

4_TYK2_Gnina_Docking_and_Scoring_with_CNN

April 8, 2022

0.1 Gnina Docking

0.1.1 Gnina - a deep learning framework for molecular docking with integrated support for scoring and optimizing ligands using convolutional neural networks

```
[1]: ! nvidia-smi
```

```
Wed Mar 23 15:10:43 2022
```

```
+-----+
| NVIDIA-SMI 460.73.01      Driver Version: 460.73.01      CUDA Version: 11.2      |
+-----+-----+-----+-----+-----+-----+
| GPU  Name                Persistence-M| Bus-Id        Disp.A | Volatile Uncorr. ECC |
| Fan  Temp  Perf  Pwr:Usage/Cap|      Memory-Usage | GPU-Util  Compute M. |
|                                       |                    |    MIG M. |
+-----+-----+-----+-----+-----+-----+
|   0  GeForce GTX 1060      Off      | 00000000:01:00.0  On  |                     N/A |
| N/A   52C    P8         7W /  N/A |    466MiB /   6075MiB |         0%      Default |
|                                       |                    |    N/A |
+-----+-----+-----+-----+-----+-----+

```

```
+-----+
| Processes:
| GPU   GI    CI          PID    Type    Process name                        GPU Memory
|       ID    ID                                   Usage
+-----+-----+-----+-----+-----+-----+
|   0   N/A   N/A         1325      G   /usr/lib/xorg/Xorg                   18MiB |
|   0   N/A   N/A         1390      G   /usr/bin/gnome-shell                 69MiB |
|   0   N/A   N/A         1605      G   /usr/lib/xorg/Xorg                   287MiB |
|   0   N/A   N/A         1681      G   /usr/lib/rstudio/bin/rstudio         1MiB |
|   0   N/A   N/A         1738      G   /usr/bin/gnome-shell                 34MiB |
|   0   N/A   N/A        17317      G   ...token=6085199307339978208        8MiB |
|   0   N/A   N/A        24555      G   /proc/self/exe                      39MiB |
+-----+-----+-----+-----+-----+-----+

```

```
[2]: ! wget -P ../tools https://github.com/gnina/gnina/releases/download/v1.0.1/gnina
```

```
--2022-03-23 15:10:43--
```

```
https://github.com/gnina/gnina/releases/download/v1.0.1/gnina
```

```
Resolving github.com (github.com)... 140.82.112.3
```

```

Connecting to github.com (github.com)|140.82.112.3|:443... connected.
HTTP request sent, awaiting response... 302 Found
Location: https://objects.githubusercontent.com/github-production-release-asset-2e65be/45548146/47de2300-8bd4-11eb-8355-430c51e07fae?X-Amz-Algorithm=AWS4-HMAC-SHA256&X-Amz-Credential=AKIAIWNJYAX4CSVEH53A%2F20220323%2Fus-east-1%2Fs3%2Faws4_request&X-Amz-Date=20220323T221043Z&X-Amz-Expires=300&X-Amz-Signature=40413772b59d7019375699594a962dea562f2e8b6888399619c3d3d14cf56e00&X-Amz-SignedHeaders=host&actor_id=0&key_id=0&repo_id=45548146&response-content-disposition=attachment%3B%20filename%3Dgnina&response-content-type=application%2Foctet-stream [following]
--2022-03-23 15:10:43-- https://objects.githubusercontent.com/github-production-release-asset-2e65be/45548146/47de2300-8bd4-11eb-8355-430c51e07fae?X-Amz-Algorithm=AWS4-HMAC-SHA256&X-Amz-Credential=AKIAIWNJYAX4CSVEH53A%2F20220323%2Fus-east-1%2Fs3%2Faws4_request&X-Amz-Date=20220323T221043Z&X-Amz-Expires=300&X-Amz-Signature=40413772b59d7019375699594a962dea562f2e8b6888399619c3d3d14cf56e00&X-Amz-SignedHeaders=host&actor_id=0&key_id=0&repo_id=45548146&response-content-disposition=attachment%3B%20filename%3Dgnina&response-content-type=application%2Foctet-stream
Resolving objects.githubusercontent.com (objects.githubusercontent.com)...
185.199.111.133, 185.199.108.133, 185.199.109.133, ...
Connecting to objects.githubusercontent.com
(objects.githubusercontent.com)|185.199.111.133|:443... connected.
HTTP request sent, awaiting response... 200 OK
Length: 562802104 (537M) [application/octet-stream]
Saving to: './tools/gnina.1'

```

```
gnina.1          100%[=====>] 536.73M  7.08MB/s   in 76s
```

```
2022-03-23 15:12:00 (7.07 MB/s) - './tools/gnina.1' saved [562802104/562802104]
```

```
[3]: ! chmod +x ../tools/gnina
```

```
[4]: ! ../tools/gnina --version
```

```
gnina v1.0.1 HEAD:aa41230   Built Mar 23 2021.
```

