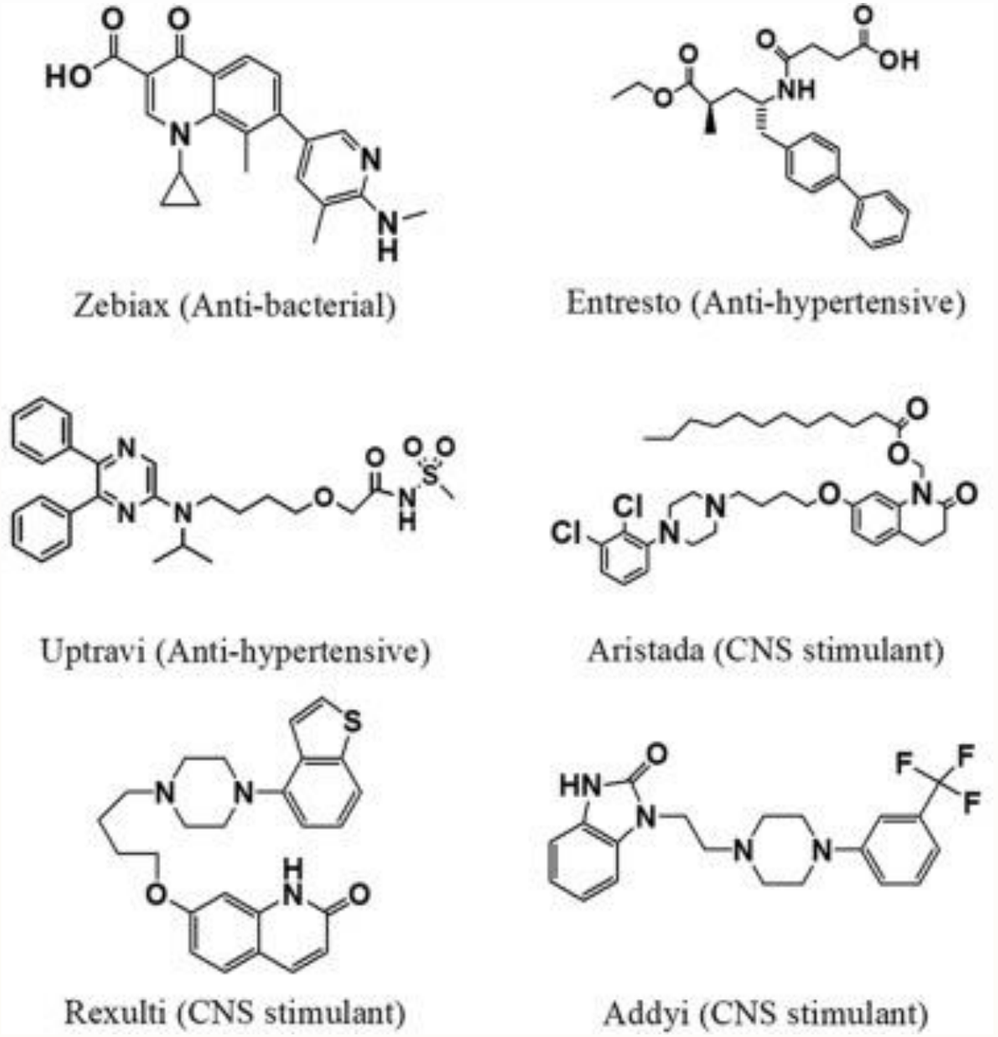

Exploring Molecular Interactions through Docking Simulations

A new approach to drug discovery and development

Chen Mingxi, GTIIT MCS

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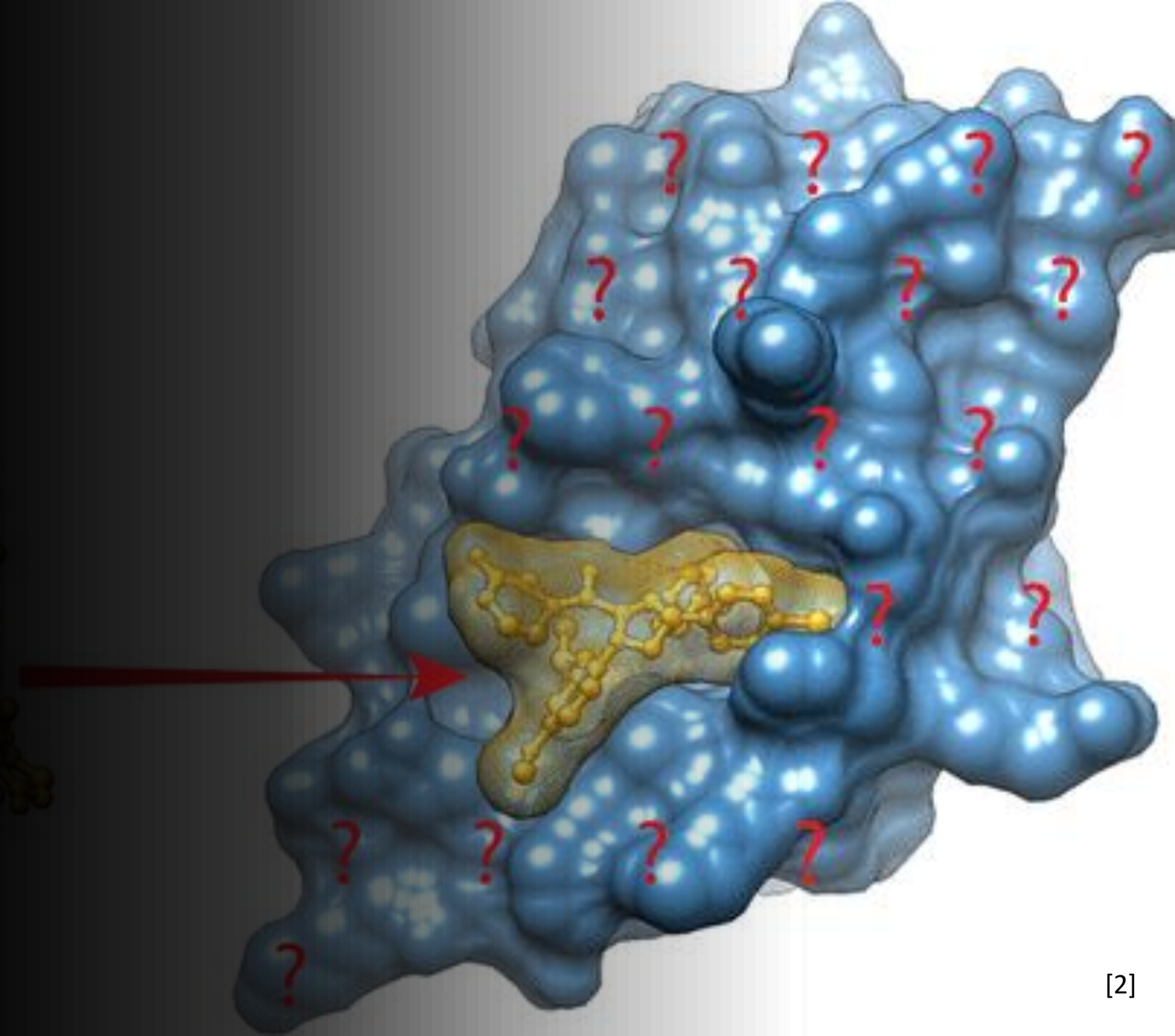
Agenda

Docking simulation

- Introduction
- Basic concepts of Docking simulation
- Application
- Summary



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1. Introduction

Docking simulation : A **computational method** to predict the preferred orientation of a ligand when bound to a target receptor.

