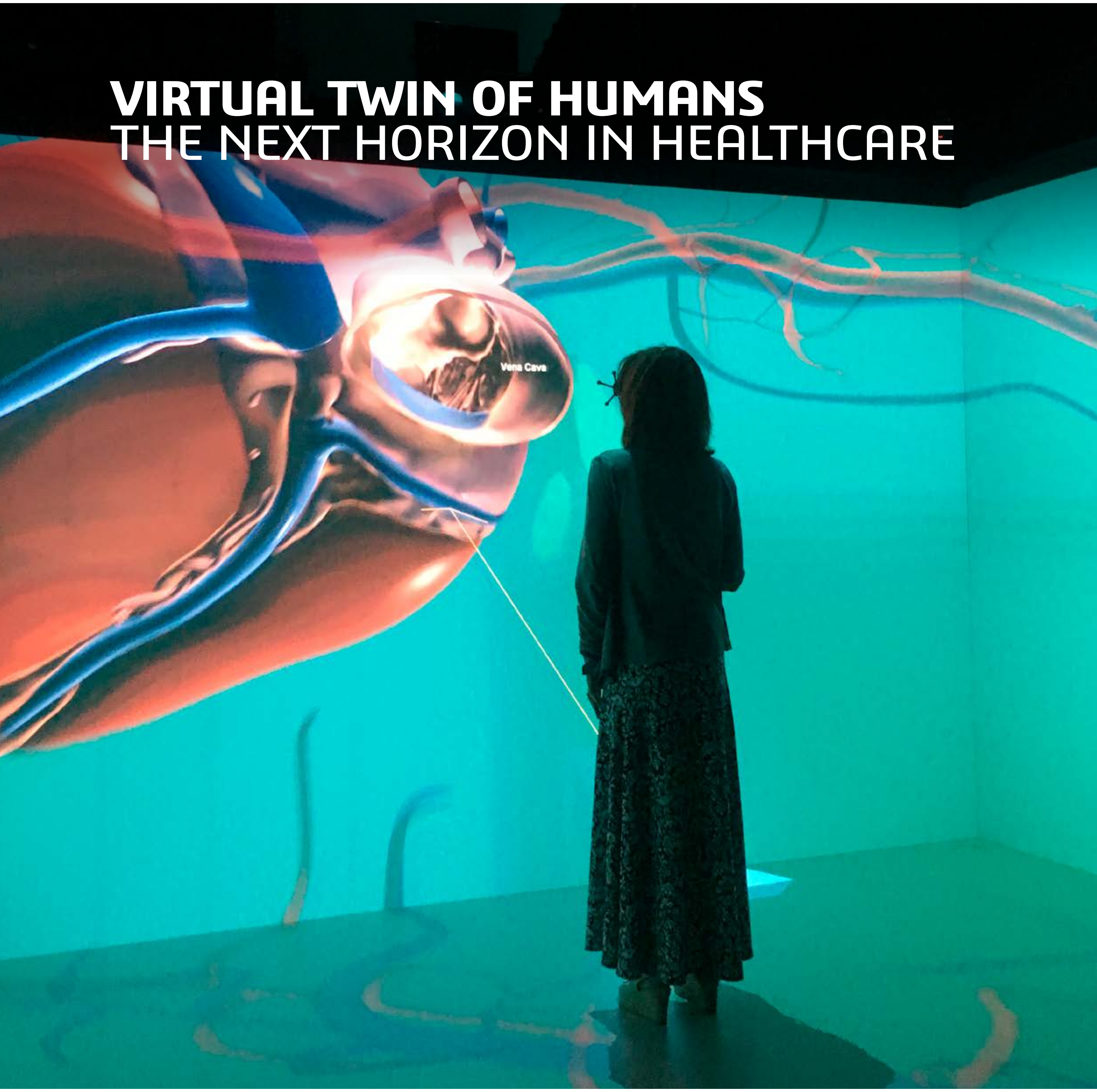
VIRTUAL TWIN OF HUMANS
THE NEXT HORIZON IN HEALTHCARE



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EXECUTIVE SUMMARY

The right treatment, for the right person at the right time. Healthcare professionals strive for this ideal. But with massive costs and limited access to cutting-edge technology, it's still more dream than reality. That is poised to change.

Modern healthcare has reached a crossroads. The era of consensus medicine has served us well, but has plateaued and actually become a barrier to a more powerful medical paradigm. Clinical evidence alone can only go so far, as it fails to capture the uniqueness of each patient or track the subtleties of chronic conditions. Moreover, it relies on diagnosis and treatment after disease is at a progressed state, which is the most reliable, yet also the most costly.

In the 21st century, we can and should do better. A new level of healthcare can be achieved if we create a digital medical system with a detailed view of each patient's anatomy, biology and relevant life exposure in the context of all we know about their condition. The system must connect fundamental knowledge gained in research with observational insights from bedside care, and close the distance between these approaches.

The vision for precision medicine is enabled by the growing ability to capture extensive data about an individual and deliver it to an entire care team. This is done through the unifying vision of a virtual twin, an integrative reference of personal health information. Created with software that conforms to known scientific principles, the twin functions as a complete dynamic "living" model, calibrated with real-world information, enabling new understanding and approaches to health diagnosis, prognosis, treatments and anticipation of future conditions.

Not only does the virtual twin serve as a 3D reconstruction of a human body and its systems, it also contains genetic code and other fundamental biomarkers. This creates a holistic integrative representation of all facets of an individual's health that over time is tuned by medical history and environmental exposures. As our understanding of human biology, physiology, biomechanics and pharmacology improves, virtual twins will become more precise, predictable and usable.

