# SCALEX

*Release 1.0.2*

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**Sep 12, 2023**

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**Contributors**

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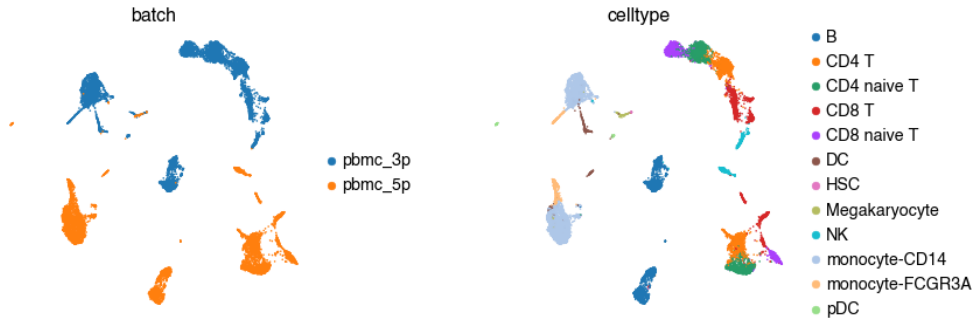
CHAPTER

# ONE

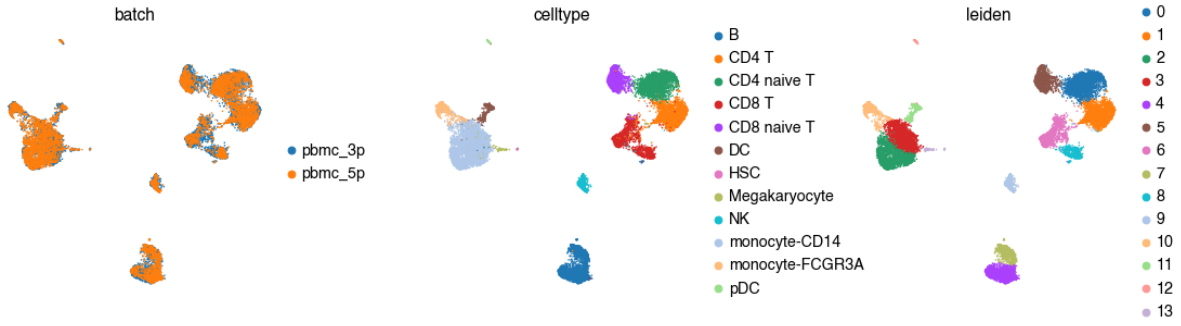
# TUTORIAL

## 1.1 Integration

before integration




after SCALEX integration

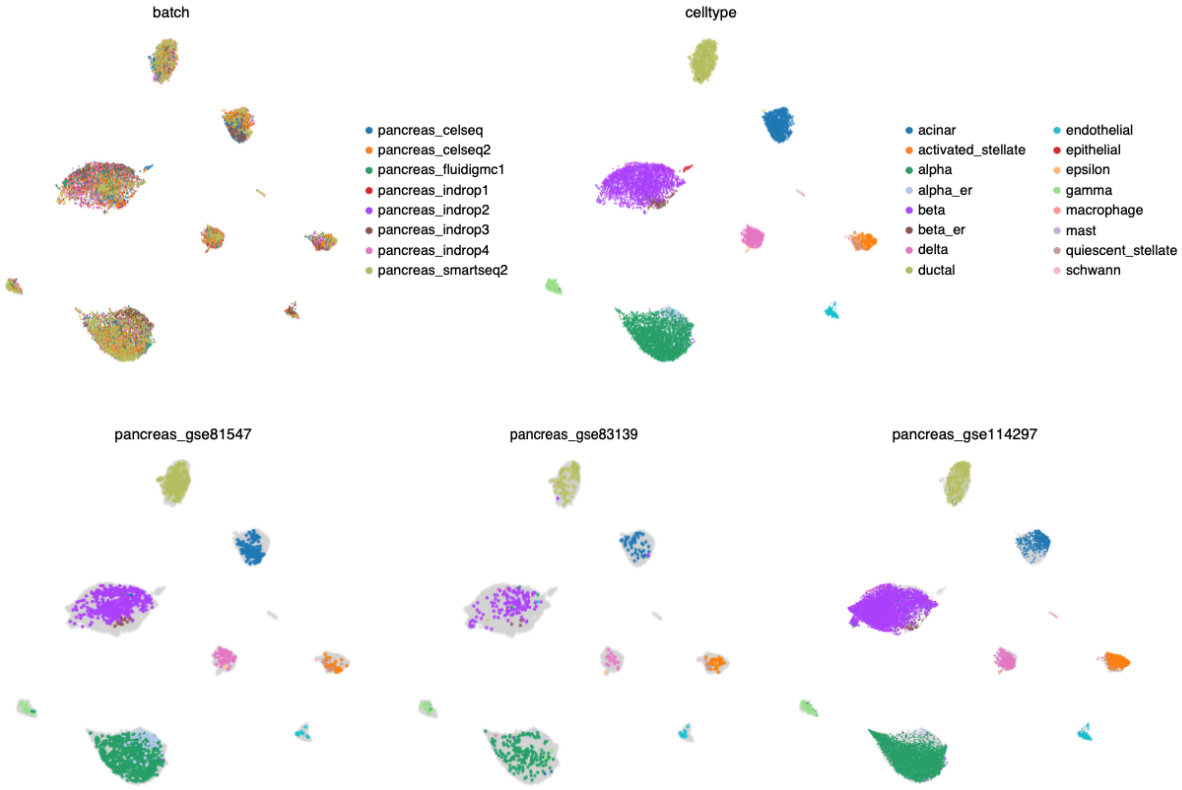



## 1.2 Projection

Map new data to the embeddings of reference

A pancreas reference was created by integrating eight batches.

Here, map pancreas_gse81547, pancreas_gse83139 and pancreas_gse114297 to the embeddings of pancreas reference.

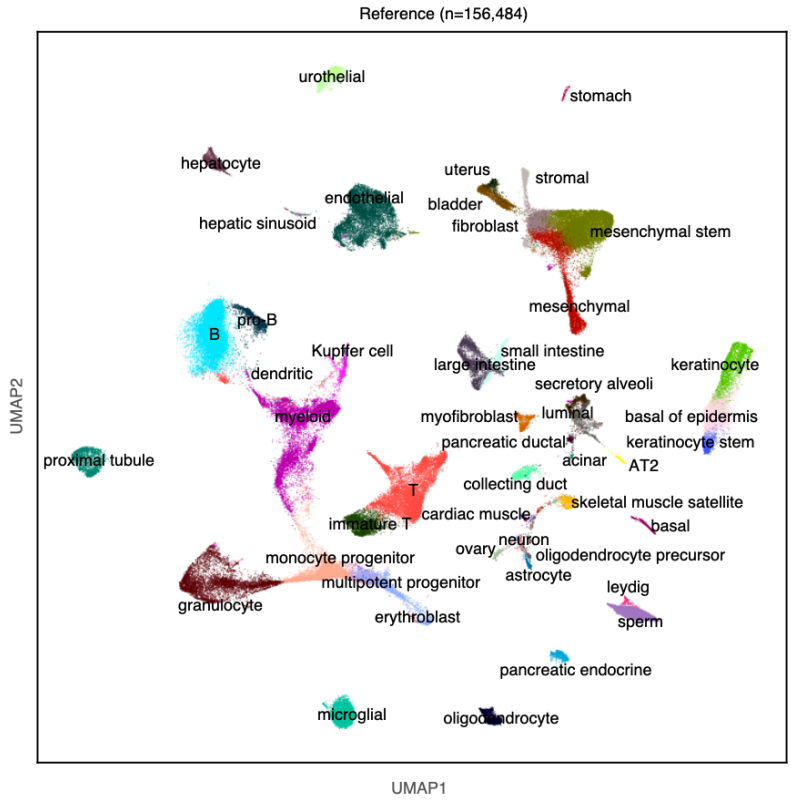



## 1.3 Label transfer

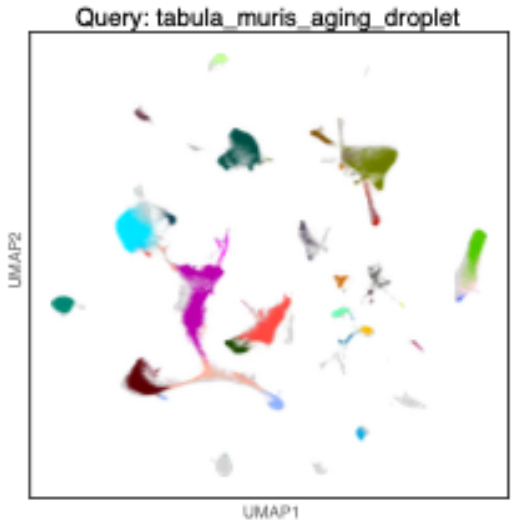
Annotate cells in new data through label transfer

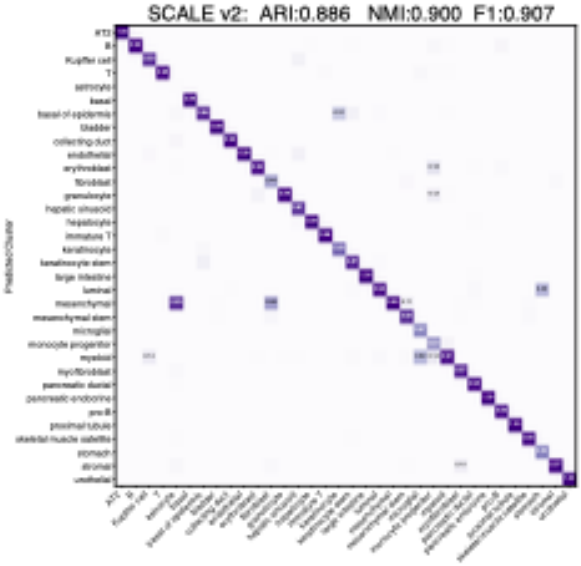
Label transfer tabula muris data and mouse kidney data from mouse atlas reference

