# Tutorial Planning: [Semi-automated workflow for docking small molecules]

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\*\*Date:\*\* 10/13/2025

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## 1. Objective

- Purpose of this tutorial: To create a workflow for docking small molecule ligands into receptors ideal for hit-to-lead or lead optimization.

- Specific learning goals: To prepare target receptors and ligands for docking, run docking itself, and analyze and process docking results.

- Target audience: beginners, intermediate, advanced users.

- Scope and limitations: allows for rigid and flexible docking (optional: free energy perturbation); covers only small molecules ligand docking; docks into known binding site of co-crystallized ligand, but grid box size adjustable, Vina can be used for quick and basic docking, while GNINA can be used for accurate pose prediction and binding affinity estimation (*we can choose either, Gnina = Vina + machine learning*)

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## 2. Source/Reference

- PDB101 tutorial by RCSB Protein Data Bank: <https://pdb101.rcsb.org/train/training-events/python4>

- McNutt, A.T., Li, Y., Meli, R. *et al.* GNINA 1.3: the next increment in molecular docking with deep learning. *J Cheminform* **17**, 28 (2025). <https://doi.org/10.1186/s13321-025-00973-x>

- Buccheri, R.; Rescifina, A. High-Throughput, High-Quality: Benchmarking GNINA and AutoDock Vina for Precision Virtual Screening Workflow. *Molecules* **2025**, *30*, 3361. <https://doi.org/10.3390/molecules30163361>

- Sunseri, J., & Koes, D. R. (2021). Virtual Screening with Gnina 1.0. *Molecules (Basel, Switzerland)*, *26*(23), 7369. <https://doi.org/10.3390/molecules26237369>

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## 3. Computational Environment

- \*\*Hardware\*\*: [13th Gen Intel(R) Core(TM) i7-1355U 1.70 GHz, 12 cores, 16GB]

- \*\*Software stack\*\*:

- Receptor and ligand preparation: [Biopython, OpenMM, Open Babel, PDBfixer, RDKit, scrubber]

- Docking/Screening: [AutoDock Vina, Gnina]

- Visualization: [py3Dmol, PyMOL]

- Analysis tools: [MDAnalysis, matplotlib, pandas]

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## 4. Tutorial Steps

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| --- | --- | --- |
| Step | Description | Expected outcome |
| Environment setup | Install dependencies, load modules | Working environment created |
| Receptor and ligand preparation | Download/clean (through scripts) input structures or datasets, compare output with commercial software e.g. Schrödinger | Input files ready |
| Run example molecules | Execute main workflow commands/scripts for docking | Simulation or calculation runs |
| Visualization | Inspect structures, trajectories, or results | Figures or visual confirmation |
| Data analysis | Process outputs, calculate metrics, compare output with commercial software e.g. Schrödinger | Tables, plots, or free energy data |
| Report/Notes | Summarize learnings, caveats, troubleshooting tips | Documentation for future reference |

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## 5. Schedule (Estimated Working Time)

\*\*The tasks are used as examples only\*\*

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| --- | --- | --- |
| Task | Description | Estimated time (hours) |
| Environment setup | Install dependencies, load modules | 2-3 |
| Receptor and ligand preparation | Download/clean (through scripts) input structures or datasets, compare output with commercial software e.g. Schrödinger | 2-3 |
| Run example molecules | Execute main workflow commands/scripts for docking | 3-4 |
| Visualization | Inspect structures, trajectories, or results | 1 |
| Data analysis | Process outputs, calculate metrics, compare output with commercial software e.g. Schrödinger | 3-4 |
| Report/Notes | Summarize learnings, caveats, troubleshooting tips | 1 |
|  |  | Total: 12-16 |

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