stagewiseNN

Release 0.1

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Jul 26, 2021

CONTENTS

stagewiseNN is a computational tool for constructing developmental tree from Multi-staged single-cell RNA-seq data.

Install from source code:

```
git clone https://github.com/XingyanLiu/stagewiseNN.git
cd stagewiseNN
python setup.py install
```

It is easy to use:

```
import swnn

# ====== Inputs ======
# data_matrix = ..
# stage_labels = ..
# group_labels = ..
# stage_order = [f'stage_{i}' for i in range(5)]

builder = swnn.Builder(stage_order=stage_order)
# step1:
# building (stage-wise) single-cell graph
distmat, connect = builder.build_graph(
        X=data_matrix, stage_lbs=stage_labels,
    )
# step2:
# build developmental tree from single-cell graph
builder.build_tree(group_labels, stage_labels,)
```

CHAPTER

ONE

CONTRIBUTE

- Issue Tracker: https://github.com/XingyanLiu/stagewiseNN/issues
- Source Code: https://github.com/XingyanLiu/stagewiseNN

CHAPTER

TWO

SUPPORT

If you are having issues, please let us know. We have a mailing list located at:

- xingyan@amss.ac.cn
- 544568643@qq.com

2.1 Installation

2.1.1 PyPI

Install stagewiseNN with PyPI, run:

```
pip install stagewisenn
```

2.1.2 GitHub

Or fetch from GitHub and manually install:

```
git clone https://github.com/XingyanLiu/stagewiseNN.git
cd stagewiseNN
python setup.py
```

END

2.2 Tutorials

To be completed!

see *Tutorial for using stagewiseNN*

2.2.1 Tutorial for using stagewiseNN

TODO: Add some descriptions

```
import os
import sys
from pathlib import Path
from typing import Sequence, Mapping, Optional, Union, Callable
import logging
import pandas as pd
import numpy as np
import scanpy as sc

ROOT = Path('../')
sys.path.append(str(ROOT))

import swnn
from swnn.utils.process import describe_dataframe, set_adata_hvgs, change_names

DATADIR = ROOT / 'sample_data'
```

```
def get_adata(datadir=DATADIR, ):
    path = datadir / 'merged_B-L0-0.2.h5ad'
    adata = sc.read_h5ad(path)
    return adata


def get_high_freq_hvgs(min_freq=3, datadir=DATADIR):
    hvg_freq = pd.read_csv(
        datadir / 'hvg_frequencies.csv', index_col=0, header=None)
    hvg_freq = hvg_freq.iloc[:, 0]
    return hvg_freq[hvg_freq >= min_freq].index.tolist()


def formulate_adata(adata, save_path=None):
    adata.obs.columns = change_names(
        adata.obs.columns, stage='stage_id', )
    adata.obs['lineage'] = change_names(
        adata.obs['lineage'],
        {'Tail bud stem cells': 'Unassigned'}
    )
    adata.obs['stage_primer'] = adata.obs[['stage_name', 'primer']].apply(
        lambda x: '_'.join(x), axis=1
    )
    adata.obs['stagewise_cluster'] = adata.obs[['stage_name', 'leiden_new']].apply(
        lambda x: '_'.join(x), axis=1
    )
    adata.obs['stagewise_cluster'] = change_names(
        adata.obs['stagewise_cluster'],
        {'B_1': 'B_0', 'B_2': 'B_1', 'B_3': 'B_2'}
    )

    if save_path is not None:
```

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```
        adata.write(save_path)
    return adata


def _inspect_data(log_file=None):
    adata = get_adata()
    adata = formulate_adata(adata)
    print(adata, file=log_file)
    describe_dataframe(adata.obs, file=log_file)
    # TODO: additional markers of prior knowledge
    hvgs = get_high_freq_hvgs()
    print('Total of %d HVGs are used.', len(hvgs), file=log_file)
```

