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Virtual Reality: Beyond Visualisation

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Abstract

Virtual reality (VR) has recently become an affordable technology. A wide range of options are available to access this unique visualisation medium, from simple cardboard inserts for smartphones to truly advanced headsets tracked by external sensors. While it is now possible for any research team to gain access to VR, we can still question what it brings to scientific research. Visualisation and the ability to navigate complex three-dimensional data is undoubtedly a gateway to many scientific applications, however, we are convinced that data treatment and numerical simulations, especially those mixing interactions with data, human cognition and automated algorithms will be the future of VR in scientific research. Moreover, VR might soon merit the same level of attention to imaging data as machine learning currently has. In this short perspective we discuss approaches that employ VR in scientific research based on some concrete examples.

Keywords: virtual reality, microscopy, data visualisation, image processing, data treatment, human-in-the-loop

*Maxime Dahan died on the 28th of July, 2018.

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1. Introduction: Virtual Reality for Everyone

Virtual reality (VR) is not a new technology. It has played a role in a number of specialised industrial applications since the 1970s, notably in the automobile and military sectors. Yet, major recent advances in the technology
5 have made it amenable to new application domains not limited to education, psychiatry and scientific research. In fact, it is the convergence of three trends that has made this possible. First, desktop computers now have graphics cards sufficiently powerful to meet the real-time rendering requirements necessary for VR. Second, the latest iterations of VR technologies have been optimised
10 to ensure visual comfort and ergonomic usage. Finally, widespread consumer availability of VR headsets such as the HTC Vive, Oculus Rift and Windows Mixed Reality at affordable prices has democratised its usage.

VR, at its core, is a technology that uses real-world visual perception within entirely artificial computer-generated environments. Concretely, it is the combination of three effects. i) A total immersion experience. Users wear an optically
15 hermetic headset designed to block external parasitic light. ii) Stereoscopic vision. Each eye sees the same scene rendered from a slightly different angle, effectively mimicking how our eyes see the world in three dimensions. iii) Motion capture. The position of the user's head and controllers are detected with
20 either three or six degrees of freedom allowing precise tracking of movements within rendered scenes.

Through these effects, VR offers a unique visualisation context that heightens perception of volumetric details. Compared to visualisation on a conventional computer monitor, where users typically view three-dimensional (3D)
25 data as a passive observer, the immersive experience of VR allows users to literally enter inside their data in a manner that feels spatially realistic. For this reason, first-time usage experiences with VR are typically characterised by a surprise or “wow effect” by the user. While applications in entertainment (*e.g.*

video games and film) have largely driven VR technology, its use in the sci-
ences is still being elaborated. So far VR remains in early adopter laboratories
30 although emerging platforms will soon bridge gaps in adoption.

The immersive and interactive experience of VR offers a new way to observe
data. It is our view that it will play a critical role in spreading scientific knowl-
edge to the non-scientist and serve to attract students to the lab. Beyond this,
35 the new opportunities that VR and related technologies confer to the scientist
are so transformative that they may permanently change how work in the lab is
performed and prompt new scientific advances. In the following, we focus our
discussion on scientific applications of VR with a focus on its use in the labo-
ratory. We will limit discussions on the advanced technical strategies core to
40 any VR application (*e.g.* real-time volume rendering, memory management, file
management, etc.) to focus rather on applications and uses of VR. Finally, we
shall emphasise the integral role VR plays in *human-in-the-loop* data analysis.

2. Data Visualisation

Arguably the main advantage of VR for visualising scientific data is the free-
dom it grants users to intuitively explore and interact with their environment.
45 Objects can be observed from entirely arbitrary angles and vantage points, just
as we observe them in the real world. Interaction using specialised VR con-
trollers available with modern headsets can be performed with millimetre pre-
cision. This sense of realism translates to a fluid and natural-feeling experience
50 for the user, in turn allowing otherwise complicated spatial tasks to be per-
formed rapidly, often by orders of magnitude, compared to conventional mouse
and monitor configurations. Moreover, the simple act of moving within a VR
scene increases the likelihood to detect patterns of interest. VR naturally en-
courages exploration and curiosity-driven action, which are essential ingredients
55 to promote discoveries.

