A DISSERTATION ON

DRUG DESIGN AND MOLECULAR DOCKING OF SARS CoV-2 VARIANT USING COMPUTATIONAL TOOLS

SUBMITTED TO THE
DEPARTMENT OF BIONGINEERING
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FOR THE
DEGREE OF MASTER OF TECHNOLOGY
IN BIOINFORMATICS
BY
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M. Tech Bioinformatics (IV Semester)
Enrollment No: 1300100768

UNDER THE SUPERVISION OF

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DECLARATION FORM

I, **Sakshi Srivastava**, a student of **M.Tech Bioinformatics** (2nd Year/ 4th Semester), Integral University have completed my six months dissertation work entitled **"Drug design and Molecular docking of SARS Cov-2 variant using Computational tools"** successfully from BPRI, Noida, under the able guidance of **Dr. Uma Kumari.**

I, hereby, affirm that the work has been done by me in all aspects. I have sincerely prepared this project report and the results reported in this study are genuine and authentic.

Sakshi Srivastava

Mohammed Kalim Ahmed Khan
Course Coordinator
Department of Bioengineering

Registered under MSME, Gov. of India and ISO 9001: 2015 certified

CERTIFICATE

This is to certify that Ms. **Sakshi Srivastava** D/o **Mr. S.K.Srivastava** , student of M.tech Bioinformatics (4th Semester), from **Integral University, Lucknow** has successfully completed her 6 months Dissertation/Project, from 17th Jan 2022 to 17th July 2022, under the guidance of Dr. **Uma Kumari, at Bioinformatics Project And Research Institute, Noida.** The project topic is "**Docking and virtual high throughput screening and insilico fragment based drug design of SARS-CoV-2 variants of concern**".

Good luck for your future endeavor.   **Certificate Number BPRI-0722-11**

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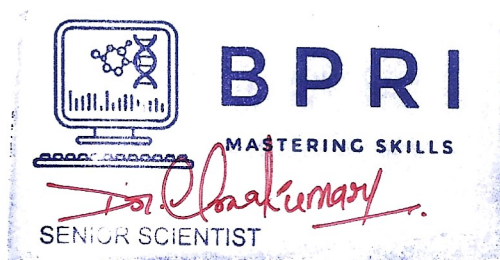
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This is to certify that **Sakshi Srivastava ,** a student of **M.Tech in Bioinformatics** (2nd Year/4th Semester), Integral University has completed his six months dissertation work entitled **"Drug design and Molecular Docking of SARS Cov-2 variants using Computational Tools"** successfully. She has completed this work from **BPRI, NOIDA** under the guidance of **Dr. Uma Kumari,** (SENIOR BIOINFORMATICS SCIENTIST) BPRI Noida, Uttar Pradesh. The dissertation was a compulsory part of his M.Tech Bioinformatics. I wish her good luck and bright future

Dr. Mohammad Haneef
Assistant Professor
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TO WHOM IT MAY CONCERN

This is to certify that **Sakshi Srivastava**, a student of **M.Tech** in **Bioinformatics** (2nd Year/ 4th Semester), Integral University has completed her six months dissertation work entitled "**Drug design and Molecular Docking of SARS Cov-2 variants using Computational Tools**" successfully. She has completed this work from **BPRI Noida**, **Uttar Pradesh** under the guidance of **Dr. Uma Kumari, Assistant Professor and Coordinator, Department of Bioinformatics**. The dissertation was a compulsory part of her, **M.Tech Bioinformatics**.

I wish her good luck and bright future.

Dr. Alvina Farooqui
Head
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ACKNOWLEDGEMENT

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ABBREVIATIONS

Abbreviations	Full Form
SARS-CoV	Severe acute respiratory syndrome coronavirus 2
ACE	Angiotensin-converting enzyme 2
RBD	Receptor-binding domain
WHO	World Health Organization
RNA	Ribonucleic acid
CDC	Centers for Disease Control and Prevention
FASTA	Fast alignment sequence test for application
NCBI	National centre for biotechnology information
BLAST	Basic local alignment search tool
CFR	Case fatality ratio
CADD	Computer Aided Drug Design
EMA	European Medicines Agency's
NIH	National Institutes of Health
VOC	variants of concern
PDB	Protein Data Bank

INTRODUCTION

Viruses are constantly evolving, and this might result in the emergence of a new virus variation, or strain. The virus's behaviour is usually unaffected by a variation. They do, however, occasionally cause it to behave in unexpected ways.

Changes in the virus that causes COVID-19 are being monitored by researchers all around the world. Their findings are assisting scientists in determining if some COVID-19 variations spread more quickly than others, how they influence your health, and how effective different vaccines are against them.

Coronaviruses have been around for a while. They're a huge viral family with a long history. Many of them can induce a variety of ailments, ranging from a simple cough to serious respiratory problems.

Coronaviruses have been investigated for almost 50 years and have been shown to infect a wide range of animals, including humans. Although the pathogenesis of diseases caused by these viruses, as well as their mechanism of replication, have been well described in previous outbreaks (severe acute respiratory syndrome coronavirus (SARS-CoV) in China in 2003 and Middle East respiratory syndrome coronavirus in Saudi Arabia in 2012), the current COVID-19 pandemic has prompted researchers around the world to study and investigate the pathogenesis of diseases caused by these viruses in greater depth. Coronaviruses are divided into four genera: Alphacoronaviruses, Betacoronaviruses, Gammacoronaviruses, and Deltacoronaviruses [1]. SARS-CoV-2, the organism that causes COVID-19, is classified as a betacoronavirus based on nucleotide sequence similarities.

Coronaviruses have a spike glycoprotein that helps them enter the host cell and gives them a crown-like shape on their surface. The critical stage in the onset of infection is the binding of SARS-CoV-2 pathogenic particles to host cell receptors. Furthermore, the virus's capacity to connect to the unique receptors of other host species is a need for cross-species transmission [2].

SARS-CoV requires human angiotensin-converting enzyme 2 (ACE2) for passage, and researchers discovered that SARS-CoV-2 requires ACE2 for entry into host cells following the COVID-19 epidemic [3][4]. Host proteases break the SARS-CoV-2 spike protein into an S1 and an S2 domain, which facilitate receptor binding and membrane fusion, respectively[5].

The S1 domain of the spike protein of SARS-CoV-2 has a receptor-binding domain (RBD), which forms a complex with human ACE2 and enhances viral entry, according to [6]. Emerging changes in the SARS-CoV-2 genome, on the other hand, might affect infection transmission and replication, as well as the virus's ability to bind to ACE2. SARS-CoV-2, according to epidemiological data, after zoonotic transmission via Malayan pangolins, SARS- CoV-2 was first detected in bats in Wuhan, China, and subsequently expanded to other regions of the [7][8]. It's critical to understand the origins of distinct strains of SARS-CoV-2 identified from different sections of India in a country with such a diverse geographical distribution as India. Knowing the RBD binding affinity of different Indian Severe acute respiratory isolates for ACE2 of natural reservoirs, including humans, is highly essential since contact with ACE2 is the major channel of entrance of this virus into its host. However, with little information available, this has remained a murky area. The goal of our research was to look at the spike sequences of Indian SARS-CoV-2 isolates obtained from COVID-19 patients.in Odisha (an eastern Indian state) to best explain the association between their RBDs and ACE2 in a variety of coronavirus natural hosts, including bats, pangolins, hamsters, and humans. One isolate's mutant RBD had a higher binding affinity for human ACE2 than the wild-type RBD, revealing critical details about its virulence and therapeutic targeting.

COVID-19 is caused by a new (or "novel") coronavirus, one of numerous known to infect humans. It's most likely been found in animals for a long time. Viruses that infect animals can occasionally infect humans. That's what scientists believe happened in this case. So, while this virus is not new to the rest of the planet, it is novel to humans. When scientists discovered it was causing illness in people in 2019, they dubbed it a new coronavirus. SARS-CoV-2 is the name given to these strains by experts.

Coronaviruses have all of their genetic information in RNA (ribonucleic acid). Although RNA and DNA have some similarities, they are not the same.

When viruses infect you, they connect to your cells, enter them, and replicate their RNA, allowing them to spread. If a copying error occurs, the RNA is altered. Mutations are the term used by scientists to describe these alterations.These modifications occur at random and by chance. It's a natural component of the process of viruses multiplying and spreading.Because the changes are unpredictably occurring, they may have little or no impact on a person's health. They may also cause disease in some cases. One reason you need a flu vaccination every year,

for example, is that influenza viruses evolve year to year. This year's flu virus isn't likely to be the same as the one that swept the country last year.

If a virus undergoes a random mutation, it becomes easier to detect.

The new variant (B.1.1.529) was first detected in specimens collected on November 11, 2021 in Botswana. Experts in South Africa first reported the Omicron variant to the World Health Organization (WHO) on Nov. 24, 2021. They discovered the variant after COVID-19 infections suddenly began to go up.

The WHO grouped Omicron as a "Variant of Concern." This category means the variant might have a higher transmissibility, cause more intense disease, and may be less likely to respond to vaccines or treatments. But researchers need more information to confirm these factors.Early evidence suggests that the Omicron variant causes a higher risk of reinfection compared to other variants.Current PCR tests for COVID-19 can effectively find Omicron cases. Experts found that one specific PCR test doesn't identify one of the three target genes (called the S gene dropout) in people infected with Omicron. Because of this, these tests can specifically mark positive Omicron cases and, because of that, can detect this variant faster than with previous surges.According to research, breakthrough infections are possible with the Omicron variant even if you're fully vaccinated. However, COVID-19 vaccines and boosters are still effective at preventing severe illness, hospitalizations, and death.

Omicron "stealth" variant (BA.2): Scientists call it Omicron BA.2 as opposed to the original Omicron variant, BA.1. At first, scientists thought BA.2 wasn't as contagious as BA.1 and would soon fade away. That didn't happen, and starting in January 2022, BA.2 appeared to be at least as easy to transmit as BA.1. As of the end of February 2022, BA.2 showed signs of spreading more easily than other variants, though it didn't seem to cause more serious symptoms. The World Health organization has said that BA.2 is a "variant of concern." The best protection is still the coronavirus vaccine. Current vaccines and boosters seem to work well against BA.2, protecting against initial infection as well as against serious illness if you do get infected.

Other Coronavirus Mutations

Alpha (B.1.1.7) . In late 2020, experts noted gene mutations in COVID-19 cases seen in people in southeastern England. This variant has since been reported in other countries, including the

U.S. Scientists estimate that these mutations could make the virus up to 70% more transmissible, meaning it could spread more easily. Some research has linked this variant to a higher risk of death, but the evidence isn't strong.The mutation on the Alpha variant is on the spike protein, which helps the virus infect its host. This is what COVID-19 vaccines target. These vaccines make antibodies against many parts of the spike protein, so it's unlikely that a single new mutation in the Alpha variant will make the vaccine less effective.

Beta (B.1.351). Other variants of the virus have been found in other countries, including South Africa and Nigeria. The Beta variant appears to spread more easily than the original virus but doesn't seem to cause worse illness.Gamma (P.1). In January 2021, experts spotted this COVID-19 variant in people from Brazil who'd traveled to Japan. By the end of that month, it was showing up in the U.S.The Gamma variant appears to be more contagious than earlier strains of the virus. And it may be able to infect people who've already had COVID-19. A report from Brazil confirms that a 29-year-old woman came down with this variant after an earlier coronavirus infection a few months before.

Some early research suggests that the variant's changes might help it evade antibodies (made by your immune system after an infection or a vaccine) that fight the coronavirus. A lab study shows that the Pfizer-BioNTech vaccine can neutralize the fast-spreading Brazil strain. But more research is needed. Delta (B.1.617.2). This variant was spotted in India in December 2020. It caused a huge surge in cases in mid-April 2021. This highly contagious variant is now found in 178 countries including the U.S., the U.K., Australia, and all of Europe. It's the dominant strain in the U.S. and the U.K.

A study of the COVID-19 vaccine's effectiveness against this variant found that:

- Two doses of the Pfizer-BioNTech vaccine were 88% effective 2 weeks after the second dose.
- Two doses of the AstraZeneca vaccine available in the U.K. were 60% effective.
- Both vaccines are only 33% effective 3 weeks after the first dose.

For people who haven't had the coronavirus vaccine, the Delta variant may cause more severe illness than the original strain of the virus. Vaccinated people may also get what's called a "breakthrough infection," but they're less likely to be seriously sick or to die. The relatively low

rate of vaccination in some areas of the country is the main reason that the Delta variant has been able to spread so rapidly and shows no signs of slowing down. Getting the vaccine is the best way to slow the spread of the coronavirus and protect yourself against serious illness or death.

Mu (B.1.621). Experts first spotted this COVID-19 variant (pronounced m'yoo) in Colombia in January 2021. Since then, countries in South America and Europe have reported outbreaks of Mu. In the U.S., the Centers for Disease Control and Prevention says Mu reached a peak in June 2021, when it made up less than 5% of variants going around the country. As of early September, it had been steadily declining. Still, scientists continue to track Mu. The World Health Organization (WHO) says this variant has mutations that might make COVID-19 vaccines and our immune systems less effective against it. Early data suggests it has certain similarities to the Beta variant, but we need more research to know for sure.In August 2021, the WHO labeled Mu a "variant of interest." In general, variants of interest might pose an emerging risk to the world's public health, with the potential to do things like spread more easily, cause worse disease, or evade vaccines or tests. But they're considered less of a threat than "variants of concern," like Alpha, Beta, Gamma, and Delta.