This advancement delivers on the promise of patient-centric digital health and transforms all aspects of the current healthcare system. The breakthroughs that manufacturing industries enjoyed thanks to virtual twins of traditional products can now be replicated in the healthcare sector. The question is no longer 'is it possible', but rather, 'when will it happen and who will deliver it?'

CREATING A VIRTUAL TWIN OF A HUMAN BODY

The human body is the result of hundreds of thousands of years of continuous evolution. Despite a changing external environment, the basic functions of the body have not changed. The architecture of a human is composed of elements and molecules organized in organelles, cells and tissues delivering physiological functions at a macro scale.

Unlike man-made machines which are version controlled and offer a design blueprint, when there is a problem with the body, there is no functional diagram to consult to deduce cause-and-effect relationships. What we understand is largely the result of deconstructing complex systems into smaller, functional parts and running trial-and-error analysis of their behavior. This knowledge had allowed us to make incredible medical advances. However, we have reached the limits of traditional approaches. We now face unsustainable hurdles to continue to more fully understand – and ultimately optimize – the human body.

How much do we understand about the human body? We know that DNA encodes our inherited genetics and adapts to meet ever-changing conditions, sending out proteins as messenger molecules to do the necessary work within our cells. But while we can now readily identify the body's coding, we still don't understand its complex language. The answers lie inside of us, and we now have the technology to decipher them.

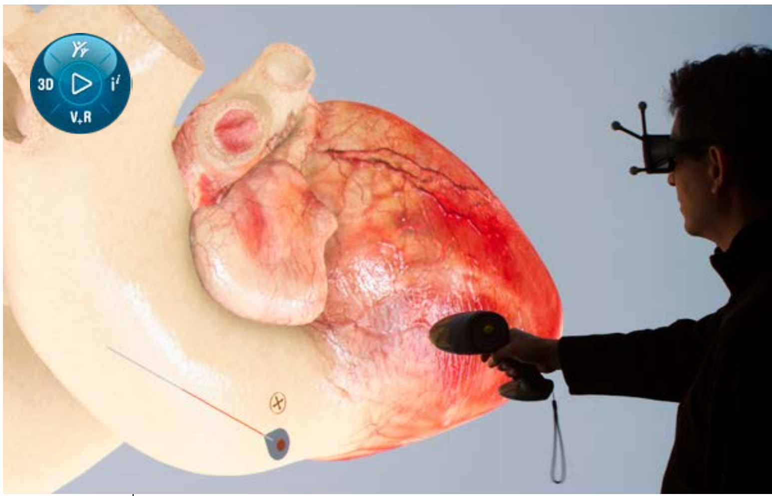
Health data is being collected at a rate unprecedented in all of human history, revealing clue after clue about the human body. But each clue is of limited value without context. If the global scientific community combines their research and understanding, can we gain new insights? Can we create a virtual representation of a human body to highlight gaps in our knowledge? Could we develop functioning models to interpret, correlate and aggregate new data and identify where to focus research? Most importantly, could we apply each individual's attributes and history to adapt this virtual human into a digital surrogate to reconcile medical uncertainties and find the optimized approach for each person?

Achieving precision medicine is the fundamental challenge for healthcare of the 21st century. This is the experiment Dassault Systèmes began with the Living Heart project.

THE REASON TO BELIEVE: THE LIVING HEART PROJECT

A Virtual Medical Reference

In 2014, the Living Heart Project (LHP) was launched to test the hypothesis that cardiovascular experts around the world from academia, industry and clinical practice already had sufficient knowledge to create a fully functioning 3D model of the human heart but were not sufficiently connected accomplish this. The experiment to properly combine their information was successful, and the group published the details of a complete virtual twin of a human heart, built from basic understanding of heart tissue, structure and electrophysiology, and completely adaptable to mimic an individual person or a population. This virtual medical reference is now in use around the world, helping to unravel structural and hemodynamic heart disease. With each use, strengths and weakness of the model are identified and



The Living Heart Project, an immersive experience

published, fueling new experts to join the project and pushing the learning and the technology further.

The LHP demonstrated that by using real-world experience of medical practitioners as the basis, computational biologists and biomedical engineers can replicate the iterative process necessary to produce functional organs in the virtual world. The project delivered a reference model of a functioning beating heart that can reproduce any cardiovascular condition and safely test treatment options.

Because it is virtual, it can be interrogated, shared and visualized to tell the complete story of its function and likely outcomes. Serving as an open reference platform, technical details and knowledge that were once fragmented and isolated is centralized, actionable and sharable. This was more than a useful computational model: the virtual human twin was born.

In an important signal to the industry, the US Food and Drug Administration (US FDA) has served as a key participant in LHP since its outset. It is now using the technology in the ENRICHMENT project, where the Living Heart represents a cohort of human patients with mitral valve disease. This first-of-a-kind *in silico* clinical trial of a medical device using a digital review process proves we can safely unleash innovation by reducing dependency on costly, time consuming animal and human studies required for clinical trials.

It can also create synthetic control arms, eliminating patients receiving only a placebo. Dassault Systèmes' Medidata Rave platform supports this approach by applying AI to data accumulated in previous clinical trials for pharmaceuticals. Combined, the LHP and the platform set the stage to not only accelerate time to market, but to serve as a data source for precision medicine.

Enabling Clinical Decisions with 3D Experiences

Visualization is crucial in healthcare diagnostics. 2D imaging provides essential visual detail to guide clinical treatment, offering a quantitative analysis of system dynamics that allows clinicians to utilize their expertise to make decisions on how to treat a patient.