Drug molecules discovery approaches

(Traditional way vs Docking simulation)

Traditional way

- Significant resources required
- Time consuming
- Potential oversight of important binding conformations
- May miss subtle interactions

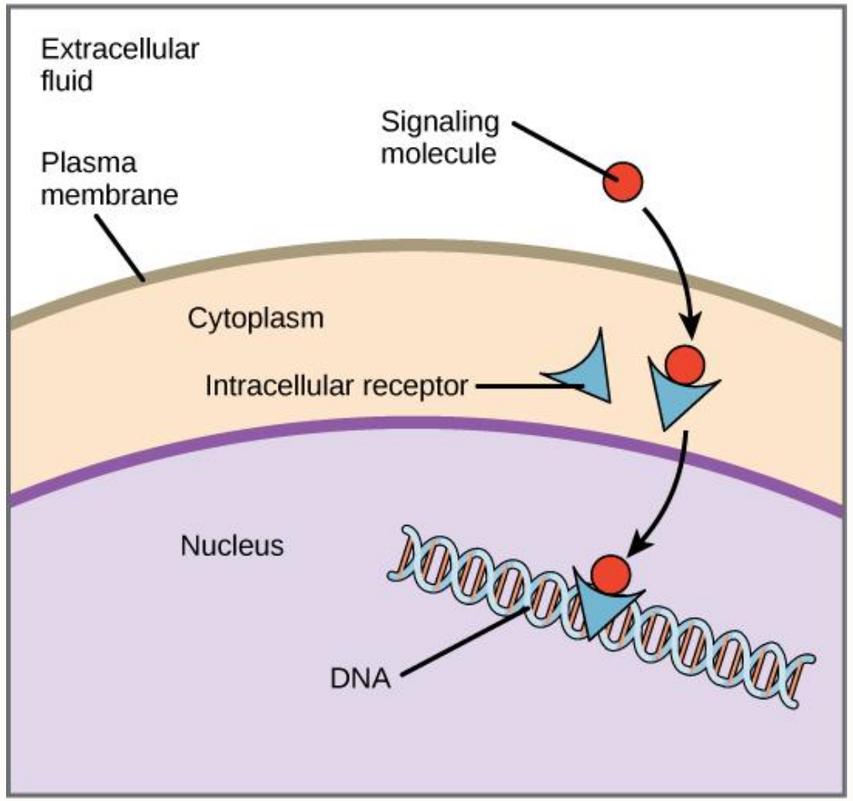
Docking simulation

- Low cost in resources
- Efficient evaluation in silico
- Captures details about conformations during the reaction

2. Basic concepts of Docking simulation

- Ligand and Receptor Interaction

Molecular docking focuses on the study of ligand-receptor interactions. Ligands, typically **small organic molecules**, interact with receptors such as proteins, nucleic acids, or other biomolecules. Understanding these interactions is critical for drug design and understanding biological processes.



