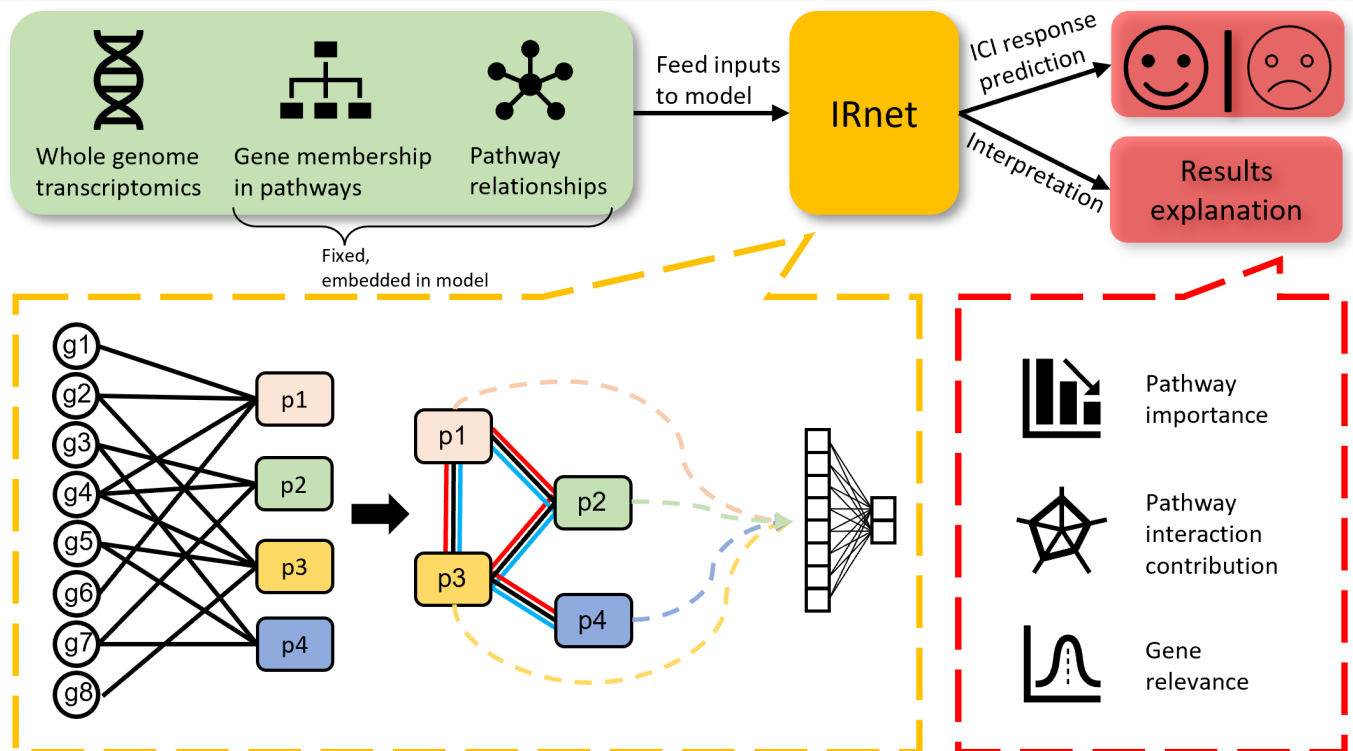


IRnet

Immunotherapy response prediction using pathway knowledge-informed graph neural network

Overview

Immunotherapy, specifically, immune checkpoint inhibitors (ICIs) are powerful and precise therapies for many cancer types and have improved the survival of patients who positively respond to them. However, only a minority of patients respond to ICI treatments. Thus, determining ICI responders before treatment would dramatically save medical resources and save time for alternative therapies. Here, we present a novel deep-learning framework that leverages graph neural network and biological pathway knowledge to predict ICI treatment response. The results indicate that the prediction performance is superior to other state-of-the-art methods or tumor microenvironment-based predictions. Moreover, the model quantifies the importance of pathways, pathway interactions, and genes to the prediction. Such interpretability of IRnet provides mechanism insights intoof different ICI treatments.



Installation

- Anaconda3 required (tested on version 4.12.0)
- Download and unzip this GitHub repo.
- Create and activate the conda environment for IRnet

```
$ conda env create -f IRnet_env.yaml
$ conda activate IRnet_env
```

Usage

Run IRnet through command line:

```
usage: predict.py [-h] -input INPUTFILE -output OUTPUTDIR -treatment DRUG

IRnet: Immunotherapy response prediction using pathway knowledge-informed
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optional arguments:
  -h, --help            show this help message and exit
  -input INPUTFILE      Gene expression matrix with values separated by Tab.
Rows
                        are named with gene symbols. Columns are named with
                        patient IDs. (default: None)
  -output OUTPUTDIR     The name of the output directory. (default: None)
  -treatment DRUG       Specify the immunotherapy treatment target, either
"anti-
                        PD1", "anti-PDL1", or "anti-CTLA4" (default: None)
```

Example

The file `example_expression.txt` contains the gene counts separated by tabs. Rows are named with gene symbols. Columns are named with patient IDs. User provided gene expression input should follow this format, the order of genes doesn't matter. To obtain the anti-PD1 immunotherapy response prediction for this dataset, you can run following code on your terminal:

```
$ python ./predict.py -input ./example_expression.txt -output
./prediction_results/ -treatment anti-PD1
```

The output file `prediction_results.txt` will be created under the fold `./prediction_results/`. It has three columns: Patient ID, Predicted score, and Predicted Immune Checkpoint Inhibitors (ICI) response.

Patient ID	Predicted score	Predicted ICI response
Patient107	0.3977815508842468	False
Patient163	0.31186426132917405	False
Patient96	0.4907291173934937	False
Patient83	0.5010034710168838	True
Patient121	0.6585307002067566	True
Patient48	0.3147367350757122	False
Patient94	0.6644996523857116	True
Patient117	0.539155526459217	True

Citation

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