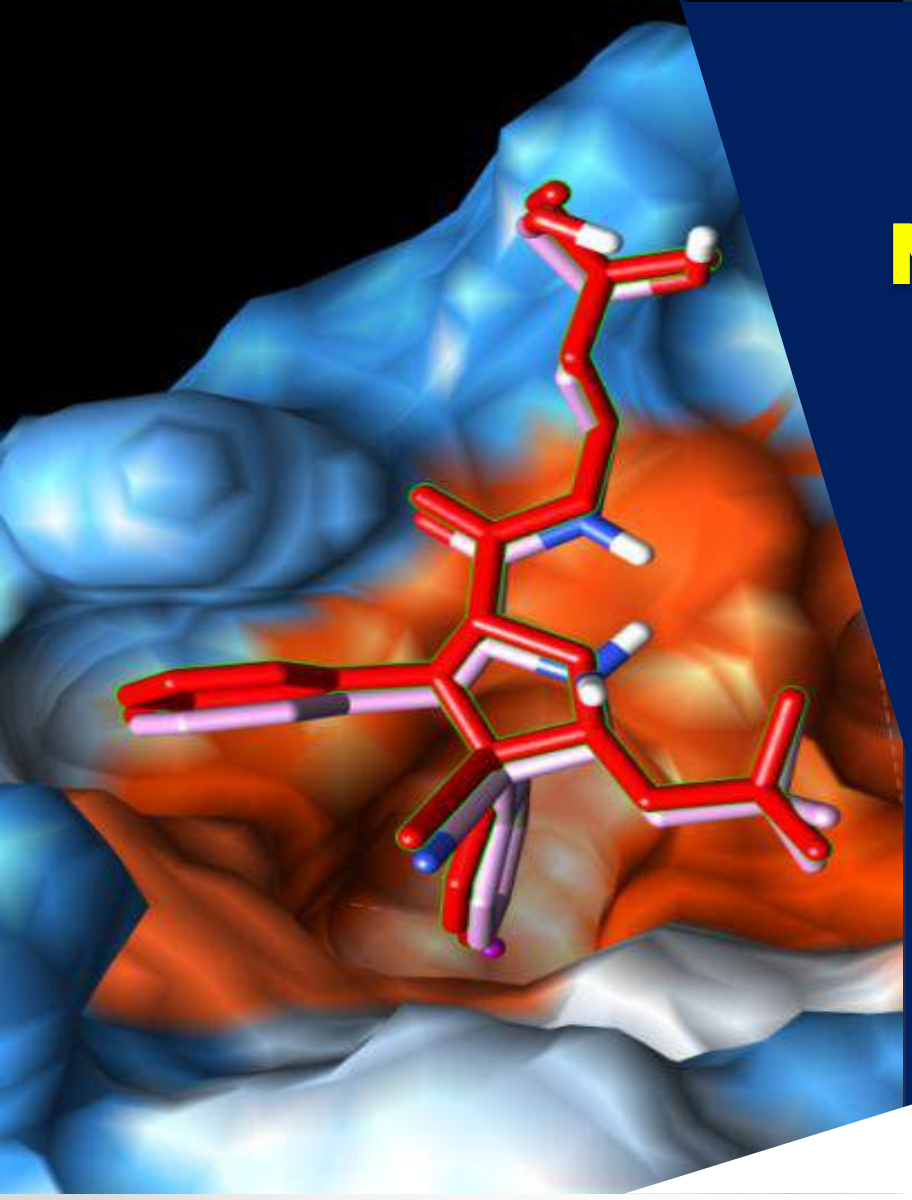

MOLECULAR DOCKING

Presented by:

Dr. Sanket P. Bapat

Associate Professor

MIT School of Bioengineering Sciences & Research
Breathe Life into Engineering Career!
A Constituent Unit of MIT ADT University

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Objective/Learning Outcome:

CO1	Understanding of levels of protein structure organization and related methods of structure determination
CO2	Knowledge of various methods of secondary structure prediction
CO3	Understanding of molecular modeling and its application
CO4	Learning the molecular dynamics and its methods
CO5	Understanding different approaches to study protein-protein interactions

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Chapters

- **Introduction**

1. Introduction to Molecular Modeling (Molecular Docking/Dynamics)
2. Application of Molecular Docking in Drug Development