The generation of a VR scene comes at a high computational cost. A dif-
ferent scene has to be rendered for each eye (*i.e.* stereoscopy) at a refresh rate

exceeding 60 Hz (often 90 Hz is recommended) for smooth navigation. The sheer size and richness of scientific data makes this requirement particularly difficult to meet on some computing platforms. The most general approach for ameliorating rendering speed is by reducing rendered image quality, although graphics card manufacturers such as NVIDIA propose VR-specific features such as single-pass stereo rendering, headset lens-matched pixel resolution and multiple graphics card configurations to improve rendering performance. Efforts to unify all VR technology under a single framework such as OpenVR and SteamVR have simplified development, however upcoming features such as foveated rendering, environment mapping and inside-out tracking imply a prolonged technological turnover that will present challenges to the widespread adoption of VR for both the developer and consumer.

The visualisation of volumetric imaging data (*i.e.* image stacks) presents some particularly difficult challenges. The first of these is the design of a 3D look-up table or *transfer function* for efficient data visualisation. The transfer function assigns optical properties such as colour and transparency to each voxel of the visualised scene. It defines the physical rule of light propagation in the sample. Moreover, it ensures optimal information representation in the visualisation of the 3D image. This can mean allowing structures inside a cell to be seen from the outside while revealing the barriers between domains with different properties. An example of such a challenge is shown in a complex microscopy image of the mouse neocortex (Figure 1(a)) [1]. Note the level of detail revealed in the corresponding VR rendering.

VR data visualisation is not limited to image stacks, it can be applied to deconvolved or post-treated images. Single-molecule localisation microscopy, a key methodology for exploring nanometric cellular function, generates spot localisations (*i.e.* point clouds) in 2D and more recently 3D from raw imaging data [2]. In general, 3D point clouds are difficult to spatially assess and VR can be instrumental in this task [3]. An example is shown in Figure 1(b). Immersive visualisation can also be facilitating complicated segmentation tasks of microscopic structures within image stacks. Figure 2(a) shows a segmented portion

of neurons in the mouse olfactory bulb imaged using confocal microscopy. Here,
90 surfaces have been pre-annotated by the user and the transfer function has been
optimised to ensure their visibility. Combined with stereoscopy, a simple glance
reveals both geometric and some topologic features of this local network.

Beyond imaging data, VR can be used to visualise many forms of scientific
data. Scientific laboratories generate large amounts of high dimensional data on
95 a daily basis and immersive environments can be exploited to more efficiently
extract information from them. In Figure 2(d) we show an example of a user
visualising and interacting with a macromolecule in VR. Similarly, we show
3D yeast chromosome geometry based on statistical properties of Hi-C maps
Figure 1(c) [4]. In both of these examples, immersive visualisation provides
100 an enhanced geometric understanding. Proximity of data points in complex
datasets can be immediately assessed and complex correlations in structures,
that may escape automated analysis, can be directly seen.

Besides visualisation, data navigation is a second major challenge. Figures
1 and 2 display screen captures of images rendered in the VR headset. The
105 supplementary video reveals how easily data is moved, rotated and scaled by the
user. Visualising data on a 2D screen is now a relatively standardised task and
consensus exists for navigation (*e.g.* using a mouse-wheel to zoom, dragging
with the mouse button clicked to rotate). This is not the case for VR and
significant work is required to establish standard modes of interaction. The use
110 of VR controllers is critical in this regard. It provides a means to perform basic
tasks such as grabbing, scaling and rotation although data-specific challenges
still exist (*e.g.* changing display parameters of the transfer function). Consensus
will emerge as the number of users increases and the technologies introduced in
VR controllers continues to mature [5, 6]. The INRIA Naviscope project [7], for
115 example, addresses a number of challenges related to data navigation.

