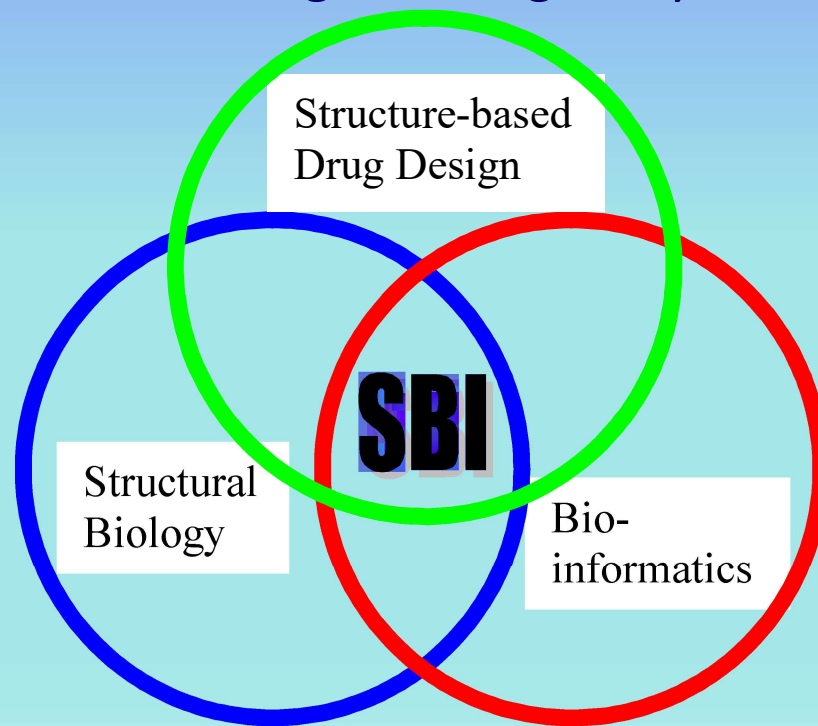


Structural Bioinformatics in Drug Discovery

Structural Bioinformatics

“Structural bioinformatics is a subset of bioinformatics concerned with the use of biological structures – proteins, DNA, RNA, ligands and complexes for understanding of biological systems.”



Impact of Structural Bioinformatics on Drug Discovery: Speeds up key steps in DD process by combining aspects of bioinformatics, structural biology, and structure-based drug design

SBI in Drug Discovery

SBI can be used to examine:

- drug **targets** (usually proteins)
- binding of **ligands**



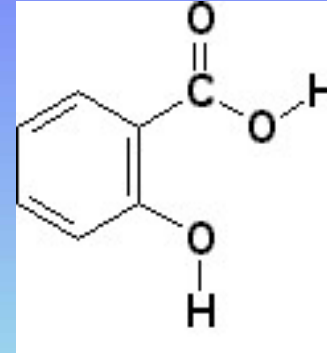
“rational” drug design

(benefits = saved time)

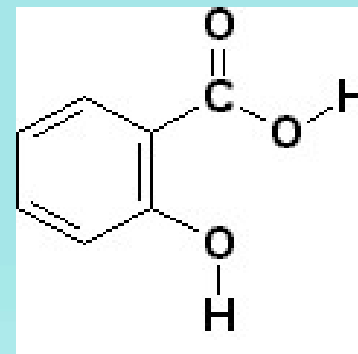
Traditional Methods of Drug Discovery



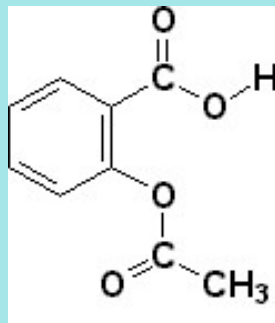
Natural (plant-derived)
treatment for illness/ailments