As of September 2021, the CDC hadn't escalated Mu to being a variant of interest in the U.S. The agency intends to keep tracking it along with the other variants.R.1. Scientists first detected R.1 in a number of countries, including Japan. There was an outbreak at a Kentucky nursing home in March 2021, when an unvaccinated health care worker passed it to about 45 other staff and residents.

The WHO labeled it a "variant under monitoring" in April 2021, meaning some of its characteristics may pose a future risk to humans.As of October 2021, the CDC hadn't labeled R.1 as a variant of concern or interest.Epsilon, Theta, and Zeta were at one point listed as variants of interest and were downgraded by the WHO. They are still being monitored.

Earlier Coronavirus Variants

Earlier in 2020, when the pandemic was new, you might have heard that there was more than one strain of the new coronavirus. Is it true? The answer appeared to be yes.The theory about different variants of the new coronavirus came from a study in China. Researchers were studying changes in coronavirus RNA over time to figure out how various coronaviruses are related to each other. They looked at 103 samples of the new coronavirus collected from people, and they looked at

coronaviruses from animals. It turned out that the coronaviruses found in humans weren't all the same.There were two types, which the researcher's called "L" and "S." They're very similar, with slight differences in two places. It looks like the S type came first. But the scientists say the L type was more common early in the outbreak.

The virus that causes COVID-19 will probably keep changing. Experts may find new variants. It's impossible to predict how those virus changes might affect what happens. But change is just what viruses do.The development of vaccines against emerging and reappearing viruses is one of the most rational approaches to controlling their rapid infection. More than 64 vaccine candidates for SARSCoV2 are currently under development . Technologies used to develop these vaccines include, but are not limited to, mRNA vaccines, replication-deficient virus vector vaccines, inactivated pathogen vaccines, protein subunit vaccines, and virus-like particles. USAFDA has granted Emergency Use Authorization (EUA) for two mRNA-based vaccines. One is from PfizerBioNTech and the other is from Moderna. In addition, the non-replicating viral vector-based vaccine developed by Johnson & Johnson received the FDA's EUA for use in the United States. These vaccines appear to be very successful in containing SARSCoV2. Variant of Concern (VOC) and Variant of Concern (VOI) of SARSCoV2 However, variants such as the Delta and Delta Plus variants that contain multiple mutations within the SRBD are effective for these vaccines. May be compromised . In addition, the efficacy and endurance of these vaccines against vulnerable populations, including children, pregnant women, immunocompromised individuals, and those with COVID19 comorbidities, is unknown . Attempts to reuse multiple drug candidates to control and / or control rapid viral infections and COVID19-related mortality and morbidity have resulted in mild to moderate efficacy. To date, remdesivir (RDV; GS5734) is the only antiviral drug approved for the treatment of patients with COVID 19 in the United States . A randomized, double-blind, placebo-controlled clinical trial conducted by the National Institutes of Health (NIH) found shorter hospital stays for COVID 19 patients when treated with RDV compared to placebo-controlled (NCT04280705). In contrast, another multicenter randomized clinical trial conducted by the World Health Organization (WHO) has not reported a significant effect of RDV on hospitalized COVID 19 patients (NCT04315948) . According to current US guidelines, the Centers for Disease Control and Prevention (CDC) does not recommend specific treatments for inpatients and in patients with mild to moderate COVID 19 disease that do not require oxygen support. For inpatients requiring oxygen supplementation (with or without

ventilation), RDV alone or with dexamethasone is recommended, depending on the patient's condition and the availability of the two drugs(www.covid19treatmentguidelines). .nih.gov). These facts underscore the need to develop effective antivirals that can serve as prophylactic and

/ or therapeutic agents for COVID19. In addition, because vaccines are hesitantly available, there are likely to be populations that may not be vaccinated, requiring the development of more effective small molecule antivirals. Since the first step in the SARSCoV2 virus life cycle involves the binding of SRBD to the ACE2 receptor in the host cell, the development of effective prophylaxis against COVID19 should preferably target the virus SRBD. Two high-resolution crystal structure complexes, SRBD and ACE2, have been reported . The crystal structure of SRBD (PDB entry 6M0J) containing the WuhanHu1 sequence complexed with human ACE2 provides atomic details for the interaction interface . Other crystal structures of the SRBD / ACE2 complex (PDB entry details the atoms of the interaction between ACE2 and SRBD on P.1.

Spike Proteins

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus behind the worldwide outbreak of COVID-19 disease. One of the key biological characteristics of SARS- CoV-2, as well as several other viruses, is the presence of spike proteins that allow these viruses to penetrate host cells and cause infection.Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus behind the worldwide outbreak of COVID-19 disease. One of the key biological characteristics of SARS-CoV-2, as well as several other viruses, is the presence of spike proteins that allow these viruses to penetrate host cells and cause infection.Coronaviruses (CoVs) like the Middle East respiratory syndrome (MERS)-CoV, which had infected almost 2,500 individuals by the end of 2019, as well as the novel severe acute respiratory syndrome (SARS)-CoV-2, are enveloped and spherical viruses that typically measure between 80 and 120 nanometers (nm) in size.The RNA genome of coronaviruses, which, at a median length of 29 kb is the longest among all RNA viruses, is comprised of six to ten open reading frames (ORFs) that are responsible for encoding both the replicase and structural proteins for the virus.Each of the components of the viral genome is packaged into a helical nucleocapsid that is surrounded by a lipid bilayer.The viral envelope of coronaviruses is typically made up of three proteins that include the membrane protein (M), the envelope protein (E), and the spike protein (S).

OBJECTIVES

1. Analysis of structure, domain and function of SARS-CoV-2 variant by genome analysis using Multiple sequence alignment.
2. Analysis of human SARS-CoV-2 variant using Molecular docking .
3. In silico analysis and Computer Aided Drug Design of SARS-CoV-2 variant for the conformation and position of binding affinity.

Review of Literature

The COVID-19 Pandemic The COVID-19 global pandemic is the greatest challenge to community health this century, and it has had the most significant impact on vulnerable populations, such as senior citizens and minorities [9][10][11]. COVID-19 is a severe respiratory syndrome coronavirus 2 (SARS-Co-V-2) transmitted through respiratory droplets from person to person contact with an infected individual, with symptoms ranging from mild to severe [12][13]. Nursing homes' congregate nature and resident population increase the risk of transmission, morbidity, and mortality associated with COVID-19 [14]. The Centers for Disease Control and Prevention (CDC, n.d.) advised that severe illness from COVID-19 could include hospitalization, placement in an intensive care unit, the use of a ventilator to assist with difficulty breathing, and death. By January 10, 2021, there had been a total of 549,852 United States nursing home residents with confirmed cases and 107,107 COVID-19 deaths (COVID- 19 Nursing Home Data, 2021). Nursing home residents represent less than.5% of the United States population; however, they made approximately 36% of the deaths related to COVID-19 in the early waves of the pandemic [15]. The pandemic highlighted the need for increased public and political attention on the inadequate preparation and unique infection control challenges nursing homes face [16]. Further confounding the pandemic in the United States was the history of racial, ethnic, and colonial oppression, which has allowed health equity to remain in the margins of the public health response efforts [17]. COVID-19 and Vulnerable Populations.

During the earlier waves of COVID-19, long-term care (LTC) facilities were the United States epicenter of COVID-19 for vulnerable populations [18][19]. By August 2020, more than 60,000 deaths occurred in United States nursing homes and LTC facilities, accounting for half of the total COVID-19 related deaths in the country [20]. Kirkland, Washington, is where the first United States nursing home confirmed COVID-19 case of infection occurred [2][21]. The initial case occurred at Life Care Center of Kirkland on January 22, 2020, and the first outbreak occurred in the same community on February 27, 2020 (Morris et al., 2020). On February 29, 2020, the Seattle & King County Public Health Department reported the first COVID-19 death [20]. By March, every state in the United States began reporting cases [20]. On March 13,

2020, the United States President declared a national emergency, with CMS issuing guidance for infection control and prevention in nursing homes and recommendations for visitor restriction [20]. SARS-CoV-2 is a newly discovered virus that is closely related to bat coronaviruses, [22] pangolin coronaviruses,[23][24] and SARS-CoV.[24] The first known outbreak started in Wuhan, Hubei, China, in November 2019. Many early cases were linked to people who had visited the Huanan Seafood Wholesale Market there,[25][26][27] but it is possible that human-to-human transmission began earlier.[28][29]

The scientific consensus is that the virus is most likely of zoonotic origin, from bats or another closely-related mammal.[28][30][31] Despite this, the subject has generated extensive speculation about alternative origins.[32] [33] The origin controversy heightened geopolitical divisions, notably between the United States and China.[34] The earliest known infected person fell ill on 1 December 2019. That individual did not have a connection with the later wet market cluster.[35][36] However, an earlier case may have occurred on 17 November.[37] Two- thirds of the initial case cluster were linked with the market.[38][39][40] Molecular clock analysis suggests that the index case is likely to have been infected between mid-October and mid- November 2019.[41][42] Official "case" counts refer to the number of people who have been tested for COVID-19 and whose test has been confirmed positive according to official protocols whether or not they experienced symptomatic disease.[43][44] Due to the effect of sampling bias, studies which obtain a more accurate number by extrapolating from a random sample have consistently found that total infections considerably exceed the reported case counts.[45][46] Many countries, early on, had official policies to not test those with only mild symptoms.[47][48] The strongest risk factors for severe illness are obesity, complications of diabetes, anxiety disorders, and the total number of conditions.[49]

In early 2020, a meta-analysis of self-reported cases in China by age indicated that a relatively low proportion of cases occurred in individuals under 20.[50] It was not clear whether this was because young people were less likely to be infected, or less likely to develop symptoms and be tested.[51] A retrospective cohort study in China found that children and adults were just as likely to be infected.[52] Among more thorough studies, preliminary results from 9 April 2020 found that in Gangelt, the centre of a major infection cluster in Germany, 15 percent of a population sample tested positive for antibodies.[53] Screening for COVID-19 in pregnant women in New York City, and blood donors in the Netherlands, found rates of positive

antibody tests that indicated more infections than reported.[54][55] Seroprevalence-based estimates are conservative as some studies show that persons with mild symptoms do not have detectable antibodies.[56] Initial estimates of the basic reproduction number (R_0) for COVID- 19 in January were between 1.4 and 2.5,[57] but a subsequent analysis claimed that it may be about 5.7 (with a 95 percent confidence interval of 3.8 to 8.9).[58] In December 2021, the number of cases continued to climb due to several factors including new COVID-19 variants. As of that 28 December, 282,790,822 individuals worldwide had been confirmed as infected.[59] As of 14 April 2022, over 500 million cases were confirmed globally.[60] Most cases are unconfirmed with the Institute for Health Metrics and Evaluation estimating the true number of cases as of early 2022 to be in the billions.[61][62] As of 14 May 2022, more than

6.26 million[63] deaths had been attributed to COVID-19. The first confirmed death was in Wuhan on 9 January 2020.[64] These numbers vary by region and over time, influenced by testing volume, healthcare system quality, treatment options, government response,[65] time since the initial outbreak, and population characteristics, such as age, sex, and overall health.[66] Multiple measures are used to quantify mortality.[67] Official death counts typically include people who died after testing positive. Such counts exclude deaths without a test.[68] Conversely, deaths of people who died from underlying conditions following a positive test may be included.[69] Countries such as Belgium include deaths from suspected cases, including those without a test, thereby increasing counts.[70] Official death counts have been claimed to underreport the actual death toll, because excess mortality (the number of deaths in a period compared to a long-term average) data show an increase in deaths that is not explained by COVID-19 deaths alone.[71] Using such data, estimates of the true number of deaths from COVID-19 worldwide have included a range from 9.5 to 18.6 million by *The Economist*,[71] as well as over 10.3 million by the Institute for Health Metrics and Evaluation[72] and ~18.2 million (earlier) deaths between Jan 1, 2020, and Dec 31, 2021 by a comprehensive international study.[73] Such deaths include deaths due to healthcare capacity constraints and priorities, as well as reluctance to seek care (to avoid possible infection).[74] Further research may help distinguish the proportions directly caused by COVID-19 from those caused by indirect consequences of the pandemic.[75] In May 2022, the WHO estimated the number of excess deaths to be 14.9 million compared to 5.4 million reported Covid deaths, with the majority of the unreported 9.5 million deaths believed to be direct deaths due the virus, rather

than indirect deaths. Some deaths were because people with other conditions could not access medical services.[76]

The time between symptom onset and death ranges from 6 to 41 days, typically about 14 days.[77] Mortality rates increase as a function of age. People at the greatest mortality risk are the elderly and those with underlying conditions.[78][79] In May 2022 the World Health Organization estimated that COVID has caused just under 15 million excess deaths worldwide. The virus directly caused most of these deaths but some were because people with other conditions could not access medical services.[80] The infection fatality ratio (IFR) is the cumulative number of deaths attributed to the disease divided by the cumulative number of infected individuals (including asymptomatic and undiagnosed infections and excluding vaccinated infected individuals).[83][84][85] It is expressed in percentage points (not as a decimal).[86] Other studies refer to this metric as the 'infection fatality risk'.[87][88]

