SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

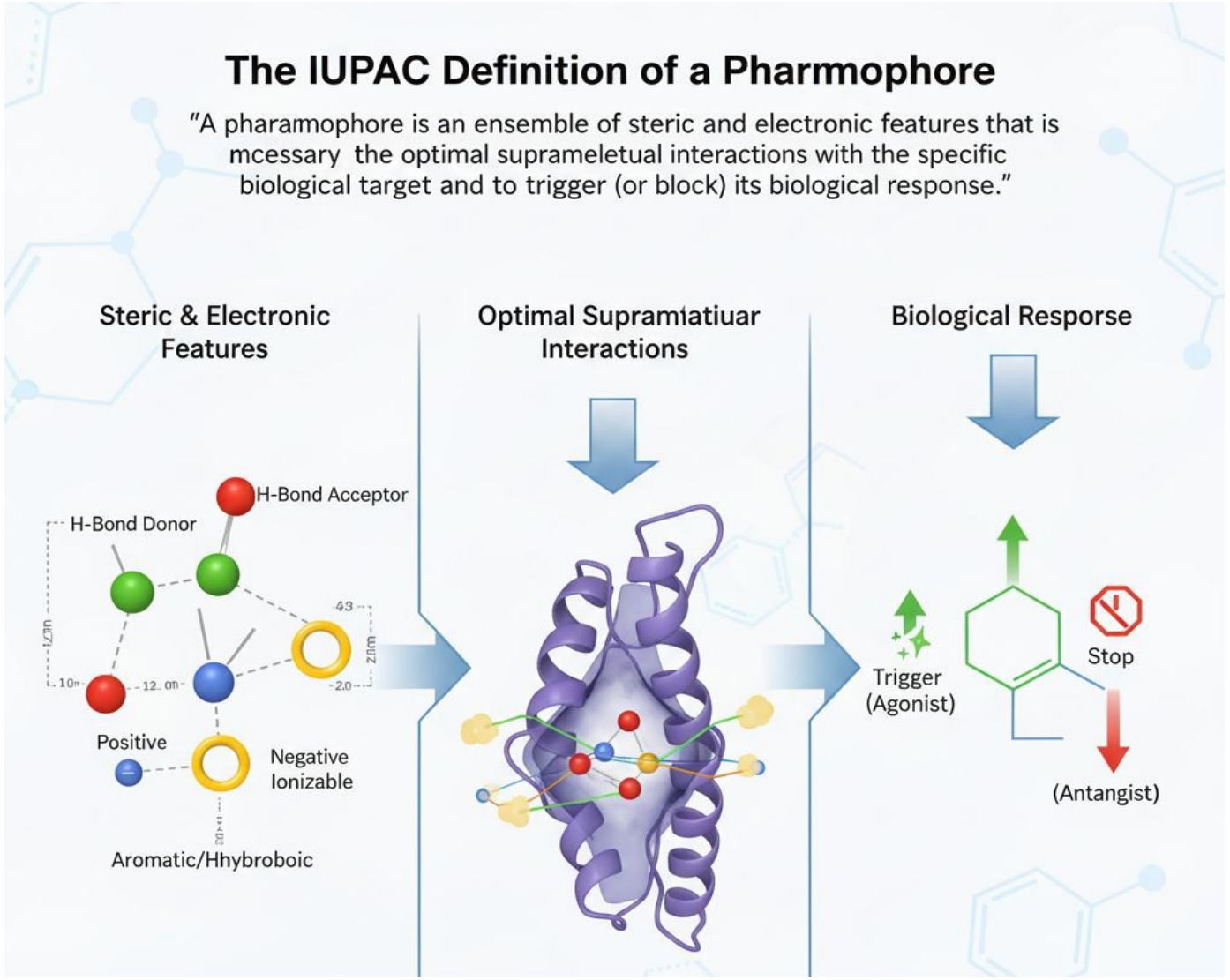
Affiliated To The Tamil Nadu Dr. MGR Medical University,
Chennai Approved by Pharmacy Council of India, New Delhi.
Coimbatore -641035

COURSE NAME : COMPUTER AIDED DRUG DESIGN(BP 807 ET)

