Review Article

Review of Innovative Immersive Technologies for Healthcare Applications

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Source of Support: The Sony Foundation and Tour de Cure Foundation provided funding support under the Virtual Reality Cancer Research Scheme. Zhonglin Qu is funded by a Western Sydney University Research Scholarship.

Conflict of Interest: None.

Received: Jun 11, 2021; Revision Received: Nov 23, 2021; Accepted: Feb 1, 2022

Qu Z, Lau CW, Simoff SJ, et al. Review of innovative immersive technologies for healthcare applications. *Innov Dig Health Diagn Bio*. 2022; 2:27–39. DOI: 10.36401/IDDB-21-04.

ABSTRACT

Immersive technologies, including virtual reality (VR), augmented reality (AR), and mixed reality (MR), can connect people using enhanced data visualizations to better involve stakeholders as integral members of the process. Immersive technologies have started to change the research on multidimensional genomic data analysis for disease diagnostics and treatments. Immersive technologies are highlighted in some research for health and clinical needs, especially for precision medicine innovation. The use of immersive technology for genomic data analysis has recently received attention from the research community. Genomic data analytics research seeks to integrate immersive technologies to build more natural human-computer interactions that allow better perception engagements. Immersive technologies, especially VR, help humans perceive the digital world as real and give learning output with lower performance errors and higher accuracy. However, there are limited reviews about immersive technologies used in healthcare and genomic data analysis with specific digital health applications. This paper contributes a comprehensive review of using immersive technologies for digital health applications, including patient-centric applications, medical domain education, and data analysis, especially genomic data visual analytics. We highlight the evolution of a visual analysis using VR as a case study for how immersive technologies step, can by step, move into the genomic data analysis domain. The discussion and conclusion summarize the current immersive technology applications' usability, innovation, and future work in the healthcare domain, and digital health data visual analytics.

Keywords: immersive technology, visualization, virtual reality, augmented reality, artificial intelligence, machine learning, innovation, digital health, extended reality

INTRODUCTION

As the years pass by, the technologies in healthcare continue to improve patient treatment outcomes, help enhance the quality of care, and lower cost. Innovative technologies including immersive technologies are used for augmented reality (AR) training, healthcare data leveraging, patient-customer experience personalization, big data analytics, and health outcome retrieval from data.[1] Immersive technologies allow the users to have the perception of being physically present in a non-physical world using different stimuli such as images and sound. These technologies are becoming more affordable, user-friendly, and pervasive. They have also been adopted and embraced by several industries, including healthcare.[2] This is particularly true with the advanced analytical methods and massive quantities of healthcare data being collected from patients and the general population. Healthcare experts will address the extensive unmet information, make a prediction, and select a treatment method based on a patient's genetic profile instead of a one-size-fits-all approach.[3] Artificial intelligence (AI), precision medicine, and immersive technology are among the most promising health technologies.[4] The convergence of AI and immersive technology trends offer opportunities currently available to health domain users that will change many of the experiences that they already have. As health data continue to become more diverse, the need for tools that facilitate interactive, versatile, and integrative visualization of complex big data is also growing. Immersive technology is developed to offer natural interactions between humans and machines, and incorporate other perception dimensions, such as sound,[5] over conventional data visualization approaches. AI, when added to the novel data visualization tools, makes them even more effective when processing complex data.[6]

Machine learning, as a branch of AI,[7] is used as one of the leading health technologies for enhancing accuracy in clinical insights, improving decision making, avoiding errors such as misdiagnosis and unnecessary procedures, helping in the ordering and interpretating of appropriate tests, and recommending treatment methods.[8] Machine learning has been used in the field of "precision medicine" for years. According to the U.S. National Library of Medicine,[9] precision medicine is "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person." Precision medicine enables physicians to determine personalized treatments for patients by interrogating the data of a patient's genetic history, location, environmental factors, lifestyle, and habits instead of a blanketed approach for all patients. Machine learning can make data visualizations dynamic with real-time analytics, find more granular and actionable insights, create better searches for visualization dashboards, and create better predictive models.[10]

Virtual reality (VR) provides users with a virtual or simulated experience that excludes their actual physical surroundings. It helps humans perceive the digital world as real and gives learning output with lower performance errors and higher accuracy. VR is an immersive technology that allows the user to explore and manipulate computer-generated three-dimensional (3D) environments in real time.[11] A VR environment, in comparison with other media, has fewer distractions, more space, and more natural interactions. VR has become more portable, immersive, and vivid, which has enabled the technology to be used in a broad range of medical applications,[12] such as neurological disease, and other domains, including education[13] and construction safety.[14] AR superimposes digital elements on top of the user's physical environment through a device. AR is another immersive environment that provides a real-time overlay of reality with digital information.[15] Mixed reality (MR) blends the digital world with the physical environment integrated with the user's physical surroundings. Immersive technology platforms can precisely translate movements from the physical world to the virtual world.[16] VR, AR, and MR together are also called *extended reality* (XR).[17] With the mature immersive game engine architecture, we can design controls that mimic novel physical actions, such as grabbing a data point to extend workflows and presenting data into the virtual world.[18]

