### 1 Virtual Reality: A Railroad for Structural Bioinformatics towards

### 2 Advanced Cancer Research

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#### 11 ABSTRACT

12 Technology has been a part of everyone's life for decades now, and its impact on our lifestyle only 13 seems to increase with time. Considering applications in the field of scientific research till date, it has made exponential advancements and created a new hallmark. 'Virtual Reality' is one of the 14 15 most applicable, impressive and recently uplifted technologies that has been implemented in 16 numerous approaches already. In the light of structural biological studies, virtual reality technology 17 enables immersive 3D visualization of molecular structures, interactions, mechanisms etc., and 18 molecular modelling at the atomic level facilitating a better understanding of the 'science behind 19 the scene'. In molecular cancer studies, this helps peruse and diagnose defective root causes and 20 unveil effective therapeutic approaches. Although this technology has primarily interested a huge 21 number of researchers and institutes performing structural bioinformatics studies, many researchers 22 across the globe and a large section of the public are still in the dark about its practicality and 23 benefits, some of the main reasons being lack of exposure and the issue with affordability. Thus, 24 besides shedding light on the various ways in which virtual reality has been lately implied to cancer 25 research and therapy, this article aims to promote and encourage usage of a simple, cost-effective 26 platform for 3D immersive visualization of molecular structures for the insufficiently funded 27 community to begin with experiencing molecular virtual reality. It also intends to propose a new 28 permutation of concepts to contribute to an advanced approach in structural cancer studies where 29 scientists can superlatively immerse into the cellular environments and seek answers by virtually 30 communicating with the entities in the microscopic realm. This versatile technology has thus far 31 inevitably proven to possess an enormous potential and is already underway in revolutionizing 32 education, training, scientific research and medical therapy. This article aims to educate more 33 people about prevailing VR technologies and primarily to help accelerate this futuristic technique 34 in cancer research and therapeutics. Albeit leading to a progress in scientific exploration, it could 35 also spread hope and soon assist in upgrading the quality of living especially for cancer victims.

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#### 37 Keywords:

38 Virtual reality (VR), 3D immersive visualization, head-mounted display (HMD)/VR headset,

39 CAVE, VR hand controls, data gloves, haptic technology.

#### 40 INTRODUCTION: The VR Story

41 Virtual Reality (VR), as the name says, is a simulated environment which does not exist in the real 42 world. Although it is visually experienced by a user wearing an external head-mounted display and 43 operating a specialized computer, it still tingles with their sensory system and creates a practical notion that he or she is present inside an artificiality<sup>1</sup>. The feature of immersive virtuality that this 44 45 technology indulges in is considered one of the pivotal hallmarks in the field of technology and has thus helped mankind to lay a bridge towards a futuristic style of research, development and 46 computing. Since the second half of the 20<sup>th</sup> century, scientists started to prove that augmented 47 reality is no longer just a made-up story in a comic but rather a complexly programmed 48 49 environment set for an individual to experience in real time.

50 The history of 'Virtual Reality' indicates that its concept and application in the real world was 51 inspired by science fiction. A short story titled "Pygmalion's Spectacles" produced by Stanley 52 Grauman Weinbaum (1935) describes unreal experiences that a character undergoes due to a virtual environment holographically projected by a pair of goggles<sup>2</sup>. Later, Morton Heilig, a 53 54 cinematographer, constructed a type of immersive theatre cabinet which could apparently evoke 55 all the senses of the user, hence the name 'Sensorama'. He invented the first ever head-mounted 56 display (HMD) called the 'Telesphere Mask' and patented it in 1960 even before patenting his 57 Sensorama in 1962. The next pioneer in the field, Ivan Sutherland, developed the 'Ultimate Display' 58 in 1965 where users could interact in the artificial environment realistically. Ivan also stated that 59 an empty room with a chair and a computer could literally be transformed into the 'Wonderland 60 into which Alice walked' through the ultimate display with proper programming. The VR HMD 61 he created in 1968 with his student, Bob Sproull, was disadvantageously heavy and had to be 62 suspended from the ceiling. Graphics generated by the computer were also poor in quality at the time. In 1987, Jaron Lanier, the founder of VPL (abbreviated as Visual Programming Lab) began 63 calling this technology "Virtual Reality" after which the name was rapidly accepted across the 64 globe. His company produced the 'data glove', the 'Eyephone HMD' and was the first to start 65 selling them contributing to a huge development. The last decade of the 20<sup>th</sup> century led to a surge 66 of VR-based games and popularized the technology through movies too. Publicly accessed arcade 67 68 machines launched by the Virtuality group indulged people to wear VR goggles, immerse in 3D 69 display and also offered multi-player gaming experience. A couple of years later, in 1993, SEGA