In November 2020, a review article in Nature reported estimates of population-weighted IFRs for various countries, excluding deaths in elderly care facilities, and found a median range of 0.24% to 1.49%.[89] IFRs rise as a function of age (from 0.002% at age 10 and 0.01% at age 25, to 0.4% at age 55, 1.4% at age 65, 4.6% at age 75, and 15% at age 85). These rates vary by a factor of ~10,000 across the age groups.[90] For comparison the IFR for middle-aged adults is two orders of magnitude more likely than the annualised risk of a fatal automobile accident and far more dangerous than seasonal influenza.[90] In December 2020, a systematic review and meta-analysis estimated that population-weighted IFR was 0.5% to 1% in some countries (France, Netherlands, New Zealand, and Portugal), 1% to 2% in other countries (Australia, England, Lithuania, and Spain), and about 2.5% in Italy. This study reported that most of the differences reflected corresponding differences in the population's age structure and the age- specific pattern of infections.[91]

Another metric in assessing death rate is the case fatality ratio (CFR), which is the ratio of deaths to diagnoses. This metric can be misleading because of the delay between symptom onset and death and because testing focuses on symptomatic individuals.[92] Based on Johns Hopkins University statistics, the global CFR is 1.20 percent (6,262,419 deaths for 520,660,058 cases) as of 14 May 2022.[93] The number varies by region and has generally declined over time.[93] Symptoms of COVID-19 are variable, ranging from mild symptoms to

severe illness.[94][95] Common symptoms include headache, loss of smell and taste, nasal congestion and runny nose, cough, muscle pain, sore throat, fever, diarrhoea, and breathing difficulties. People with the same infection may have different symptoms, and their symptoms may change over time. Three common clusters of symptoms have been identified: one respiratory symptom cluster with cough, sputum, shortness of breath, and fever; a musculoskeletal symptom cluster with muscle and joint pain, headache, and fatigue; a cluster of digestive symptoms with abdominal pain, vomiting, and diarrhoea. In people without prior ear, nose, and throat disorders, loss of taste combined with loss of smell is associated with COVID-19 and is reported in as many as 88% of cases.[96][97][98]

Transmission of COVID-19

The disease is mainly transmitted via the respiratory route when people inhale droplets and small airborne particles (that form an aerosol) that infected people exhale as they breathe, talk, cough, sneeze, or sing.[99][100][101][102] Infected people are more likely to transmit COVID-19 when they are physically close. However, infection can occur over longer distances, particularly indoors. [103] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to the broad family of viruses known as coronaviruses.[104] It is a positive-sense single- stranded RNA (+ssRNA) virus, with a single linear RNA segment. Coronaviruses infect humans, other mammals, including livestock and companion animals, and avian species.[105] Human coronaviruses are capable of causing illnesses ranging from the common cold to more severe diseases such as Middle East respiratory syndrome (MERS, fatality rate ~34%). SARS-CoV-2 is the seventh known coronavirus to infect people, after 229E, NL63, OC43, HK3U1, MERS-CoV, and the original SARS-CoV.[106]

COVID-19 Diagnosis

The standard methods of testing for presence of SARS-CoV-2 are nucleic acid tests,[107] which detects the presence of viral RNA fragments.[108] As these tests detect RNA but not infectious virus, its "ability to determine duration of infectivity of patients is limited."[109] The test is typically done on respiratory samples obtained by a nasopharyngeal swab; however, a nasal swab or sputum sample may also be used.[110][111] The WHO has published several testing protocols for the disease.[112]

Prevention

Preventive measures to reduce the chances of infection include getting vaccinated, staying at home, wearing a mask in public,[113] avoiding crowded places, keeping distance from others, ventilating indoor spaces, managing potential exposure durations,[114] washing hands with soap and water often and for at least twenty seconds, practising good respiratory hygiene, and avoiding touching the eyes, nose, or mouth with unwashed hands.[115][116] Those diagnosed with COVID-19 or who believe they may be infected are advised by the CDC to stay home except to get medical care, call ahead before visiting a healthcare provider, wear a face mask before entering the healthcare provider's office and when in any room or vehicle with another person, cover coughs and sneezes with a tissue, regularly wash hands with soap and water and avoid sharing personal household items.[117][118]

Vaccines

A COVID-19 vaccine is intended to provide acquired immunity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). Prior to the COVID-19 pandemic, an established body of knowledge existed about the structure and function of coronaviruses causing diseases like severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). This knowledge accelerated the development of various vaccine platforms during early 2020.[119] The initial focus of SARS-CoV-2 vaccines was on preventing symptomatic, often severe illness.[120] On 10 January 2020, the SARS-CoV-2 genetic sequence data was shared through GISAID, and by 19 March, the global pharmaceutical industry announced a major commitment to address COVID-19.[121] The COVID-19 vaccines are widely credited for their role in reducing the severity and death caused by COVID-19.[122][123]

As of late-December 2021, more than 4.49 billion people had received one or more doses[124] (8+ billion in total) in over 197 countries. The Oxford-AstraZeneca vaccine was the most widely used.[125]

Treatment -

For the first two years of the pandemic, no specific and effective treatment or cure was available.[126][127] In 2021, the European Medicines Agency's (EMA) Committee for Medicinal

Products for Human Use (CHMP) approved the oral antiviral protease inhibitor, Paxlovid (nirmatrelvir plus AIDS drug ritonavir), to treat adult patients.[128] FDA later gave it an EUA.[129] Most cases of COVID-19 are mild. In these, supportive care includes medication such as paracetamol or NSAIDs to relieve symptoms (fever,[130] body aches, cough), adequate intake of oral fluids and rest. [131] Good personal hygiene and a healthy diet are also recommended.[132] Supportive care includes treatment to relieve symptoms, fluid therapy, oxygen support and prone positioning, and medications or devices to support other affected vital organs.[133] More severe cases may need treatment in hospital. In those with low oxygen levels, use of the glucocorticoid dexamethasone is recommended, to reduce mortality.[134] Noninvasive ventilation and, ultimately, admission to an intensive care unit for mechanical ventilation may be required to support breathing.[135] Extracorporeal membrane oxygenation (ECMO) has been used to address the issue of respiratory failure.[136][137]

Variants -

Several variants have been named by WHO and labelled as a variant of concern (VoC) or a variant of interest (VoI). They share the more infectious D614G mutation:[141][142][143] Delta dominated and then eliminated earlier VoC from most jurisdictions. Omicron's immune escape ability may allow it to spread via breakthrough infections, which in turn may allow it to coexist with Delta, which more often infects the unvaccinated.[144]

Prognosis -

The severity of COVID-19 varies. The disease may take a mild course with few or no symptoms, resembling other common upper respiratory diseases such as the common cold. In 3–4% of cases (7.4% for those over age 65) symptoms are severe enough to cause hospitalization.[146] Mild cases typically recover within two weeks, while those with severe or critical diseases may take three to six weeks to recover. Among those who have died, the time from symptom onset to death has ranged from two to eight weeks. Prolonged prothrombin time and elevated C-reactive protein levels on admission to the hospital are associated with severe course of COVID-19 and with a transfer to intensive care units (ICU).[147][148]

History of Sars-CoV-2   -

 The outbreak was discovered in Wuhan in November 2019. It is possible that human-to- human transmission was happening before the discovery. Based on a retrospective analysis starting from December 2019, the number of cases in Hubei gradually increased, reaching 60 by 20 December and at least 266 by 31 December. A pneumonia cluster was observed on 26 December and treated by Doctor Zhang Jixian. She informed the Wuhan Jianghan CDC on 27 December.[149] Vision Medicals reported the discovery of a novel coronavirus to the China CDC (CCDC) on 28 December.[150][151] On 30 December, a test report from CapitalBioMedlab addressed to Wuhan Central Hospital reported an erroneous positive result for SARS, causing doctors there to alert authorities. Eight of those doctors, including Li Wenliang (who was also punished on 3 January),[152] were later admonished by the police for spreading false rumours; and Ai Fen was reprimanded.[153] That evening, Wuhan Municipal Health Commission (WMHC) issued a notice about "the treatment of pneumonia of unknown cause".[154] The next day, WMHC made the announcement public, confirming 27 cases[155][156][157] enough to trigger an investigation.[158]

On 31 December, the WHO office in China was informed of cases of the pneumonia cases[159][160] and immediately launched an investigation.[161] Official Chinese sources claimed that the early cases were mostly linked to the Huanan Seafood Wholesale Market, which also sold live animals.[162] However, in May 2020, CCDC director George Gao indicated the market was not the origin (animal samples had tested negative).[163] On 11 January, WHO was notified by the Chinese National Health Commission that the outbreak was associated with exposures in the market, and that China had identfied a new type of coronavirus, which it isolated on 7 January. Initially, the number of cases doubled approximately every seven and a half days.[164] In early and mid-January, the virus spread to other Chinese provinces, helped by the Chinese New Year migration. Wuhan was a transport hub and major rail interchange.[165] On 10 January, the virus' genome was shared through GISAID.[166] A retrospective study published in March found that 6,174 people had reported symptoms by 20 January. A 24 January report indicated human transmission, recommended personal protective equipment for health workers, and advocated testing, given the outbreak's "pandemic potential".[167][168]On 31 January the first published modelling study warned of inevitable

"independent self-sustaining outbreaks in major cities globally" and called for "large-scale public health interventions."[169]

On 30 January, 7,818 infections had been confirmed, leading WHO to declare the outbreak a Public Health Emergency of International Concern (PHEIC).[170][171] On 11 March, WHO elevated it to a pandemic.[172][173]

MATERIALS AND METHODS

The basic tool in bioinformatics is a computer program that mimics the way biological information systems function in order to predict and provide new insights into the biological world. The program performs computations that provide biologists with information about DNA/RNA sequences, protein structures, gene regulatory mechanisms, and other biological structures and processes. The use of computer software in bioinformatics is the basic underlying principle of the field.

The abundance of available biological information through the production of large-scale genomes has spurred on the development of the field of genomics. In the past two decades, the types of bioinformatics analysis methods have expanded to include a variety of computational methods, including sequence alignment, annotation of eukaryotic proteins and nucleic acids, and genetic programming. The latest paradigm in bioinformatics analysis is that of phylogenetic analysis, where a whole phylogenetic tree is used to infer relationships between disparateorganisms

CBI
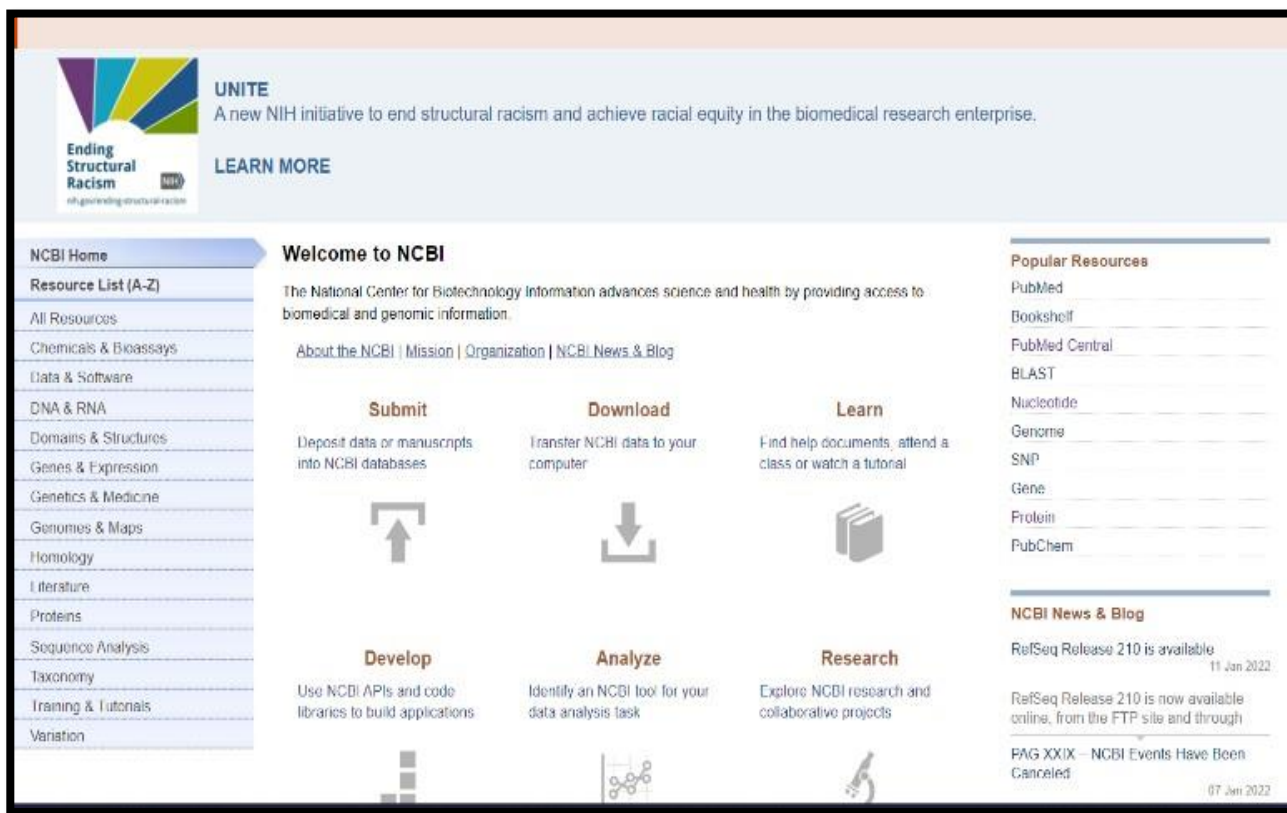
Figure 1- NCBI official website

1. NCBI- National Centre for Biotechnology Information
2. NCBI is the source of public biomedical databases, different software tools used for analysing molecular and genomic data, and research in computational biology.
3. NCBI creates and maintains more than 40 integrated databases which are used by the medical and scientific communities as well as the general public
4. The National Centre for Biotechnology Information (NCBI) provides a comprehensive overview of the scientific literature and databases that authors and publishers can use to support their research.
5. Available free for use at https://www.ncbi.nlm.nih.gov/