The field of healthcare discovery demands such visualization tools for the clear and comprehensive representation of data exploration to lead to new insights and discovery. Immersive technologies anchor virtual objects to the real world and allow users to interact with the virtual objects.[19] Machine learning and immersive technology are both technologies that present opportunities independently; however, combining them will make various experiences even more interactive and engaging.[20] XR and immersive environments open up new opportunities for diagnostics, medical education, preoperative planning, and intraoperative support because their 3D interactive and immersive nature allows users to absorb and retain more information.[21] VR has been used in pain management, physical therapy, fears and phobias, and cognitive rehabilitation for its unrivaled engagement ability.[22] Visual data analytics has proven essential in genomics research to gain insight into biological processes, find correlations and trends in large data sets, and communicate outcomes to others.[23] Big complex genomic data analysis needs methods to support flexible and dynamic queries to search for informative insights over very large collections in very high dimensions.[24] Immersive technologies could improve scientific genomic data visualization and interpretation by combining the natural 3D environment with natural human pattern recognition to uncover multidimensional relationships in data, especially when VR visualization tools are integrated with machine learning models. The VR display environment could amplify human perception and assist users in recognizing patterns in genomic data, as has been shown in multiple studies[25–27] in the digital health domain.

The AR and VR industries were valued at $14.1 billion in 2017 according to Statista. The compound annual growth rate of the AR/VR industry is expected to be in the range of 40% to 80%. Statista predicts that the AR/VR industry will be valued at $209 billion by 2022.[28] There is no doubt that healthcare will also jump in on the action. More commercial VR headsets are launched, which is expected to accelerate the growth of the market. Making the VR experience more realistic is a key driver for market adoption and penetration.[29] As immersive technology is only now starting to find its way into the healthcare domain, its innovative potential has yet to be fully realized. For example, there are thousands of exciting and innovative immersive technology projects coming along in clinical studies listed at ClinicalTrials.gov[30] and NIH (National Institutes of Health) RePORTER.[31] There was a dramatic fund increase from 2018 to 2021. At this stage, more than 85% of the projects are for the clinical management of children or older adults. It is encouraging to see almost 5% of the projects that are using immersive and XR technologies for health data analysis. However, there are not many reviews and research work that highlight the gaps and discuss the possible solutions, and there are limited works on genomic data visualization in immersive environments, especially on the approaches to integrate different technologies such as machine learning and game engine theory. This paper contributes a comprehensive review on the existing immersive projects for healthcare with a focus on patient-centric projects, medical education, and data visual analytics. We use a case study to find how immersive technologies step, can by step, move into the genomic data analysis domain. We review and discuss the combination of immersive technology, human-machine interaction, data visualization, and machine learning to solve real clinical cases. Current issues and future trends also are discussed.

The following section, "Immersive Technology Projects for HealthCare," reviews the current immersive projects and applications directly used by the patient, physician, or practitioner in healthcare, including dementia, remote consultation, aged care, children's anxiety, psychiatric care, distraction therapy, and healthcare education. Immersive technology used for healthcare education inspires the use of digital health data visualizations because users potentially engage more in an immersive environment to understand the patterns and insights from the complex big health data. The section, "Immersive Technologies for Visual Analytics of Health Data," focuses on reviewing immersive technology used for data analysis, especially for health data analysis. A research use case is also reviewed for the evolution of immersive technology used for healthcare data analysis. The final two sections discuss the current issues and the future work for VR technologies in healthcare data analytics.

IMMERSIVE TECHNOLOGY PROJECTS FOR HEALTHCARE

Interactive visualization seeks to go beyond the traditional environment into emerging platforms such as VR, AR, MR, large and high-resolution displays, and mobile devices. Complex data visualization and interaction tools in the XR environments could enhance humans' perception of where the interactions could be more natural or more effortless.[32] There has been increasing use of immersive technologies in the healthcare sector, such as medical training, patient treatment, medical marketing, and disease awareness.[33]

We frame this onto healthcare data resolution with a specific focus on the use of both immersive technology and machine learning for genomic data visualizations for the period between 2000 and 2020. It commences with a general search on a search engine, such as Google Scholar and Google search engine, and then in several databases, such as Springer, Nature, Genome Research, IEEE, and ACM. We also collect information through relevant market reports, such as the Mordor Intelligence Analysis Report. The search terms included "Genomic VR project," "Healthcare VR applications," "Machine learning combines immersive technology," and "VR data visualization tools." These words were used for all the other database searches. Only studies published in the English language were included for review. The main reviewer extracted and analyzed data from all articles in consultation with the other authors.

Healthcare Immersive Technology Projects

In clinical practice, immersive technologies offer the potential to facilitate the manipulation of patient-specific needs.[34] Immersive technology is being used in many ways in the healthcare domain, as shown in Figure 1. Each branch represents one type of use in the healthcare domain. Immersive technologies are gaining insight into life with dementia, enabling remote general practitioner (GP) consultation, activating aged care, easing child anxiety, automating psychiatric care delivery, supporting healthcare education, providing distraction therapy for patients with cancer, and delving into health data analytics. Some finished and ongoing immersive healthcare projects related to Figure 1 are listed in Tables 1 and 2. Detailed project description and discussion are listed in the following paragraphs "Patient-Centric Immersive Solutions in the Healthcare Domain" and "Physician- or Practitioner-Centered Immersive Technology for Healthcare Education." We can find that immersive technology can enhance learning and improve productivity in healthcare domain training from these projects. Data analytics and visualization then use this better perception advantage to help users find patterns and insights from complex big data. Data analytics projects and health data analytics with immersive technology are listed in Table 2. The discussion about these projects is also listed and discussed in section "Immersive Technologies for Visual Analytics of Health Data."

