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Host-Virus Interactions at Atomic Resolution

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ABSTRACT

Host-virus interactions are a significant area of research, as understanding these interactions can help to prevent, manage, and cure diseases more effectively. This is particularly evident during a pandemic, such as COVID-19, when it is crucial to gain a better understanding of the disease in order to prevent and manage it. Studying these interactions at the atomic level has proven to be beneficial, as it allows for a more comprehensive understanding of the receptor-spike interactions that lead to the virus entering cells. In this article, I will analyze the omicron variant of the coronavirus, using a combination of structural analysis and molecular dynamics software to examine the receptor binding domain of the omicron variant and track the movement of its atomic-level structures over time.

Keywords: Structure; Virus; Coronavirus; Omicron; Computational Biology; Molecular Dynamics

Abbreviations: VMD: Visual Molecular Dynamics; NAMD: Nanoscale Molecular Dynamics; UCSF: University of California San Francisco; RCSB: Research Collaboratory for Structural Bioinformatics; PDB: Protein Data Bank; ps: picosecond; ns: nanosecond; hACE2: human Angiotensin-converting enzyme 2; VMD: Visual Molecular Dynamics; NAMD: Nanoscale Molecular Dynamics

Introduction

The interactions between hosts and viruses are complex and involve multiple factors. These interactions are shaped by the dynamic interplay between the strategies employed by viruses to infect host cells and the defenses mounted by the host organism [1]. As obligate intracellular pathogens, viruses have evolved various mechanisms to exploit host cellular processes for replication and evade host immune responses [1]. This relationship can be viewed as a molecular arms race, where both the virus and the host continuously adapt to each other's strategies [2]. It is interesting to note that while viruses are often perceived as purely pathogenic entities, some studies suggest that they can also play beneficial roles in host survival, particularly in isolated ecosystems such as deep-sea hydrothermal vents [3]. Moreover, the study of viruses in non-traditional model organisms has the potential to unveil novel insights into virology and host-virus dynamics [4]. Conversely, viruses can manipulate host metabolic pathways through lateral gene transfer, which contributes to their diversification and the regulation of infection mechanisms [5].

Additionally, the co-evolution of viruses and hosts has significance for the evolution of plant viruses, which must balance adaptability to the host with transmissibility by vectors [6]. Host-virus interactions are characterized by an ongoing evolutionary struggle in which viruses develop sophisticated methods to hijack host mechanisms, and hosts evolve defenses to counteract these viral strategies. The study of these interactions not only provides insights into cellular and immune system functions but also has implications for the development of antiviral therapeutics and understanding the ecological roles of viruses [7-9]. The diversity of viral strategies and host responses underscores the complexity of these interactions and the importance of continued research in this field [10]. Host-virus interactions are a critical component of disease prevention and management, providing valuable insights into effective strategies against illnesses. Understanding these interactions is a crucial step in combating diseases. In 2024, the widespread use of computers in research and other areas of human life led to the development of sophisticated computational tools, such as structural biology and molecular dynamics software [11].

These tools enable researchers to determine protein structures at the atomic resolution and observe protein movement over time, respectively. As a result, researchers can now study host-virus interactions in great detail, gaining a deeper understanding of disease mechanisms and developing more effective prevention and treatment strategies. In this examination, I will focus on the structure and molecular dynamics of the latest COVID-19 variant, the Omicron variant (Figures 1-3).