introduced its VR headsets comprising of inbuilt stereo sound and an LCD screen on the inside but failed to enter the market due to technical faults. Similarly, the Nintendo Virtual Boy, a portable gaming console with 3D graphics, also failed commercially due to lack of software support, graphic colours and users' discomfort while wearing it. Movies such as *Lawnmower Man* (released in 1992, inspired by the company VPL) and *The Matrix* (released in 1999) had massive impacts in the film industry and promoted the idea of augmented reality<sup>3</sup>.

76 In the 21<sup>st</sup> century, with the exponential advancement of technology, 'Virtual Reality' has seemed 77 to have seeped into numerous aspects of development. Not only do the gaming industries utilize 78 this technology extensively in the present day but even architectural organisations, research 79 communities, medical and educational institutions etc., seem to be keeping up their pace. Oculus 80 VR, the most successful company to manufacture VR headsets released its product Oculus Rift in 81 early 2016. However, it was bought by Facebook in 2014 and is considered a division of Facebook 82 Inc. since then. Similarly, more internationally popular companies have taken a leap towards 83 development using the VR technology. Google marketed their product 'Google Cardboard', a 'do-84 it-yourself' headset which needs a smartphone to be slipped inside it before experiencing an 85 immersive view. Sony, Samsung and HTC have also popularized their products in the market 86 successfully. These products have enthralled and helped a huge number of institutions and 87 organisations across the globe to think in a broader perspective and identify futuristic approaches.

Apart from VR technology having greatly aided in entertainment, psychological, educational 88 89 aspects etc., this article is going to focus on the medical accomplishments that VR is responsible for. Cancer research and therapy, being the topic of focus in this article, has made an advancement 90 91 due to VR technology in the last decade. To treat patients undergoing painful therapies against 92 cancer, VR has made a grand entry into the field as a different form of ailment to alleviate mental and physical stress<sup>4,22</sup>. Apart from aiding in numerous medical approaches to ultimately help 93 94 patients suffering from cancer and providing them with emotional support and encouragement<sup>5</sup>, 95 VR has shown great potential to improvise structural bioinformatics research. The idea of visualising, modelling or examining a molecule in an immersive 3D space is a huge improvement 96 97 compared to doing the same on a conventional 2D computer screen. The provision of interacting 98 with objects in the virtual environment by only making bodily gestures and not having to 99 necessarily stay put in one place makes it much more relaxing, easier, and faster for users to 100 understand the environment and perform their tasks. With these privileges, VR has provided us

101 with the most futuristic manner of performing biological research at the molecular level and it is

sure that this technology is going to elevate the scope of structural bioinformatics in the upcomingyears.

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#### 105 **PRACTICAL RELEVANCE**

#### 106 Virtual Reality – Cancer: In Medical Training and Therapeutics

107 Wang SS et al (2012) studied the value of VR during the planning of resections of tumours in the 108 sellar region of 60 participative patients. In this case, VR technology helped neurosurgeons with 109 3D images of the anatomy in the sellar region after all patients underwent CT angiographies. The 110 data provided by the VR system were printed and used as references by the doctors during surgery<sup>6</sup>. 111 Essig H et al (2011) claimed that a technique, computer-assisted preoperative planning or 'CAPP', 112 helped to improve 3D virtual marking of anatomical specimen and mapping of macroscopic 113 tumours, important surgical sections, margins etc. This technique can be used to store the 114 information in a particular format and later be shared with oncologists, pathologists etc., in order to specifically illustrate the patient's tumour data<sup>7</sup>. Zanzonico P talked about a clever approach 115 116 undertaken by Sgouros G et al (2011) where VR is considered a much healthier alternative to 117 diagnose cancer patients compared to traditional clinical practices which involve imaging 118 procedures using potentially harmful radiation which could increase the risk of cancer<sup>8</sup>. The year 119 2011 also introduced the Robotic Surgical Simulator or 'RoSS', a virtual reality simulator to train 120 aspiring surgeons. This study involved a cohort which included surgeons experienced with robotic 121 surgeries. 88% of the group strongly felt that it is appropriate for training and testing an individual's 122 skills before their participation in the actual operation theatre, and 77% thought that this novel 123 invention is fit to be certified in robotic surgery<sup>9</sup>. In favour of the same concept, Anupama 124 Rajanbabu et al (2014) stated that training surgeons with robotic approaches are imperative even in India, by using VR robotic simulators before a live surgery<sup>10</sup>. Whether robotic surgeries, manual 125 brain tumor resections which may involve VR simulators like NeuroTouch<sup>11</sup>, 3D VR simulations 126 using the Dextroscope system for pre-surgical procedures<sup>12</sup> or 3D anatomical study of tumors 127 which is superior to existing imaging techniques<sup>13</sup>, it is imperative that global education and 128 129 training systems should start keeping pace with such technology in order to improve manual