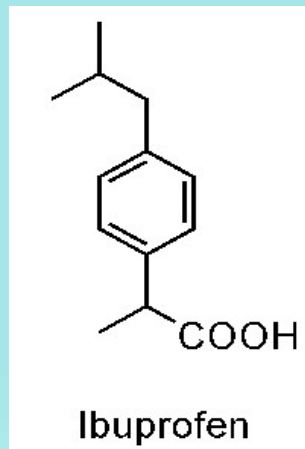
Isolation of active compound
(small, organic)



Synthesis
of compound



Aspirin



Ibuprofen



Manipulation of structure
to get better drug

(greater efficacy, fewer side effects)

Modern Drug Discovery

disease → genetic/biological target



discovery of a "lead" molecule

- design assay to measure function of target
- use assay to look for modulators of target's function



high throughput screen (HTS)

- to identify "hits" (compounds with binding in low nM to low μ M range)

Modern Drug Discovery

Small molecule hits



Manipulate structure to increase potency



Optimization of lead molecule into candidate drug

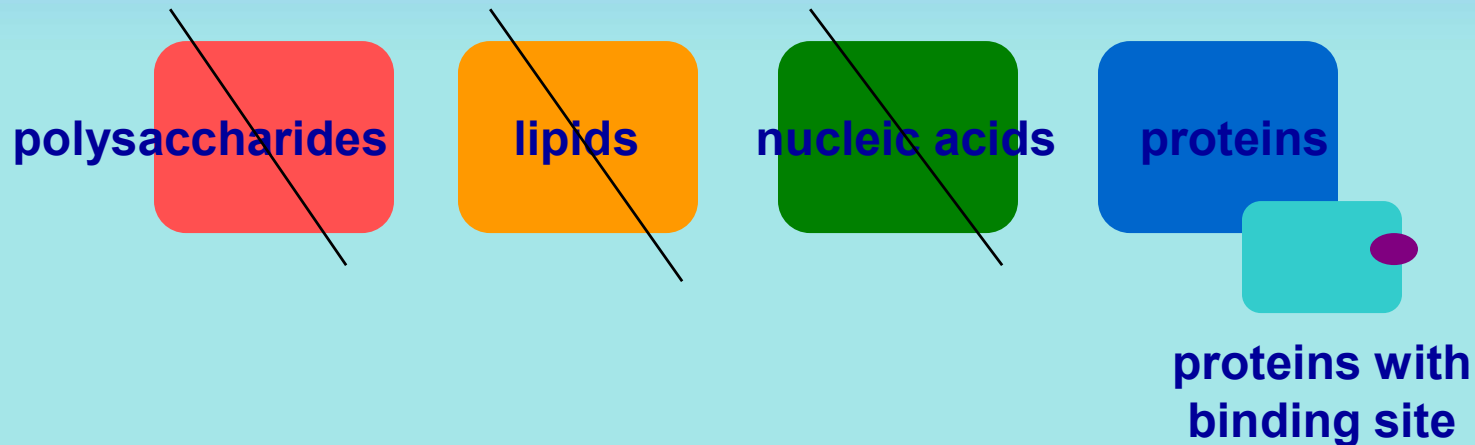
**Fulfillment of required pharmacological properties:
potency, absorption, bioavailability, metabolism, safety**



Clinical trials

Identifying Targets: The “Druggable Genome”

