# **SpaOTsc**

Release 0.2

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**CHAPTER** 

ONE

### SPAOTSC API REFERENCE

## 1.1 The SpaOTsc module

```
spaotsc.SpaoTsc.choose\_landmarks(pts, n, dmat=None, method='maxmin', assignment='nearest') \\
```

Choose a set of landmark points from a set of points.

[1] De Silva, Vin, and Gunnar E. Carlsson. "Topological estimation using witness complexes." SPBG 4 (2004): 157-166.

#### **Parameters**

- pts (class:numpy.ndarray) coordinates of points (n\_points, nD) needed if dmat not given
- **n** (*int*) number of landmark points to select
- dmat (class:numpy.ndarray) the distance matrix for the points (n\_points, n\_points)

**Returns** the indices of selected points and an assignment matrix to assign original points to landmark points (n\_landmarks, n\_points)

**Return type** class:numpy.ndarray

```
\verb|spaotsc.SpaOTsc.compute_mcc|| \textit{true\_labels}, \textit{pred\_labels})|
```

Compute matthew's correlation coefficient.

#### **Parameters**

- true\_labels (class:numpy.ndarray) 1D integer array
- pred\_labels (class:numpy.ndarray) 1D integer array

Returns mcc

Return type float

```
spaotsc.SpaOTsc.knn\_graph(D, k)
```

Construct a k-nearest-neighbor graph as igraph object.

#### **Parameters**

- D (class:numpy.ndarray) a distance matrix for constructing the knn graph
- **k** (*int*) number of nearest neighbors

Returns a knn graph object

**Return type** class:*igraph.Graph* 

```
spaotsc.SpaOTsc.knn\_graph\_nx(D, k)
```

Construct a k-nearest-neighbor graph as networkx object.

#### **Parameters**

- D (class:numpy.ndarray) a distance matrix for constructing the knn graph
- **k** (*int*) number of nearest neighbors

**Returns** a knn graph object and a list of edges

**Return type** class: networkx. Graph, list of tuples

```
spaotsc.SpaOTsc.phi_exp (x, eta, nu, p)
```

The exponential weight kernel. Computes  $\exp(-(x/eta)^{n}(p*nu))$ .

#### **Parameters**

- **x** (float or class:*numpy.ndarray*) the input value
- eta (float) the cutoff for this soft thresholding kernel
- **nu** (*int*) a possitive integer for the power term, a bigger nu gives sharper threshold boundary
- **p** (*int*) p=1: emphasize elements lower than cutoff; p=-1: emphasize elements higher than cutoff

**Returns** the kernel output with same shape of x

Return type same as x

```
spaotsc.SpaOTsc.sci(x, y, W, scale=False)
```

Computes the spatial correlation index in Eq. (9) of [1].

[1] Chen, Yanguang. "A new methodology of spatial cross-correlation analysis." PloS one 10.5 (2015): e0126158.

#### **Parameters**

- **x** (class:*numpy.ndarray*) the variable's values at the spatial locations
- y (class:numpy.ndarray) the other variable's values at the spatial locations
- W (class: numpy.ndarray) weight matrix (symmetric) among the locations with W[i,i] = 0
- scale (boolean) whether to scale the inputs s.t. (1) sum\_{i,j}W\_{ij} = 1 and (2) x = (x-mu(x))/sigma(x)

Returns a global spatial cross correlation index

#### Return type float

```
class spaotsc.SpaOTsc.spatial_sc(sc_data=None, is_data=None, sc_data_bin=None, is_data_bin=None, is_pos=None, is_dmat=None, sc_dmat=None)
```

An object for connecting and analysis of spatial data and single-cell transcriptomics data.

A minimal example usage: Assume we have (1) a pandas DataFrame for single-cell data df\_sc with rows being cells and columns being genes (2) a numpy array for distance matrix among spatial locations is\_dmat (3) a numpy array for dissimilarity between single-cell data and spatial data cost\_matrix (4) a numpy array for dissimilarity matrix within single-cell data sc\_dmat

#### **Parameters**

- sc\_data (class:pandas.DataFrame) single-cell data of size (n\_cells, n\_genes)
- is\_data (class:pandas.DataFrame) spatial data of size (n\_locations, n\_genes)
- sc\_data\_bin (class:pandas.DataFrame) binarized single-cell data
- is\_data\_bin (class:pandas.DataFrame) binarized spatial data
- is\_pos (class:numpy.ndarray) coordinates of spatial locations (n\_locations, n dimensions)
- **is\_dmat** (class:*numpy.ndarray*) distance matrix for spatial locations (n\_locations, n\_locations)
- **sc\_dmat** (class:*numpy.ndarray*) dissimilarity matrix for single-cell data (n\_cells, n\_cells)

#### List of instance attributes:

#### **Variables**

- **sc\_data** (class:pandas.DataFrame) single-cell data of size (n\_cells, n\_genes) \_\_init\_\_
- is\_data (class:pandas.DataFrame) spatial data of size (n\_locations, n\_genes) \_\_init\_\_
- sc\_data\_bin (class:pandas.DataFrame) binarized single-cell data \_\_\_init\_\_\_
- is\_data\_bin (class:pandas.DataFrame) binarized spatial data \_\_init\_\_
- **is\_pos** (class:*numpy.ndarray*) coordinates of spatial locations (n\_locations, n\_dimensions) \_\_init\_\_
- **is\_dmat** (class:*numpy.ndarray*) distance matrix for spatial locations (n\_locations, n\_locations) \_\_init\_\_
- **sc\_dmat** (class:*numpy.ndarray*) dissimilarity matrix for single-cell data (n\_cells, n\_cells) \_\_init\_\_
- gamma\_mapping (class:numpy.ndarray) the mapping matrix between single-cell data and spatial data (n\_cells, n\_locations) transport\_plan
- sc\_dmat\_spatial (class:numpy.ndarray) the spatial cell-cell distance for single-cell data (n cells, n cells) cell cell distance
- clustering\_ncluster\_org (int) number of clusters in original clustering of single-cell data clustering
- clustering\_nsubcluster (list of int) number of cell spatial subclusters within each original cluster clustering
- clustering\_partition\_org (list of numpy integer arrays) the cell indices for each original cluster clustering

- **clustering\_partition\_inds** (*dictionary*) the cell indices for the cell spatial subclusters, e.g. the key (0,1) returns the cell indices for the second spatial subcluster within the first original cell cluster. clustering
- **gene\_cor\_scc** (class:*pandas.DataFrame*) the intracellular spearmanr correlation between genes nonspatial\_correlation
- **gene\_cor\_is** (class: pandas. DataFrame) the intercellular spatial correlation between genes spatial\_correlation
- **g\_bin\_edges** (dictionary) the bin edges for the discretization of gene expressions with gene name string as dictionary key discretize\_expression

cell\_cell\_distance (epsilon=0.01, rho=inf, scaling=True, sc\_dmat\_spatial=None, use\_landmark=False, n\_landmark=100)

Compute spatial distance between single cells using optimal transport.

Generates: self.sc\_dmat\_spatial: (n\_cell, n\_cell) numpy.ndarray

Requires: self.gamma\_mapping, self.is\_dmat

#### **Parameters**

- epsilon (float, defaults to 0.01) weight for entropy regularization term
- **rho** (float, defaults to inf) weight for KL divergence penalizing unbalanced transport
- scaling (boolean, defaults to True) whether to scale the cost\_matrix (is\_dmat) to avoid numerical overflow
- sc\_dmat\_spatial (class:numpy.ndarray, optional) the spatial distance matrix for single cells (n\_cells, n\_cells). If given, simply set the distance matrix without computing.
- use\_landmark (boolean, defaults to False) whether to use landmark points for computing transport distance.
- n\_landmark (int, defaults to 100) number of landmark points to use if use\_landmark

**Returns** (spatial) cell-cell distance matrix (n\_cells, n\_cells)

**Return type** class:numpy.ndarray

**clustering** (*genes=None*, *pca\_n\_components=None*, *res\_sc=0.5*, *res\_is=0.3*, *min\_n=3*) Clustering and spatial subclustering.

#### Generates:

*self.clustering\_nsubcluster*: list of int, numbers of subclusters in each cluster obtained in regular clustering of single-cell data

self.clustering\_partition\_inds: list of cell index arrays for clusters

*self.clustering\_partition\_org*: a dictionary for cell index arrays of spatial subclusters. The key (1,0) gives the first subcluster for the second cluster.

#### Requires:

self.sc\_dmat\_spatial, self.sc\_data

#### **Parameters**

• **genes** (list) – genes to use when clustering single-cell data. All genes in self.sc\_data are used if not specified.

- pca\_n\_components (int) number of pca components when clustering single-cell data
- res\_sc (float, defaults to 0.5) resolution parameter in louvain clustering for single-cell data
- **res\_is** (*float*, *defaults* to 0.3) resolution parameter in louvain clustering for spatial subclustering of single-cel data
- min\_n (int, defaults to 3) minimum number of members to be considered a cluster

#### discretize\_expression(genes=None, p0=1e-15)

Discretize gene expression using Bayesian blocks.