FASTA

Figure 2- FASTA official website

1. FASTA is a DNA and protein sequence alignment software which was first described by David J. Lipman and William R. Pearson in 1985.
2. It uses the FASTA format which is now ubiquitous in bioinformatics.
3. The Fasta file format is one of the most common text file formats in bioinformatic
4. FASTA is one of the most used sequence alignment tools which is generally used to search similarities between DNA sequences and proteins...FASTA is one of the fine tools used for similarity searches.
5. FASTA format is a text-based format for presenting either nucleotide sequences or peptide sequences, in which base pairs or amino acids are represented using single- letter codes.
6. In FASTA format a sequence begins with a single-line description, which is followed by lines of sequencedata

   BLAST

1. BLAST finds regions of similarity between biological sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance.
2. https://blast.ncbi.nlm.nih.gov/Blast.cgi
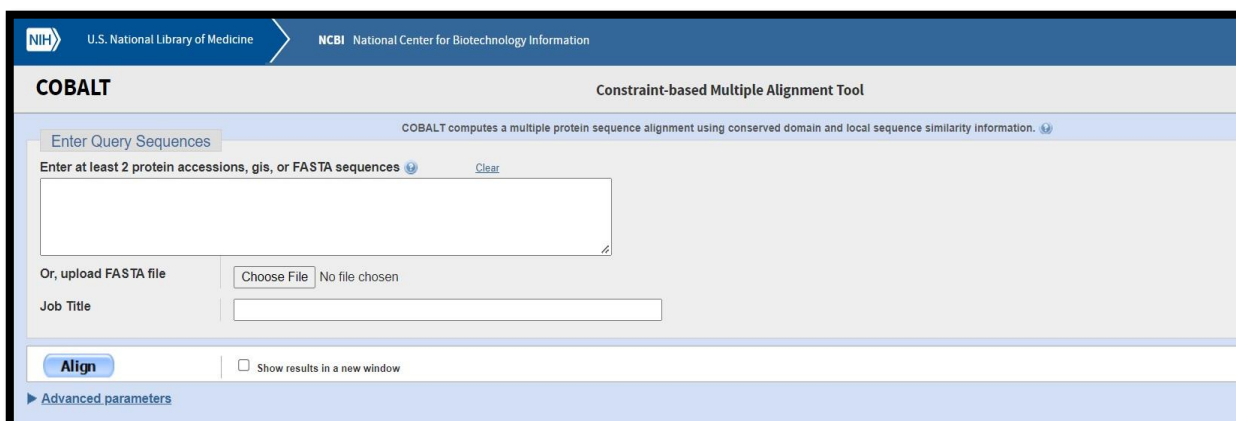

Figure 4- BLAST home page

Figure 5- Home age of COBALT software

1. COBALT is a multiple protein sequence alignment program which uses conserved domain and local sequence similarity information.

2. Pairwise constraints are then incorporated into a progressive multiple alignment.

3. https://www.ncbi.nlm.nih.gov/tools/cobalt/re_cobalt.cgi

Protein Data Bank

Figure 6- Official website of Protein data bank OR homepage of Protein data bank

1. PDB is a database of biological macromolecules such as proteins and nucleotides.
2. Each macromolecule of PDB have a unique ID number which makes it easy for searching particular protein or nucleic acid.
3. There are 3 file formats of PDB
a) PDB file format
b) mmCIF format
c) PDBML format
4. PDB have data submitted by the biologist and biochemist from all over the world.
5. Macromolecule's 3-d structures are obtained by NMR or X-RAY diffraction.
https://www.rcsb.org/
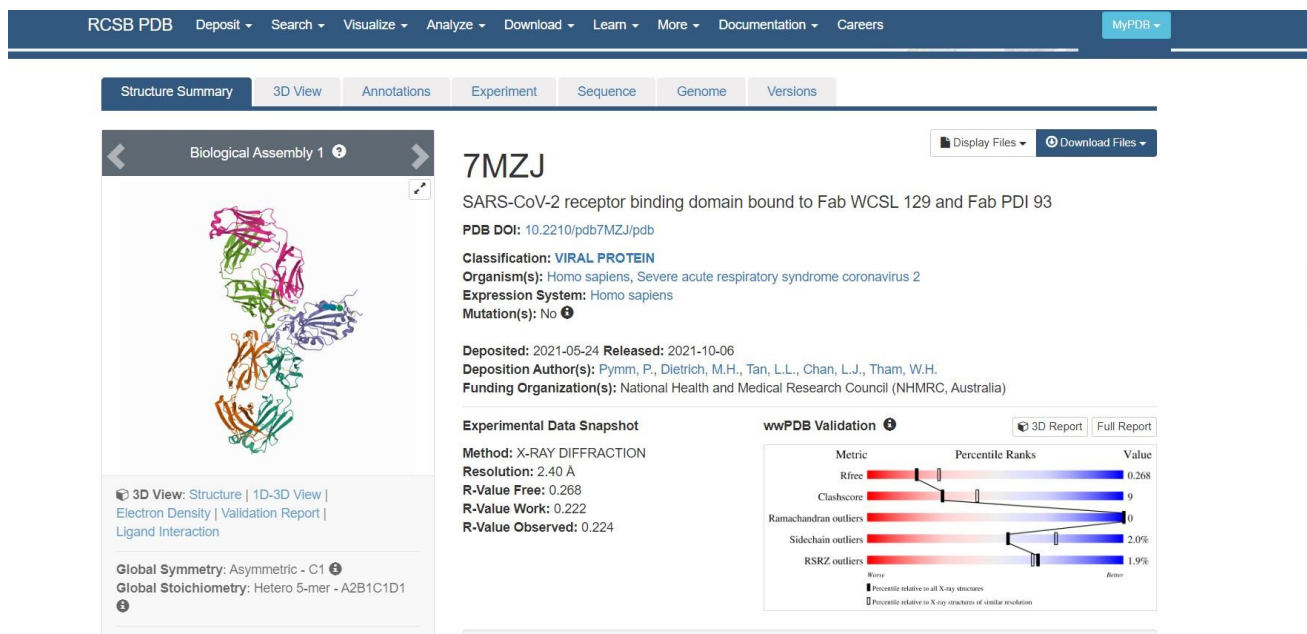
7MZJ PROTEIN SEQUENCE –

Figure 7- 7MZJ PROTEIN SEQUENCE IN PDB

Potent neutralizing monoclonal antibodies are one of the few agents currently available to treat COVID-19. SARS-CoV-2 variants of concern (VOCs) that carry multiple mutations in the viral spike protein can exhibit neutralization resistance, potentially affecting the effectiveness of some antibody-based therapeutics. Here, the generation of a diverse panel of 91 human, neutralizing monoclonal antibodies provides an in-depth structural and phenotypic definition of receptor binding domain (RBD) antigenic sites on the viral spike. These RBD antibodies ameliorate SARS-CoV-2 infection in mice and hamster models in a dose-dependent manner and in proportion to in vitro, neutralizing potency. Assessing the

effect of mutations in the spike protein on antibody recognition and neutralization highlights both potent single antibodies and stereotypic classes of antibodies that are unaffected by currently circulating VOCs, such as B.1.351 and P.1. These neutralizing monoclonal antibodies and others that bind analogous epitopes represent potentially useful future anti-SARS-CoV-2 therapeutics.
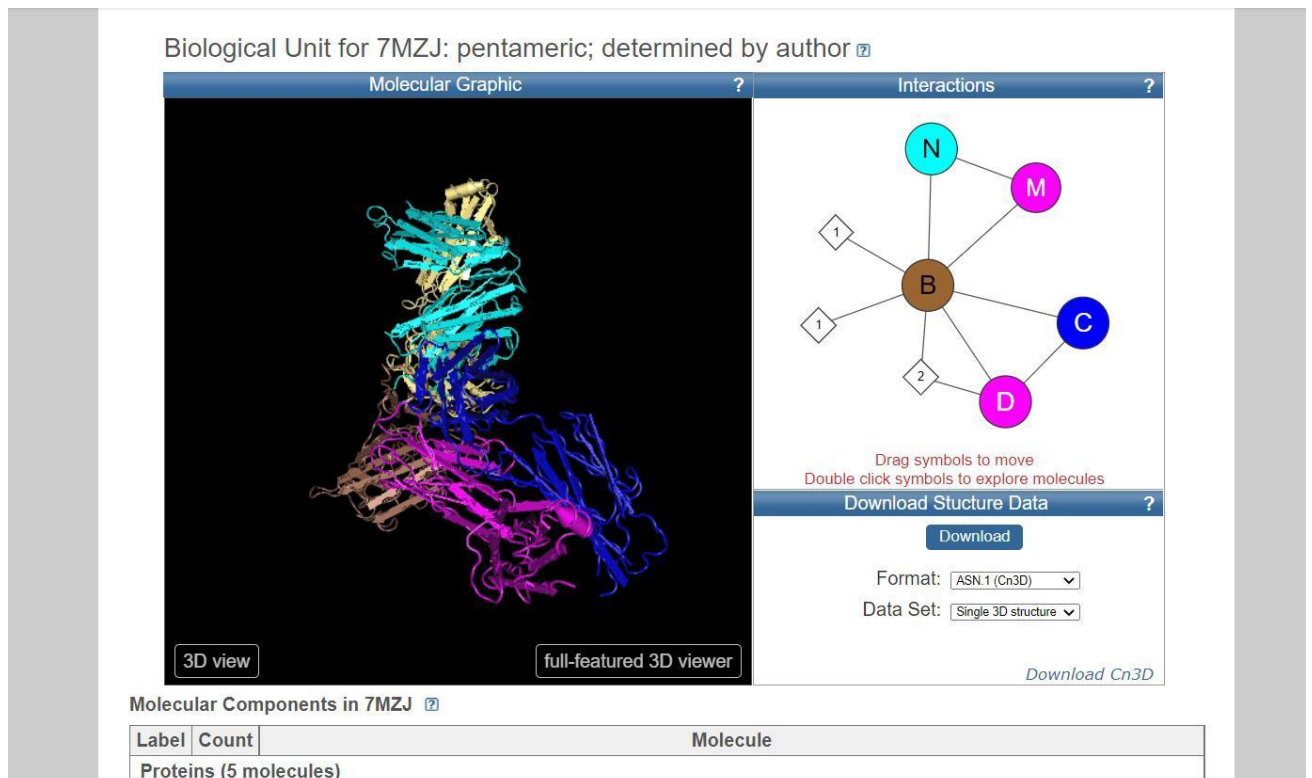

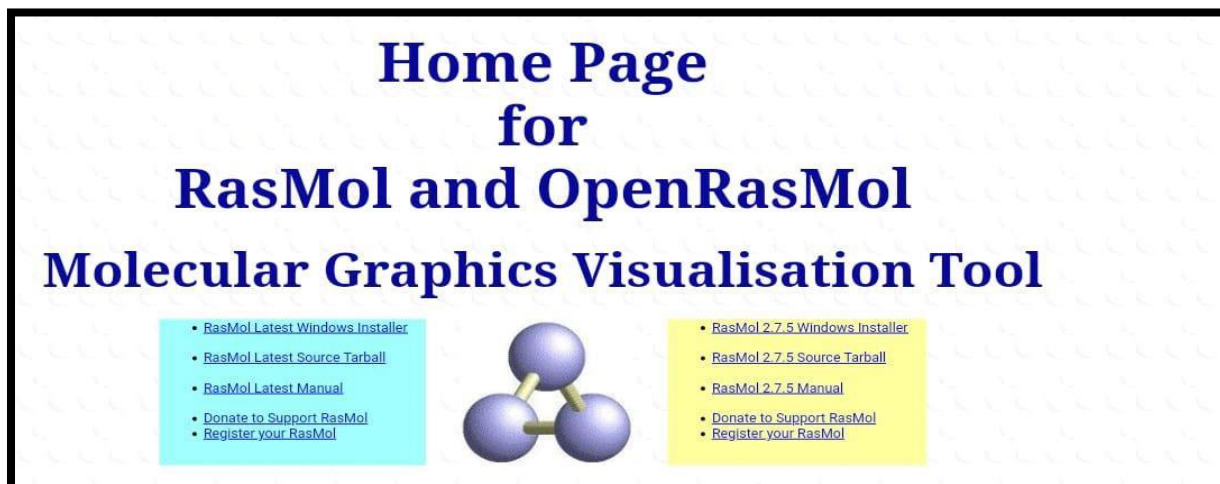**Figure 8- 3D structure prediction of 7MZJ protein sequence**