Patient-Centric Immersive Solutions in the Healthcare Domain

User-centric design (UCD) is an iterative design process to bring the users into every stage of the design process to create highly usable and accessible products for users. Many immersive technology applications have been prioritized for patient-centric immersive solutions.

Immersive technologies can help with distraction therapy. Patients are often anxious, which is known as white coat syndrome.[35] Immersive technologies can help provide an immersive experience for patients to tour a health facility visually, to help patients cope with pain, and to ease children's anxiety.[36] For example, there is a project Distraction Therapy for Cancer Patients,[37] which Samsung ran under a collaboration of Start VR and Chris O'Brien Lifehouse. When patients

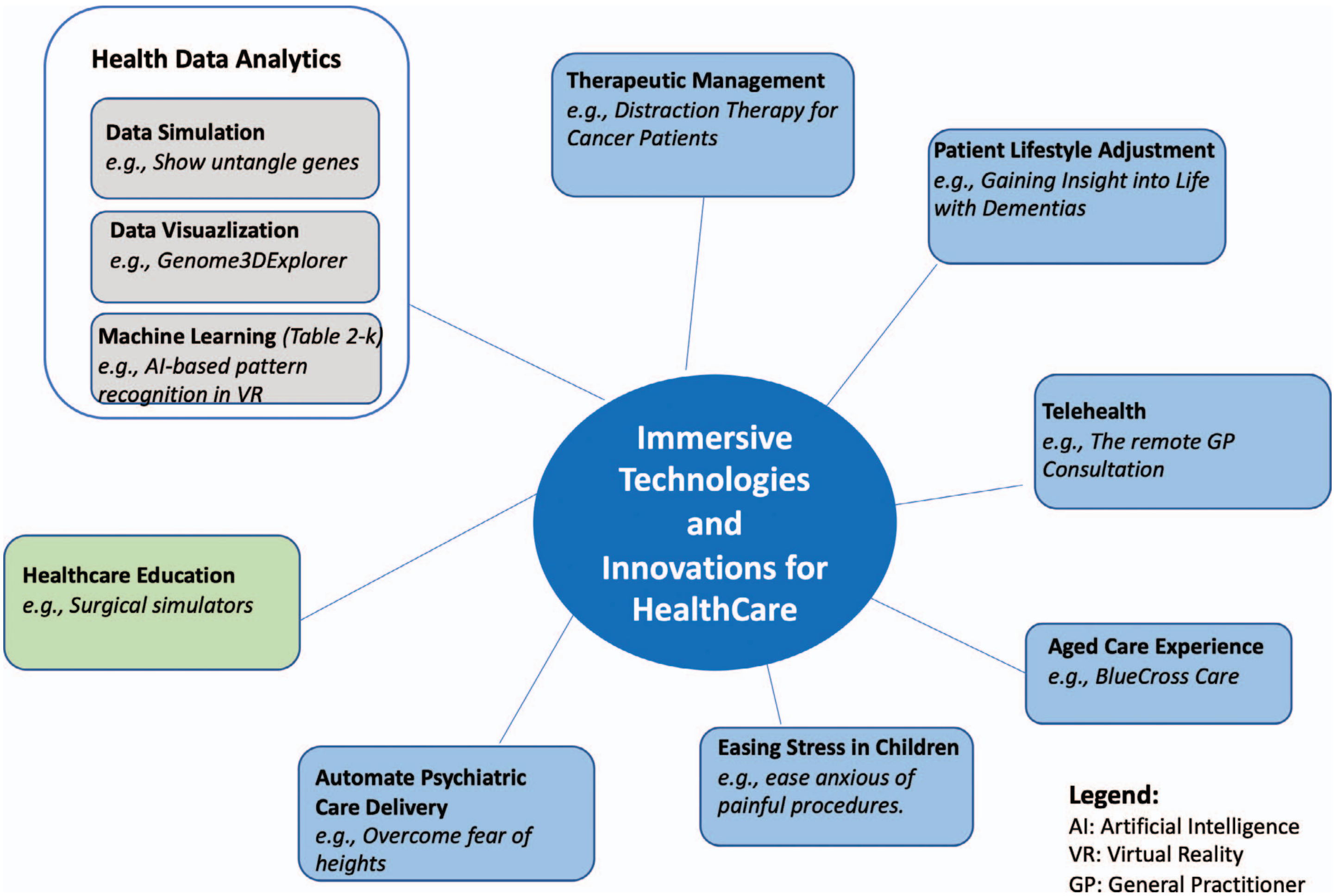

Figure 1. Immersive technology has been used in the healthcare domain in many ways including health data analytics. Each branch stands for one type of healthcare domain that immersive technology is used for. See Tables 1 and 2 for additional details on each technology.

become worried about unknown outcomes during sitting and waiting for periods of time, the VR application allows them to escape the experience of chemotherapy and give them a perception of 3D blended space to temporarily forget what is going on. Also, such an immersive experience before surgery distracts patients and allows them to keep their spirits up.