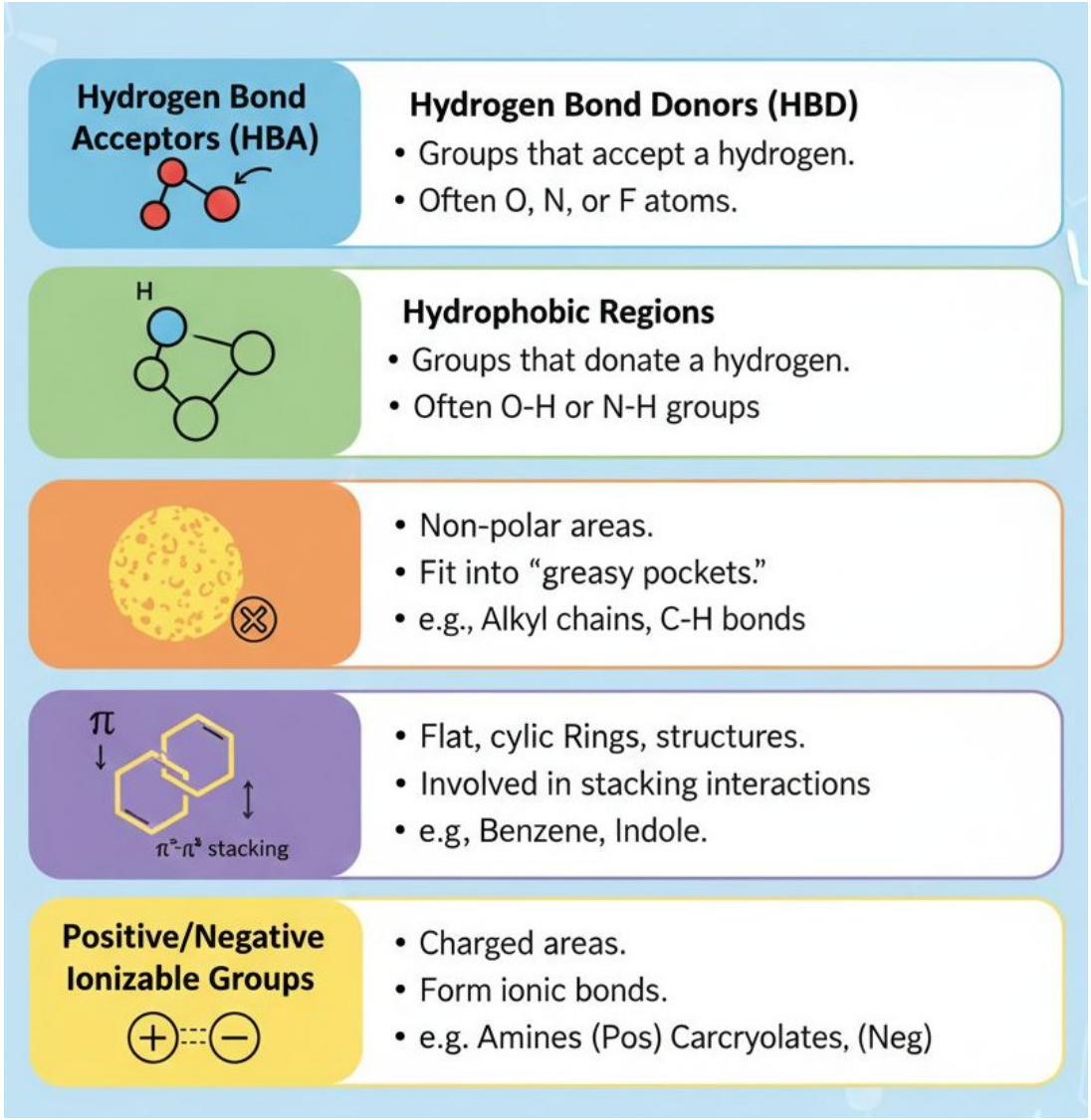
VIII SEM / IV YEAR

TOPIC: CONCEPT OF PHARMACOPHORE MAPPING AND PHARMACOPHORE BASED SCREENING

WHAT IS PHARMACOPHORE..?



