The Demonstration of AutoDock as an Educational Tool for Drug Discovery

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Typical Student Results

Following the completion of the experiment, students were asked to submit the docking output files (those with the extension .dlg) for review by the instructors. Generally, the students correctly docked the compounds and generated meaningful output consistent with the results generated by the instructors (Figure SR1). The predicted binding affinities (Table SR1, column 3) were similar in value to those appearing in the manuscript (Table 1) with the exception of compound **1** (student mean = 179 μM, instructor value = 69.0 μM). The disagreement regarding compound **1** is the result of the small size of the inhibitor and the fact that there are only two strong binding interactions between the protein and ligand. However, some of the data submitted by students revealed predicted binding poses and affinities that were not representative of the expected output. When these values are included in the statistical analysis of the student results, the mean values are dramatically altered (Table SR1, column 2). For example, the mean predicted binding affinity (K_i) changes from 0.936 to 10.7 μM for compound **2**. There are two factors that contributed to students incorrectly docking the compounds and obtaining inaccurate binding affinities. The students either docked the wrong compound (for example, the incorrect tautomer of compound **3**, Figure SR2), or the students incorrectly centered the grid box over the protein active site, altering the target docking region of the protein (Figure SR3). However, following consultation with the instructors, the students were able to re-dock the compounds and obtained reasonable docking poses and predicted binding affinities.

Table SR1: Output binding affinities representing typical student results

Compound	K_i Range w/outliers (μM)[a, b]	K_i Range w/o outliers (μM)[b]
1	42.3 – 456 (135 ± 159)	76 – 456 (179 ± 185)
2	0.585 – 65.3 (10.7 ± 24.1)	0.585 – 1.09 (0.936 ± 0.240)
3	0.104 – 7.91 (3.04 ± 3.59)	0.104 – 0.221 (0.208 ± 0.140)
4	16.2 – 181.2 (54.9 ± 60.8)	16.2 – 44.4 (25.8 ± 13.0)

a. The large Ki ranges are the result of the inclusion of values generated by students who incorrectly docked the compounds on their initial attempts to complete the experiment.
b. Means with standard deviation in parentheses.

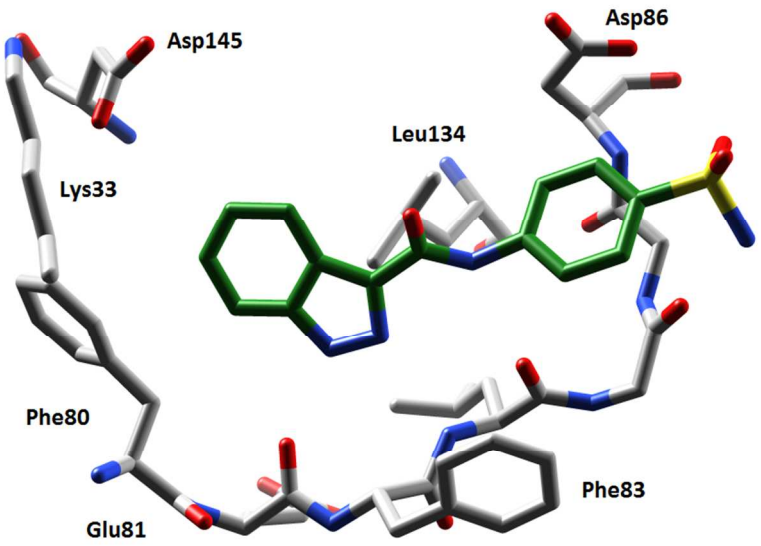

Figure SR1: Example docking output for a student who correctly docked the ligand. This image was generated by the authors with Chimera 1.11.