As the use of VR technologies will increase for scientific research, automating
some procedures for visualisation and navigation will become appealing and,
in some cases, necessary. Naturally, this shall be determined based on user
testimonials and case studies. Several publications have already investigated the

120 reaction of users using VR in specific tasks [8, 9, 10, 11, 12]. These studies serve
the purpose of surveying user preferences and will enable developers to address
their requirements. This is particularly vital for user-centric technologies such
as VR, where development based on the needs of domain experts can be a
conduit for transmitting knowledge to novices. In our experience, we have
125 observed consistent trends in user behaviour when trying our VR applications.
For example, it is not uncommon to witness users standing up, moving the data
vertically, moving around the data in order to explore its spatial extents before
manipulating it. Automated protocols to encourage initial data exploration can
aid in this regard.

130 **3. Data Treatment and Numerical Simulations**

The visual intuition provided by VR extends further than facilitating spatial
understanding of complex volumetric data. In our view it provides an excellent
canvas for data treatment and interaction. It is its place at the frontier of
human cognition, data visualisation and direct treatment that VR could have
135 its greatest impact. Through some examples we discuss some major topics where
we predict VR to have an immediate impact.

A direct form of interaction is the selection of 3D regions of interest (ROIs)
for exportation and performing analysis. As an example, 3D single-molecule
imaging has emerged as a powerful approach to probe complex biological pro-
140 cesses at the nanometric scale in native cellular environments. Identifying 3D
patterns (static or dynamic) indicative of biological activity is neither a simple
task nor is it easily automated. Figure 2(b) illustrates an example where the
user defines ROIs using the VR controller, upon which an inference program is
executed to estimate the local value of diffusivity of all single molecules moving
145 in that volume [14]. Similarly, being immersed in data provides valuable intu-
ition of data with complex geometries. In Figure 2(c) we show an example of
a user effectively mapping the inside of a mammalian cell by using the VR con-
troller to perform a planar projection in a high-resolution electron microscopy