130 performance during pre-surgical and surgical procedures, as suggested by Lendvay TS et al 131 (2013)<sup>14</sup>. Endoscopy (importantly upper endoscopy) is the most probable test carried out to detect 132 stomach cancer<sup>15</sup>. Being a non-surgical procedure, endoscopy too has also found its way out of few 133 complications due to the applications of virtual reality. Professionals in this field were introduced 134 to and trained in using a VR simulator as practice. Thus, during real-time operations, patient's 135 discomfort and the procedure time significantly decreased when the job was handled by a group 136 trained by the simulator. In 2005, this trial which involved many gastroenterologists had strongly supported the plan of adding simulator-training sessions to the endoscopy education syllabus<sup>16</sup>. In 137 138 the field of Urology, compared to conventional cystoscopy, VR has much aided clinicians in 139 examining the interior of bladders through virtual images and predict the probabilities of cancer<sup>17</sup>.

140 Although this powerful technology leads to futuristic approaches to enhance training and practice 141 in the surgical field, there persist few limitations at present such as high maintenance costs, high 142 power consumption or limited battery life of the machinery, heavily sized devices, bulky and 143 unhandy cables, ethical obligations while handling patient data and using recordable VR HMDs 144 during medical protocols etc. Apart from undoubtedly becoming a part of these practices very soon, 145 it will turn out to be a challenge to tackle and consider their advantages over demerits in all aspects 146 of medical care<sup>18</sup>. But some techniques may eliminate the need for burdensome cables and heavy 147 machinery. One of them being the ones which have been used for immersive visualization and 148 study of computed tomographic (CT) images in 3D virtual reality, in the year 2013. Here, the user 149 can interact with the data and study it in his/her own visual perspective by wearing a HMD and a 150 data glove. This has won over the conventional old-school infrastructure of viewing multiple 151 images captured in different angles in 2D. Although it is mentioned that this technology has not 152 been actively implied clinically yet, it does offer chances to improve and optimize medical 153 operative planning and training<sup>19</sup>.

Another simple and efficient way by which cancer patients have been benefitted involves only a VR headset and a pair of headphones to be worn by them. This introduces and helps the individual participate in a desired virtual environment and thereby deviates his/her mind from the unpleasant physical ambience, aiding in their psychological and bodily endurance against bothersome treatments and overcoming distressful symptoms<sup>20</sup>. This technique which electronically simulates a separate visual world also triggers the sense of touch and hearing corresponding to the augmented

image that the person is interacting with<sup>21</sup>. Thus, it can stimulate the secretion of 'happy hormones' 160 161 in cancer patients consequently minimizing physical and mental stress<sup>22</sup>. Mary Dacuma (2016) 162 mentioned that, according to scientific research and demonstrations, the advantages of VR included 163 reducing fatigue and side effects while cancer patients underwent chemotherapy, and the ones who 164 experienced VR seemed to face lesser negative psychological symptoms and improved 165 emotionally<sup>23</sup>. Schneider SM et al (2011) experimented on a cohort of patients suffering from 166 breast, colon or lung cancer. Diagnosis, being the strongest predicting factor of the study, explained 167 that those suffering from colon and breast cancer perceived time to have passed faster while receiving chemotherapy treatment<sup>24</sup>. However, Schneider SM and Hood LE (2007) stated that 168 169 although patients say that chemotherapy treatments seem shorter and better with experiencing VR 170 as a distraction intervention, their findings confirmed that VR only helps patients tolerate the 171 treatment and not necessarily improve symptoms associated with chemotherapy. On the other hand, 172 patients being able to simultaneously enjoy and tolerate their symptoms very well, and VR being 173 a cost-efficient distraction technique for chemotherapy, are few reasons why it is suggested that it 174 should be implemented clinically to treat the ones are prone to suffering. While the HMD was easy 175 to use for the patients, they mentioned that they did not face cyber-sickness and it was found that 82% of the participants were keen to experience VR along with therapy again<sup>20</sup>. Steven-Charles 176 177 Jaffe, American producer, director, writer, CEO of Springbok Entertainment (2016), after having 178 supported his daughter battle cancer in a hospital, remarked that the capability of VR technology 179 to virtually teleport cancer patients away from the torment of chemotherapy or from the hospital's 180 constrainment is critical for them to be in contact with positive experiences. He expressed his 181 gratitude to collaborate with Keck School of Medicine and USC Norris Comprehensive Cancer 182 Center as a parent of a cancer survivor and mentioned that VR will fill the void in chemotherapy and help support patients for better health<sup>23</sup>. 183