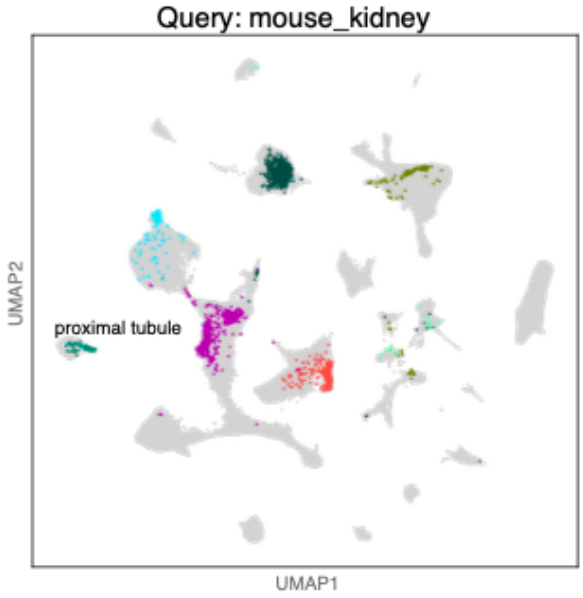
mouse atlas reference

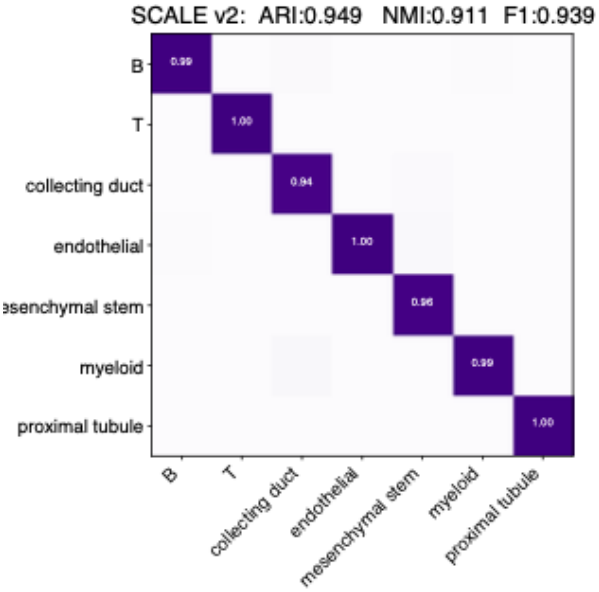



query tabula muris aging and query mouse kidney

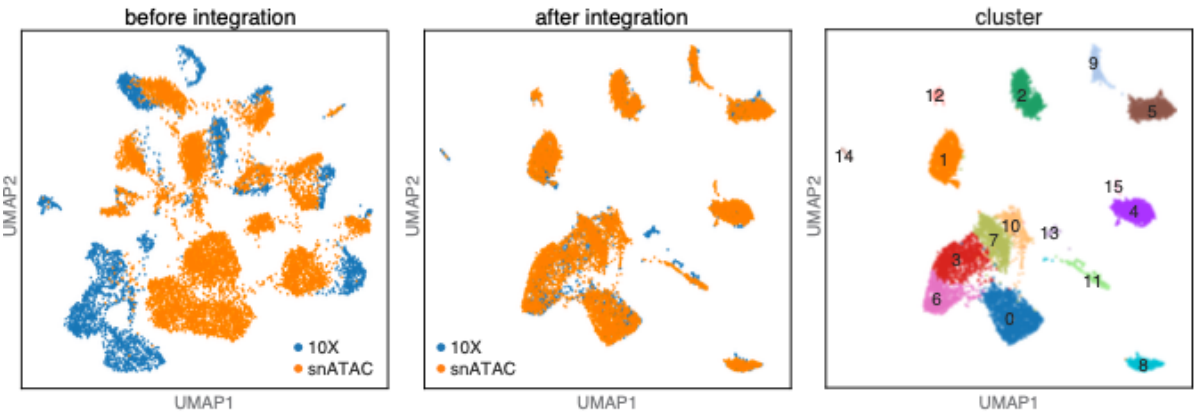

Query: tabula_muris_aging_droplet
UMAP2
UMAP1


SCALE v2: ARI:0.886 NMI:0.900 F1:0.907


Query: mouse_kidney
proximal tubule
UMAP2
UMAP1

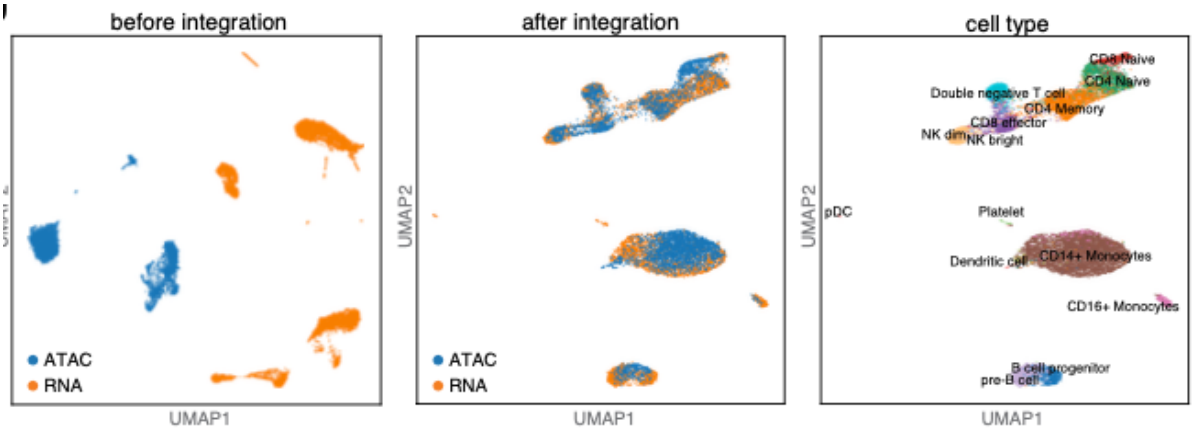

SCALE v2: ARI:0.949 NMI:0.911 F1:0.939
B
T
collecting duct
endothelial
esenchymal stem
myeloid
proximal tubule
0.99
1.00
0.94
1.00
0.96
0.99
1.00
B
T
collecting duct
endothelial
mesenchymal stem
myeloid
proximal tubule

## 1.4 Integration scATAC-seq data




## 1.5 Integration cross-modality data

Integrate scRNA-seq and scATAC-seq dataset




## 1.6 Spatial data (To be updated)

Integrating spatial data with scRNA-seq

## 1.7 Examples

### 1.7.1 Integrating PBMC data using SCALEX

The following tutorial demonstrates how to use SCALEX for *integrating* PBMC data.

There are two parts of this tutorial:

- **Seeing the batch effect.** This part will show the batch effects of two PBMC datasets from single cell 3' and 5' gene expression libraries that used in SCALEX manuscript.

- **Integrating data using SCALEX.** This part will show you how to perform batch correction using SCALEX function in SCALEX.

[1]:
```
import scalex
from scalex.function import SCALEX
from scalex.plot import embedding
import scanpy as sc
import pandas as pd
import numpy as np
import matplotlib
from matplotlib import pyplot as plt
import seaborn as sns
```

[2]:
```
sc.settings.verbosity = 3
sc.settings.set_figure_params(dpi=80, facecolor='white',figsize=(3,3),frameon=True)
sc.logging.print_header()
plt.rcParams['axes.unicode_minus']=False
```

```
scanpy==1.6.1 anndata==0.7.5 umap==0.4.6 numpy==1.20.1 scipy==1.6.1 pandas==1.1.3 scikit-
↪learn==0.23.2 statsmodels==0.12.0 python-igraph==0.8.3 louvain==0.7.0 leidenalg==0.8.3
```

[3]:
```
sns.__version__
```

[3]:
```
'0.10.1'
```

[4]:
```
scalex.__version__
```

[4]:
```
'0.2.0'
```

### Integrating data using SCALEX

The batch effects can be well-resolved using SCALEX.

---

**Note**

Here we use GPU to speed up the calculation process, however, you can get the same level of performance only using cpu.

---

[12]:
```
# ! wget http://zhanglab.net/scalex-tutorial/pbmc.h5ad
adata=SCALEX('pbmc.h5ad', batch_name='batch', outdir='pbmc_output/')
```

```
2021-03-30 20:16:38,586 - root - INFO - Raw dataset shape: (15476, 33694)
2021-03-30 20:16:38,588 - root - INFO - Preprocessing
2021-03-30 20:16:38,616 - root - INFO - Filtering cells
Trying to set attribute `.obs` of view, copying.
2021-03-30 20:16:39,462 - root - INFO - Filtering features
```

```
filtered out 13316 genes that are detected in less than 3 cells
```

```
2021-03-30 20:16:39,952 - root - INFO - Normalizing total per cell
```

```
normalizing counts per cell
    finished (0:00:00)
```

```
2021-03-30 20:16:40,076 - root - INFO - Log1p transforming
2021-03-30 20:16:40,493 - root - INFO - Finding variable features
```

```
If you pass `n_top_genes`, all cutoffs are ignored.
extracting highly variable genes
    finished (0:00:01)
--> added
    'highly_variable', boolean vector (adata.var)
    'means', float vector (adata.var)
    'dispersions', float vector (adata.var)
    'dispersions_norm', float vector (adata.var)
```

```
2021-03-30 20:16:42,776 - root - INFO - Batch specific maxabs scaling
2021-03-30 20:16:44,173 - root - INFO - Processed dataset shape: (15476, 2000)
2021-03-30 20:16:44,192 - root - INFO - model
VAE(
  (encoder): Encoder(
    (enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=2000, out_features=1024, bias=True)
          (norm): BatchNorm1d(1024, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
          (act): ReLU()
        )
      )
    )
    (mu_enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=1024, out_features=10, bias=True)
        )
      )
    )
    (var_enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=1024, out_features=10, bias=True)
        )
      )
    )
  )
  (decoder): NN(
    (net): ModuleList(
      (0): Block(
        (fc): Linear(in_features=10, out_features=2000, bias=True)
        (norm): DSBatchNorm(
          (bns): ModuleList(
            (0): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (1): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
          )
        )
```

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```
        (act): Sigmoid()
      )
    )
  )
)
Epochs: 100%|| 125/125 [06:11<00:00,  2.97s/it, recon_loss=182.388,kl_loss=3.988]
2021-03-30 20:23:03,050 - root - INFO - Output dir: pbmc_output//
2021-03-30 20:23:07,564 - root - INFO - Plot umap
```

```
computing neighbors
    finished: added to `.uns['neighbors']`
    `.obsp['distances']`, distances for each pair of neighbors
    `.obsp['connectivities']`, weighted adjacency matrix (0:00:03)
computing UMAP
    finished: added
    'X_umap', UMAP coordinates (adata.obsm) (0:00:12)
running Leiden clustering
    finished: found 15 clusters and added
    'leiden', the cluster labels (adata.obs, categorical) (0:00:05)
WARNING: saving figure to file pbmc_output/umap.pdf
```

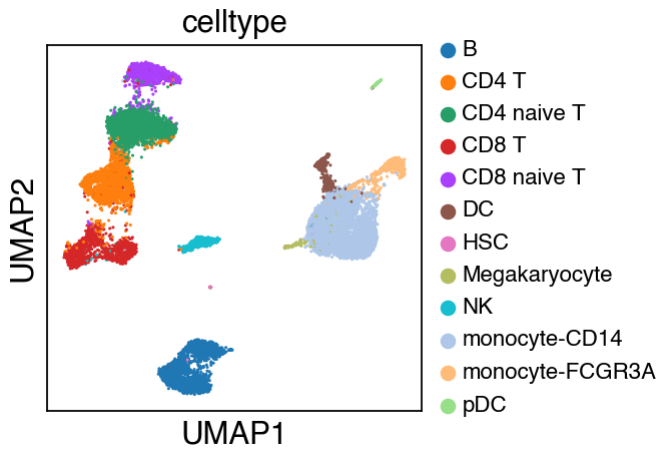
[13]:
```
adata
```

[13]:
```
AnnData object with n_obs × n_vars = 15476 × 2000
    obs: 'batch', 'celltype', 'protocol', 'celltype0', 'n_genes', 'leiden'
    var: 'n_cells', 'highly_variable', 'means', 'dispersions', 'dispersions_norm',
↪'highly_variable_nbatches', 'highly_variable_intersection'
    uns: 'log1p', 'hvg', 'neighbors', 'umap', 'leiden', 'batch_colors', 'celltype_colors
↪', 'leiden_colors'
    obsm: 'latent', 'X_umap'
    obsp: 'distances', 'connectivities'
```

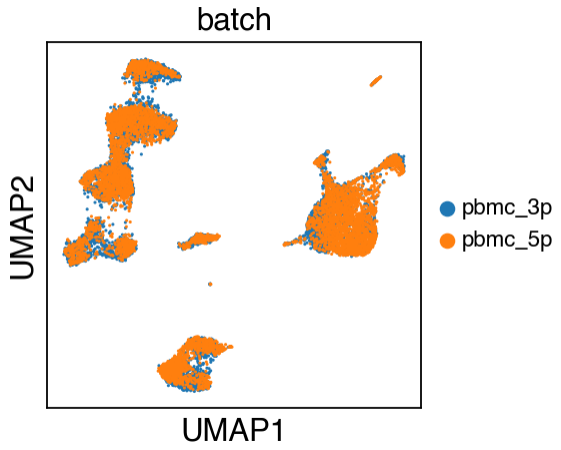
While there seems to be some strong batch-effect in all cell types, SCALEX can integrate them homogeneously.

[14]:
```
sc.settings.set_figure_params(dpi=80, facecolor='white',figsize=(3,3),frameon=True)
```

[15]:
```
sc.pl.umap(adata,color=['celltype'],legend_fontsize=10)
```



[16]:
```
sc.pl.umap(adata,color=['batch'],legend_fontsize=10)
```




The integrated data is stored as `adata.h5ad` in the output directory assigned by `outdir` parameter in SCALEX function.

### 1.7.2 Projection pancreas data using SCALEX

The following tutorial demonstrates how to use SCALEX for *integrating* data and *projection* new data `adata_query` onto an annotated reference `adata_ref`.

There are five parts of this tutorial:

- **Seeing the batch effect.** This part will show the batch effects of eight pancreas datasets that used in SCALEX manuscript.
- **Integrating data using SCALEX.** This part will show you how to perform batch correction and construct a reference batch `adata_ref` using SCALEX function in SCALEX.
- **Mapping onto a reference batch using projection function.** The third part will describe the usage of projection function in SCALEX to map three batches query dataset `adata_query` onto the reference batch `adata_ref` you construetd in part two.
- **Visualizing distributions across batches.** Often, batches correspond to experiments that one wants to compare. SCALEX v2 offers embedding function to convenient visualize for this.
- **Label transfer.** SCALEX offers label_transfer function to conveniently transfer labels from reference datasets to query datasets.

[1]:
```
import scalex
from scalex import SCALEX, label_transfer
from scalex.plot import embedding
import scanpy as sc
import pandas as pd
import numpy as np
import matplotlib
from matplotlib import pyplot as plt
import seaborn as sns
```

[2]:
```
sc.settings.verbosity = 3
sc.settings.set_figure_params(dpi=80, facecolor='white',figsize=(3,3),frameon=True)
sc.logging.print_header()
plt.rcParams['axes.unicode_minus']=False
```