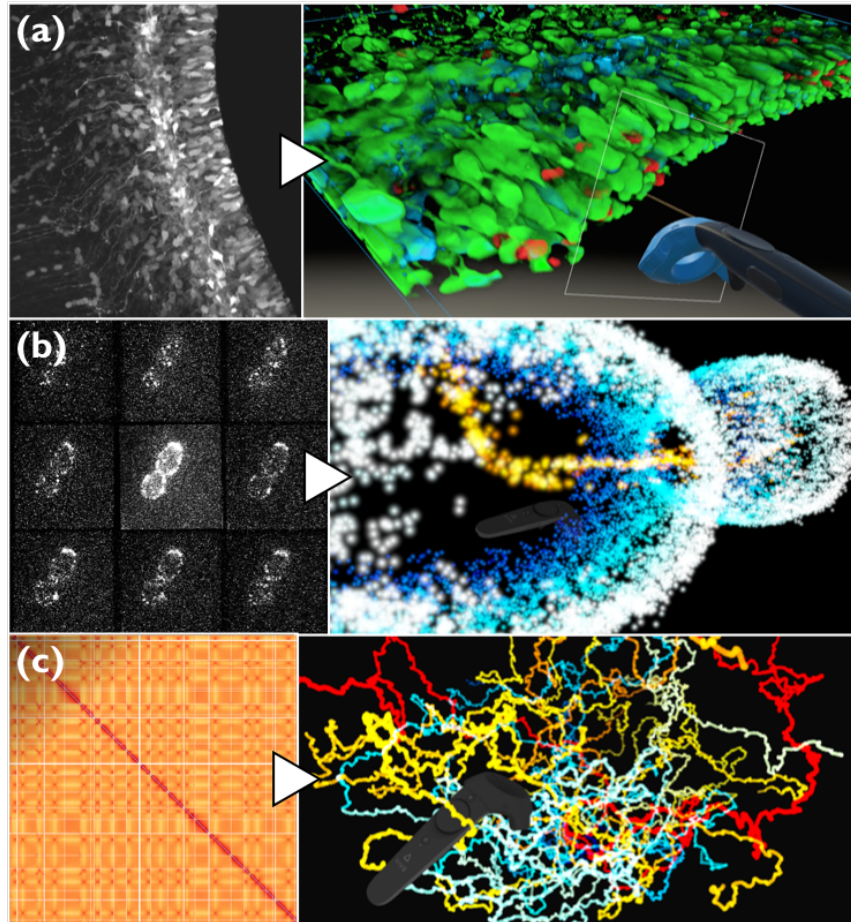


Figure 1: **Visualising data in VR.** **A)** Example of visual representations of scientific data using VR. On the left, a maximum intensity projection of an image stack of neurons imaged by spinning disk confocal microscopy [1]. On the right a capture of the same dataset in VR. There is a significant increase in volumetric cues and information in the VR mode (see supplementary material); 3D geometry is accessible, boundaries can be enhanced and complex geometrical relation between neurons is clearly observed. **B)** Single-molecule point cloud originating from multifocus microscopy [13]. On the left, the raw image acquisition. On the right, the VR representation. In blue-white, the wall of a *saccharomyces cerevisiae* yeast, in red-yellow a filament of alpha tubulin passing between the dividing mother and daughter cells. **C)** A volumetric representation of the simulated positions of sixteen *saccharomyces cerevisiae* yeast chromosomes (distinguished by colour) based on the statistical properties in a Hi-C map, an example of which is shown on the left [4]. All VR screen captures were generated with the DIVA software platform.

dataset. In being able to arbitrary position the projection plane with the VR
150 controller, this function allows structures of interest to be easily revealed to the
user. Finally, and similarly to the previous example, the user can directly cre-
ate 3D annotations to data and perform simple measurements that are difficult
and taxing to perform outside of the VR context. We show an example in Fig-
ure 2(e), where dendrites of a segmented neuron are interactively and precisely
155 measured. These annotations can be exported and fed to other programs to
characterise the geometrical properties of the tagged structures. Notably, all
these examples demonstrate we can transform, in a matter of seconds, intuition
and perception into quantitative results.

Another possibility is to couple human interaction with simulation to under-
160 stand the processes driving the dynamics of living systems. A direct example
is that of molecular simulations. The high dimensional energy landscapes as-
sociated with biomolecule folding problems entails a significant combinatorial
complexity of solutions. Optimised molecular dynamics software packages show
continuous improvements but the task remains computationally intensive, es-
165 pecially for large molecules [15, 16]. Introducing visual intuition and external
knowledge can massively improve performance. In [10] the authors created a
software platform where interactive simulations enable multiple users to simul-
taneously manipulate molecules and observe their dynamics, computed from
physical equations in the cloud, in VR. Here, VR is the vehicle that provides
170 the geometric intuition, where the user can pull, push and introduce or re-
lease molecules and observe the resultant physical effects of the interactions.
Note that the authors added an innovative “multi-user presence” in VR as a
component of their software. Researchers can learn and interact in virtual envi-
ronments together while they manipulate the molecules. Similarly, UnityMol is
175 a software package that brings VR and human interaction to molecule editing
and prototyping, an photo of which is shown in Figure 2(d) [17].

Finally, we address the concept of *human-in-the-loop* (HITL) data treatment
and the integral role that VR plays. HITL means that the user and the machine
(*i.e.* learning algorithm) work simultaneously to achieve a specific data treat-