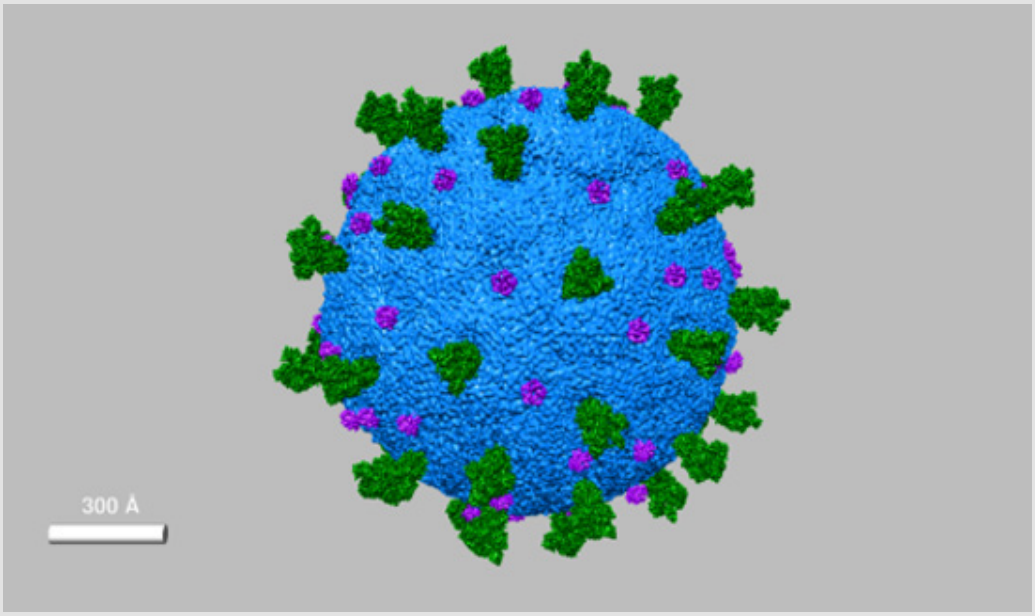

Figure 1: The structure of SARS-CoV-2 was created at atomic resolution and real scale using the UCSF Chimera software. The bar depicted in the image represents a length of 300 angstroms.

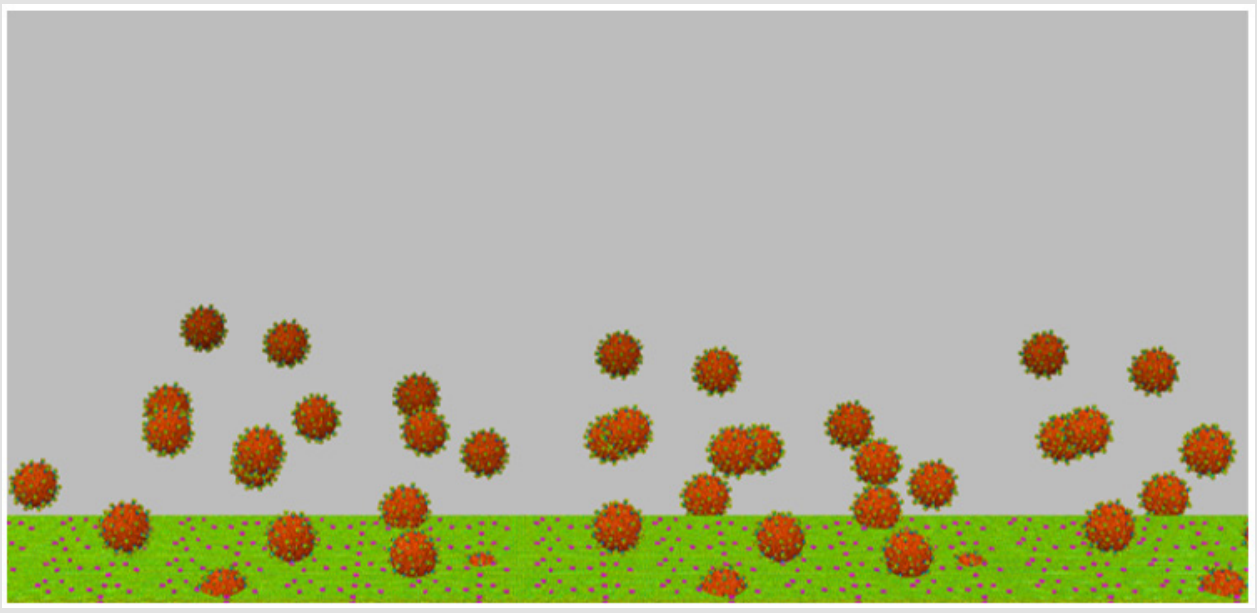

Figure 2: The composition of SARS-CoV-2 infection, encompassing the cell membrane featuring hACE2 receptors (magenta) at an atomic level of detail and scale, was visualized using UCSF Chimera software.