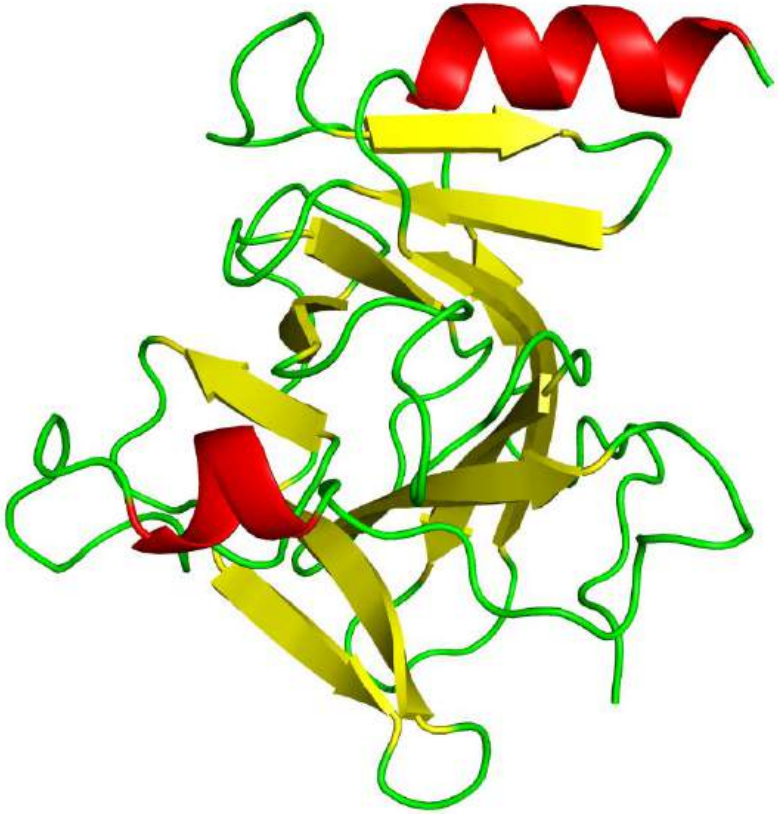
- **Molecular Docking**

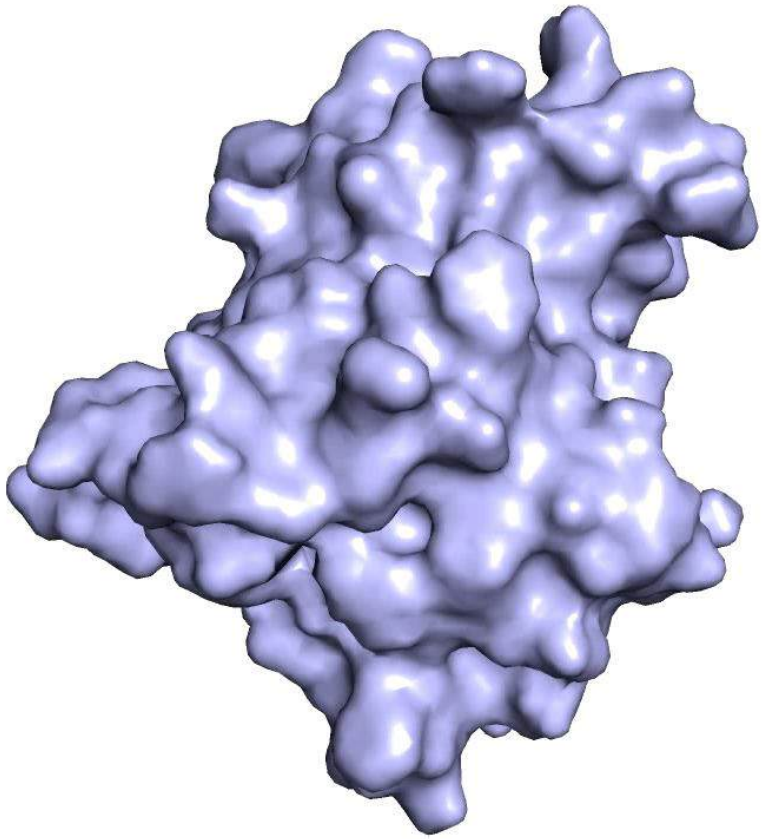
1. Introduction to Molecular Docking
2. Understanding Concepts behind the Steps in Molecular Docking

- **Docking Tools**

1. Explanation about various tools in Molecular Docking
2. Installation of Autodock Vina

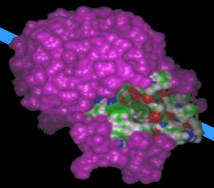
Protein Structures



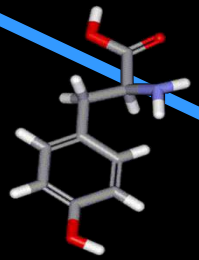


Drug Discovery & Development

Identify disease



Isolate protein involved in disease (2-5 years)



Find a drug effective against disease protein (2-5 years)

Preclinical testing (1-3 years)