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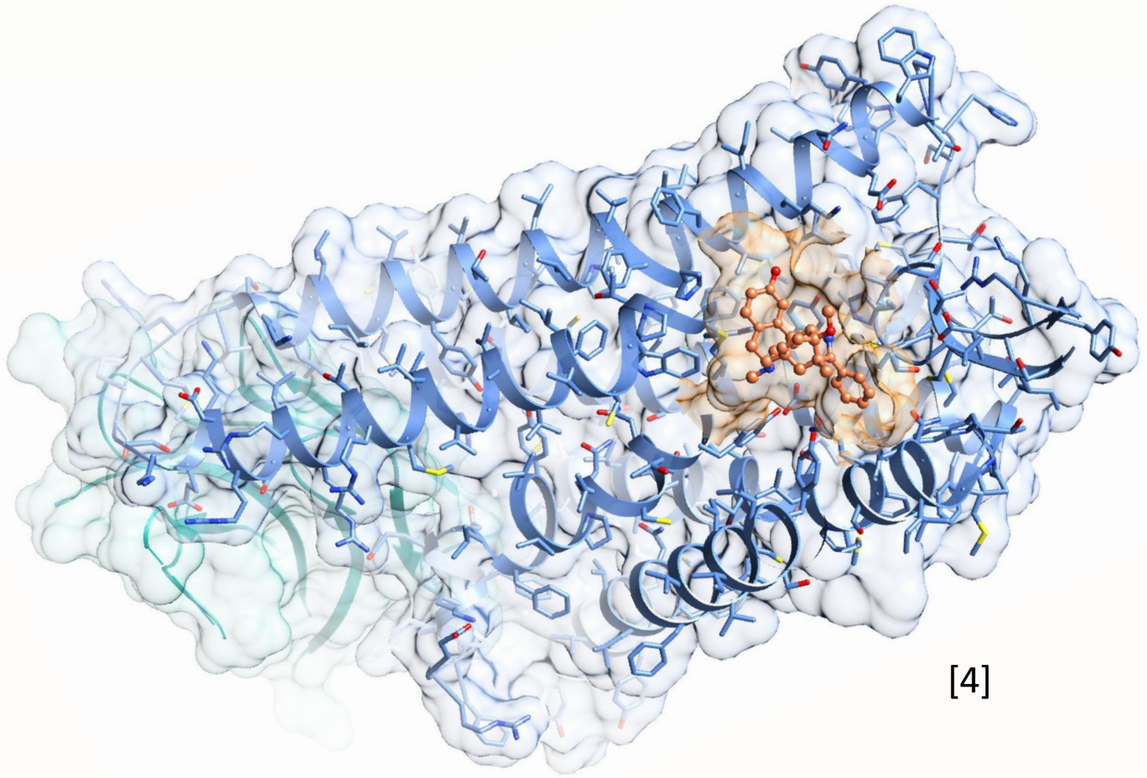

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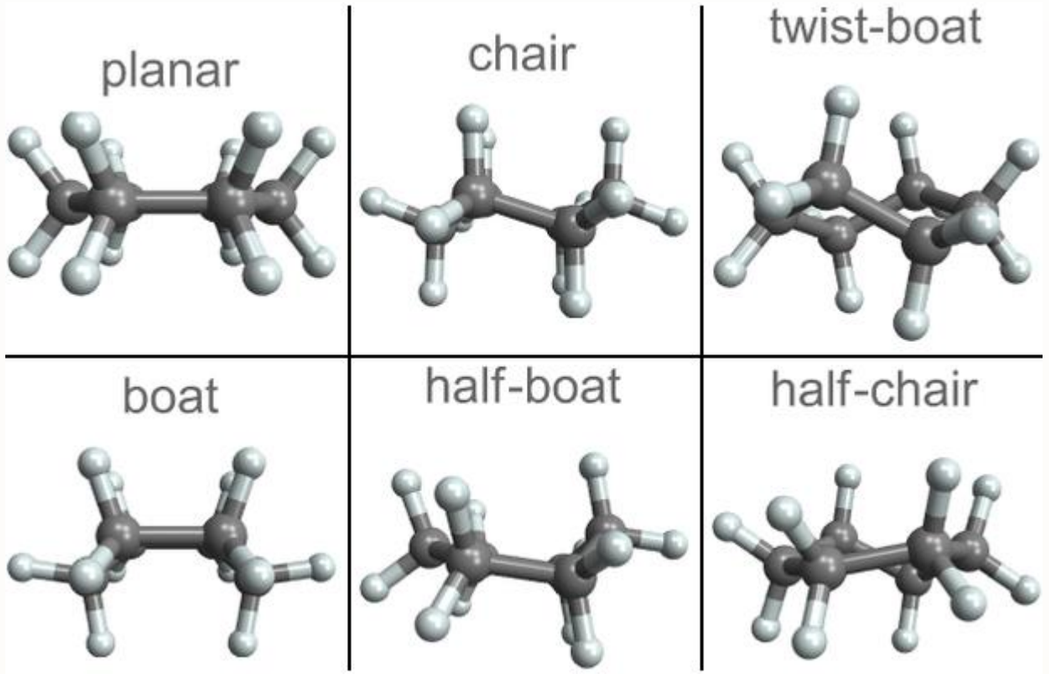
2. Basic concepts of Docking simulation

- Conformational Search

Conformation refers to the spatial arrangement of atoms in a molecule, particularly the relative positions of atoms that result from rotation about single bonds. It describes the **different shapes** a molecule can adopt due to the free rotation of single bonds while maintaining the **same connectivity** of atoms.



