Manual of Unicon3D

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1. **Github access:** https://github.com/multicom-toolbox/UniCon3D

2. **Files and Directories (All under root):**

    1. examples/: contains the test files to run Unicon3D
    2. scripts/: contains the scripts for preparing the input files of Unicon3D, please type **python2 <script name>.py -h** to see the parameters
    3. lib/: contains the trained model
    4. src/: contains the source codes of Unicon3D project
    5. bin/: contains binaries for linux and osx
    6. test/: contains test fasta sequence that used in this manual
    7. README: the installation and usage manual
    8. Manual.pdf: The detailed guide of how to run the Unicon3D

3. **Run Unicon3D:**

    Follow the below steps:

    Step 1: Go through the README file.

    Step 2: Run the following commands to execute the program with example data:

    ```
    > cd examples/
    >../bin/linux/UniCon3D -i test -f test.fa -s test.ss -c test.cm -m
    ../lib/UniCon.iohmm -d 10
    ```

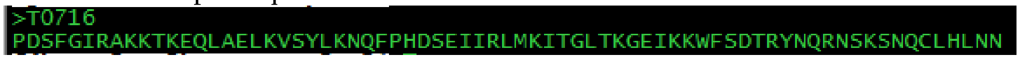
    Note: 10 decoys are generated in the examples folder starting from test_000001.pdb to test_000010.pdb and test_stats.txt contains the folding statistics.

    Step 3 (optional): Use a test protein of your choice. Get the fasta file, secondary structure and contact matrix. Then run the UniCon3D program with it to sample decoys.

4. **Required inputs for Unicon3D**

    1) Fasta sequence

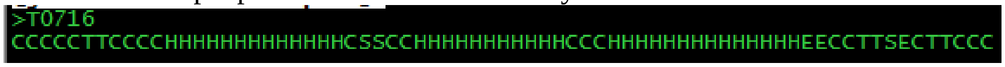
    Unicon3D accepts sequence file with FASTA format as follows:



```
>T0716
PDSFGIRAKKTKEQLAELKVSYLKNQFPHDSEIIRLMKITGLTKGEIKKWFSDTRYNQRNSKSNQCLHLNN
```

    2) Predicted secondary structure

    Unicon3D accepts predicted 8-class secondary structure as follows:



```
>T0716
CCCCCTTCCCCHHHHHHHHHHHHHCSSCCHHHHHHHHHHHCCCHHHHHHHHHHHHHHEECCTTSECTTCCC
```

    Please refer to Section 5 (1) to learn how to generate 8-class secondary structure.

3) Predicted contact map

Unicon3D accepts predicted contact map matrix, which will be used as part of energy score function. We provide different functions for users to handle typical three situations:

a) No residue-contact information:

If users don’t have contact information, we provide one script to help user generate fake contact map, in which all confidence are 0.

```
> cd scripts
> python2 init_cm.py -h
> python2 init_cm.py  --fasta ../test/T0700.fasta  >
../test/T0700.cm.init
```

b) Residue-contact without confidence probability (2-column)

If users only have a list of residue-residue contact without any confidence weight, we provide one script to generate contact map matrix, where the confidence is set to 1

```
> cd scripts
> python2 rr2cm.py -h
> python2 rr2cm.py --fasta ../test/T0700.fasta  --rr
../test/T0700.rr_2col --format 2 > ../test/T0700.cm.2col
```

c) Residue-contact with confidence probability (3-column)

If users have list of residue-residue contact with confidence level (3-column format, for example, DNcon results), we provide one script to generate contact map matrix, where the confidence is set to weight in the third column.

```
> cd scripts
> python2 rr2cm.py -h
> python2 rr2cm.py --fasta ../test/T0700.fasta  --rr
../test/T0700.DNcon_3col  --format 3 > ../test/T0700.cm.3col
```

d) Residue-contact with confidence probability (CASP format, 5-column)