```
resdir = ROOT / '_temp'
swnn.check_dirs(resdir)

adata0 = get_adata()
adata0 = formulate_adata(adata0)
# TODO: additional markers of prior knowledge
hvgs = get_high_freq_hvgs()
adata = swnn.quick_preprocess_raw(
    adata0, hvgs=hvgs, copy=True, batch_key='stage_primer')

X = adata.X
stage_lbs = adata.obs['stage_name']
stage_order = ("B", "G3", "G4", "G5", "G6", "N0", "N1", "N3", "L0")
ks = [10] * 7 + [5] + [3]
n_pcs = [30] * 5 + [50] * 4
```

```
already exists:
    ../_temp
```

```
distmat, connect = swnn.stagewise_knn(
    X, stage_lbs, stage_order,
    k=ks,
    leaf_size=1, # 1 for brute-force KNN
    pca_base_on='stacked',
    n_pcs=n_pcs,
    binary_edge=False,
    )
connect_bin = swnn.make_binary(connect)
swnn.set_precomputed_neighbors(adata, distmat, connect_bin, )
```

```
AnnData object with n_obs × n_vars = 29775 × 3569
    obs: 'stage_id', 'primer', 'n_genes', 'n_counts', 'stage_primer', 'stg_leiden',
↪'stage_stg_leiden', 'refined_group', 'leiden_new', 'parent_bcd', 'lineage', 'stage_name
↪', 'stagewise_cluster'
    var: 'highly_variable'
    uns: 'log1p', 'neighbors'
    obsp: 'distances', 'connectivities'
```

```
# sc.tl.umap(adata, min_dist=0.1)
# sc.settings.figdir = resdir
# sc.set_figure_params(fontsize=14)
#
# lin_colors = pd.read_csv(
#     'sample_data/lineage_colors.csv', index_col=0).iloc[:, 0]
# adata.obs['lineage'] = pd.Categorical(
#     adata.obs['lineage'], categories=lin_colors.index)
# adata.uns['lineage_colors'] = lin_colors.tolist()
# sc.pl.umap(adata, color='lineage', ncols=1, save='_lineage.pdf')
# sc.pl.umap(adata, color='stage_name', palette='plasma_r', save='_stage.pdf')
```

```
from scipy import sparse
obs = adata.obs
group_lbs = obs['stagewise_cluster'].values
stage_lbs = obs['stage_name'].values
KEY_TREE_NODE = 'tree_node'

# graph to tree
conn_upper = sparse.triu(connect).tocsc()
adj_max = swnn.max_connection(conn_upper)
edgedf, new_group_lbs = swnn.adaptive_tree(
    adj_max, group_lbs, stage_lbs=stage_lbs, stage_ord=stage_order)

obs[KEY_TREE_NODE] = new_group_lbs
edgedf.prop.hist() # voting proportions
logging.info("edgedf = %s", edgedf)

df_tree = edgedf[['node', 'parent']].copy()
df_tree['label'] = df_tree['node'].copy()
df_tree['stage'] = df_tree['node'].apply(lambda x: x.split('_')[0])
groupby = KEY_TREE_NODE
props_all = swnn.group_mean_adata(adata, groupby, use_raw=True, binary=True)
means_all = swnn.group_mean_adata(adata, groupby, use_raw=True, )
```

```
connecting stage B and G3
---> aggregating edges...
unique labels of rows: ['B_1' 'B_0' 'B_2']
unique labels of columns: ['G3_1' 'G3_0' 'G3_3' 'G3_4' 'G3_2' 'G3_5']
grouping elements (edges)
shape of the one-hot-labels: (1596, 3) (1826, 6)
parent nodes that had no descendent: ['B_2']
Taking descendant-points from other nodes (groups)
pasting stage labels
---> aggregating edges...
unique labels of rows: ['B_1' 'B_0' 'B_2']
unique labels of columns: ['G3_1' 'G3_0' 'G3_3' 'G3_4' 'G3_2' 'G3_5' 'G3_6']
grouping elements (edges)
shape of the one-hot-labels: (1596, 3) (1826, 7)