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#### 185 Virtual Reality – Cancer: In Biological Research and Development

The big question that intrigues today's society is if Virtual Reality can ever develop to an extent when it could genuinely replace reality<sup>25</sup> so that we use the technology to interact with things and perform tasks realistically more efficiently. Like the common objects that we see and interact with frequently in the real world, VR has significantly proved to us that it can do so too. We can even expect this technology to become a colossal trend and take over our lives in the future. On the other

hand, what is more challenging for scientists is to virtualize life at the cellular and molecular level
based on reality. Apart from conventional medical research studies, this technology has a strong
potential to extensively aid researchers to indirectly/directly help patients fight cancer.

194 Dr John McGhee, director of 3D Visualization Aesthetics Lab<sup>26</sup>, University of New South Wales, 195 Australia, is one of the very popular scientists dealing with this technology. He leads a team of 196 researchers and has made it possible to virtually travel on a living cell and even look inside it to 197 study its inner dynamics by wearing headphones, HTC Vive VR headsets and using its hand 198 controls. He demonstrates this by maneuvering through different locations of a cancerous cell's 199 outer surface using a switch on the hand control, and shows viewers how a targeted nanoparticle 200 gets absorbed by the cell. Moreover, Dr Angus Johnston from Monash University, who designs 201 mechanisms for delivery of nano-sized drugs, states that a close-up study on the structural 202 properties of the drug or vector such as its size, shape etc., is the key to decipher the mechanism of 203 drug uptake, aiding in drug designing, and to ultimately fight cancer. The switch also allows Dr 204 McGhee to enter the cell's cytoplasm through a virtual portal. He further virtually penetrates his 205 head into a mitochondrion to view its inner structure and confidently shows us how we can now 206 immerse into a desired molecular environment and perform studies on every detail in 3D by just 207 physically walking around. Dr Kara Perrow, University of Wollongong, mentions that this 208 technology can certainly help to design drugs and nanotherapies. Dr Johnston who also contributed 209 to the development of the model with Dr McGhee, agrees that our understanding of drug 210 interactions will evolve for the better. This visualization of a breast cancer cellular system in VR 211 was built by developing its high-resolution data (taken from the University of Queensland) into a 212 3-dimensional mesh using the same technology employed in gaming industries. Colours, textures, 213 animation etc., were computationally added to the same 3D data by designing experts in Dr 214 McGhee's laboratory to impart a naturalistic feel when studied in the virtual environment. Dr 215 McGhee states that it was the first time in history that such an interactive VR model was developed 216 based on data from an actual cell. Although, this demonstration did not include an explanation on 217 targeted drug delivery to endosomes<sup>27</sup>.

The experience of studying molecular structure and dynamics at the cellular level in VR is currently meant for educational purposes, but on the other hand, Dr McGhee has collaborated with Dr Steven Faux, director of rehabilitation at St. Vincent's Hospital in Sydney, on another project to