RASMOL

Figure 9- Homepage of RasMol

1. RasMol was developed by Roger Sayle in the early 1990s.

2. RasMol is molecular graphics visualisation program.

3. It is useful in viewing rotating protein molecules.

4. RasMol reads molecular coordinate files and displays the molecule on screen in variety of representation and colours.

5. Different parts of the molecules can be coloured independently from the rest of the molecule.

6. The displayed molecule can be rotated, translated, zoomed using mouse, scroll bars and command bar line.

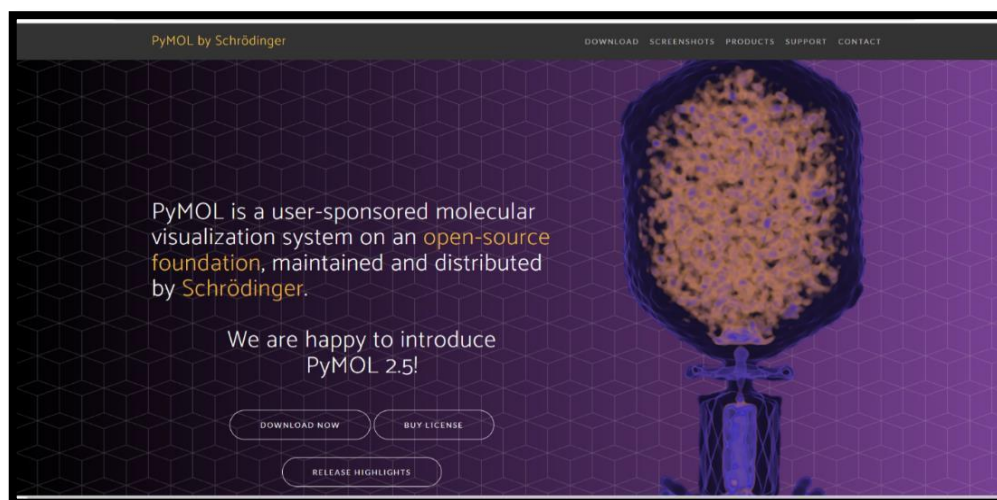7. https://www.rcsb.org/

PyMOL

Figure 10- Homepage of PyMol

1. PyMol was created by Warren Lyford DeLano

2. PyMOL is a cross-platform molecular graphic tool.

3. It is widely used for 3D visualization of macromolecule and proteins.

4. It is a Python based program

5. PyMol is also capable of editing the molecules.

6. PyMol was created by Warren Lyford DeLano

7. PyMOL is an open-source molecular visualization system.

8. This program can produce high-quality 3D images of small molecules and biological macromolecules and is one of the few open-source model visualization tools available for use in education, specifically structural biology.

9. It is universally accessible to scientific way - https://pymol.org/2/
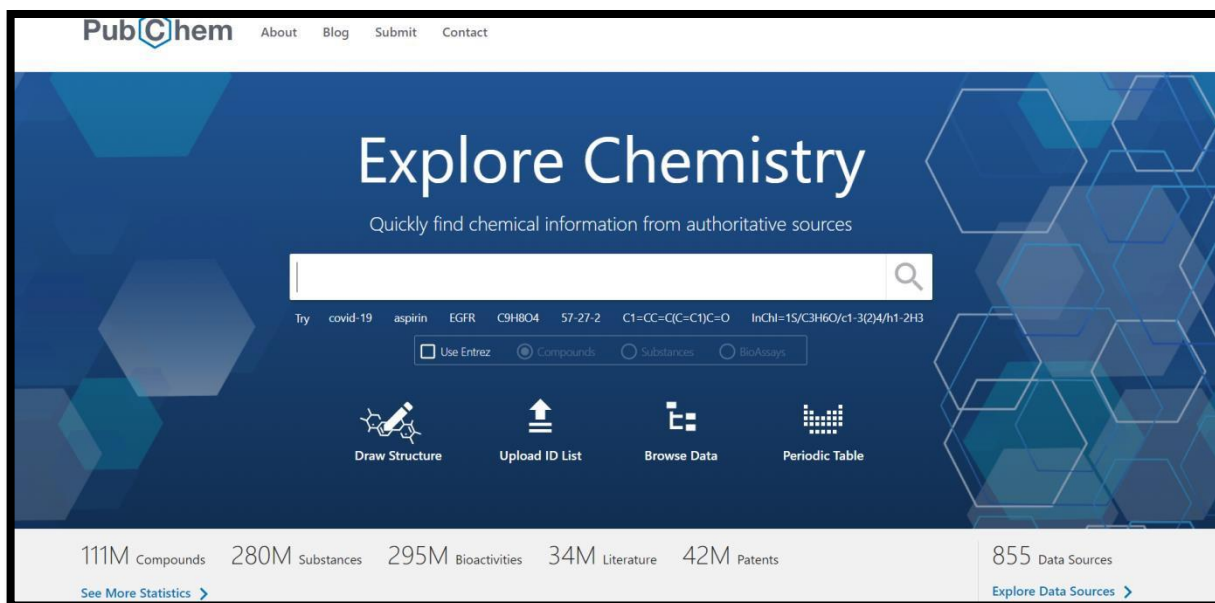
PUBCHEM -

Figure 11- Homepage of PubChem

1- PubChem is a database of chemical molecules and their activities against biological assays.

2- This is maintained by the National Center for Biotechnology Information (NCBI), a component of the National Library of Medicine,part of the United States National Institutes of Health (NIH).

3- PubChem can be accessed for free through a web user interface.

4- Millions of compound structures and descriptive datasets can be freely downloaded via FTP.

5- PubChem contains multiple substance descriptions and small molecules with fewer than 100 atoms and 1000 bonds. More than 80 database vendors contribute to the growing PubChem database.

Figure 12- PubChem official websit
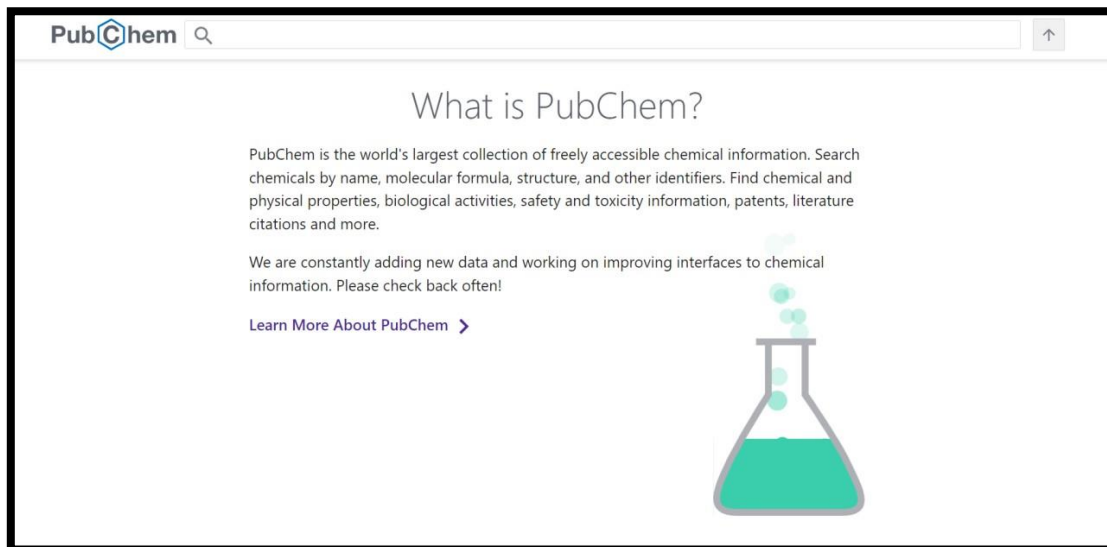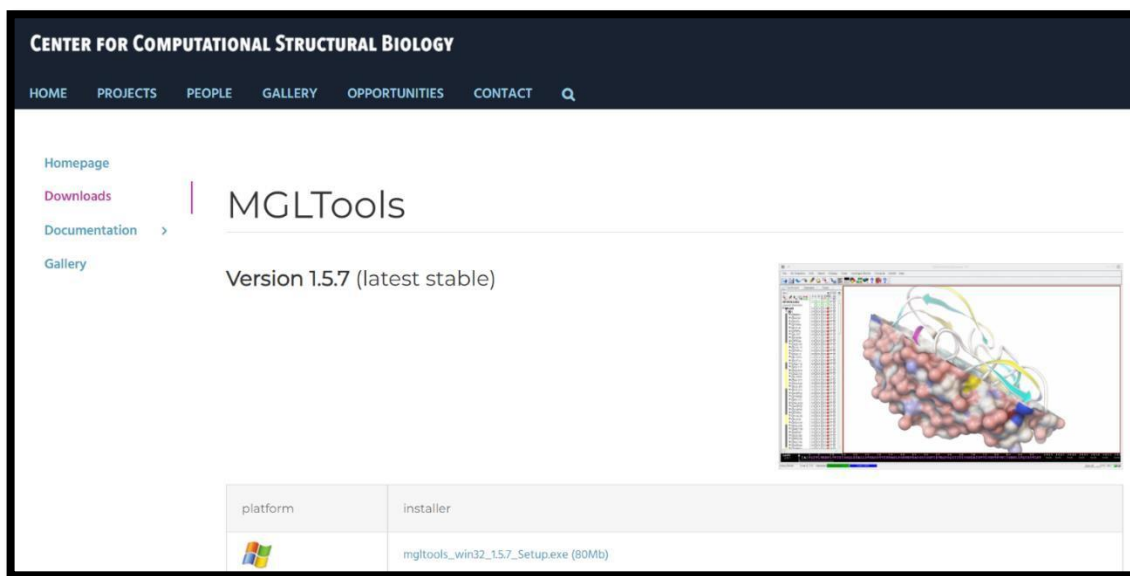
AutoDock

AutoDock is molecular modeling simulation software. It is especially effective for protein- ligand docking. AutoDock 4 is available under the GNU General Public License. AutoDock is one of the most cited docking software applications in the research community. It isused by the FightAIDS@Home and OpenPandemics - COVID-19 projects run at World Community Grid, to search for antivirals against HIV/AIDS and COVID-19. In February 2007, a search of the ISI Citation Index showed more than 1,100 publications had been cited using the primary AutoDock method papers. As of 2009, this number surpassed 1,200.AutoDock Vina is a successor of AutoDock, significantly improved in terms of accuracy and performance. It is available under the Apache license. Both AutoDock and Vina are currently maintained by Scripps Research, specifically the Center for Computational Structural Biology. AutoDock is a suite of automated docking tools. It is designed to predict how small molecules, such as substrates or drug candidates, bind to a receptor of known 3D structure. Current distributions of AutoDock consist of two generations of software: AutoDock 4 and AutoDock Vina.

Figure 13- Autodock official website

RESULTS AND DISCUSSION

Conserve Domain

Chain B, Spike protein S1

PDB: 7MZJ_B

```
>pdb|7MZJ|B Chain B, Spike protein S1
NITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSF
VIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDIST
EIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPGSHHHHHH
```

Receptor-binding domain of the S1 subunit of severe acute respiratory syndrome coronavirus 2 Spike (S) protein; This group contains the receptor-binding domain of the S1 subunit of the spike (S) protein from highly pathogenic human virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as 2019 novel coronavirus (2019-nCoV).