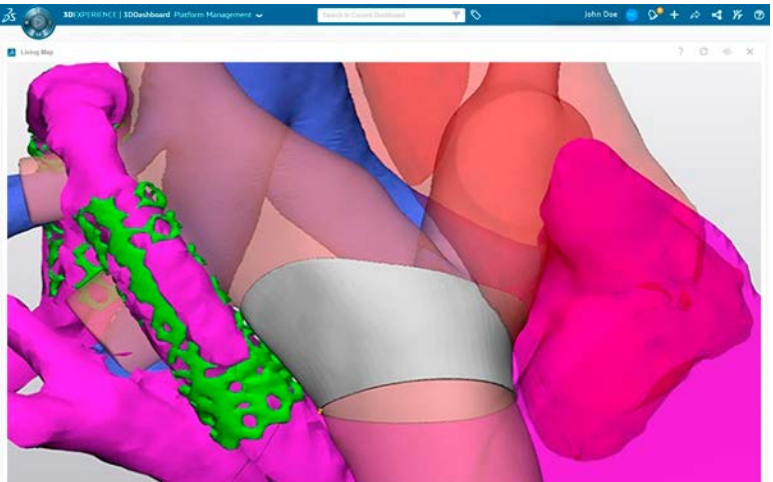
By leveraging breakthrough 3D virtual twin technology, scientists have the power to test and simulate scenarios to predict real-world outcomes. Such a "3D experience" creates the ability to safely push the boundaries of innovation and learning, while minimizing undesirable impacts.

By reconstructing a patient's heart in 3D, for example, doctors can virtually try out invasive measures that consider that specific patient's anatomy, such as testing the pressure differential across a stenosis to be replaced. It also makes it possible to deliver directly to a radiologist a full blood flow analysis of that person's entire coronary vascular system, showing the impact of each interventional option. These insights can not only help guide the right treatment, but also reveal insights that could allow clinicians to lower re-hospitalization rates and sudden deaths.

Helping Underserved Patient Populations

Eight million children each year are born with some kind of birth defect. Nearly half will die by age five. For economic and ethical reasons, the pharmaceutical and medical device industries are unable to properly serve them.

Clinicians typically adapt adult treatments or experiment on their young patients with wide variations in success. Premiere medical centers have the volume and resources to develop reliable treatments for children, but due to limited knowledge sharing, many young patients are not able to be helped despite knowledge being out there. The LHP is an example of how information can be shared to help more precisely treat patients.



A 3D cardiovascular reconstruction from Boston Children's Hospital

While not yet commonplace, these virtual twins of the heart are saving lives in Europe and in the US, and are in development in Asia. For example, in one of the leading pediatric cardiovascular groups at Boston Children's Hospital, Dr. David Hoganson works closely with a Harvard bioengineering team led by Peter Hammer, and together they've shown that computer models of complex cardiovascular reconstructions can be more effective in determining the best treatment than expert opinions.

Online communities can be established to share best practices, giving clinicians from around the world the opportunity to quickly learn from what the leaders in their field have experienced, helping them to address their most challenging cases and successfully plan protocols, test surgical options and techniques and predict outcomes for their patients.

Using virtual twins to address these underserved populations signals the future of precision medicine, where each patient is a cohort of one. Heart disease and stroke cost the world more than $3B per day; imagine what could be saved if only a fraction was channeled into building online collaborative communities instead?

REACHING A NEW STEP WITH THE BRAIN

The success of the Living Heart Project demonstrated the power of the virtual twin to combine and apply cross-disciplinary experience. The rapid pace of technical achievements confirmed the theory that establishing a collective understanding provides far greater benefit than relying on what any one individual can know. With that realization, the door opened to virtually model other organs and systems in the body, and the Living Brain project was launched.

Having a virtual twin of the brain holds great possibilities in neurology, where the level of uncertainty is high and the impact of error can be catastrophic. Indeed, modeling and simulating the brain could provide critical guidance for mechanical or electrophysiological interventions, and one day at the level of brain function itself.

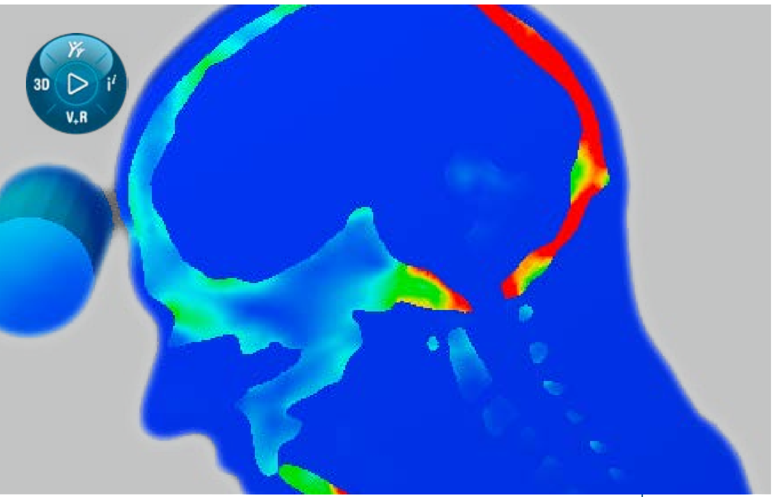
Using high quality imaging, 3D reconstructions can reliably reproduce the physical structure of the head, neck and brain. Rigid structures (skull, vertebra) are the most reliable, but visualizing soft tissue (gray matter, white matter fibers (tractography), the spine) and fluids (sines, ventricles, cerebrospinal fluid) is also needed to get a complete understanding of the brain's structure.