human genome



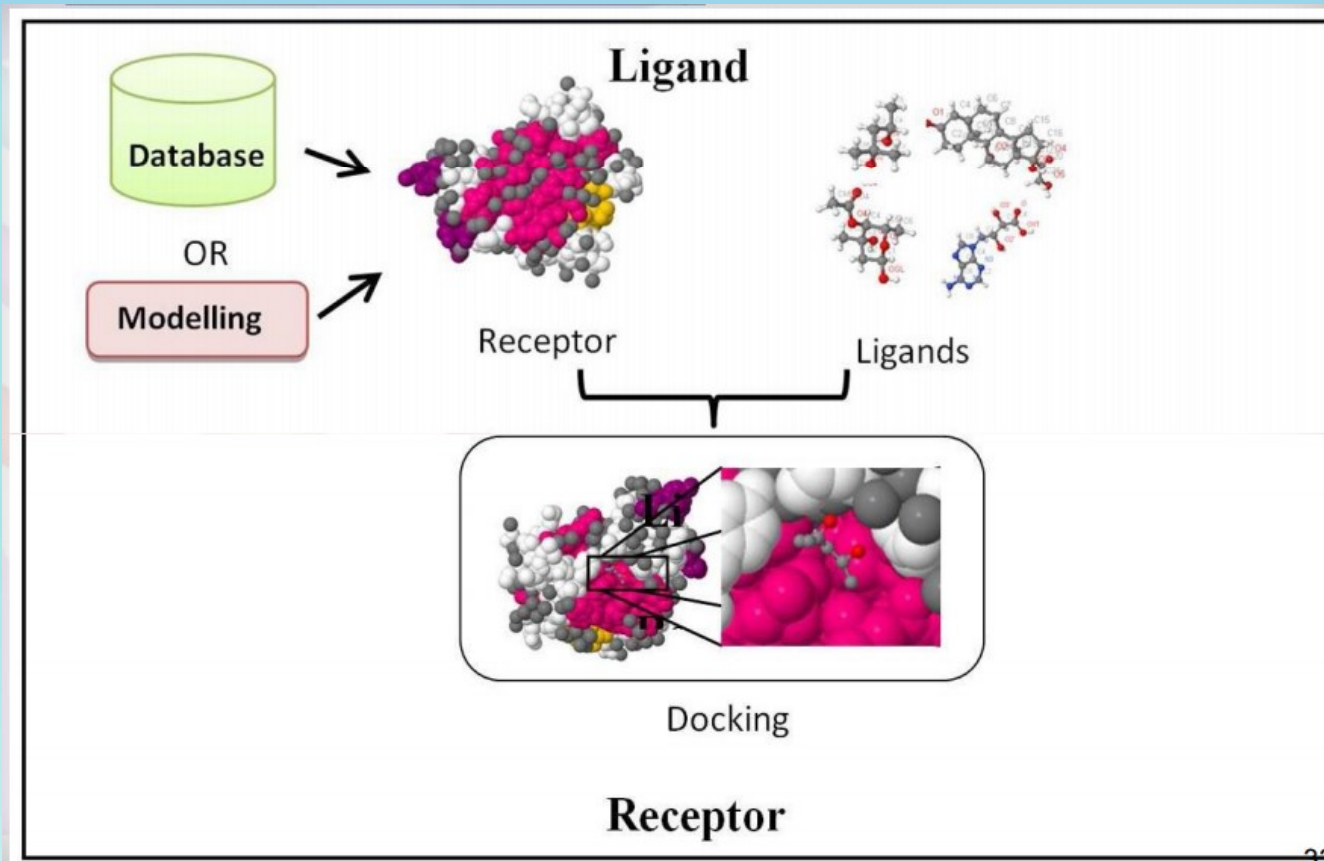
“Druggable genome” = subset of genes which express proteins capable of binding small drug-like molecules

Roles for SBI in drug discovery

- **Binding pocket modeling**
- **Lead identification**
 - Similarity with known proteins or ligands
- **Chemical library design / combinatorial chemistry**
- **Virtual screening**
- ***Lead optimization***
 - Binding
 - ADMET

SBI in drug discovery

- Insilico Methods in Drug Discovery-Computational tools offer the advantage of delivering new drug candidates more quickly and at a lower cost.
- Molecular docking



Molecular Docking

- Docking is the computational determination of binding affinity between molecules (protein structure and ligand). Given a protein and a ligand find out the binding free energy of the complex formed by docking them.
- stages of High throughput docking for protein –ligand complex binding...

