# A Beginner's Manual for PyRx

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## PyRx Installation

**Pre-Installation**: Ensure that you have Python 2.6 (or newer) and MS Visual C++ 2008 RP installed prior to installing PyRx.

1. Obtain PyRx installer from: http://pyrx.sourceforge.net/downloads
2. Run "PyRx-0.9.2-Setup.exe" → Click "next"
3. Install to default destination folder → Click "next"'
    a. Note: PyRx should install to C:\Program Files (x86)\PyRx
4. Deselect "Launch PyRx" and Select "Create Desktop Shortcut"
5. Create a shortcut for your desktop linked to: C:\Users**YOURNAME** \.PyRx_workspace
    a. PyRx automates many intermediate steps that would normally be manually performed in the AutoDock Suite. PyRx, by default, uses this folder as its workspace. Thus, it is convenient to have quick access to it.

**Optional (but recommended): Open Babel**

1. Open Babel is an extremely helpful and diverse program that allows for the GUI conversion of several file types, such as PDB, PDBQT, and SDF files.
2. Open Babel can used within PyRx or independently. This allows conversions seamlessly within PyRx's GUI. Additionally, Open Babel can be used to convert files for use in AutoDock, when necessary.

## PyRx Environment:

1. Click the PyRx desktop shortcut to run the GUI
    a. If any errors present STOP and troubleshoot. If all of PyRx's dependencies have been installed, a reboot and/or a reinstallation would be my first recommendations.
    b. Running PyRx with underlying errors will cause severe issues and likely cause computations to abort.
2. Obtain PDB file for ligand and receptor.
    a. In this case I will be using the following:
        i. Receptor: 2ZCK
        ii. Ligand: ZAP
3. Load Receptor and Ligand by going to FILE>LOAD MOLECULE
    a. Both the ligand and receptor can be loaded from this interface
4. Click the + next to 2ZCK
    a. Right click and remove the S, L, and H chain
    b. This leaves only the PSA (P chain) in the interface

    c. The PSA can be saved as a .PDB by right clicking the P and choosing “save as PDB”
5. At this point, we are ready to prepare the files for the AutoDock wizard
    a. Right click the P-chain and select “AUTODOCK>MAKE MACROMOLECULE”
    b. Right click the ZAP (ligand) and select “AUTODOCK>MAKE LIGAND”
        i. NOTE: This will do all necessary preliminary steps such as removing water, adding hydrogens, merging non-polar hydrogens, and adding partial charges
6. Select the AutoDock Wizard under the controls tab
7. Click LOCAL and then NEXT
8. Click the corresponding ligand in the AutoDock Navigator
9. Click the corresponding macromolecule in the AutoDock Navigator
10. Confirm that the AutoDock Wizard is set to Select Molecules and shows that 1 ligand and 1 macromolecule has been selected
11. Input AutoGrid Dimensions
    a. Grid Center:
        i. X-Dimension: -36.636
        ii. Y-Dimension: -37.475
        iii. Z-Dimension: -21.304
    b. Number of Points
        i. X-Dimension: 100
        ii. Y-Dimension: 100
        iii. Z-Dimension: 100
    c. Spacing (Angstrom): 0.200
12. Click NEXT
13. Click Genetic Algorithm
    a. Click Docking Parameters
    b. Change:
        i. Number of GA runs to 25
        ii. Maximum number of energy evaluations to medium
        iii. Click OK
14. Analyze results
    a. Can be saved as comma separated value (CSV) for use in excel
    b. FILE>EXPORT can be used to export all files into a tar.gz file that allows for later importation of the data and computations directly into PyRx
        i. This removes the need to recalculate AutoGrid and AutoDock data

NOTE: Unlike AutoDockTools some features are not possible. For example, the covalent map function is not available in PyRx.