Immersive technology is being used for Alzheimer's disease, for example, the project "Gaining Insight into Life with Dementias" created by Alzheimer's Research UK and VISYON.[38] An innovative smartphone app named "A Walk-Through Dementia" is provided to users with an immersive space to feel what it is like to live with dementia. The main goal of this application is to provide the users with a clearer view of the challenges that patients with Alzheimer's disease face in everyday life and give a feeling into the emotional impact of symptoms. The Android phones application uses a combination of 360-degree video and VR environments to illustrate how even the most common everyday tasks for someone living with dementia, such as making a cup of tea, can become a challenge. Immersive technology helps people to engage with the impact of dementia on a new level.[39]

In addition, VR can be used for remote GP consultation. One example is the Remote GP Consultation project, which is run by the Silver Chain Group.[40] This project made it possible for a nurse to check the patients' health data and consult with a remote holographic doctor enabled with AR technology. This project is seeking methods to help a nurse who needs to speak to a doctor but is busy helping patients, so he or she can look through Microsoft HoloLens[41] to see patients' data and speak to a holographic doctor. The HoloLens VR/AR/MR technology makes it possible for the doctors to stay in their current location while still helping out and finishing their job. The project can potentially save the healthcare system considerable time and money. Patients then could receive similar care in the comfort of their own homes.

Immersive technologies can be used for aged care, such as aged care project[42] run by a Melbourne aged care, called BlueCross Care. They use VR technology in aged care to enable elderly individuals to experience travel, adventure, aquatics, even classical concerts and theatri-

Table 1. Immersive technologies and innovations used in the healthcare domain

Solution	Reference Project(s)	Immersive Device	Outcome and Innovation	Contribution in Digital Health
Therapeutic Management	Distraction Therapy for Cancer Patients[37]	Samsung Gear VR headsets	Such VR experience before surgery allows patients to keep their spirits up by giving them a distraction.	Creates engaging immersive content and actions that positively impact the lives of patients with cancer.
Patient Lifestyle Adjustment	Gaining Insight into Life With Dementias[38]	Android phones application with the combination of VR environments and 3D video	An innovative smartphone app named "A Walk-Through Dementia" is provided to users with an immersive insight into the condition.	The application provides the users a clearer view of the challenges that patients with Alzheimer disease face in everyday life and gives a feeling into the emotional impact of symptoms.
Telehealth	The Remote GP Consultation project is run by the Silver Chain Group[40]	Microsoft HoloLens[41]	The technology allows nurses to use the hands-free data while they are at their in-home visits. Doctors can see live biometric data, see what the nurses are doing, and speak to the patients and the family members.	The HoloLens VR and AR mixed reality technology makes it possible for the doctors to stay in their location while still doing consultation job and helping out.[40]
Aged Care Experience	An aged care project[42] run by a Melbourne aged care named BlueCross Care	Specific VR system on a smart phone, goggles, and Bluetooth headphones	VR technologies enable elderly individuals to experience what they could not reach, for example, travel, adventure, aquatics, even classical concerts and theatrical performances, from their home.	Takes residents to their familiar places based on the Google Maps. Staff and family can also watch simultaneously on another device or screen to enjoy the VR experience.
Easing Stress in Children	Helps children feel less anxious for pain management using VR[43]	VR goggles	Distracts children by taking them on an underwater adventure with VR technologies. Children are visibly more relaxed and clinicians need less time to complete blood tests and other painful procedures.	Helps children feel less anxious when they have simple but sometimes painful procedures.[102]
	Distracts patients in pathology and emergency departments[44]	No specific device	An engaging and interactive 3D "virtual world" is provides an escape from the real world associated with needle-based procedures.	Immersive technologies help to reduce the fear and pain.
Automate Psychiatric Care Delivery	Psychiatric Care Delivery led by the University of Oxford's Department of Psychiatry[45]	No specific device	VR helps patients overcome their fear of heights and patients with schizophrenia silence the voices in their heads.	VR helps automate psychiatric care delivery, empower patients to confront the sources of their anxieties. The result is even better than expected from face-to-face therapy.
Healthcare Education	VR systems are used to assist surgeons in planning upcoming operations, train residents, and educate patients[52]	No specific device	VR is used in training skills such as laparoscopic surgery, education of orthopedic residents, gynecology residents, suturing, ultrasound, nursing procedures and paramedical interventions.[49]	Compared with those trained by conventional approaches, people trained by VR systems have fewer performance errors and higher accuracy.[54,55]
	MR and VR surgical simulators[53]	Active optical motion tracking system VICON allows users to in real-time track the motion of the surgical tools and plastic spine models	With a VICON motion tracking system, MR and VR are used to rasp procedure in the artificial cervical disc replacement surgery.	MR and VR surgical simulators can work as an indispensable part of physicians' training, and offer a risk-free training environment.

GP: general practitioner; MR: mixed reality; VR: virtual reality.

cal performances that they may have not been able to reach due to their age, from the comfort of their homes. Staff and family can also watch simultaneously on another device or screen to enjoy the VR experience.