If users have list of residue-residue contact with confidence level (5-column format,http://predictioncenter.org/casproll/index.cgi?page=format), we provide one script to generate contact map matrix, where the confidence is set to weight in the third column.

```
> cd scripts
> python2 rr2cm.py -h
> python2 rr2cm.py --fasta ../test/T0700.fasta  --rr
../test/T0700.DNcon_5col  --format 5 > ../test/T0700.cm.5col
```

5. Recommended tools:

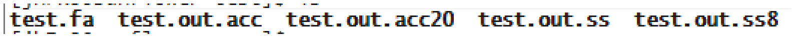
1) Secondary structure prediction:

Unicon3D project originally applied SSpro5 in the package 'SCRATCH-1D release 1.1' to predict the secondary structure, which can be downloaded from http://download.igb.uci.edu/, and it is easy to install and use.
Please try following steps after you have 'SCRATCH-1D release 1.1' installed.

a. > cd UniCon3D/test/

b. > <SCRATCH-1D_1.1 path>/bin/run_SCRATCH-1D_predictors.sh test.fa test.out 1

c. The expected output should be as follows:



```
test.fa  test.out.acc  test.out.acc20  test.out.ss  test.out.ss8
```

Note: Unicon3D project used 8-class secondary structure information in the training models. So please use file 'test.out.ss8' as secondary structure input for Unicon3D

2) **Contact map prediction**:

Unicon3D project originally applied in-house contact prediction pipeline tools to get contact map prediction which haven't released to community at this moment. Users can use any residue-residue contact prediction tool (ex. DNcon) to get the predicted residue contacts and convert the residue contact predictions to contact map matrix. Or users can also applied contact map prediction tool (ex.NNcon) directly to get the predicted contact map.

- Here we gave an example to show how to use '**NNcon**' to generate contact map prediction:

  a. Download 'NNcon1.0' from MULTICOM-Toolbox (http://sysbio.rnet.missouri.edu/multicom_toolbox/tools.html)

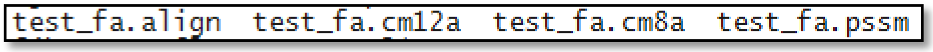
  b. Follow the installation manual to install the tool

  c. > cd UniCon3D/test/

  d. > mkdir ConMap/

  e. > perl <nncon1.0 path>/bin/predict_ss_sa_cm.sh test.fa ConMap/

  f. The expected output should be as follows:



```
test_fa.align  test_fa.cm12a  test_fa.cm8a  test_fa.pssm
```

You can choose either 'test_fa.cm8a' or 'test_fa.cm12a' as contact map input for Unicon3D

Note: When use 'NNcon' results, please remove the top 4 lines which contains sequence information and secondary structure/solvent accessibility information, only keep the contact matrix

g. **Run Unicon3D**:

```
>../bin/linux/UniCon3D -i test -f test.fa -s test.out.ss8  -c ConMap/test_fa.cm8a -m ../lib/UniCon.iohmm -d 10
```

Note: 10 decoys are generated in the examples folder starting from test_000001.pdb to test_000010.pdb and test_stats.txt contains the folding statistics.

- Here we gave an example to show how to use ‘**DNcon**’ to generate contact residue-residue prediction and convert it to contact map prediction:

  a. Download ‘DNcon1.0’ from MULTICOM-Toolbox (http://sysbio.rnet.missouri.edu/multicom_toolbox/tools.html)

  b. Follow the installation manual to install the tool

  c.
  ```
  > cd UniCon3D/test/
  ```

  d.
  ```
  > mkdir ConRes/
  ```

  e.
  ```
  > perl <dncon1.0 path>/run_dncon.pl <dncon1.0 path>/local_submit_job.cgi  <UniCon3D path>/test/FASTA/ <UniCon3D path>/test/ConRes/  'l' CPU
  ```

