3D PARAMETRIC FULL EYE MODEL GIVES 20+ YEARS OF BETTER VISION

A research team at Kejako, a medical device company based in Switzerland, share how they are using multiphysics simulation to develop an innovative solution that will delay the need for reading glasses or invasive surgery for decades.

By **GEMMA CHURCH**

PRESBYOPIA IS A NATURAL EFFECT of aging in which a loss of elasticity in the lens of the eye causes far-sightedness. As a result, your visual accommodation gradually declines, as your eyes can no longer effectively change their optical power to maintain a clear image or focus on an object as its distance varies.

The current solutions to this problem are at opposite ends of the treatment spectrum: You can either wear a pair of glasses or opt for an invasive surgical solution that could compromise the quality of your vision (Figure 1).

A novel solution developed by medical device company Kejako will provide a viable treatment that treads the middle ground between surgery and spectacles. Their 3D parametric full-eye model is providing invaluable insights into the root cause of the eye's degeneration over time. As a result, Kejako is edging closer to an innovative solution that will delay the need for reading glasses or invasive surgery for over 20 years.

PERSONALIZED TREATMENT OPTIONS

KEJAKO'S COFOUNDER AND CEO, David Enfrun, explained: "Our solution has the potential to become the next generation's standard of care in personalized ophthalmic anti-aging medicine," explained David Enfrun, Kejako's cofounder and CEO. We focus on early treatments to maintain enough capacity of visual accommodation by offering personalized anti-aging laser treatments that could give patients an additional 20 years of comfortable vision."

Kejako's solution is designed to treat the root causes of presbyopia and features a series of noninvasive laser eye surgeries, which are prescribed from when a patient starts to develop presbyopia until cataracts develop. This keeps a patient's visual accommodation amplitude above where spectacles are required (Figure 2).

To correct presbyopia, the team is combining the noninvasive treatment with simulation to provide an all-in-one solution called phakorestoration.

Their simulation work features a 3D parametric full-eye model, which the company developed using multiphysics simulation. Enfrun said: "We began our development work in 2015 with an alternative software that we were familiar with. However, it soon became clear that this solution was too restrictive. Our project is quintessentially multiphysics."

"In 2016, we started to work with

Figure 1. Current surgical solutions result in visual compromises, including halos (top), glare (middle), and poor acuity in dim light (bottom).

COMSOL because of the multiphysics nature of the software and the high quality of customer support."

The full-eye model has the potential to provide a personalized treatment for every patient. This is important because every patient is different in terms of their physiology and the severity of their presbyopia. Enfrun explained: "One size will not fit all when treating presbyopia, and our model will be fundamental to addressing that issue. We can use the model to optimize each patient's treatment and provide a personalized procedure."

EYEING THE PHYSICS

TO CREATE AN accurate 3D parametric model of the eye, a full description of this organ must be taken into account and several physics phenomena considered. Aurélien Maurer,

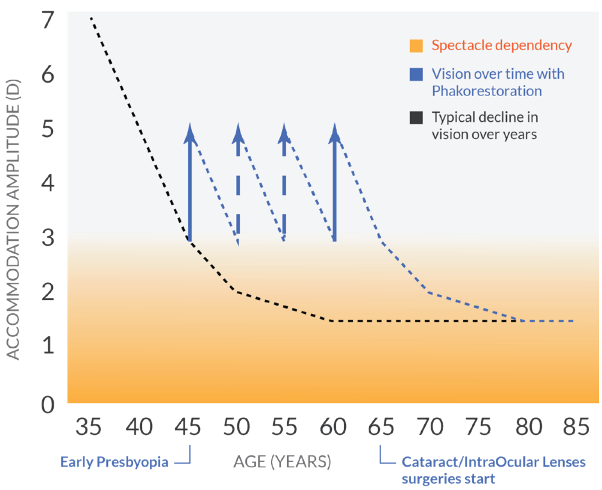

Figure 2. Principle of phakorestoration's action on visual accommodation as a function of age.

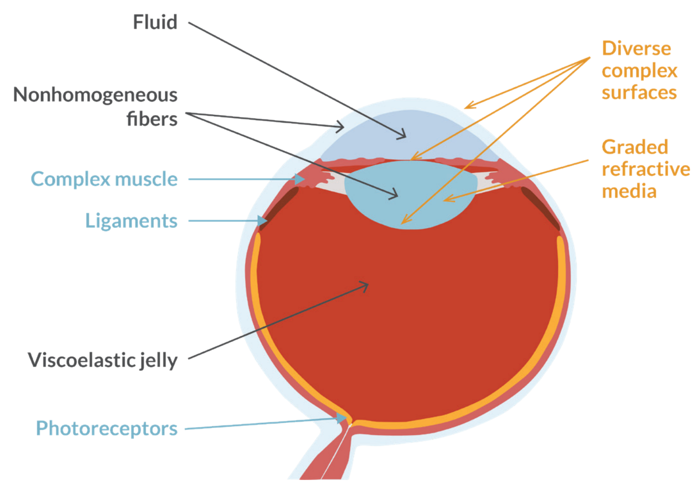

Figure 3. Various components of the eye that needed to be considered for the multiphysics model.