```
scanpy==1.6.1 anndata==0.7.5 umap==0.4.6 numpy==1.20.1 scipy==1.6.1 pandas==1.1.3 scikit-
↪learn==0.23.2 statsmodels==0.12.0 python-igraph==0.8.3 louvain==0.7.0 leidenalg==0.8.3
```

[3]:
```
sns.__version__
```

[3]:
```
'0.10.1'
```

[4]:
```
scalex.__version__
```

[4]:
```
'0.2.0'
```

### Seeing the batch effect

The pancreas data has been used in the Seurat v3 and Harmony paper.

On a unix system, you can uncomment and run the following to download the count matrix in its anndata format.

[5]:
```
# ! wget http://zhanglab.net/scalex-tutorial/pancreas.h5ad
# ! wget http://zhanglab.net/scalex-tutorial/pancreas_query.h5ad
```

[6]:
```
adata_raw=sc.read('pancreas.h5ad')
adata_raw
```

[6]:
```
AnnData object with n_obs × n_vars = 16401 × 14895
    obs: 'batch', 'celltype', 'disease', 'donor', 'library', 'protocol'
```

Inspect the batches contained in the dataset.

[7]:
```
adata_raw.obs.batch.value_counts()
```

[7]:
```
pancreas_indrop3       3605
pancreas_celseq2       3072
pancreas_smartseq2     2394
pancreas_indrop1       1937
pancreas_celseq        1728
pancreas_indrop2       1724
pancreas_indrop4       1303
pancreas_fluidigmc1     638
Name: batch, dtype: int64
```

The data processing procedure is according to the scanpy tutorial [Preprocessing and clustering 3k PBMCs].

[8]:
```
sc.pp.filter_cells(adata_raw, min_genes=600)
sc.pp.filter_genes(adata_raw, min_cells=3)
adata_raw = adata_raw[:, [gene for gene in adata_raw.var_names if not str(gene).
↪startswith(tuple(['ERCC', 'MT-', 'mt-']))]]
sc.pp.normalize_total(adata_raw, target_sum=1e4)
sc.pp.log1p(adata_raw)
sc.pp.highly_variable_genes(adata_raw, min_mean=0.0125, max_mean=3, min_disp=0.5)
```

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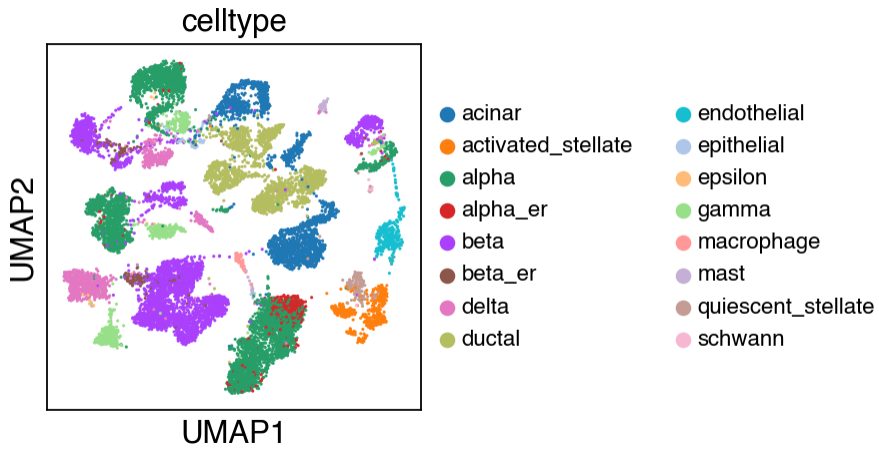
```
adata_raw.raw = adata_raw
adata_raw = adata_raw[:, adata_raw.var.highly_variable]
sc.pp.scale(adata_raw, max_value=10)
sc.pp.pca(adata_raw)
sc.pp.neighbors(adata_raw)
sc.tl.umap(adata_raw)
```

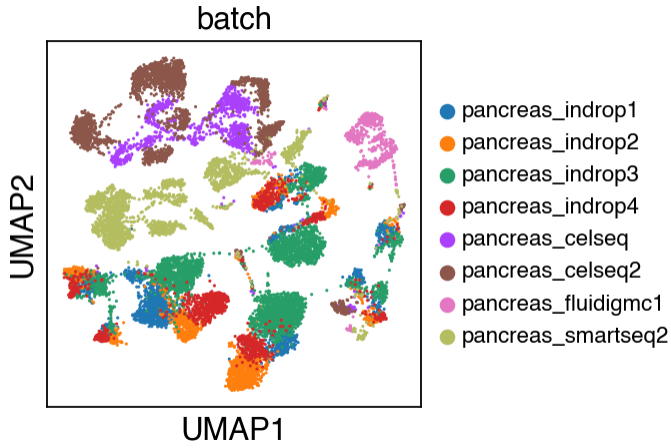
```
filtered out 1124 cells that have less than 600 genes expressed
normalizing counts per cell
    finished (0:00:00)
extracting highly variable genes
    finished (0:00:01)
--> added
    'highly_variable', boolean vector (adata.var)
    'means', float vector (adata.var)
    'dispersions', float vector (adata.var)
    'dispersions_norm', float vector (adata.var)
... as `zero_center=True`, sparse input is densified and may lead to large memory␣
↪consumption
computing PCA
    on highly variable genes
    with n_comps=50
    finished (0:00:03)
computing neighbors
    using 'X_pca' with n_pcs = 50
    finished: added to `.uns['neighbors']`
    `.obsp['distances']`, distances for each pair of neighbors
    `.obsp['connectivities']`, weighted adjacency matrix (0:00:15)
computing UMAP
    finished: added
    'X_umap', UMAP coordinates (adata.obsm) (0:00:09)
```

We observe a batch effect.

[9]:
```
sc.pl.umap(adata_raw,color=['celltype'],legend_fontsize=10)
```




[10]:
```
sc.pl.umap(adata_raw,color=['batch'],legend_fontsize=10)
```




[11]:
```
adata_raw
```

[11]:
```
AnnData object with n_obs × n_vars = 15277 × 2086
    obs: 'batch', 'celltype', 'disease', 'donor', 'library', 'protocol', 'n_genes'
    var: 'n_cells', 'highly_variable', 'means', 'dispersions', 'dispersions_norm', 'mean
↪', 'std'
    uns: 'log1p', 'hvg', 'pca', 'neighbors', 'umap', 'celltype_colors', 'batch_colors'
    obsm: 'X_pca', 'X_umap'
    varm: 'PCs'
    obsp: 'distances', 'connectivities'
```

### Integrating data using SCALEX

The batch effects can be well-resolved using SCALEX.

**Note**

Here we use GPU to speed up the calculation process, however, you can get the same level of performance only using cpu.

[12]:
```
adata_ref=SCALEX('pancreas.h5ad',batch_name='batch',min_features=600, min_cells=3,␣
↪outdir='pancreas_output/',show=False,gpu=7)
```

```
2021-03-30 20:21:06,757 - root - INFO - Raw dataset shape: (16401, 14895)
2021-03-30 20:21:06,759 - root - INFO - Preprocessing
2021-03-30 20:21:06,785 - root - INFO - Filtering cells
```

```
filtered out 1124 cells that have less than 600 genes expressed
```

```
Trying to set attribute `.obs` of view, copying.
2021-03-30 20:21:09,107 - root - INFO - Filtering features
2021-03-30 20:21:10,607 - root - INFO - Normalizing total per cell
```

```
normalizing counts per cell
    finished (0:00:00)
```

```
2021-03-30 20:21:10,850 - root - INFO - Log1p transforming
2021-03-30 20:21:11,759 - root - INFO - Finding variable features
```

```
If you pass `n_top_genes`, all cutoffs are ignored.
extracting highly variable genes
    finished (0:00:04)
--> added
    'highly_variable', boolean vector (adata.var)
    'means', float vector (adata.var)
    'dispersions', float vector (adata.var)
    'dispersions_norm', float vector (adata.var)
```

```
2021-03-30 20:21:17,003 - root - INFO - Batch specific maxabs scaling
2021-03-30 20:21:19,528 - root - INFO - Processed dataset shape: (15277, 2000)
2021-03-30 20:21:19,566 - root - INFO - model
VAE(
  (encoder): Encoder(
    (enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=2000, out_features=1024, bias=True)
          (norm): BatchNorm1d(1024, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
          (act): ReLU()
        )
      )
    )
    (mu_enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=1024, out_features=10, bias=True)
        )
      )
    )
    (var_enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=1024, out_features=10, bias=True)
        )
      )
    )
  )
  (decoder): NN(
    (net): ModuleList(
      (0): Block(
        (fc): Linear(in_features=10, out_features=2000, bias=True)
        (norm): DSBatchNorm(
          (bns): ModuleList(
            (0): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (1): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (2): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (3): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
```

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```
            (4): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (5): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (6): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (7): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
          )
        )
        (act): Sigmoid()
      )
    )
  )
)
Epochs: 100%|| 127/127 [09:11<00:00,  4.34s/it, recon_loss=266.572,kl_loss=4.667]
2021-03-30 20:30:38,361 - root - INFO - Output dir: pancreas_output//
2021-03-30 20:30:47,018 - root - INFO - Plot umap
```

```
computing neighbors
    finished: added to `.uns['neighbors']`
    `.obsp['distances']`, distances for each pair of neighbors
    `.obsp['connectivities']`, weighted adjacency matrix (0:00:03)
computing UMAP
    finished: added
    'X_umap', UMAP coordinates (adata.obsm) (0:00:10)
running Leiden clustering
    finished: found 13 clusters and added
    'leiden', the cluster labels (adata.obs, categorical) (0:00:02)
WARNING: saving figure to file pancreas_output/umap.pdf
```

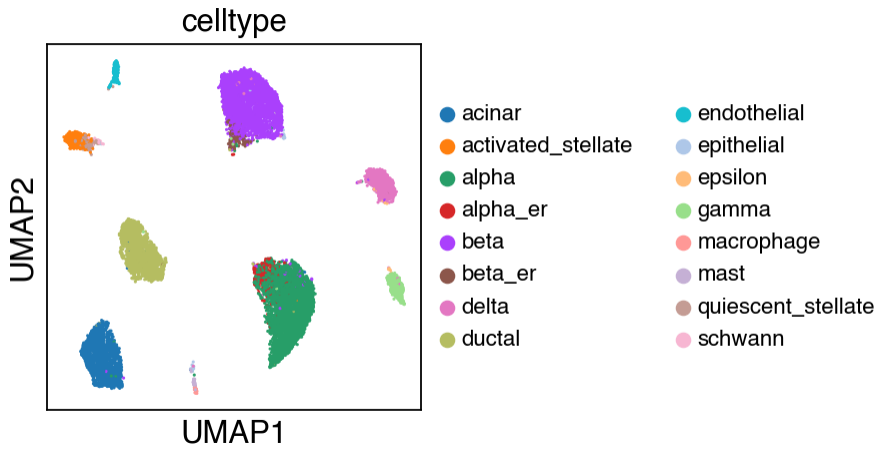
[13]:
```
adata_ref
```

[13]:
```
AnnData object with n_obs × n_vars = 15277 × 2000
    obs: 'batch', 'celltype', 'disease', 'donor', 'library', 'protocol', 'n_genes',
↪'leiden'
    var: 'n_cells', 'highly_variable', 'means', 'dispersions', 'dispersions_norm',
↪'highly_variable_nbatches', 'highly_variable_intersection'
    uns: 'log1p', 'hvg', 'neighbors', 'umap', 'leiden', 'batch_colors', 'celltype_colors
↪', 'leiden_colors'
    obsm: 'latent', 'X_umap'
    obsp: 'distances', 'connectivities'
```

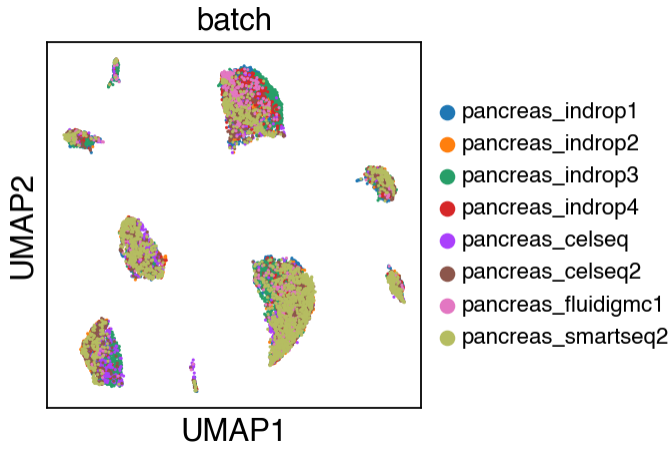
While there seems to be some strong batch-effect in all cell types, SCALEX can integrate them homogeneously.

[14]:
```
sc.settings.set_figure_params(dpi=80, facecolor='white',figsize=(3,3),frameon=True)
```

[15]:
```
sc.pl.umap(adata_ref,color=['celltype'],legend_fontsize=10)
```




[16]:
```
sc.pl.umap(adata_ref,color=['batch'],legend_fontsize=10)
```




The integrated data is stored as `adata.h5ad` in the output directory assigned by `outdir` parameter in SCALEX function.

### Mapping onto a reference batch using projection function

The pancreas query data are available through the Gene Expression Omnibus under accession GSE114297, GSE81547 and GSE83139.

[17]:
```
adata_query=sc.read('pancreas_query.h5ad')
adata_query
```

[17]:
```
AnnData object with n_obs × n_vars = 23963 × 31884
    obs: 'batch', 'celltype', 'disease', 'donor', 'protocol'
```

Inspect the batches contained in `adata_query`.