Furthermore, immersive technologies can be easily accepted by children for easing anxiety. At St John of God Health Care hospitals, a promising future is seen in VR goggles that are used to help children when they have blood tests and other painful procedures to feel less anxious.[43] The immersive technology distracts children by taking them on an underwater adventure, and the children who are in the virtual world with the VR goggles

Table 2. Immersive technologies for data analysis

Solution	Reference Project(s)	Immersive Device	Outcome and Innovation	Contribution in Digital Health
General Data Analytics	iViz[67]	Oculus Rift VR goggles	Enables the user to easily select and shuffle which data parameters are mapped.	Shows large digital sky surveys data.
	Bader[68]	No specific device	Users can adjust the data and visualize the results and then collaborate on how to proceed.	Considered as the first immersive data analytics platform, it allows users to see the whole picture and real-time collaboration.
	Virtualitics[69]	No specific device	An innovator in the data visualization space that has an AI-driven feature.	This platform can help companies to get actionable insights quicker than with traditional data analytics tools and it also supports multiple users and faster decisions.
	3Data[70]	No specific device	Immersive 3D platform that is developed for enterprise IT and cybersecurity operations.	With this platform, users can "step into" the command and control of complex networks allows better and faster decisions.
Genomic Data Simulation	Shows untangling of genes[74]	HTC VIVE	With this technology, researchers can efficiently combine their data to gain a much broader understanding of how the organization of the genome affects gene expression, and how mutations and variants affect such interactions.	Combines data on the genome sequence with data on gene interactions to create a 3D model that shows where regulatory elements and the genes they control sit relative to each other. It makes it easier to understand the processes going on within a living cell.
	Molecular Rift[76]	Oculus Rift	Provides access to powerful cheminformatics functions.	Reflections on VR's future capabilities in chemistry and education.
	VMD[77]	6-degree-of-freedom input gadgets, and haptics accessories	Provides a classical molecular viewer with other features along with VR capabilities.	Supports immersive visualization and advanced input devices.
Genomic Data Visualization	Genome3DExplorer[79]	No specific device	The exploration is based on a well-adapted graphical paradigm that automatically helps to build a graph-based representation.	Visualize textual and factual genomic data based on adapted federator description language. Allows biologist to highlight some global topological characteristics of data.
	iCAVE[80]	No specific device	Visualizes large and complex biomolecular interaction networks in the immersive environment. Allows development with algorithms, data sets, or features.	The first freely available open-source tool that enables 3D visualizations of complex, dense, or multilayered biomolecular networks.
Genomic Data Analysis with Machine Learning	3Data[70]	No specific device	Immersive 3D platform that is developed for enterprise IT and cybersecurity operations.	With this platform, users can "step into" the command and control of complex networks allows better and faster decisions.
	Children Cancer Data Visualization Tool[83]	The tool can run on HoloLens and Oculus Rift	This tool can show the whole group of patients' data processed with AI algorithms in a 3D scatter plot and check a single patient's details.	Combines AI and VR to enable an important possibility of AI-based pattern recognition reporting results in a VR display.[32]

AI: artificial intelligence; IT: information technology; VR: virtual reality; 3D: three dimensional.

are visibly more relaxed. Moreover, when clinicians need to complete simple but sometimes painful procedures for children, using VR goggles can also reduce the time. Another similar VR research study is being conducted at Monash Children's Hospital and Monash University; the clinicians use immersive technologies to help distract pediatric patients from painful procedures in the Pathology and Emergency Departments.[44] With immersive technologies, the users are transported to an engaging and interactive 3D "virtual world" that provides an escape from the real world. When the painful procedure is performed, the fear and pain associated with needle-based procedures are reduced.

There are more possible applications of VR/AR/MR in the healthcare domain. Adult automated psychiatric care delivery can use immersive technologies as well. For example, the patients can be empowered by VR to confront the sources of their anxieties when maintaining their dignity and skirting painful consequences. The research study, led by the University of Oxford's

Department of Psychiatry,[45] shows that immersive technologies not only potentially help patients with schizophrenia silence the voices in their heads, but is also proven to help patients overcome their fear of heights. New evidence shows that the results are even better than what is expected from face-to-face therapy.

Physician- or Practitioner-Centered Immersive Technology for Healthcare Education

Immersive technology implementations for a physician not only have a distinct focus on the patient, but also concentrate on aspects of healthcare education for its better engagement feature. XR creates a computer-generated real or artificial 3D multimedia sensory environment and allows users to explore and manipulate it in real time.[46] Immersive technologies allow the human to percept the digital world as real and interact with objects and/or perform a series of actions in this digital world.[11] Through different levels of immersion based on engagement, empowerment, and self-actualization, immersive technologies also allow for a first-person active learning experience.[47]

Immersive technologies have the ability to enable the individualized repetitive practice of motor function while engaging and stimulating cognitive processes,[48] so the technologies are suitable to be used in training such skills as laparoscopic surgery, education of orthopedic residents, gynecology residents, suturing, ultrasound, nursing procedures, and paramedical interventions.[49] Immersive technologies provide a great way to teach and train surgeons, assist nurses and other medical professionals, and offer the next level of education in the healthcare domain.

Immersive technologies in surgery provide an opportunity to be fully immersed in a situation that is nearly identical to an actual operation.[50] Immersive technology such as VR can potentially improve and standardize both cognitive and technical skills and make it free from the demands of traditional clinical environments.[51] VR used for teaching purposes has already been successfully implemented in many clinics around the world. For example, Stanford University has a VR system that is used to help train residents, assist surgeons in planning upcoming operations, and educate patients.[52] The system also helps surgeons in the operating room by guiding them in a 3D space. VR and MR surgical simulators provide a risk-free training environment and can work as an indispensable part of physicians' training. For example, MR is used for rasping procedures in the artificial cervical disc replacement surgery with a VICON motion tracking system.[53] VICON is an active optical motion tracking system that allows users to in real-time track the motion of the surgical tools and plastic spine models. Evidence showed that people trained by VR/MR had lower performance errors and higher accuracy than those trained by conventional approaches.[54,55] Immersive technologies also start to be used in digital health data visualizations because users potentially engage more when in the immersive environment to understand the patterns and insights from the complex big health data.[56,57]