connecting stage G3 and G4
---> aggregating edges...
```

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```
unique labels of rows: ['G3_0', 'G3_1', 'G3_2', 'G3_3', 'G3_4', 'G3_5', 'G3_6']
unique labels of columns: ['G4_0' 'G4_4' 'G4_2' 'G4_3' 'G4_1']
grouping elements (edges)
shape of the one-hot-labels: (1826, 7) (1477, 5)
parent nodes that had no descendent: ['G3_3', 'G3_6']
Taking descendant-points from other nodes (groups)
pasting stage labels
---> aggregating edges...
unique labels of rows: ['G3_0', 'G3_1', 'G3_2', 'G3_3', 'G3_4', 'G3_5', 'G3_6']
unique labels of columns: ['G4_0' 'G4_4' 'G4_2' 'G4_3' 'G4_5' 'G4_1' 'G4_6']
grouping elements (edges)
shape of the one-hot-labels: (1826, 7) (1477, 7)

connecting stage G4 and G5
---> aggregating edges...
unique labels of rows: ['G4_0', 'G4_1', 'G4_2', 'G4_3', 'G4_4', 'G4_5', 'G4_6']
unique labels of columns: ['G5_2' 'G5_0' 'G5_3' 'G5_1' 'G5_5' 'G5_8' 'G5_6' 'G5_4' 'G5_7
↪']
grouping elements (edges)
shape of the one-hot-labels: (1477, 7) (4098, 9)
parent nodes that had no descendent: ['G4_5', 'G4_6']
Taking descendant-points from other nodes (groups)
pasting stage labels
---> aggregating edges...
unique labels of rows: ['G4_0', 'G4_1', 'G4_2', 'G4_3', 'G4_4', 'G4_5', 'G4_6']
unique labels of columns: ['G5_2' 'G5_0' 'G5_3' 'G5_1' 'G5_5' 'G5_8' 'G5_6' 'G5_4' 'G5_7
↪' 'G5_9'
 'G5_10']
grouping elements (edges)
shape of the one-hot-labels: (1477, 7) (4098, 11)

connecting stage G5 and G6
---> aggregating edges...
unique labels of rows: ['G5_0', 'G5_1', 'G5_2', 'G5_3', 'G5_4', 'G5_5', 'G5_6', 'G5_7',
↪'G5_8', 'G5_9', 'G5_10']
unique labels of columns: ['G6_1' 'G6_0' 'G6_3' 'G6_4' 'G6_8' 'G6_7' 'G6_5' 'G6_6' 'G6_2
↪']
grouping elements (edges)
shape of the one-hot-labels: (4098, 11) (4775, 9)
parent nodes that had no descendent: ['G5_8', 'G5_9', 'G5_10']
Taking descendant-points from other nodes (groups)
pasting stage labels
---> aggregating edges...
unique labels of rows: ['G5_0', 'G5_1', 'G5_2', 'G5_3', 'G5_4', 'G5_5', 'G5_6', 'G5_7',
↪'G5_8', 'G5_9', 'G5_10']
unique labels of columns: ['G6_1' 'G6_0' 'G6_3' 'G6_4' 'G6_8' 'G6_7' 'G6_5' 'G6_6' 'G6_2
↪' 'G6_10'
 'G6_9']
grouping elements (edges)
shape of the one-hot-labels: (4098, 11) (4775, 11)

connecting stage G6 and N0
```