[18]:
```
adata_query.obs.batch.value_counts()
```

[18]:
```
pancreas_gse114297    20784
pancreas_gse81547      2544
```

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```
pancreas_gse83139       635
Name: batch, dtype: int64
```

SCALEX provides a projection function for mapping new data `adata_query` onto the reference batch `adata_ref`.

[19]:
```
adata=SCALEX('pancreas_query.h5ad',batch_name='batch',min_features=600, min_cells=3,
             outdir='pancreas_projection/', projection='pancreas_output/',show=False,
↪gpu=7)
```

```
2021-03-30 20:31:47,177 - root - INFO - Raw dataset shape: (23963, 31884)
2021-03-30 20:31:47,177 - root - INFO - Raw dataset shape: (23963, 31884)
2021-03-30 20:31:47,180 - root - INFO - Preprocessing
2021-03-30 20:31:47,180 - root - INFO - Preprocessing
2021-03-30 20:31:47,236 - root - INFO - Filtering cells
2021-03-30 20:31:47,236 - root - INFO - Filtering cells
```

```
filtered out 219 cells that have less than 600 genes expressed
```

```
Trying to set attribute `.obs` of view, copying.
2021-03-30 20:31:49,744 - root - INFO - Filtering features
2021-03-30 20:31:49,744 - root - INFO - Filtering features
2021-03-30 20:31:51,094 - root - INFO - Normalizing total per cell
2021-03-30 20:31:51,094 - root - INFO - Normalizing total per cell
```

```
normalizing counts per cell
    finished (0:00:00)
```

```
2021-03-30 20:31:51,430 - root - INFO - Log1p transforming
2021-03-30 20:31:51,430 - root - INFO - Log1p transforming
2021-03-30 20:31:52,607 - root - INFO - Finding variable features
2021-03-30 20:31:52,607 - root - INFO - Finding variable features
```

```
There are 2000 gene in selected genes
```

```
2021-03-30 20:31:56,488 - root - INFO - Batch specific maxabs scaling
2021-03-30 20:31:56,488 - root - INFO - Batch specific maxabs scaling
2021-03-30 20:31:59,442 - root - INFO - Processed dataset shape: (23744, 2000)
2021-03-30 20:31:59,442 - root - INFO - Processed dataset shape: (23744, 2000)
2021-03-30 20:32:04,207 - root - INFO - Output dir: pancreas_projection//
2021-03-30 20:32:04,207 - root - INFO - Output dir: pancreas_projection//
... storing 'batch' as categorical
... storing 'celltype' as categorical
... storing 'disease' as categorical
... storing 'donor' as categorical
... storing 'library' as categorical
... storing 'protocol' as categorical
... storing 'leiden' as categorical
2021-03-30 20:32:08,411 - root - INFO - Plot umap
2021-03-30 20:32:08,411 - root - INFO - Plot umap
```

```
computing neighbors
    finished: added to `.uns['neighbors']`
    `.obsp['distances']`, distances for each pair of neighbors
    `.obsp['connectivities']`, weighted adjacency matrix (0:00:08)
computing UMAP
    finished: added
```

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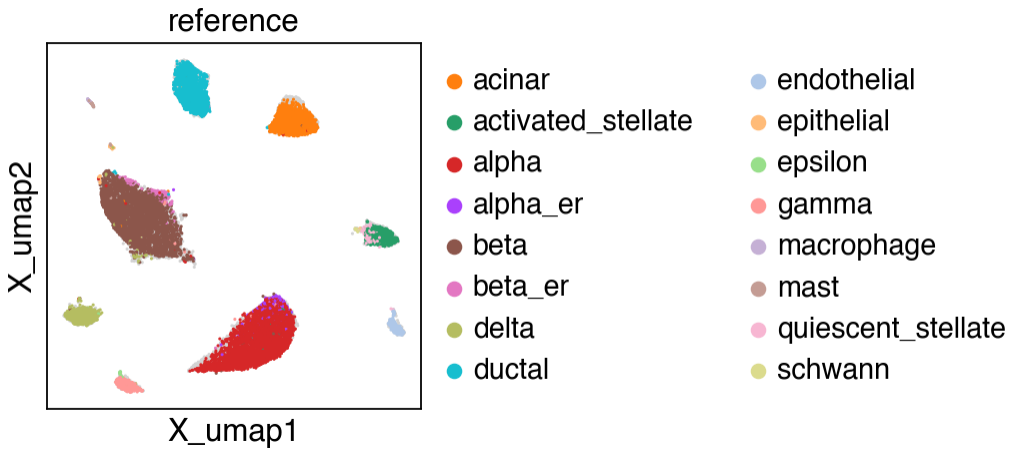
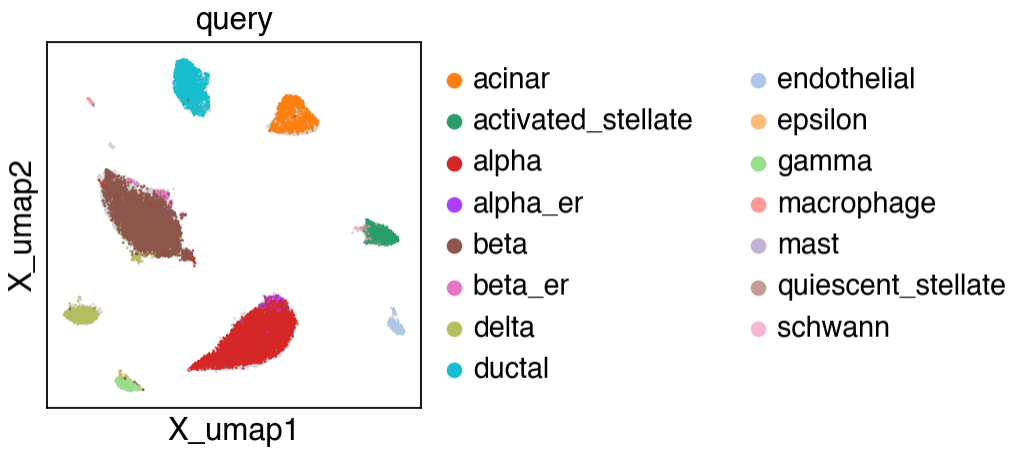
```
    'X_umap', UMAP coordinates (adata.obsm) (0:00:26)
running Leiden clustering
    finished: found 13 clusters and added
    'leiden', the cluster labels (adata.obs, categorical) (0:00:10)
WARNING: saving figure to file pancreas_projection/X_umap_reference.pdf
WARNING: saving figure to file pancreas_projection/X_umap_query.pdf
```

Load integrated data `adata` that contained `adata_ref` and `adata_query`.

[20]:
```
sc.settings.set_figure_params(dpi=80, facecolor='white',figsize=(3,3),frameon=True)
```

[21]:
```
embedding(adata,groupby='projection')
```




[22]:
```
adata
```

[22]:
```
AnnData object with n_obs × n_vars = 39021 × 2000
    obs: 'batch', 'celltype', 'disease', 'donor', 'library', 'protocol', 'n_genes',
↪'leiden', 'projection'
    var: 'n_cells-reference', 'highly_variable-reference', 'means-reference',
↪'dispersions-reference', 'dispersions_norm-reference', 'highly_variable_nbatches-
↪reference', 'highly_variable_intersection-reference'
```

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```
    uns: 'neighbors', 'umap', 'leiden'
    obsm: 'latent', 'X_umap'
    obsp: 'distances', 'connectivities'
```

Inspect the batches contained in adata.

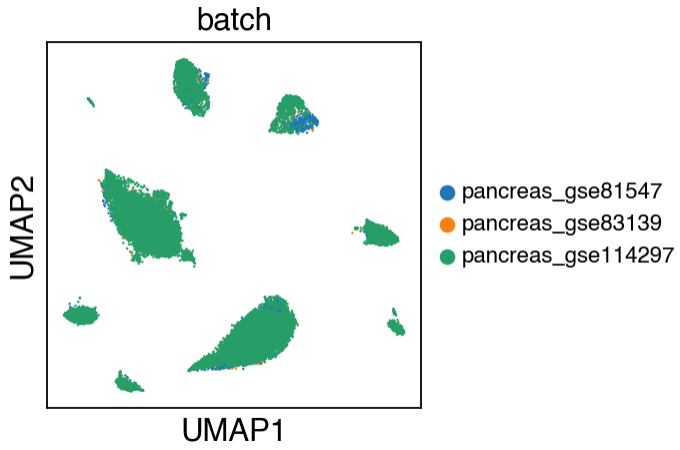
[23]:
```
adata.obs.batch.value_counts()
```

[23]:
```
pancreas_gse114297     20573
pancreas_indrop3        3605
pancreas_gse81547       2536
pancreas_celseq2        2440
pancreas_smartseq2      2394
pancreas_indrop1        1937
pancreas_indrop2        1724
pancreas_indrop4        1303
pancreas_celseq         1236
pancreas_fluidigmc1      638
pancreas_gse83139        635
Name: batch, dtype: int64
```

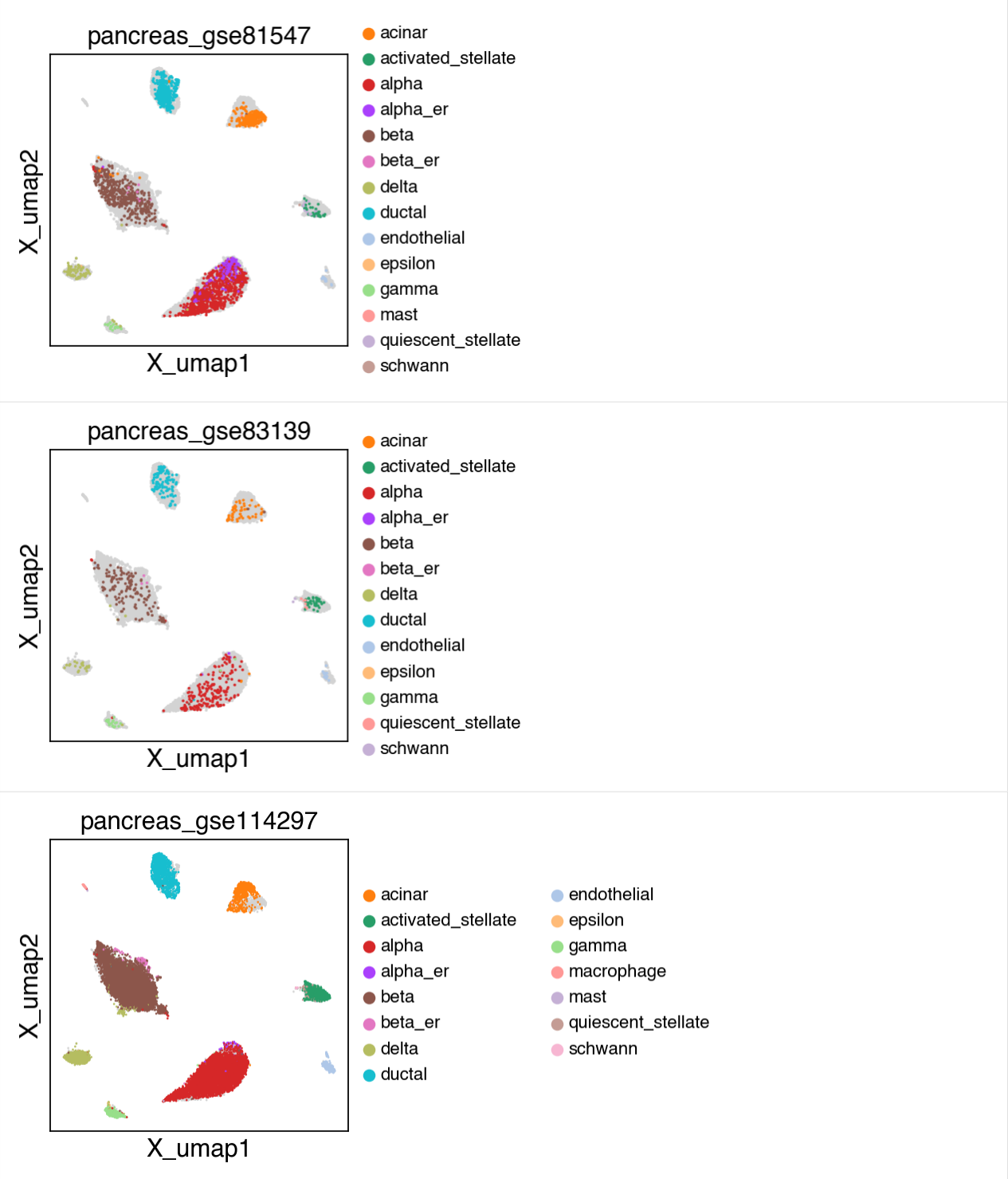
### Visualizing distributions across batches

[24]:
```
sc.pl.umap(adata[adata.obs.batch.isin(['pancreas_gse114297','pancreas_gse81547',
↪'pancreas_gse83139'])],color='batch',legend_fontsize=10)
embedding(adata[adata.obs.batch.isin(['pancreas_gse114297','pancreas_gse81547','pancreas_
↪gse83139'])],legend_fontsize=10)
```

```
Trying to set attribute `.uns` of view, copying.
```




```
Trying to set attribute `.obs` of view, copying.
```




The projection results is stored as `adata.h5ad` in the output directory assigned by `outdir` parameter in SCALE function.

### Label transfer

We can also use SCALEX to transfer data from one dataset to another. Here, we demonstrate data transfer between two scRNA-seq datasets by transferring the cell type label from the `adata_ref` and the `adata_query`.