THE KEY PHARMACOPHORIC FEATURES

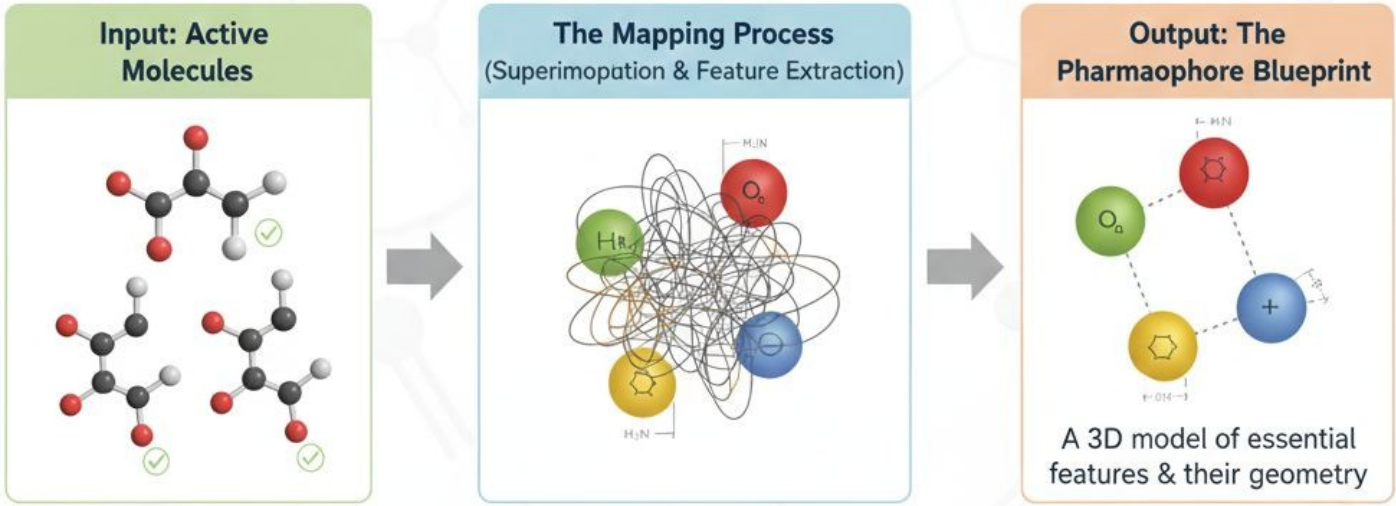


WHAT IS PHARMACOPHORE MAPPPING

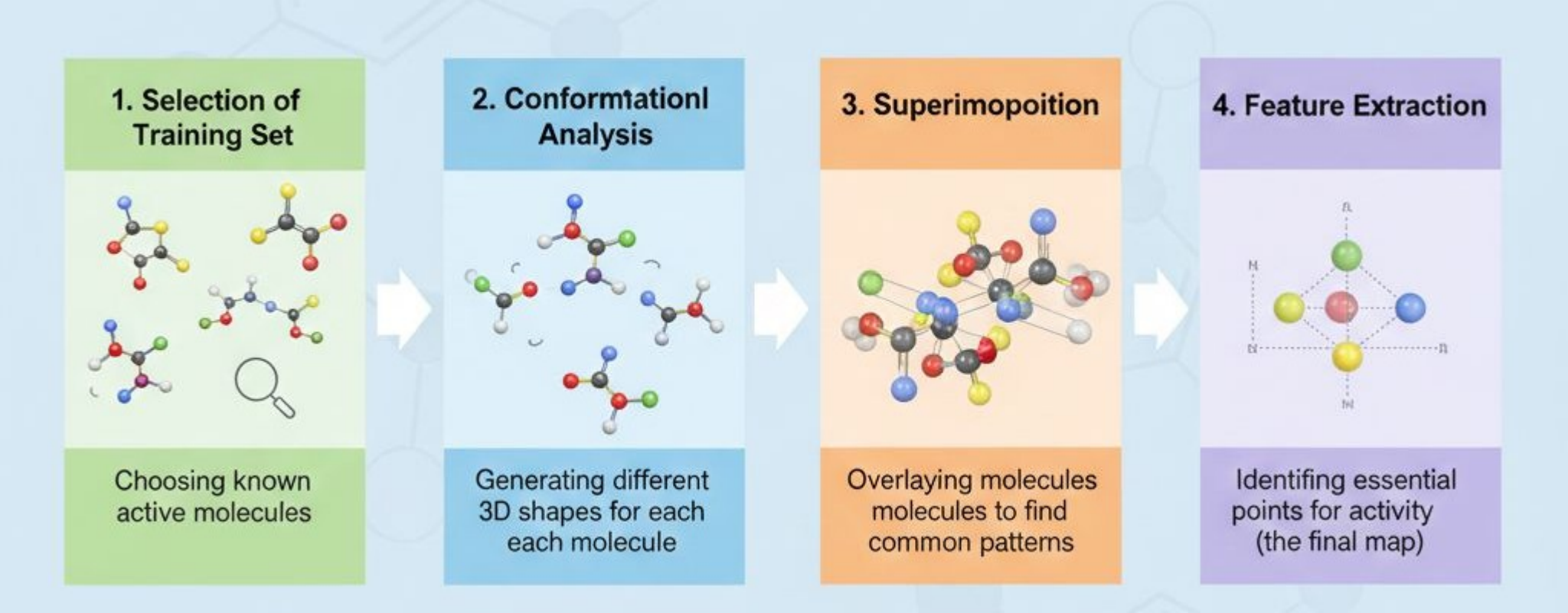
Pharmacohore Mapping: The Bluepinting Process

IUPAC definition:

The compuational process of identifing the essential 3D arrangnent of chemical features required for biological activity.



PROCESS OF PAHRMACOPHORE MAPPING

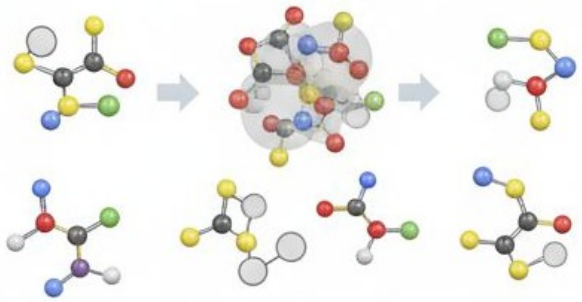


PHARMACOPHORE MAPPPING : 2 MAIN STRATEGIES

Pharamochore Mapping: Two Main Strategies

1. Ligand-Based Mapping
(Target Structure Unknown)

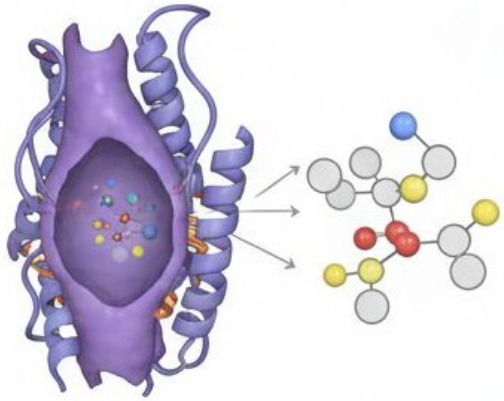
- Based on active molecules. Finds common features.



- Thate Ra pative a Shapes " stacking each fatures
- Identifies common 3D arrangement

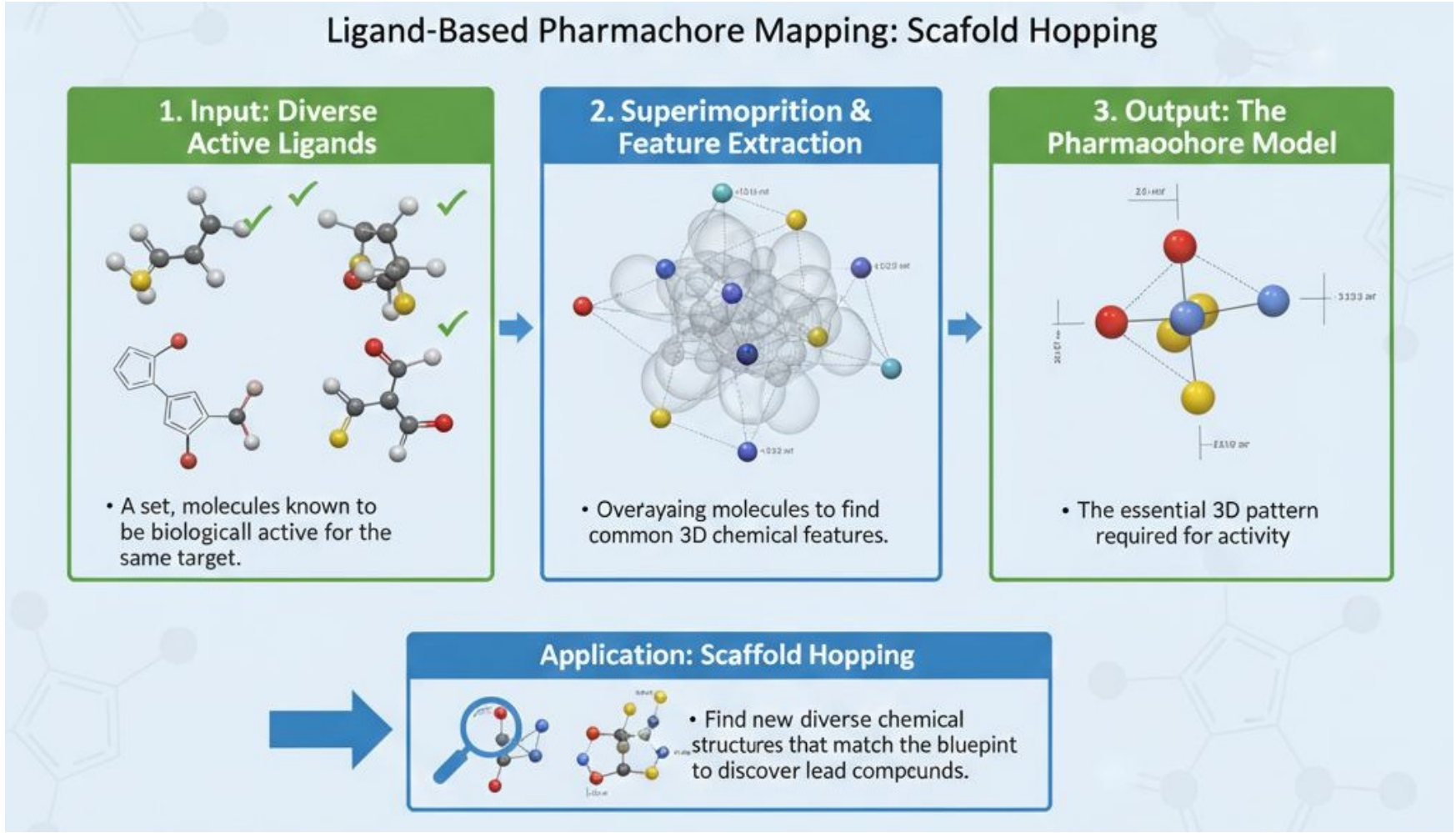
2. Structure-Based Mapping
(Target Structure Known)