IMMERSIVE TECHNOLOGIES FOR VISUAL ANALYTICS OF HEALTH DATA

VR Benefits Visual Data Analytics

As immersive analytics combine the use of immersive technologies, natural user interface, and visualization, best-known techniques to achieve transparent cognitive experience and to enable visual analytics in the immersive environment,[58–60] it provides novel opportunities to enhance digital data analysis. As a platform for interactive, collaborative, visual exploration, VR is one of the immersive technologies and is also used as big data visual analytics. VR for data visual analytics has advantages such as more data visualization possibilities, intuitive approach, multiple users, and elimination of distractions.[61] VR technology can lead to a demonstrably better perception of a data scape geometry, more intuitive data understanding, and better retention of the perceived relationship in the data.[62] Interactive 3D VR platforms can reduce distractions and apply more interactions to maintain attention and focus on learning.[63] VR allows users to interact with the data surrounding them just like the data are in front of, behind, above, and to either side of them. VR uses a human's natural instinct[64] to think about and process data in multiple dimensions and makes it possible to communicate data attributes in numerous positions.[65] VR can make data analysis more fun, as it allows "stepping into the data" and avoids the exercise of pouring over complex data. More humans then can be involved in monitoring machine learning models to ensure the machine's decisions continue to be ethical, fair, and reasonable.[66]

Some VR platforms for other domain data analysis combine all the modern technologies together to get better data analysis outcomes, as shown in the top part of Table 2. For example, iViz[67] is VR for a visual data analytics tool that uses Oculus Rift VR goggles as a display device to show large digital sky surveys data. The user interface for iViz enables the user to easily select and shuffle which data parameters are mapped to determine the optimal mapping choice for a given scientific. This flexibility allows for a more powerful visual data exploration and discovery. Bader[68] immersive data analytics platform allows users to see the whole picture and real-time collaboration. Users can adjust the data and visualize the results and then collaborate on how to proceed. Virtualitics[69] is another VR platform that is an innovator in the data visualization space with an AI-driven feature. This platform can help practitioners get actionable insights that are quicker than with traditional data analytics tools, and it also supports multiple users. 3Data[70] is another VR 3D platform that is developed for enterprise information technology and cybersecurity operations. With such VR platform, users can get illusory experiences that they are in reality, "stepping into" the command and control of complex networks.[71]

VR for Health Data Analytics

Genomic data is getting bigger and more complex for advanced computing technologies. For example, a single-cell data set can have tens of thousands to millions of cells and hundreds to tens of thousands features created by a total-seq platform.[72] For complex health data, especially genomic data, VR is a remarkable technology to control the subconscious mind and understand patterns in big data sets efficiently.[73] Immersive technology is used for health data analysis in many ways, such as data simulation, data visualization, and the combination of data visualization and machine learning. The bottom part of Table 2 shows some immersive using healthcare data analysis.

Immersive technology can be used for genomic data simulation. For example, VR is used to combine data on the genome sequence with data on gene interactions to create a 3D model that shows where regulatory elements and the genes they control sit relative to each other. It also makes it easier to understand the processes going on within a living cell.[74] With this technology, researchers can efficiently combine their data to gain a much broader understanding of how the organization of the genome affects gene expression, and how mutations and variants affect such interactions. Immersive technology is also used for showing the molecular structure of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[75] Immersive environment tools such as Molecular Rift[76] and VMD[77] help to improve the understanding of the virus action mechanism and to accelerate the drug discovery process. Using VR to visualize such genomic data is important because the human brain is very good at pattern recognition, and people think visually. Immersive technology can assist microscopy data visualization and colocalization analysis.[78]

In such systems, fully immersive manipulation of the microscopy data and analysis tools are offered by using hand gestures interface and a conventional gamepad as an alternative input method. The user's perception in data handling is maximized in the immersive environment.

Immersive technology is used for genomic visualization in many projects such as Genome3DExplorer[79] and iCAVE.[80] The immersive tools help biologists highlight some global topological characteristics of data and make better decisions based on the visualizations. Some data visualization tools combine VR and AI as a better solution for health data analysis, such as Deep Learning Development Environment in Virtual Reality.[81] It is also used to explain deep learning algorithms. This software runs as a standalone application on the Oculus Rift VR headset.[82] Another health data visualization tool, the Children Cancer Data Visualization tool,[83] already combines AI and VR to enable an important possibility of AI-based pattern recognition reporting results in a VR display.[32] This tool can be used to show the whole group of patients' data processed with AI algorithms in a 3D scatter plot, and then individually check each patient's detail. It can also zoom and rotate the visualization plot, compare genes among several patients, as well as interact with users and show the comparison visualization between selected patients. The tool can run on different VR environments such as HoloLens and Oculus Rift. It allows the users to see and manipulate the data in different and immersive ways in comparison with ordinary displays and portable devices. Then the users can look and feel the patients' avatars moving and positioned in a cohort and interact with the 3D visualization.

An Evolution of Integrating Immersive Technologies to a Visual Analytics of Genomic Data

Visual analytics or machine learning platforms for genomic data analysis have been in the research domain for more than a decade. Genomic data research trends to integrate immersive technologies. For example, as shown in Figure 2, a genomic data visual analytic research project starts from focusing on statistics and data mining, and then on blending 3D visualizations to 2D screen and mobile devices, and recently focuses on building it to an immersive 3D VR environment. Machine learning models are also integrated into the genomic data visualization in the immersive environment.