Results

| Ligand | Binding Energy | Intermol Energy | Internal Energy | Torsional Energy | Unbound Energy |
|---|---|---|---|---|---|
| 2zck_p_zap | -7.22 | -10.2 | -1.46 | 2.98 | -1.46 |
| 2zck_p_zap | -5.67 | -8.66 | -1.67 | 2.98 | -1.67 |
| 2zck_p_zap | -5.1 | -8.08 | -1.54 | 2.98 | -1.54 |
| 2zck_p_zap | -5.82 | -8.8 | -0.84 | 2.98 | -0.84 |
| 2zck_p_zap | -5.62 | -8.61 | -2.59 | 2.98 | -2.59 |
| 2zck_p_zap | -5.05 | -8.03 | -1.45 | 2.98 | -1.45 |
| 2zck_p_zap | -5.32 | -8.3 | -0.97 | 2.98 | -0.97 |
| 2zck_p_zap | -5.18 | -8.16 | -1.1 | 2.98 | -1.1 |
| 2zck_p_zap | -7.28 | -10.26 | -1.48 | 2.98 | -1.48 |
| 2zck_p_zap | -5.66 | -8.64 | -0.66 | 2.98 | -0.66 |
| 2zck_p_zap | -6.6 | -9.58 | -1.53 | 2.98 | -1.53 |
| 2zck_p_zap | -4.5 | -7.49 | -1.73 | 2.98 | -1.73 |
| 2zck_p_zap | -5.29 | -8.28 | -1.84 | 2.98 | -1.84 |
| 2zck_p_zap | -7.55 | -10.53 | -1.41 | 2.98 | -1.41 |
| 2zck_p_zap | -7.55 | -10.54 | -1.58 | 2.98 | -1.58 |
| 2zck_p_zap | -5.9 | -8.88 | -1.77 | 2.98 | -1.77 |
| 2zck_p_zap | -6.81 | -9.8 | -1.03 | 2.98 | -1.03 |
| 2zck_p_zap | -4.59 | -7.57 | -1.72 | 2.98 | -1.72 |
| 2zck_p_zap | -4.4 | -7.39 | -1.87 | 2.98 | -1.87 |
| 2zck_p_zap | -5.62 | -8.6 | -1.52 | 2.98 | -1.52 |
| 2zck_p_zap | -4.98 | -7.97 | -1.78 | 2.98 | -1.78 |
| 2zck_p_zap | -5.9 | -8.88 | -2.14 | 2.98 | -2.14 |
| 2zck_p_zap | -5.53 | -8.51 | -1.53 | 2.98 | -1.53 |
| 2zck_p_zap | -4.43 | -7.41 | -2.2 | 2.98 | -2.2 |
| 2zck_p_zap | -7.23 | -10.21 | -1.51 | 2.98 | -1.51 |
| 2zck_p_zap | -5.5 | -8.48 | -1.96 | 2.98 | -1.96 |
| 2zck_p_zap | -5.43 | -8.41 | -1.79 | 2.98 | -1.79 |
| 2zck_p_zap | -6.03 | -9.01 | -1.75 | 2.98 | -1.75 |
| 2zck_p_zap | -6.15 | -9.13 | -1.25 | 2.98 | -1.25 |
| 2zck_p_zap | -4.53 | -7.52 | -2.49 | 2.98 | -2.49 |
| 2zck_p_zap | -7.16 | -10.14 | -1.63 | 2.98 | -1.63 |
| 2zck_p_zap | -5.02 | -8 | -1.6 | 2.98 | -1.6 |
| 2zck_p_zap | -6.48 | -9.46 | -1.68 | 2.98 | -1.68 |
| 2zck_p_zap | -7 | -9.98 | -1.46 | 2.98 | -1.46 |
| 2zck_p_zap | -7.19 | -10.17 | -1.41 | 2.98 | -1.41 |
| 2zck_p_zap | -4.79 | -7.77 | -2.57 | 2.98 | -2.57 |
| 2zck_p_zap | -4.46 | -7.44 | -1.43 | 2.98 | -1.43 |
| 2zck_p_zap | -4.52 | -7.5 | -1.68 | 2.98 | -1.68 |
| 2zck_p_zap | -5.03 | -8.01 | -1.68 | 2.98 | -1.68 |

| | | | | | |
|---|---|---|---|---|---|
| 2zck_p_zap | -4.12 | -7.1 | -2.43 | 2.98 | -2.43 |
| 2zck_p_zap | -5.84 | -8.83 | -1.39 | 2.98 | -1.39 |
| 2zck_p_zap | -7.29 | -10.27 | -1.46 | 2.98 | -1.46 |
| 2zck_p_zap | -6.12 | -9.11 | -2.51 | 2.98 | -2.51 |
| 2zck_p_zap | -5.58 | -8.56 | -1.62 | 2.98 | -1.62 |
| 2zck_p_zap | -5.97 | -8.96 | -2.6 | 2.98 | -2.6 |
| 2zck_p_zap | -5.62 | -8.6 | -1.56 | 2.98 | -1.56 |
| 2zck_p_zap | -6.37 | -9.35 | -0.91 | 2.98 | -0.91 |
| 2zck_p_zap | -5.1 | -8.08 | -1.54 | 2.98 | -1.54 |
| 2zck_p_zap | -4.81 | -7.79 | -1.12 | 2.98 | -1.12 |
| 2zck_p_zap | -5.16 | -8.14 | -1.77 | 2.98 | -1.77 |