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```
---> aggregating edges...
unique labels of rows: ['G6_0', 'G6_1', 'G6_2', 'G6_3', 'G6_4', 'G6_5', 'G6_6', 'G6_7',
↪'G6_8', 'G6_9', 'G6_10']
unique labels of columns: ['N0_6' 'N0_2' 'N0_8' 'N0_5' 'N0_4' 'N0_3' 'N0_1' 'N0_0' 'N0_9
↪' 'N0_7']
grouping elements (edges)
shape of the one-hot-labels: (4775, 11) (4992, 10)
parent nodes that had no descendent: ['G6_9', 'G6_10']
Taking descendant-points from other nodes (groups)
pasting stage labels
---> aggregating edges...
unique labels of rows: ['G6_0', 'G6_1', 'G6_2', 'G6_3', 'G6_4', 'G6_5', 'G6_6', 'G6_7',
↪'G6_8', 'G6_9', 'G6_10']
unique labels of columns: ['N0_6' 'N0_2' 'N0_8' 'N0_5' 'N0_4' 'N0_3' 'N0_1' 'N0_0' 'N0_9
↪' 'N0_7'
 'N0_11']
grouping elements (edges)
shape of the one-hot-labels: (4775, 11) (4992, 11)

connecting stage N0 and N1
---> aggregating edges...
unique labels of rows: ['N0_0', 'N0_1', 'N0_2', 'N0_3', 'N0_4', 'N0_5', 'N0_6', 'N0_7',
↪'N0_8', 'N0_9', 'N0_11']
unique labels of columns: ['N1_4' 'N1_3' 'N1_2' 'N1_0' 'N1_7' 'N1_6' 'N1_5' 'N1_8' 'N1_1
↪' 'N1_9']
grouping elements (edges)
shape of the one-hot-labels: (4992, 11) (4399, 10)
parent nodes that had no descendent: ['N0_11']
Taking descendant-points from other nodes (groups)
pasting stage labels
---> aggregating edges...
unique labels of rows: ['N0_0', 'N0_1', 'N0_2', 'N0_3', 'N0_4', 'N0_5', 'N0_6', 'N0_7',
↪'N0_8', 'N0_9', 'N0_11']
unique labels of columns: ['N1_4' 'N1_3' 'N1_2' 'N1_0' 'N1_7' 'N1_6' 'N1_5' 'N1_8' 'N1_1
↪' 'N1_9'
 'N1_10']
grouping elements (edges)
shape of the one-hot-labels: (4992, 11) (4399, 11)