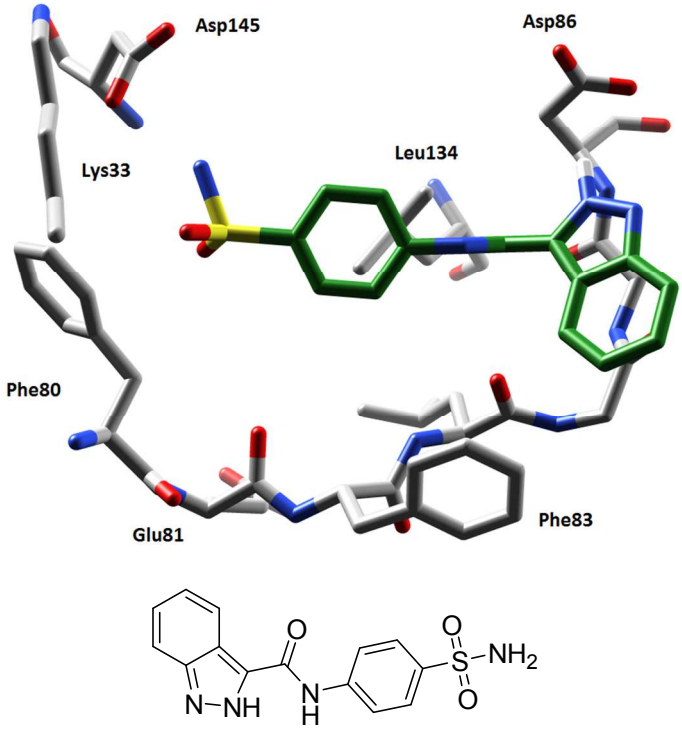

Figure SR2: Example docking output for a student who docked the incorrect compound (wrong tautomer of compound **3**). This image was generated by the authors with Chimera 1.11.

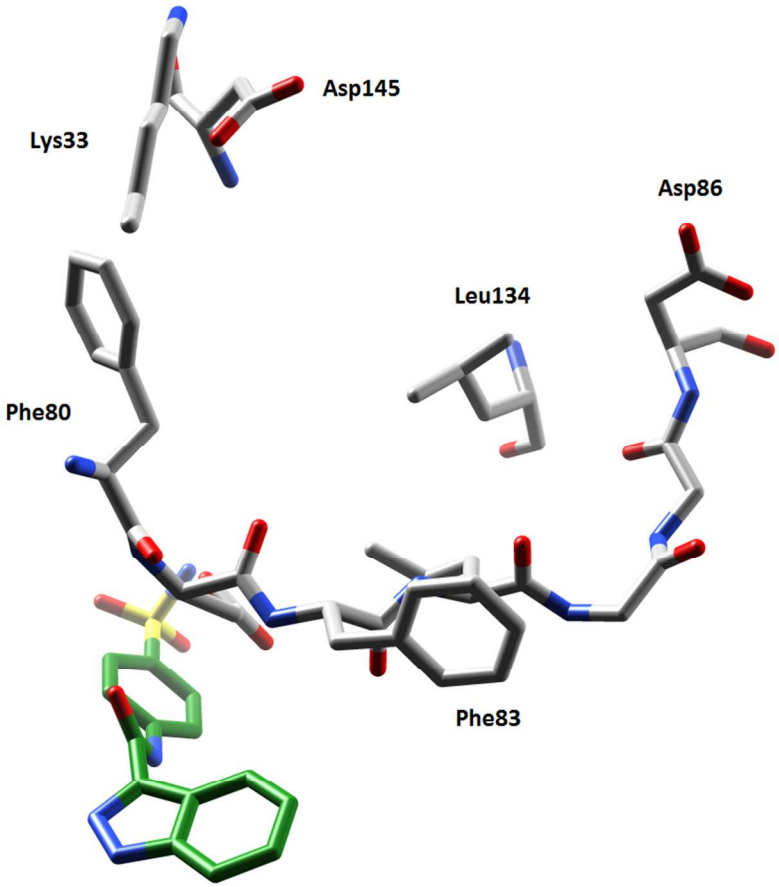

Figure SR3: Example docking output for a student who incorrectly centered the grid box prior to docking the ligand. The ligand was predicted to bind outside of the known active site. This image was generated by the authors with Chimera 1.11.