R&D engineer at Kejako and eye model project leader, explained: "We needed a complete solution, including the mechanics and optics of the eye. We wanted to model the entire eye and adapt its properties to look at different outcomes."

A range of complex physics must be considered to achieve this. Within the eye, there are a lot of different physics and material properties to take into consideration, such as the fluidics of the aqueous humor; optical behavior of the lens and cornea material; and the refractive index, which involves modeling the muscle ligaments as they deform the lens.

The team also wanted to model the gradient of the refractive index as light penetrates the crystalline lens, so they coupled structural mechanics and ray optics. Maurer said: "No one before had looked at the relation between the mechanical deformation and the refractive index gradient in the crystalline lens, so we decided to put this in a model and test it against the existing results in the literature."

The team's dual approach of modeling both the mechanical and optical elements of the eye was validated using existing measurements. "If we only model the mechanics or the optics, then we do not get all the information we need. But if we put all of this together, that's where the magic happens," Maurer added.

» MULTIPHYSICS FOCUS

USING GEOMETRIES FROM statistical measurements and standard optical coherence tomography (OCT) imaging techniques, the team began to develop their model by imaging the eye and then translating this information into a parameterized 3D geometry imported in the COMSOL® software.

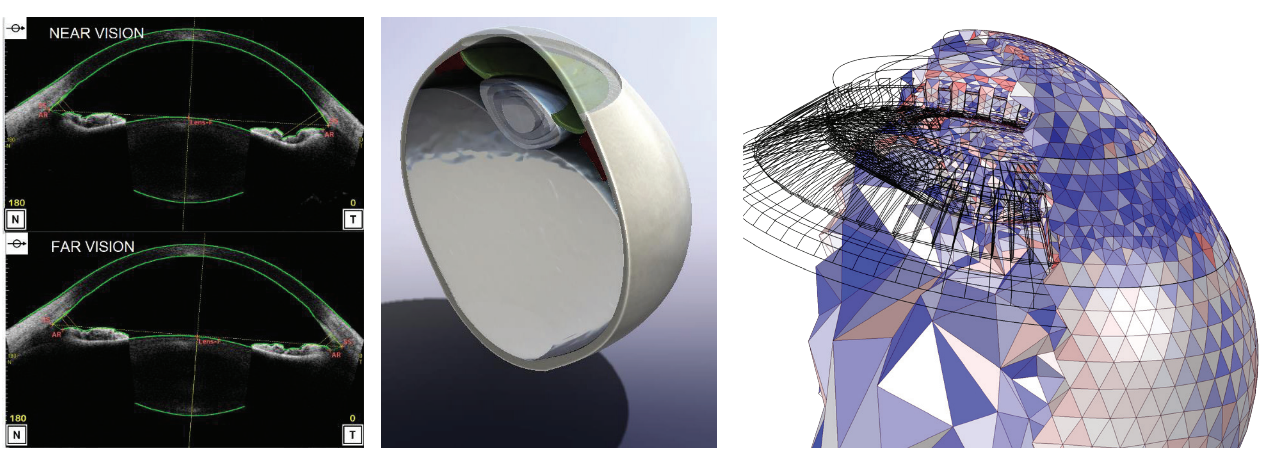

Figure 4. From measurement to simulation. Left: A typical eye imaging from an OCT. Middle: A cross section of the 3D model based on the measurement from the OCT results, created using the SOLIDWORKS® software. Right: Mesh of the 3D model created using COMSOL®.