Scale-up

Formulation

File IND

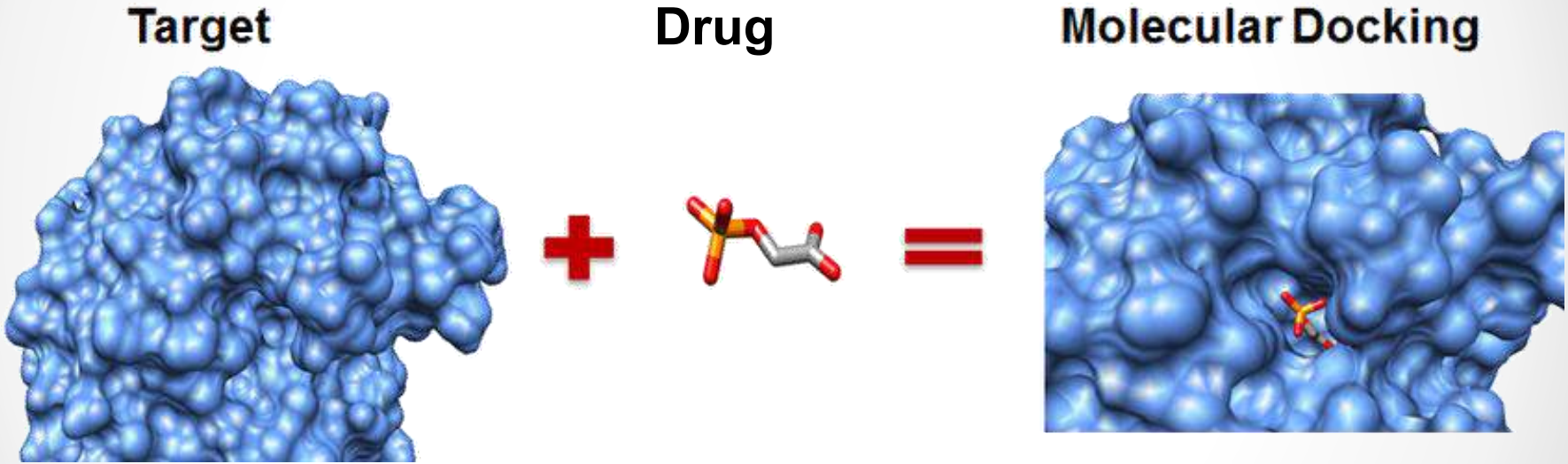
Human clinical trials (2-10 years)

File NDA

FDA approval (2-3 years)

IND: Investigational New Drug
NDA: New Drug Application

Molecular Modeling: Molecular Docking



Molecular Docking

Molecular docking is a method which predicts the preferred **orientation of one molecule to a second** when bound to each other at a **site** to form a stable complex.

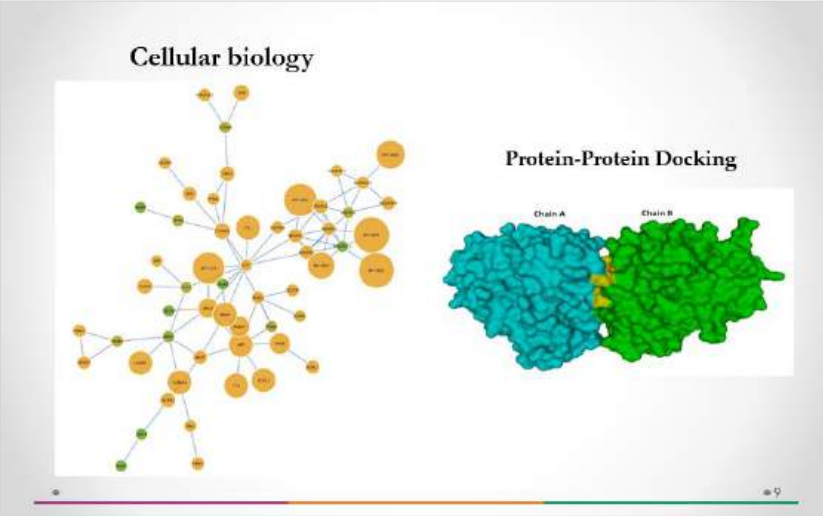
Knowledge of the **preferred orientation** in turn may be used to predict the strength of association or **binding score** between two molecules.