Table 1: This table is the resulting data from PyRx's facilitated docking. The receptor is an isolated prostate-specific antigen from PDB ID: 2ZCK. The ligand is an unmodified [N-(BENZYLOXYCARBONYL)AMINO](4-AMIDINOPHENYL)METHANE-PHOSPHONATE obtained from PDB ID: ZAP.

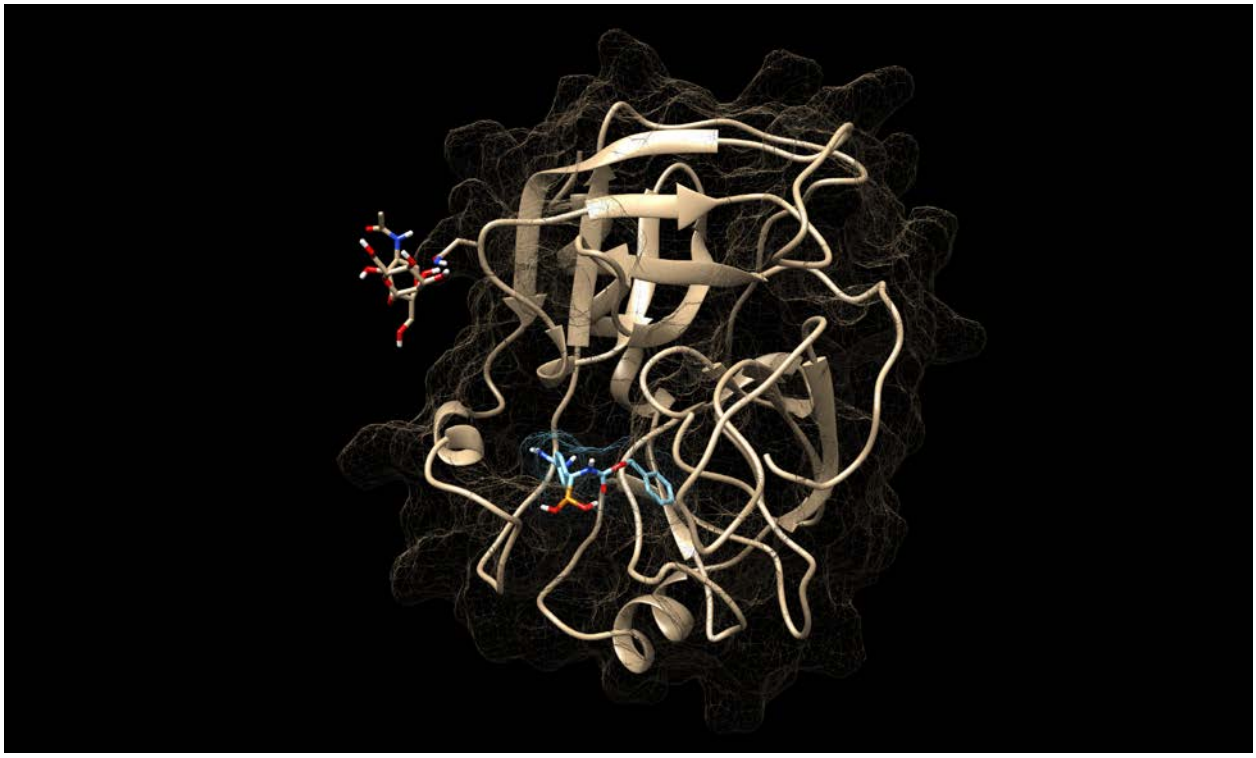

Figure 1: This image depicts the highest energy confirmation produced through PyRx. This image was produced in a manner that did not use a covalent map; thus, results differ from those obtained via AutoDockTools.