connecting stage N1 and N3
---> aggregating edges...
unique labels of rows: ['N1_0', 'N1_1', 'N1_2', 'N1_3', 'N1_4', 'N1_5', 'N1_6', 'N1_7',
↪'N1_8', 'N1_9', 'N1_10']
unique labels of columns: ['N3_0' 'N3_6' 'N3_2' 'N3_8' 'N3_4' 'N3_10' 'N3_9' 'N3_1' 'N3_
↪13' 'N3_3'
 'N3_7' 'N3_5' 'N3_11' 'N3_12']
grouping elements (edges)
shape of the one-hot-labels: (4399, 11) (4448, 14)
parent nodes that had no descendent: ['N1_3', 'N1_9', 'N1_10']
Taking descendant-points from other nodes (groups)
pasting stage labels
---> aggregating edges...
```

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```
unique labels of rows: ['N1_0', 'N1_1', 'N1_2', 'N1_3', 'N1_4', 'N1_5', 'N1_6', 'N1_7',
↪'N1_8', 'N1_9', 'N1_10']
unique labels of columns: ['N3_0' 'N3_6' 'N3_2' 'N3_8' 'N3_4' 'N3_10' 'N3_9' 'N3_1' 'N3_
↪13' 'N3_3'
 'N3_7' 'N3_5' 'N3_11' 'N3_12' 'N3_15' 'N3_14']
grouping elements (edges)
shape of the one-hot-labels: (4399, 11) (4448, 16)

connecting stage N3 and L0
---> aggregating edges...
unique labels of rows: ['N3_0', 'N3_1', 'N3_2', 'N3_3', 'N3_4', 'N3_5', 'N3_6', 'N3_7',
↪'N3_8', 'N3_9', 'N3_10', 'N3_11', 'N3_12', 'N3_13', 'N3_14', 'N3_15']
unique labels of columns: ['L0_4' 'L0_1' 'L0_0' 'L0_14' 'L0_6' 'L0_7' 'L0_12' 'L0_10'
↪'L0_11' 'L0_5'
 'L0_8' 'L0_2' 'L0_9' 'L0_16' 'L0_3' 'L0_15' 'L0_13']
grouping elements (edges)
shape of the one-hot-labels: (4448, 16) (2164, 17)
parent nodes that had no descendent: ['N3_5', 'N3_9', 'N3_11', 'N3_14', 'N3_15']
Taking descendant-points from other nodes (groups)
pasting stage labels
---> aggregating edges...
unique labels of rows: ['N3_0', 'N3_1', 'N3_2', 'N3_3', 'N3_4', 'N3_5', 'N3_6', 'N3_7',
↪'N3_8', 'N3_9', 'N3_10', 'N3_11', 'N3_12', 'N3_13', 'N3_14', 'N3_15']
unique labels of columns: ['L0_4' 'L0_1' 'L0_0' 'L0_14' 'L0_6' 'L0_7' 'L0_12' 'L0_10'
↪'L0_11' 'L0_5'
 'L0_8' 'L0_2' 'L0_9' 'L0_16' 'L0_3' 'L0_15' 'L0_19' 'L0_13' 'L0_17'
 'L0_20' 'L0_18' 'L0_21']
grouping elements (edges)
shape of the one-hot-labels: (4448, 16) (2164, 22)

Binarized...the results will be the expression proportions.
Calculating feature averages for 99 groups
['B_0' 'B_1' 'B_2' 'G3_0' 'G3_1' 'G3_2' 'G3_3' 'G3_4' 'G3_5' 'G3_6' 'G4_0'
 'G4_1' 'G4_2' 'G4_3' 'G4_4' 'G4_5' 'G4_6' 'G5_0' 'G5_1' 'G5_10' 'G5_2'
 'G5_3' 'G5_4' 'G5_5' 'G5_6' 'G5_7' 'G5_8' 'G5_9' 'G6_0' 'G6_1' 'G6_10'
 'G6_2' 'G6_3' 'G6_4' 'G6_5' 'G6_6' 'G6_7' 'G6_8' 'G6_9' 'L0_0' 'L0_1'
 'L0_10' 'L0_11' 'L0_12' 'L0_13' 'L0_14' 'L0_15' 'L0_16' 'L0_17' 'L0_18'
 'L0_19' 'L0_2' 'L0_20' 'L0_21' 'L0_3' 'L0_4' 'L0_5' 'L0_6' 'L0_7' 'L0_8'
 'L0_9' 'N0_0' 'N0_1' 'N0_11' 'N0_2' 'N0_3' 'N0_4' 'N0_5' 'N0_6' 'N0_7'
 'N0_8' 'N0_9' 'N1_0' 'N1_1' 'N1_10' 'N1_2' 'N1_3' 'N1_4' 'N1_5' 'N1_6'
 'N1_7' 'N1_8' 'N1_9' 'N3_0' 'N3_1' 'N3_10' 'N3_11' 'N3_12' 'N3_13'
 'N3_14' 'N3_15' 'N3_2' 'N3_3' 'N3_4' 'N3_5' 'N3_6' 'N3_7' 'N3_8' 'N3_9']
Calculating feature averages for 99 groups
['B_0' 'B_1' 'B_2' 'G3_0' 'G3_1' 'G3_2' 'G3_3' 'G3_4' 'G3_5' 'G3_6' 'G4_0'
 'G4_1' 'G4_2' 'G4_3' 'G4_4' 'G4_5' 'G4_6' 'G5_0' 'G5_1' 'G5_10' 'G5_2'
 'G5_3' 'G5_4' 'G5_5' 'G5_6' 'G5_7' 'G5_8' 'G5_9' 'G6_0' 'G6_1' 'G6_10'
 'G6_2' 'G6_3' 'G6_4' 'G6_5' 'G6_6' 'G6_7' 'G6_8' 'G6_9' 'L0_0' 'L0_1'
 'L0_10' 'L0_11' 'L0_12' 'L0_13' 'L0_14' 'L0_15' 'L0_16' 'L0_17' 'L0_18'
 'L0_19' 'L0_2' 'L0_20' 'L0_21' 'L0_3' 'L0_4' 'L0_5' 'L0_6' 'L0_7' 'L0_8'
 'L0_9' 'N0_0' 'N0_1' 'N0_11' 'N0_2' 'N0_3' 'N0_4' 'N0_5' 'N0_6' 'N0_7'
 'N0_8' 'N0_9' 'N1_0' 'N1_1' 'N1_10' 'N1_2' 'N1_3' 'N1_4' 'N1_5' 'N1_6'
 'N1_7' 'N1_8' 'N1_9' 'N3_0' 'N3_1' 'N3_10' 'N3_11' 'N3_12' 'N3_13'
```