[25]:
```
adata_query=adata[adata.obs.projection=='query']
adata_query
```

[25]:
```
View of AnnData object with n_obs × n_vars = 23744 × 2000
    obs: 'batch', 'celltype', 'disease', 'donor', 'library', 'protocol', 'n_genes',
↪'leiden', 'projection'
    var: 'n_cells-reference', 'highly_variable-reference', 'means-reference',
↪'dispersions-reference', 'dispersions_norm-reference', 'highly_variable_nbatches-
↪reference', 'highly_variable_intersection-reference'
    uns: 'neighbors', 'umap', 'leiden'
    obsm: 'latent', 'X_umap'
    obsp: 'distances', 'connectivities'
```

[26]:
```
adata_ref=adata[adata.obs.projection=='reference']
adata_ref
```

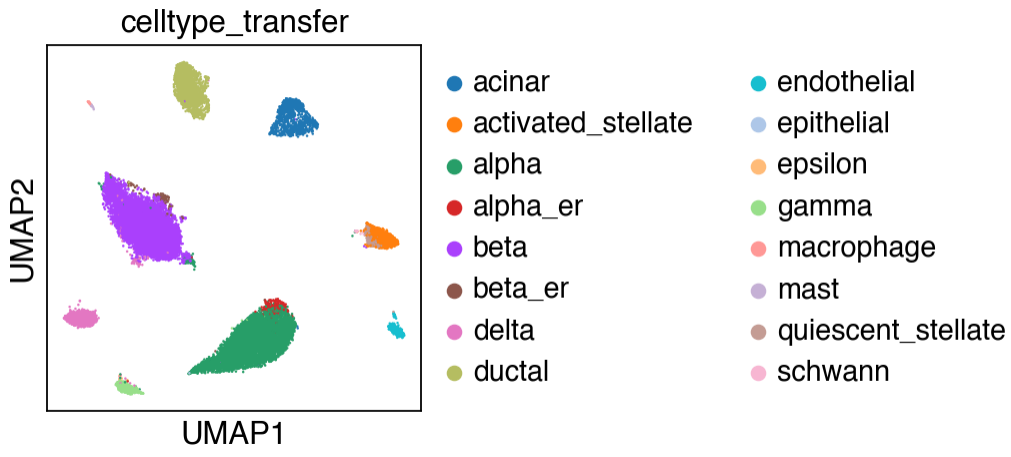
[26]:
```
View of AnnData object with n_obs × n_vars = 15277 × 2000
    obs: 'batch', 'celltype', 'disease', 'donor', 'library', 'protocol', 'n_genes',
↪'leiden', 'projection'
    var: 'n_cells-reference', 'highly_variable-reference', 'means-reference',
↪'dispersions-reference', 'dispersions_norm-reference', 'highly_variable_nbatches-
↪reference', 'highly_variable_intersection-reference'
    uns: 'neighbors', 'umap', 'leiden'
    obsm: 'latent', 'X_umap'
    obsp: 'distances', 'connectivities'
```

[27]:
```
adata_query.obs['celltype_transfer']=label_transfer(adata_ref, adata_query, rep='latent',
↪ label='celltype')
```

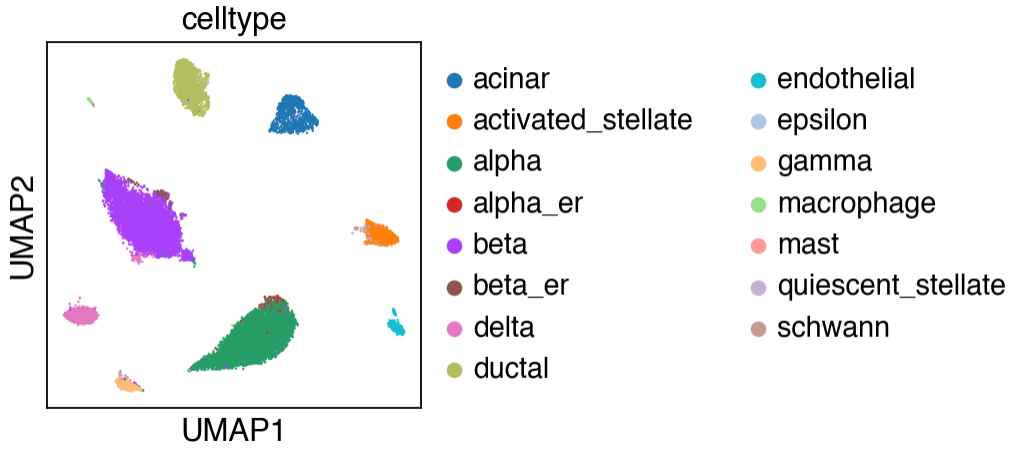
```
Trying to set attribute `.obs` of view, copying.
```

[28]:
```
sc.pl.umap(adata_query,color=['celltype_transfer'])
```

```
... storing 'celltype_transfer' as categorical
```



[29]:
```
sc.pl.umap(adata_query,color=['celltype'])
```




Let us first focus on cell types that are conserved with the reference.

[30]:
```
obs_query = adata_query.obs
conserved_categories = obs_query.celltype.cat.categories.intersection(obs_query.celltype_
↪transfer.cat.categories)  # intersected categories
obs_query_conserved = obs_query.loc[obs_query.celltype.isin(conserved_categories) & obs_
↪query.celltype_transfer.isin(conserved_categories)]  # intersect categories
obs_query_conserved.celltype.cat.remove_unused_categories(inplace=True)  # remove unused␣
↪categoriyes
obs_query_conserved.celltype_transfer.cat.remove_unused_categories(inplace=True)  #␣
↪remove unused categoriyes
obs_query_conserved.celltype_transfer.cat.reorder_categories(obs_query_conserved.
↪celltype.cat.categories, inplace=True)  # fix category ordering
pd.crosstab(obs_query_conserved.celltype, obs_query_conserved.celltype_transfer)
```

[30]:

| celltype_transfer | acinar | activated_stellate | alpha | alpha_er | beta |
|---|---|---|---|---|---|
| celltype | | | | | |
| acinar | 1346 | 0 | 3 | 0 | 3 |
| activated_stellate | 0 | 1033 | 0 | 0 | 2 |
| alpha | 2 | 0 | 7527 | 83 | 13 |
| alpha_er | 0 | 0 | 159 | 105 | 2 |
| beta | 3 | 0 | 119 | 4 | 8683 |
| beta_er | 0 | 0 | 0 | 0 | 41 |
| delta | 1 | 0 | 8 | 0 | 34 |
| ductal | 2 | 0 | 3 | 0 | 2 |
| endothelial | 0 | 1 | 0 | 0 | 1 |
| epsilon | 1 | 0 | 0 | 0 | 0 |
| gamma | 0 | 0 | 7 | 2 | 3 |
| macrophage | 0 | 0 | 0 | 0 | 0 |
| mast | 1 | 0 | 0 | 0 | 1 |
| quiescent_stellate | 0 | 53 | 0 | 0 | 2 |
| schwann | 1 | 0 | 2 | 0 | 0 |

| celltype_transfer | beta_er | delta | ductal | endothelial | epsilon | gamma |
|---|---|---|---|---|---|---|
| celltype | | | | | | |
| acinar | 0 | 0 | 2 | 0 | 0 | 0 |

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```
activated_stellate        0      0       0             0       0      0
alpha                     0      3       0             0       0     11
alpha_er                  1      0       0             0       0      0
beta                     34     17       1             0       0      3
beta_er                  56      0       1             0       0      0
delta                     0   1099       0             0       1      6
ductal                    0      3    1889             0       0      0
endothelial               0      1       0           456       0      0
epsilon                   0      3       0             0      10      3
gamma                     0      1       0             0       2    578
macrophage                0      0       0             0       0      0
mast                      0      0       0             0       0      0
quiescent_stellate        0      0       0             0       0      0
schwann                   1      0       0             0       0      0

celltype_transfer   macrophage  mast  quiescent_stellate  schwann
celltype
acinar                       0     0                   1        0
activated_stellate           0     0                 119        1
alpha                        0     1                   0        0
alpha_er                     0     0                   0        0
beta                         0     0                   0        0
beta_er                      0     0                   0        0
delta                        0     0                   0        0
ductal                       0     0                   0        0
endothelial                  0     0                   1        0
epsilon                      0     0                   0        0
gamma                        0     0                   0        0
macrophage                  58    14                   0        0
mast                         3     6                   0        0
quiescent_stellate           0     0                  68        1
schwann                      0     0                   0       34
```

Let us now move on to look at all cell types.

[31]:
```
pd.crosstab(adata_query.obs.celltype, adata_query.obs.celltype_transfer)
```

[31]:
```
celltype_transfer   acinar  activated_stellate  alpha  alpha_er  beta  \
celltype
acinar                1346                   0      3         0     3
activated_stellate       0                1033      0         0     2
alpha                    2                   0   7527        83    13
alpha_er                 0                   0    159       105     2
beta                     3                   0    119         4  8683
beta_er                  0                   0      0         0    41
delta                    1                   0      8         0    34
ductal                   2                   0      3         0     2
endothelial              0                   1      0         0     1
epsilon                  1                   0      0         0     0
gamma                    0                   0      7         2     3
macrophage               0                   0      0         0     0
mast                     1                   0      0         0     1
quiescent_stellate       0                  53      0         0     2
```

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```
schwann                  1                  0      2         0     0

celltype_transfer   beta_er  delta  ductal  endothelial  epithelial  epsilon  \
celltype
acinar                   0      0       2            0           0        0
activated_stellate       0      0       0            0           0        0
alpha                    0      3       0            0           1        0
alpha_er                 1      0       0            0           0        0
beta                    34     17       1            0           0        0
beta_er                 56      0       1            0           0        0
delta                    0   1099       0            0           0        1
ductal                   0      3    1889            0           0        0
endothelial              0      1       0          456           0        0
epsilon                  0      3       0            0           0       10
gamma                    0      1       0            0           0        2
macrophage               0      0       0            0           0        0
mast                     0      0       0            0           1        0
quiescent_stellate       0      0       0            0           0        0
schwann                  1      0       0            0           0        0

celltype_transfer   gamma  macrophage  mast  quiescent_stellate  schwann
celltype
acinar                  0           0     0                   1        0
activated_stellate      0           0     0                 119        1
alpha                  11           0     1                   0        0
alpha_er                0           0     0                   0        0
beta                    3           0     0                   0        0
beta_er                 0           0     0                   0        0
delta                   6           0     0                   0        0
ductal                  0           0     0                   0        0
endothelial             0           0     0                   1        0
epsilon                 3           0     0                   0        0
gamma                 578           0     0                   0        0
macrophage              0          58    14                   0        0
mast                    0           3     6                   0        0
quiescent_stellate      0           0     0                  68        1
schwann                 0           0     0                   0       34
```

### 1.7.3 Integrating scATAC-seq data using SCALEX

The following tutorial demonstrates how to use SCALEX for *integrating* scATAC-seq data.

There are two parts of this tutorial:

- **Seeing the batch effect.** This part will show the batch effects of two adult mouse brain datasets from single nucleus ATAC-seq (snATAC) and droplet-based platform (Mouse Brain 10X) that used in SCALEX manuscript.
- **Integrating data using SCALEX.** This part will show you how to perform batch correction using SCALEX function in SCALEX.

[1]:
```
import scalex
from scalex.function import SCALEX
```

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```
from scalex.plot import embedding
import scanpy as sc
import pandas as pd
import numpy as np
import matplotlib
from matplotlib import pyplot as plt
import seaborn as sns
import episcanpy as epi
```

[2]:
```
sc.settings.verbosity = 3
sc.settings.set_figure_params(dpi=80, facecolor='white',figsize=(3,3),frameon=True)
sc.logging.print_header()
plt.rcParams['axes.unicode_minus']=False
```