The S1 subunit contains a receptor-binding domain (RBD), while the S2 subunit contains a hydrophobic fusion peptide and two heptad repeat regions. S1 contains two structurally independent domains, the N-terminal domain (NTD) and the C-terminal domain (C-domain).
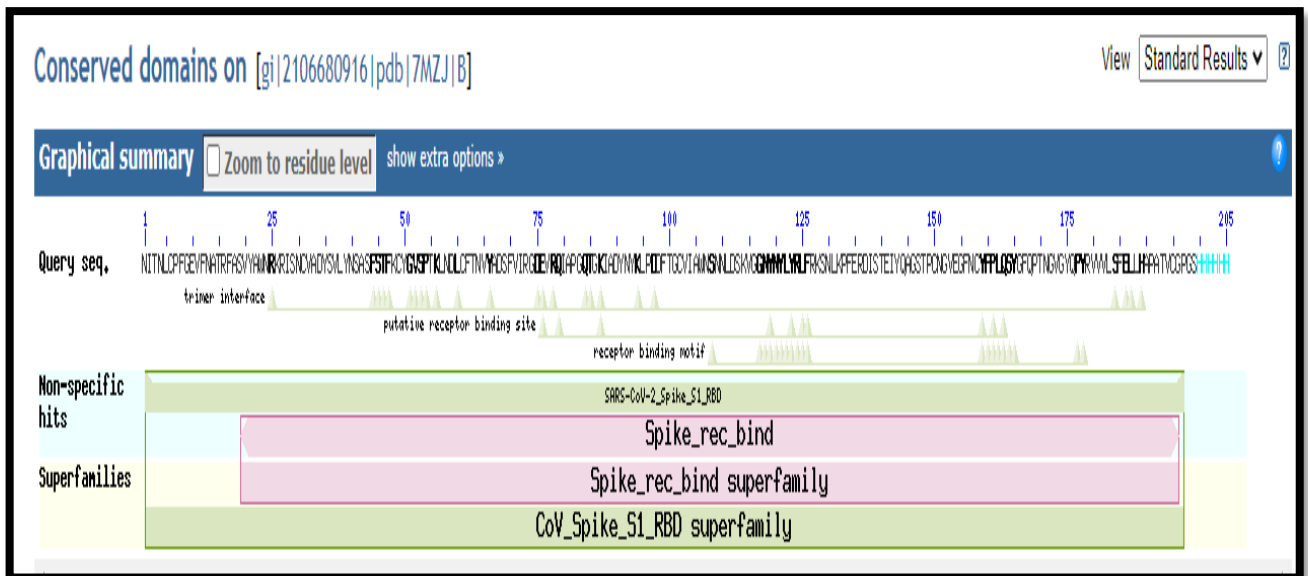
Figure: 14 Conserve Domain Result of Spike Protein
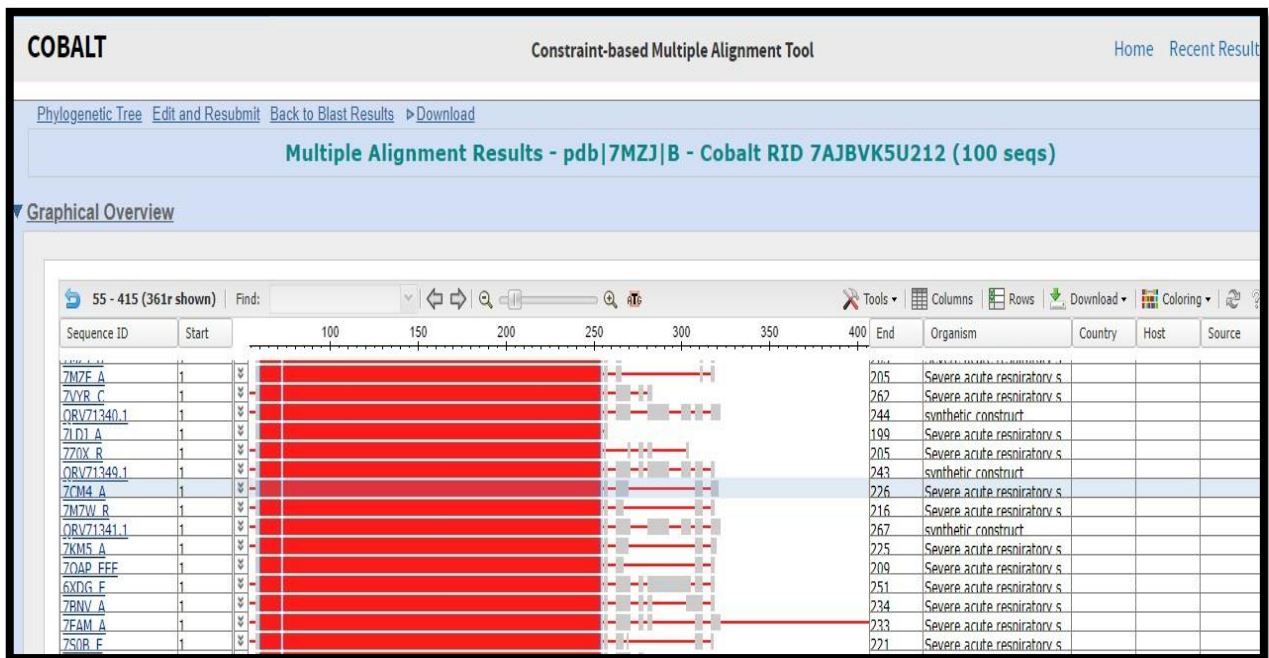
Figure: 15- COBALT

- Panorama at the top with the Alignment view below it, with the first row representing the consensus sequence.
- The Panorama viewer shows the coverage and quality of the alignment.
- Positions where the majority of sequences match the consensus are colored in gray, while positions that contain a large proportion of mismatches are colored in red.
- Alignment view, mismatches are highlighted in red by default.
- Gaps are indicated by a gray line while insertions relative to the consensus/anchor sequence are indicated by a blue bracket

PyMol Results-

- In PyMol software, we analysed the ligand and protein confirmation.

- And analysis of different demonstration.

- Ligands interacts with protein in target cells.
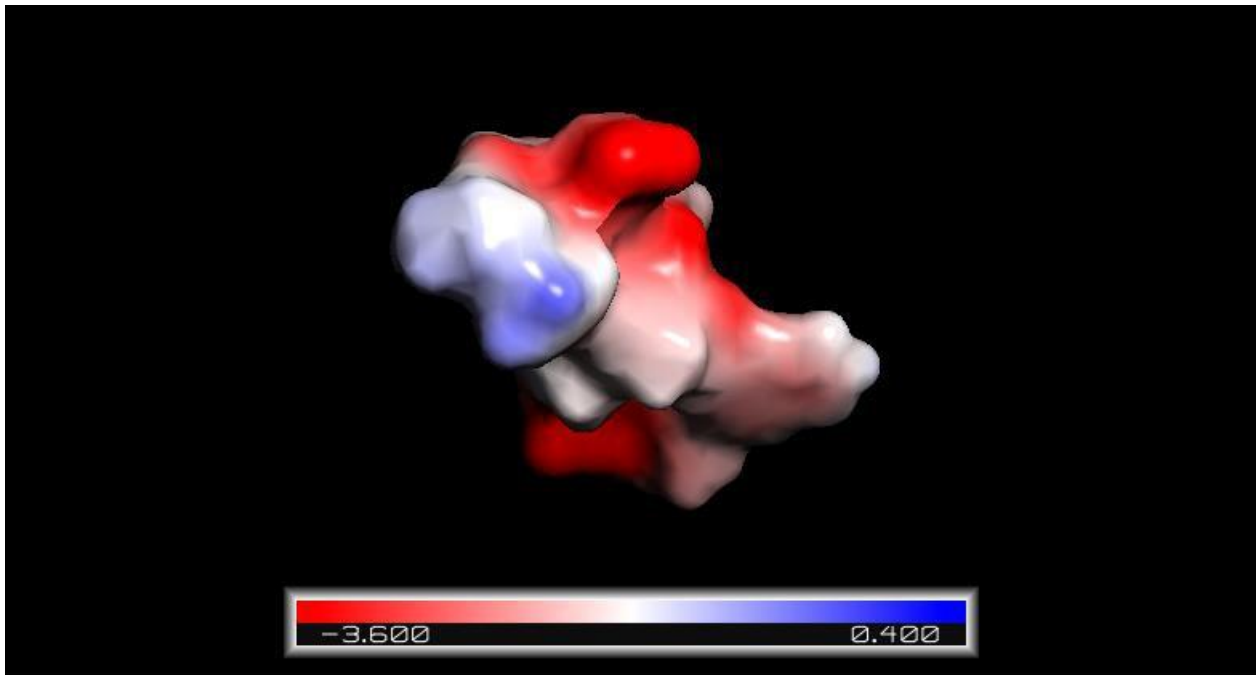
Figure: 16 -Electrostatic Potential image in Pymol

A molecule is rendered as a surface that is colored according to the electrostatic potential. The red color (negative potential) arises from an excess of negative charges near the surface and the blue color (positive potential) occurs when the surface is positively charged. White regions correspond to fairly neutral potentials. Alter the low and high range to -3 and +3, respectively to identify areas that have strong potentials
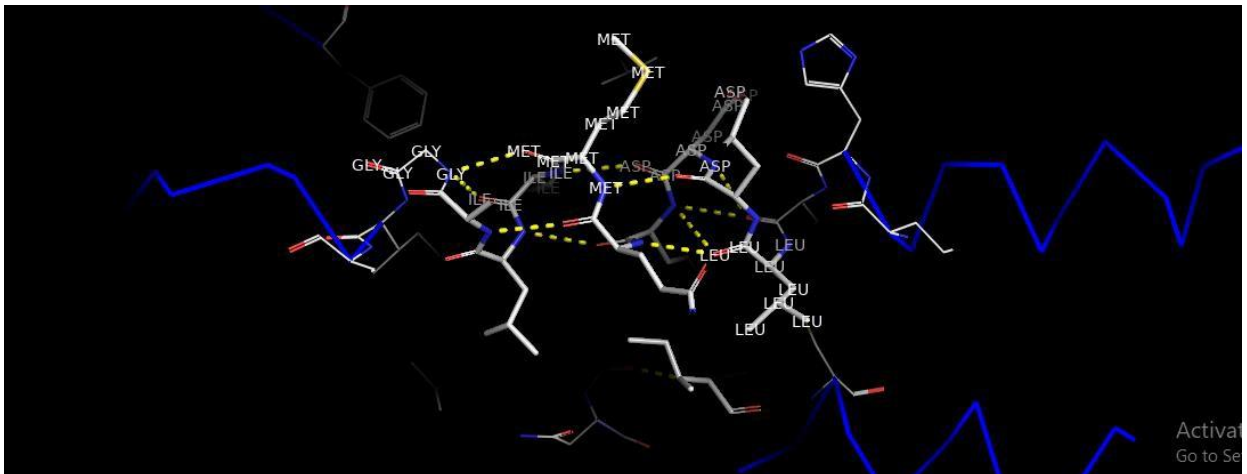
Figure 17- ROVING DENSITY (Active site of Atom)

Results in RasMol

- In RasMol , we analysed the proteins
- We did a different representation such as a stick form, cartoon form,ribbon form
- It is showing the classical format such as alphanbeta.
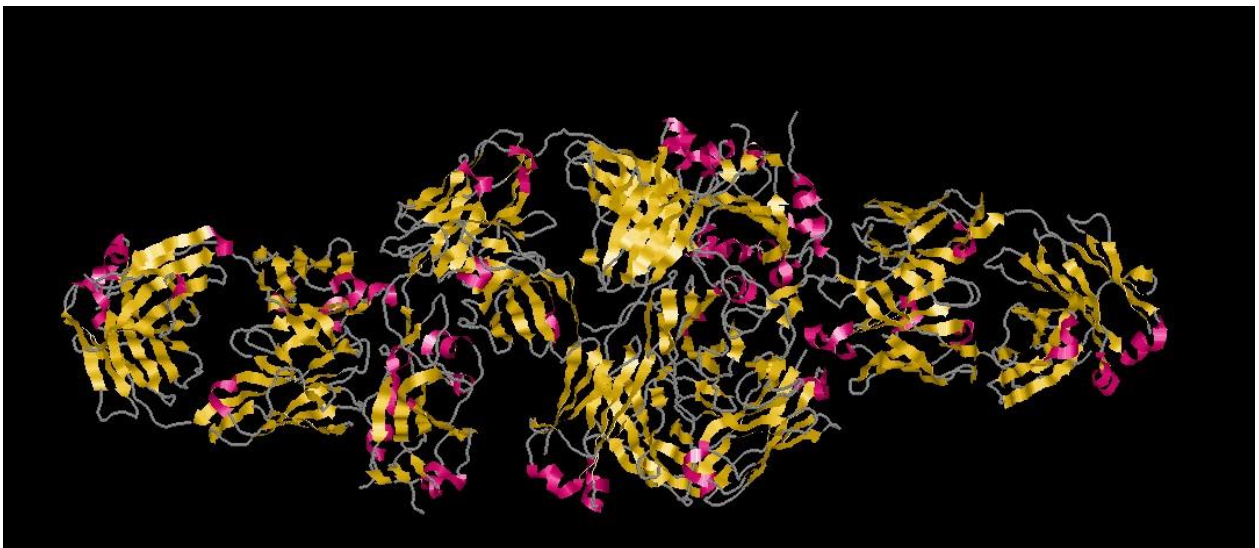
Figure 18- Structure Representation in Rasmol (7MZJ)(Alpha n Beta)

In protein visualization of protein, *Magenta* color represents the *alpha helix* of the protein and *Yellow* color represents the *Beta sheets* of protein.

<u>Spacefill</u>

Syntax: spacefill {<boolean>} Spacefill temperature

Spacefill user Spacefill<value>

- The RasMolspacefill command is used to represent all of the currently selected atoms as solid spheres.

- This command is used to produce both union-of-spheres and ball-and-stick models of a molecule.

- The command, spacefilll true, the default, represents each atom as a sphere of Van der Waals radius.

- The command spacefill off turns off the representation of the selected atom as spheres.

- A sphere radius may be specified as an integer in RasMol units ($1/250^{th}$ Angstrom) or a value containing a decimal point. A value of 500 (2.0 Angstroms) or greater results in a "Parameter value too large" error.