A model of a brain must encompass both the physical anatomy and the behavioral activity, which is defined by electric current flow. A virtual twin can create understanding of the brain during different experiences, recreating activity inside the skull such as during sport, automobile accidents, work-related injuries or epilectic seizures. It can also help us better understand brain development. For example, while we know that many people accumulate brain lesions throughout life, we don't know enough about their impact.

As we become more able to track the physical health of the brain, we may better understand and predict behavioral changes or guide treatments when the cause is seemingly unknown. Critically, a virtual twin can report information in a standard way, often more reliably than the patient, who paradoxically becomes decreasingly reliable as getting information from and about them becomes increasingly important.

Developing a better understanding of the brain's 3D structural layout could help identify early development of a neurodegenerative disease. For example, if we measure the volume of cortical or subcortical brain regions over years, clinicians will have a reference point to understand their individual patient's connectome, a comprehensive map of neural connections in the brain.

Knowing these leading indicators can be discovered could encourage patients to not only seek care early, but to help



Simulating the impact of a head injury through the Living Brain

them and their medical team select the best care plan for their precise situation. Properly managed, virtual twins of the brain can become essential references for the industry to develop new and more precise diagnoses and treatments, increasingly using virtual patients as fidelity improves.

Testing the Living Brain: Epilepsy Research

In acute brain diseases such as epilepsy, personalized virtual twins are already helping to guide accurate diagnosis and treatment. At the earliest onset of seizure symptoms, the complex signals from the brain can be captured, diagnosed and tracked as care is administered.

In the 30% of epilepsy patients who are drug-resistant, a localized part of the brain's tissue is defective and responsible for seizures. Precisely targeted brain surgery can be an effective therapeutic strategy. The patient's virtual twin can help to ensure the region to resect is well identified and precisely delineated, allowing the removal of damage while preserving critical functions of neighboring regions.

This is the goal one of the programs of the Living Brain project, EPINOV: a public-private partnership coordinated by Aix-Marseille University and composed of Dassault Systèmes, the Assistance-Publique Hôpitaux de Marseille, the Hospices Civils de Lyon and the French Institute of Health and Medical Research (Inserm). After learning of the success of the LHP, clinicians and renown neurologists came to Dassault Systèmes to help accomplish their goal of improving epilepsy surgery management and prognosis by modeling each patient's brain in 3D.

Since 2019, a clinical trial is using virtual twins of the brain constructed from patient imaging and electrophysiological data, calibrated to the typical seizures of a patient. Bringing together the 3D anatomy of each patient's brain with its connectomic structure, combining detailed electrophysiological models of brain regions (neural mass models) with high-dimensional data fitting algorithms, has the potential to raise the success rate of surgery for these patients. Further, data from the clinical trial will validate the added value of the virtual brain technology to surgical decisions or point toward improvements.

EXPANDING TO NEW HORIZONS

With the successes and lessons learned from leveraging the virtual world to extend and improve the real world for the heart and the brain, advances in using twins to model other parts of the human body are also underway. While the idea of having virtual twins of all organs such as the lungs and kidney and body parts such as feet appear in scientific literature almost daily, here we will focus on three nascent uses for virtual human twins: skin, cells and the gut.

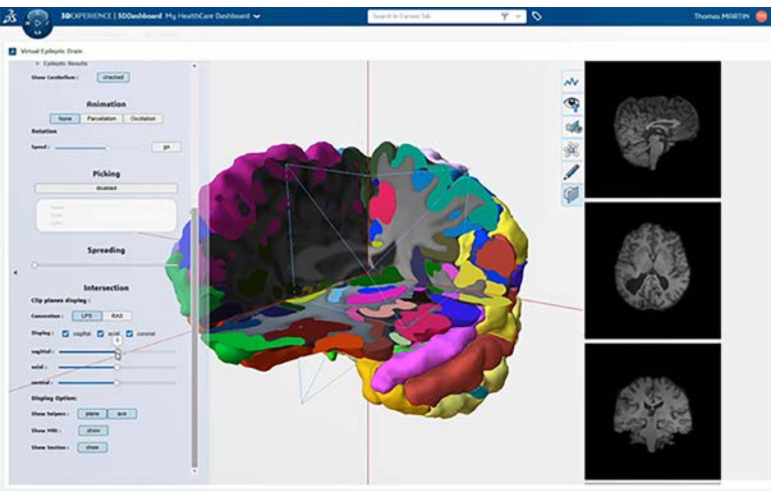
Living Skin: From Biologics Testing to Healing

Human testing is the last stop for any new medical innovation. Most testing begins at the bench or in animals, never seeing a human environment until late in the cycle. Both public opposition and ethical considerations, however, have limited animal testing to only situations when it is absolutely necessary. Animal testing is already banned for the majority of development and testing of cosmetics, which must be compatible with human skin.

As the largest organ, skin provides many essential functions: from shielding against external aggressions by pathogens, chemicals and radiation to thermoregulation and serving as the alert system against harm. To serve these functions, skin contains many different cell types, organized into multiple layers and distinct structures that collaborate together.

Moving away from live animal models, petri dishes of laboratory-grown *in vitro* skin samples are now the norm to test cosmetic products. However, *in silico* skin models are maturing and are poised to take over. While still early in development, these models offer many potential advantages, including eventually becoming part of a virtual twin. And it is not only consumer companies who are set to benefit from these advances: the pharmaceutical industry is taking note, since for non-oral treatments such as biologics, access to the body through the skin is critical.