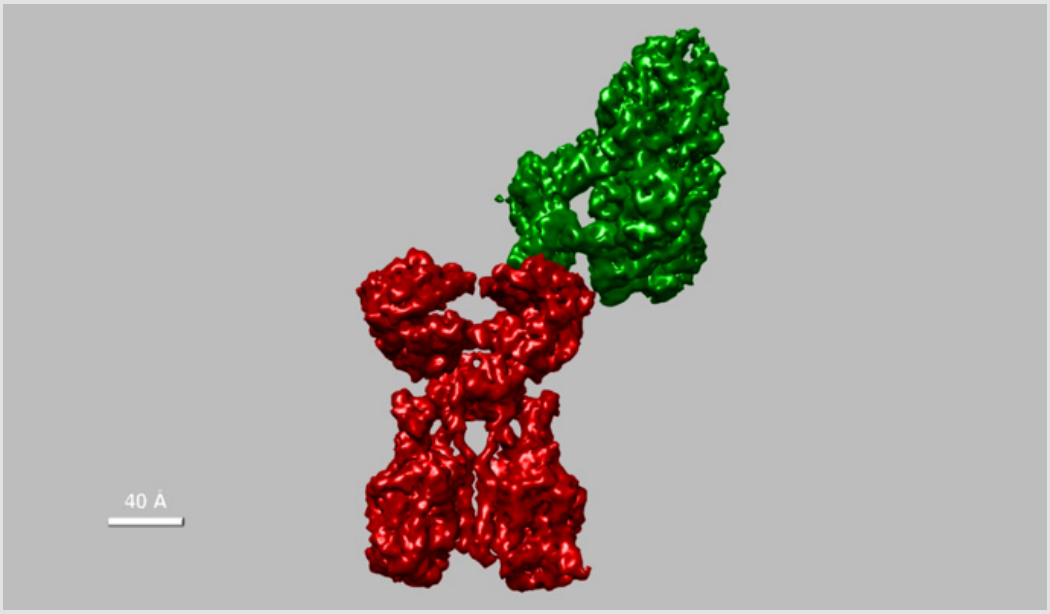

Figure 3: The interaction between the hACE2 receptor (in red) and the SARS-CoV-2 spike glycoprotein (in green) is depicted, with a bar indicating a distance of 40 angstroms.

Materials and Methods

Structural Biology and Molecular Dynamics

In performing in silico analyses of static structures, I have utilized UCSF Chimera software. To specifically identify the spike glycoprotein of the omicron variant bound to the hACE2 receptor in the RCSB databank, I used the PDB ID 7WK6 [12]. I executed molecular dynamics simulations using NAMD software [13], from within VMD [14], with the Qwikmd tool [15], for approximately 8 nanoseconds at 37 degrees Celsius with 0.15 mol/L NaCl concentration and used implicit solvent. The resulting trajectory was analyzed using UCSF Chimera software [16].

Results

The Omicron variant (B.1.1.529) of SARS-CoV-2 has been reported to possess a significant number of mutations, particularly in the spike protein, which is a key factor in the virus's ability to enter host cells and evade immune responses. The World Health Organization (WHO) designated Omicron as a variant of concern due to these mutations, which may affect transmissibility, immune evasion, and possibly the efficacy of existing vaccines. The emergence of the Omicron variant, which constitutes the latest phase of the COVID-19 pandemic, has attracted attention to its extensive mutations. This particular variant showcases the highest level of mutations among SARS-CoV-2 viruses discovered thus far, with over 30 unique alterations that have engendered apprehensions about its capacity for transmission and its ability to evade immune responses. Furthermore, this variant has garnered global attention due to its swift dissemination, thereby engendering heightened concerns about its capacity to circumvent prevailing vaccines and therapeutic modalities. The atomic resolution analysis of the receptor-binding domain (RBD) of the Omicron variant bound to the human ACE2 receptor is feasible in real time.

By scrutinizing specific amino acid interactions, it becomes possible to gain insight into the behavior of this particular variant. For instance, the binding interactions between the positively charged amino acids N440K and Q498R and the negatively charged amino acids can be explained. These interactions result in strong binding between the virus spike and the receptor, thereby forming two binding interfaces. The mutations responsible for these amino acids are N440K and Q498R [17,18]. As illustrated in Figure 4, the interaction between the receptor and the RBD of the Omicron spike is depicted in red and green, respectively. These binding interactions involve conserved mutations that increase the affinity of the virus spike for the receptor. Furthermore, these binding interactions play a crucial role in determining the virulence and transmissibility of the virus. In Figure 5, the two distances of the binding interactions are shown.

