DockTData

Automated Integration of Binding Affinity and Molecular Structure Data for Receptor—Ligand Interaction Modeling

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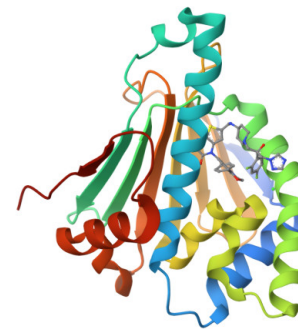
1 Background

The Central Role of Data

- **Binding affinity** as central task in **drug design**
- **Structural data** as a **rich information** reference
- **Structure-based affinity prediction models** are as key components for **Virtual Screening**, ***De Novo*** **Drug Design**
- Need for **open** and FAIR-compliant resources



Current Data Landscape

1 Background

- Data availability is the **bottleneck**: *no data = no AI/ML*
- **PDBbind**[1] was valuable but constrained by **restrictive licensing**
- **Boltz-2**[2] recent success highlights how **large-scale, curated datasets can unlock affinity prediction models**
  - but the pipelines for obtaining the data are **not readily available**
- **DockTData** contributes to this ecosystem as a **free and open resource**

[1] S. Passaro et al., *bioRxiv*, **2025**, 10.1101/2025.06.14.659707.

[2] Z. Liu et al., *Acc. Chem. Res.*, **2017**, 50.

Bridging Disciplines Through Data

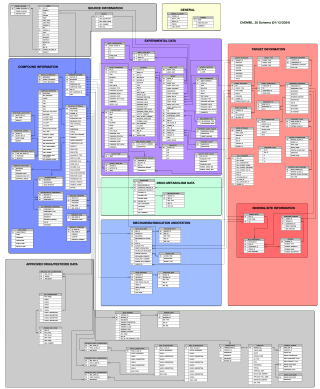
1 Background

- **Medicinal Chemists:** a hub for deposition, extraction and curation of experimental binding data
- **Machine Learning Community:** comprehensive training material with multiple representations of proteins and ligands
- **Bioinformatics & Molecular Modeling:** consolidated datasets for validation of docking, virtual screening & QSAR simulations

Data Integration Challenges

1 Background

- Missing **structural–functional links**
- Lack of supporting information and **documentation**
- **Data quality** and consistency issues
- **Scalability** for large datasets
- **Standardization** of data formats and identifiers
- Understanding different **data source structures**



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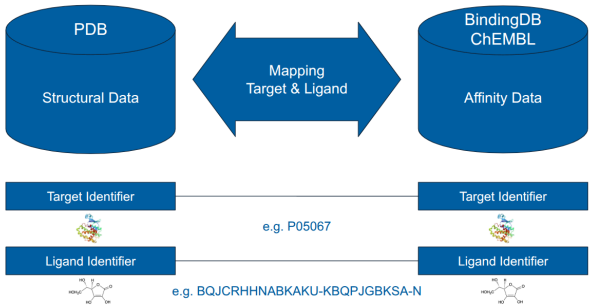
ETL Architecture

- **Extract:** PDB[3] (API), BindingDB[4] (flat files), ChEMBL[5] (relational DB)
- **Transform:** Validation, Filtering, Processing, Cross-linking
- **Load:** Structure the integrated set

[1] Berman, H. M. et al *Nucleic Acids Res.* **2000**, 28.
[2] Z. Liu, T. et al. *Nucleic Acids Res.*, **2025**, 53.
[3] Mendez, D. et al. *Nucleic Acids Res.* **2019**, 47.