~Berry, 2015

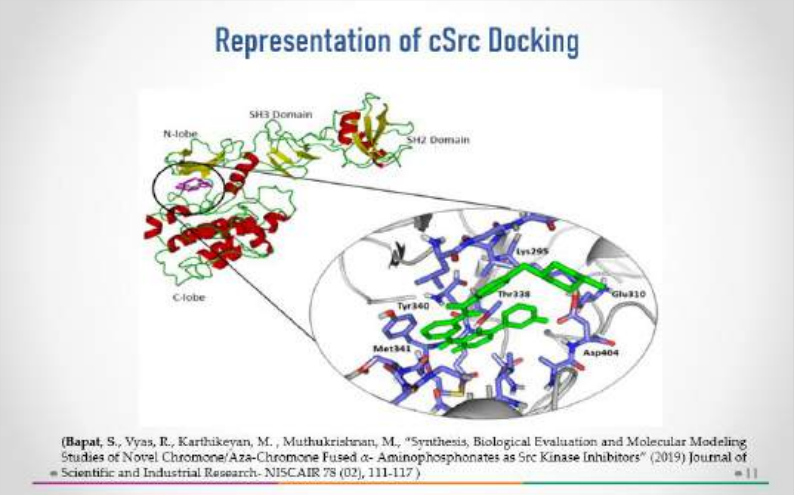
*Berry, Michael, Burtram Fielding, and Junaid Gamieldien. "Practical considerations in virtual screening and molecular docking." *Emerging trends in computational biology, bioinformatics, and systems biology* (2015): 487.

Why is docking important?