- Based on protein's binding pocket. Designs ideal fit

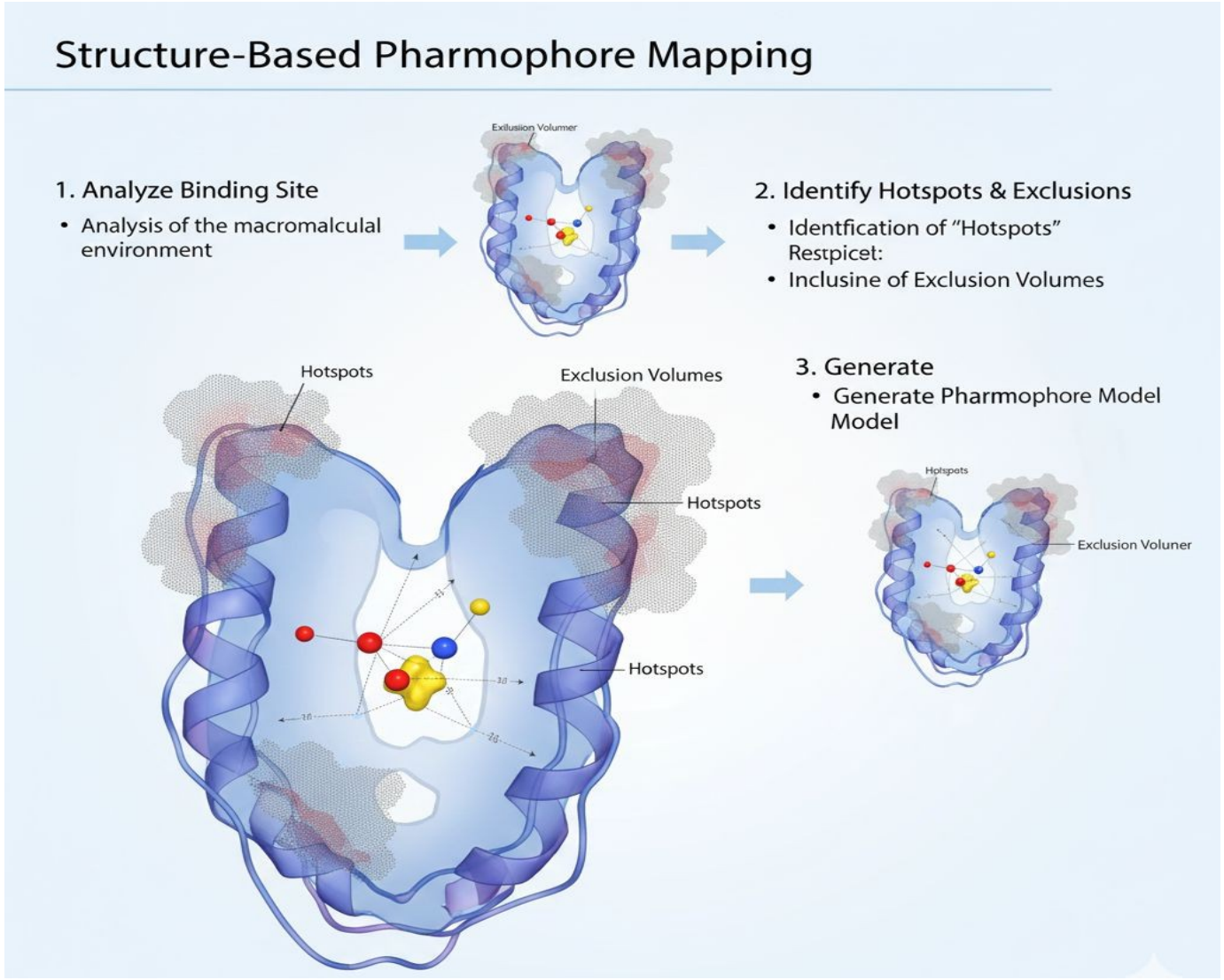


Features: H-bond D/A, Hydrophobic, Ionic
Hinos: Virtual Screening & Scaffold Hopping