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Note: LYS 440.A NZ <-> GLU 329.B CD: 6.85 (towards the left side)
ARG 498.A CZ <-> ASP 38.B CG: 4.75 (towards the right side)

Figure 4: The interaction between the hACE2 domain (shown in red) and the RBD (green) of the omicron spike is depicted. Four residues, which form electrostatic binding interactions, are displayed in sticks. The scale bar represents a distance of 15 angstroms.

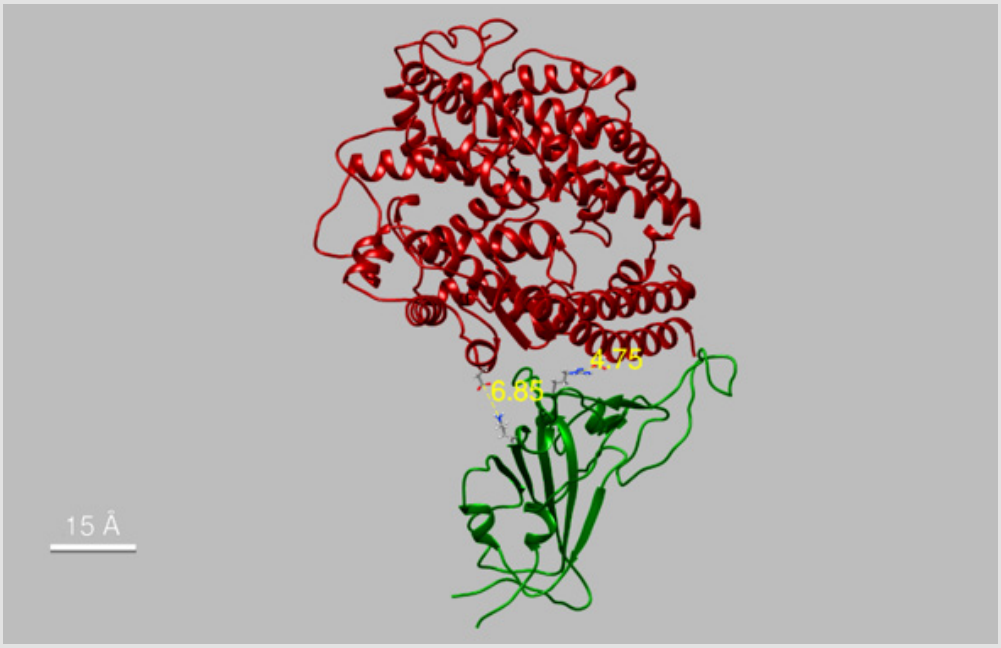

Figure 5: This figure depicts the close proximity of the distances in angstroms, which are crucial for strong interactions.

Figure 6: Zoomed-in view of the interactions, emphasizing the positions of the amino acids.

(Figure 6) Ultimately, the molecular dynamics simulations over a duration of approximately 8 nanoseconds illustrate the temporal development of these interactions. Specifically, residue R498 exhibits its stable interactions with residue D38, while residue K440 exhibits more extensive movement but generally remains in close proximity to residue E329. See two videos: https://youtu.be/5-EvJb7oI3Y and https://youtu.be/BAWgmGMmjqs The RBD region of the spike glycoprotein in the Omicron variant possesses two novel mutations that enhance its binding capabilities, leading to more efficient infection. Through the use of structural analysis and molecular dynamics at the atomic resolution, valuable insights have been gained that are instrumental in combating the COVID-19 pandemic.

Conclusion

Structural examination of proteins and macromolecular complexes, including viruses, cell organelles, bacteria, and cells, can offer insights that traditional research methods cannot. This enables us to better comprehend biological processes and develop innovative solutions to address biological challenges. Molecular dynamics is an additional step in research that allows us to analyze interactions at the atomic level, providing more information than was previously possible. The utilization of computational power and techniques is essential to achieve this type of analysis [19-24]. The development of more sophisticated computing capabilities, such as the emergence of powerful quantum computers, will undoubtedly enhance our comprehension of viruses and cellular structures. The application of these analytical tools to larger macromolecular entities, such as cells, represents an exciting prospect. Although these advances may still be some way off, technological progress is rapid, and it is reasonable to anticipate that such capabilities will be realized in the not-too-distant future. The avoidance of invasive techniques that can inflict harm on patients is a significant advantage of computational methods, which are also more precise than traditional approaches. As scientific research continues to push the boundaries, it is likely that many breakthroughs will be achieved in the years to come [25,26].

Conflict of Interest

The author declares no conflict of interests.

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