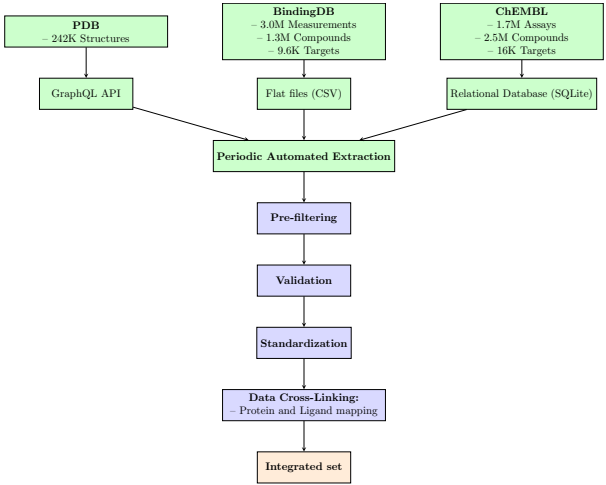
Data Cross-Linking

- **Protein mapping:** UniProt IDs (ChEMBL), sequence identity $\geq 85\%$ (BindingDB)
- **Ligand mapping:** InChIKey and CCD



Pipeline

2 The DockTData Project



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Dataset Composition

3 What We Have

- **37.0K** unique PDB structures
- **13.8K** unique ligands
- Binding affinity types: **Ki, Kd, IC50 & EC50**
- Protein- & Nucleic acid- ligand complexes

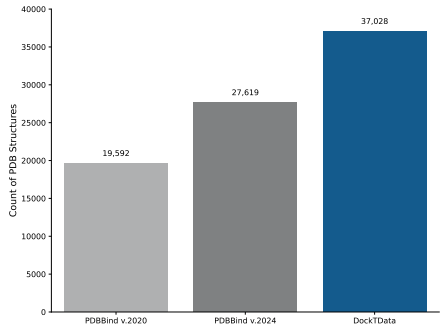
Democratizing data

3 What We Have

- **DockTData** (Last update 17-Set-25)
  Unique PDB structures: **37.0K**

- **PDBbind*** v.2020 (Free)
  Unique PDB structures: **19.5K**

- **PDBbind*** v.2024 (Paid**)
  Unique PDB structures: **27.6K**



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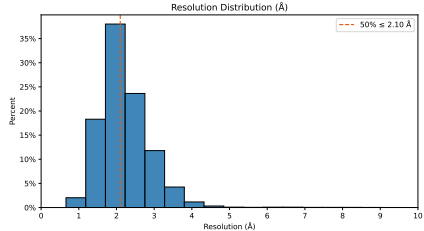
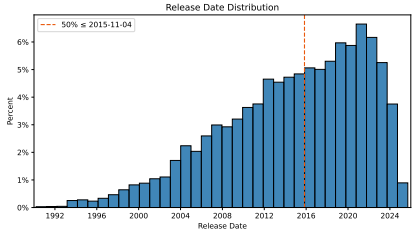
* Subject to a highly restrictive license

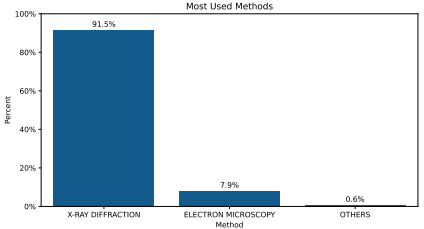
** Cost for academic users: USD 2,000

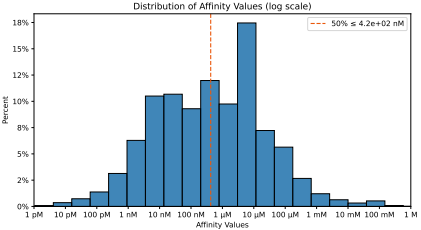
Dataset Characterization

3 What We Have









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4 Perspectives

Conclusions

4 Perspectives

- **Scalable, reproducible, automatic pipeline** integrating structural–functional data
- A resource for many purposes:
  - ML-based **Affinity Prediction**
  - **Virtual Screening** Validation
  - **Generative Models** for **Drug Design**
  - and **more**

Work-In-Progress

4 Perspectives

- **Peptide** and **Oligosaccharides** as ligands
- Target mapping by **sequence alignment** (MMseqs2)
- Subsets with **refined** filters
- Availability of **prepared structures** (e.g. protonation, cofactors)

Future Perspectives

4 Perspectives

- **Expansion:** Multi-ligand Complexes, Nucleotide Receptors
- Public **web portal** and **collaborative curation**
- **Call-to-action:** *from the community to the community*

Acknowledgement

4 Perspectives

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Obrigado!