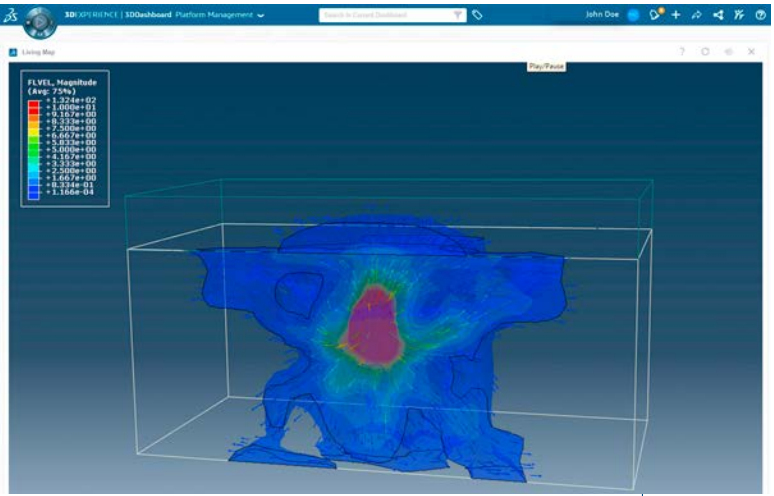
Dassault Systèmes develops solutions that provide a multiscale model of skin, based on its fundamental molecular properties, and that can accurately predict the penetration of chemicals through skin layers. Virtual models can reflect individual skin types and properties such as age, levels of hydration or damage due to exposure, and can test formulations of cosmetic creams and lotions.



Living Brain links 2D medical images to 3D Experience Twins anatomical brain regions

The models are also used to design predictable drug delivery systems for painless injections, secure wearables and eventually injectables that correct for an individual's shape, size, body chemistry and mobility. These same delivery systems will also monitor dosage, seamlessly feeding this information back to a person's unique virtual twin for accurate clinical tracking.

Even more complex models of skin are being used to understand the dynamic process of wound healing, a major burden on the healthcare system. An aging population and rising incidence of diabetes are among the major drivers behind a rise in wound care, which is expected to reach USD 16.5 billion by 2025, up from USD 10.3 billion in 2020.



Simulation of fluid velocity to simulate perfusion into a porous medium of skin

In particular, deep chronic wounds such as diabetic foot and venous ulcers are painful, slow-healing conditions and it is not always clear which available interventions and treatments are best for a given patient. Creating a virtual twin of an individual with a wound allows doctors to develop a personalized prognosis and test different treatment options. If the outcome doesn't go as hoped, that information can also be fed back into the twin to study the body's healing process.

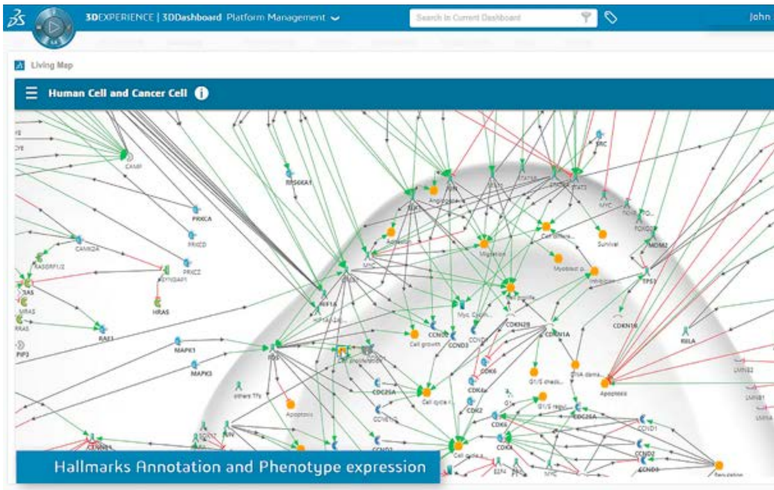
Living Cells: Stopping Diseases at Their Source

The myriad of cells in the body are ultimately responsible for its functions. Modeling can provide critical insights by reproducing cells that can in turn be studied for a variety of diseases. While we are not yet at the stage of being able to map all cells and personalize them in a virtual twin, we can model some cells that are known to directly impact patient health.

Cancer cells, for example, can be modeled to reproduce key behaviors such as disease evolution and treatment efficacy, and virtualized through the concept of intracellular pathways where a healthy cell is represented by an equilibrium of chained molecular reactions. Each pathway is controlled by cellular functions, such as growth and division. Pathways that are deregulated in cancer have been extensively described, perhaps most notably in the book 'The Biology of Cancer' by Massachusetts Institute of Technology professor Robert Weinberg. The 3DS Cancer Map was developed based on this research, offering a logical system view of all biological entities (genes, proteins) and interactions that are most important in human cancer. This allows the scientific community to visualize and learn from:

- oncogenes (entities responsible for cancer initiation & progress)
- tumor suppressors (entities that prevent cancer)
- major cancer hallmarks (subsystems than can become dysfunctional and lead to cancer)

Virtual cells can become part of the virtual twin of the body, and used to reproduce likely biochemical alterations and help target the right drug treatments. With a virtual twin, trial-and-error treatment of diseases can happen in the lab before experimenting on a patient. Cell automates can take into account heterogeneous cell populations and reproduce, for instance, the genetic diversity observed in cancer. At each cell division, genetic modifications may occur with a defined probability. For example, intra-tumor heterogeneity can be used to predict targeted cancer treatments depending on the level of HER2 gene amplification observed in different breast cancer patients and treatment combinations can be tested through the virtual twin model of an individual.