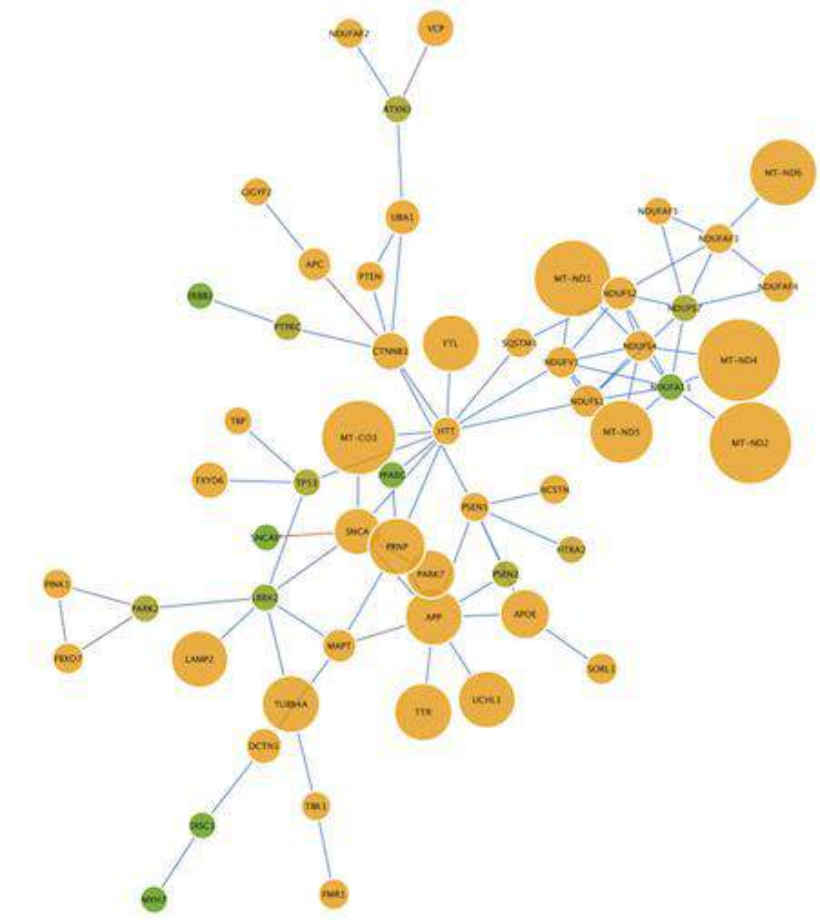
Cellular biology



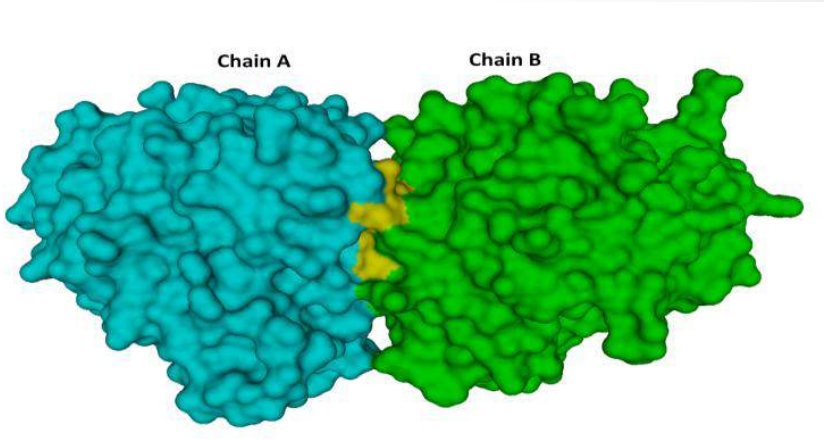
Rational drug design



Cellular biology

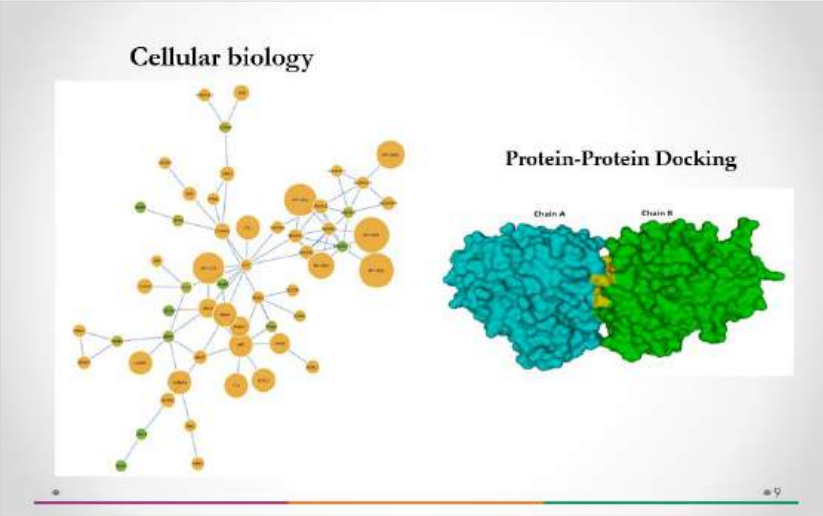


Protein-Protein Docking

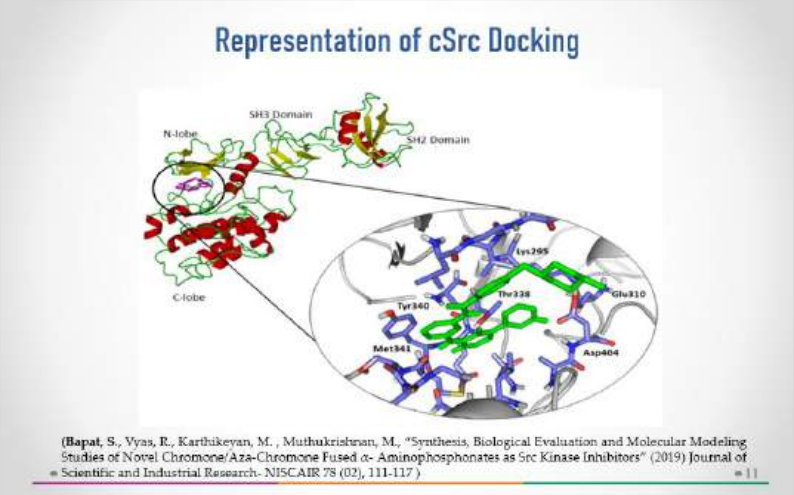


Why is docking important?