0.1.2 Extract receptor and ligand atomic coordinates from the X-ray structure PDB ID 6NZP

```
[5]: cd ../pipeline/3_Gnina_docking/
```

```
/home/cv/TECHX/pipeline/3_Gnina_docking
```

```
[6]: ! wget http://files.rcsb.org/download/6NZP.pdb
```

```
6NZP.pdb.1          [  <=>          ] 390.52K   612KB/s    in 0.6s

2022-03-23 15:12:02 (612 KB/s) - '6NZP.pdb.1' saved [399897]
```

```
! awk '$1=="ATOM" && $5=="B"' 6NZP.pdb > rec_tyk2B.pdb
```

```
! awk ' $1=="HETATM" && $4=="LB7" && $5=="B" ' 6NZP.pdb > lig_tyk2B.pdb
```

Note: with receptor and ligand .pdb files converted with AutoDockTools to .pdbqt format for docking

```
[9]: ! ../../tools/gnina -r rec_tyk2B.pdbqt -l lig_tyk2B.pdbqt --autobox_ligand_
    ↪ lig_tyk2B.pdbqt ↵
    -o docked_gnina_lig_tyk2B.sdf --seed 0
```

$$\begin{array}{c} \bar{(_)} \\ / _ \backslash | | _ \backslash / _ \backslash | \\ | (_ | | | | | | | (_ | \\ _ , _ | _ | _ | _ | _ | _ | \\ _ / | \\ | / \end{array}$$

```

Commandline: ../../tools/gnina -r rec_tyk2B.pdbqt -l lig_tyk2B.pdbqt
--autobox_ligand lig_tyk2B.pdbqt -o docked_gnina_lig_tyk2B.sdf --seed 0
Using random seed: 0

```

0% 10 20 30 40 50 60 70 80 90 100%

```
| pose 0 | ligand outside box
| pose 0 | ligand outside box
| pose 0 | ligand outside box
| pose 0 | ligand outside box
| pose 0 | ligand outside box
| pose 0 | initial pose not within box
```

```
[10]: ! obrms -firstonly lig_tyk2B.pdbqt docked_gnina_lig_tyk2B.sdf
```

Binding site defined with `-autobox` ligand option around the ligand surface

[illegible]

gnina v1.0.1 HEAD:aa41230 Built Mar 23 2021.
gnina is based on smina and AutoDock Vina.
Please cite appropriately.

Commandline: ../../tools/gnina -r rec_tyk2B.pdbqt -l dock22.sdf --autobox_ligand
lig_tyk2B.pdbqt -o docked_22.sdf.gz --num_modes 1 --seed 0
Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.75	0.9932	7.073

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

ZINC72454514 | pose 1 | ligand outside box

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-10.15	0.9899	7.377

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

ZINC09224703 | pose 2 | ligand outside box

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-10.96	0.6465	6.937

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
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```

1      -9.61      0.9896      7.118
Using random seed: 0

0%  10  20  30  40  50  60  70  80  90  100%
|----|----|----|----|----|----|----|----|----|
*****

mode | affinity | CNN | CNN
    | (kcal/mol) | pose score | affinity
-----+-----+-----+-----
1      -10.56      0.9889      7.157
Using random seed: 0

0%  10  20  30  40  50  60  70  80  90  100%
|----|----|----|----|----|----|----|----|----|
*****

mode | affinity | CNN | CNN
    | (kcal/mol) | pose score | affinity
-----+-----+-----+-----
1      -9.73      0.9111      7.118
Using random seed: 0

0%  10  20  30  40  50  60  70  80  90  100%
|----|----|----|----|----|----|----|----|----|
*****

mode | affinity | CNN | CNN
    | (kcal/mol) | pose score | affinity
-----+-----+-----+-----
1      -9.66      0.8762      7.066
Using random seed: 0

0%  10  20  30  40  50  60  70  80  90  100%
|----|----|----|----|----|----|----|----|----|
*****
ZINC02638281 | pose 7 | ligand outside box
ZINC02638281 | pose 7 | ligand outside box
ZINC02638281 | pose 7 | ligand outside box

mode | affinity | CNN | CNN
    | (kcal/mol) | pose score | affinity
-----+-----+-----+-----
1      -9.52      0.9644      7.291
Using random seed: 0