Genomic data analysis focused on statistics and data mining before 2010, such as Kadupitige et al [84] created a "MINER" to apply exploratory analysis of gene interaction networks by machine learning from expression data. And then 3D visualization tools were developed, such as Nguyen et al[85] for visual analytics of clinical and genetic data sets of acute lymphoblastic leukemia. This paper highlighted methods to support the decision-making process by processing data mining, interactive visualization, analytical views and gene comparison. Then the research team created an improved work[86] for a novel 3D interactive visualization for medical data analysis. This work used better selection strategies to choose a group of data in a blended 3D environment. Machine learning models were then added to the 3D visualization models in the research, for example the study by Nguyen et al,[87] unlocked the complexity of genomic data of patients with rhabdomyosarcoma by using visual analytics. Then another interactive visualization work for patient-to-patient comparison was created by Nguyen et al.[88] This work improved the work by adding multiple interactions and provided a comprehensive framework solution for analyzing large and complex integrated genomic and biomedical data.

Following this, Khalifa et al[89] developed a visualization system for analyzing biomedical and genomic data

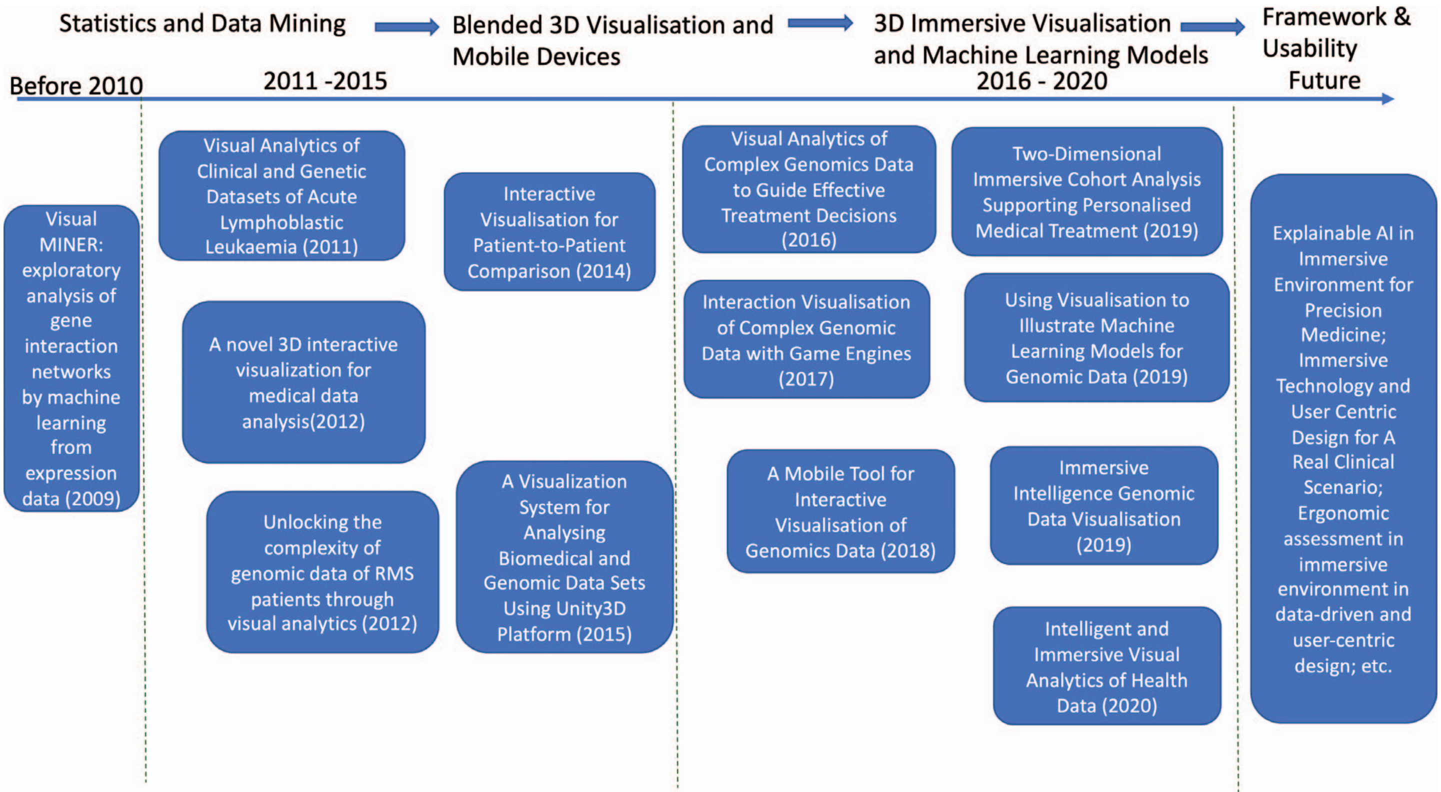

Figure 2. The genomic data analytics timeline that uses machine learning, mobile, and immersive technologies in the development evolution.