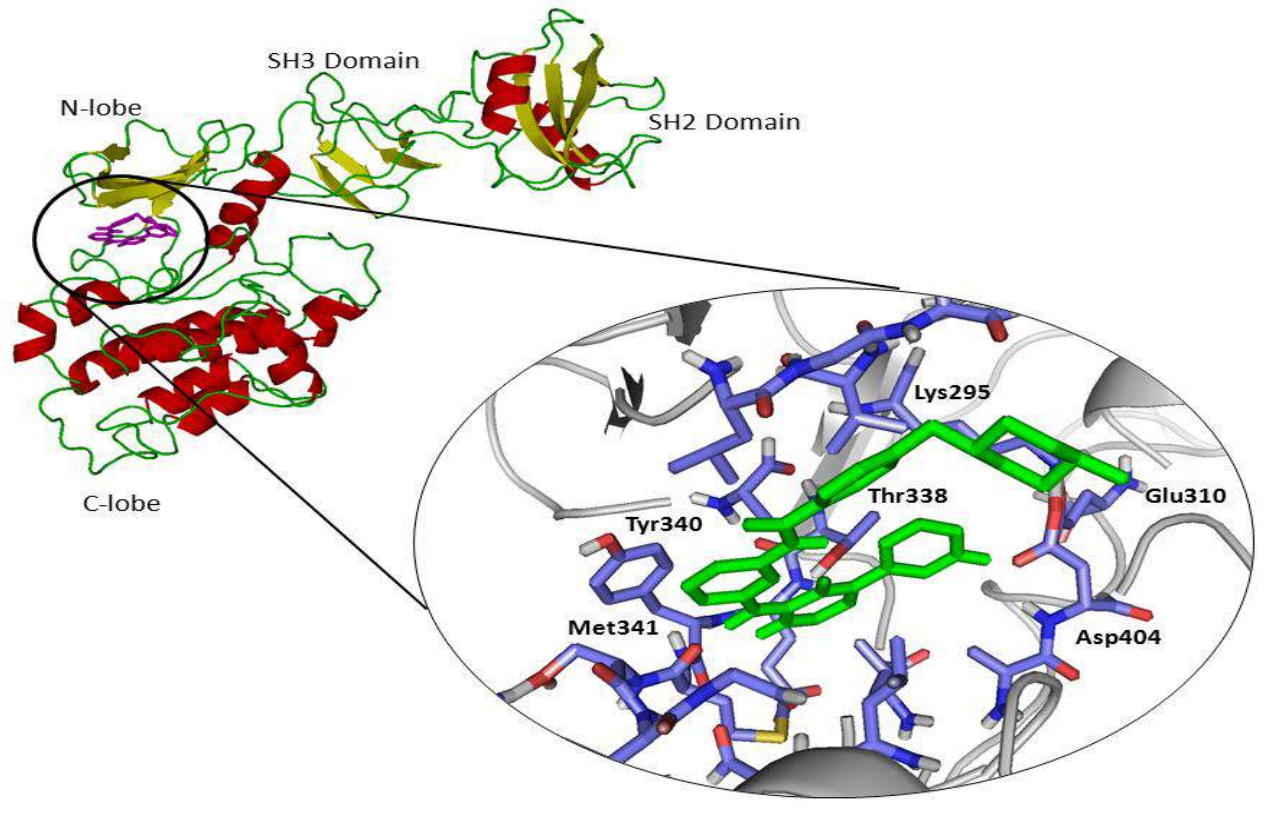
Cellular biology



Rational drug design



Representation of cSrc Docking

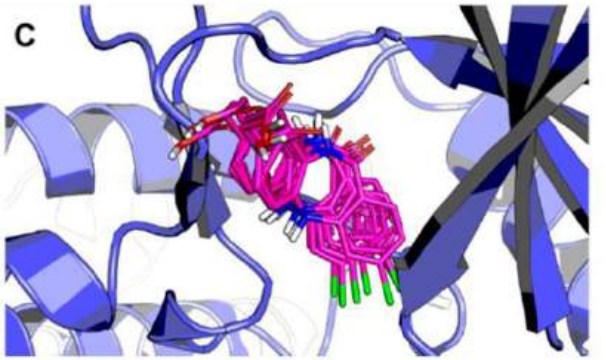


(Bapat, S., Vyas, R., Karthikeyan, M. , Muthukrishnan, M., "Synthesis, Biological Evaluation and Molecular Modeling Studies of Novel Chromone/Aza-Chromone Fused α- Aminophosphonates as Src Kinase Inhibitors" (2019) Journal of Scientific and Industrial Research- NISCAIR 78 (02), 111-117)