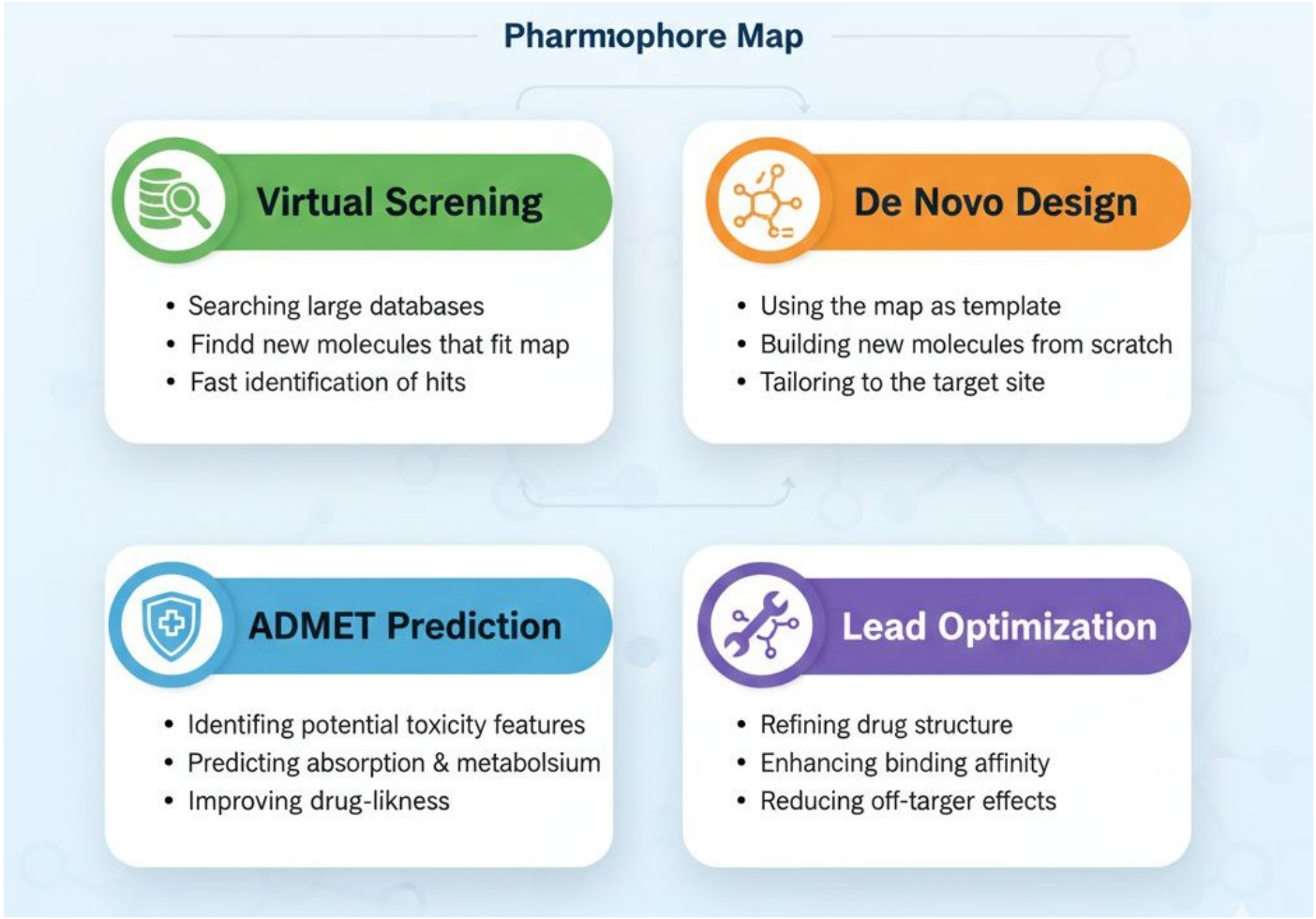
LIGAND BASED DRUG DESIGN



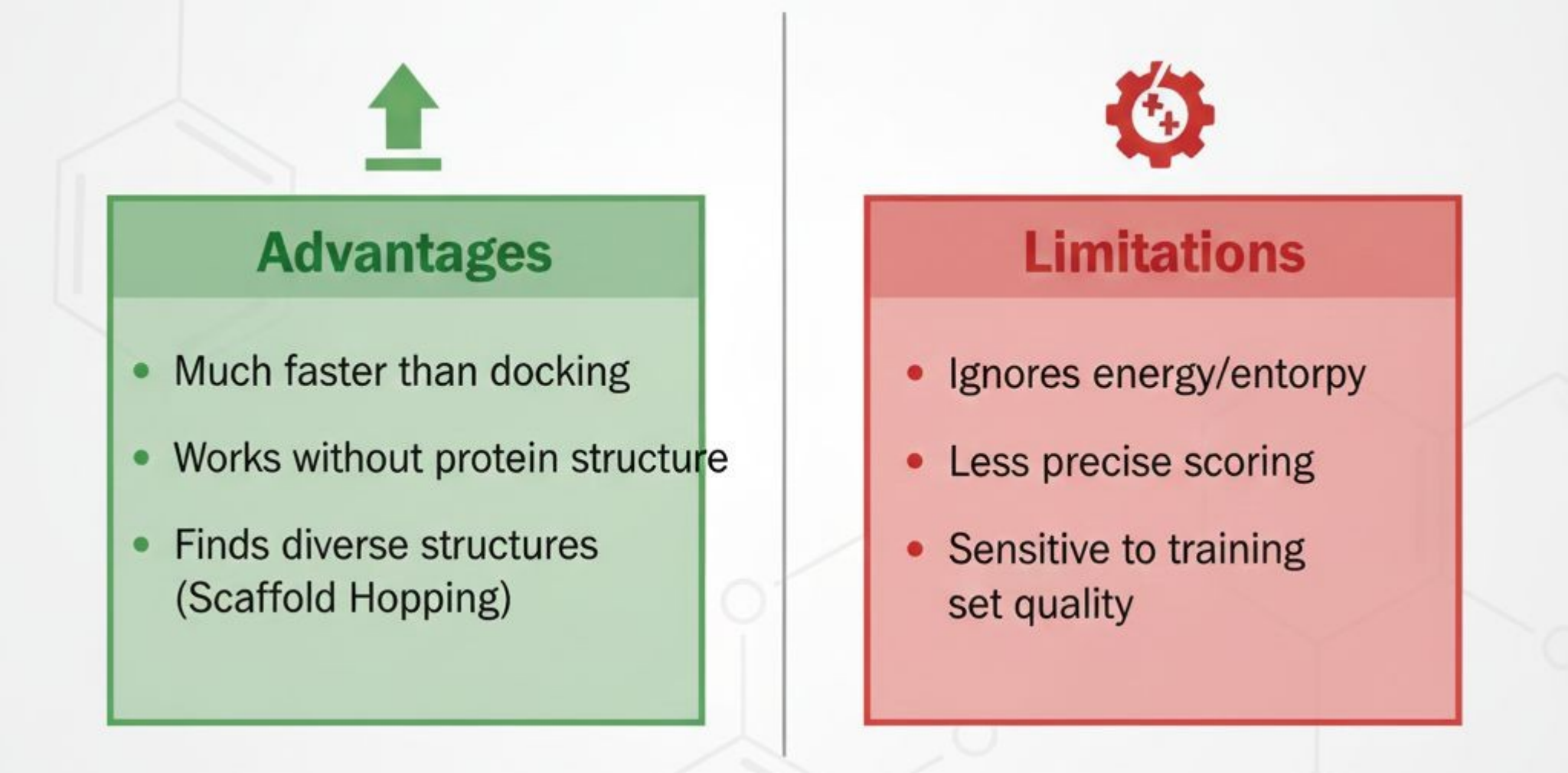
STRUCTURE BASED DRUG DESIGN (SBDD)