0%  10  20  30  40  50  60  70  80  90  100%
|----|----|----|----|----|----|----|----|----|

```

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.59	0.9716	7.089

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

ZINC02472304 | pose 9 | ligand outside box
ZINC02472304 | pose 9 | ligand outside box
ZINC02472304 | pose 9 | ligand outside box
ZINC02472304 | pose 9 | ligand outside box
ZINC02472304 | pose 9 | ligand outside box
ZINC02472304 | pose 9 | initial pose not within box
ZINC02472304 | pose 9 | ligand outside box

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.50	0.9126	7.358

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

ZINC02472318 | pose 10 | ligand outside box
ZINC02472318 | pose 10 | ligand outside box
ZINC02472318 | pose 10 | ligand outside box
ZINC02472318 | pose 10 | ligand outside box
ZINC02472318 | pose 10 | ligand outside box
ZINC02472318 | pose 10 | initial pose not within box
ZINC02472318 | pose 10 | ligand outside box
ZINC02472318 | pose 10 | ligand outside box

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.39	0.8882	7.141

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity	CNN	CNN
------	----------	-----	-----

	(kcal/mol)	pose score	affinity
1	-9.34	0.9790	7.353

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-8.74	0.9718	6.735

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.34	0.9749	7.106

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

ZINC20939765 | pose 14 | initial pose not within box

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.54	0.9741	7.370

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.55	0.9846	7.566

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-8.97	0.6628	7.359

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-8.99	0.8915	7.184

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

ZINC09728763 | pose 18 | ligand outside box
ZINC09728763 | pose 18 | ligand outside box
ZINC09728763 | pose 18 | ligand outside box
ZINC09728763 | pose 18 | ligand outside box
ZINC09728763 | pose 18 | ligand outside box
ZINC09728763 | pose 18 | initial pose not within box

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-7.96	0.8993	7.245

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

ZINC13131298 | pose 19 | ligand outside box
ZINC13131298 | pose 19 | ligand outside box
ZINC13131298 | pose 19 | ligand outside box
ZINC13131298 | pose 19 | ligand outside box
ZINC13131298 | pose 19 | ligand outside box
ZINC13131298 | pose 19 | initial pose not within box

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.07	0.9230	7.247

Using random seed: 0

```
0%  10  20  30  40  50  60  70  80  90 100%
|----|----|----|----|----|----|----|----|----|
*****
```

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.02	0.9611	7.008

Using random seed: 0

```
0%  10  20  30  40  50  60  70  80  90 100%
|----|----|----|----|----|----|----|----|----|
*****
```

ZINC06901595 | pose 21 | ligand outside box

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.39	0.9347	7.119

Using random seed: 0

```
0%  10  20  30  40  50  60  70  80  90 100%
|----|----|----|----|----|----|----|----|----|
*****
```

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-10.33	0.9980	7.853

0.1.5 Blind Docking with Gnina on selected compounds

Binding site defined with `--autobox_ligand` option around the entire receptor surface

```
[12]: ! ../../tools/gnina -r rec_tyk2B.pdbqt -l dock22.sdf --autobox_ligand rec_tyk2B.
      ↪pdbqt -o docked_22_blind.sdf.gz --num_modes 1 --seed 0
```

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  _/ |
 | _/
```

gnina v1.0.1 HEAD:aa41230 Built Mar 23 2021.
 gnina is based on smina and AutoDock Vina.
 Please cite appropriately.

Commandline: ../../tools/gnina -r rec_tyk2B.pdbqt -l dock22.sdf --autobox_ligand
 rec_tyk2B.pdbqt -o docked_22_blind.sdf.gz --num_modes 1 --seed 0

=====

*** Open Babel Warning in PerceiveBondOrders

Failed to kekulize aromatic bonds in OBMol::PerceiveBondOrders

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%

|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.91	0.9924	7.036

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%

|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-10.04	0.9882	7.343

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%

|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-8.13	0.7042	6.860

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%

|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
------	------------------------	-------------------	-----------------

```

-----+-----+-----+-----
      1      -5.63      0.6010      5.002
Using random seed: 0

0%   10   20   30   40   50   60   70   80   90  100%
|----|----|----|----|----|----|----|----|----|
*****

mode |  affinity  |    CNN    |    CNN
      | (kcal/mol) | pose score | affinity
-----+-----+-----+-----
      1      -10.57      0.9888      7.165
Using random seed: 0

0%   10   20   30   40   50   60   70   80   90  100%
|----|----|----|----|----|----|----|----|----|
*****

mode |  affinity  |    CNN    |    CNN
      | (kcal/mol) | pose score | affinity
-----+-----+-----+-----
      1      -6.33      0.6914      5.055
Using random seed: 0

0%   10   20   30   40   50   60   70   80   90  100%
|----|----|----|----|----|----|----|----|----|
*****

mode |  affinity  |    CNN    |    CNN
      | (kcal/mol) | pose score | affinity
-----+-----+-----+-----
      1      -10.23      0.8146      6.942
Using random seed: 0

0%   10   20   30   40   50   60   70   80   90  100%
|----|----|----|----|----|----|----|----|----|
*****

mode |  affinity  |    CNN    |    CNN
      | (kcal/mol) | pose score | affinity
-----+-----+-----+-----
      1      -9.74      0.9628      7.370
Using random seed: 0

0%   10   20   30   40   50   60   70   80   90  100%
|----|----|----|----|----|----|----|----|----|
*****

```

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.60	0.9685	7.082

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.90	0.8494	7.042

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-10.03	0.8722	7.037

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.36	0.9801	7.348

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.06	0.9680	6.919

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.30	0.9750	7.082

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-6.32	0.4769	5.136

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-8.99	0.4465	6.857

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-7.52	0.7271	6.651

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
|----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-6.97	0.4843	5.607

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-5.91	0.3935	5.918

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-7.97	0.7516	6.952

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-8.39	0.7197	6.574

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-9.44	0.9178	7.078

Using random seed: 0

0% 10 20 30 40 50 60 70 80 90 100%
 |----|----|----|----|----|----|----|----|----|----|

mode	affinity (kcal/mol)	CNN pose score	CNN affinity
1	-10.28	0.9978	7.875

[]: