CFD results."

— DR. DAVID HOGANSON, Co-director, Boston Children's Hospital Cardiovascular 3D Modeling and Simulation Program

physiology. "We build parameter models for the boundary conditions of individual CHD patients in Ansys Fluent and it's a really seamless process," he says. Using Fluent, Hoganson and his team can code outlet boundary conditions and parameter models. Then using physiologic information from the patient, they can fine-tune the parameter models so they have responsive boundary conditions that change over time depending upon different physiological states they've tested.

The results? Staggeringly similar CFD and MRI results.

Even so, there will always be biological variables that can't be accounted for, but Hoganson and his team are taking every step to ensure the cardiac community trusts in their simulations. "We've been really thrilled with our results, but we're nowhere near a position to stop validating every single patient that we do," he says.

ACCELERATING THE PROCESS

Like most plans in life, things change, and surgical planning is no exception. Hoganson explains that using simulation for preoperative planning is an inherently iterative process that takes time to do.

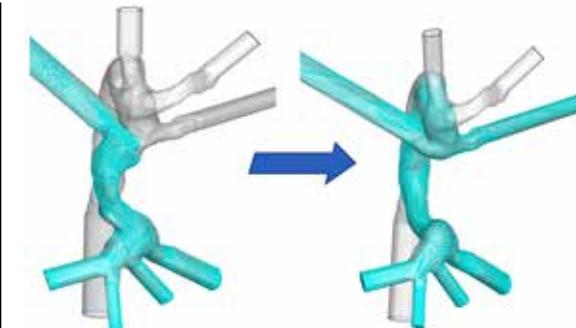
"The first simulation we ever did took like three-and-a-half months," he says. "Now the entire iterative process of simulating multiple surgical options including all of the 3D modeling and virtual surgery work takes us around three and a half weeks." But the more complex the defect, the longer it takes. So the modeling and simulation team have used Discovery as a screening tool. Discovery gives them an initial 4D visualization of the defect before they do the full CFD simulation in Fluent.

"We've done well over 20 clinical CFD patients and not one single time have we done the CFD and then did the surgery that the surgeon had proposed," Hoganson says. "One hundred percent of the time we have changed the operation based on the CFD results."

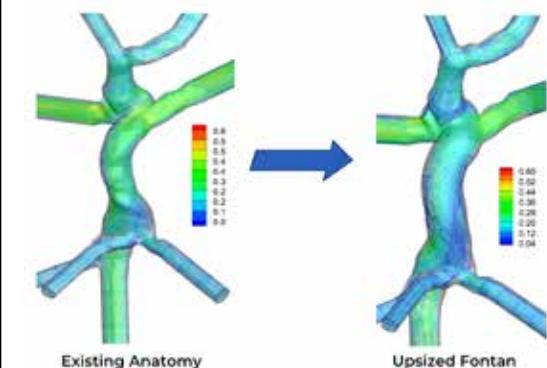
IT'S NOT ROCKET SCIENCE, BUT IT IS HEART SURGERY

Pediatric cardiac surgeons spend roughly 12 years training to do these types of repairs. CHD patients and their parents only get a few months, or even weeks, to understand it. Hoganson uses the 3D simulation to explain how the surgical team will approach a patient's specific defect.

"These simulations have proven to be great



Clinical use of computational flow modeling to determine best approach for Fontan or Fontan revision



Modeling to optimize conduit size

communication tools. You don't need a doctorate in engineering to look at a simulation and see where the flow is going," he says. "The parents have a much clearer understanding of their child's condition and how we are going to repair it."

THE DIFFERENCE BETWEEN LIFE AND DEATH

Different departments within Boston Children's Hospital are seeing the benefits of 3D modeling and simulation, and want in on the success. Hoganson and team recently helped create a model for an entire chest wall reconstruction.

Not only are others within the hospital interested, but other medical centers are as well. "We're working closely with several other leading centers in the U.S. and trying to help them get up to speed with some of the work that we're doing," says Hoganson.

He and the rest of the modeling and simulation team are working hard to expand their capabilities and drive innovation for CHD patients.

"For every simulation patient, it's life or death. This makes a big difference for every single child," he says. ▲



Improving Human Health: Philips Uses Simulation to Bring Bright Ideas to Life

By Ansys Advantage Staff

Ever since the visionary father-son duo of Frederik and Gerard Philips started selling incandescent lightbulbs in the 1890s, their eponymous company has improved people's lives with a steady flow of ground-breaking innovations.

Though consumers may know the company best for closer-shaving razors, deeper-cleaning toothbrushes, and the world's first consumer video cassette recorder, Philips has been developing medical technology from the start. Among other achievements, its groundbreaking 1929 work on X-ray tubes made it possible to obtain quality images of organs, not just bones, enabling the early detection of tuberculosis and saving countless lives. Nearly a century later, the principle behind the original Philips "Rotalix" tube is still in use.

"At Philips, we're empowering people to take care of their health and well-being and helping doctors and nurses to provide better, more sustainable, and more convenient care — in hospitals, clinics, and the home."

— ROY JAKOBS, CEO, Philips

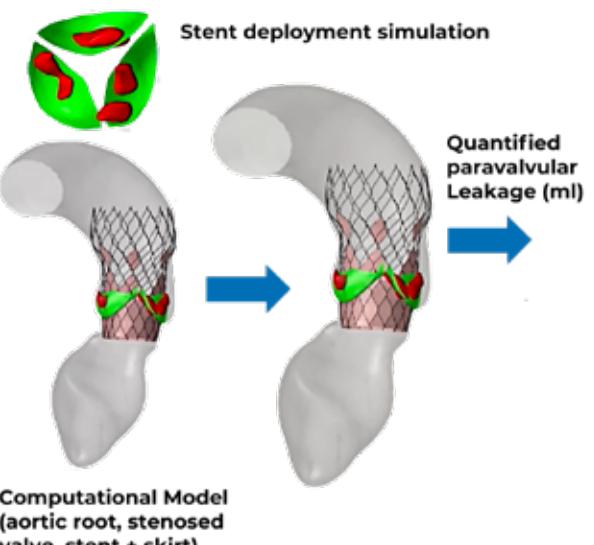
Today, Philips is focused exclusively on improving people's health and well-being through meaningful innovations, and it aims to improve the lives of 2.5 billion people per year by 2030. As stated by its CEO, Roy Jakobs: "At Philips, we're empowering people to take care of their health and well-being and helping doctors and nurses to provide better, more sustainable and more convenient care — in hospitals, clinics, and the home."

The company is organized around three pillars:

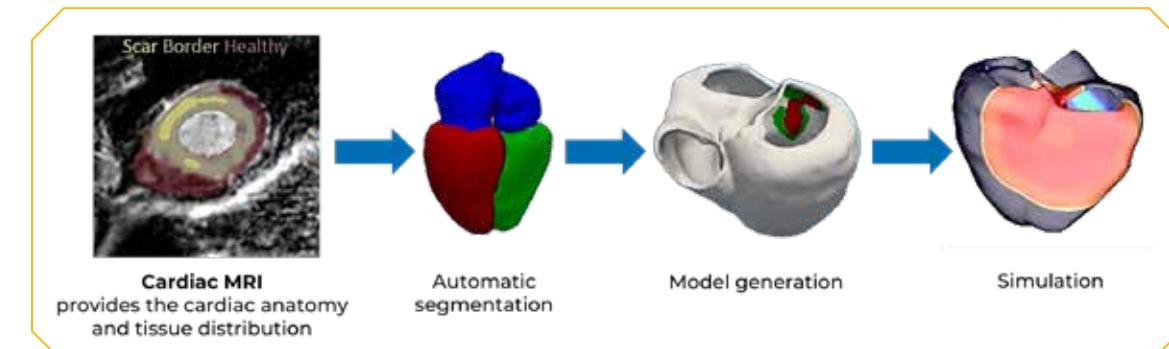
1. Precision diagnosis and image-guided, minimally invasive treatment.
2. Connected care (including digital solutions such as hospital monitors and workflow systems).
3. Personal health products like sleep and respiratory aids, and those ubiquitous Sonicare toothbrushes.

According to Ger Janssen, principal data and artificial intelligence (AI) scientist, Philips is leveraging what it calls "meaningful innovation" to optimize product performance and reliability, move away from expensive physical prototyping, and reduce time to market. That includes using Ansys multiphysics simulation software across a broad range of physics domains: heat and flow, mechanics, dynamics, optics, electromagnetics, acoustics, and electronics design. Philips deploys virtual design and

testing for internal product development process acceleration and leverages the developed simulation models sometimes in the field of operational applications. The company is also working to integrate hybrid modeling — combining traditional simulation with AI — into its development capabilities.



Pre-operative risk assessment of paravalvular leakage using a computational transcatheter aortic valve replacement (TAVR) deployment model (left) and a dynamic simulation of the device to determine the radial force that should be applied.



A future hybrid modeling workflow using artificial intelligence to go from magnetic resonance imaging (MRI) to the cardiac simulation

“We’re looking for an appropriate trade-off between the virtual world and experimental input and validation, between detailed physical simulation and more simplified approaches.”

— GER JANSSEN, Principal Data and Artificial Intelligence Scientist, Philips

FIRST-TIME SUCCESS

Janssen says that to accelerate the product development process, Philips aims to virtually design as much as possible. That enables them to minimize hardware design cycles and design testing, and to eliminate problems before building physical prototypes.

“We’re looking for an appropriate trade-off between the virtual world and experimental input and validation, between detailed physical simulation and more simplified approaches,” says Janssen.

As an example, he points to the drop impact testing workflow developed by close cooperation of Janssen’s team with a few businesses, which proved its value across multiple Philips businesses.

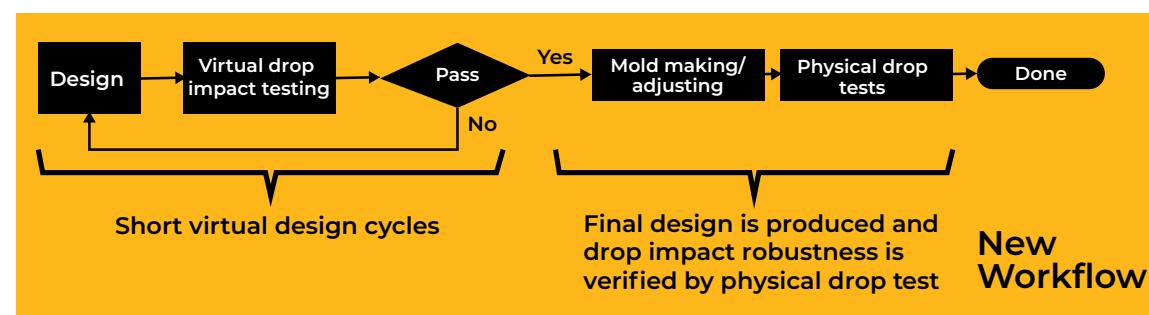
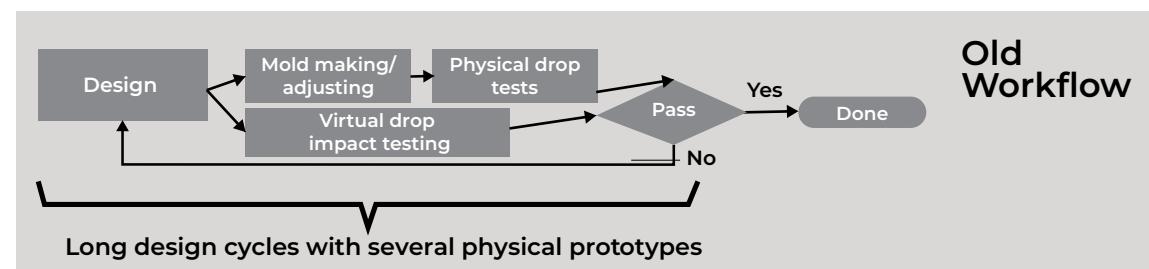
In the traditional way, engineers simultaneously subjected physical prototypes to physical and virtual drop impact testing. The physical test would tell engineers if the prototype passed or failed, but the virtual test would tell them why. When a prototype failed to perform as planned, a new development cycle began.

Now, however, Philips has the ability to perform a simpler, shorter, and more effective strategy — a “first-time-right” approach that delivers detailed insight into impact dynamics and improves design confidence. Only after the product design “passes” the virtual drop impact testing, a prototype is made for physical verification. This means there are fewer hardware iterations, fewer tooling changes, and less testing, all of which generate considerable savings.

In a similar vein, Philips engineers use virtual qualification to understand how a product functions under different scenarios and stresses before they move to hardware qualification. This helps them make the right critical design choices early on, reducing cost, time, and uncertainty.

DIGITAL TWINS MODEL PATIENTS

In addition to their role in research and development, Philips’ virtual design and qualification activities can also form the basis for digital twins in the operational and clinical space.



An example of how Philips has saved time by optimizing a digital product design workflow.



One way Philips uses simulation is in virtual design and qualification. The example above shows how clamping affects the mechanical stresses inside a catheter.

A digital twin is a virtual representation of real-world entities and processes, synchronized at a specified frequency and fidelity. Digital twins allow companies to monitor the real-time behavior of a system or product and compare it to a virtual model that is constantly being updated. This makes it possible to optimize performance, predict and avoid failure, and plan for maintenance of complex systems.

In the clinical space, a digital twin enables the dynamic combination of multiple models: a model of the patient’s anatomy plus computational and system models from the imaging device used to diagnose or treat their health issue. As a result, the clinician has unique insight into the patient’s current status, can test different scenarios, and can better predict the outcome.

For example, to help clinicians diagnose structural heart problems, the Philips Dynamic HeartModel automatically extracts the anatomic detail of the patient’s heart from an ultrasound image and calculates again automatically some cardiac function

parameters. The clinician is then also able to use the same technology in the planning and the performance of a cardiovascular intervention.

Ultimately, the digital twin — a virtual representation of a person’s health status — will enable clinicians to deliver the right care in the right way at the right time. It reduces patient adverse events, shortens hospital stays, and minimizes the likelihood of readmission..

ROOM FOR LIMITLESS INNOVATION
Philips drives innovation and efficiency through a global, collaborative network where locally relevant solutions are created.

In the future, Janssen says, many of those locally relevant solutions will come from the interaction of AI with traditional, knowledge-driven modeling and simulation. The process is already underway at Philips, in fact. It underscores Philips’ commitment to advancing highly personalized, digital healthcare through leading-edge technology — which is central to Philips’ strong healthcare legacy. ▲

All Eyes on SIMULATION

By Ansys Advantage Staff

In recent years, biomedical engineering has made remarkable strides in developing treatments for eye conditions that once caused millions to suffer from impaired vision or blindness. Groundbreaking innovations — such as polymeric intraocular lenses (IOLs) used to replace cataract-clouded natural lenses — have revolutionized vision restoration procedures. LASIK surgery has become a widely recognized method for correcting common refractive errors like near sightedness, far sightedness, and astigmatism, while advancements in surgical techniques targeting retina issues and managing conditions like glaucoma have significantly improved patient outcomes. Additionally, noninvasive alternatives such as contact lenses, eye drops, and dietary supplements have advanced and benefited from biomedical research.

At the forefront of these advancements is Alcon, the global eye care leader renowned for its innovative eyecare solutions, headquartered in Geneva, Switzerland. Alcon develops advanced instrumentation for diagnosis and surgery in its surgical division, as well as consumer products in its vision care division. Both support the company's goal of helping people worldwide "See Brilliantly."

"Alcon is dedicated to providing long-term value for patients by delivering cutting-edge

innovation and breakthrough technology, transforming the way we treat eye diseases and eye conditions," says Sonalee Tambat, Senior Director and Head of Modeling and Simulation in Alcon's research and development (R&D) organization.

"To uphold its leadership position, Alcon continuously seeks to pioneer next-generation products and processes to improve patient outcomes and get these solutions to market as fast as possible." Engineering simulation software is helping them in this effort.



"By integrating simulation at the inception of the design cycle and optimizing virtually assessed designs, we've reduced the number of prototypes and in some cases eliminated an entire build phase."

— SONALEE TAMBAT, Senior Director and Head of Modeling and Simulation, Alcon

SIMULATION SHORTENS THE DEVELOPMENT CYCLE

Drawing upon her extensive academic background in mechanical engineering and over 25 years of experience in modeling and simulation, Tambat has been instrumental in leading the company's modeling and simulation group for the past eight years. Her expertise enables her team to effectively leverage modeling and simulation to expedite product development and time-to-market.

"A couple years ago, we launched a drive to fast-track digital transformation at Alcon," she explains. "As a crucial aspect of this endeavor, we broadened the scope of modeling and simulation across our entire portfolio of products. Our team has tripled in size and we've been rolling out customized simulations to global R&D teams working on surgical consoles (cataract, vitreoretinal, and refractive), diagnostics and visualization tools, consumables, intraocular lenses, contact lenses, and a range of ocular drug therapies."

The company invested in its infrastructure, deploying a high-performance computing (HPC) system with global access, as well as cloud computing and cloud bursting for problems that need large scale-up in central processing units (CPUs).

Through digital integration, Tambat and her group have reduced the development cycle timeline to just a few months for many products. They achieved this by simultaneously modeling multiple designs, materials, and load conditions and streamlining workflows to optimize and achieve desired safety and efficacy requirements. This not only accelerates development time and enhances products but also produces cost savings.

"By integrating simulation at the inception of the design cycle and optimizing virtually assessed designs, we've reduced the number of prototypes and in some cases eliminated an entire build phase. Simulation provides comprehensive answers upfront, enabling us to streamline the process. Additionally, we're

SHARING A COMPASSION FOR SIMULATION



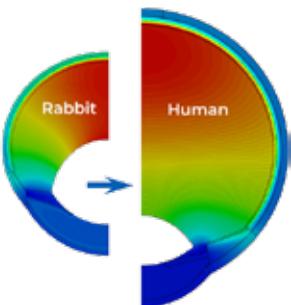
Sonalee Tambat, Senior Director and Head of Modeling and Simulation at leading eye care provider Alcon, spoke at Ansys' virtual SimCare conference in March 2023 to promote computational modeling and simulation (CM&S) in biomedical.

now assessing product concepts during the ideation phase, allowing us to swiftly and efficiently halt projects early on if needed, saving valuable time and resources."

MULTIPHYSICS SOLUTIONS ARE REQUIRED

Given the diverse range of products within Alcon's portfolio, which includes large electro-mechanical surgical consoles, intraocular lenses, contact lenses and ocular drugs, the demand for multiphysics solvers and integration platforms is paramount. "We have implemented several Ansys modeling and simulation platforms, helping us build an integrated approach, optimize results, and efficiently manage, secure, and store simulation data," says Tambat.