- The RasMol command cpk is synonymous with the spacefill command.
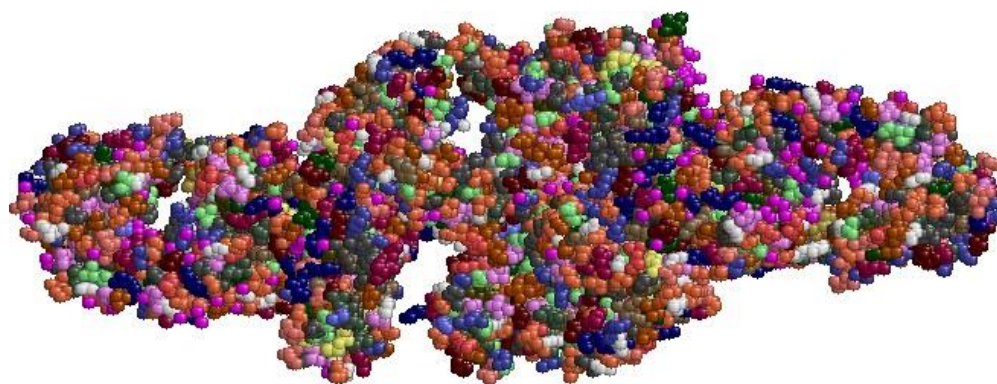
Figure 19- SpacefillRepresntation in RASMOL 7MZJ

- The temperature option sets the radius of each sphere to the value stored in its temperature field. Zero or negative values causes have no effect and values greater than

2.0 are truncated to 2. The user option allows the radius of each spheres to be specified by additional lines in the molecule's PDB file using Raster 3D's COLOR record extension.
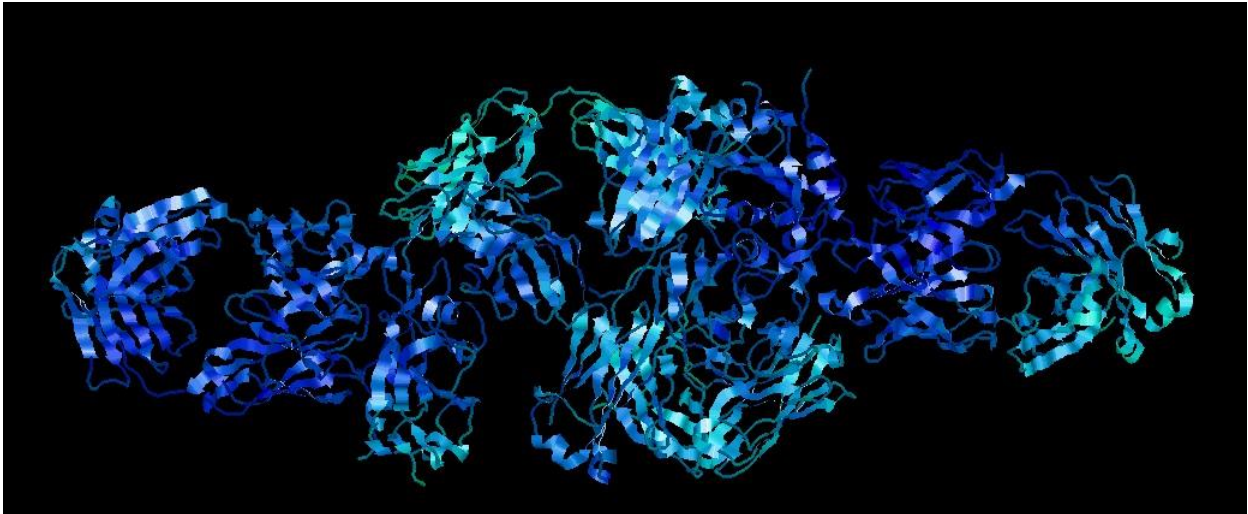
Figure 20 - Temperature Representation in RasMol
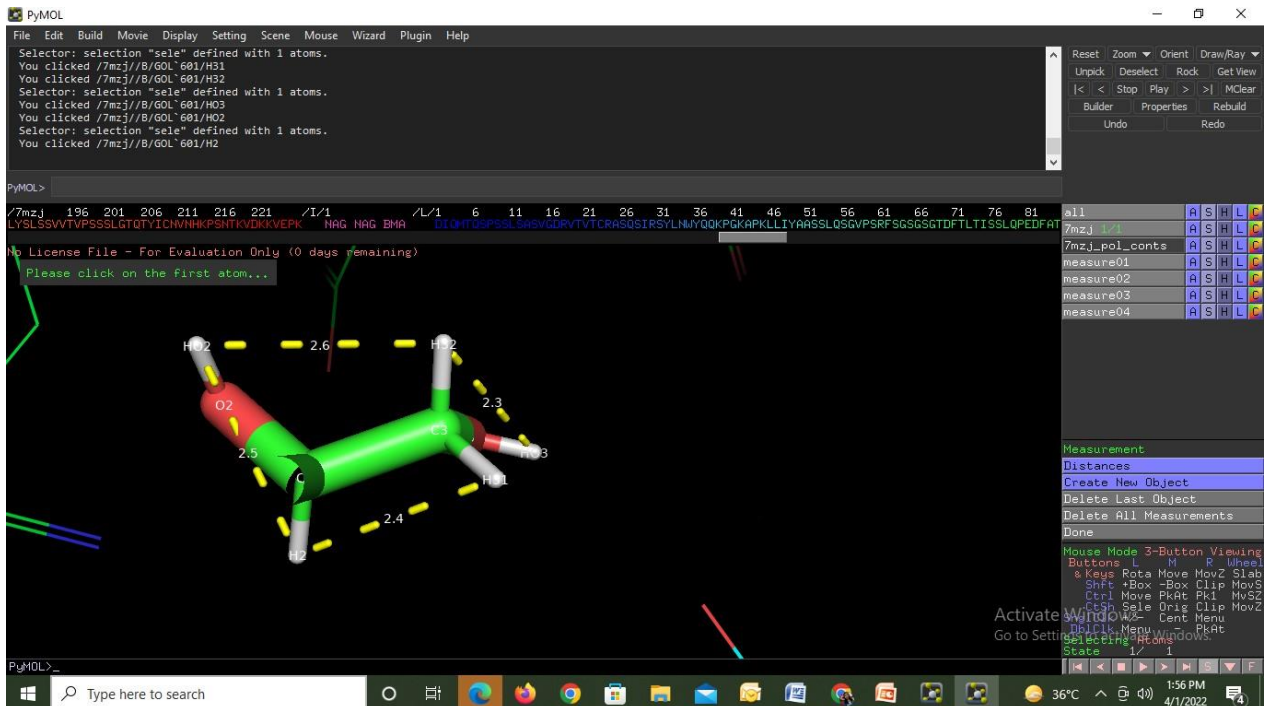
Figure 21 - Analysis of 7MZJ in PyMol
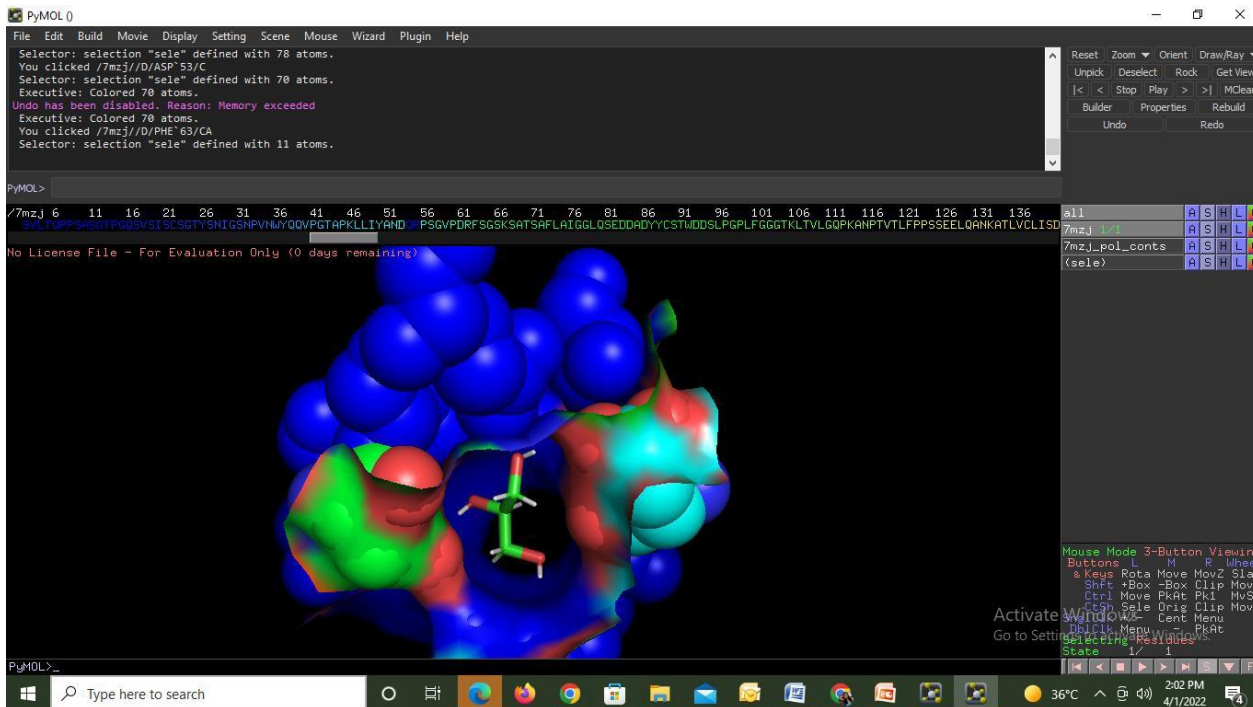
Figure 22- Protein-Ligand Interactions in Pymol (Protein structure)
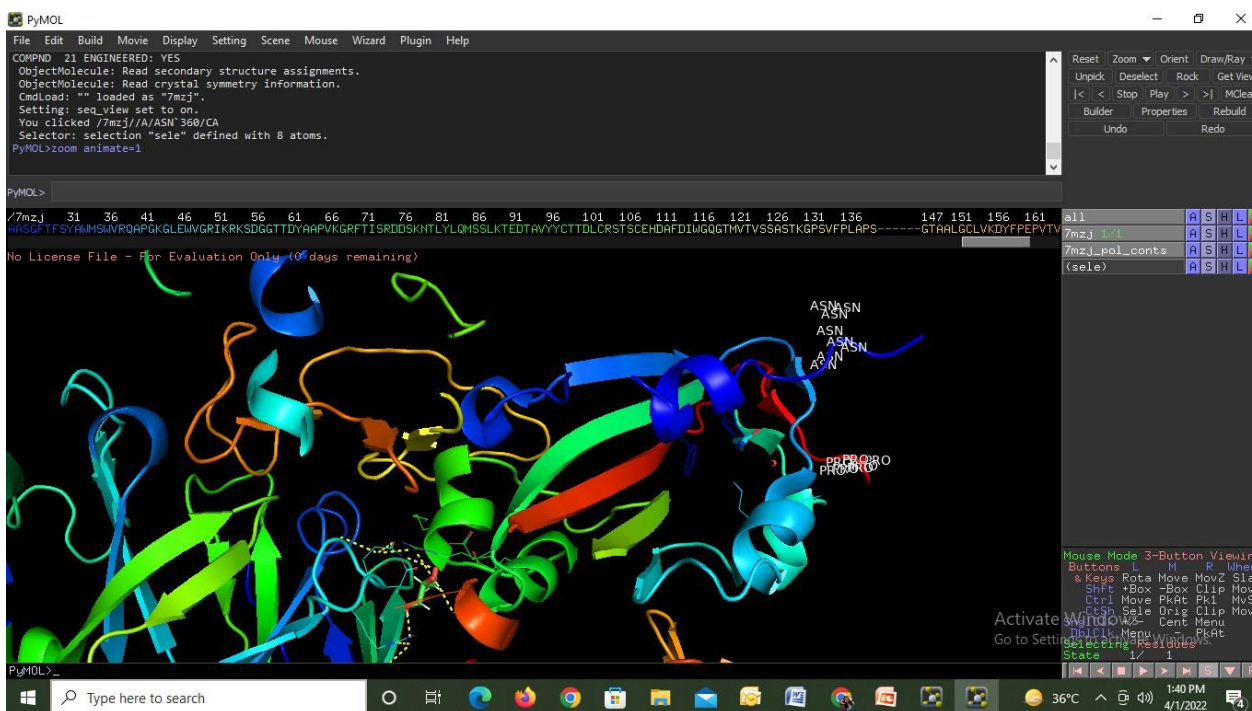
Figure 23 - Ribbon structure in PyMol showing H-bonds with yellow dotted color

Figure 24- Analysis of molecular docking with pymol visualizer to have information about the Various conformations of the ligand on the protein

AUTODOCK RESULT
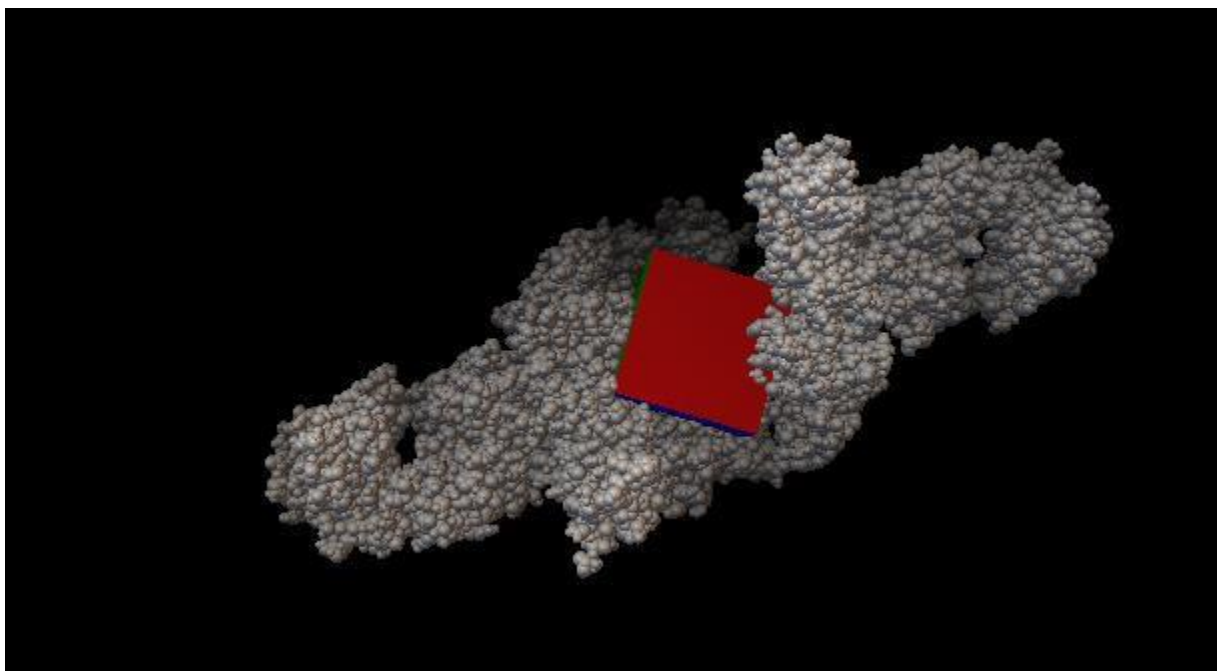
FIGURE 25- AUTODOCK (Grid formation)

