Editorial

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Future Medicinal Chemistry

Virtual and augmented reality applications in medicinal chemistry

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"Although the metaverse is in its infancy and is still largely unexplored, it has already begun to provide important support in research and development, manufacturing, training and marketing as well as the launch of new drugs."

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Since the early 1980s, computer applications and computational tools have been widely used to facilitate and aid drug discovery. These applications have allowed the emergence of so-called computer-aided drug design (CADD) [1]. The progress made in accelerating the discovery of new drugs has been possible thanks to the innovative discoveries of chemistry and physics, especially the new synthetic methodologies, as well as the development of information technology, with the increase in computing power and statistics [2].

The growth in information technologies and the great power of the computers at our disposal have made possible a rapid evolution in every field of science, especially drug discovery, and enabled us to acquire considerable knowledge in a relatively short time. The recent advent of user-friendly software has further enabled the widespread use of innovative computational tools in all environments where drugs are designed. Today, we have several software applications that simplify the visualization of molecular models – including Avogadro, Molekel, Molden, RasMol, Visual Molecular Dynamics, PyMOL and Chimera – and allow users to examine them in a mock 3D environment [3–5]; therefore, the visualizations turn out to be approximations of real 3D structures.

More recently, we are witnessing a new revolution in the visualization of molecular models because, thanks to the virtual technologies of the metaverse, these models can be inspected not only visually, as is currently the case, but also interactively in a 3D environment that is very similar to the real world. These virtual methods can be used to quickly obtain detailed information valuable for the discovery of new drugs [6].

The recent introduction of computer methodologies defined as 'immersive virtual reality', which creates a 3D virtual environment, is revolutionizing the processes related to drug discovery since they allow us to visualize and understand the 3D space and to interact with and manipulate objects in the 3D environment. Thanks to its remarkable innovative potential, this new drug discovery approach has aroused considerable interest in both the academic world and Big Pharma, which sees a further step forward in optimizing the development of new molecular entities [7–9].

The idea of developing virtual reality systems to be used in science is not novel, as it was born a few years after the introduction of the first computers; however, because of the high cost of technology, it was inaccessible until a few years ago. With recent technological advances and the ability to operate in a virtual environment with the help of the latest smartphones, this technology has become more widely accessible [5]. The recent introduction of new digital visual devices connected to a helmet or headset worn by the user has further enhanced the virtual approach. This technological innovation has allowed the rapid emergence of two new computer-assisted technologies, virtual reality and augmented reality, opening paths and new potentials not yet well defined even in drug discovery. Although these technologies are often associated with one another, they are, in fact, quite different. Virtual reality makes possible a simulated experience that may or may not be similar to the real world. Alternatively, augmented reality

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is a mixed technology that superimposes a 3D image onto reality, thus digitally positioning computer-generated information within the real-world environment [10,11].

The application of virtual reality in drug discovery is no longer a promise and is now starting to be realized through the development of various applications that allow the 3D molecular models obtained with conventional computational software to be moved into virtual environments [7]. These virtual applications allow us to overcome the limitations of 3D molecular models and obtain a better perception of the spatial arrangement of the protein binding interaction sites and, therefore, of the protein–ligand interactions [12]. Compared with traditional viewing approaches, virtual reality techniques provide a wider field of view, allowing us to observe molecules from the inside – with only a simple movement of the head to change the viewing direction – with the use of the new viewers (Microsoft, Redmond, WA, USA and Meta Quest 2, Menlo Park, CA, USA).

In addition to a more detailed understanding of the system to be studied, providing more information for the design of a drug, the use of controllers, which devices are equipped with today, allows the operator to grasp and interact with a molecule as if it were a normal real-world object. This approach allows for manipulation of the protein–ligand system being studied as well as modification of its structure and makes it possible to carry out all interactions directly and in a very short time [13].

In other words, modern virtual technology (hardware and software) is not simply a graphical update to better visualize 3D molecular models. Rather, it is primarily concerned with the ability to directly manipulate simulations and create and modify the molecular structure from within the program using virtual reality (augmented or virtual reality). In essence, this new technology makes it possible to move from a simple visualization tool to a valid system for the design of new molecules. However, it should not be forgotten that, like all new technologies, this approach is also extremely useful in the training field, where it is already enjoying enormous success in training at all levels, especially in the academic field [14]. The application advantage of these technologies is most evident in scientific subjects such as chemistry, where the 3D complexities of molecular symmetry, chirality and solid-state structures are difficult to visualize on paper or computer liquid crystal display screens and can be confusing for students. The novelty of virtual reality can also involve and motivate students more than current teaching approaches – which are considered almost obsolete – and can therefore have a high motivational impact on learning [15].

Nevertheless, even virtual technologies have their limitations; for example, controllers paired with suboptimal headsets that cannot be controlled with hand movements. This limitation can only be overcome with the use of special gloves that allow more complex movements than the hands are capable of or wrist trackers, which require just two simple bracelets placed on the wrists [16]. Both technologies, at the time of this writing, are quite expensive but certainly represent a further step in affirming the importance of virtual technologies in drug design. Moreover, virtual reality, which is part of the metaverse, will change many other aspects of drug development. Certainly, the metaverse will be used for the development of drugs in areas where it is still difficult to achieve adequate results, as in the case of the development of effective agents in the fight against neurodegenerative diseases such as Alzheimer's and Parkinson's.

Currently, companies are preparing to enter a very different future than the one they had in mind when they began operating. Companies will soon find themselves at the intersection of many new worlds, where they will manage the physical and virtual realities they have built and provide services in environments created by other companies [17]. Pharmaceutical companies are exploring how to integrate virtual reality into the workflow to improve its collaborative and educational aspects.

Without a doubt, the innovations of the metaverse have opened new doors for the development of the pharmaceutical sector, not only in the field of drug discovery but also with regard to better showing how a drug works and helping patients understand the criticality of their pathologies and how to solve them [18]. Although the metaverse is in its infancy and is still largely unexplored, it has already begun to provide important support in research and development, manufacturing, training and marketing as well as the launch of new drugs. We will remain vigilant and carefully observe what happens in the next 2 years, especially with the advent of new technologies that could further alter this scenario. We will also stay up to date with technologies, equipping ourselves with an adequate smartphone since this device will be very important in the future, not only for daily communications but also for connecting and interacting with the world around us: the metaverse.

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