sets using the Unity3D platform. This system applied the use of a 3D platform to analyze biomedical and genomic data. Furthermore, Nguyen et al[90] used 3D gaming environments and interfaces to improve the user-centric interaction and exploration experience. Khalifa et al[91] started to integrate the game engine to create an interactive visualization of complex genomic data. It presented a visual analytics model that enables the analysis of large and complex genomic data using Unity3D game technology. Genomics data visualization was also extended to the other platforms, including mobile[92] and large- and high-resolution display.[93]

Some platforms combined machine learning models with 3D space visualization, such as that of Qu et al,[94] which used visualization to illustrate machine learning models for genomic data. New research should apply popular visualization techniques in biology fields, such as scatter plot and heatmap visualization to train genomic data and explain a decision tree machine learning algorithm. Some visual analytical tools have been built in the VR platform; one of them was by Lau et al[83] for immersive intelligence genomic data visualization. This tool visualizes a 3D space scatter plot with data processed by a machine learning model. A review [95] of intelligent and immersive visual analytics of health data discusses the intelligent visualization, AI, and immersive technologies in the health domain with various VR case studies in genomic data visual analytics.

DISCUSSION

Immersive technology can potentially improve humans' perception. Humans are born into and are best adapted to a multidimensional world. Immersive VR technology allows the users to see, hear, smell, or touch things as in the real world.[96] VR makes it possible for sensory information processing in more natural conditions.[97] More and more VR clinical uses are created because of the benefits of its warm, inviting environment for engagement, and distraction-free and therapeutic care environment.[96]

Immersive technology, especially VR, is a potential technology for collaboration among different teams in different locations. Most VR is single user now, but some have or can be changed to multiple users. This enables the opportunities on the technology side for developers to create and share multi-user immersive MR experiences.[98] VR has the ability to collaborate in 3D environments and link data with natural human pattern recognition to uncover multidimensional relationships in data and to extract actionable knowledge that may not be discoverable by any other means.

Immersive technology as a promising technology combines different data analysis frameworks such as machine learning, and data visual analytics. VR can bridge knowledge gaps between experts and newcomers in the digital health domain.[99] With better perception and natural interaction ability, VR can be used to visualize and explain complex machine learning models to clinical users to improve trust. Researchers use immersive technology to assist in explaining AI in the medical domain, such as for simulation-based training in surgery and medicine[100] and reinforcement learning as a tool to make people move to a specific location in Immersive VR.[101] More and more research projects seek to combine XR with machine learning approaches to improve medicine or precision therapy through digital data genetic analysis.

Immersive technology has been used in the health industry for both the patient and the professional, such as aged care, remote GP, dementia, child anxiety, psychiatric care, distraction therapy, education, and health data analytics. These existing and ongoing projects are already helping to enhance patient outcomes, improve medical education, and interact with data visualizations in an intuitive way. All the projects are very new, most started from 2014, and most are ongoing projects. VR used for the digital health domain still needs time to develop its full potential. Data visualization starts to extend to the VR environment for its more interactive and more natural way to understand big genomic data.

Although there has already been some research on immersive technology for genomic data visual analytics, it is still in the early stages. Big complex genomic data analysis needs innovative immersive technology to improve human engagement and find more patterns and insights. Knowing how to make the immersive technology applications useful for the domain users also has a long way to go. Future research needs to know "why" before "how" by collecting end users' domain knowledge before and after developing the genomic data visual analytics tools in the immersive technology environment. The users' real requirements should be merged into the tool design and development. The immersive technology projects for genomic data visualization have the ability to inherit and integrate the previous research outcomes such as derived through AI and add new features to make the outcome really useful for domain users. Usability studies with domain users also need to address more ergonomic assessment to improve data-driven and UCD with immersive technology.

CONCLUSION

This paper provides a comprehensive review on the current immersive and XR technology projects for healthcare, XR for medical domain education, and health data analysis, especially genomic data visualizations. We also use an evolution of a genomic data analysis research case study to demonstrate how VR integrates with other technologies such as AI and mobile devices to solve clinical questions. Immersive technology applications for healthcare are still in their infancy.

Within the authors' knowledge, there are few works on genomic data visualization in VR environments, especially on how to integrate different technologies such as machine learning and game theories. The potential remains largely unexplored for VR used for genomic data analysis. A new framework may be useful for analyzing and interacting visualization genomic data in the XR environment. The new framework should aim to solve real clinical cases such as combining data processing, machine learning models, visual design and interactions, game optimization, and visual analytics with domain expert knowledge to deliver an effective analysis process to the domain users. New usability studies should evaluate the integration of all the preceding technologies to analyze complex genomic data in a user-friendly way. Ergonomic assessment in the virtual environment is also needed to get the immersive space design more data-driven and user-centric. Moreover, the genomic data visualization user interface also needs to improve to better use the XR and 3D environment as a more natural way of interacting. Last, the genomic data analysis ways need to combine different analysis strategies such as machine learning and add suitable explanations to make the results useful, trustable, and interpretable for domain users. Immersive technology as an innovative technology will be used more and more to improve the accuracy and effectiveness of current procedures and enhance the capabilities of humans in the digital health domain.

The individual nature of XR implementation has not allowed for widespread adoption within larger healthcare networks yet, so this paper could not review leading examples of widespread immersive technologies, nor study the quantifiable impacts. Immersive technologies combined with cameras and cloud servers have the potential to lead to widespread adoption. This article might exclude some potential works in other languages because we only searched to find the immersive projects written in English.

Acknowledgments

The authors thank The Sony Foundation and Tour de Cure Foundation for funding support under the Virtual Reality Cancer Research Scheme.

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