```
scanpy==1.6.1 anndata==0.7.5 umap==0.4.6 numpy==1.20.1 scipy==1.6.1 pandas==1.1.3 scikit-
↪learn==0.23.2 statsmodels==0.12.0 python-igraph==0.8.3 louvain==0.7.0 leidenalg==0.8.3
```

[3]:
```
sns.__version__
```

[3]:
```
'0.10.1'
```

[4]:
```
scalex.__version__
```

[4]:
```
'0.2.0'
```

### Seeing the batch effect

The following data has been used in the SnapATAC paper, has been used here, and can be downloaded from here.

On a unix system, you can uncomment and run the following to download the count matrix in its anndata format.

[5]:
```
# ! wget http://zhanglab.net/scalex-tutorial/mouse_brain_atac.h5ad
```

[6]:
```
adata_raw=sc.read('mouse_brain_atac.h5ad')
adata_raw
```

[6]:
```
AnnData object with n_obs × n_vars = 13746 × 479127
    obs: 'batch'
```

Inspect the batches contained in the dataset.

[7]:
```
adata_raw.obs.batch.value_counts()
```

[7]:
```
snATAC    9646
10X       4100
Name: batch, dtype: int64
```

The data processing procedure is according to the epiScanpy tutorial [Buenrostro_PBMC_data_processing].

[8]:
```
epi.pp.filter_cells(adata_raw, min_features=1)
epi.pp.filter_features(adata_raw, min_cells=5)
adata_raw.raw = adata_raw
adata_raw = epi.pp.select_var_feature(adata_raw,
```

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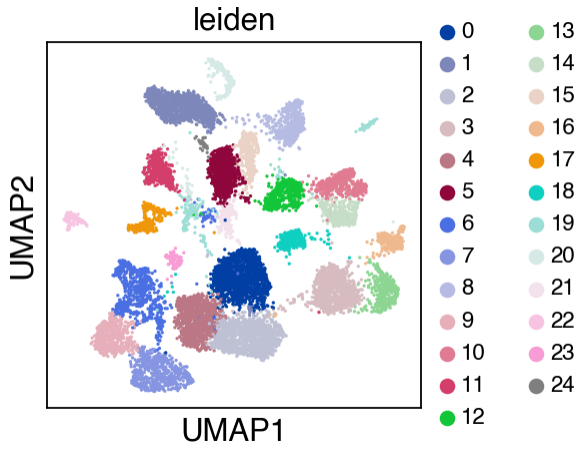
```
                                    nb_features=30000,
                                    show=False,copy=True)
adata_raw.layers['binary'] = adata_raw.X.copy()
epi.pp.normalize_total(adata_raw)
adata_raw.layers['normalised'] = adata_raw.X.copy()
epi.pp.log1p(adata_raw)
epi.pp.lazy(adata_raw)
epi.tl.leiden(adata_raw)
```

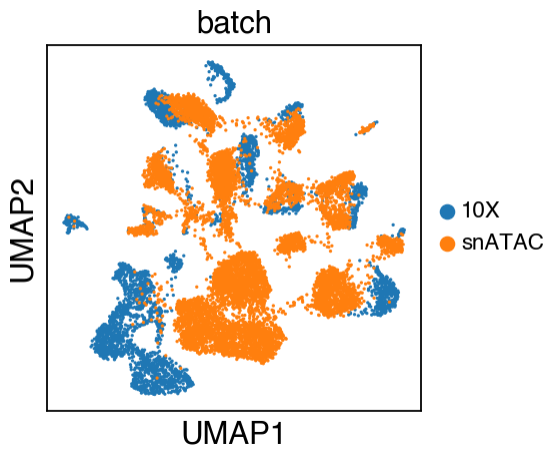
```
filtered out 11140 genes that are detected in less than 5 cells
normalizing counts per cell
    finished (0:00:00)
computing PCA
    with n_comps=50
    finished (0:01:46)
computing neighbors
    using 'X_pca' with n_pcs = 50
    finished: added to `.uns['neighbors']`
    `.obsp['distances']`, distances for each pair of neighbors
    `.obsp['connectivities']`, weighted adjacency matrix (0:00:14)
computing tSNE
    using 'X_pca' with n_pcs = 50
    using the 'MulticoreTSNE' package by Ulyanov (2017)
    finished: added
    'X_tsne', tSNE coordinates (adata.obsm) (0:01:35)
computing UMAP
    finished: added
    'X_umap', UMAP coordinates (adata.obsm) (0:00:09)
running Leiden clustering
    finished: found 25 clusters and added
    'leiden', the cluster labels (adata.obs, categorical) (0:00:01)
```

We observe a batch effect.

[9]:
```
sc.pl.umap(adata_raw,color=['leiden'],legend_fontsize=10)
```




[10]:
```
sc.pl.umap(adata_raw,color=['batch'],legend_fontsize=10)
```




[11]:
```
adata_raw
```

[11]:
```
AnnData object with n_obs × n_vars = 13746 × 30076
    obs: 'batch', 'nb_features', 'leiden'
    var: 'n_cells', 'prop_shared_cells', 'variability_score'
    uns: 'log1p', 'pca', 'neighbors', 'umap', 'leiden', 'leiden_colors', 'batch_colors'
    obsm: 'X_pca', 'X_tsne', 'X_umap'
    varm: 'PCs'
    layers: 'binary', 'normalised'
    obsp: 'distances', 'connectivities'
```

### Integrating data using SCALEX

The batch effects can be well-resolved using SCALEX.

**Note**

Here we use GPU to speed up the calculation process, however, you can get the same level of performance only using cpu.

[12]:
```
adata=SCALEX('mouse_brain_atac.h5ad',batch_name='batch',profile='ATAC',
            min_features=1, min_cells=5, n_top_features=30000,outdir='ATAC_output/',
↪show=False,gpu=8)
```

```
2021-03-30 20:21:45,161 - root - INFO - Raw dataset shape: (13746, 479127)
2021-03-30 20:21:45,166 - root - INFO - Preprocessing
2021-03-30 20:21:45,639 - root - INFO - Filtering cells
2021-03-30 20:21:47,224 - root - INFO - Filtering features
```

```
filtered out 11140 genes that are detected in less than 5 cells
```

```
2021-03-30 20:21:49,461 - root - INFO - Finding variable features
2021-03-30 20:21:51,582 - root - INFO - Normalizing total per cell
```

```
normalizing counts per cell
    finished (0:00:00)
```

```
2021-03-30 20:21:51,690 - root - INFO - Batch specific maxabs scaling
2021-03-30 20:22:16,926 - root - INFO - Processed dataset shape: (13746, 30076)
2021-03-30 20:22:17,234 - root - INFO - model
VAE(
  (encoder): Encoder(
    (enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=30076, out_features=1024, bias=True)
          (norm): BatchNorm1d(1024, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
          (act): ReLU()
        )
      )
    )
    (mu_enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=1024, out_features=10, bias=True)
        )
      )
    )
    (var_enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=1024, out_features=10, bias=True)
        )
      )
    )
  )
  (decoder): NN(
    (net): ModuleList(
      (0): Block(
        (fc): Linear(in_features=10, out_features=30076, bias=True)
        (norm): DSBatchNorm(
          (bns): ModuleList(
            (0): BatchNorm1d(30076, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (1): BatchNorm1d(30076, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
          )
        )
        (act): Sigmoid()
      )
    )
  )
)
Epochs: 100%|| 141/141 [10:53<00:00,  4.63s/it, recon_loss=992.783,kl_loss=3.643]
2021-03-30 20:33:17,866 - root - INFO - Output dir: ATAC_output//
2021-03-30 20:33:22,489 - root - INFO - Plot umap
```

```
computing neighbors
    finished: added to `.uns['neighbors']`
```

(continues on next page)

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```
    `.obsp['distances']`, distances for each pair of neighbors
    `.obsp['connectivities']`, weighted adjacency matrix (0:00:03)
computing UMAP
    finished: added
    'X_umap', UMAP coordinates (adata.obsm) (0:00:09)
running Leiden clustering
    finished: found 16 clusters and added
    'leiden', the cluster labels (adata.obs, categorical) (0:00:01)
WARNING: saving figure to file ATAC_output/umap.pdf
```

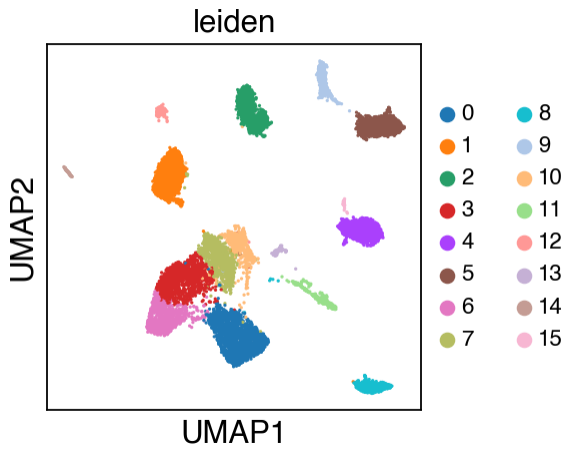
[13]:
```
adata
```

[13]:
```
AnnData object with n_obs × n_vars = 13746 × 30076
    obs: 'batch', 'n_genes', 'leiden'
    var: 'n_cells', 'prop_shared_cells', 'variability_score'
    uns: 'neighbors', 'umap', 'leiden', 'batch_colors', 'leiden_colors'
    obsm: 'latent', 'X_umap'
    obsp: 'distances', 'connectivities'
```

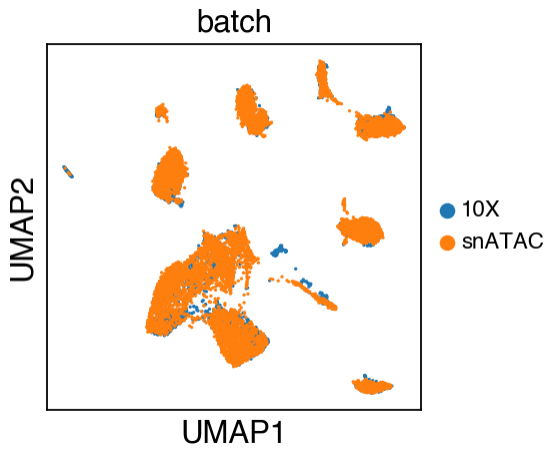
While there seems to be some strong batch-effect in all cell types, SCALEX can integrate them homogeneously.

[14]:
```
sc.settings.set_figure_params(dpi=80, facecolor='white',figsize=(3,3),frameon=True)
```

[15]:
```
sc.pl.umap(adata,color=['leiden'],legend_fontsize=10)
```




[16]:
```
sc.pl.umap(adata,color=['batch'],legend_fontsize=10)
```




The integrated data is stored as `adata.h5ad` in the output directory assigned by `outdir` parameter in SCALE function.

### 1.7.4 Integration cross-modality data using SCALEX

The following tutorial demonstrates how to use SCALEX for *integrating* scRNA-seq and scATAC-seq data

There are mainly two steps:

- **Create a gene activity matrix from scATAC-seq data.** This step follows the standard workflow of Signac for scATAC-seq data analysis. We uses the function GeneActivity of Signac and calculate the activity of each gene in the genome by assessing the chromatin accessibility associated with each gene, and create a new gene activity matrix derived from the scATAC-seq data. More details are here.
- **Integrate.** We regard gene expression matrix and gene activity matrix as two batches of one dataset and use SCALEX for integration.

For this tutorial, we used a cross-modality PBMC data between scRNA-seq and scATAC-seq provided by 10X Genomics, and both scRNA-seq and scATAC-seq data are available through the 10x Genomics website.

#### Create a gene activity matrix (R)

[1]:
```
suppressPackageStartupMessages(library(Signac))
suppressPackageStartupMessages(library(Seurat))
suppressPackageStartupMessages(library(GenomeInfoDb))
suppressPackageStartupMessages(library(EnsDb.Hsapiens.v75))
suppressPackageStartupMessages(library(ggplot2))
suppressPackageStartupMessages(library(patchwork))
set.seed(1234)
options(warn=-1)
```

### Pre-processing

We follow the pre-processing workflow of Signac when pre-processing chromatin data. First we creat a Seurat object by two related input files: cell matrix and fragment file.

[2]:
```
counts <- Read10X_h5(filename = "atac_v1_pbmc_10k_filtered_peak_bc_matrix.h5")
metadata <- read.csv(
  file = "atac_v1_pbmc_10k_singlecell.csv",
  header = TRUE,
  row.names = 1
)

chrom_assay <- CreateChromatinAssay(
  counts = counts,
  sep = c(":", "-"),
  genome = 'hg19',
  fragments = 'atac_v1_pbmc_10k_fragments.tsv.gz',
  min.cells = 10,
  min.features = 200
)

pbmc <- CreateSeuratObject(
  counts = chrom_assay,
  assay = "peaks",
  meta.data = metadata
)
```

```
Computing hash
```

Now add gene annotations to the pbmc object for the human genome. genome is suggested to be as same as the genome for scRNA-seq reads mapping on.

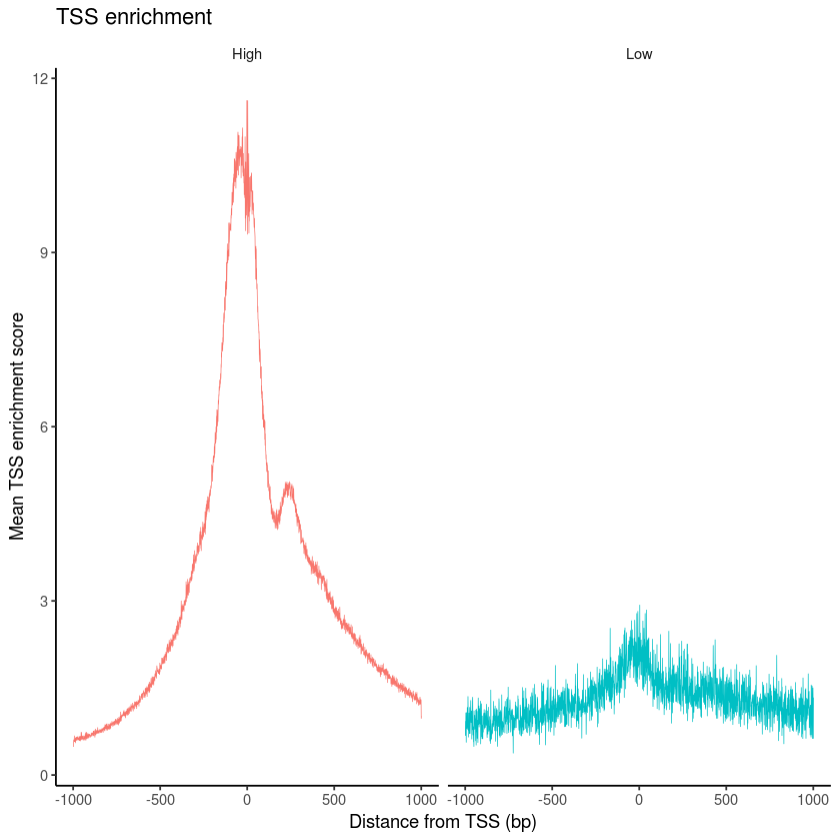
[4]:
```
# extract gene annotations from EnsDb
annotations <- GetGRangesFromEnsDb(ensdb = EnsDb.Hsapiens.v75)

# change to UCSC style since the data was mapped to hg19
seqlevelsStyle(annotations) <- 'UCSC'
genome(annotations) <- "hg19"

# add the gene information to the object
Annotation(pbmc) <- annotations
```