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Conformational search is a computational exploration of the different spatial arrangements or conformations, which are crucial for understanding the flexibility and behavior of molecules.

2. Basic concepts of Docking simulation

- Force Fields and Energy Calculations

Force fields are mathematical models that describe the interactions between atoms and molecules in molecular modeling. They include parameters for atom types, **bonded interactions** (bonds, angles, dihedrals), and **non-bonded interactions** (Van der Waals, electrostatic).

Potential Energy (U): It represents the stored energy in a system due to its configuration and intermolecular interactions. Force fields provide the mathematical expressions for calculating potential energy.

Kinetic Energy (K): It accounts for the energy associated with the motion of atoms and molecules within the system. In molecular dynamics simulations, kinetic energy is calculated based on the velocities of particles.

Total Energy (E): The sum of potential and kinetic energy gives the total energy of the system (E = U + K).

Energy Minimization: In molecular modeling, energy minimization is often performed to find the most stable configuration of a molecular system by adjusting atomic coordinates to minimize potential energy.

The energy calculations help predict the **stability** of different binding poses between the ligand and receptor.

3. Application

01

Accelerating Drug Discovery: **Reducing time and cost** by prioritizing potential drug candidates.

02

Lead Identification and Optimization: Guiding the **optimization** of drug candidates for improved efficacy.

03

Drug Repurposing: Finding new uses for existing drugs.

04

Targeting Specific Proteins: Designing drugs for specific molecular targets.

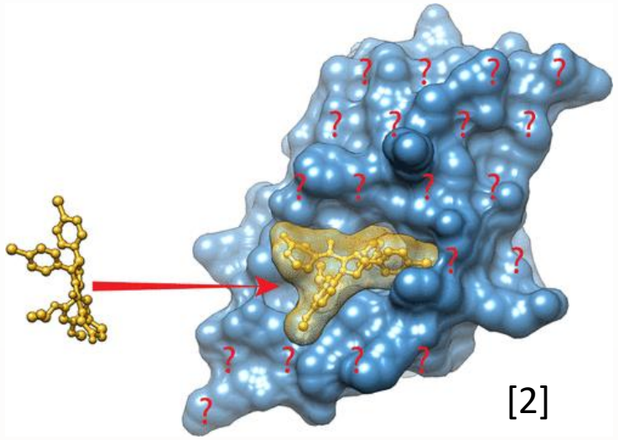
3. Application

Existing algorithms can be categorized through different computational approaches and objects:

- **Rigid Docking**
  - Suitable for **small** molecules and proteins with **low flexibility**
  - Algorithms: **Autodock, Vina**
- **Flexible Docking**
  - Suitable for molecules with **complex conformation**, supports flexible molecules
  - Algorithms: **FlexX, Glide**
- **Protein-Protein docking**
  - Predicting protein-protein interactions
  - Algorithms: **ZDOCK, ClusPro**

4. Summary

In conclusion, docking simulations are more than predictive tools; they are gateways to the molecular realm.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Docking simulation : Key approach to accelerate drug discovery

Challenges

- High-precision simulations consume large amounts of computational resources
- The lack of generality. (Certain methods are only suitable for specific type of molecules)
- Accuracy is still limited, especially flexibility and solvent effects are concerned.

Future

- Integrating multi-scale and multi-mode simulation methods
- Using Machine learning to improve the precision and accuracy
- Developing AI-based methods to reduce the costs of computational resources

Guangdong Technion
Israel Institute of Technology
广东以色列理工学院

Reference & QA session

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