180 ment task [18, 19, 20, 21]. It is our view that such mixed approaches will be instrumental in the context of explainable artificial intelligence (xAI), where human intuition and reasoning is used to justify predictions in artificial intelligence systems. Motivation for HITL approaches derives from two often-encountered scenarios present in scientific research. In the first, data is complex to acquire, 185 non-standardised and limited in number (*e.g.* images of neural connectomes, organism atlases, etc). Developing fully automated algorithms or leveraging machine learning in these situations is challenging. The time required to develop efficient algorithms can exceed the time for semi-manual analysis in its own right. Furthermore, generalisation is not ensured due to complexities in 190 data acquisition protocols and the limited number of examples to train on. Relating physical interactions to learning algorithms in VR may greatly reduce the time to treat data, improve the efficiency in performing tasks and reveal possible strategies to automate treatment. For example, in [22] the authors developed a manual interface to trace neurons from 3D image stacks. VR allows for easy 195 vision of neurons in 3D, even within noisy confocal microscopy datasets. In this context, the user trace neurons by simply moving the VR controller within the data as if it were a real object. Eventually, human intervention can be used to simply define initial “starting points” in the segmentation task after which an algorithm will perform the optimisation. Human intervention can also be 200 intermittent in the training of a learning algorithm, similar to the workflow described in software such as ilastik and others [23, 24]: VR would be used for fast data tagging in 3D and afterwards the algorithm locally learn rules to classify data.

HITL is equally applicable in cases of massive, complex and standardised 205 data. A direct example is the collaborative efforts to trace neurons from EM serial imaging [25, 26, 27, 28]. As mentioned prior, VR human interaction will most likely be used to accelerate data tagging. Interacting and learning is possible on small portions of data loaded in the VR environment, which can then be propagated to the remainder of the dataset. Several challenges will still have 210 to be resolved, namely loading and visualising image files that are significantly

larger than the graphics card live memory. Approaches such as MaMuT [29] and hierarchical file encoding [30, 31] offer a promising path. Although it will be challenging to ensure efficiency and robustness of results across multiple users performing tagging, testing and visual verification.

215 An interesting concept that is bound to drive the development of data treatment procedures in VR is that of “gamification” or “serious games”. Recently, numerous initiatives have used video games as inspiration (*e.g.* point scoring, competition, rules) to facilitate scientific discovery for specialists and non-specialists alike. VR seems an ideal setting for such approaches [32]. The design
220 of visually appealing environments, efficient human-data interaction procedures and various game-like features will motivate the non-specialist. It will also ensure the continuous motivation of the specialist for complex tasks that may otherwise be tedious. The examples of protein folding and EM neuron tracing are relevant [33].

225 Another important feature of treating data in VR is the transfer of expert knowledge to the uninitiated. Immersive environments engage the user to interact with the data. Active interaction promotes better learning than passive observation. The possibility of following the actions of experts performing tasks while being inside data can be transformative in training and education. Mutual
230 interaction in the environment can also drastically reduce learning curves [10].

4. Conclusion

We are in a period where the impacts of VR technologies on scientific research are starting to be understood and realised. All signs indicate that VR will have a major and sustained impact on the way research is done. Naturally,
235 visualisation will provide intuitive visual comprehension of volumetric data and promote rapid knowledge transmission and training in the lab. It is data treatment, however, that will most likely dominate future uses of VR in scientific research. Bridging of knowledge gaps between experts and newcomers, the facilitation of segmentation tasks and the streamlining of studies of system