Generate: self.g\_bin\_edges: a dictionary of block edges with gene names as keys

Requires: self.sc\_data

**Parameters p0** (*float*, *defaults to 1E-15*) – the p0 score in Bayesian blocks. A smaller p0 has lower tolerance of false rate, i.e. resulting in fewer blocks.

gene\_clustering (gene\_dmat, res=3, k=5, rng\_seed=48823)

Cluster the genes based on their spatial pattern difference.

#### **Parameters**

- **gene\_dmat** (class:numpy.ndarray) the distance matrix for genes (n\_gene, n\_gene)
- **res** (*float*, *defaults* to 3) resolution parameter used by louvain clustering, higher res gives more clusters
- **k** (int, defaults to 5) the k for knn graph fed to louvain algorithm
- rng\_seed (int) random seed for louvain algorithm to get consistent results

**Returns** a list of index vectors for the clusters

Return type list of list of int

Compute Wasserstein distance between gene expressions in scRNA-seq data.

#### **Parameters**

- **genes** (list of str) the gene names to compute distance
- epsilon (float, defaults to 0.01) weight for entropy regularization term
- **rho** (float, defaults to inf) weight for KL divergence penalizing unbalanced transport
- scaling (boolean, defaults to True) whether to scale the cost matrix
- **sc\_dmat\_spatial** (class:*numpy.ndarray*) spatial distance matrix over the single cells
- use\_landmark (boolean, defaults to False) whether to use landmark points to accelarate computation
- n\_landmark (int, defaults to 100) number of landmark genes to use

**Returns** gene-gene distance matrix

Return type class:numpy.ndarray

Deriving scores for intercellular gene regulation (how much effect does gene\_1 in neiborhood have on gene\_2) using random forest.

Requires: self.sc\_dmat\_spatial, self.sc\_data, self.gene\_cor\_scc

#### **Parameters**

- gene\_1 (str) the name of source gene whose expression in the neighborhood will be examined
- gene\_2 (str) the name of target gene whose cellular expression will be used
- background\_genes (list of str) a name list for gene that are correlated to gene\_2
- **cor\_cut** (*float*) the cut\_off choosing background genes. used when background\_genes is not specified
- n\_top\_g (int) the number of genes with highest correlation to gene\_2 to be used as background\_genes. used when both background\_genes and cor\_cut are not specified
- effect\_ranges (list of float) list of spatial distances to consider
- **method** (str, defaults to 'Importance') 'Importance': interpret the feature importance as regulation strength; 'Prediction': interpret prediction accuracy in cross-validation as regulation strength.

**Returns** a (n\_distance, 2) array with the first row recording the spatial distances examined and the second row being the effect strength

**Return type** class:numpy.ndarray

 $\begin{tabular}{ll} \begin{tabular}{ll} \beg$ 

The unique information provided by G1\_nb (within various ranges) to G2 considering background genes Gi

Requires: self.sc\_dmat\_spatial, self.sc\_data, self.gene\_cor\_scc

- gene\_1 (str) the name of source gene whose expression in the neighborhood will be examined
- gene\_2 (str) the name of target gene whose cellular expression will be used
- background\_genes (list of str) a name list for gene that are correlated to gene 2
- **cor\_cut** (*float*) the cut\_off choosing background genes. used when background\_genes is not specified
- n\_top\_g (int) the number of genes with highest correlation to gene\_2 to be used as background\_genes. used when both background\_genes and cor\_cut are not specified
- effect\_ranges (list of float) list of spatial distances to consider
- **p0** (*float*, *defaults* to 1E-15) the p0 score in Bayesian blocks. A smaller p0 has lower tolerance of false rate, i.e. resulting in fewer blocks.
- output\_individual (boolean, defaults to False) where to output the information computed with each background gene

**Returns** a (n\_distance, 2) array with the first row recording the spatial distances examined and the second row being the effect strength

Return type class:numpy.ndarray

Determine spatial distance for given signaling using random forest.

Requires: self.sc\_dmat\_spatial, self.sc\_data, self.gene\_cor\_scc

#### **Parameters**

- Lgenes (list of str) name list of ligand genes
- Rgenes (list of str) name list of receptor genes
- **Dgenes** (list of str) name list of downstream genes
- n\_top\_g (int, defaults to 50) number of background genes to use when building predictive model.
- effect\_ranges (list of float) the spatial distances to examine
- method (str, defaults to 'Importance') the way of interpreting likelihood for each spatial distance
- **custom\_dmat** (class:numpy.ndarray) a cell-cell distance matrix given by user. self.sc\_dmat\_spatial is used if not given.

**Returns** (n\_distance, 2) array for spatial distances (first row) and effect strengths (second row); and a (n\_distance, n\_DSgenes) array for the effect strength of each downstream genes.

**Return type** two class:*numpy.ndarray* 

#### nonspatial\_correlation(genes=None)

Compute gene-gene correlation matrix for pre-screening of genes.

Generates: *self.gene\_cor\_scc* 

Requires: self.sc\_data', self.sc\_genes

**Parameters genes** (list of str) – list of gene names. If not specified, all genes in self.sc data are used.

rank\_marker\_genes (cid, genes=None, method='ranksum', return\_scores=False)

Rank genes to identify markers for cell clusters.

#### **Parameters**

- cid (class:numpy.1darray) cell indices for the cluster
- **genes** (list) candidate genes to examine. If not specified, all genes are used.
- method(str, defaults to 'ranksum') method to use. 1. 'roc', using auc-roc score to rank; 2. 'ranksum', using ranksum statistics.
- return\_scores (boolean, defaults to False) whether to return scores instead of sorted gene indices

**Returns** sorted gene indices (if return\_scores==False) or gene scores (if return\_scores==True)

**Return type** class:*numpy*.*1darray* 

**spatial\_correlation** (*genes=None*, *effect\_range=None*, *kernel='lorentz'*, *kernel\_nu=10*) Computes spatial correlation between genes for pre-screening.

Generates: self.gene\_cor\_is pandas DataFrame

Requires: self.sc\_data

#### **Parameters**

- genes (list of str) list of gene to examine
- effect\_range (float) spatial distance
- **kernel** (str, defaults to 'lorentz') type of kernels for weight matrix
- kernel\_nu (int, defaults to 10) power for weight kernel

Generate the spatial map for intercellular gene-gene regulatory information flow.

Requires: self.sc\_data, self.sc\_dmat\_spatial, self.gene\_cor\_scc, self.gene\_cor\_is

#### **Parameters**

- genes (list of str) name list of genes to be examined
- effect\_range (float) spatial distance for analyzing the intercellular processes
- **cor\_cut** (*float*) the cutoff for spatial correlation between two genes for further examination (used if n\_top\_edge not specified)
- n\_top\_edge (int) the number of gene pairs to examine with highest spatial correlation
- **cor\_cut\_bg** (float) the cutoff for intracellular gene correlation to select background genes
- n\_top\_g\_bg (int) the number of genes with highest intracellular gene correlation with the target gene to use as background genes (used if cor\_cut\_bg not specified)
- p0 (float, defaults to 1E-15) the p0 value for Bayesian blocks (lower p0 gives fewer number of bins)
- output\_individual (boolean, defaults to False) whether to output the individual values computed with each background gene

**Returns** a data frame with rows being source genes and columns being target genes

Return type class:pandas.DataFrame

```
\begin{tabular}{ll} {\bf signaling\_ot} (Lgenes, & Rgenes, & Tgenes=[], & Rbgenes=[], & DSgenes\_up=[], \\ & DSgenes\_down=[], & gene\_bandwidth=\{\}, & effect\_range=None, \\ & rho=10.0, & epsilon=0.2, & kernel\_nu=5, & use\_kernel\_ligand=False, \\ & use\_kernel\_receptor=False, & return\_weight\_only=False) \end{tabular}
```

Generate cell-cell signaling using optimal transport for a list of ligands and a list of receptors.

Requires: self.sc\_dmat\_spatial, self.sc\_data

- **Lgenes** name list of the ligand gene
- Rgenes (list of str) name list of receptor genes
- Tgenes (list of str, optional) name list of genes for transporters of ligands
- **Rbgenes** (*list of str*, *optional*) name list of genes for proteins bound to receptor for the receptor to work
- DSgenes\_up (list of str) name list of up regulated genes by the ligand-receptor

- DSgenes\_down (list of str) name list of down regulated genes by the ligandreceptor
- gene\_bandwidth (dictionary (str to scalar), all outputs default to 1)—the cutoffs for each gene to be considered expressed
- effect\_range (float) spatial distance cutoff for the signaling
- epsilon (float, defaults to 0.2) weight for entropy regularization term
- **rho** (float, defaults to inf) weight for KL divergence penalizing unbalanced transport
- **kernel\_nu** (*float*, *defaults* to 5) the power parameter for the exponential kernel, bigger nu means sharper soft cutoff
- use\_kernel\_ligand (boolean, defaults to False) whether use kernel function to rescale ligand expression
- use\_kernel\_receptor (boolean, defaults to False) whether use kernel function to rescale receptor expression
- return\_weight\_only (boolean, defaults to False) whether to only return the weight for source distribution and destination distribution

**Returns** a scoring matrix for the given signaling genes (cells, cells), (i,j) entry is the score for cell i sending signals to cell j

**Return type** class:numpy.ndarray

Generate cell-cell signaling using optimal transport for a single ligand.

Requires: self.sc\_dmat\_spatial, self.sc\_data

#### **Parameters**

- Lgene (str) name of the ligand gene
- Rgene (list of str) name list of receptor genes
- Tgenes (list of str, optional) name list of genes for transporters of ligands
- **Rbgene** (list of str, optional) name list of genes for proteins bound to receptor for the receptor to work
- DSgenes\_up (list of str) name list of up regulated genes by the ligand-receptor
- DSgenes\_down (list of str) name list of down regulated genes by the ligand-receptor
- effect\_range (float) spatial distance cutoff for the signaling
- epsilon (float, defaults to 0.2) weight for entropy regularization term
- **rho** (float, defaults to inf) weight for KL divergence penalizing unbalanced transport

**Returns** a scoring matrix for the given signaling genes (cells, cells), (i,j) entry is the score for cell i sending signals to cell j

**Return type** class:numpy.ndarray

Generate cell-cell signaling using predefined scoring function.

Requires: self.sc\_dmat\_spatial, self.sc\_data

#### **Parameters**

- Lgene (str) name of the ligand gene
- Rgene (list of str) name list of receptor genes
- **Rbgene** (list of str, optional) name list of genes for proteins bound to receptor for the receptor to work
- **Tgenes** (list of str, optional) name list of genes for transporters of ligands
- DSgenes\_up (list of str) name list of up regulated genes by the ligand-receptor
- DSgenes\_down (list of str) name list of down regulated genes by the ligand-receptor
- effect\_range (float) spatial distance cutoff for the signaling
- **kernel** (str, defaults to 'exp') weight kernel to use for soft thresholding
- **kernel\_nu** (*float*, *defaults* to 5) power for weight kernel, a higher power gives a shaper edge
- gene\_eta (list of float, defaults to 1s) a list of threshold values for the downstream genes
- **penalty\_type** (str, defaults to 'addition') how to penalize inconsistency of downstream genes. 'addition': relaxed penalty; 'multiplication': strict penalty

**Returns** a scoring matrix for the given signaling genes (cells, cells), (i,j) entry is the score for cell i sending signals to cell j

Return type class:numpy.ndarray

transport\_plan (cost\_matrix, cor\_matrix=None, alpha=0.1, epsilon=1.0, rho=100.0, G\_sc=None, G\_is=None, scaling=False)

Mapping between single cells and spatial data as transport plan.

Generates: self.gamma\_mapping: (n\_cells, n\_locations) numpy.ndarray

- **cost\_matrix** (class:*numpy.ndarray*) dissimilarity matrix between single-cell data and spatial data (cells, locations)
- cor\_matrix (class:numpy.ndarray, optional) similarity matrix between single-cell data and spatial data (cells, locations)
- alpha (float, [0,1], defaults to 0.1) weight for structured part (Gromov-Wassertein loss term)
- epsilon (float, defaults to 1.0) weight for entropy regularization term
- **rho** (float, defaults to 100.0) weight for KL divergence penalizing unbalanced transport
- G\_sc (class:numpy.ndarray) dissimilarity matrix within single-cell data (cells, cells)
- G\_is (class:numpy.ndarray) distance matrix within spatial data (locations, locations)

• scaling (boolean, defaults to False) - whether scale the cost\_matrix to have max=1

**Returns** a mapping between single-cell data and spatial data (cells, locations)

Return type class:numpy.ndarray

**Parameters type** (*int*) – the type of visualization type=1 dimension reduction with spatial distance, label with original clusters; type=2 dimension reduction with scRNAseq, label with spatial subclusters; type=3 dimension reduction with spatial distance, label with spatial subclusters; type=4 dimension reduction with scRNAseq, label with original clusters.

Visualize subclusters as a summary and distributions over the original geometry (2D).

- pts (class:numpy.ndarray) the coordinates of original geometry (n\_locations, 2)
- **k** (*int*) the number nearest neighbors to connect in the subcluster summary plot
- vmin (float) the vmin for colormap of the edges in the summary plot
- vmax (float) the vmax for colormap of the edges in the summary plot
- $umap_k(int)$  the n\_neighbors parameter in umap dimension reduction

### **CHAPTER**

# TWO

# **INDICES AND TABLES**

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