A cancer cell with pathways

Over the last three years, a similar model has been built in a collaboration between Dassault Systèmes and scientists at the French Institute of Research and Health (Inserm) describing key pathways in cellular aging.

Aging is a major risk factor for many chronic and neurodegenerative diseases. As the human life span increases, understanding the impact and the underlying mechanism of aging on the onset and evolution of these diseases is important to act preventively and help people age in better condition.

Cellular aging is a protection mechanism to avoid cells becoming cancerous. But as aging cells induce their neighbors to prematurely age too, the body cannot keep up with cleaning them all. Cleaning up prematurely aged cells a as treatment is under investigation in arthrosclerosis, and a virtual twin can be deployed to study the impact and test treatment options.

An additional advantage in using virtual twins of cells is to advance the development of personalized drugs. Connecting cellular level function with organ or system-level behavior is the missing link in this pursuit. The Living Heart Project took this on, modeling drug interactions that could alter organ-level function. Models of the individual-action potentials responsible for voltage changes across cell membranes were substituted for the phenomenological electrical model. By mapping the cells into the whole heart, researchers could predict when an irregular heart rate would occur and at what point circulation of blood through the body is compromised. This allows dosage sensitivity to be robustly mapped across a virtual patient population, providing data for AI models that predict safety based on chemical function, rather than waiting for clinical observation.

Living Microbiota: Virtual Gut Health

Many diseases, and in particular chronic ones, do not develop only due to genetic predisposition: environmental factors highly influence their course and gravity. Eating and living habits, pollution, past disease and taken medication shapes the community of microbes living in each person's gut. The gut microbiota community integrates all environmental influences, making it a foe when it resists treatment, or a friend when it helps defeats diseases and promotes healing.

Because microbiota is highly diverse from person to person, creating a virtual twin of it holds great promise in medicine, since both genetics and microbiota play a part in disease.

Physiological based kinetic model

Over the last three years, Dassault Systèmes and Inserm have collaborated to integrate existing knowledge of the interaction between the gut microbiota and the human body into a physiologically-based kinetic (PBK) computational model describing the cycling of some key metabolites throughout several organs of the digestive system. Inserm scientists use this model in their quest to better understand the role of microbiota in human health. This modeling enriches the virtual human twin by introducing a functional, physiological layer, completing the far more advanced 3D physics, fluidics and electrical parts.

To personalize a fully functional virtual twin requires substantial innovation in minimally invasive technologies able to measure critical metabolites and microbiota community composition over time, as well as leveraging AI and deep learning technologies to fit patient data. Achieving this could open an entirely new way to support personalized diagnoses, prognosis, predict responses to drugs and preventively apply nutritional intervention.

VIRTUAL TWINS IN ACTION

Population & Disease Models

Over time, the collection of virtual twins will behave as a virtual clinic that represents the entire population. A virtual twin is descriptive of its real equivalent, but it can also be predictive. An effective way to model predicted response to treatment is with Pharmacokinetic/Pharmacodynamics models (PKPD).

These models represent "what a body does to a drug" and "what a drug does to a body." When a drug is administered, a body will absorb, distribute, metabolize and eliminate it. The efficacy of each step is different for each person, depending, in particular, on the phenotypic expression of its genes.

PKPD models are key to developing a new drug. However, they generally are not refined enough to be able to predict a specific patient's response, partially because the phenotypic expressions of genes are not available for each patient. To improve the predictive power of PKPD models, several approaches have been developed.

One approach uses quantitative system pharmacology models built on the underlying physiology that integrate diverse data from micro-scale to macro-scale, considering the body as a unique, complex, biological network. The mechanistic consideration of processes underlying drug absorption, distribution, metabolism, excretion and action makes possible to study the behavior of drugs in more realistic models, such as the combined effect of multiple drugs with polypharmacology.

Quantitative system pharmacology models can also explicitly introduce variability terms (e.g. inter-patient variability), to model and predict a population's response to a treatment. Combining mechanistic and population-based approaches will generate virtual populations to show variability equivalents to real populations. These virtual populations allow for the exploration of observed uncertainty, to explain the causes of inter-patient variability. This means that defining the similarity of a patient to a population makes it possible to predict how a patient will react to a drug.

Virtual twins of patient populations are expected to soon become part of the evidence supporting preclinical and clinical evaluations of new treatments. Currently, randomization is the gold standard method to generate clinical evidence. However, its feasibility is limited when it comes to rare diseases or to personalized medicine.

Cohort Models

Synthetic Control Arm is a modeling method that uses historical claims and observational data to approximate the effect of randomization by comparing patient populations across different clinical trials. For any new experimental arm, a specific control arm is created using patient data from selected clinical trials. Synthetic Control Arms accelerate approval of new drugs by combining virtual and clinical evidences, avoiding large randomized clinical trials in situations where innovation is most needed.

By merging personalized models with models defined at the population level along with machine learning, the virtual twin will help patients get the best available treatment for them.

Uniting Virtual + Real to Go Beyond Health Records

A critical aspect of successfully creating a reliable digital healthcare system is having complete and consistent information, to support every step: from day-to-day monitoring to diagnosis to surgical planning. A complete representation of the condition and its supporting data must be available to the entire patient care team, in a form suitable for each team member.

At the center of that team is the patient, their family or their surrogate. Point of care becomes dynamic and often location-free. The patient may be at home, with the clinician in their office or with the surgeon in the hospital. Regardless, the information should be always available.