Outline of Docking

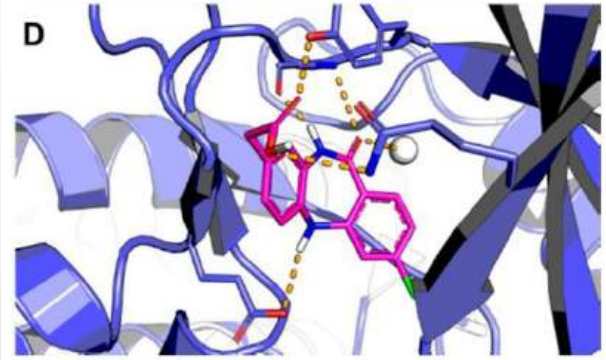
bind

Ligand poses



Binding energy

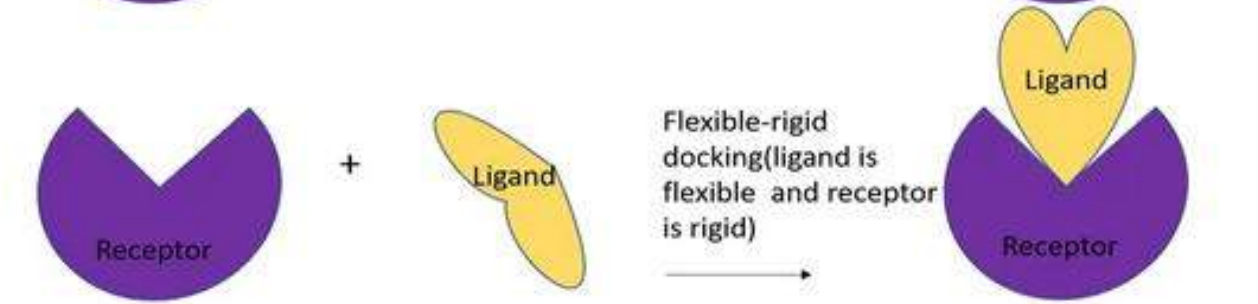
Best Pose



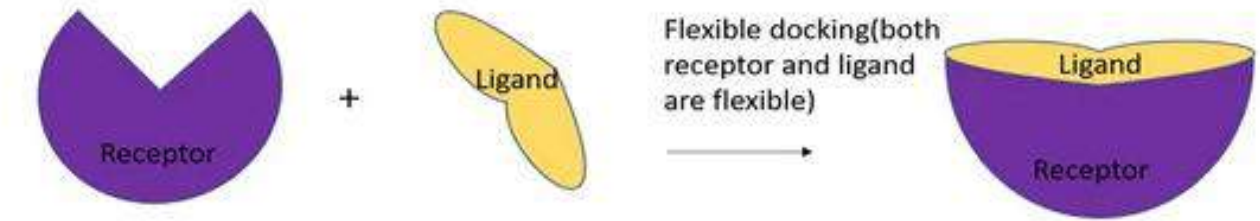
Types of Docking

Rigid Docking

Flexible - Rigid Docking



Flexible Docking



Steps for Docking

1. Choose the protein target and ligand molecule.
2. Energy minimize both protein and ligand.
3. Select the docking site in protein.
4. Carry out protein-ligand docking using docking tool.
5. Different ligand poses are generated.
6. The ligand pose with maximum score and least energy (best docked with protein) is selected.

Softwares required

- The software required for performing Autodock are mentioned below along with their link.

1. AutoDock MGL Tools [http://mgltools.scripps.edu/]

2. AutoDock Vina [http://vina.scripps.edu/index.html]

3. Pymol visualization tool [https://pymol.org/2/]

Case Study 1

- Docking studies on tuberculosis proteins.

PDB target	Compound 1		Compound 2		Compound 10		Compound 11	
	MOE	Autodock Vina	MOE	Autodock Vina	MOE	Autodock Vina	MOE	Autodock Vina
1U2P	-10.00	-7.1	-9.65	-6.8	-10.15	-7.6	-11.25	-8.0
2OZ5	-12.41	-8.16	-12.37	-8.1	-13.96	-9.0	-11.36	-8.2
2NSD	-12.20	-8.1	-11.84	-7.8	-12.37	-7.1	-12.51	-6.8
1DG5	-12.79	-8.4	-12.47	-8.28	-11.80	-8.0	-10.40	-7.9

Case Study 2

- Docking studies on Src proteins,

Sr. No	Entry	Unphosphorylated Protein: 1Y57		Phosphorylated Protein: 2H8H	
		Amino acids involved in intermolecular interactions	GLIDE Score (kcal/mol)	Amino acids involved in intermolecular interactions	GLIDE Score (kcal/mol)
1	4c	Lys295 Asp404	-4.5	Lys295 Ala390	-5.0
2	4i	Asp404	-4.4	Lys295	-4.6
3	4j	Lys295 Ala390	-5.4	Asn391 Lys295	-6.5
4	Staurosporine	Met341	-8.3	-	-
5	PP2	Met341	-7.6	-	-

Rahul Chavan et al /J. Pharm. Sci. & Res. Vol. 7(2), 2015, 70-75

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Protein Modeling and Docking of Curcurin Against Neuraminidase, Hemagglutinin Proteins o Pandemic Influenza H1N1/2009

Rahul Chavan[1*], Lalit Samant[2], Sanket Bapat[3], Abhay Chowdhary[4]

Computational Approach to study the effect of point mutations in the development of antifungal resistance to Azoles and Flucytosine Drugs in Candida auris

Shreeya Mhade [1], Gursimran Kaur Uppal [1,*], Sanket Bapat [2,*]

Synthesis, Biological Evaluation and Molecular Modeling Studies of Novel Chromone/Aza-Chromone Fused α-Aminophosphonates as Src Kinase Inhibitors

S Bapat[1,2], N Viswanadh[1,3], M Mujahid[1], A N Shirazi[4], R K Tiwari[4], K Parang[4], M Karthikeyan[1,3], M Muthukrishnan[1,3] and Renu Vyas[5]*

In silico binding analysis of lutein and rosmarinic acid against envelope domain III protein of dengue virus

Ritesh Panchal[1], Sanket Bapat[2], Sandeepan Mukherjee[3], Abhay Chowdhary[4]

Abstract:

OBJECTIVE: The study was performed to evaluate *in silico* binding ability of lutein and rosmarinic acid (RA) with the envelope domain III (EDIII) proteins of the four serotypes of dengue virus (DENV),

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Research

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Cite this article: Nalla V, Shaikh A, Bapat S, Vyas R, Karthikeyan M, Yogeeswari P, Sriram D, Muthukrishnan M. 2018 Identification of potent chromone embedded [1,2,3]-triazoles as novel anti-tubercular agents. *R. Soc. open*

Identification of potent chromone embedded [1,2,3]-triazoles as novel anti-tubercular agents

Viswanadh Nalla[1,2], Aslam Shaikh[1,2], Sanket Bapat[3], Renu Vyas[3], M. Karthikeyan[1,2], P. Yogeeswari[4], D. Sriram[4] and M. Muthukrishnan[1,2]