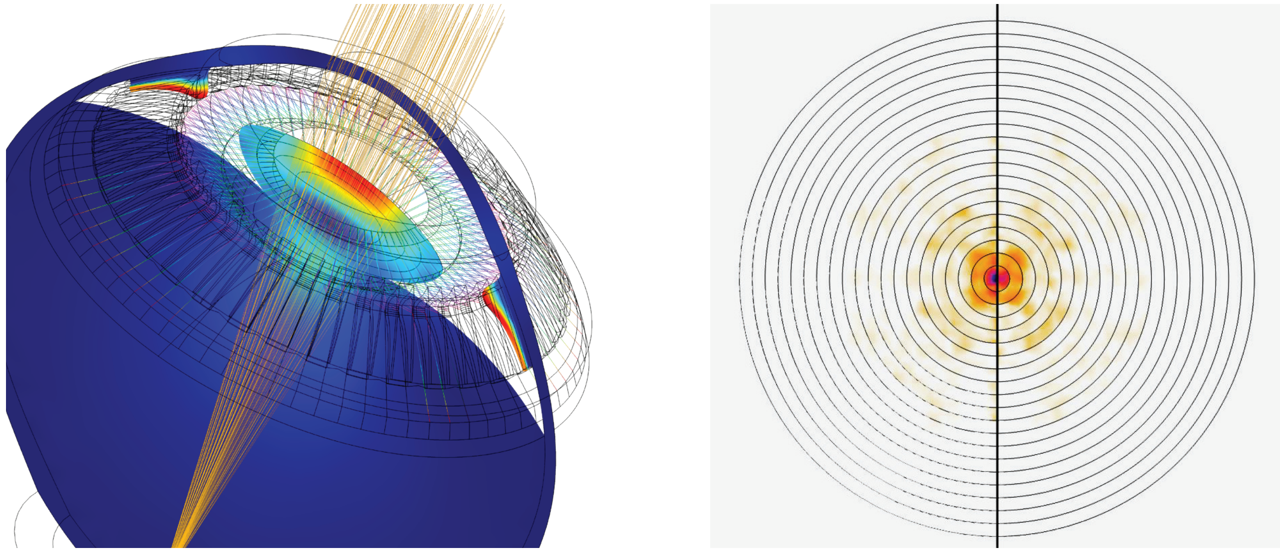

Figure 5. Left: Simulation results showing eye deformation and ray tracing in far vision. Right: Ray focusing after traveling through the eye's optical system. Dark colors represent higher ray density.

The mechanical elements of the eye were then modeled, including the complex muscle ligaments that pull the lens into shape and the viscoelastic properties of the vitreous fluid that fills the eye.

The fibrous nonhomogeneous nature of the sclera was also modeled. Charles-Olivier Zuber, a biomedical PhD student at Kejako and Rostock University, Germany, explained: "The sclera is the white part of the eye and it is made of collagen fibers. Because those fibers are made of collagen, we needed to examine their nonlinear mechanical properties in a multiphysics environment." The displacement of the eye material for a specified accommodation relative to the resting state can be determined by taking all of the elements into account (Figure 5, left).

> *We started to work with COMSOL because of the multiphysics nature of the software and the high quality of customer support.*
>
> —DAVID ENFRUN, COFOUNDER AND CEO, KEJAKO

The ray optics capabilities of the software were used to trace the light rays, modeling the refractive properties of the lens and ray focusing on the retina, considering parallel incoming rays (as if they were emitted by an infinitely far source). This enabled simulations of the patient's sharpness of vision and the objective amplitude of accommodation to be determined. Ray focusing of the eye optical system (cornea and crystalline lens) can be simulated (Figure 5, right). How rays distribute on the retina depends on individual visual acuity. "We can provide models that produce exactly what the patient sees, enabling us to better understand and treat presbyopia. For example, we can see how the image forms on the retina for each individual, so sharpness of vision can be addressed," Maurer added. The team validated its visual accommodation analysis and the presbyopia simulation using measurements from more than 50 eyes.

The ability to model this vast range of parameters was key to the creation and success of the 3D parametric full-eye model. Zuber, explained: "What we appreciate about COMSOL is that we have access to all of these parameters driving the geometric configuration, material properties, and physics involved. Such flexibility is very helpful to improve our comprehension of the problem and find the most effective solution."

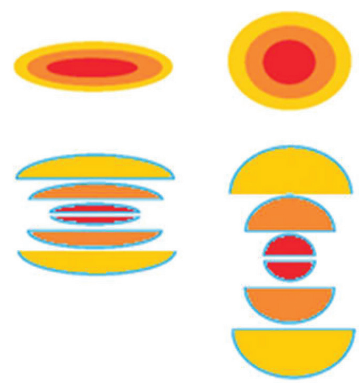

Figure 6. Simplified finite multilayer representation of the GRIN with decomposition in equivalent lens. Far vision is pictured on the left, near vision on the right. Colors represent the value of the refractive index with the highest values in red.