The virtual twin serves as a next-generation functional health representation, allowing for a common understanding, efficient sharing and data-driven care to reduce preventable errors. This is only possible if the medical systems communicate through the use of standards on a cloud-based platform, which helps reduce inconsistencies introduced by separate tools and reliably drive surgical robots for maximum precision.

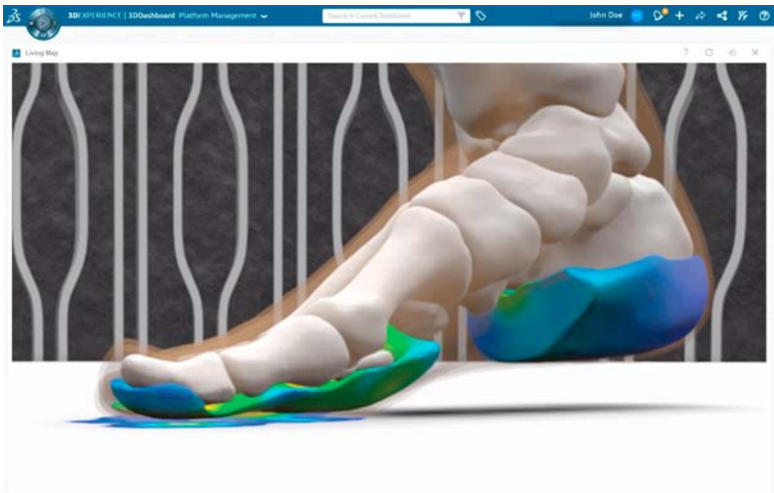
Supporting an Emerging Ecosystem of Virtual Twin Innovators

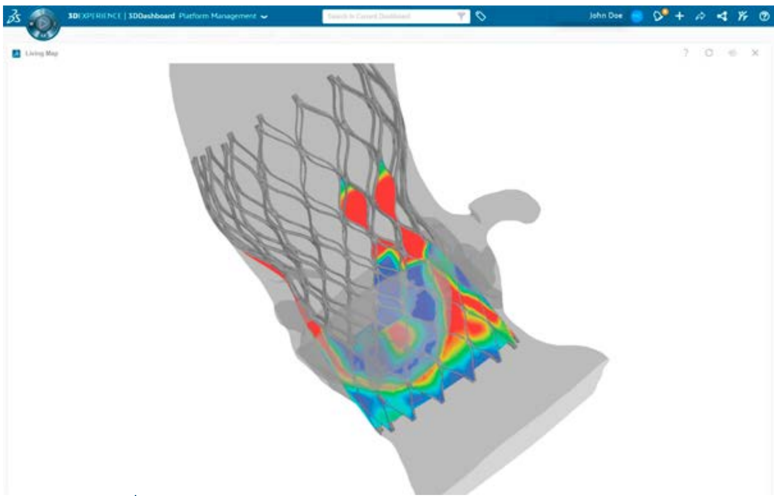
We are still at the beginning of the digitalization of healthcare, including the virtual twin. As the industry embraces this transformation and ushers in a new era of medical innovation, a cloud-based, common platform must be deployed as the technical underpinning.

Incubators, such as the **3D**EXPERIENCE Lab, allow disruptive startup companies to gain access to state of the art platform capabilities to develop virtual twins. Though their work is in the early stages, these companies are already delivering improved diagnosis and treatment services, including outcome-optimized surgical planning. Some examples:

- **BioSerenity** develops mobile sensors for high risk patients to track detailed neurological and cardiovascular signals. These are loaded to the cloud and tracked by the physician to immediately identify a condition, such as an epileptic seizure, wherever it occurs. The neurologist can use the data from the sensors to plan surgical intervention.
- **Digital Orthopaedics** provides optimized orthopedic surgical plans, based on simulated outcomes derived from detailed, personalized foot and ankle pathology reconstructions combined with motion-driven healing predictions. This provides a surgeon with knowledge of the expected healing process before beginning a procedure.
- **FEops** addresses the growing practice of replacing failed heart valves through non-invasive procedures. Though less costly and far less invasive, success is contingent on achieving a precise pressure fit for the newly implanted valve. Accurate sizing, shape and location can be predicted by reconstructing an individual patient's heart in 3D and performing virtual surgery options, reporting the best approach to the surgeon.

These three companies are delivering their innovations through a cloud-based Clinical Decision Support System (CDSS) supported on the **3D**EXPERIENCE platform. Today, their focus is on treating each patient individually, but over time their learnings will be aggregated into a knowledge base of parametric models used to train clinicians and feed AI systems.





On top: Digital Orthopaedics
Below: FEops

Additionally, researchers throughout the world are now using virtual twins of humans to develop innovative solutions to a wide range of medical challenges. Here are a few examples that Dassault Systèmes La Fondation India supports:

- **Smart CPR**: For a person suffering a heart attack, time can be the difference between life and death. CPR administered correctly can save a life, but requires 30-40 minutes of demanding physical effort, sufficient to exhaust even a healthy person. A Smart CPR device that can provide advanced cardiac life support based on a patient's specific physiological condition is under development by a team at the Indian Institute of Technology. Virtual patients, today represented by the LHP, are being used for inverse electro-mechanical modeling of the cardiac resuscitation process. Fundamental insights into the cardiovascular tissue correlation of external measurements will feed the development of the device, fine tuning treatment based on that patient's physiology. This type of specific biomechanical study would be impossible without virtual modeling.