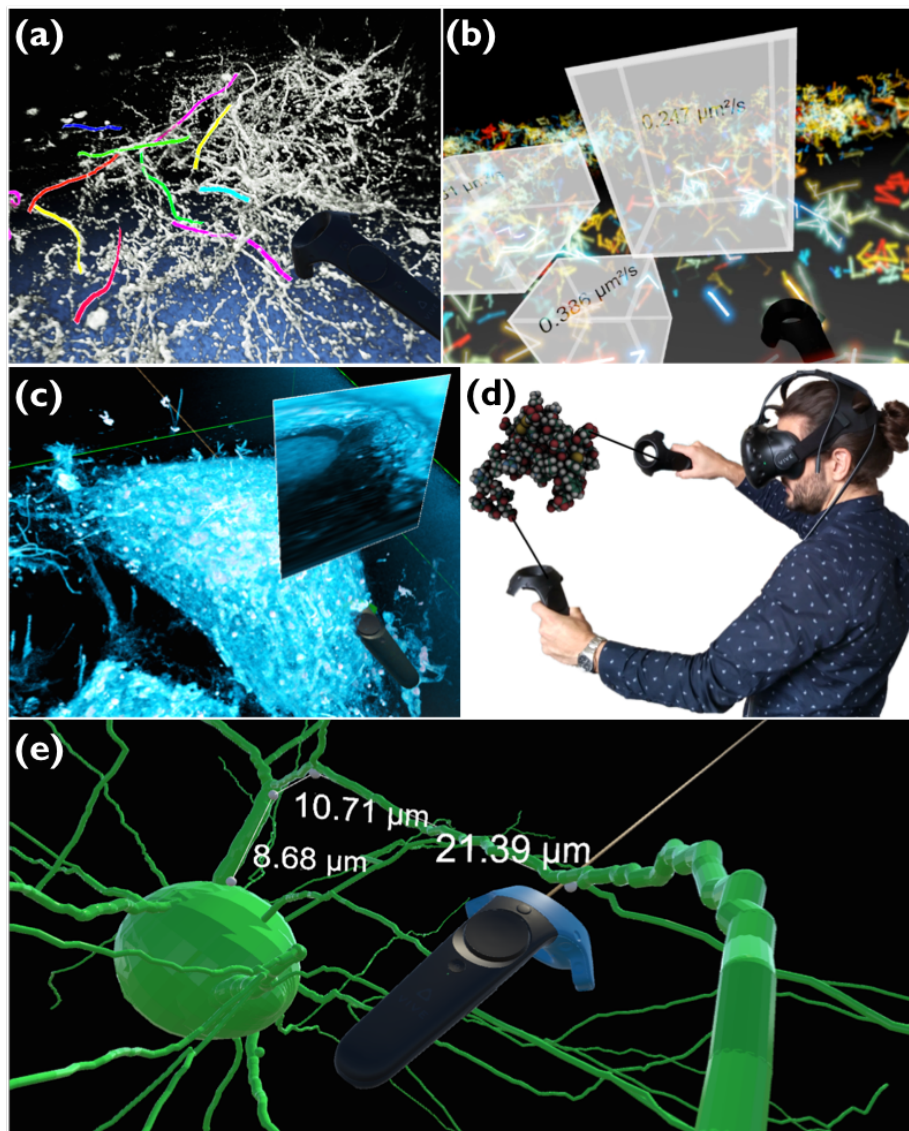


Figure 2: **Data treatment in VR: a human-in-the-loop approach.** **A)** Bayesian inference of local diffusivity of tracer fluorescent beads in the nucleus of a U2OS cell using VR. A video demonstration can be seen in <http://goo.gl/dnNueu>. The user identifies a local region of interest (ROI) in 3D, uses the VR controller to define the limits of the ROI and triggers a program (based on the InferenceMAP software [14]) that computes the diffusion using a Bayesian inference approach. The results is then overlaid. **B)** UnityMol VR [17]. This software allows the user to visualise and interact with large molecules in VR **C)** Use of VR in a *human-in-the-loop* segmentation task. Raw confocal images of fluorescent mouse olfactory bulb neurons with a reduced signal-to-noise ratio. VR allows easy determination of axon position and direction permitting a rapid segmentation with the VR controller. **D)** Projection tool aligned to the VR controller used to map the inside of a plated HeLa cell in a serial block-face scanning electron microscopy image stack [34]. **E)** Precise measurement of axon segments using the VR controller in a segmented mouse neuron database. All VR screen captures were generated with the DIVA software platform.

240 dynamics, are just a few applications that demonstrate how VR is positioned
to accelerate scientific discovery. Even still, we emphasise that two main chal-
lenges lie ahead. The first centres on arriving to a consensus on how to properly
interact with data in VR. The second will focus on numerical and hardware
challenges, as real-time stereoscopic data visualisation remains a demanding
245 task. Simultaneously performing analysis and simulations in the same context
will require skillfully designed software and optimised hardware configurations.

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