During most eye surgeries, doctors must ensure that the intraocular pressure of the eye is maintained. Alcon engineers can now model this pressure in advance. Similarly,



Computational modeling allows scaling of drug distribution kinetics from animals to humans.

“While modeling and simulation have long been present in various industries, what’s particularly promising now is the significant advancements in computing power and artificial intelligence technologies.”

— SONALEE TAMBAT, Senior Director and Head of Modeling and Simulation, Alcon



fluid-structure interaction simulation is extremely helpful for developing tools for surgeries done on the retina, which involve extremely small instruments that are used to make an incision, control a laser beam, or other tasks that require careful precision. With computational fluid dynamics, engineers can understand the flow field surrounding the tip of the instrument, which is critical for surgeons to determine how close the device can get to the back of the eye without damaging the retina.

BALANCING THE SCALES

In addition to her dedication to advancing simulation technologies, Tambat is equally passionate about promoting diversity and inclusion within the engineering field. Drawing upon her own experiences as a trailblazer in a male-dominated industry, Tambat actively mentors young engineers and champions diversity initiatives within Alcon and beyond. She believes that fostering a diverse and inclusive workforce not only enhances creativity and innovation but also ensures that the engineering profession reflects the diverse communities it serves.

SIMULATION IS EVOLVING

As emerging technology demands more sophisticated engineering each day, Tambat emphasizes the potential benefits of evolving digital capabilities in product development.

“While modeling and simulation have long been present in various industries, what’s particularly promising now is the significant advancements in computing power and artificial intelligence technologies. Moreover, healthcare regulatory bodies are establishing pathways to utilize computational modeling and simulation to validate medical device claims, facilitating the feasibility of swift development and delivery of new technologies for enhanced patient care,” she explains. “This presents a pivotal moment for healthcare companies to embrace these technologies, gaining a competitive edge, advancing products, and accelerating innovation.”

The field of biomedical engineering is experiencing a transformative period, driven by innovations in simulation technologies. With a steadfast commitment to innovation, companies like Alcon are poised to lead the way in delivering groundbreaking solutions that enhance the lives of millions worldwide. ▲

DIGITAL TWIN OF THE EYE

As a global leader in ophthalmic healthcare, Alcon is continuously striving to use new technologies to drive breakthrough innovation and champion progress. One such initiative they have embarked on is the development of a digital twin of the eye — a modeling and simulation-driven research and development project aimed at building patient-specific computational models of the human eye.

“These models will enable accurate modeling of key aspects of ocular physiology pertaining to the interaction with our devices and therapies in order to further improve the outcome and impact on patients,” says Sonalee Tambat, Senior Director and Head of Modeling and Simulation in Alcon’s research and development (R&D) organization.

Simulation Helps GSK Bring Medicines to Patients Faster

By **Aliyah Mallak**,
Senior Marketing
Communications Writer, Ansys

In the world of pharmaceuticals, most drugs can be broken up into two categories: small-molecule, chemically derived drugs and large-molecule biologics. Small-molecule drugs are compounds with low molecular weight and relatively simple chemical structures. These make up most of the drugs we have in our medicine cabinets, such as antihistamines and blood pressure medications. Biologics, however, consist of large, complex molecules such as proteins, carbohydrates, or nucleic acids that have a high molecular weight. As the name suggests, biologics are derived from living cells and make up hormones, vaccines, gene and cellular therapies, growth factors, insulin, and more.

Due to their simple structures, the pharmacokinetics and pharmacodynamics of small-molecule drugs are more predictable than biologics, making manufacturing processes simpler and reproduction easier. Biologics’ extreme sensitivity to physical conditions make them notorious for their manufacturing difficulty and tend to have smaller yields. While small-molecule drugs might seem like the easier option to manufacture, both are necessary to prevent, treat, and cure the vast number of ailments humans face.

Small-molecule chemically derived drugs	Large-molecule biologics
Made from chemical processes	Made from living cells
Low molecular weight	High molecular weight
Simple structure	Complex structure
Easy manufacturing processes	Difficult manufacturing processes

The differences between small-molecule and large-molecule drugs

“Fundamentally, it’s a lot easier to use CFD combined metabolic models to look at how our small-scale data will apply in the larger scale than it is to try and really mimic 2,000-liter conditions exactly in the small scales.”

— LUISA ATTFIELD, Associate Data Scientist, GSK

Historically, small-molecule drugs have dominated the U.S. Food and Drug Administration (FDA) new drug approvals (NDAs). But as new innovations surface and patients' medical needs grow, biologics are becoming more and more common. In 2023, 20 new biological license applications (BLAs) were approved by the FDA for indications including the treatment, prevention, or immunization of sickle cell disease, hemophilia A, Type 1 diabetes, Duchenne muscular dystrophy, and more.

But the process that goes into the creation of these drugs is far from simple. Drug development in general can take more than a decade and cost billions of dollars. From cell line selection to scaling the manufacturing processes, biologics are often riskier than their small-molecule counterparts. In an attempt to mitigate inconsistencies observed in the performance of their processes and cell lines between different bioreactor scales, the GSK Drug Substance Development (DSD) team turned to simulation.

ESTABLISHING CELL LINES

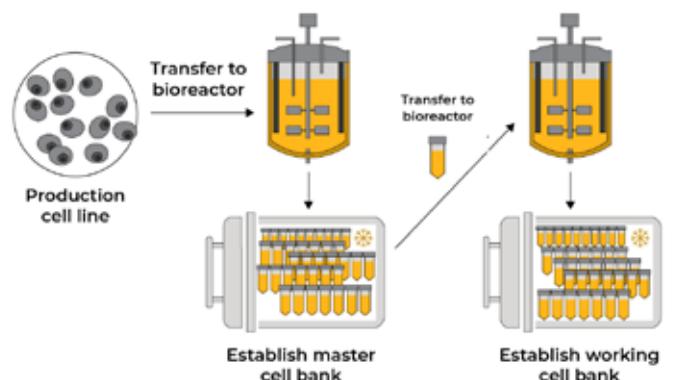
The generation of commercial, clonal cell lines expressing the biologic of interest is one of many important roles the GSK DSD team has. This involves engineering a cell to produce a specific, desired protein. Scientists transfer a gene encoding the desired protein into a cell, producing a pre-clonal pool of cell lines expressing the desired protein. The scientist then performs single cell cloning, generating multiple different cell lines all expressing the desired protein. These cell lines are then evaluated for growth, productivity, and quality in small-scale production bioreactors, such as the Ambr15. The best performing cell line is selected, becoming the production line.

Scientists then transfer the production cell line to a bioreactor to establish a master cell bank (MCB) that creates genetically identical cells. The cells multiply for a few generations, creating hundreds of millions of identical copies. The cells are portioned into vials and frozen with liquid nitrogen. The deep freeze stops cell growth so it can be thawed and used later.

A working cell bank (WCB) is then created by thawing one of the vials containing the MCB cells, allowing the cells to multiply in a bioreactor, and are then frozen again. Each new production run starts by thawing a vial from the WCB.

Because these cells are intended for human use, stable longevity is key, as the quality and safety need to be guaranteed throughout the entire life cycle of a drug. If the cell line does not create the appropriate quality in a stable and reproducible manner, the whole manufacturing process is at risk.

Cell Bank Production



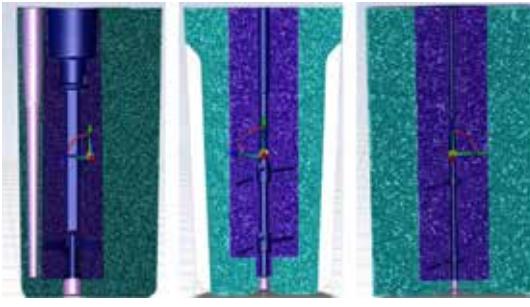
A biomanufacturing workflow adapted from: Burke, Emily. “Biomanufacturing: How Biologics Are Made.” Biotech Primer Inc., Biotech Primer, Inc., 31 Aug. 2023, biotechprimer.com/how-biologics-are-made.

SCALING UP IN SIZE

In addition to establishing cell lines, the GSK DSD team is responsible for the development of scalable, robust, and efficient upstream and downstream processes and the transfer of those processes to commercial manufacturing scale.

They select their cell lines and start them in a 15-milliliter bioreactor, but eventually these need to be scaled up to 2,000-liter bioreactors. Biological processes scale unpredictably; not only must differences between the bioreactor sizes be accounted for, but the cells' sensitivity to changes must also be taken into consideration.

While the DSD team uses predictive modeling to plan production processes, it is still nearly impossible to account



A comparison of 15-milliliter to 2,000-liter computational fluid dynamics bioreactor models in Ansys Fluent

for every single parameter. Cell line and bioreactor conditions need to be tightly controlled or the cell lines could die, which would require the DSD team to start production over again.

Predictive models developed at small scale require additional (often expensive) testing to calibrate for larger scales, and detailed vessel models may require proprietary third-party data. The DSD team also needed their solution to transfer code from the cell culture bioreactor model from gPROMS, the software on which it was developed.

The DSD team used Ansys Fluent to model the hydrodynamic profiles in GSK's bioreactors and in different conditions using computational fluid dynamics (CFD). The CFD-based investigation was critical for achieving better scale-down

models of the large-scale bioreactors, therefore enabling less expensive and more efficient experimentation for progressing biopharmaceutical assets through the pipeline.

“Fundamentally, it’s a lot easier to use CFD combined metabolic models to look at how our small-scale data will apply in the larger scale than it is to try and really mimic 2,000-liter conditions exactly in the small scales,” says Luisa Attfield, Associate Data Scientist at GSK.

The DSD team used the CFD models to create static reduced-order models (ROMs) in Ansys Twin Builder to predict selected outputs at each scale, primarily the mass transfer coefficient (k_{La}). The ROMs acted as virtual sensors that provided inputs to the cell compartment model, created with the Modelica language.

“We know that cell growth is dependent on different things like oxygen concentration,” said Attfield. “So within Twin Builder, what we’re looking at is dissolved oxygen. Any gradients of dissolved oxygen across the large bioreactor scales — oxygen transfer being the mass transfer coefficient — and combining that oxygen transfer into the metabolic models to see how the cells will behave and what we expect the local environment to be like.”

The ROMs and cell compartment model were linked in a system model created in Twin Builder and exported as a digital twin runtime. Ansys Twin Deployer was used to convert these into a scaffolding Python command line application that connected to an industrial Internet of Things (IIoT) platform. It was important to transfer the code for the cell culture bioreactor model from gPROMS to Modelica to enable the deployment of the L1 digital twin. For that reason, Ansys engineers developed a Python code that translates the gPROMS code to a language that is compatible with Fluent. This is critical because it enables a seamless translation of future changes that GSK might apply in the gPROMS model to the Modelica language.

“We definitely benefited from this collaboration — not just the software, but the help and support that we had from Ansys,” said Pavlos Kotidis, Digital and Data Analytics Leader at GSK. “There were a lot of conversations between us and Ansys to upskill our team in the CFD space. Otherwise, it would have taken us much longer to get the project going.” ▲

Sartorius Finds Simulation Is the Perfect Prescription

The world's leading pharmaceutical companies depend on Sartorius for high-quality, reliable equipment used in drug discovery. In turn, Sartorius relies on simulation to drive rapid, cost-effective, innovative product development.

By Ansys Advantage Staff

You might not have heard the name Sartorius, but you've almost certainly used prescription drugs that were developed using its advanced solutions for the pharmaceutical industry. Headquartered in Göttingen, Germany, Sartorius is a €3.4 billion company with over 14,000 employees and 60 locations worldwide. The Sartorius Group is a leading international partner of life sciences research and the biopharmaceutical industry. With its products and solutions, Sartorius enables the development and production of new and better therapies as well as affordable medicine. From lab products and services to custom bioprocessing solutions, Sartorius supports the critical drug discovery efforts of every major biopharmaceutical company.

“If we can replace iterative prototyping with simulation, then that's a huge savings of time and money. And if we can replace a single 30-day test cycle with one week of iterative simulations, then obviously we can deliver solutions to customers much faster, while still having a high degree of confidence.”

— CHRISTIAN BECKER, Senior Engineer, Sartorius

“One of the great things about being part of Sartorius is that our work has obvious importance and a demonstrated impact on society,” says Christian Becker, the company’s Senior Engineer for computer aided engineering (CAE) simulations. “As just one example, almost every COVID-19 vaccine was produced using equipment from Sartorius.”

On the way to the marketplace, new drugs face tough challenges and create enormous costs for biopharmaceutical companies. Only one out of 10,000 drug candidates actually reaches the market, with an average cost of \$2.18 billion and a development cycle, from discovery to regulatory approval, that can span 10 years. To protect those investments, drug makers need to ensure they’re working with partners that represent the leading edge in technology innovation, as well as uncompromising quality standards.

For biopharmaceuticals — a key area of focus for Sartorius — the challenges and risks are amplified. This class of drugs, which includes vaccines and insulin, consists of complex molecules that are obtained from living cells via cell culture processes. Their development costs, and their handling and quality-control requirements, are even greater than for other pharmaceuticals. Sartorius’ global leadership in this tough market segment is a testament to its own investments in world-class product development.

TAKING DEVELOPMENT TO THE NEXT LEVEL WITH SIMULATION

Since 2019, simulation via Ansys has become a key component of the company’s product development strategy. Becker joined Sartorius that year to head up the company’s simulation efforts, bringing hands-on experience from the aerospace, automotive, and oil and gas industries.

“I think most people associate engineering

simulation with those industries, and they’re surprised that a biopharma supplier would be leveraging such sophisticated product development methods,” notes Becker. “It’s evidence of how committed Sartorius is to providing advanced, leading-edge solutions to our customers.”

Together, the simulation team at Sartorius conducts multiphysics studies using Ansys Mechanical and Ansys Fluent that reveals



The world's leading biopharma research teams rely on high-performing, high-quality solutions from Sartorius.

detailed performance of many of the company’s equipment — providing an “inside” view that would otherwise be impossible.

While many of Sartorius’ equipment offerings are constructed of single-use plastic parts, the simulation team helps perfect the design of the company’s single-use plastic bags that line bioreactors and other equipment during customer use.

“As our customers are developing drugs, they’re running 30-day batches, and then they see afterward if the product is fine or not,” explains Abhinav Hazarika Product Development Scientist and Engineer, Sartorius.

“In addition to growing the team, our goal is to enable our colleagues to do their own preliminary studies in easy-to-use tools, like Ansys Discovery, then we’ll move those into Mechanical or Fluent to conduct deeper analysis. We need to increase our simulation bandwidth to keep driving innovation and answer our customers’ needs.”

— CHRISTIAN BECKER, Senior Engineer, Sartorius

“So during that month of continuous operation, the conditions must be tightly controlled. We need to understand exactly what’s happening inside the bioreactor. For example, are shear stresses being created? If so, how can we minimize them?”

“We not only need to design our single-use bioreactors for structural strength and robustness to perform for 30 days, but we also need to optimize the behavior of the fluids inside them,” says Friedrich Maier, Senior Scientist for CAE Simulation at Sartorius. “After a certain time period, how will the viscosity change? How will the density change? With our visualizations enabled by Ansys, we can look directly into the reactor, which in many cases would not be possible in any other way.” Maier points out that the company’s bioreactors range from 15 ml to 2,000 liters in working volume.

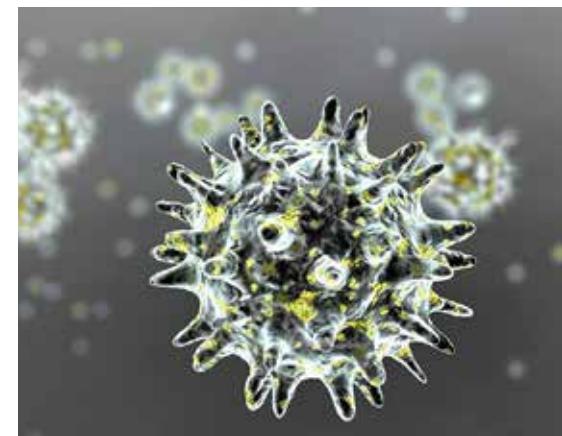
“Running a single physical prototype of a bioreactor takes one month and cost up to €50,000,” Becker says. “If we can replace iterative prototyping with simulation, then that’s a huge savings of time and money. And if we can replace a single 30-day test cycle with one week of iterative simulations, then obviously we can deliver solutions to customers much faster, while still having a high degree of confidence. We can’t eliminate experimental testing, but we can reduce it.”

TACKLING THE CHALLENGE OF INCREASED SUSTAINABILITY

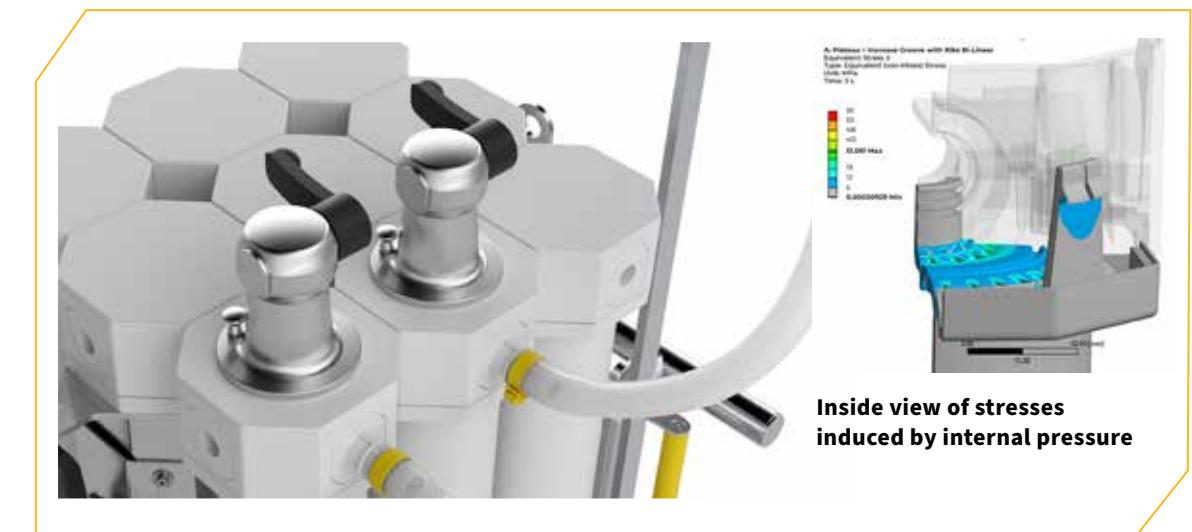
“Sartorius is committed to maximizing cost and ease-of-use for our customers, as well as supporting sustainability,” explains Becker. “After a multiuse bioreactor has been used, it takes a lot of chemicals, hot water, and energy to clean the steel tank before another batch process can take place. We’ve addressed that by designing single-use plastic liners for our vessels, which are material or thermal recycled after use.”



Single-use bioreactors from Sartorius can range dramatically in size and volume, from 10 ml to 2,000 liters.



Biopharmaceutical development often requires 30-day batch processing, during which conditions must be tightly controlled to protect living cells.



“Designing those bags with its stirring unit and connectors is a significant engineering challenge because you’re dealing with injection molding processes and complex part assemblies,” he continues. “And when you’re talking about plastic, there is a lot of nonlinear material behavior.

“Engineering a product that includes both a reusable reactor and single-use liners for a customer application can easily cost over €1,000,000,” Becker says. “Ansys helps us predict how that product is going to perform in advance, accounting for nonlinear behaviors and other complexities.”

When Becker joined Sartorius, single-use plastics design was one of his first priorities, because they provide huge development speed and cost payback in addition to sustainability.

A HEALTHY OUTLOOK FOR THE FUTURE

Simulation has proven so valuable at Sartorius that Becker predicts his team will be doubling in size in the next five years or so. “Today, our three-person team is located in Gottingen, at the headquarters of Sartorius, but we want to get team members in India, France, and other regions more involved in simulation,” he says.

“In addition to growing the team our goal is to enable our colleagues to do their own preliminary studies in easy-to-use tools, like Ansys Discovery, then we’ll move those into Mechanical or Fluent to conduct deeper analysis,” Becker continues. “We need to increase our simulation bandwidth to keep driving innovation and answer our customers’ needs.”

With the rapid commercialization of COVID-19 vaccines and the emergence of mRNA technology, the global biopharmaceutical industry is experiencing incredible growth, which brings both opportunities and challenges for Sartorius’ customers. The company prides itself on helping customers drive product and process innovation via its own leading-edge solutions.

“Simulation with Ansys helps us maximize both development cost-effectiveness and speed, along with product confidence and reliability,” notes Becker. “As the benefits of engineering simulation become apparent, I expect more and more healthcare companies to adopt it as a standard product development practice.” ▲



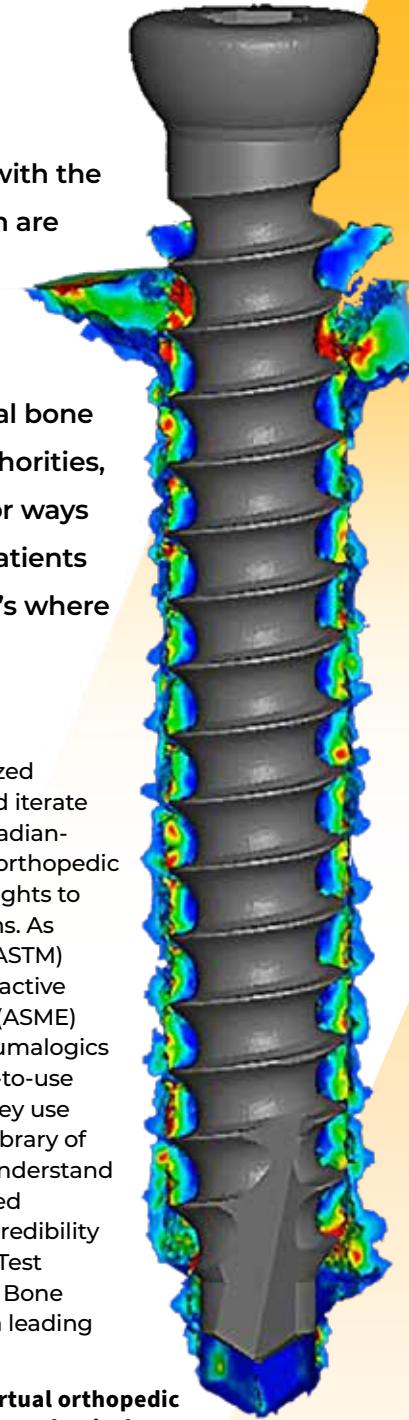
Accelerating In Silico Medical Device Testing

By Aliyah Mallak, Senior Marketing Communications Writer, Ansys

There are thousands of medical devices registered with the Food and Drug Administration (FDA), some of which are implanted orthopedic devices. Bone screws are the most common type of orthopedic implant because they are used in just about every joint replacement, plate fastening, and fixation device. While the typical bone screw has specific parameters set by regulatory authorities, medical device manufacturers are always looking for ways to create new, innovative screws that are safer for patients and more convenient for orthopedic surgeons. That's where Numalogics comes in.

Numalogics helps small-, medium-, and large-sized medical device manufacturers design, test, and iterate on their devices using virtual models. This Canadian-based company was founded in 2010 by three orthopedic spinal surgeons whose goal was to provide insights to the biomechanics of human-device interactions. As a member of the American Society for Testing and Materials (ASTM) committee on medical and surgical materials and devices, an active contributor to the American Society of Mechanical Engineers (ASME) V&V40 committee, and a member of the Avicenna Alliance, Numalogics democratizes *in silico* medical device testing by creating easy-to-use applications with embedded ASTM and ISO standard tests. They use high-fidelity finite element analysis (FEA) models to create a library of different *in silico* tests so medical device manufacturers can understand the behavior and performance of their implants under modeled biological system (biofidelic) loading conditions. To establish credibility of their computational models, specifically for ASTM F543-A3: Test Method for Determining the Axial Pullout Strength of Medical Bone Screws, Numalogics joined forces with Ansys and Sawbones, a leading provider of bone surrogate materials.

A virtual orthopedic implant mechanical test



“You only need the 3D model of the screw to run the simulation, which takes just a few minutes, to evaluate its anchoring performance. The model is ideal for conducting experimental design studies and converge towards the most optimal design while significantly reducing the time and resources required for prototyping and experimentally testing new designs.”

— DAVID BENOIT, Biomechanical Simulation R&D Specialist, Numalogics

BONE IN, PLEASE

Designing, prototyping, and conducting experimental testing of the screws is a frequent challenge for medical device manufacturers and can take months.

This wastes up valuable time and resources that could otherwise be spent somewhere else or delay a device's submission to the FDA, therefore slowing down entry to market or inhibiting even engaging in such projects. Numalogics aims to shorten timelines and reduce R&D costs by replicating the ASTM standard that is used to test the performance of orthopedic bone screws with their virtual models. But before they could model the screws, they needed the other half of the equation: bone.

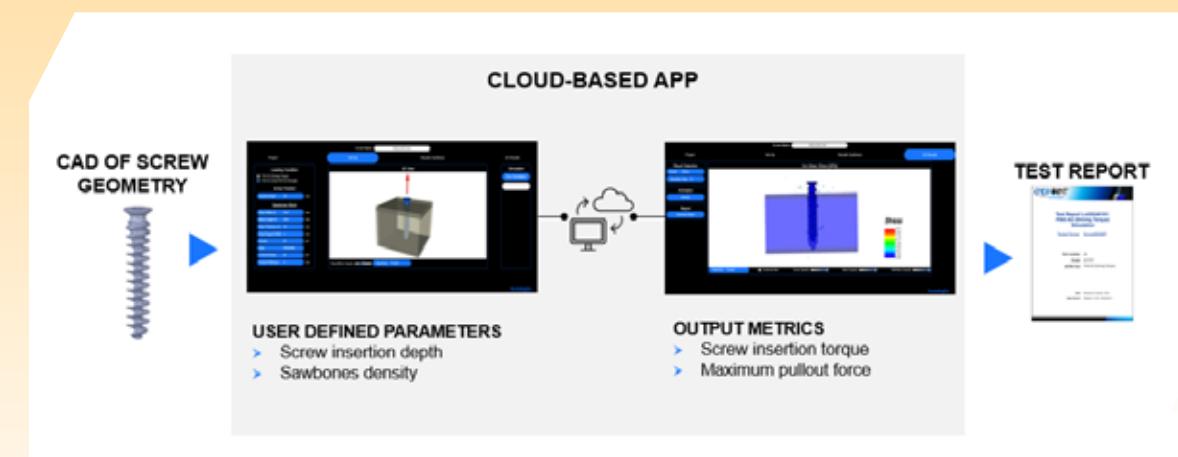
Cadaver bone might seem like the logical option for testing, but it's not. Bone density varies wildly depending on sex, age, diet, previous medical conditions, etc., so there would be no way to guarantee consistency between the mechanical properties of the bone from test to test. It's also not easy to acquire cadaver bone. So, Numalogics turned to Sawbones.

Sawbones creates a bone surrogate material that cuts, drills, and feels like real bone; is recognized by the FDA; and conforms to ASTM F-1839-08: Standard Specification for Rigid

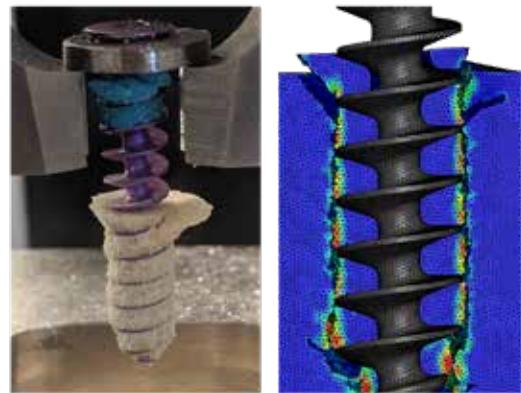
Polyurethane Foam for Use as a Standard Material for Testing Orthopaedic Devices, making it the perfect base for Numalogics to test their models. They offer a variety of models that cover the entirety of the skeletal system and even have veterinary models for dogs, cats, and horses. Companies all over the world use their products to test orthopedic devices and provide hands-on learning to aspiring medical professionals. The rigid polyurethane foam block offers a standard way to evaluate the performance of orthopedic screws, as they offer consistent mechanical properties and enable performance comparisons between different screw designs.

“We virtualized the Sawbones material in a finite element model,” says David Benoit, Biomechanical Simulation R&D Specialist at Numalogics. “The material’s mechanical behavior was characterized through extensive experimental testing across various loading modes, which enabled us to incorporate all material properties into the model. The credibility of the model was then evaluated by conducting a validation study using real orthopedic screws.”

An obvious but complex feature of a bone screw is its anchoring performance once



Workflow of the Numalogics and Sawbones app, Endpoint™



Physical experimental testing of a bone screw versus the FEA testing of a bone screw (section view)

fixed in the bone. Throughout its entire life cycle, regardless of bone density, it is ideal for the screw to never move. Numalogics used 17 different screws from five implant manufacturers and conducted experimental screw pullout testing for all of them. The team then simulated the screw pullout tests and compared the physical results to the predictions of the models. The numerical model showed excellent reliability in predicting the maximum pullout force of the screw.

NO LOOSE SCREWS HERE

The success of the validation study led Numalogics and Sawbones to create an app that democratizes the use of simulation by making it easier to test bone screws in a virtual environment. Endpoint™, launched in early 2024, is a cloud-based app that enables engineers to easily test orthopedic screw designs using Numalogics' latest computational modeling and simulation techniques and obtain results quickly, even before the first physical prototype can be manufactured.

"You only need the 3D model of the screw to run the simulation, which takes just a few minutes, to evaluate its anchoring performance," says Benoit. "The model is ideal for conducting experimental design studies and converge towards the most optimal design while significantly reducing the time and resources required for prototyping and experimentally testing new designs."

For now, to assist with usability and understanding, customers submit their computer-aided design (CAD) files and testing requirements to Sawbones and Numalogics engineers run the simulations in the app for them. The app automatically creates the geometry in Ansys SpaceClaim, then creates the model in Ansys Mechanical and

runs the simulation using Ansys LS-DYNA. The automation is handled via a dedicated ACT extension, and they use the Ansys Data Processing Framework (DPF) from PyAnsys for results visualization.

Eventually users will be able to independently upload their CAD files, specify a few simple parameters such as Sawbones' block density and screw insertion depth, then let the app do the rest. And not only will this version of the app provide test results, but it will also provide the user with more control to gain insight to the mechanism of bone failure — something very important to optimizing and understanding bone screws.

"When you do experimental testing, it's hard to discover the reason of the failure or the failure mechanism inside the block of foam," says Loïc Degueldre, Simulation Automation R&D Manager at Numalogics. "In the numerical simulation, we provide an animation of the failure. So, you can see what's really happening inside the bone and compare mechanisms of the failure between different designs."

VALIDATED, VERIFIED, AND ACCEPTED

While this app will help many medical device manufacturers design new screws, it's just the tip of the iceberg for the benefits Numalogics can provide.

"The next step is to facilitate the results evaluation by the regulatory bodies for our customers," says Benoit. "Our goal is to have simulation results be accepted as evidence to demonstrate the screws' performance so that it can be used to reduce or replace experimental testing."

"In democratizing this simulation tool when it is eventually available as a web-based app," says Degueldre, "we will help screw manufacturers significantly reduce time and resources for evaluating new screw designs before going to market." ▲

PAVING THE WAY TO Personalized Medicine

By Aliyah Mallak, Senior Marketing Communications Writer, Ansys

When we need an orthopedic implant or a cardiovascular device such as a stent, we may assume it's personalized, customized, or selected for us. Yet almost all orthopedic and cardiovascular surgeons use off-the-shelf products and select them based on experience. They are rarely, if ever, personalized for an individual patient. The one-size-fits-all approach to healthcare fails to recognize the significant differences among the anatomical and physiological characteristics of individual patients. This creates inefficiencies and cost overruns, but also affects the quality of care provided. Personalized healthcare could help provide optimal, patient-specific treatment plans, from diagnosis to therapy.

“PyAnsys is a game-changer for the development of Simq products and our digital twin technologies. PyAnsys provides a modern, state-of-the-art Pythonic interface. This is a huge advantage for developers.”

— ALEXANDER VOLF, Chief Technology Officer, Simq

While this concept might seem like science fiction, advanced technology is poised to speed up patient recovery and improve the quality of life for people around the world. Smart medical devices and wearables are already bridging the gap between hardware and software, with heart rate and blood pressure monitoring, sleep cycle tracking, and more.

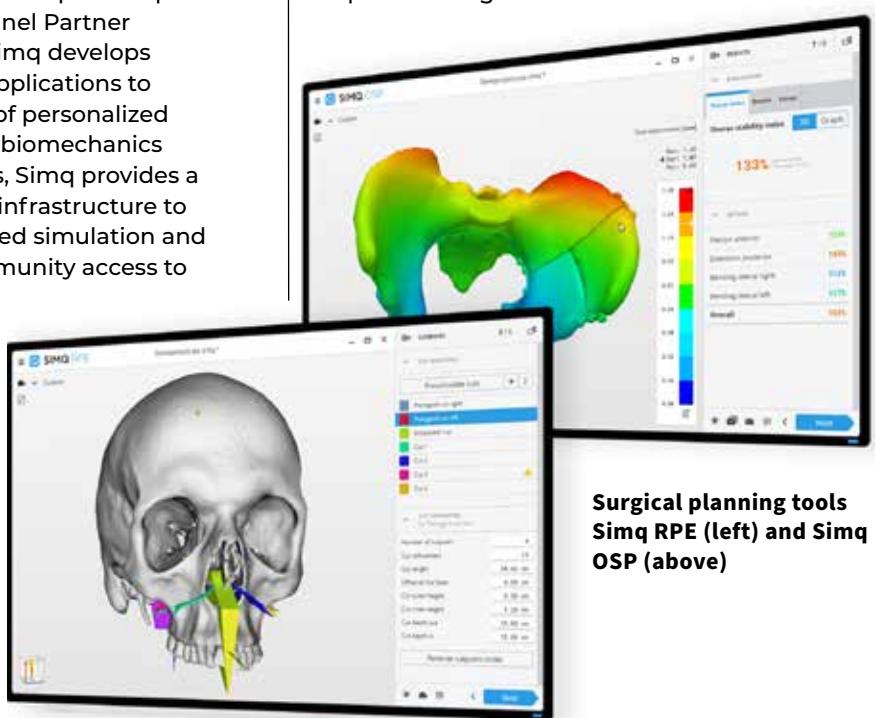
Yet personalized healthcare still requires a significant paradigm shift and new technology tool kits for collecting and creating data used to customize treatment. Biomechanical simulations offer a fast and straightforward solution for personalization at the point of care to treat patients with devices or implants that interact optimally with their body. In this way, healthcare providers can create truly personalized treatment plans and rule out possible complications.

One company leading the charge to personalized medicine is Simq — a corporate spin off from Ansys Channel Partner CADFEM International. Simq develops easy-to-use healthcare applications to accelerate the adoption of personalized medicine. By combining biomechanics and *in silico* technologies, Simq provides a compliant development infrastructure to democratize physics-based simulation and give the healthcare community access to more information and personalized insights. Their team of experts is committed to delivering the highest quality solutions to make the potential of digital twin simulation — a patient-specific computer model — artificial intelligence, and machine learning broadly available.

DEMOCRATIZING SIMULATION FOR MEDICAL PROFESSIONALS

While simulation is a tremendous asset in many industries, companies may be reluctant to hire experienced engineers to perform simulations. With high costs and long delays prominent in the healthcare industry, most companies don't have the budget to hire engineers, nor the time to train healthcare professionals to use simulation software.

As a company, Simq offers several solutions for specific purposes, such as virtual implant testing (Simq VIT), surgical planning tools for complex osteosynthesis (Simq OSP) and rapid palatal expansion (Simq RPE), and a medical device to improve diagnosis in sleep apnea patients (Simq OSA). They use PyAnsys — a technology combining Python and Ansys solutions to democratize simulation — to assist biomedical engineers, and eventually medical professionals, with diagnostics, research and development, treatment planning, and implant testing.



Surgical planning tools
Simq RPE (left) and Simq OSP (above)

By giving Simq access to Ansys' physics-based engineering tools, Simq developers can focus on the implementation and adoption of digital twins in medicine and regulatory requirements.

Simq is developing applications with an easy-to-use, easy-to-interpret user interface (UI), which prevents the need to hire specialty engineers in hospitals or train medical professionals on all the intricacies of simulation.

“PyAnsys is a game-changer for the development of Simq products and our digital twin technologies,” says Alexander Wolf, Chief Technology Officer of Simq. “PyAnsys provides a modern, state-of-the-art Pythonic interface. This is a huge advantage for developers. Beyond its immediate usability, it also opens access to the extensive capabilities of the Python ecosystem in the simulation process, as well as the combination of simulation with mathematical, statistical, and machine learning methods.”

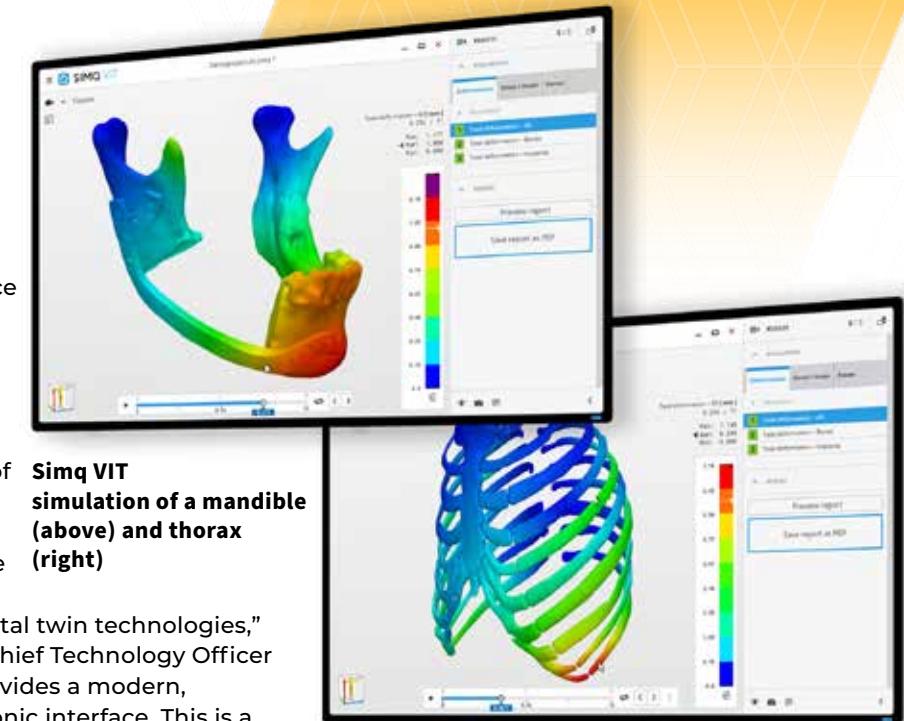
SIMULATION EMPLOYED AS A MEDICAL DEVICE

Meeting regulatory requirements is one challenge faced by Simq and its customers. Medical devices of any kind are subject to approval from regulatory authorities such as the Food and Drug Administration (FDA) in the United States or the notified bodies in Europe. To approve a medical device, the manufacturer must provide extensive documentation and clinical data showing that the device is safe and effective.

But Simq doesn't produce physical devices; their customers do. So, are they responsible for following regulatory guidelines? Yes, they are.

As with medical devices, whether software qualifies as a medical device is determined by the manufacturer's intended purpose for the software. From a regulatory perspective, medical software is subject to the same requirements as a physical medical device. Accordingly, medical software must meet certain standards.

Simq's VIT, OSP, and RPE medical software solutions enable medical device



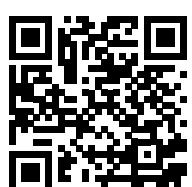
Simq VIT
simulation of a mandible (above) and thorax (right)

manufacturers to check their devices for compliance and work towards personalized medicine. They provide verification, validation, and uncertainty quantification following FDA standards for patient-specific simulation models and quality assurance for products according to ISO 13485. Simq can reuse their regulatory framework and validation process for precision medicine and digital twins, which helps to speed up the development processes.

To ensure that as many patients as possible benefit from Simq's solutions, they make the basic technologies available to other medical device manufacturers. Instead of starting from scratch every time, manufacturers can use Simq's development framework, which saves time and money through reusable technical documentation. This gives customers valuable resources back so they can focus on the next big innovative medical device. ▲

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Diagnosing Aneurysms in a Heartbeat with Ansys

By Ansys Advantage Staff

Ascending aortic aneurysms (ATAAs) are very common, life-threatening cardiovascular diseases characterized by an abnormal bulging or a weak spot in the aorta, the main artery in the human body. Most of us are familiar with aneurysms, as they have a scary reputation for causing a blood vessel to burst suddenly — and, too often, fatally.

However, an ATAA diagnosis isn't always a death sentence. In some cases, effective treatment requires a few lifestyle changes or — in more severe cases — surgery. The good news is that among those who elect ATAA surgery, studies have shown that 79% will survive for at least 10 years after treatment.

In the case of a rupture, however, the first 48 hours are critical. Without emergency surgery during those 48 hours, only half can expect to survive. In any event, a detailed clinical assessment and definitive diagnosis based on family history, medical expertise, and relevant testing involving different imaging technologies can factor heavily in a patient's survival.

In the future — within a simulation environment — it may be possible for a medical team to more quickly and accurately identify what to do in the case of an aneurysm, then take immediate action to successfully treat it. To be clear, this activity would not happen in a vacuum. It would also be guided by the expertise of the attending physician, the assessment of a greater medical team, and various imaging and test results.

A TWINNING STRATEGY FOR THE FUTURE OF ANEURYSM PREVENTION AND TREATMENT

Thanks to MeDITATE — the Medical Digital Twin for Aneurysm prevention and Treatment — simulation may become an important factor in the diagnosis and treatment of aneurysms. MeDITATE research is supported by a longstanding partnership between Ansys and software company RBF Morph.

There are currently three MeDITATE research projects focused on using digital twins that are interconnected with some participant overlap. RBF Morph is enabling the use of mesh morphing with Ansys computer-aided engineering (CAE) solutions and Ansys Twin Builder software in all three projects to develop a better understanding of ATAA and other medical conditions.

"Coming into MeDITATE we already have activities around this topic," says Dr. Marco Evangelos Biancolini, RBF Morph CTO and founder and associate professor of machine design at the University of Rome Tor Vergata. "We consider aneurysm research to be really important and really difficult, involving academia and the medical industry working together for a common objective. We have a \$4 million budget for this project with many partners including Ansys, plus 14 researchers that are 100% committed to this effort, which

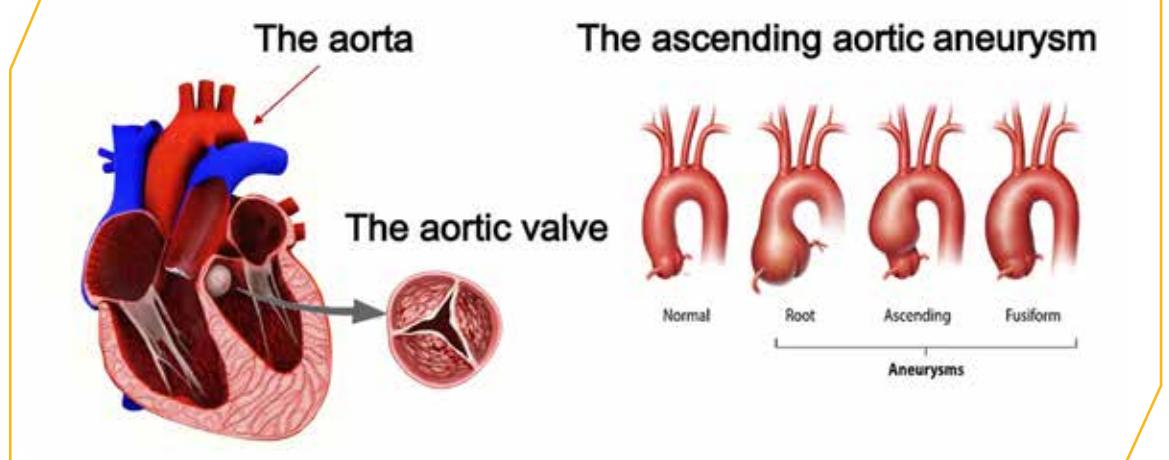
amounts to a medical digital twin task force of almost 100 people."

MeDITATE's large consortium of researchers are working together with Ansys using medical imaging segmentation software. Researchers compare the images of a patient with the reduced-order model (ROM) generated in Twin Builder software to see, in real time, the evolution of the pathology. Using this medical digital twin model, they can then augment the images with simulation results, enabling them to extract indexes/biomarkers and further understand what's going on medically.

DIGITAL TWIN AND REAL TIME SIMULATION.

Ultimately, the creation of a medical digital twin in Twin Builder could enable a high-fidelity simulation of the patient for a patient-specific geometry. The goal is to provide additional information to the surgeon and reduce the mortality rate of an aneurysm. Using a medical digital twin introduces greater certainty in the medical decision-making process, supported by additional evidence and knowledge.

"Obviously, if I'm a patient and I have this condition, and you provide one more perspective or additional information to help me make this decision, that's always better," says Biancolini. "Introducing simulation gives you more authoritative, well-defined



The anatomy and the clinical problem. The criterion to perform ascending aortic aneurysm surgery is currently based only on the evaluation of the ascending aorta diameter.

“Twin Builder enables us to extract a large amount of data, then use it to create a model that — instead of running many hours of calculations — can run in real time.”

— DR. MARCO EVANGELOS BIANCOLINI,
RBF Morph CTO and Founder,
and Associate Professor of
Machine Design, University
of Rome Tor Vergata

information based on additional technology. In the future, it's also possible that a digital twin may become an important component or part of a medical device, such as a digital twin onboard of an ultrasound."

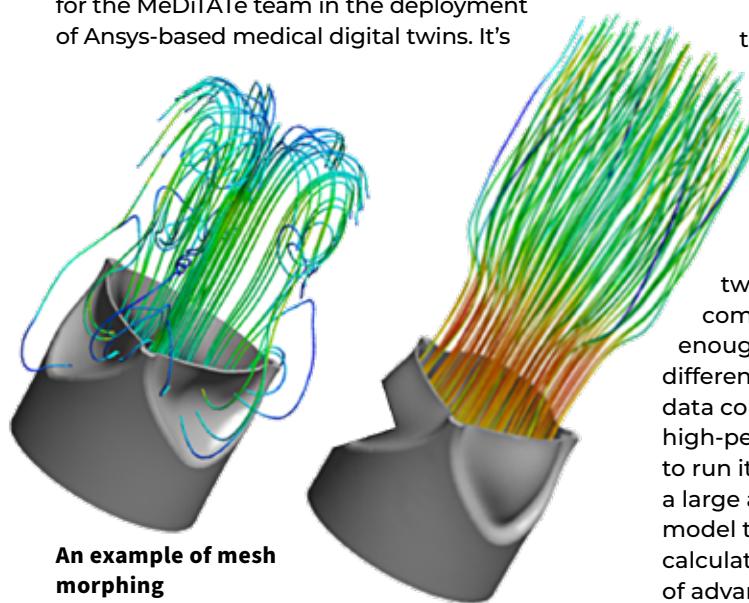
ANSYS SOFTWARE ENABLES NEW PATHWAYS TO RECOVERY

In the face of many unknowns, the extensive use of simulation comes with several benefits for the MeDiTATe team in the deployment of Ansys-based medical digital twins. It's

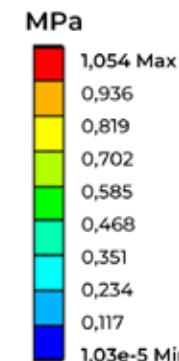
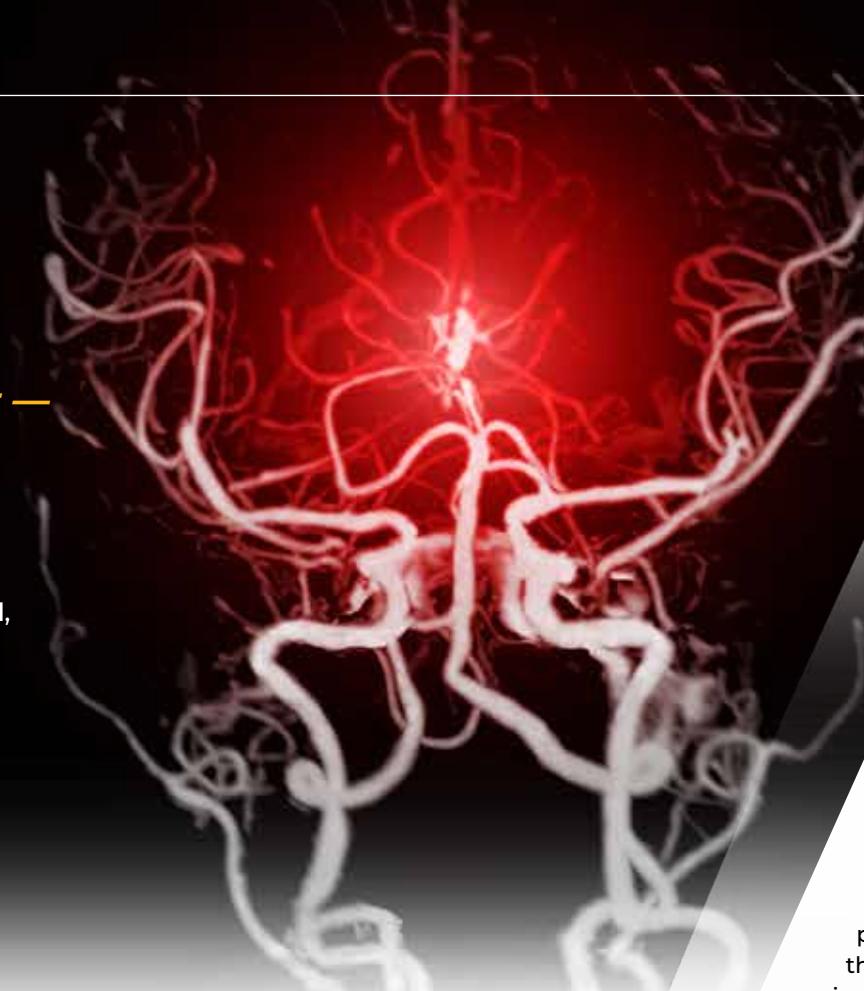
reflected first in the collective experience using high-fidelity simulation software including Ansys Fluent, Ansys Mechanical, and Ansys LS-DYNA. All three are integral in the study of fluids, structures, and electrophysiology fluid-structural interactions that are a big part of the team's work. MeDiTATe researchers are also deploying solutions with Twin Builder that make ROM generation effective and user friendly in the process.

Working with very well-established tools in support of new technologies for digital twin development enables researchers to approach their work with more clarity. It enables them to know where they are headed, and understand the challenges they can expect.

"To deploy effective medical digital twins, you need the state-of-the-art data coming out of our research, yet this is not enough," says Biancolini. "You also need two different things — one is reduced-order model data compression, which can be obtained by high-performance computing, and a model to run it on. Twin Builder enables us to extract a large amount of data then use it to create a model that, instead of running many hours of calculations, can run in real time. The ability of advanced visualization makes translation



An example of mesh morphing

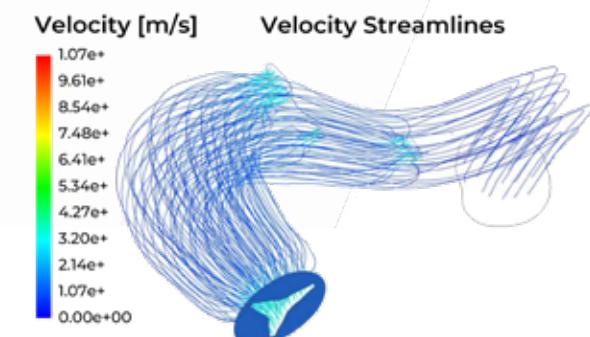


A study of the aortic valve using RBF mesh morphing technology

possible so this data can be used in the medical world."

MESH MORPHING AND TWIN BUILDING INTO THREE DIMENSIONS

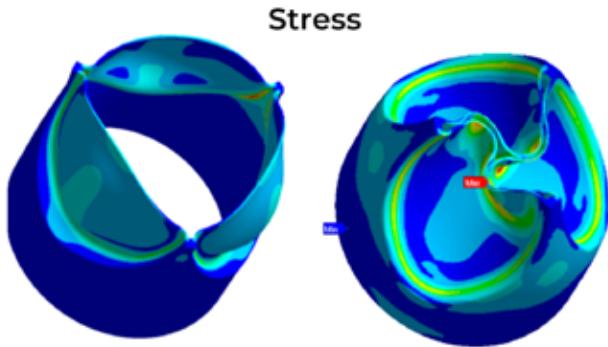
RBF Morph mesh morphing technology is a key enabler of parametric shapes and forms — shapes that have a curving nature. The software is not only useful in defining shape parameters — for instance, the positioning of a prosthetic part — but is also needed for statistical shape modeling (i.e. to extract common shape features of a patient cohort). It's extremely helpful during projects when researchers are tasked with creating generic patients. If a statistical model is built with a large cohort, the software enables the digital



Study of the computational fluid dynamics simulation of an aorta opening and closing

twin coming out of Twin Builder to easily adapt to and represent a new patient without the need for further CAE computations.

Currently this method is being applied to an aortic arch so that a full-flow simulation of a new patient is readily available in the 3D slicer software used for medical image segmentation. This leads to successful 3D image data extraction of regions of interest



(ROIs) from cross-sectional imaging modalities such as magnetic resonance imaging (MRI) or computed tomography (CT) scans. Using a similar process, the DITAID (digital twin for airflow and drug delivery in human airways) team is also creating parametric airways to enable a more patient-based approach to decide which drug deliveries are needed to treat various pulmonary conditions.

REPLICATING A CIRCULATORY LOOP WITH SIMULATION

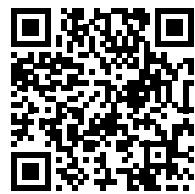
Beyond imaging and the associated *in vivo* data, MeDiTATe uses 3D printing to create medical mockups that are perfect reproductions, all done within a simulation environment. In this case, high-fidelity simulation working in concert with several tools, including 3D printing, enables the team to arrive at the most accurate representation possible.

It's the combination of surgical expertise and material analysis that ultimately leads to the creation of an accurate 3D-printed mockup of a circulatory loop, which not only considers the vessel, but is connected with everything that makes the heart beat in the actual patient. During the process, tissues extracted during ATAA-related procedures are used for mechanical testing to develop a better understanding of their structural characteristics. The result is a valuable, scientifically accurate physical representation useful in making further medical discoveries about heart conditions, with Ansys simulation being the key enabler. ▲

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Simulating for Earlier Melanoma Detection

By Aliyah Mallak, Senior Marketing Communications Writer, Ansys

"Don't forget the sunscreen!" How often did we hear Mom or Dad yelling at us to put on sunscreen as a child?