- **Cervical Spine Surgery**: Heterotopic ossification is one of the most common major complications after artificial disc replacement, limiting the patient's range of motion. People who have undergone surgery to implant an artificial disc in their spine can face severe problems after a few years. Abnormal bone growth occurs due to severe loading on the artificial disc, often requiring expensive and painful revision surgery. At the Vellore Institute of Technology in Chennai, researchers are simulating bone remodeling and growth to develop a personalized artificial disc that will balance the load and heal with predictability.
- **Personalized Psychiatric Treatments**: Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique in which low intensity direct current is applied to the head for several minutes to modulate neural activity in specific regions of the brain. It is increasingly being used to treat neurological and psychiatric disorders such as depression, stroke recovery and schizophrenia. The simplicity, affordability and portability of tDCS make it ideal for developing countries that suffer from a high prevalence of mental disease and low access to pharmacological therapy. However, efficacious personalized application of tDCS can be problematic since the tDCS-induced current patterns in the brain show marked inter-subject variation due to underlying differences in cranial anatomy and brain tissue characteristics. To address this challenge, India's National Institute of Mental Health and Neuro Sciences (NIMHANS) has demonstrated that computational modeling techniques can integrate multimodal brain imaging with other clinical and biological metrics to improve the efficacy and personalization of neuromodulation. High-fidelity 3D head-brain models created from MRI images of schizophrenia patients and multiple predictive studies determined the optimal treatment protocol for each person. Ultimately, machine learning approaches will be used to build a predictive framework based on 3D imaging and physics-based simulation, as well as on subject-specific genetic, clinical, biometric, behavioral and environmental information to better guide the diagnosis and treatment of neurological and psychiatric disorders.

CONCLUSION

Improving human health relies on gaining a much deeper understanding of the human body. Nearly fifty years after the dawn of the digital revolution, we understand the power that results from when we capture, grow and apply research and understanding from teams throughout the world.

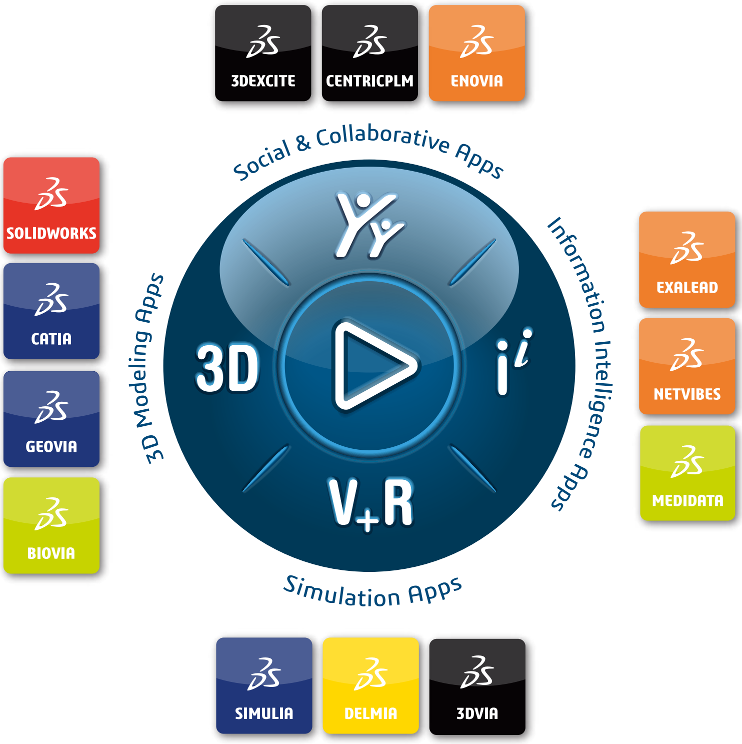
In the 1980s and 1990s, Dassault Systèmes helped pioneer the use of digital mock ups to revolutionize how products were developed, by using 3D to represent entire complex systems, outside and inside. Each piece came together to simulate a complete engineering context in a virtual model, replacing physical mock-ups. This ushered in an era of collaborative innovation that revolutionized how non-organic products were designed and manufactured.

We are on the cusp of the next revolution, where these same approaches are now applied to the organic world. By fusing real-world knowledge and know-how with multidiscipline, multiscale modeling and simulation technology, we can gain never-before possible insights into the human body.

Harnessing data from medical records and collating insights and intelligence from a range of disciplines – industry, research, practitioners – and even patients themselves can unlock the means to prevent and battle disease and to speed healing. This data must be stored on a secure, cloud-based common platform that can be accessed by anyone, anywhere.

By leveraging that data, we can create virtual twins of the human body to visualize, test, understand and predict what cannot be seen – from the way drugs affect a disease to surgical outcomes – before a patient is treated. The virtual twin can be built to represent most, then personalized for each patient.

In the same way companies who create non-organic products have innovated using the virtual world to improve the real world – (V+R) – we can now leverage the virtual world to improve the organic world. The potential to use V+R to create an entirely new approach to healthcare is unprecedented; we will benefit from next-generation medical practices, precision medicine and surgery, and informed predictions to individualize care. The time has come to act.



Our **3D**EXPERIENCE® platform powers our brand applications, serving 11 industries, and provides a rich portfolio of industry solution experiences.

Dassault Systèmes, the **3D**EXPERIENCE Company, is a catalyst for human progress. We provide business and people with collaborative virtual environments to imagine sustainable innovations. By creating 'virtual experience twins' of the real world with our **3D**EXPERIENCE platform and applications, our customers push the boundaries of innovation, learning and production.

Dassault Systèmes' 20,000 employees are bringing value to more than 270,000 customers of all sizes, in all industries, in more than 140 countries. For more information, visit **www.3ds.com**.

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