Compute QC Metrics. If you don't need to filter cells, ignore this step

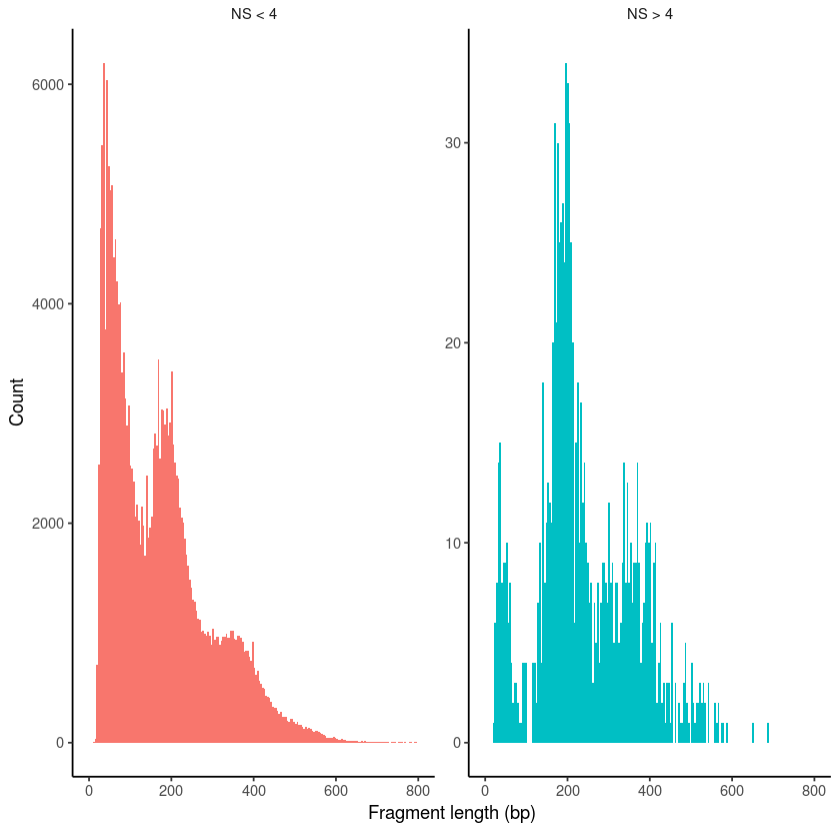
[13]:
```
# compute nucleosome signal score per cell
pbmc <- NucleosomeSignal(object = pbmc)

# compute TSS enrichment score per cell
pbmc <- TSSEnrichment(object = pbmc, fast = FALSE)

# add blacklist ratio and fraction of reads in peaks
pbmc$pct_reads_in_peaks <- pbmc$peak_region_fragments / pbmc$passed_filters * 100
pbmc$blacklist_ratio <- pbmc$blacklist_region_fragments / pbmc$peak_region_fragments
```

```
Extracting TSS positions

Finding + strand cut sites

Finding - strand cut sites

Computing mean insertion frequency in flanking regions

Normalizing TSS score
```

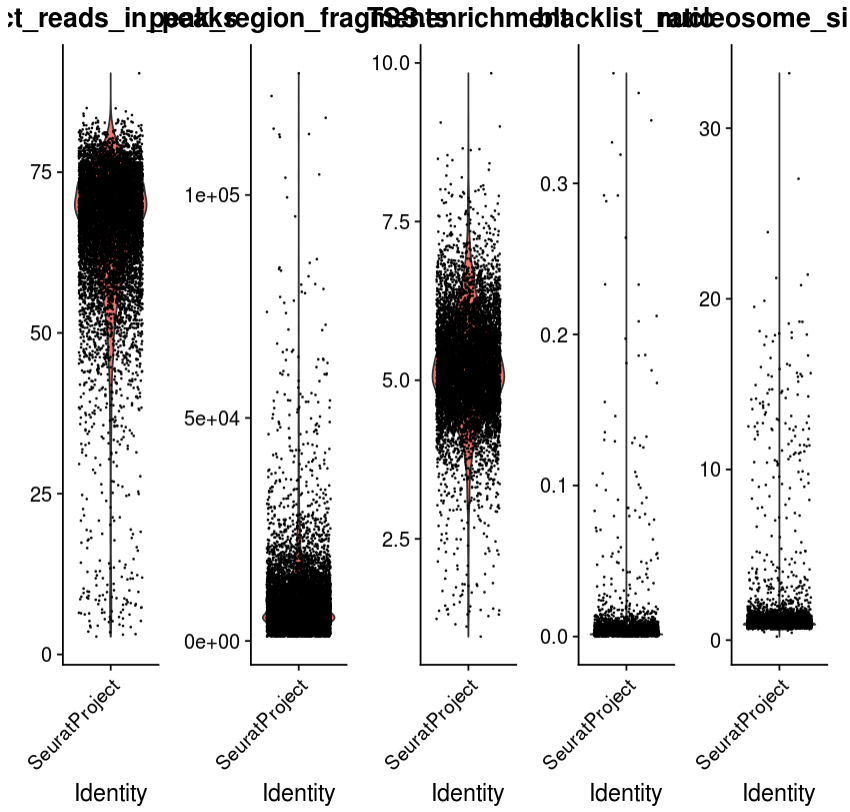
[14]:
```
pbmc$high.tss <- ifelse(pbmc$TSS.enrichment > 2, 'High', 'Low')
TSSPlot(pbmc, group.by = 'high.tss') + NoLegend()
```




[15]:
```
pbmc$nucleosome_group <- ifelse(pbmc$nucleosome_signal > 4, 'NS > 4', 'NS < 4')
FragmentHistogram(object = pbmc, group.by = 'nucleosome_group')
```




[16]:
```
VlnPlot(
  object = pbmc,
  features = c('pct_reads_in_peaks', 'peak_region_fragments',
               'TSS.enrichment', 'blacklist_ratio', 'nucleosome_signal'),
  pt.size = 0.1,
  ncol = 5
)
```




Filter cells that are outliers for the QC metrics.

[17]:
```
pbmc <- subset(
  x = pbmc,
  subset = peak_region_fragments > 3000 &
    peak_region_fragments < 20000 &
    pct_reads_in_peaks > 15 &
    blacklist_ratio < 0.05 &
    nucleosome_signal < 4 &
    TSS.enrichment > 2
)
pbmc
```

```
An object of class Seurat
87561 features across 7060 samples within 1 assay
Active assay: peaks (87561 features, 0 variable features)
```

### Calculate gene activity matrix by GeneActivity() function

[5]:
```
gene.activities <- GeneActivity(pbmc)
```

```
Extracting gene coordinates

Extracting reads overlapping genomic regions
```

save results

[ ]:
```
wk_dir <- './'
```

[2]:
```
write.table(t(gene.activities), paste(wk_dir,"gene_activity_score.txt",sep=''), sep='\t',
↪quote = F)
```

### Integrate (python)

Now you can use the gene_activity_score together with the gene expression matrix for integration.

You can run SCALE command line directly: SCALEX.py –data_list data1 data2 –batch_categories RNA ATAC -o output_path

- **data1:** path or file of scRNA-seq data
- **data2:** file of gene_activity_score

and here we show the results before integration and after integration.

[3]:
```
import scalex
from scalex import SCALEX
from scalex.plot import embedding
import scanpy as sc
import pandas as pd
import numpy as np
import matplotlib
from matplotlib import pyplot as plt
import seaborn as sns
```

[19]:
```
sc.settings.verbosity = 3
sc.settings.set_figure_params(dpi=80, facecolor='white',figsize=(3,3),frameon=True)
sc.logging.print_header()
plt.rcParams['axes.unicode_minus']=False
```

```
scanpy==1.7.0 anndata==0.7.5 umap==0.5.0 numpy==1.19.2 scipy==1.5.2 pandas==1.1.3 scikit-
↪learn==0.23.2 statsmodels==0.12.0 python-igraph==0.9.0 leidenalg==0.8.3
```

[3]:
```
scalex.__version__
```

[3]:
```
'2.0.3.dev'
```

First we merge the RNA and ATAC data and add metadata information, and this processed data is available here

[ ]:
```
wk_dir = './'
```

[10]:
```
adata = sc.read_h5ad(wk_dir+'pbmc_RNA-ATAC.h5ad')
```

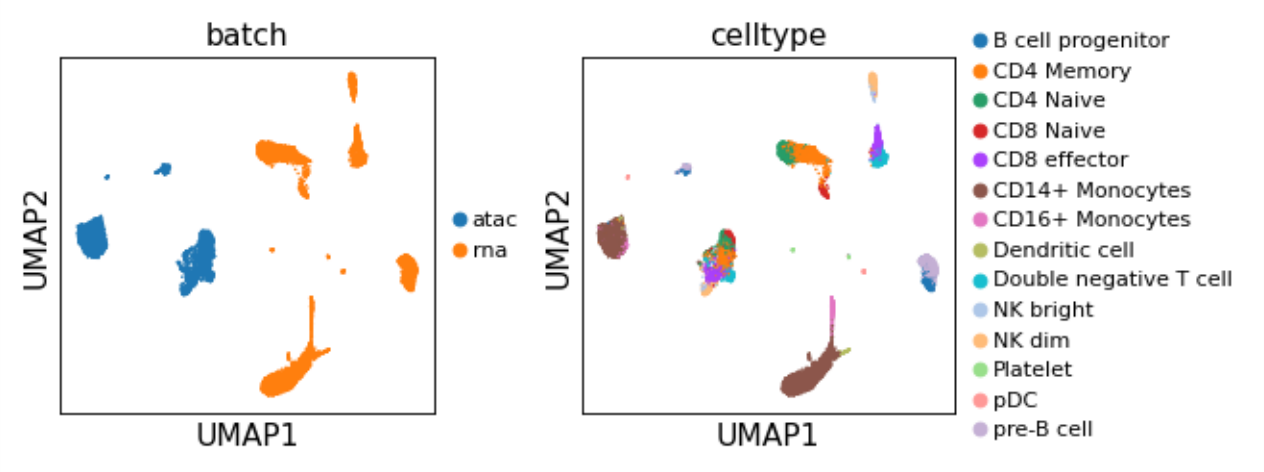
[11]:
```
adata
```

[11]:
```
AnnData object with n_obs × n_vars = 16492 × 13928
    obs: 'celltype', 'tech', 'batch'
```

[12]:
```
sc.pp.filter_cells(adata, min_genes=0)
sc.pp.filter_genes(adata, min_cells=0)

sc.pp.normalize_total(adata, inplace=True)
sc.pp.log1p(adata)
sc.pp.highly_variable_genes(adata, n_top_genes=2000)
adata = adata[:, adata.var.highly_variable]

sc.pp.scale(adata, max_value=10)
sc.tl.pca(adata)
sc.pp.neighbors(adata, n_pcs=30, n_neighbors=30)
sc.tl.umap(adata, min_dist=0.1)
```

```
normalizing counts per cell
    finished (0:00:00)
If you pass `n_top_genes`, all cutoffs are ignored.
extracting highly variable genes
    finished (0:00:01)
--> added
    'highly_variable', boolean vector (adata.var)
    'means', float vector (adata.var)
    'dispersions', float vector (adata.var)
    'dispersions_norm', float vector (adata.var)
... as `zero_center=True`, sparse input is densified and may lead to large memory␣
↪consumption
computing PCA
    on highly variable genes
    with n_comps=50
    finished (0:00:02)
computing neighbors
    using 'X_pca' with n_pcs = 30
    finished: added to `.uns['neighbors']`
    `.obsp['distances']`, distances for each pair of neighbors
    `.obsp['connectivities']`, weighted adjacency matrix (0:00:14)
computing UMAP
    finished: added
    'X_umap', UMAP coordinates (adata.obsm) (0:00:29)
```

[15]:
```
sc.pl.umap(adata,color=['batch','celltype'],legend_fontsize=10, ncols=2)
```




[16]:
```
wk_dir='./' # wk_dir is your local path to store data and results
```

[17]:
```
adata = SCALEX(data_list = [wk_dir+'RNA-ATAC.h5ad'],
               min_features=0,
               min_cells=0,
               outdir=wk_dir+'/pbmc_RNA_ATAC/',
               show=False,
               gpu=7)
```

```
2021-03-26 11:46:17,234 - root - INFO - Raw dataset shape: (16492, 13928)
2021-03-26 11:46:17,237 - root - INFO - Preprocessing
2021-03-26 11:46:17,260 - root - INFO - Filtering cells
Trying to set attribute `.obs` of view, copying.
2021-03-26 11:46:21,627 - root - INFO - Filtering features
2021-03-26 11:46:24,745 - root - INFO - Normalizing total per cell
normalizing counts per cell
    finished (0:00:00)
2021-03-26 11:46:25,022 - root - INFO - Log1p transforming
2021-03-26 11:46:26,014 - root - INFO - Finding variable features
If you pass `n_top_genes`, all cutoffs are ignored.
extracting highly variable genes
    finished (0:00:03)
--> added
    'highly_variable', boolean vector (adata.var)
    'means', float vector (adata.var)
    'dispersions', float vector (adata.var)
    'dispersions_norm', float vector (adata.var)
2021-03-26 11:46:30,637 - root - INFO - Batch specific maxabs scaling
2021-03-26 11:46:32,857 - root - INFO - Processed dataset shape: (16492, 2000)
2021-03-26 11:46:32,908 - root - INFO - model
VAE(
  (encoder): Encoder(
    (enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=2000, out_features=1024, bias=True)
          (norm): BatchNorm1d(1024, eps=1e-05, momentum=0.1, affine=True, track_running_
```