References:

References	Book Name	Library
Rastogi, S. C.	Bioinformatics: Methods and Applications: Genomics, Proteomics and Drug Discovery	Present in Library
Szabo, Gabor Naray	Protein Modelling	Present in Library
Sternberg, M. J. E.	Protein structure Prediction A Practical approach	Present in Library
Bourne, P. E.	Structural Bioinformatics	Present in Library

- **Molecular Docking Tutorial | Autodock Vina | Part 1**
- **Link:** https://youtu.be/Sux91FJ3Xe8?si=4elWVOncwNO050K_

- **Molecular Docking Tutorial | Autodock Vina | Part 2**
- **Link:** https://youtu.be/vU2aNuP3Y8I?si=CCA3T49ruYRK4wgX

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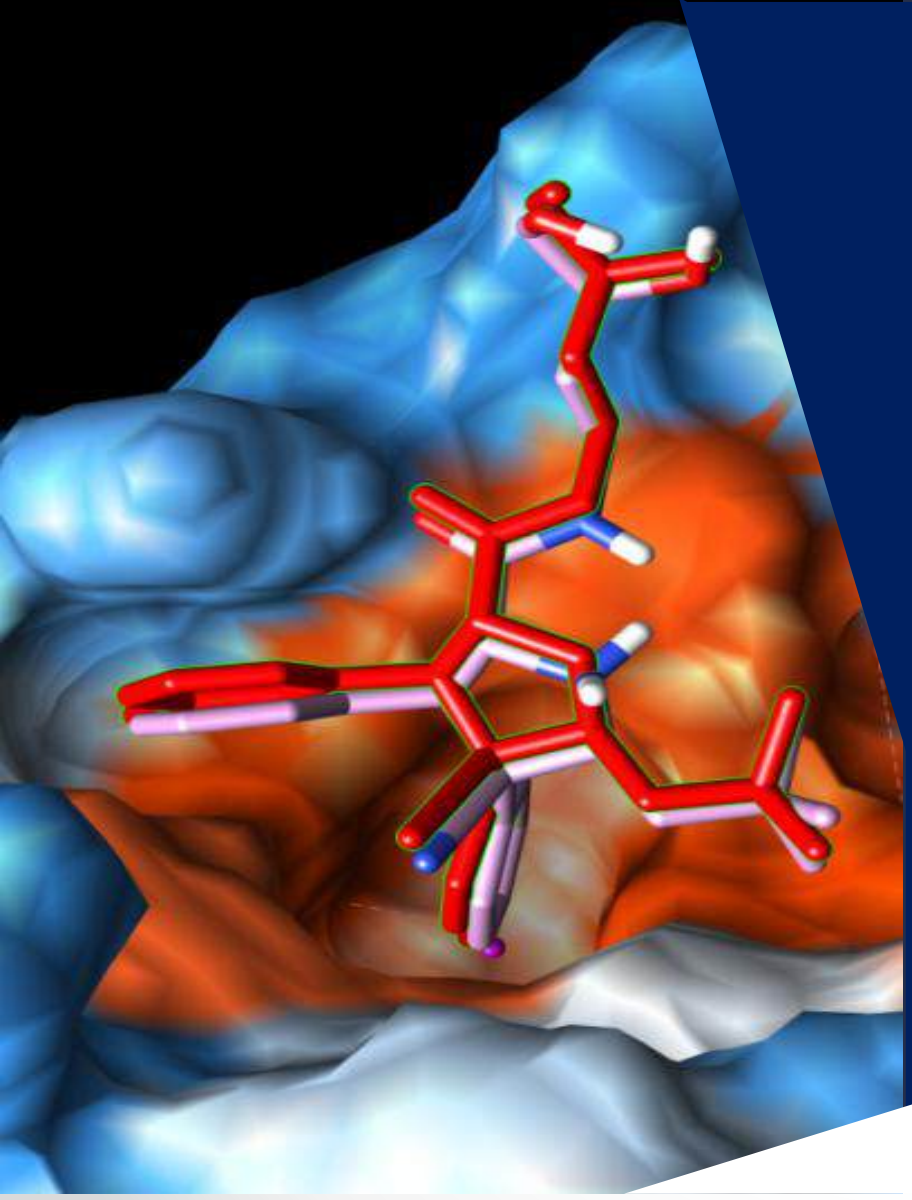
The following questions can be asked for 2 marks, 5marks, 10 marks

1. What is molecular docking and why is it used in drug discovery?
2. What is the difference between rigid docking and flexible docking?
3. What is a binding site in molecular docking?
4. Name any two commonly used molecular docking tools/software.
5. What is a docking score and what does it indicate?
6. Why is protein–ligand interaction important in molecular docking?



THANK YOU

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