» GIVE US A GRIN

MULTIPHYSICS SIMULATION ALLOWED the team to deduce some of the nonmeasurable mechanical properties of the lens, including the gradient of refractive index (GRIN) used in the

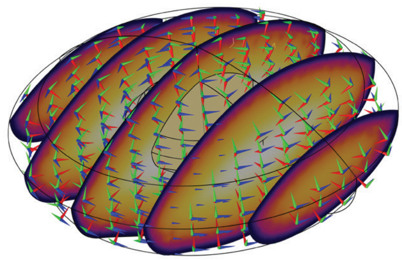

Figure 7. Curvilinear coordinate system used to represent the anisotropic material properties of the lens. The GRIN distribution is shown.

3D parametric model of the eye. The refractive index of the human eye lens has subtle fluctuations and this creates a particular reflectance pattern. The GRIN consists of spatial continuous variation of the refractive index over the lens, which increases from the surface to the center. This repartition has a strong influence on focalization of light, aberration, and thus visual acuity. Through simulation, the GRIN of the eye lens can be calculated, which is vital to understanding how light passes through the structure.

The GRIN acts as a multiplicative factor for the visual accommodation of the eye. As the lens tissues (with their specific refractive index) move with the lens accommodation, it results in two different optical configurations for each extreme state, either far or near vision (Figure 6).

The lens is made of fiber-shaped cells arranged in concentric layers like an onion. This organization is responsible for the lens transparency, but this also has a strong influence on its anisotropic mechanical properties. The model accounts for this microstructure, using the curvilinear coordinate tool available in the software to represent the fiber arrangement (Figure 7). The GRIN value is incredibly difficult to measure directly, but its incorporation into the team's parametric model (Figure 8) was vital to ensure the accuracy of the model and, subsequently, the effectiveness of any proposed treatment.

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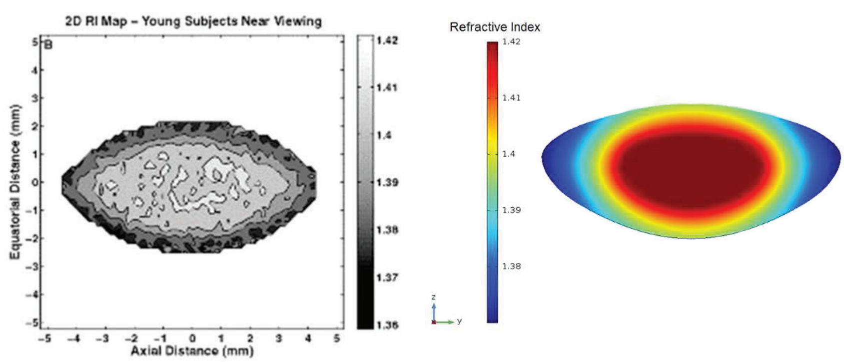


Figure 8. Left: Example of a GRIN measured with magnetic resonance imaging (MRI). Right: Parametric model of the GRIN.

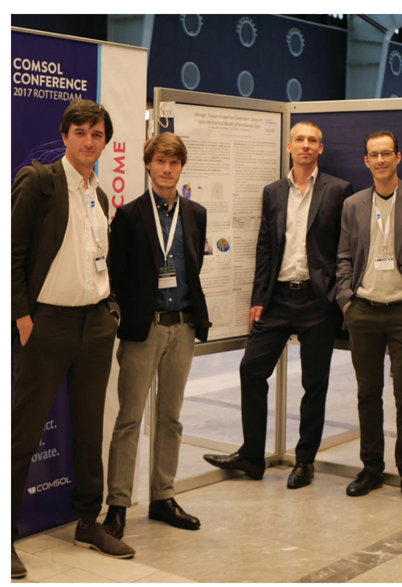
SIMULATION FOR ALL

THE TEAM IS NOW BUILDING SIMULATION apps, using the Application Builder available in the software to extend the reach of the 3D parametric full-eye model and prepare the company for market maturity.

Once the multiphysics model is packaged into a simulation app with an easy-to-use interface, Kejako's work is ready for a clinical setting through a straightforward process. A clinician can use standard OCT imaging to image the patient's eye. This information is sent to Kejako, where the team of experts can create a personalized 3D parametric full-eye model. This model is then further optimized and a customized phakorestoration procedure is created.

The projected prevalence of presbyopia is predicted to reach more than 1.3 billion people by 2020, so apps will be fundamental to keep up with the demand, as nonexperts in simulation can benefit from multiphysics to create each patient's phakorestoration treatment.

"Simulation and modeling have allowed for time savings with regards to our *in vivo* and *ex vivo* tests. We will move to trial when we are confident that we can do something significant in the human body and are convinced of our solution, and COMSOL Multiphysics will help us to achieve that in a much shorter time frame," Enfrun added. ◎



From left to right: Aurélien Maurer, Charles-Olivier Zuber, David Enfrun, and John Speyrer.