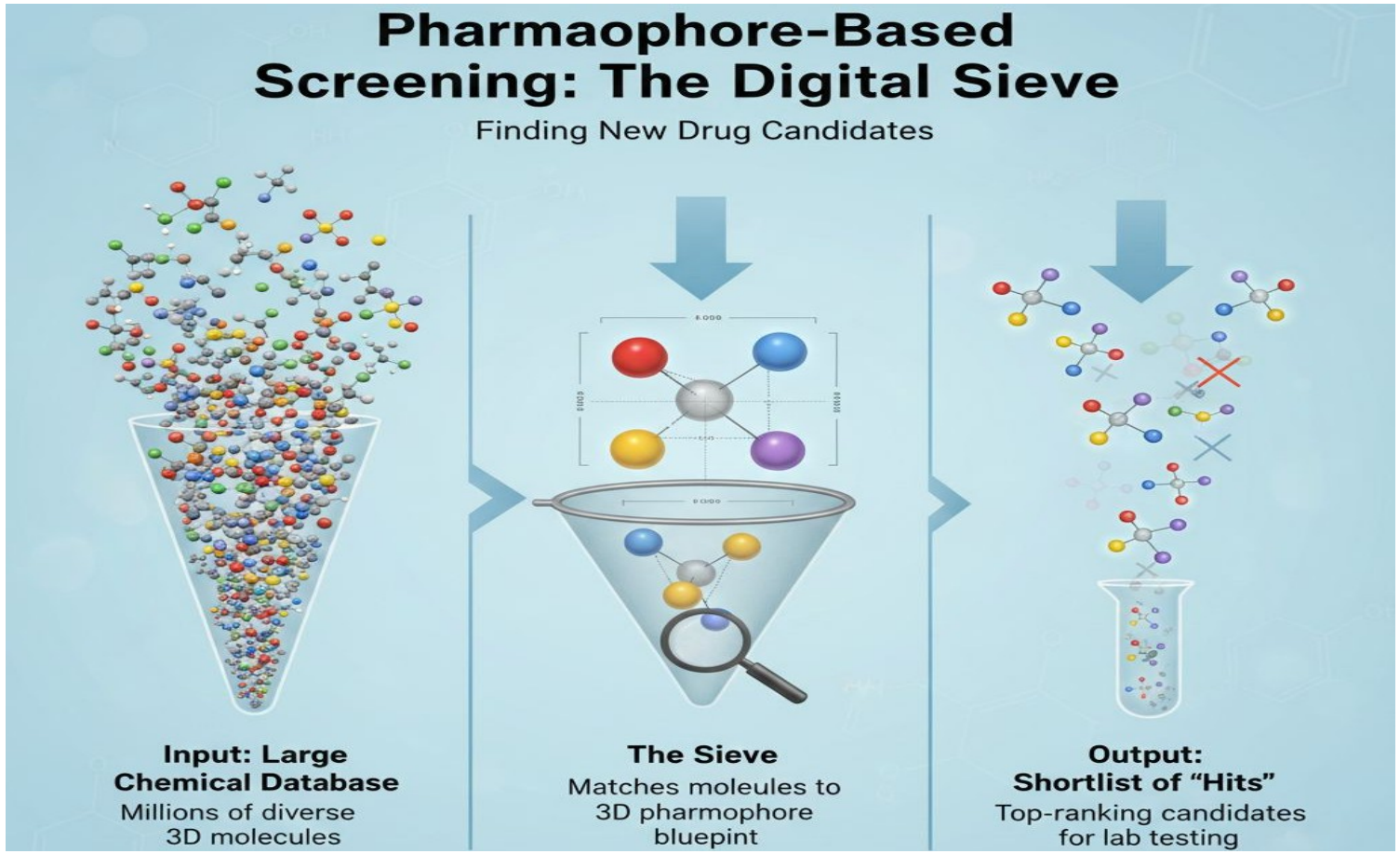
APPLICATIONS OF PHARMACOPHORE MAPPING IN DRUG DISCOVERY



PHARMACOPHORE MAPPING ADVANTAGES AND DISADVANTAGES

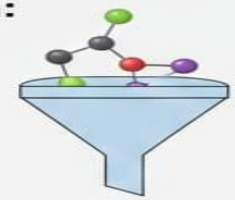


PHARMACOPHORE BASED SCREENING



Introduction to Pharmophore-Based Screening

Definition:



- Ligand-based virtual screening technique
- Identifies potential drug candidates
- Identifies essential on essential molecular features.