Parameter of Grid

7mzj:

- **spacing 0.964**
- **npts   40 40 40**
- **X-Dimension 40**
- **y-Dimension 40**
- **Z-Dimension 40**
- **center   x = -6.359**
  - **y = 8.352**
  - **z = 2.871**
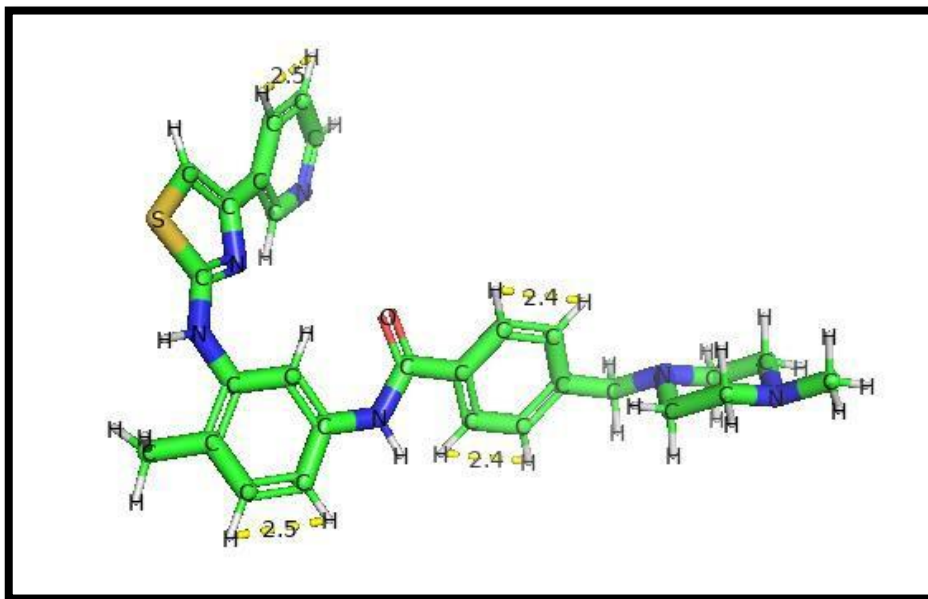
Figure 26- Masitinib visualisation in Pymol
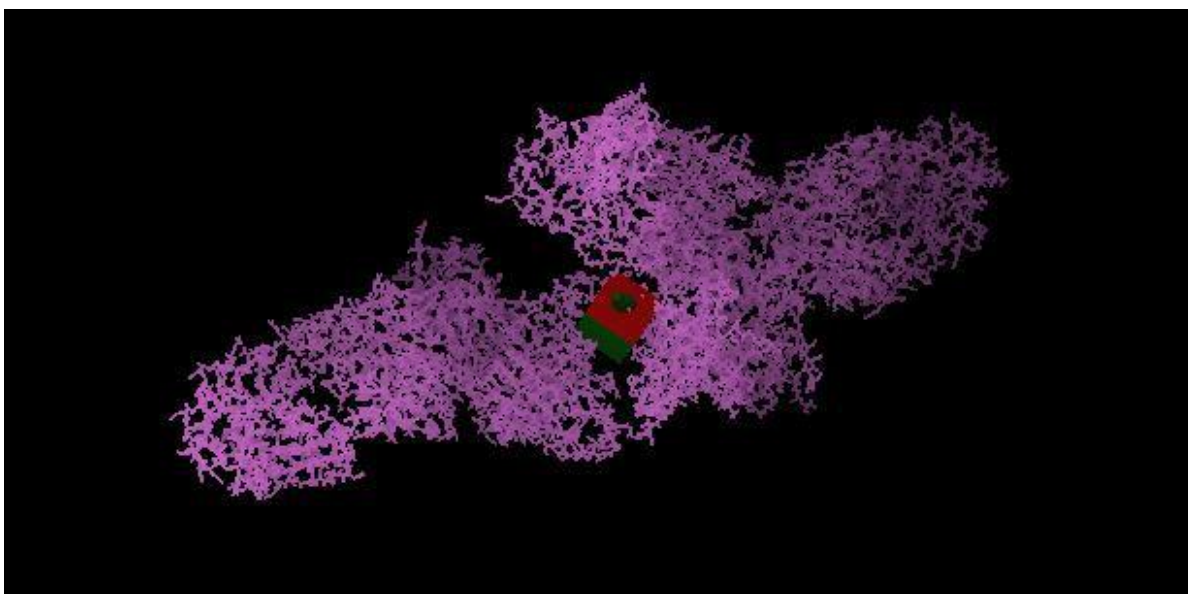
Figure 27 :Protein and Ligand Interaction (Molecular Docking)

S.No	Ligand Masitinib mesylate	Binding affinity (kcal/mol)
1	x-axis	-0.141
2	y-asix	-0.133
3	z-axis	0.009

Table 1 Binding affinity of ligand with target proteins
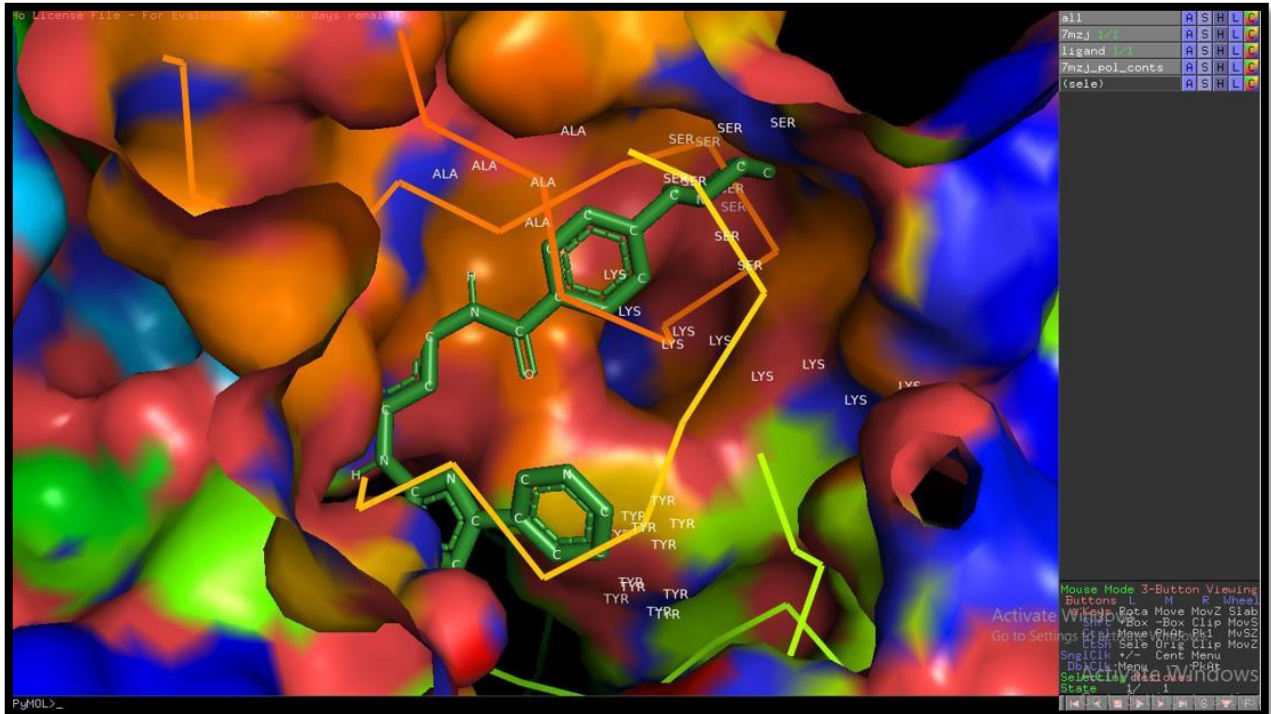
Figure 28- Protein (7MZJ) and Ligand (Masitinib) Molecular Docking
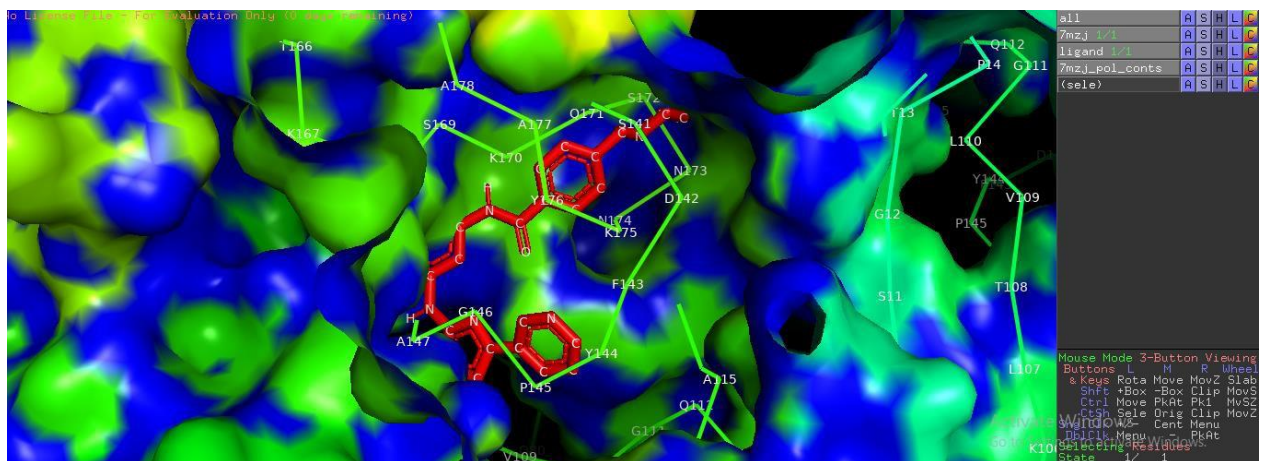
Figure 29- Red one is ligand and Protein interaction

The CoV S protein is an envelope glycoprotein that plays the most important role in viral attachment, fusion, and entry into host cells, and serves as a major target for the development of neutralizing antibodies, inhibitors of viral entry, and vaccines. It is synthesized as a precursor protein that is cleaved into an N-terminal S1 subunit (~700 amino acids) and a C-

terminal S2 subunit (~600 amino acids) that mediates attachment and membrane fusion, respectively. Three S1/S2 heterodimers assemble to form a trimer spike protruding from the viral envelope. Depending on the virus, either the NTD or the C-domain can serve as the receptor-binding domain (RBD). While RBD of mouse hepatitis virus (MHV) is located at the NTD, most of other CoVs, including SARS-CoV-2 use the C-domain to bind their receptors. Recent studies found that the receptor-binding domain (RBD) of SARS-CoV-2 S protein binds strongly to human and bat angiotensin-converting enzyme 2 (ACE2) receptors. Moreover, SARS-CoV-2 RBD exhibited significantly higher binding affinity to the ACE2 receptor than SARS-CoV RBD. Due to the key role of the S protein RBD in viral attachment, it is the major target for antibody-mediated neutralization. This model corresponds to the S1 subunit C- domain that serves as the RBD for SARS-CoV-2 and most CoVs.

CONCLUSION

The project is based on docking and protein ligand interaction of Sars -Cov-2 variant.The development of broad-spectrum antiviral drugs and vaccines against SARS-CoV-2 and its variants will require a long-term strategy in the search for clinical treatments. High infectivity of SARS-CoV-2 by revealing the exceptional binding affinity between SARS-CoV-2 RBD and its receptor ACE2, the diversity of receptor usage by SARS-CoV-2, and the multibasic motif at the S1/S2 boundary of SARS-CoV-2 S protein.The dashboard also describes the summary of models of docked structures i.e., binding modes of receptor and Ligand Docking score, Ligand modeled structures using homologous templates shows a quality report of the docking predicted the ability of protein pocket to bind with high affinity as a drug candidate .

The fundamental role of the spike protein in infectivity indicates that it is a major target for immunogenic development.

Present study describes docking poses ,binding sites and drug ability that is aimed towards molecular associations certain to infection and replication. Therefore, these findings would help to control the exploiting pandemic condition.

This study further describes docking poses ,binding sites and drug ability, hydrogen bonding that is aimed towards molecular associations certain to infection and replication. Therefore, these findings would help to control the exploiting pandemic condition.

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Viruses are constantly evolving, and this might result in the emergence of a new virus variation, or strain. The virus's behaviour is usually unaffected by a variation. They do, however, occasionally cause it to behave in unexpected ways.

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Coronaviruses have a spike glycoprotein that helps them enter the host cell and gives them a crown-like shape on their surface.