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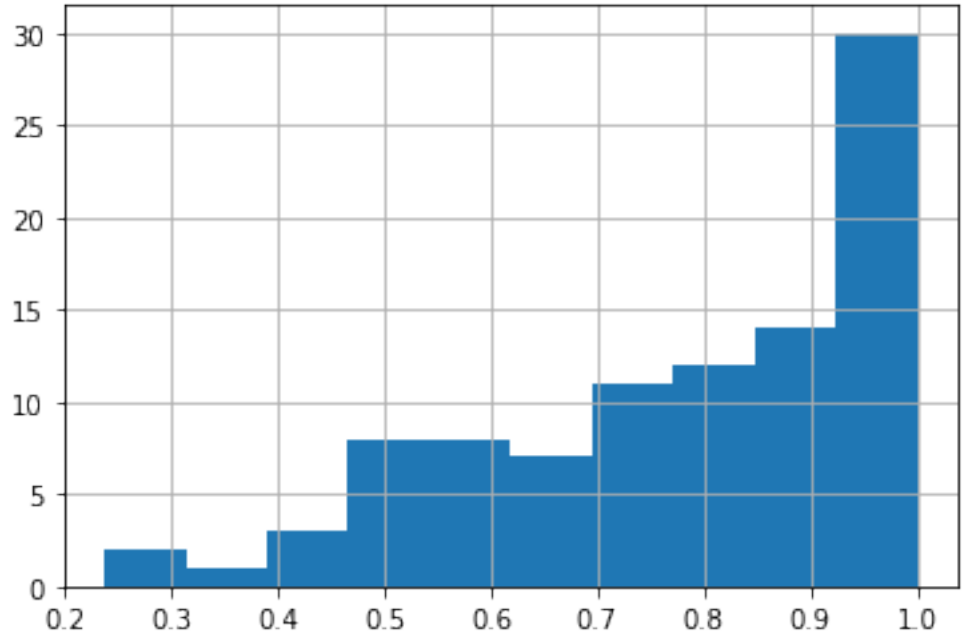
```
 'N3_14' 'N3_15' 'N3_2' 'N3_3' 'N3_4' 'N3_5' 'N3_6' 'N3_7' 'N3_8' 'N3_9']
```




```
# props_all.to_csv(resdir / f'expr_prop_all.csv', index=True, header=True)
# means_all.to_csv(resdir / f'avg_expr_all.csv', index=True, header=True)
```

2.3 API

Import stagewiseNN as:

```
import swnn
```

2.3.1 Object for Management

See apidoc/swnn.builder for detailed information.

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2.3.2 Data Processing

—

2.3.3 Make Graph

—

2.3.4 Others

—

2.4 Citation

Please cite XXX

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THREE

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