GR-389

Molecular Dynamics and Protein-Protein Interactions (PPIs) on SARS-CoV-2 coronavirus

Abstract

In this study, Molecular Dynamics simulations and hydrogen bond analyses were conducted on six variants of SARS-CoV-2 to examine their behavior and protein interactions in an environment resembling the human body. The findings provide valuable insights into the molecular dynamics and stability of the protein structures, which could aid in the development of effective treatments and vaccines against COVID-19. Further research in this area is crucial to combat the ongoing pandemic and prevent future outbreaks.

Introduction

The ongoing COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has had a massive impact on global health, economies, and societies, resulting in millions of infections and deaths worldwide. One of the primary reasons for the continuous evolution of the pandemic is the emergence of new SARS-CoV-2 variants, including the Original, alpha, beta, gamma, delta, and omicron variants, which have caused concerns due to their potential to cause increased transmission, severe illness, or reduced vaccine effectiveness. Understanding the molecular behavior of these SARS-CoV-2 variants is crucial for developing targeted therapeutics and vaccines, as well as predicting the potential consequences of future mutations.

Figure 1: Structural Comparisons

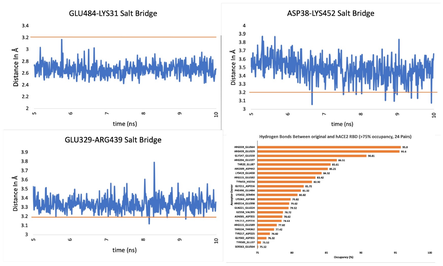
To gain a better understanding of the molecular dynamics and protein-protein interactions of the SARS-CoV-2 variants, computational methods such as Molecular Dynamics (MD) simulations and protein-protein interaction analyses have emerged as powerful tools. In a recent study, researchers performed a comparative analysis of the Original, alpha, beta, gamma, delta, and omicron variants of SARS-CoV-2 using MD simulations in a human-like environment. The study aimed to investigate the differences in molecular behavior, protein stability, and interactions between amino acid residues in these variants, which may contribute to their unique biological properties. In addition to MD simulations, the researchers conducted salt bridge and hydrogen bond analyses to further elucidate the protein-protein interactions and their implications on the stability of the viral proteins. The results of this study could provide valuable insights for the development of effective treatments and vaccines against COVID-19, as well as inform strategies for mitigating the spread of the virus. However, computational methods offer several advantages, including the ability to simulate complex biological systems over longer timescales and the flexibility to manipulate various parameters and conditions. By combining experimental and computational approaches, researchers can obtain a more comprehensive understanding of the molecular behavior and protein-protein interactions of SARS-CoV-2 variants, facilitating the development of effective therapeutic interventions against COVID-19.

Results

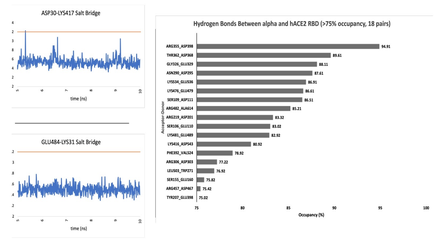
Below are the results obtained from MD simulations

- Bar chart represents Hydrogen bonds of that Variant of Concern (VOC) MD simulation Results with occupancy > 75%
- Line graph is the representation of salt bridges formed during PPI of that variant.
- A orange line on salt bridge chart is the base line (3.2 Å) which is used for stabilization evaluation.

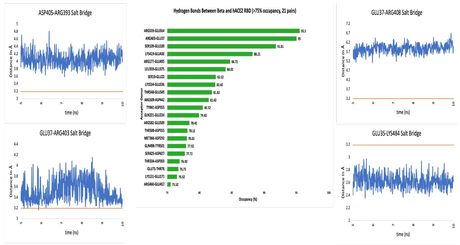
Original:



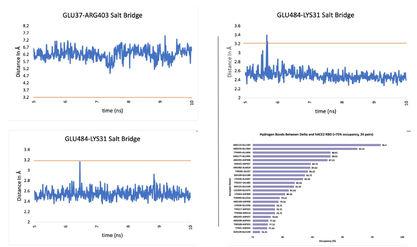
Alpha:



Beta:



Gamma:



Delta:

Omicron:

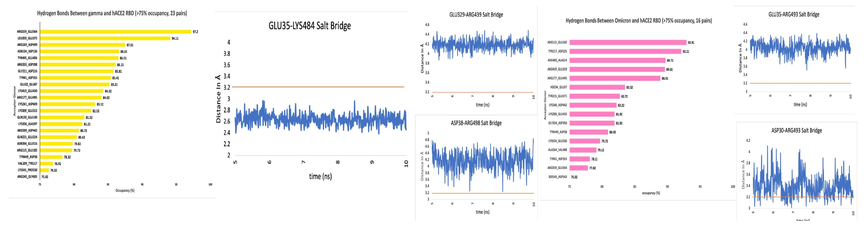


Figure 2: Hydrogen Bonds (with occupancy >75%) and salt bridges of the VOC (Variants of Concern)

Tools and Methods

The first step in our study was to obtain the protein structures of the Original, alpha, beta, gamma, delta, and omicron variants of SARS-CoV-2 coronavirus from the Chimera tool. We then utilized the tool to align the protein structures and remove non-similar regions. This allowed us to compare the variants more accurately and gain a better understanding of their structural differences.
After aligning and refining the protein structures, we configured an environment for Molecular Dynamics (MD) simulations using the VMD tool. We generated Protein Structure Files (PSF) for each variant and used NAMD2 to perform MD simulations, which simulate the physical movement and interactions of atoms in the protein structures over time. This allowed us to observe the changes in the protein structures of each variant and analyze their dynamic behavior.
To analyze the results of the MD simulations, we utilized VMD to generate data on hydrogen bonds and salt bridges for each variant. Hydrogen bonds are a type of chemical bond between hydrogen atoms and other atoms in the protein, while salt bridges are electrostatic interactions between oppositely charged amino acids. We analyzed the number, length, and strength of these interactions for each variant to determine their stability and behavior. We then visualized and analyzed this data using Microsoft Excel to gain a better understanding of the variants' behavior.

Conclusions

Our study has provided valuable insights into the molecular behavior and protein-protein interactions of the SARS-CoV-2 variants, which are crucial for the development of targeted therapeutics and vaccines. Our analysis highlights the importance of hydrogen bonding and salt bridge interactions in stabilizing the protein-protein interactions across all variants, with the gamma variant exhibiting the highest hydrogen bond occupancy and the alpha variant having the highest number of stable salt bridges with shorter distances. We have also identified key amino acids involved in forming these interactions, such as arginine and aspartic acid. Importantly, our results suggest that the delta variant forms the most stable interaction with hACE2 among all the variants analyzed. This finding may provide useful information for the development of targeted therapeutics and vaccines against the delta variant. Our molecular dynamics simulations have also provided insights into the potential consequences of specific frames and mutations in the variants, which could aid in predicting the effects of future mutations. Overall, our study demonstrates the power of computational methods such as MD simulations and protein-protein interaction analyses in understanding the molecular behavior of SARS-CoV-2 variants and informing strategies for mitigating the spread of the virus.

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