  f. The expected output ‘test.DNcon’ should be generated

  Note: It is better to format residue-residue contact to CASP format with 5 column, please refer to (http://predictioncenter.org/casproll/index.cgi?page=format)

  g. Generate contact map prediction:
  ```
  > python2 ../scripts/rr2cm.py --fasta test.fa --rr  ConRes/test.DNcon –format 3 > ConRes/test.DNcon.cm
  ```

  h. **Run Unicon3D**:
  ```
  > ../bin/linux/UniCon3D -i test -f test.fa -s test.out.ss8  -c ConRes/test.DNcon.casp.cm -m ../lib/UniCon.iohmm -d 10
  ```

  Note: 10 decoys are generated in the examples folder starting from test_000001.pdb to test_000010.pdb and test_stats.txt contains the folding statistics.

3) **(Option) All-atom model generation**: PULCHRA software can be used to generate all-atom model from UniCon3D models.

  a. Download ‘PULCHRA’ from http://www.pirx.com/pulchra/index.shtml

  b. Follow the installation manual to install the tool

  c.
  ```
  > cd UniCon3D/test/
  ```

  d.
  ```
  > <pulchra path>/pulchra  -g -v  test_000010.pdb
  ```

  e. The full-atom model ‘test_000010.pdb.rebuilt.pdb’ will be generated

6. Built-in Functions

We wrote several simple program to call the tools to generate inputs for users to run Unicon3D smoothly. All the scripts can be copied and modified to users’ preference.

```
> cd <UniCon3D path>/test
```

1) **Get secondary structure prediction**:

```
> python2 ../scripts/Getsecondary.py --fasta <UniCon3D path>/test/test.fa  --id test
```

Note:

a. Please change the ‘**SCRATCH_1D**’ installation path to yours in script ‘scripts/Getsecondary.py’.

b. Please give the full path of fasta file

c. The predicted secondary structures are inside folder ‘**secondary/**’

2) Get contact map prediction from NNcon:

```
> python2 ../scripts/GetNNcon.py --fasta <UniCon3D path>/test/test.fa
```

Note:

a. Please change the '**NNcon**' installation path to yours in script 'scripts/GetNNcon.py'.

b. Please give the full path of fasta file

c. The predicted contact map files are inside folder '**NNcon_contact/test_fa.cm8a**'

3) Get contact map prediction from DNcon:

```
> python2 ../scripts/GetDNcon.py --fasta <UniCon3D path>/test/test.fa    --range
'l' --device CPU
```

Note:

a. Please change the '**NNcon**' installation path to yours in script 'scripts/GetNNcon.py'.

b. Please give the full path of fasta file

c. The predicted contact files are inside folder '**DNcon_contact/output/test.DNcon**'

d. Convert DNcon results to CASP format:

```
> perl ../scripts/dncon2casp.pl DNcon_contact/output/test.DNcon
DNcon_contact/output/test.DNcon.casp
```

e. Generate contact map prediction:

```
> python2 ../scripts/rr2cm.py --fasta test.fa --rr
DNcon_contact/output/test.DNcon.casp >
DNcon_contact/output/test.DNcon.casp.cm
```

4) Run Unicon3D on NNcon contact map and secondary structure

```
>  ../bin/linux/UniCon3D -i test -f test.fa -s secondary/test.ss8  -c
NNcon_contact/test_fa.cm8a -m ../lib/UniCon.iohmm -d 10
```

Note: 10 decoys are generated in the examples folder starting from test_000001.pdb to test_000010.pdb and test_stats.txt contains the folding statistics.

5) Run Unicon3D on DNcon contact map and secondary structure

```
>  ../bin/linux/UniCon3D -i test -f test.fa -s secondary/test.ss8  -c
DNcon_contact/output/test.DNcon.casp.cm -m ../lib/UniCon.iohmm -d 10
```

Note: 10 decoys are generated in the examples folder starting from test_000001.pdb to test_000010.pdb and test_stats.txt contains the folding statistics.