221 rehabilitate stroke patients with virtual reality using the Oculus Rift headset. Here, Dr McGhee is 222 responsible for creating a virtual trip inside the patient's inner organ system after the MRI or CT 223 scan image is optimally filtered (and the inappropriate parts of the image are removed) by a 224 neuroradiologist. Dr Faux said that the impact on patients was remarkable and they have genuinely understood what went wrong in their body because of Dr McGhee's work<sup>28</sup>. For example, patients 225 226 can literally travel inside their own arteries and observe the size and location of cholesterol 227 accumulation in 3 dimensions instead of trying hard to understand from a 2D image in the conventional way<sup>29</sup>. This technique could truly motivate patients to readily participate in their 228 229 rehabilitation. Moreover, other than hoping 3D visualizations to have a positive impact on scientific 230 discoveries by helping scientists to view their data from a new perspective, Dr McGhee also intends to create a virtual world where they can observe the movement of cancer cells in the  $body^{28}$ . 231

232 Parallely, scientists at Weill Cornell Medical College, New York City, have started employing VR 233 to even clearly study and comprehend the mutated genes responsible for evoking cancer. An 234 individual wearing an Oculus Rift VR headset is privileged to visualize and interact with the 235 molecular structures of proteins in immersive 3D space. This program introduced to the Oculus 236 Rift VR has been called 'IPM VR', named after the Institute of Precision Medicine. Its objective 237 is to make it convenient for researchers to identify the genetic mutative cause to cancer, and for 238 doctors and clinicians to further decipher the optimal treatment accordingly. Dr Oliver Elemento, 239 a specialist in precision medicine at Weill Cornell, says that it is only by studying a protein that a 240 genetic mutation can be discovered because the mutation functionally expresses itself only when a 241 gene is translated into a protein. A clinician can position him/herself as close to the mutation in 3D 242 VR unlike in flat, 2D images. Apart from navigating in VR in and around the protein structure, the 243 individual can even refer to 2D medical documents/reports of the patient inside the VR program 244 just by looking in the corresponding direction. Hand gestures help to zoom in/out, move 245 away/towards, scroll through patient's medical records and choose options to change molecular 246 representations for a better view of genetic hotspots and mutations. This could help the clinician to 247 identify a drug to target the specific molecular site and even bring fortune to the patient at the end 248 of the day. As for now, this technology is only available to research but this technology will soon 249 turn into an integrative platform among clinicians to deal with patient data and to even discuss 250 issues with experts from various fields in immersive VR, just by wearing the HMD. Alexandros 251 Sigaras, a research associate in Dr Elemento's team, thinks that the prices for VR equipment will eventually drop and every clinician will own a VR headset within a decade from now. He has been testing various VR platforms and been trying to quickly spread the word to clinicians along with Dr Elemento. Sigaras mentions that they intend to make medical professionals experience and grasp large quantities of information much faster. Fundamentally, it is believed that this technology will become the best way of linking genetic and health data in order to most favourably treat patients<sup>30</sup>.

258 CAVE (CAVE Automatic Virtual Environment) is another 3D-enabled technological, but Java-259 dependent, approach through which one can perform immersive computational molecular studies. 260 It is a physical platform which provides the user with a physical rectangular space to walk around 261 and interact the elements in the virtual environment without a conventional headset but with LCD shutter eyeglasses which give a 3D effect to the viewer's eyes<sup>31,32</sup>. The individual is surrounded by 262 263 large wall-like screens behind which powerful video graphics hardware are used to generate the 264 images<sup>33</sup>. These screens help him/her visualize the virtual world and even share the same 265 experience with another person simultaneously. This technology aims towards overcoming 266 demerits of HMDs. The first version of this technology was developed at the Electronic 267 Visualization Laboratory (EVL), University of Illinois in 1992 and then upgraded (as CAVE2) in 268 1994 at the National Center for Supercomputing Applications (NCSA), University of Illinois. 269 CAVE2 had a more dedicated objective of helping scientists visualize their data effectively. In 2000, the Vis Group at NCSA founded 'Visbox' to provide CAVE technology with upgraded 270 digital projection and graphics hardware<sup>32</sup>. The high-performance VR system even comes with a 271 272 tracking system, which tracks the user's movement and shifts the environment accordingly. A wide 273 range of studies can be performed, from visualizing anatomical images in 3D to studying molecular realms in an immersive virtuality<sup>31</sup>. About a decade ago, Visbox was experimented for educational 274 275 purposes at few universities in the U.S. and was brought to classrooms for the betterment of 276 students' learning. As a result, the cost and efforts spent by lecturers to build models reduced and the majority of students using VR did claim that they understood better. This research hoped that 277 this technology be implemented in a wide variety of engineering courses<sup>34</sup>. Back in 1993, Carolina 278 279 Cruz-Neira et al, EVL, University of Illinois, Chicago, researched on the behaviour of p21 protein 280 (translated by an oncogene) in association with a GTP molecule to function as a cell growth 281 regulator. A molecular dynamics (MD) simulation was performed in a CAVE to study this 282 potentially cancer-causing protein and its behaviour at a desired magnitude of detail. Viewers could 283 explore atoms and molecules by holding and rotating them virtually. They could also maneuver 284 and focus on a desired section of the molecular system during its dynamics simulation. At that time, 285 to enhance the experience, it was needed to improve the hardware and software interfaces, improve 286 the physical design of the wand (hand control provided with buttons) and tackle the severe memory 287 constraints of the CAVE technology (because computational programs tend to generate huge data and all of it are not required to perform visualization)<sup>35</sup>. Kamran Ahsan and Muhammad Shahzad 288 289 (2015) mentioned few different types of CAVE environments used for biomolecular research 290 including a VR-oriented software plug-in for PyMOL developed by a high-end visualization 291 company named 'Virtalis', to innovatively improve the user's comprehension of the relationship between molecular structures and functions<sup>36</sup>. As of today, even the institute of Weill Cornell 292 Medicine utilizes CAVE to easily visualize medical data in 3D with the upgraded version of CAVE. 293 294 It surely comes in handy to doctors and clinicians of various fields including oncology to study the 295 patient's body parts on the macro and micro-levels in virtual reality after the 3D view of images is 296 obtained from MRI scans. Alex Sigaras (2017) mentions that it is important to be able to 297 communicate with other people while studying the molecule in VR instead of standing alone in a 298 virtual room while visualizing it and thus they also prefer to extensively use the Microsoft 299 HoloLens HMD to interactively study cancer-causing proteins, mutations etc. in real time, and 300 simultaneously discuss with other people while the molecule floats in 3D space in front of them $^{37}$ . 301

#### 302 DISCUSSION

#### 303 Cost-Efficient Methods to Experience VR: For Learning and Molecular Visualization.

304 Virtual Reality has undoubtedly upgraded the style of research and discovery in many institutions 305 and organizations. Although these organizations can handle the expenses for the technology that 306 they use, they too face some minor disadvantages during its maintenance. This minor problem is 307 an obvious major disadvantage when referring to so many other institutions that simply cannot 308 afford it. This issue of affordability in the current scenario builds a barrier for ardent researchers 309 who aren't sufficiently funded and keeps them away from the privilege of experiencing VR in 310 biological research. YouTube has fortunately been providing everyone with VR and 360-degree 311 videos for about a couple of years now. Apart from enabling people to upload VR and 360-degree 312 videos onto its website, it also provides an option to its viewers to immerse into a virtual movie 313 theatre to watch any video on YouTube using a VR headset. This feature was officially launched 314 and has been actively utilized in Android and iOS smartphones till date. The requirements are quite 315 simple, all that are needed is a smartphone (Android or iOS-based) with the YouTube app pre-316 installed and a conventional VR headset like the widely known 'Google Cardboard'. Here's how 317 to experience immersion into YouTube's online videos: After the link (URL) to view the particular 318 video is accessed in the YouTube application on the smartphone, the user needs to just open the 319 setting and turn the VR mode on by tapping on the 'view in cardboard' option. The video is then 320 supposed to be watched using the headset; these headsets are simple, much cheaper ones which 321 enable smartphones itself to be inserted into them after which the user experiences an immersive 322 feel. Even though there are many different brands of such headsets available in the market today 323 for a very reasonable price even for the public to possess, Google's do-it-yourself Cardboard HMD, which has been in action since 2014, makes it more convenient and cost-effective for individuals 324 325 to buy or to even make a smartphone-insertable headset for themselves using cardboard material 326 and some simple stationery.

327 Regarding molecular biological research and molecular visualization in the field of Structural 328 Bioinformatics, researchers and scientists can now have a basic immersive experience in 329 visualizing proteins in virtual reality using a VR headset without the need of owning any expensive 330 or sophisticated devices. To view a structure file from the Protein Data Bank (PDB), an individual 331 does not have to own an Oculus Rift or any such expensive headset, nor does he/she have to view 332 it on a 2D computer screen. There is an intermediate which is a simple, efficient way of 333 experiencing VR along with 3D immersive molecular visualization. Autodesk, an American 334 multinational software company, created a unique web-based molecule visualization tool 335 (https://moleculeviewer.bionano.autodesk.com/) to achieve this intermediate so that everybody 336 including students and learners can afford to view molecules in VR. With an access to the internet, 337 users can download or directly import a structure onto the molecule viewer platform from PDB, 338 view it from different angles, take snapshots, measure distances, change representations and 339 colours to acquire vibrant and high quality images etc., and create a unique URL for their saved 340 work on the laptop or desktop computer. The same URL helps share their data with others or be 341 pasted in a smartphone's internet browser to view the saved structure in a virtual environment using an ordinary VR headset<sup>38</sup>. After performing several experiments to visualize proteins in immersive 342 343 VR using Android smartphones, Mozilla Firefox resulted to be the fastest and most responsive

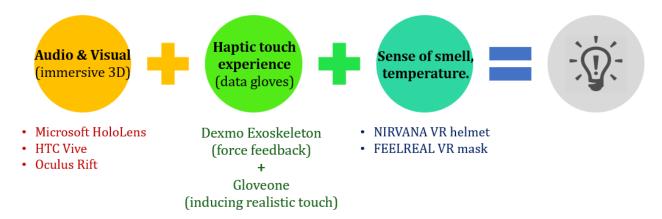
Android browser for Autodesk's online platform over Google Chrome, Opera Mini and UC browser. As a fact, Mozilla Firefox again seemed to respond quickest during preparation of molecular representations on desktop computers / laptops. For iOS and Mac OS based platforms, this online platform created by Autodesk is supposed to be optimized for use on the Safari browser.

#### 349 A Hypothesis to Revolutionize Structural Biological Research

350 This article proposes a hypothesis that some aspects of currently advanced VR-oriented gaming 351 technologies can be applied to cancer research and therapeutics as well. This technology which is 352 being referred to involves the sensation of 'touch' apart from just an immersive visual experience. 353 Apart from many great minds who have constructed VR gloves and enthusiasts who get to wear 354 them to interact with virtual objects, Mark Zuckerberg, CEO of Facebook, also appears in the big picture and says that the very new VR gloves recently built by Oculus which is to be connected 355 356 with its VR headset can help type on a virtual keyboard, draw in the air and even shoot webs like Spider-Man<sup>39</sup>. But the hypothesis proposed in this article is much more than just gaming or 357 358 touching virtual objects like the ones we interact with in the real world. Imagine being able to 359 'touch a biomolecular compound in a microscopic virtual reality and feel its physical characteristics 360 such as texture, mass, density, flexibility, temperature etc.' This could greatly aid especially in the 361 field of cancer research and create another trademark.

362 By combining the advanced 3D immersive audio-visual technology (incorporated into VR headsets 363 like Oculus Rift, Microsoft HoloLens, HTC Vive) with the latest gaming technology such as the 364 'FEELREAL' VR mask (an add-on compatible with four of currently available headsets) or the 365 NIRVANA VR helmet (both of which provide a sensation of smell, taste, a feel of the environmental atmosphere and temperature)<sup>40</sup> and with haptic data glove technologies such as 366 367 'Gloveone' created by NeuroDigital Technologies (which induces a realistic sense of touch of the virtual object)<sup>41</sup> and 'Dexmo exoskeleton' created by Dexta Robotics (which reduces the error rate 368 by providing a realistic force feedback by the virtual object)<sup>42</sup> (Figure 1), how would it be if we 369 370 were to equip researchers so that they virtually dive into the cellular level to study the activity of 371 cancer in VR after being privileged to even normally 'touch' the cancerous cell to easily understand 372 its morphological and biophysical properties, perform comparative research between a healthy 373 cell/tissue and a suspected tumour to study the differences and the stage of infection etc., without

374 having to consciously hold and operate the usual VR hand controls? During comparative studies, 375 apart from observing for the rate of proliferation of the cells, their behavior, influence of drugs or 376 external agents on the activity or viability of the cells etc., users could even feel their size, shape, 377 mass, density, surficial temperature, elasticity etc. at the same time by wearing a pair of data gloves instead of using hand controls. In this way, the limitation of conventional VR hand controls which 378 379 do not help much activate the human touch sensation can be overcome by the data glove technology 380 which genuinely creates realistic sensations corresponding to the individual's actions and 381 interaction with objects in the virtual world. These futuristic approaches unified may not replace 382 the usual computational manner of obtaining answers from the atomic and molecular realms, but 383 is speculated to be a humongous upgradation to the technique of virtual visualization. Other data glove technologies such as Manus VR gloves (integrated with HTC Vive)<sup>43</sup>, Hands OMNI glove 384 (sponsored by Virtuix)<sup>44</sup> and Control VR<sup>45</sup> also provide a sense of touch with respect to elements 385 386 in VR. Although they all employ different approaches, they do work towards intensifying a user's 387 VR experience.



#### 388

#### **Figure 1:** Combining various VR-associated technologies to form a new idea.

390 The illustrative equation depicts a concept of combining immersive 3D audio-visuals, sensation of touch and feel of the VR environment to build an all-in-one package and strengthen cancer 391 392 research through virtuality. VR headsets like Microsoft HoloLens, HTC Vive, Oculus Rift etc., 393 suit well for the 3D immersive audio-visual component. The NIRVANA VR helmet or 394 FEELREAL VR mask are best for the user to feel the surrounding temperature and smell the 395 virtual environment. Haptic data gloves like Gloveone and Dexmo exoskeleton combined would 396 provide appropriate force feedback and a realistic touch simultaneously. These technologies are 397 primarily targeted so that cancer research is made revolutionarily interactive and beneficial.

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399 Concerning applications in cancer research, all data gloves may fill some void by indulging 400 scientists to interact with or 'touch' virtual objects almost the way they do with things in the real 401 world. For example, the Dexmo exoskeleton glove exerts a force back on the user's hand while a 402 virtual object is touched or held. The exoskeleton does not allow the user to fully close his fist if 403 he/she is virtually holding something solid and rigid, due to which the user gets to feel the object's 404 mass and robustness in the hand. Otherwise, when an object is spongy, the glove allows you to 405 compress it up to an extent just like in reality. Utilizing the mechanism of force feedback (as 406 incorporated in the Dexmo exoskeleton created by Dexta Robotics) for its uniqueness and reduction 407 in error rates combined with the 'Gloveone' product (created by NeuroDigital Technologies) would 408 not only permit the non-scientific community to enjoy a higher grade of touch sensation during 409 learning, training, gaming etc. in VR, but also benefit scientists to experience molecular research 410 in greater depth by naturally involving them in an immersive environment where they can touch, 411 hold and communicate with substances superlatively, helping them understand the molecular 412 scenario better and thus acquiring more data.

This hypothesis, as depicted in figure 1, shares an opinion that the sensation of touch and feel while virtually handling and studying a previously detected cancer cell for instance, using a synergistic combination of data glove technologies as aforementioned, in collaboration with advanced audiovisual technology such as Dr McGhee's innovation (where it is even possible to virtually peep into the cell's inner structure) would greatly contribute to structural cellular/molecular research, transform the idea of computational study by visualization and modelling, and have a colossal impact on cancer research and therapeutics all the more.

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#### 421 SUMMARY AND CONCLUSION

The concept of Virtual Reality has prevailed among us for decades now, but has technologically been revamped and modernized lately. Today, it is already underway in taking education, medical therapy, scientific research including cancer research etc. to a much advanced level by employing sophisticated techniques and devices. Soon, the wearable products involved in this technology will probably become more affordable and available, and help instigate people to involve more with this innovation and spread awareness to ultimately uplift the lifestyle of society in many regions across the globe.

The idea proposed in this article, if practically implied, would help VR technology take an upswing and minimize the need for experts to create alternative models and spend extra efforts to understand molecular mechanisms. The sensation of touch and feel using haptic data gloves in addition to a realistic audio-visual experience with VR headsets would naturally involve a person's mind in the virtual environment to a greater extent. Till date, these technologies have been massively used to upgrade the standard of gaming. It is probably time that we implement it to facilitate advanced scientific research to indirectly help save lives from the wrath of diseases.

436 A combination of the technologies as hypothesized could help us make a breakthrough and climb 437 the ladder to experience the next level of futurism just like the way scientists have contributed 438 towards transforming mere imaginations to actual real-time experiences throughout the years. In 439 the current scenario, it does seem like the efforts spent towards improvising this futuristic 440 technology are never ending because the applications of it have proved to be of paramount 441 assistance in various scientific and educational fields, and the scope for improvement is 442 unknowingly vast. A possible justification for its further advancement is that 20<sup>th</sup>-century fiction 443 has now turned into a reality and possibly today's fiction will do the same soon.

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