Pharmacphore-Based Screening

Finds molecules with matching 3D feature patterns.

Used When:

- Protein structure is unknown

- Known active ligands available

Early-Stage Drug Discovery

Finding New Leads: Focusing on What Matters Most

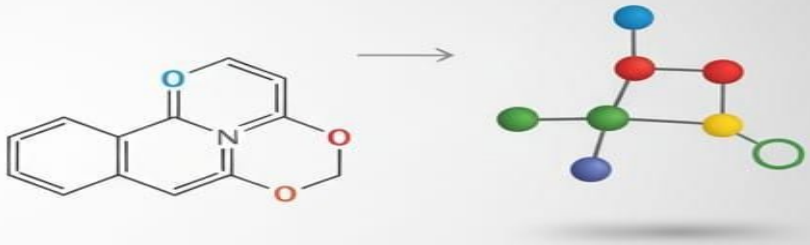
The Concept of a Pharmaophore

Definition:

- 3D arrangment of chemical features.
- Required for biological activity.
  Focuss on functionality, not structure.

Understanding SAR:

Lead Molecule



- Represents features for target–ligand interaction. Helps understand Structure–Activity Relationship (SAR).

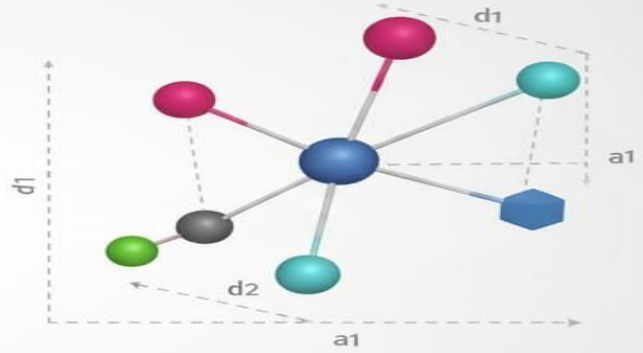
Pharmacophore: The Key 3D Features for Biological Function

Pharmaophoric Features

Common Features:

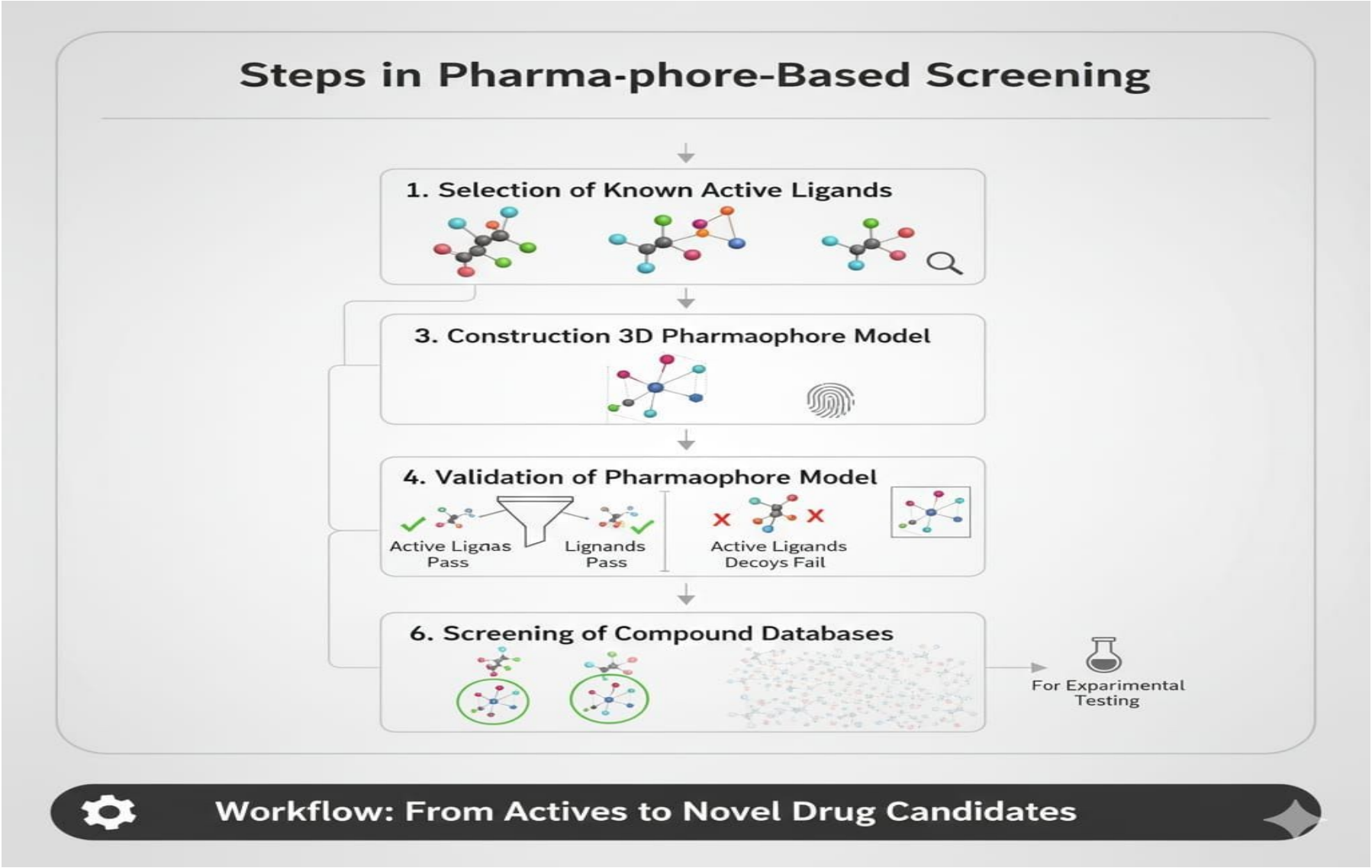
- **Hydrogen bond doners (HBD)** - H Atom bonded to O/N)
- **Hydrogen bond acceptors** - O/N Atoms
- **Hydroboboic regions** - Alkyl/Aryl groups
- **Aromatic rings** Pi-stacking
- **Positive Ionizable** Basic groups
- **Negative Ionizable** - Acidic groups

