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Support Vector Machine on Graph Kernels for Protein-Protein Docking Scoring

The software supports the publication of the following articles:


iScore uses a support vector machine (SVM) approach to rank protein-protein interfaces. Each interface is represented by a connection graph in which each node represents a contact residue and each edge the connection between two contact residues of different protein chain. As feature, the node contains the Position Specific Similarity Matrix (PSSM) of the corresponding residue.

To measure the similarity between two graphs, iScore use a random walk graph kernel (RWGK) approach. These RWGKs are then used as input of the SVM model to either train the model on a training set or use a pretrained model to rank new protein-protein interface.
Installation

2.1 Install via pip

In most cases you can use pip to install iScore. Simply use:

```
pip install iScore
```

2.2 Install from source

If the pip install fails or if you want to modify the code you can install iScore manually. The code is hosted on Github (https://github.com/DeepRank/iScore)

To install the code

- `git clone https://github.com/DeepRank/iScore.git`
- `cd iScore`
- `pip install -e ./`

To test the module go to the test folder `cd ./test` and execute the following test:

```
pytest
```
One of the main features of the software are the serial and MPI binaries that fully automatize the workflow and that can be used directly from the command line. To illustrate the use of these binaries go to the folder iScore/example/training_set/. This folder contains the subfolders pdb/ and pssm/ that contain the PDB and PSSM files of our training set. The binary class corresponding to these PDBs are specified in the file ‘caseID.lst’.

Training a model using iScore can be done in a single line using MPI binaries with the command:

$ mpiexec -n 2 iScore.train.mpi

This command will first generate the graphs of the conformations stored in pdb/ using the PSSM contained in pssm/ as features. These graphs will be stored as pickle file in graph/. The command will then compute the pairwise kernels of these graphs and store the kernel files in kernel/. Finally it will train a SVM model using the kernel files and the caseID.lst file that contains the binary class of the model.

The calculated graphs and the svm model are stored in a single tar file called here training_set.tar.gz. This file contains all the information needed to predict binary classes of a test set using the trained model.

To predict binary classes (and decision values) of new conformations go to the subfolder test/. Here 5 conformations are specified by the PDB and PSSM files stored in pdb/ and pssm/ that we want to use as a test set. Ranking these conformations can be done in a single command using:

$ mpiexec -n 2 iScore.predict.mpi --archive ../training_set.tar.gz

This command will first compute the graph of the conformation in the test set and store them in graph/. The binary will then compute the pair wise kernels of each graph in the test set with all the graph contained in the training set that are stored in the tar file. These kernels will be stored in kernel/. Finally the binary will use the trained SVM model contained in the tar file to predict the binary class and decision value of the conformations in the test set. The results are then stored in a text file and a pickle file iScorePredict.pkl and iScorePredict.txt. Opening the text file you will see:
<table>
<thead>
<tr>
<th>Name</th>
<th>label</th>
<th>pred</th>
<th>decision_value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1ACB_2w</td>
<td>None</td>
<td>0</td>
<td>-0.994</td>
</tr>
<tr>
<td>1ACB_3w</td>
<td>None</td>
<td>0</td>
<td>-0.994</td>
</tr>
<tr>
<td>1ACB_4w</td>
<td>None</td>
<td>0</td>
<td>-0.994</td>
</tr>
<tr>
<td>1ACB_5w</td>
<td>None</td>
<td>0</td>
<td>-0.994</td>
</tr>
</tbody>
</table>

The ground truth label are here all None because they were not provided in the test set. This can simply be done by adding a caseID.lst in the test/ subfolder.

### 3.1 Serial Binaries

Serial binaries are also provided and can be used in a similar way than the MPI binaries: iscore.train and iscore.predict
CHAPTER 4

Computing PSSM files

As a preprocessing step one must compute the PSSM files corresponding to the PDB files in the training/testing dataset. This can be achieved with the PisBLast library (https://ncbiinsights.ncbi.nlm.nih.gov/2017/10/27/blast-2-7-1-now-available/). The library BioPython allows easy use of these libraries.

iScore contains wrapper that allows to compute the PSSM data, map them to the PDB files and format them for further processing. The only input needed is the PDB file of the decoy. To compute the PSSM file one can simply use:

```python
>>> from iscore.pssm.pssm import PSSM

>>> gen = PSSM('1AK4')

>>> # generates the FASTA query
>>> gen.get_fasta()

>>> # configure the generator
>>> gen.configure(blast=<path to blast binary>, database=<path to the blast db>)

>>> # generates the PSSM
>>> gen.get_pssm()

>>> # map the pssm to the pdb
>>> gen.map_pssm()
```
5.1 Generating the Graphs:

The first step in iSCore is to generate the connections graph of the interface. In this graph each node is represented by the PSSM of a residue. The nodes are connected if they form a contact pair between the two proteins.

To create the graph one needs the PDB file of the interface and the two PSSM files (one for each chain) created by the PSSMGen tool. To generate the graph simply use:

```python
>>> from iScore.graph import GenGraph, Graph

>>> pdb = name.pdb
>>> pssm = {'A':'name.A.pdb.pssm','B':'name.B.pdb.pssm'}

>>> g = GenGraph(pdb,pssm)
>>> g.construct_graph()
>>> g.export_graph('name.pkl')
```

This simple example will construct the connection graph and export it in a pickle file. A working example can be found in `example/graph/create_graph.py`.

The function `iscore_graph()` facilitate the generation of a large number of conformations. By default this function will create the graphs of all the conformations stored in the subfolder ./pdb/ using the pssm files stored in the subfolder ./pssm/. The resulting graphs will be stored in the subfolder ./graph/.

5.2 Generating the Graph Kernels:

Once we have calculated the graphs of multiple conformation we can simply compute the kernel of the different pairs using iScore. An example can be found at `example/kernel/create_kernel.py`

```python
>>> from iScore.graph import Graph, iscore_graph
>>> from iScore.kernel import Kernel
```

(continues on next page)
The kernel between the two graphs computed above is calculated with the class `Kernel()`. By default the method `Kernel.import_from_mat()` will read all the graphs stored in the subfolder `graph/`. To compute all the pairwise kernels of the graphs loaded above we can simply use the method `Kernel.run()`. We can here specify the value of lambda and the length of the walk.
Visualizing the connection graphs

iSore allows to easily visualize the connection graphs using the HDF5 browser provided with the software and pymol. First the connections graphs must be stored in a HDF5 file. To do that simply generate the graphs as following:

```python
>>> from iScore.graphrank.graph import iscore_graph
>>> iscore_graph(pdb_path=<pdb_path>,
>>>             pssm_path=<pssm_path>,
>>>             export_hdf5=True)
```

where you have to specify the folder containing the PDB files abd PSSM files in pdb_path and pssm_path. By default this are simply ./pdb/ and ./pssm/. The script above will create a HDF5 file containing the graph.

This HDF5 file can be explored using the the dedicated HDF5 browser. Go to the ./h5x/ folder and type:

```
./h5x.py
```

This will open the hdf5 browser. You can open a hdf5 file by clicking on the file icon in the bottom left of the browser. Once opened, you will see the content of the file in the browser. Right-click on the name of a conformation and choose 3D Plot. This will open PyMol and allow you to visualize the connecton graph.
All the prototypes of the class/methods are here specified

7.1 Graph

7.2 Kernel

7.3 SVM
CHAPTER 8

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