We might have found it annoying back then, but it was for good reason. More than 1 out of 3 Americans reports getting a sunburn every year. As many of us know, sunburn is not very pleasant. But the pain and itching are the least of our worries. Overexposure to ultraviolet (UV) rays — either from the Sun or tanning beds — is a major cause of skin cancer. Skin cancer is the most common cancer in the United States, with roughly 5 million people treated every year. There are a few common types of skin cancer, but the most serious is skin melanoma because it can metastasize, or spread, to other areas of the body.

Melanoma starts in the melanocytes, which are the cells responsible for giving our skin its color. Many melanomas start on a mole, but most occur on normal skin. While melanoma only accounts for 1% of skin cancer, it makes up the majority of skin cancer-related deaths. This might sound scary, but melanoma is treatable if caught early. Early intervention includes self-checks and regular visits to the dermatologist.

Current screening methods involve total body examinations, checking each individual pigmented lesion for melanoma signs. This can be very time consuming, especially for patients with many moles or pigmentations. In an effort to make early melanoma detection easier and more efficient, the European Union's Horizon Europe program provided funding for the Intelligent Total Body Scanner for Early Detection of Melanoma (iTBoS) project.

Partners working on iTBoS are developing an artificial intelligence (AI) diagnostic platform to help detect melanoma. The platform includes a total body scanner and computer-aided diagnosis tool to integrate patient-specific data such as:

- Classical demographic data: age and sex.
- Clinical phenotypes: anatomical locations of every lesion and skin phototype.
- Genotype: mutations in hereditary melanoma genes and genetic variations in melanoma susceptibility genes.



- Imaging phenotype: number and size of moles and the degree and area of UV-damaged skin.
 - Clinical dermoscopic image: characteristics of the lesions acquired by the high-resolution total body scanner.
- Combining all this data will provide healthcare professionals with an accurate, detailed, and structured assessment of pigmented skin lesions specific to that patient.

The total body scanner will be based on an existing prototype developed by three of the project partners and powered by Optotune's high-resolution cameras equipped with liquid lenses. These novel lenses, based on two immiscible fluids of different refractive indexes, will provide unprecedented image quality of the whole body. The integration of such images with all available patient data using machine learning will lead to a new dermoscopic diagnostic tool that can provide prompt, reliable, and highly personalized diagnostics for optimal judgment in clinical practice.

CHANGING FOCUS BY REPLICATING NATURE

Founded in 2008, Optotune develops and manufactures different kinds of optical components for applications in machine vision, microscopy, laser processing, healthcare, automotive, and more. They started with their core technology, the focus tunable lens. Also known as a liquid lens, this innovation was inspired by the anatomy of the human eye.

Traditional optics are based on solid glass or plastic lenses, which move back and forth to focus or zoom. Simply put, light passes through the lens and the lens moves back and forth to converge the light to a specific point. If the light converges before or after the point, the image is out of focus.

Your eye, however, consists of an elastic lens material that bends in order to focus. When looking at things far away, your eye muscles relax and your lens looks slim. When looking at things close up, your eye muscles contract and your lens gets thicker.

Optotune's focus tunable lenses are shape-changing lenses based on a combination of optical fluids and a polymer membrane. The core element consists of a container filled with an optical liquid and sealed off with a thin, elastic polymer membrane. A circular ring that

pushes onto the center of the membrane shapes the tunable lens. The deflection of the membrane — and with that, the radius of the lens — can be changed by pushing the ring toward the membrane.

This process occurs by exerting pressure to the outer part of the membrane or pumping liquid into or out of the container.

There are five main advantages of focus tunable lenses over traditional optics:

- Compact designs
- High reliability
- Less tolerance sensitivity
- Fast response
- Robust system design

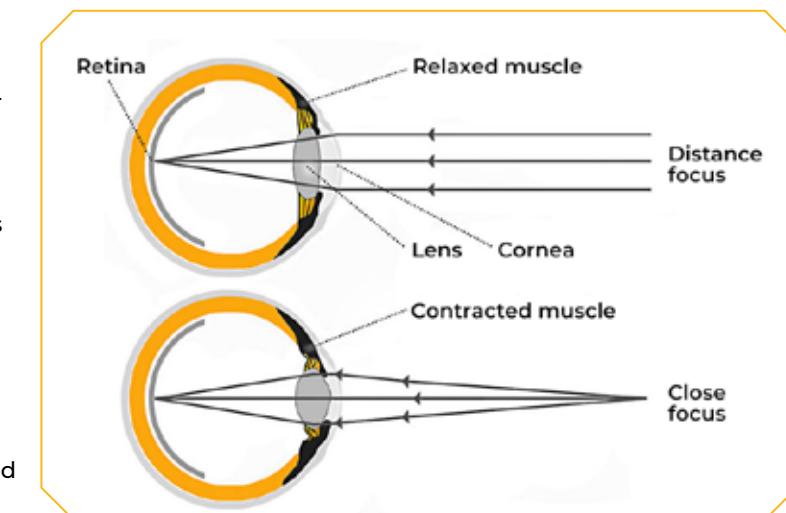


AN MRI MACHINE FOR MOLES

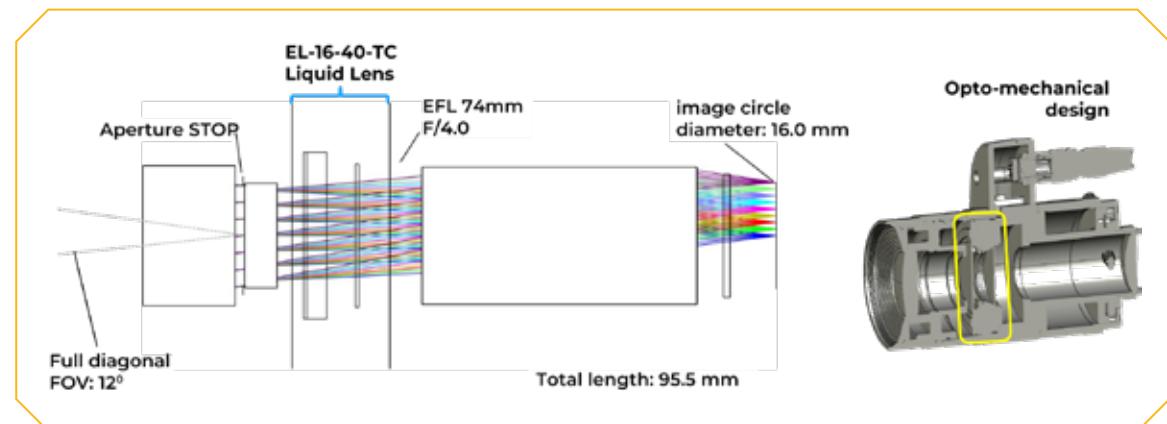
The iTBoS construction is similar to a magnetic resonance imaging (MRI) or computerized tomography (CT) scanner. The patient lays on a bed with five arches over it. Each arch has three camera modules that can move laterally and vertically. Each camera module has a:

- | | |
|-------------------|--------------------------|
| • Lighting system | • Objective lens |
| • Distance sensor | • High-resolution camera |

The lenses had a few parameters they needed to meet in addition to technical specifications. The camera needed to be roughly half a meter away from the patient to ensure their safety. Because of this, the camera would have to have a small field of view (FOV) to be able to depict the same high-



How the eye focuses on near and far objects



Camera module layout with performance characteristics (left) in Ansys Zemax OpticStudio and the opto-mechanical design of the module with the yellow rectangle indicating where the liquid lens is housed (right)

resolution images as if they were located just centimeters away. A small depth of field (DOF) was important to account for the 3D object (the patient), so the camera would have to stack several images by moving the focus a small distance each time. Lastly, as typical MRIs can take anywhere from 20 minutes to over an hour, a patient's time in the scanner needed to be reduced to increase their comfort level during the scan.

Accounting for all of these parameters, the iToBoS team decided to use the EL-16-40-TC liquid lens from Optotune — a large, electrically focused lens that comes in a small, compact design.

TESTING REQUIREMENTS IN OPTICSTUDIO

To test the different requirements of the lens, Optotune turned to Ansys Zemax OpticStudio. They started with the nominal design. When using a liquid lens in an optical design, it needs to be dynamic. In this case, Optotune wanted to adjust the working distance — the distance between the patient and the camera



Nominal design of scanner camera with liquid lens simulated in Ansys Zemax OpticStudio

module — from 350 to 650 mm, with an intermediate distance of 420 mm. Unlike other lenses, a liquid lens doesn't need to undergo a large change in focal power (+1 diopter to -1.7 diopters) to adjust the focus according to these different working distances. The curvature of the liquid lens to adjust the focal strength is very minimal compared to the adjustment a fixed lens would make in its own operating environment.

The performance of the lens needed to have a distortion of less than 1.5% and relative illumination greater than 70%. At all three distances, the lens achieved a distortion rate of less than 1% and a relative illumination of 95%, even in the corners. The nominal design was well above the target specifications; however, they were tricky to meet because the required optical quality of the iToBoS is so high.

After determining the nominal design, Optotune wanted to simulate the real performance of the lenses. Because liquid lenses have liquid inside of them (as their name suggests), Optotune had to account for the effect gravity would have on the lens. When a lens is held vertically, the liquid inside the lens pools at the bottom, creating what's known as coma. Coma caused by gravity in human eyes is small enough to not affect our vision, but optics are so sensitive that coma can affect resulting images. In most cases, this type of error isn't enough to matter, but to doctors trying to determine if a mole or pigmentation is a melanoma, it does.

Optotune simulated the effect of gravity on their lenses in OpticStudio, which showed that the results were indeed no longer within the accepted limits.

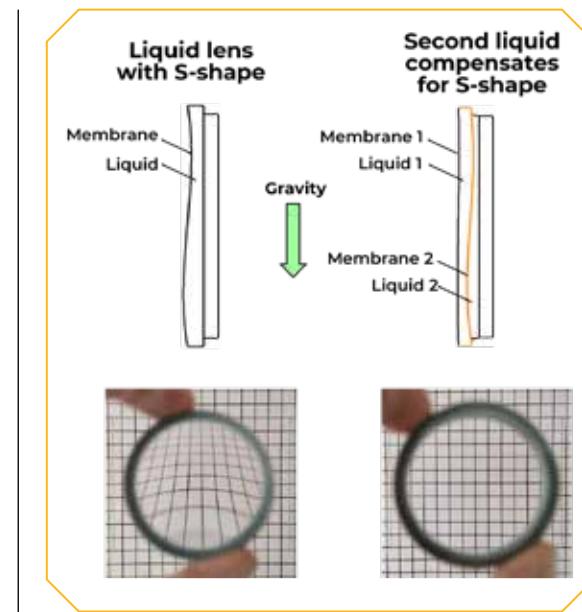
To compensate for gravity's effect on

extremely sensitive optics like the iToBoS, Optotune created gravity-compensated (GC) lenses. These lenses use the same technology as a normal liquid lens, but they contain two membranes and two liquids instead of one.

After implementing the GC lens for the iToBoS, Optotune wanted to simulate maximum residual coma caused by gravity and maximum allowed astigmatism of the lenses. While the GC lenses compensate for nearly all coma caused by gravity, there will always be some left over due to manufacturing tolerances. Optotune lenses have very low high-order aberrations, but some magnitude of low-order aberrations like astigmatism will appear. After simulating this worst-case scenario in OpticStudio, the Optotune team determined that the GC lenses still meet the minimum allowable parameters for all three distances.

After simulating the worst-case scenario, Optotune tested it against the real deal. They took the 420-mm working distance simulation with residual coma caused by gravity and astigmatism and compared it to two real measured cases from the iToBoS. The simulated results from OpticStudio and the real results from the scanner are comparable and fall within minimum production requirements.

Optotune and the iToBoS team are hard at work developing a novel skin scanner to enable an integrative diagnosis platform that detects and diagnoses relevant changes over time in pigmented skin lesions. Optotune lent their



To compensate for the effect of gravity on extremely sensitive optics like the iToBoS, Optotune created gravity-compensated (GC) lenses.

optical expertise and world-class optical lenses to make melanoma detection even easier. By simulating the optical performance of the lens in OpticStudio and comparing it to the real deal, the iToBoS team is ready for the next step in the project. ▲

SELF-CHECKS AND SUNSCREEN

To help reduce your chances of skin cancer, dermatologists recommend you:

- Avoid the sun whenever possible, especially when it's at its peak.
- Wear sunscreen. Many lotions and moisturizers have SPF in them already!
- Wear clothes that protect your skin from the Sun, such as Sun protection shirts.
- Don't use tanning beds or other tanning equipment.
- Make regular dermatology appointments. Dermatology might not be on your list of regular doctors' appointments, but as we age, our chance of getting skin cancer increases. Perform self-checks.

To help people check themselves for possible melanoma spots, dermatologists created the ABCDEs.

Asymmetry: One half of a spot is unlike the other half.

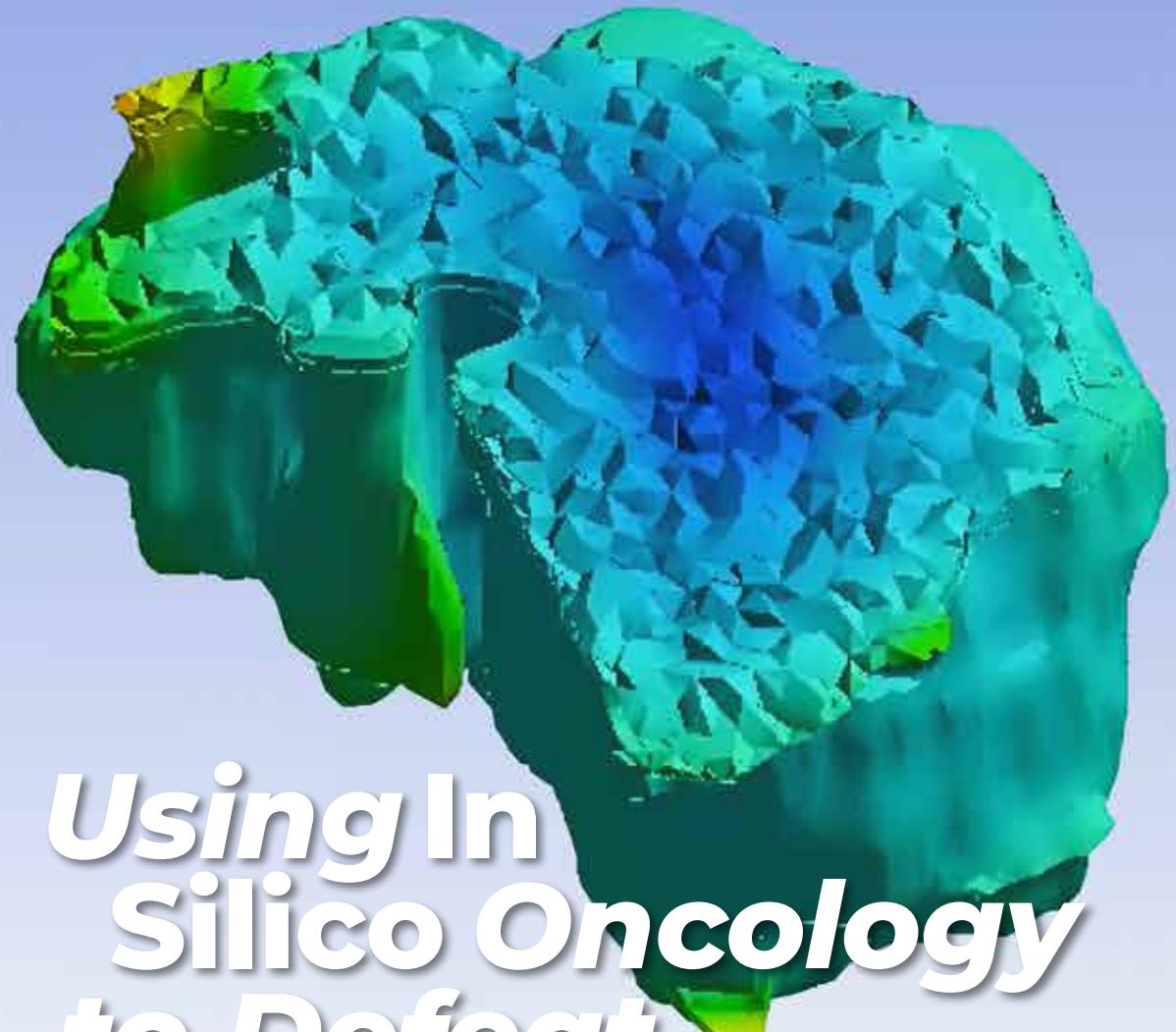
Border: A spot's border is irregular, scalloped, or poorly defined.

Color: A spot contains different colors, including shades of tan, brown, or black. Some areas may also be white, red, or blue.

Diameter: Melanomas are usually more than 6 mm in diameter, but they can be smaller.

Evolving: A spot has changed in size, shape, or color.

This is a guidance created by board-certified dermatologists. It is not a diagnostic tool. If you think you may be at risk for melanoma, please consult your doctor.



Using In Silico Oncology to Defeat Pediatric Cancer

By Ansys Advantage Staff

Dr. María Ángeles Pérez Ansón envisions a world without cancer, and she sees simulation as a key to making that vision a reality. If oncologists can simulate treatments on patient-specific digital models of cancerous tumors accurately, doctors could quickly choose the best therapy options and alleviate patient stress.

Pérez has been working on human body simulations for over two decades. Her 2004 thesis "Simulation of Cement Deterioration and Interfaces Debonding in Cemented Hip Implants" earned her a doctorate from the University of Zaragoza and subsequently won Best Technical Thesis of the year.

She is now a professor of structural mechanics at the University of Zaragoza's department of mechanical engineering. She continues to work at the forefront of simulation technology as part of the Multiscale in Mechanical and Biological Engineering (M2BE) research group at the university's Aragon Institute of Engineering Research.

"The models we are creating could help the oncologist to decide which treatment or therapeutic strategy could be most appropriate for a certain patient."

— DR. MARÍA ÁNGELES PÉREZ ANSÓN

Professor of Structural Mechanics, University of Zaragoza

The members of M2BE are experts in computational modeling, material strength, and structural mechanics. Instead of directing their expertise toward fields like architecture or aerospace engineering, Pérez and her team are exploring the intricacies of biological processes and the mechanobiology of cancer. They aim to enhance healthcare through advancements in tissue engineering, computer-aided diagnosis, and patient-specific modeling.

Ultimately, they hope these efforts will facilitate the establishment of a cloud-based platform to assist decision-making for cancer management and improve the planning behind the administration of therapeutics or surgical intervention.

A PAIR OF FORMIDABLE FOES

Pérez's work closely relates to the PRIMAGE Project. PRIMAGE stands for PRedictive *In-silico* Multiscale Analytics to support cancer personalized diaGnosis and prognosis, Empowered by imaging biomarkers.

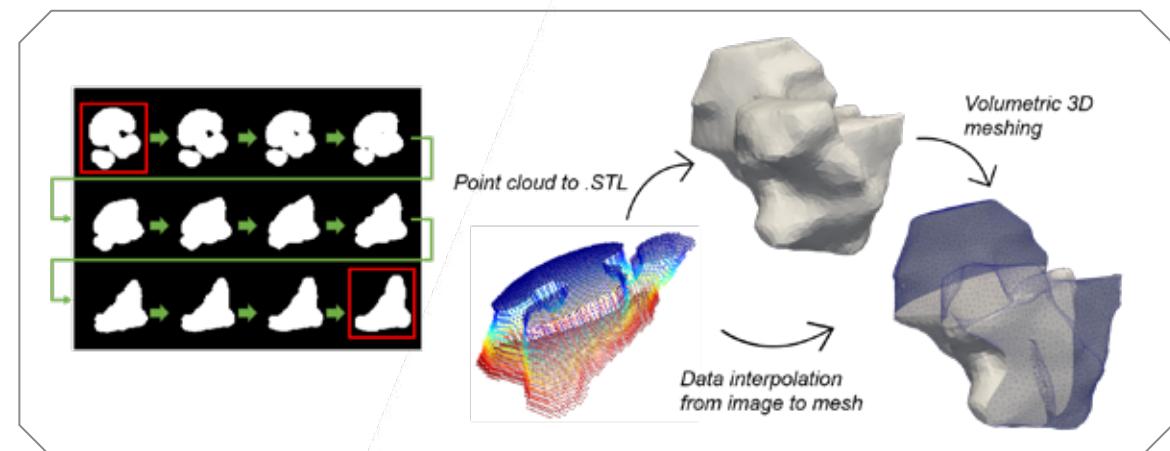
Financed by the European Commission, the project aims to develop ways to apply computational modeling and simulation (CM&S), or *in silico*, medicine to traditional

medical imaging to evaluate and treat childhood cancers, specifically two types that, while rare, have higher mortality rates: neuroblastoma and diffuse intrinsic pontine glioma (DIPG).

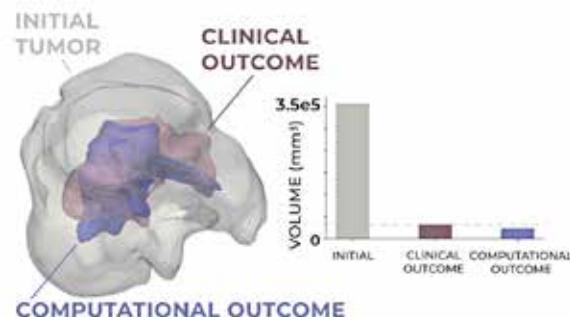
DIPG is a type of brain tumor that occurs in the pons, a portion of the brainstem that controls much of the body's unconscious vital functions like breathing, blood pressure, heart rate, and the sleep cycle. Only one to two children in 100,000 are diagnosed with DIPG each year. Unfortunately, mortality rates are very high. On average, 90% of patients with DIPG will die within the first two years of diagnosis.

Neuroblastoma, the focus of Pérez's work with M2BE for the PRIMAGE Project, is a solid tumor that can appear anywhere in the body. Though rare, neuroblastoma is the most common form of solid cancer affecting children under five. Overall, the five-year survivability rate for high-risk cases is 50%.

For both types of cancer, researchers wanted to understand how effective a treatment would be before it's even administered. With more targeted therapies, doctors could sidestep the risks of overtreatment and the subsequent health



Researchers took T2w-MRI slices and converted them to an .STL file to enable volumetric 3D meshing.



The initial size of a tumor and the clinical size after chemotherapy are shown, compared to the computational prediction.

complications it may cause. M2BE's work with simulation might eventually equip cancer researchers with that very ability.

"We are trying to reproduce a real physiological phenomenon and learn how a treatment could affect or modify the tumor's behavior," Pérez explains. "The models we are creating could help the oncologist to decide which treatment or therapeutic strategy could be most appropriate for a certain patient."

DEVELOPING A DIGITAL ADVANTAGE

To build a digital model of a neuroblastoma tumor, M2BE drew upon their earlier work with bones and cells.

Previously, the team successfully modeled how human bones respond to mechanical loads and produced simulations demonstrating how skeletal tissue heals after fracture. They validated their models with *in vitro* laboratory work involving microfluidics and cell cultures. The team applied techniques derived from this experience to the development of multiscale computational

"Our analyses are extremely complex, and Ansys software allows a high level of customization and control."

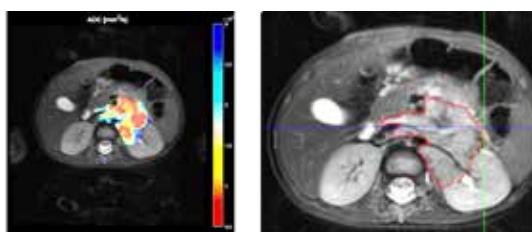
— DR. MARÍA ÁNGELES PÉREZ ANSÓN

Professor of Structural Mechanics,
University of Zaragoza

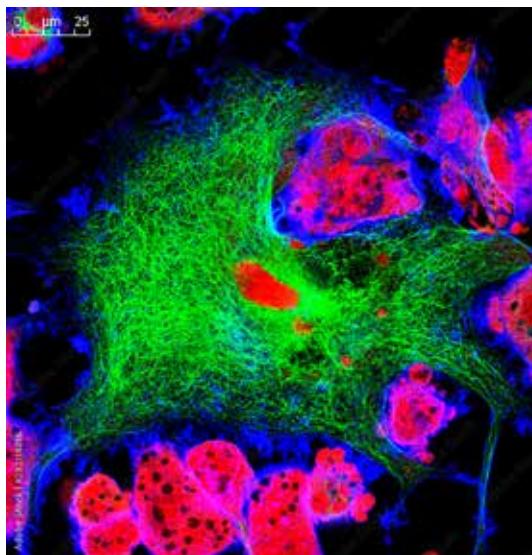
models that can predict and simulate tumor growth and degrowth in response to treatment.

The simulation capabilities of Ansys products are fundamental to the research and experimentation that M2BE engages in at the University of Zaragoza. "Our analyses are extremely complex, and Ansys software allows a high level of customization and control." By leveraging the capabilities of Ansys Mechanical APDL and Ansys Workbench software, the M2BE team took existing magnetic resonance imaging (MRI) data from a neuroblastoma scan and translated it to the basis of a digital model.

Different MRI sequences offer a detailed view of the body and tumor physiology. T2-weighted images (T2w) give the geometry of the organ or tumor. Dynamic contrast-enhanced (DCE) images offer detailed information about organ vascularization while diffusion weighted images (DWI) provide insight to the cellularity of the tumor. Armed with these details on their subject, the team



Magnetic resonance imaging (MRI) scan of a neuroblastoma



Fluorescence microscopic view of a neuroblastoma cell line in mice

set out to inform a working finite element (FE) mesh for their model.

By stacking the T2w-MRI slices of the tumor, the team built a basic point cloud for the model, which was then converted to an .STL file — the same file type used in 3D printing — allowing for volumetric 3D meshing.

Next, to improve the foundation for the mesh and prevent potential convergence problems, the team smoothed the model's geometry. Then, they integrated the clinical data on the tumor's vascularity and cellularity, which essentially offered a roadmap of its interior vessels and a cell-by-cell blueprint of how it grew.

This allowed the team to create a patient-specific species diffusion model, or a more comprehensive model of the tumor that reflects its inner makeup and how fluids move through it.

Finally, the team developed a patient-specific mechanical model of the tumor and the formulas that would govern its FE mesh. This model could simulate the cellular processes that occur during tumor growth. It could also respond to the availability of oxygen and nutrients or the introduction of chemotherapeutic drugs. These developments enabled the team to simulate the effect of a particular drug or its absence.

When applying their model to a clinical case, the team's predictions — derived from simulations of tumor growth and shrinkage on a patient-specific mechanical model — aligned with actual post-treatment outcomes, achieving roughly 90% accuracy. This promising initial result secured the validity of multiscale computational modeling for cancer research and set the stage for further development in the field.

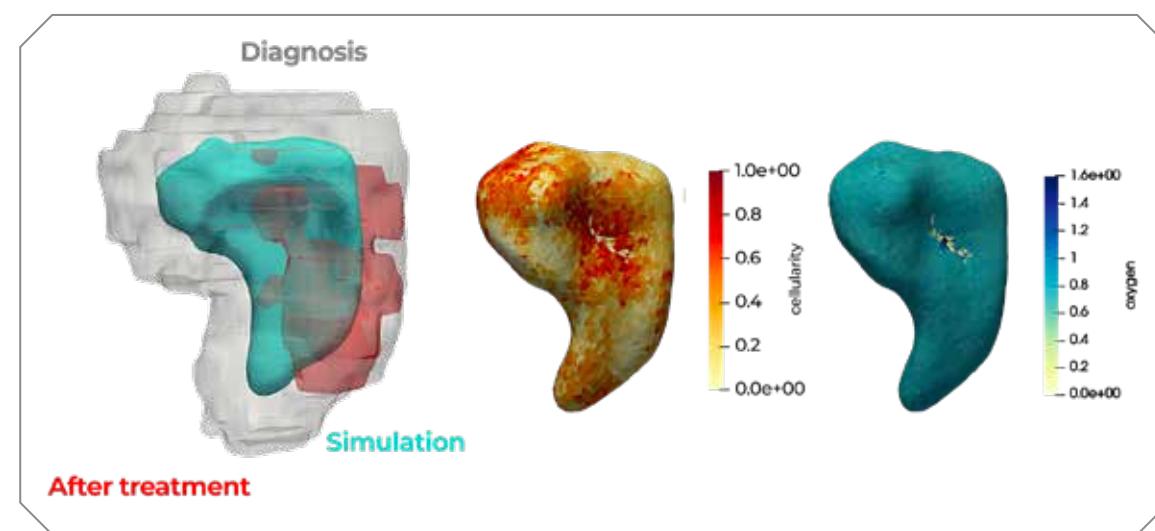
ANSYS PARTNERSHIP

Dr. María Ángeles Pérez Ansón's involvement with the Multiscale in Mechanical and Biological Engineering (M2BE) research group is linked to the Avicenna Alliance and the PRIMAGE Project, two initiatives that are closely connected to Ansys.

As a founding member, Ansys plays a crucial role in the Avicenna Alliance, a Brussels-based global nonprofit organization committed to enhancing healthcare through the use of computer modeling and simulation. The Alliance focuses on the development, regulation, and widespread adoption of *in silico* medicine (see page 6). Along with the University of Zaragoza, Ansys is also a technical partner in the PRIMAGE Project, the principal effort that Pérez's work supports.

ENTERING A NEW ERA OF CANCER RESEARCH
While Pérez admits that the models helping even 1% of cancer cases would be an incredible achievement, the significance of the progress already achieved by the group is undeniable.

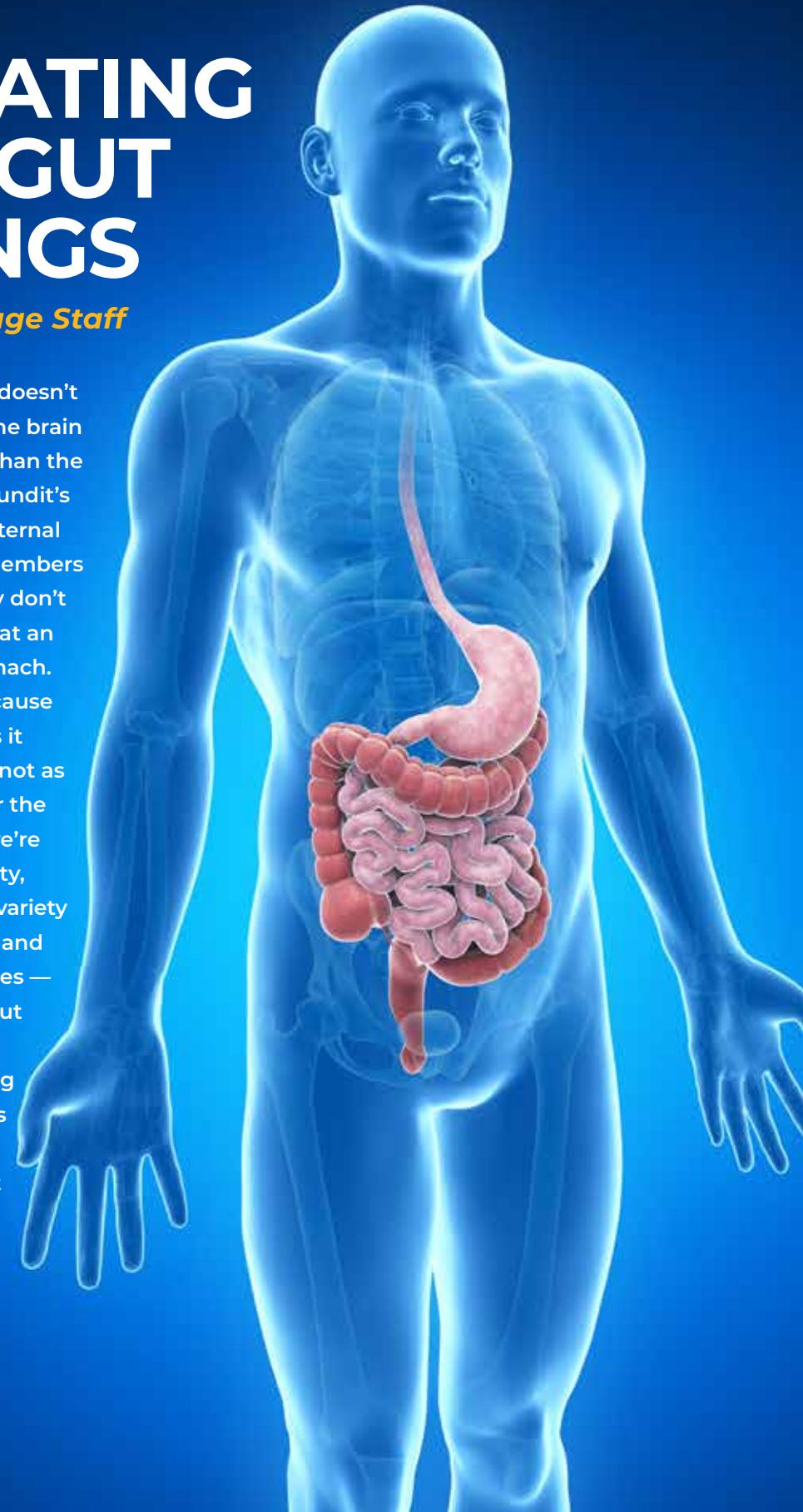
By establishing the protocol for creating a digital model of a neuroblastoma, M2BE has opened the door for other researchers to do the same with all types of cancer. And with the advancements in digital engineering software making all this possible, it feels as though a global, cloud-based knowledge bank is possible. Suddenly, the notion of a cancer-free future doesn't seem all that far-fetched. ▲



VALIDATING YOUR GUT FEELINGS

By Ansys Advantage Staff

Consider the stomach. It doesn't garner the respect that the brain does. It also ranks lower than the heart on every Internet pundit's top 10 list of important internal organs. Yet everyone remembers the assertion, even if they don't remember who said it, that an army marches on its stomach. The line is clever only because of the complicated truths it contains: The stomach is not as glamorous as the brain or the heart, but when it's full we're happy and when it's empty, we're not. We put a wide variety of things into it — liquids and solids, foods and medicines — and generally it goes about its business of breaking things down and facilitating the absorption of nutrients and medications. At the same time, it can be upset easily if we put things into it that disagree with it.



“In vivo studies of digestion are very complex, expensive, and time-consuming. They are invasive and very difficult to perform, requiring both specific technical skills and the prior approval of an ethics and human subjects review board.”

— DR. XINYING LIU, Research Associate in the School of Chemical and Biomolecular Engineering, University of Sydney

All of this we know from experience, but past experience is not always predictive. Around the world, food companies are striving to develop new foods that can sustain a hungry world more effectively and at lower cost. Pharmaceutical companies are striving to develop new medications that can cure or lessen the effects of diseases. The success of innovations in these fields will often be determined by what happens in the stomach.

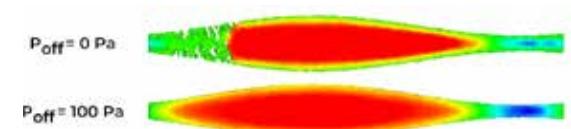
The difficulty, though, lies in developing an understanding of what will actually happen when a novel food or medication arrives in the stomach. “*In vivo* studies of digestion are very complex, expensive, and time-consuming,” notes Dr. Xinying Liu, a research associate in the School of Chemical and Biomolecular Engineering of the University of Sydney. “They are invasive and very difficult to perform, requiring both specific technical skills and the prior approval of an ethics and human subjects review board.” *In vitro* models of the digestive system can address some of these issues, but the complexities of the stomach — with its ability to layer foods for optimal digestion, its moving walls, and its complex acid and enzyme interactions — are quite difficult to reproduce accurately in an *in vitro* model.

For all these reasons, Dr. Liu and Dr. David F. Fletcher, an adjunct professor at the School of Chemical and Biomolecular Engineering at the University of Sydney, have been working to refine a computer model, also known as an *in silico* model, of the digestive system. With an accurate, operational *in silico* model of the digestive system and all its component parts — from the esophagus through the stomach and into the small and large intestine — food and drug developers, as well as other researchers in related commercial and academic fields, could gain insights to how the digestive system might respond to new or modified foods and drugs long before they actually engage human subjects to test them.

DEVELOPING AND VALIDATING AN IN SILICO MODEL OF THE DIGESTIVE SYSTEM

Liu and Fletcher did not start from nothing when developing their simulations of the digestive system. Some work had already been done within Australia's government-funded research entity, the Commonwealth Scientific and Industrial Research Organization (CSIRO) by Drs. Simon Harrison and Paul Cleary. The efforts at CSIRO had involved the development of a stomach simulation using tools based on a smooth-particle hydrodynamics (SPH) approach. While the SPH-based approach had its strengths — particularly for simulating a highly dynamic system like a stomach — Liu and Fletcher wanted to verify and validate these simulations using a different set of approaches. These efforts became the core of Liu's doctoral dissertation, which was shepherded to completion under Dr. Fletcher's supervision.

Using a range of tools from Ansys — including Ansys Mechanical, Ansys Fluent, and Ansys System Coupling — Liu and Fletcher set about validating and, as necessary, refining the SPH-based models. One of the first simulations they developed involved simulating peristaltic flow over time. This is crucial to any digestive model because peristalsis effectively mixes food and nutrients and pushes the contents of the stomach through the digestive tract. Their simulation involved modeling the contraction and expansion of muscle fibers within the digestive tract to create a wave-like motion that influences the contents of the digestive tract. As the peristaltic wave propagates, it mixes the



Without incorporating a pressure offset into the SPH code, as illustrated in the lower simulation, the fluids in the top simulation appear to cavitate, which does not occur in reality.

materials within the digestive tract and moves them along. At the same time, the physical characteristics of the stomach, the pylorus valve, and different sections of the intestines introduce variables such as velocity, pressure, and material concentrations — all of which must be accommodated in any complete simulation of the digestive process.

Liu and Fletcher used the finite volume method (FVM) embedded in Fluent and the SPH code the team at CSIRO had built, and then compared the volumetric flow results of both simulations to results from an analytic solution. This work exposed issues with the SPH code that resulted in tensile instabilities. Using the results gained through FVM, the team showed that by adding a pressure offset component in the SPH code, the tensile instability could be resolved.¹

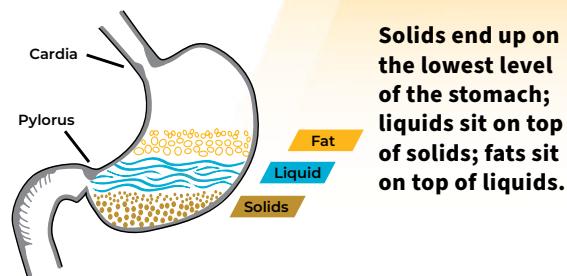
MODELING THE DYNAMICS OF THE STOMACH

Building on their experience with modeling peristaltic flow, Liu and Fletcher went on to verify the findings of the SPH-based model of the stomach itself, with specific attention to the manner in which the stomach mixes and separates different types of solids and liquids. Because the acids and enzymes in the stomach break down different types of food and medicine into smaller particles that can be digested more completely in the intestines, different types of food have different residence times in the stomach. This is achieved via layering, so that the acids and enzymes within the stomach have time to break them down.

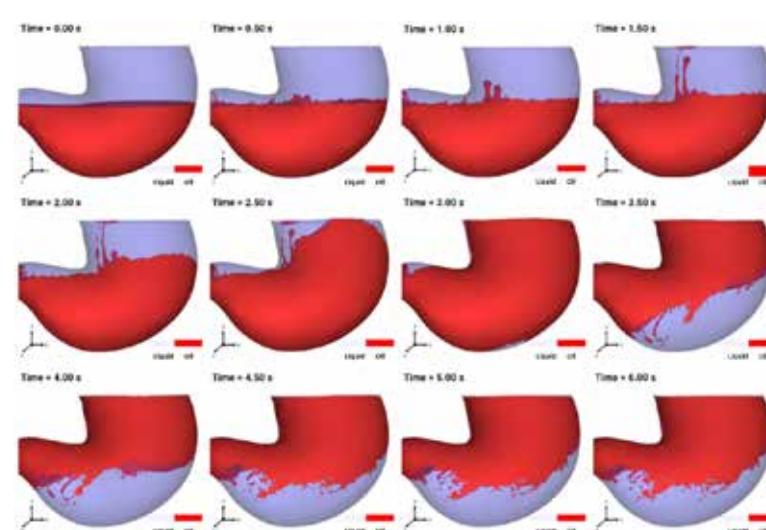
From a simulation standpoint, any model of digestion within the stomach must accurately reflect the mechanisms within the stomach that orchestrate this layering. Solids will end up on the lowest level of the stomach; liquids will sit

on top of solids; fats will sit on top of liquids and provide a buoyant layer that drug developers can use to float medications that require prolonged exposure to the gastric conditions of the stomach.

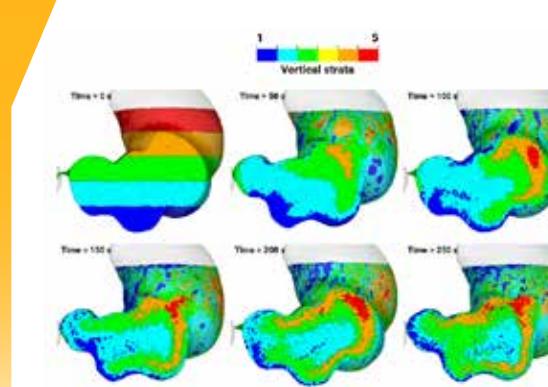
Simulating the physics of the stomach that create and maintain this layering is complicated. Moreover, incorporating the effects of stomach acids and enzymes that break down the components of the different layers (which will break down at different rates in different layers) adds further complication to any modeling efforts.



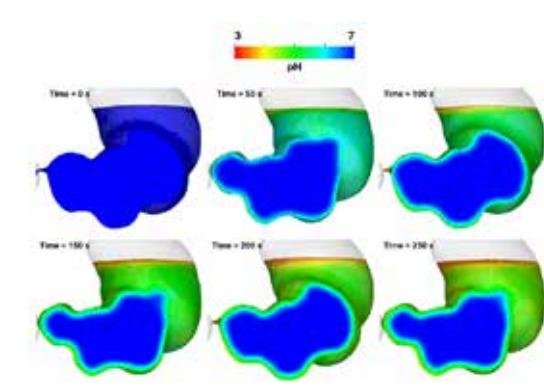
The models that Liu, Fletcher, and the CSIRO team analyzed were focused on the physics of the buoyancy-driven separation of these layers.² They did not yet attempt to model the complexities of real-world food digestion (with different types of food and numerous digestive layers) but focused, rather, on simulating the manner in which just two liquid layers — one fatty and one aqueous — would separate under gravity as a consequence of what is called Rayleigh-Taylor instability, which arises from the differences in density and the surface tension that naturally try to stabilize the layers. In the simulation, the aqueous layer begins above the fatty layer (with liquid oil representing a



In the SPH simulation, the oil and water layers invert over the course of six seconds and the details of the Rayleigh-Taylor instabilities are quite visible. However, the smooth surface between the oil and water layers that should exist at the completion of this inversion does not appear in the SPH simulation. In the FVM simulation, the Rayleigh-Taylor instabilities are less well-defined, but the oil and aqueous layer boundary is more accurately presented.



Mixing behavior within the stomach with initial fluid volume divided into five bands



Acid distribution within the stomach with acid secreted from the stomach wall

fatty layer) and the Rayleigh-Taylor instabilities naturally initiate a buoyancy-driven flow that causes the layers to invert so that the fatty layer ends up above the aqueous layer.

As with the peristalsis simulations, Liu and Fletcher relied on the FVM methodology of Fluent to replicate and validate the SPH model. In the SPH model, the oil and water invert over the course of six seconds and the details of the Rayleigh-Taylor instabilities that initiate this inversion are quite distinct.

The FVM simulation conducted using Fluent verifies many aspects of the SPH model but also highlights distinct differences. In the FVM simulation, the Rayleigh-Taylor instabilities are less well-defined, but the oil and aqueous layer boundary is more accurately presented at the conclusion of the simulation. Repeated running of the SPH model — even for longer durations — never results in as distinct a layer between the newly inverted liquids.

"The smoothed buoyancy force may become less effective in the SPH model when the thickness of the fluid fragments is smaller than the kernel width," notes Liu. "It may be that the density difference is smoothed over the kernel diameter, resulting in a smaller magnitude which results in a reduced buoyancy force — and the smaller the region of fluid, the worse this effect becomes. As for the lack of detail in the growth of the Rayleigh-Taylor instabilities in the FVM model, that may be the result of errors induced by the grid that was used rather than any specific shortcoming in the FVM approach itself."

MARCHING ORDERS

Liu and Fletcher have gone on to develop simulations of peristaltic movement in the stomach wall and models mimicking the mixing and distribution of acid within the

stomach; they have also developed simulations modeling the effect of viscosity on the speed with which the fluid layers within the stomach are mixed. Further models must still be built and validated before a complete and accurate *in silico* model of the digestive system can be said to exist, but the models developed so far appear to be on the right track.

"It is quite tricky to get set up a good simulation of the stomach," says Fletcher. "You need the tools that can model non-Newtonian flow — with particles, complex rheology, complex chemistry, moving walls, free surfaces, and the like. There is a whole range of physics that is needed, too, and that is where the ability to bring together mechanical and fluids — and then the ability to model particles within fluids — becomes critical. We need to be able to model everything from very small particles that move with the fluids all the way up to large chunks that break down over time and as a function of the physics and the chemistry of the gastric environment. Ansys has the technology to do all this, so we can see where this is going and what the future will hold."

These first encouraging results show that it is possible to reliably model the complexity of the digestive system. It paves the way toward future digital twins of the entire digestive system, a necessary step to optimize the absorption of drugs throughout the stomachal wall, test the consumption of new nutrients ... and allow us to keep enjoying food. ▲

1. X. Liu, S.M. Harrison, P.W. Cleary and D.F. Fletcher, Evaluation of SPH and FVM models of kinematically prescribed peristalsis-like flow in a tube. *Fluids*, 8, 6, (2023).

2. X. Liu, S.M. Harrison, D.F. Fletcher and P.W. Cleary, Numerical simulation of buoyancy-driven flow in a human stomach geometry: Comparison of SPH and FVM models. *Appl. Math. Model.*, 124, 367-392, (2023).



ACADEMIC SPOTLIGHT:

Exploring Healthcare Solutions Through SIMULATION

By Jennifer Procaro, Senior Corporate Communications Writer, Ansys

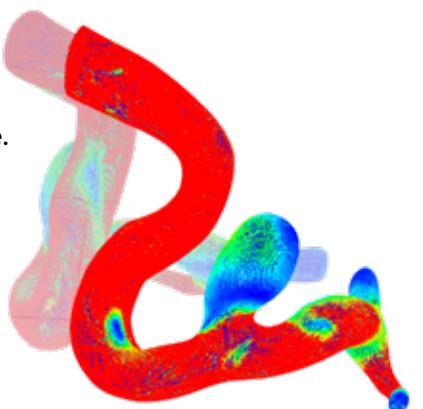
“Ansys is more user friendly and accurate than other software, and it provides more options like post-processing visualization. ... It has high reliability and is easy to import different files.”

— MAHSA DABAGH,
Assistant Professor of Biomedical Engineering, University of Wisconsin-Milwaukee

From the stress of carrying a heavy backpack to artery plaque, students around the world are discovering innovative healthcare solutions one simulation at a time.

With access to Ansys simulation through the Ansys Academic Program, students are leveraging multiphysics modeling to advance their studies and, potentially, the healthcare industry as a whole. The program provides universities with deeply discounted software for use in the classroom or in research while offering students access to free downloadable software and additional online resources for self-learning. In connection, students can access more than 400 free Ansys Innovation Courses, as well as other open-learning material available to academia through Ansys Innovation Space. Currently, the program reaches more than 2,800 universities across 86 countries with software and resources spanning a wide range of engineering disciplines, including structures, fluids, and electromagnetics.

Let's explore some of the exciting ways students and educators are integrating Ansys simulation to unlock new possibilities within the healthcare industry.



APPLYING FEA FOR MUSCULOSKELETAL HEALTH

High schooler Anish Sarkar used Ansys Mechanical finite element analysis (FEA) simulation for his project “Impact of Heavy Loads on the Human Backbone.” His research not only concluded the safest way to wear a backpack for optimal musculoskeletal health, but also landed him second place at the Golden Gate STEM Fair in California. The regional fair welcomes local science, technology, engineering, and mathematics (STEM) students in grades six through 12.

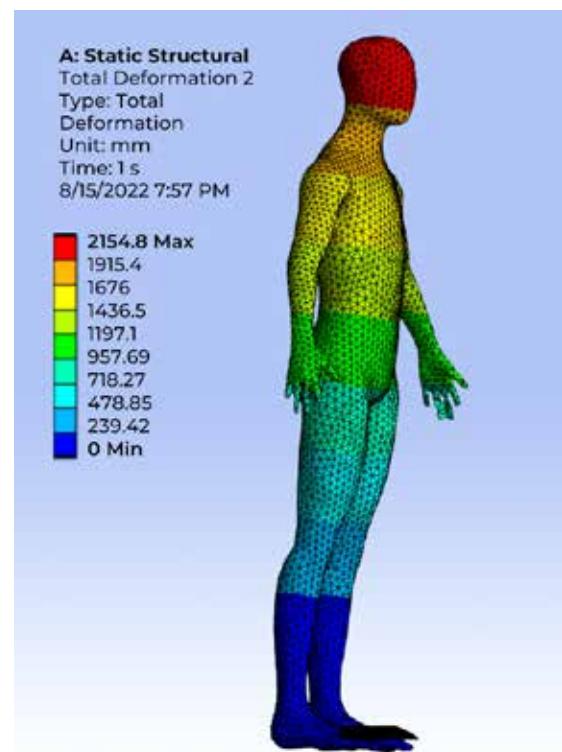
Sarkar used three models for his simulations: a basic spine and ribcage model that he created using Ansys SpaceClaim and two models he found online of a skeleton and a muscle-focused model of the human body. After refitting the online models using SpaceClaim, he generated mesh for each model in Mechanical. Next, he added pressure points to indicate where the pressure and weight of the backpack was present in each

scenario. He also used Ansys Granta MI Enterprise to set up organic material properties for the simulations.

Sarkar determined that the healthiest way to wear a backpack is to position the straps on both shoulders without pulling or tightening the shoulder straps downward. This ensures that the pressure and weight of the backpack sits loosely at the lower back instead of the upper or middle back.

The following year, Sarkar turned his focus toward amputees, aiming to improve prosthetic design for veterans. He used SpaceClaim and Mechanical to prepare prosthetic socket models and conduct a comprehensive analysis of stress, strain, and load distribution in the interface between the residual limb and the prosthetic socket throughout the gait cycle.

Sarkar's software-based design approach and analysis demonstrated the ability to customize sockets for every patient much more efficiently than traditional socket lamination techniques, which are time consuming and require more physical resources. He submitted this project to the Golden Gate Science Fair as well and received the Lemelson Young Inventor and Chevron Special awards.



High school student Anish Sarkar used Ansys Mechanical to analyze stress and pressure points along the spine for his project “Impact of Heavy Loads on the Human Backbone.”



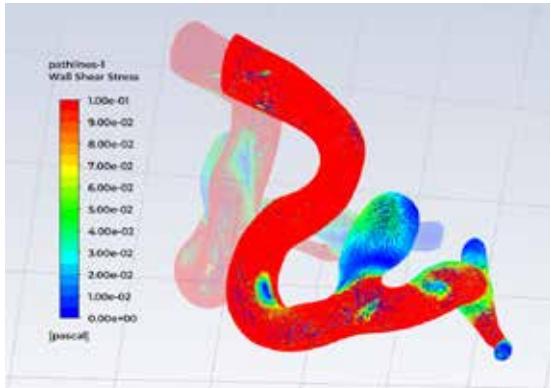
Students in the EnQuest program helped Mahsa Dabagh, an assistant professor of biomedical engineering at the University of Wisconsin-Milwaukee, with real-world vascular research.

INTEGRATING CFD FOR VASCULAR AND RESPIRATORY HEALTH

Female high schoolers participating in the EnQuest program explored real-life patient case studies involving artery blood flow and aneurysms using Ansys Fluent computational fluid dynamics (CFD) software. Hosted by the University of Wisconsin-Milwaukee (UWM), EnQuest is one of many female-focused programs hoping to bridge gender gaps in the engineering industry.

Students in a 2022 summer program participated in real-world research thanks to their session leader Mahsa Dabagh, an assistant professor of biomedical engineering at UWM whose research focuses on cancer and vascular diseases.

The group helped her analyze patient case studies concerning artery blood flow and aneurysm detection. Based on patient-specific images, the team built 3D geometries of large cerebral vascular arteries, most of which contained aneurysms. With Fluent, the team examined correlations between blood distribution inside aneurysms and regions of aneurysms that are more prone to rupture. "Ansys is more user friendly and accurate than other software, and it provides more options like post-processing visualization," says Dabagh. "I wanted students to learn as much as possible and not struggle with learning how to choose boundary conditions or how to post-process, and Ansys is easier to follow for students with user-friendly interfaces and trustable results. It has



EnQuest students used Ansys Fluent to simulate the wall shear stress of an aneurysm within an artery.

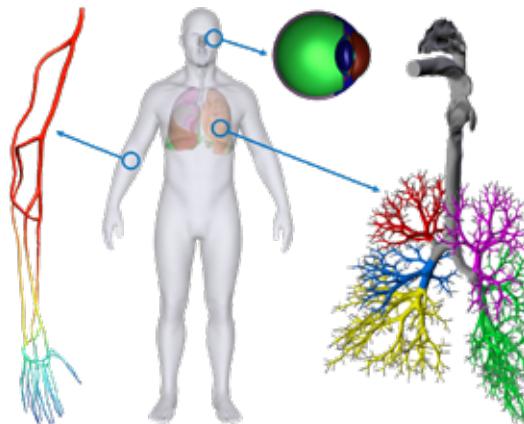
high reliability and is easy to import different files. These are all features that Ansys has that are quite unique."

In another example of applying CFD to vascular research, several students at Oklahoma State University (OSU) also use Fluent to examine artery blood flow, thanks to chemical engineering associate professor Yu Feng. Feng integrates Fluent into select undergraduate and graduate courses to complete research projects, including the examination of transient blood flow in arm arteries, topical ocular drug delivery through 3D eyeball models, and airborne transmission of virus-laden droplets in between digital twin human respiratory systems.

In addition, Feng incorporates other Ansys tools into coursework, including:

- Mechanical for solid mechanics simulation and fluid-structure interaction
- Ansys CFX for CFD simulations
- Ansys EnSight for post-processing simulation data and visualization
- Ansys Discovery for quick engineering simulation and analysis
- Ansys Workbench for fluid-structure interaction and batch process for simulations, as well as training and testing for reduced-order models (ROMs)
- Ansys Rocky for particle-particle interaction simulations

"Chemical engineering students who master Ansys Fluent and CFX have achieved remarkable success in their careers after completing their undergraduate education," says Feng. "They have skillfully applied the knowledge they gained from my multiphase flow course, and their success can be attributed to their proficiency in Ansys software, including Fluent, CFX, Mechanical, Rocky, and others."



Research examples of lung aerosol dynamics, hemodynamics in arm arteries, and topical ocular delivery optimization demonstrated using Ansys simulation and a virtual human model developed by the Computational Biofluidics and Biomechanical Laboratory (CBBL) at Oklahoma State University (OSU)

LEARNING BEYOND THE CLASSROOM

Outside of the classroom, Feng implements Ansys software to promote the next generation of STEM through multiple outreach activities for K-12 students, undergraduate students, and the local community in Oklahoma. Main activities include the Lungevity initiative hosted by the OSU Alumni Association and the Summer Bridge program, which is organized by the OSU's College of Engineering, Architecture, and Technology (CEAT).

Along with outreach, Feng's students have access to an on-site research lab with state-



Thierry Marchal, an industry director for healthcare solutions at Ansys (second from right), visits Yu Feng, a chemical engineering associate professor at OSU (far right), and past lab members at the CBBL.

of-the-art models and equipment. Through the academic partnership between Ansys, Engineering Simulation and Scientific Software (ESSS), and the Computational Biofluidics and Biomechanics Laboratory (CBBL) at OSU, Feng and peers developed a CFD-discrete element method (DEM)-based human respiratory system modeling framework that includes a clinically validated elastic whole-lung model.

Ansys is committed to the advancement of STEM education while ensuring the accessibility and affordability of simulation tools. For more information, visit ansys.com/academic.

SUPPORTING LEARNING BEYOND THE CLASSROOM

Ansys attends many healthcare-focused academic events and conferences. Some of these events include:

- International Brain Stimulation Conference
- Cardiac Digital Twin Workshop at King's College of London
- International Symposium on Computer Methods in Biomechanics and Biomedical Engineering
- Masters of Aorta and Structural Heart Surgery
- IA4Care Forum hosted by Santenov
- Functional Imaging and Modeling of the Heart
- Digital Engineering Advancing Healthcare: RF Electromagnetics for Medical Implants hosted by CADFEM, an Ansys channel partner

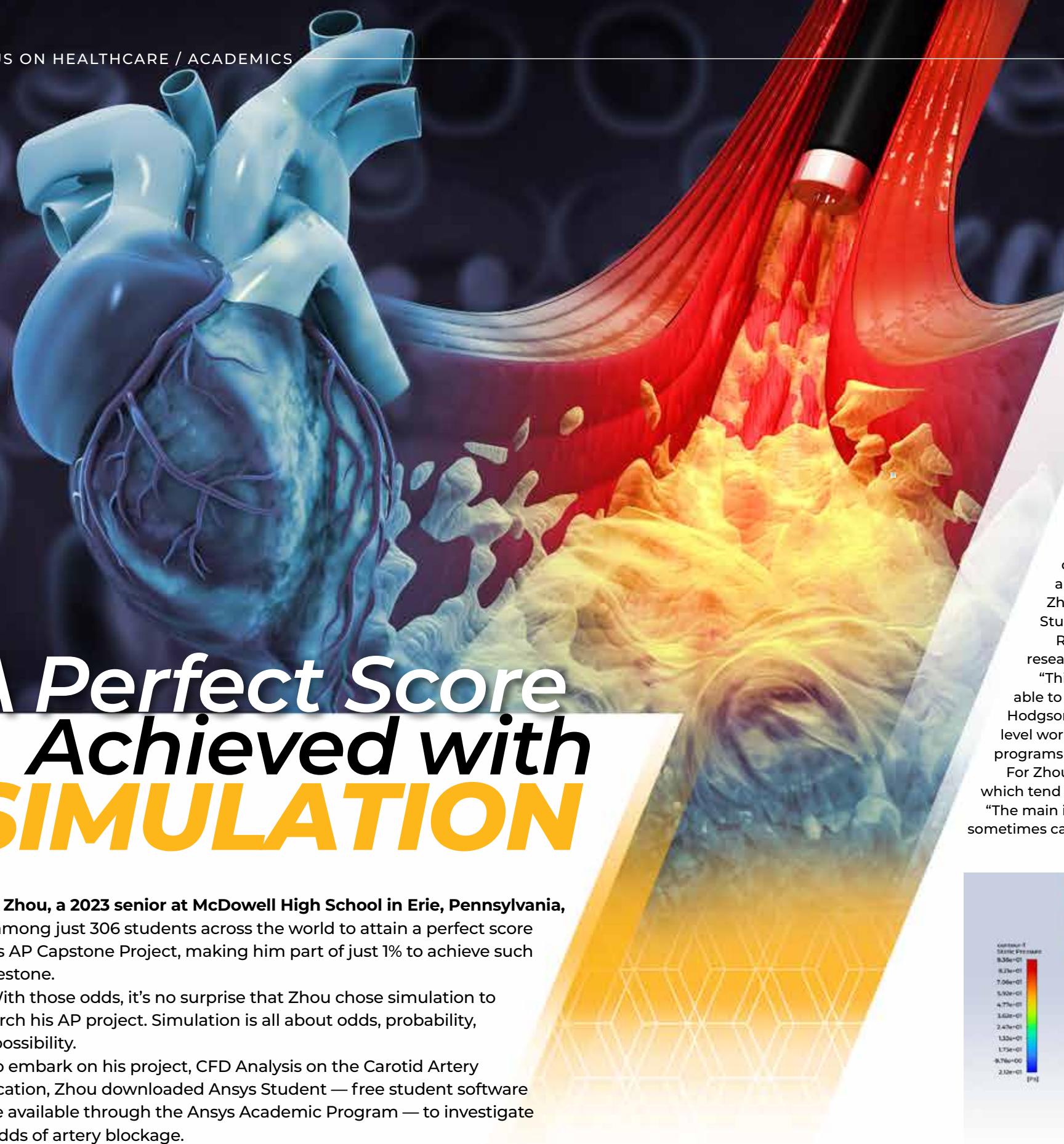
A Perfect Score Achieved with **SIMULATION**

Chris Zhou, a 2023 senior at McDowell High School in Erie, Pennsylvania, was among just 306 students across the world to attain a perfect score on his AP Capstone Project, making him part of just 1% to achieve such a milestone.

With those odds, it's no surprise that Zhou chose simulation to research his AP project. Simulation is all about odds, probability, and possibility.

To embark on his project, CFD Analysis on the Carotid Artery Bifurcation, Zhou downloaded Ansys Student — free student software made available through the Ansys Academic Program — to investigate the odds of artery blockage.

With Ansys Student, Zhou accessed Ansys Fluent computational fluid dynamics (CFD) simulation and Ansys SpaceClaim 3D modeling software to analyze and model blood flow in the carotid artery.



SIMULATING TO PREVENT ARTERY PLAQUE

Zhou began his junior year with a full course load, yet just one class would prove to be life changing: AP Research. The class is part of the AP Capstone program, a diploma program offered through College Board to develop students' skills in research, analysis, writing, and more.

The core requirement of the class is for students to select a topic to research in depth throughout the year and then share their findings at the end of the term with a presentation and paper.

At the time, Zhou was interested in the medical field and participating in a job-shadowing opportunity at the nearby UPMC Hamot Hospital. Through this experience, Zhou was exposed to several labs, piquing his interest in blood flow.

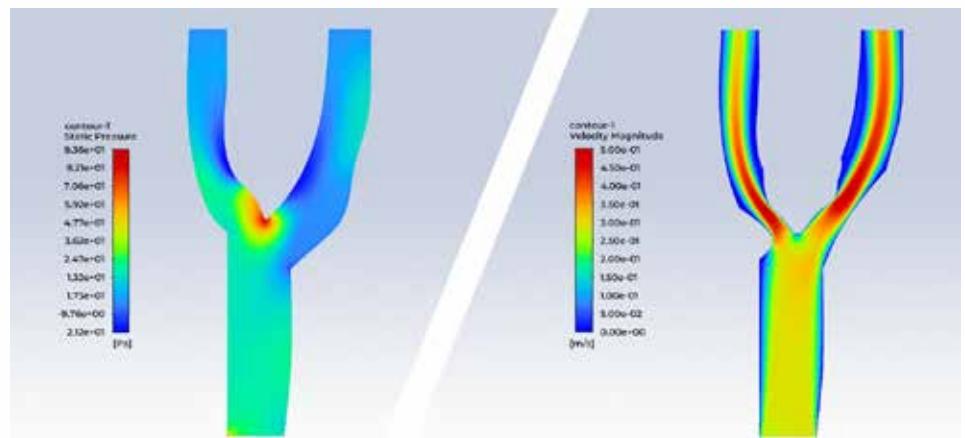
Coupled with this, Zhou's father, Jun Zhou, is an engineering professor at Penn State Behrend and is familiar with CFD. With encouragement from his dad, Zhou decided to use CFD to dive deeper into artery blood flow, particularly the carotid artery bifurcation. This is the point where the common carotid artery ends and splits into the internal and external carotid arteries that go on to supply blood to the head and neck. To begin, Zhou explored available CFD tools online and discovered Ansys Student.

Robert Hodgson, Zhou's AP teacher — who also encouraged Zhou's research — commended the program for offering these tools to students.

"This enables students to do work that they otherwise would not be able to do without access to much more expensive equipment," says Hodgson. "It increases the accessibility and ability for students to do high-level work like Chris did, which would not be possible without access to programs like this."

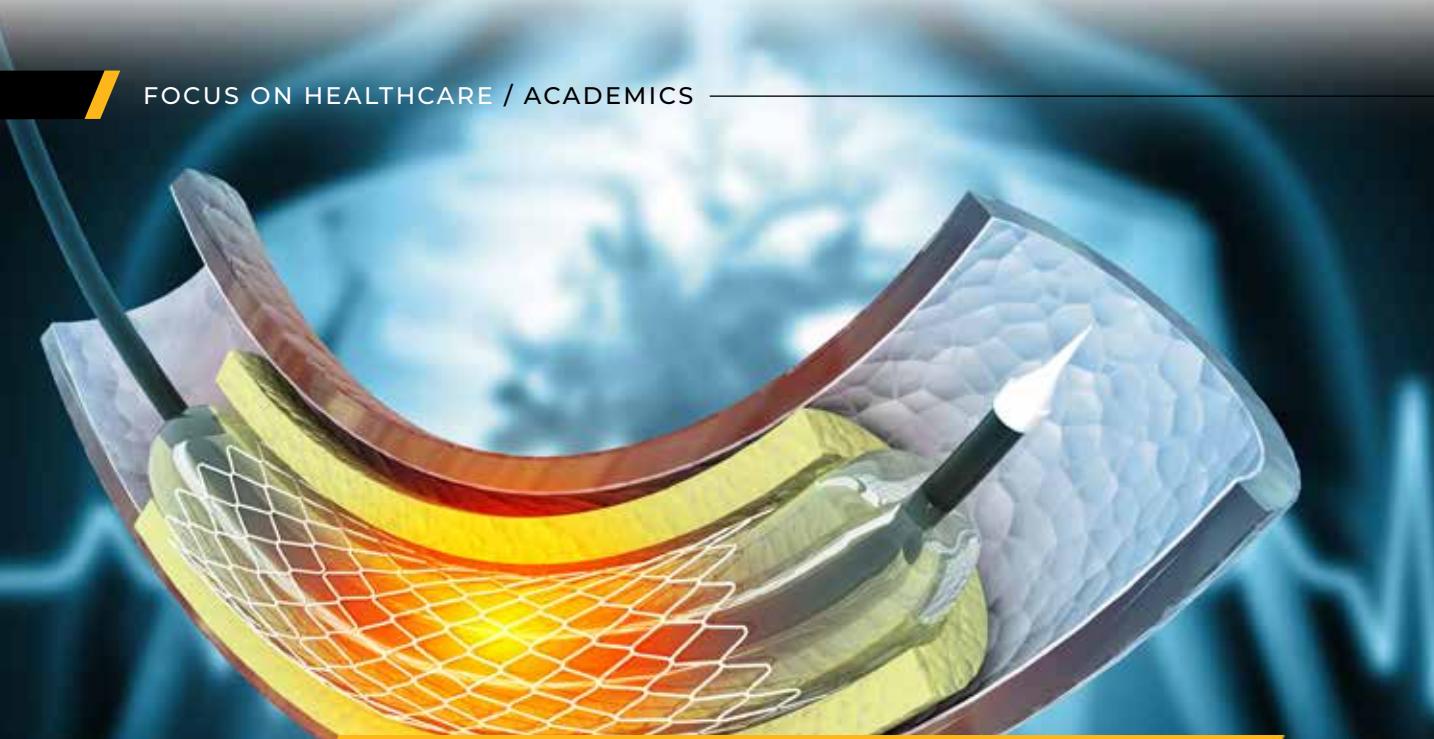
For Zhou's project, he used CFD to observe the carotid arteries of the neck, which tend to have a lot of plaque buildup, he says.

"The main issue is that modern imaging techniques such as MRI or CT scans sometimes can't fully or accurately depict if there is plaque buildup within these



A base model of the carotid artery was simulated in Ansys Fluent.

Ansys Fluent simulation illustrates the carotid artery's velocity flow during stage three of plaque buildup.



“I think Ansys made this all possible for a high school student and did a great job. Otherwise, I don’t see that it would be possible at this level, but Ansys provides these tools to students and enables them to think from a big-picture view and that stimulates further interest.”

— JUN ZHOU, Chris Zhou’s father

veins,” says Zhou. “So, instead I used CFD and Ansys to build a two-dimensional model and then run simulations of the blood flowing through the vessel.”

In addition to working on the project during class, Zhou conducted research at home and participated in Cornell’s popular edX course, “A Hands-on Introduction to Engineering Simulation,” which includes online simulation resources and tutorials for supplementary learning outside of the classroom.

Due to privacy restraints, time constraints, and limitations through the local Institutional Review Board (IRB) — which requires projects to meet certain guidelines of research — Zhou could not use patient-specific data for his testing. Instead, Zhou conducted his research on previous studies and publicly available models.

A main challenge in investigating the carotid artery bifurcation, he says, is that the vessels are thin and small, and plaque buildup

accumulates over a very long time, which makes it difficult to physically monitor, test, or see the buildup.

After reading past examinations, Zhou learned that previous researchers used CFD to build more accurate models, frequently based on actual models gained from hospitals and patient case studies. By comparing the improved models to actual cases, researchers determined patterns in blood velocity pressure and things such as wall shear stress. These analyses enabled them to determine if the patient was building up plaque or developing any other complications.

To expand upon these concepts, Zhou used Fluent to create geometry, meshing, and boundary conditions to make predictively accurate models to understand blood flow characteristics and study the correlations between healthy flowing arteries and arteries in which blockage is forming.

The class ran the length of the school year, so after nearly 10 months of research,

Zhou submitted his completed project to College Board in late May 2022. The program requires a two-part submission, consisting of a 20-minute research presentation — 15 minutes for the presentation and five minutes for an oral defense from the panel of judges — and a paper of approximately 4,000 – 5,000 words.

He received his first installment of good news in late July 2022, learning his project landed a five out of the one-to-five general scoring range, but did not know specifics such as any problems missed or minor points deducted. However, in September 2022, Zhou received an additional email from College Board informing him of his perfect score.

SIMULATING FOR THE FUTURE

Although Zhou was not sure which college he wanted to attend, he had a clearer idea of what he would pursue and applied to Ivy League schools, including Harvard University, the University of Pennsylvania, and Cornell University.

“Originally, I wasn’t sure what I wanted to do, torn between either going into a medical-based career or maybe more of an engineering aspect,” says Zhou. “But with this project, I was able to combine the two into one area, having the medical part of blood vessels and hemodynamics, and the engineering part using Ansys software and computer simulation. This really helped me get a better idea of what I would like to do in the future and how I can blend both of my interests.”

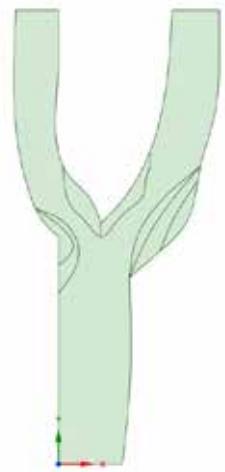
Based on his parallel passions, Hodgson and Zhou’s father encouraged him to consider a dual doctorate track incorporating biology and other science, technology, engineering, and math (STEM) subjects so he can enter the medical field as a practicing physician, while pursuing research and experiments.

With no prior experience using simulation, Zhou felt at ease using the tools crediting the Cornell edX course, Ansys, his dad, and teacher for the support and resources. His dad, however, passed any credit over to the Ansys Academic Program.

“I think Ansys made this all possible for a high school student and did a great job,” says Jun Zhou. “Otherwise, I don’t see that it would be possible at this level but Ansys provides these tools to students and enables them to think from a big-picture view and that stimulates further interest.”

Zhou agreed with his dad, and now that he has experienced simulation firsthand, he’s a big proponent of it for the future of healthcare.

“A lot of the times in the medical field,



An Ansys Fluent simulation illustrates the carotid artery’s velocity flow during stage three of plaque buildup.

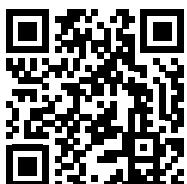
research or tests need to be run on actual subjects, which places constraints on if you can find the subject and if they’re willing to do the experiment,” he says. “But with simulation you take all of that out of play and can run everything by yourself or with a couple of colleagues and a lab where everything is controlled by you and you can just keep retrying and retesting until you think you get to your final solution.”

He’s also grateful for the Ansys Academic Program for supplying simulation to students at no cost, which gives many students like him valuable opportunities.

“If I tried to do this without simulation, I would need access to things only found in hospitals used by professionals such as expensive imaging technology, MRI machines, or CT scanners,” he says. “It wouldn’t be feasible, especially for someone at my level. But this program was completely free and very accessible. I’m just a typical high school student who was able to run all of these tests and simulations from the comfort of my own home, even on my own computer. I think that’s really nice because if any student has the passion and wants to do this, they have the opportunity to.” ▲

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