Spaial Orientation is Key:

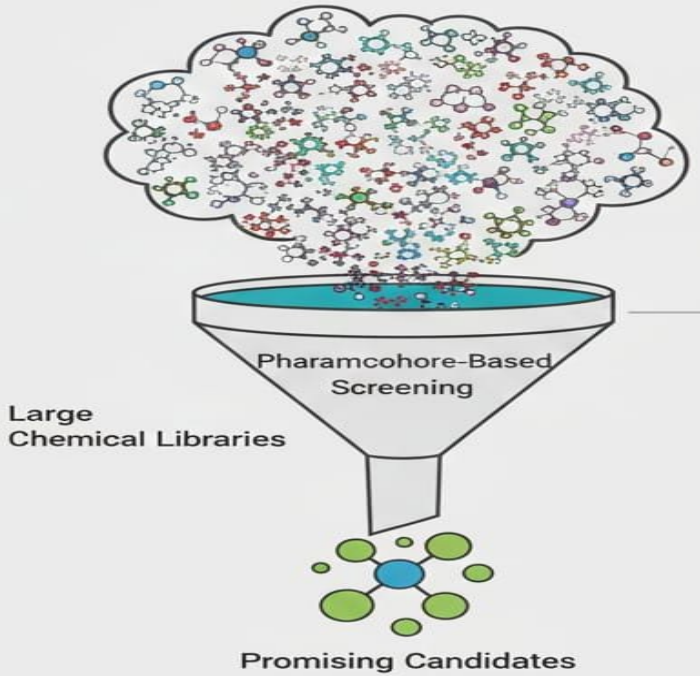


Essential for Biological Activity

Pharmacophore: The 3D Key to Unlocking Biological Function.


Steps in Pharma-phore-Based Screening
1. Selection of Known Active Ligands
3. Construction 3D Pharmaophore Model
4. Validation of Pharmaophore Model
Active Ligands Pass
Lignands Pass
Active Ligrands Decoys Fail
6. Screening of Compound Databases
For Exparimental Testing
Workflow: From Actives to Novel Drug Candidates

Advantages / Pharmoohore-Based Screening



No 3D Target Structure

- Uses known active ligands

Rapid Screening

- Filters millions of compounds quickly

Identifies Novel Scaffolds

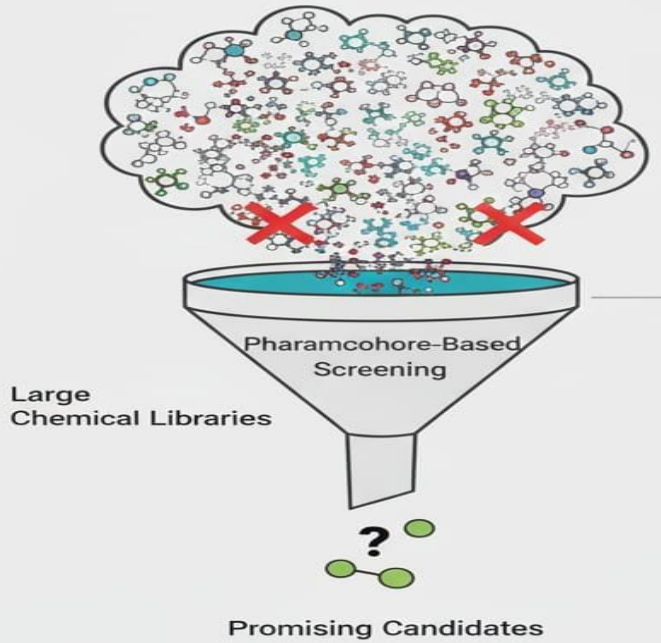
- Finds new chemical starting points

Cost-Effective & & Time-Saving

- Reduces experimental testing Crucial for lead identification

Maximazing Efficiency in Early Drug Discovery: A Ligand-Centric Approach

Limitations of Pharmoohore-Based Screening



Requires Active Compounds
- Needs known active ligands
  Cannot ths used without data

Cannot Predict Affinity
- Predicts presence, not strength
  Requires docking for scoring

Misss Novel Binding Modes
- Excludes different dat chemical series

Model Quality Dependent
- Input ligands dictate output
  Poor data = poor model

Balimazing Power & Pitfals in Ligand-Based Design

ASSESSMENT

Q1. Pharmacophore mapping mainly focuses on:
A) Complete molecular structure
B) Molecular weight and solubility
C) Spatial arrangement of functional features
D) Protein folding pattern

Q2. Pharmacophore mapping helps in understanding:
A) Drug synthesis cost
B) Structure–activity relationship (SAR)
C) Drug storage conditions
D) Packaging requirements

Q3. Pharmacophore mapping helps in understanding:
A) Drug synthesis cost
B) Structure–activity relationship (SAR)
C) Drug storage conditions
D) Packaging requirements

REFERENCES

1) Wermuth, C. G., Ganellin, C. R., Lindberg, P., & Mitscher, L. A. (1998). Glossary of terms used in medicinal chemistry (IUPAC Recommendations). Pure and Applied Chemistry, 70(5), 1129–1143

2) Yang, S. Y. (2010).
Pharmacophore modeling and applications in drug discovery: Challenges and recent advances. Drug Discovery Today, 15(11–12), 444–450

3) Patel, Y., Gillet, V. J., Bravi, G., & Leach, A. R. (2002).
A comparision of pharmacophore identification programs. Journal of Computer Aided Molecular Design, 16, 653–681.


Thank You!