# Using electrostatic forces to see which drug is most efficient for Sars Cov-2

**Elvis Lin, Dr. Mojgan Asadi, Dr. Matt Colopy, Prof. Arieh Warshel**

*Dept of Chemistry, Bridge Institute, University of Southern California, Los Angeles, CA , USA*

**Bridge UnderGrad Science (BUGS)** ***Summer Research Program***

USC University of Southern California

## Abstract

A protein is a macromolecule that is made of a chain of amino acids and plays a crucial role in facilitating the essential functions of viruses. This is why disrupting the activity of a protein is important in drug discovery, especially when finding treatments for drugs, such as SARS-CoV-2.

In order to disrupt the normal activity of a protein, we use an inhibitor. There are two types of inhibition: competitive and noncompetitive.

Noncompetitive inhibition is when the inhibitor binds to a different part of the enzyme, thereby reducing its efficiency.

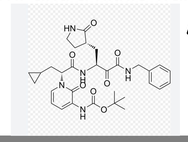
Competitive inhibition is when the inhibitor competes with the natural substrate for binding to the active site, and this inhibition is used in SARS-CoV-2.

In order to find which drug inhibits SARS-CoV-2 the best we have to look at electrostatic interactions between neighboring residues.

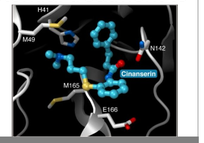
## SARS-CoV-2

SARS CoV-2 is virus that has a main protease known as $M^{pro}$, which is important in viral replication. We have found that targeting $M^{pro}$ with nirmatrelvir and a nitrile warhead is a potential treatment to SARS CoV-2.

*Chemdraw*

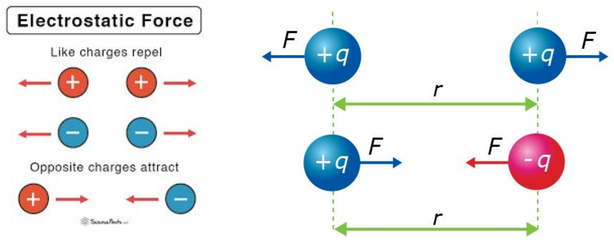


*Biorxiv*

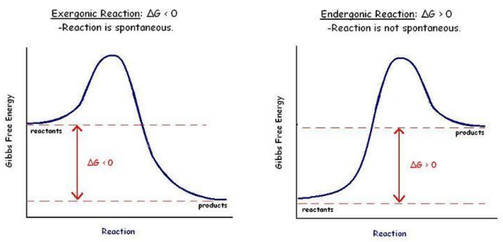



**What are the interactions that allow for us to determine binding affinity?**

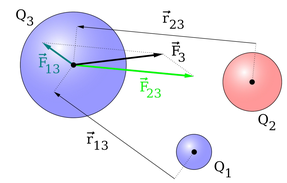
**Electrostatic forces**: is the study of charged particles



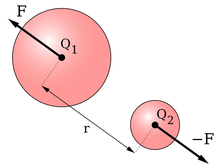

**Free energy**: is the energy that is available to do work



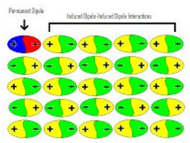

**Coulomb's Law**: calculates the strength of the electrostatic forces

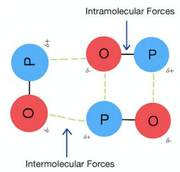



$$F = k\frac{q_1 q_2}{r^2}$$




**Van der Waals**: weak electrostatic forces that attract molecules to each other

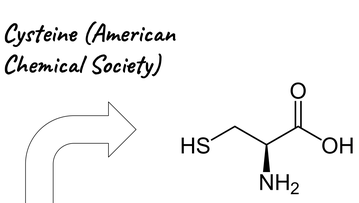


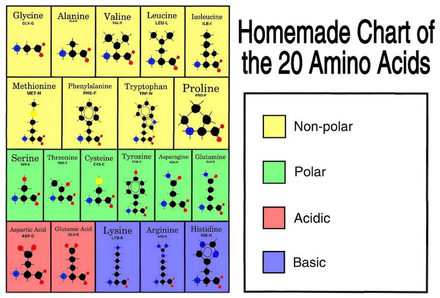



**These interactions allow us to determine which drug is most efficient**

## Cycle

*Cysteine (American Chemical Society)*

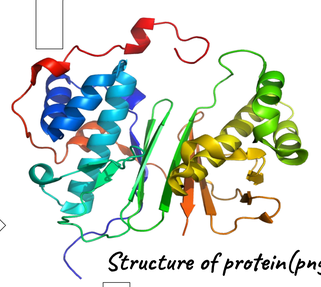


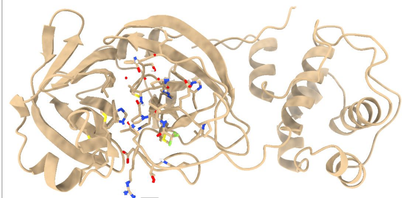

*20 amino acids(Wikimedia Commons)*

*The Protein of Covid(Chimera)*

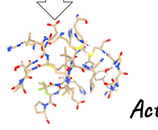




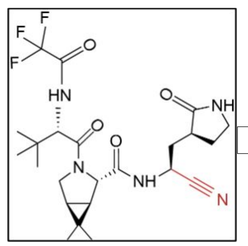
*Structure of protein(pngwing)*



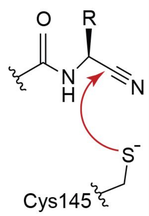
*7RFS(Chimera)*



*Active Site*



*Inhibitor of 7RFS*




*The nitrogen bond is what makes it irreversible*

## Experimental Findings

In order to find which drug is most efficient we used PDLD (Protein Dipole Langevin Dipole) calculations that are based on electrostatic forces.

Using PDLD calculations we have determined that the binding affinity for Covid with nirmatrelvir is -6.18 kcal/mol.This concludes that the drug is favorable and inhibitor binds effectively to active site.

Although a potential drug was found, drug designers are constantly trying to find ways to improve designing more effective drugs. A potential solution to improve drug design is finding more advanced computer simulations to improve efficiency and increase accuracy for finding a suitable drug for each disease.

With improved technology, diseases that were considered to be incurable such as cancer and HIV could potentially be cured.

## Summary

The binding pocket for SARS-CoV-2 is covalently bonded and exhibits the potential for both irreversible and reversible interactions to cysteine.

This bonding pocket is defined not only by the presence of negative and positive charges but also by the distances between neighboring residues.

In our calculations, we kept the distances fixed without imposing any restraints to accommodate the inhibitor within the protein.

To visualize the proteins and gain a better understanding, we used Chimera, which allowed us to find the differences between neighboring residues.

## Acknowledgments

OWEN, DAFYDD R., et al. An Oral SARS-COV-2 Mpro Inhibitor Clinical Candidate for the ... - Science, www.science.org/doi/10.1126/science.abl4784. Accessed 24 July 2023.

Mehrotra, Neha, and Saurabh Singh. Periodontitis - StatPearls - NCBI Bookshelf, www.ncbi.nlm.nih.gov/books/NBK541126/. Accessed 30 July 2023.

Thank you for Dr.Asadi for taking care of me throughout this whole summer and giving me such valuable information.

## CONTACT US

**bridge.usc.edu/bugs**