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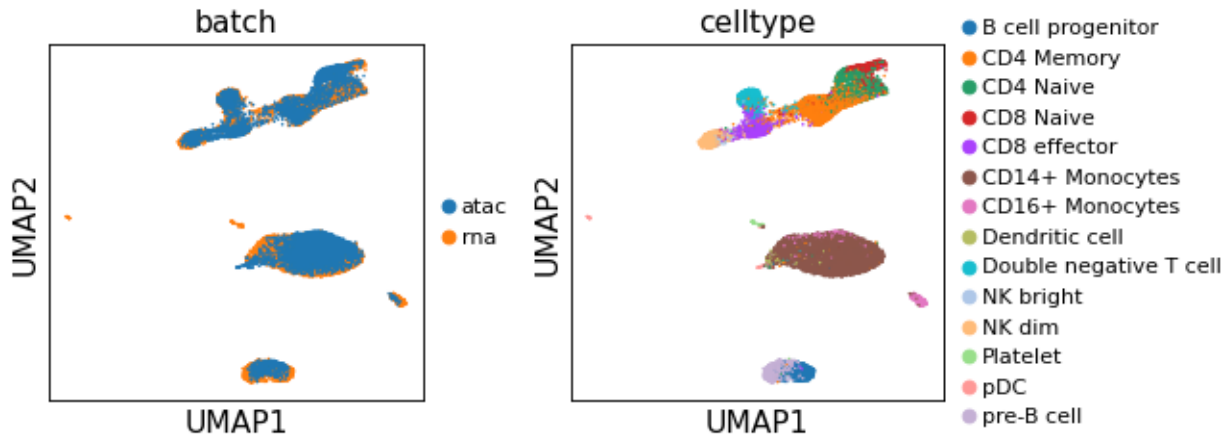
```
↪stats=True)
          (act): ReLU()
        )
      )
    )
    (mu_enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=1024, out_features=10, bias=True)
        )
      )
    )
    (var_enc): NN(
      (net): ModuleList(
        (0): Block(
          (fc): Linear(in_features=1024, out_features=10, bias=True)
        )
      )
    )
  )
  (decoder): NN(
    (net): ModuleList(
      (0): Block(
        (fc): Linear(in_features=10, out_features=2000, bias=True)
        (norm): DSBatchNorm(
          (bns): ModuleList(
            (0): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
            (1): BatchNorm1d(2000, eps=1e-05, momentum=0.1, affine=True, track_running_
↪stats=True)
          )
        )
        (act): Sigmoid()
      )
    )
  )
)
Epochs: 100%|| 117/117 [06:54<00:00,  3.54s/it, recon_loss=274.876,kl_loss=2.892]
2021-03-26 11:53:35,672 - root - INFO - Output dir: .//pbmc_RNA_ATAC//
2021-03-26 11:53:45,553 - root - INFO - Plot umap
computing neighbors
    finished: added to `.uns['neighbors']`
    `.obsp['distances']`, distances for each pair of neighbors
    `.obsp['connectivities']`, weighted adjacency matrix (0:00:03)
computing UMAP
    finished: added
    'X_umap', UMAP coordinates (adata.obsm) (0:00:26)
running Leiden clustering
    finished: found 14 clusters and added
    'leiden', the cluster labels (adata.obs, categorical) (0:00:05)
WARNING: saving figure to file pbmc_RNA_ATAC/umap.pdf
```

[20]:
```
sc.pl.umap(adata,color=['batch','celltype'],legend_fontsize=10, ncols=2)
```




[ ]:

CHAPTER

TWO

# INSTALLATION

## 2.1 PyPI install

Pull SCALE from PyPI (consider using `pip3` to access Python 3):

```
pip install scalex
```

## 2.2 Pytorch

If you have cuda devices, consider install Pytorch cuda version.:

```
conda install pytorch torchvision torchaudio -c pytorch
```

## 2.3 Troubleshooting

## 2.4 Anaconda

If you do not have a working installation of Python 3.6 (or later), consider installing Miniconda (see *Installing Miniconda*).

## 2.5 Installing Miniconda

After downloading Miniconda, in a unix shell (Linux, Mac), run

```
cd DOWNLOAD_DIR
chmod +x Miniconda3-latest-VERSION.sh
./Miniconda3-latest-VERSION.sh
```

and accept all suggestions. Either reopen a new terminal or *source ~/.bashrc* on Linux/ *source ~/.bash_profile* on Mac. The whole process takes just a couple of minutes.

CHAPTER

THREE

# USAGE

SCALEX provide both commanline tool and api function used in jupyter notebook

## 3.1 Command line

Run SCALEX after installation:

```
SCALEX.py --data_list data1 data2 --batch_categories batch_name1 batch_name2
```

`data_list`: data path of each batch of single-cell dataset

`batch_categories`: name of each batch, batch_categories will range from 0 to N if not specified

### 3.1.1 Input

Input can be one of following:

- single file of format h5ad, csv, txt, mtx or their compression file
- multiple files of above format

---

**Note:** h5ad file input

---

- SCALEX will use the `batch` column in the obs of adata format read from h5ad file as batch information
- Users can specify any columns in the obs with option: `--batch_name` name
- If multiple inputs are given, SCALEX can take each file as individual batch by default, and overload previous batch information, users can change the concat name via option `--batch_key` other_name

### 3.1.2 Output

Output will be saved in the output folder including:

- **checkpoint**: saved model to reproduce results cooperated with option `--checkpoint` or -c
- **adata.h5ad**: preprocessed data and results including, latent, clustering and imputation
- **umap.png**: UMAP visualization of latent representations of cells
- **log.txt**: log file of training process

### 3.1.3 Useful options

- output folder for saveing results: [-o] or [–outdir]
- filter rare genes, default 3: [–min_cell]
- filter low quality cells, default 600: [–min_gene]
- select the number of highly variable genes, keep all genes with -1, default 2000: [–n_top_genes]

### 3.1.4 Help

Look for more usage of SCALEX:

```
SCALEX.py --help
```

## 3.2 API function

Use SCALEX in jupyter notebook:

```
from scalex.function import SCALEX
adata = SCALEX(data_list, batch_categories)
```

**or**

adata = SCALEX([adata_1, adata_2])

Function of parameters are similar to command line options. Input can be the files of adata or a list of AnnData or one concatenated AnnData Output is a Anndata object for further analysis with scanpy.

## 3.3 AnnData

SCALEX supports `scanpy` and `anndata`, which provides the `AnnData` class.

At the most basic level, an `AnnData` object *adata* stores a data matrix *adata.X*, annotation of observations *adata.obs* and variables *adata.var* as *pd.DataFrame* and unstructured annotation *adata.uns* as *dict*. Names of observations and variables can be accessed via *adata.obs_names* and *adata.var_names*, respectively. `AnnData` objects can be sliced like dataframes, for example, *adata_subset = adata[:, list_of_gene_names]*. For more, see this blog post.

To read a data file to an `AnnData` object, call:

```
import scanpy as sc
adata = sc.read(filename)
```

to initialize an `AnnData` object. Possibly add further annotation using, e.g., *pd.read_csv*:

```
import pandas as pd
anno = pd.read_csv(filename_sample_annotation)
adata.obs['cell_groups'] = anno['cell_groups']  # categorical annotation of type pandas.
↪Categorical
adata.obs['time'] = anno['time']                # numerical annotation of type float
```

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```
# alternatively, you could also set the whole dataframe
# adata.obs = anno
```

To write, use:

```
adata.write(filename)
adata.write_csvs(filename)
adata.write_loom(filename)
```

CHAPTER

# FOUR

# API

Import SCALEX:

```
import scalex
```

## 4.1 Function

| | |
|---|---|
| *SCALEX*([data_list, batch_categories, ...]) | Online single-cell data integration through projecting heterogeneous datasets into a common cell-embedding space |
| *label_transfer*(ref, query[, rep, label]) | Label transfer |

### 4.1.1 scalex.SCALEX

scalex.**SCALEX**(*data_list=None*, *batch_categories=None*, *profile='RNA'*, *batch_name='batch'*, *min_features=600*, *min_cells=3*, *target_sum=None*, *n_top_features=None*, *join='inner'*, *batch_key='batch'*, *processed=False*, *fraction=None*, *n_obs=None*, *use_layer='X'*, *backed=False*, *batch_size=64*, *lr=0.0002*, *max_iteration=30000*, *seed=124*, *gpu=0*, *outdir=None*, *projection=None*, *repeat=False*, *impute=None*, *chunk_size=20000*, *ignore_umap=False*, *verbose=False*, *assess=False*, *show=True*, *eval=False*, *num_workers=4*)

Online single-cell data integration through projecting heterogeneous datasets into a common cell-embedding space

**Parameters**

- **data_list** (Union[str, AnnData, List, None]) – A path list of AnnData matrices to concatenate with. Each matrix is referred to as a 'batch'.
- **batch_categories** (Optional[List]) – Categories for the batch annotation. By default, use increasing numbers.
- **profile** (str) – Specify the single-cell profile, RNA or ATAC. Default: RNA.
- **batch_name** (str) – Use this annotation in obs as batches for training model. Default: 'batch'.
- **min_features** (int) – Filtered out cells that are detected in less than min_features. Default: 600.
- **min_cells** (int) – Filtered out genes that are detected in less than min_cells. Default: 3.

- **n_top_features** (Optional[int]) – Number of highly-variable genes to keep. Default: 2000.
- **join** (str) – Use intersection ('inner') or union ('outer') of variables of different batches.
- **batch_key** (str) – Add the batch annotation to obs using this key. By default, batch_key='batch'.
- **batch_size** (int) – Number of samples per batch to load. Default: 64.
- **lr** (float) – Learning rate. Default: 2e-4.
- **max_iteration** (int) – Max iterations for training. Training one batch_size samples is one iteration. Default: 30000.
- **seed** (int) – Random seed for torch and numpy. Default: 124.
- **gpu** (int) – Index of GPU to use if GPU is available. Default: 0.
- **outdir** (Optional[str]) – Output directory. Default: 'output/'.
- **projection** (Optional[str]) – Use for new dataset projection. Input the folder containing the pre-trained model. If None, don't do projection. Default: None.
- **repeat** (bool) – Use with projection. If False, concatenate the reference and projection datasets for downstream analysis. If True, only use projection datasets. Default: False.
- **impute** (Optional[str]) – If True, calculate the imputed gene expression and store it at adata.layers['impute']. Default: False.
- **chunk_size** (int) – Number of samples from the same batch to transform. Default: 20000.
- **ignore_umap** (bool) – If True, do not perform UMAP for visualization and leiden for clustering. Default: False.
- **verbose** (bool) – Verbosity, True or False. Default: False.
- **assess** (bool) – If True, calculate the entropy_batch_mixing score and silhouette score to evaluate integration results. Default: False.

**Return type**
AnnData

**Returns**

- *The output folder contains*
- *adata.h5ad* – The AnnData matrice after batch effects removal. The low-dimensional representation of the data is stored at adata.obsm['latent'].
- *checkpoint* – model.pt contains the variables of the model and config.pt contains the parameters of the model.
- *log.txt* – Records raw data information, filter conditions, model parameters etc.
- *umap.pdf* – UMAP plot for visualization.

### 4.1.2 scalex.label_transfer

scalex.**label_transfer**(*ref*, *query*, *rep='latent'*, *label='celltype'*)

Label transfer

**Parameters**

- **ref** – reference containing the projected representations and labels
- **query** – query data to transfer label
- **rep** – representations to train the classifier. Default is *latent*
- **label** – label name. Defautl is *celltype* stored in ref.obs

**Return type**
transfered label

## 4.2 Data

### 4.2.1 Load data

| | |
|---|---|
| *data.load_data*(data_list[, ...]) | Load dataset with preprocessing |
| *data.concat_data*(data_list[, ...]) | Concatenate multiple datasets along the observations axis with name batch_key. |
| *data.load_files*(root) | Load single cell dataset from files |
| *data.load_file*(path[, backed]) | Load single cell dataset from file |
| *data.read_mtx*(path) | Read mtx format data folder including: |

#### scalex.data.load_data

scalex.data.**load_data**(*data_list*, *batch_categories=None*, *profile='RNA'*, *join='inner'*, *batch_key='batch'*, *batch_name='batch'*, *min_features=600*, *min_cells=3*, *target_sum=None*, *n_top_features=None*, *backed=False*, *batch_size=64*, *chunk_size=20000*, *fraction=None*, *n_obs=None*, *processed=False*, *log=None*, *num_workers=4*, *use_layer='X'*)

Load dataset with preprocessing

**Parameters**

- **data_list** – A path list of AnnData matrices to concatenate with. Each matrix is referred to as a 'batch'.
- **batch_categories** – Categories for the batch annotation. By default, use increasing numbers.
- **join** – Use intersection ('inner') or union ('outer') of variables of different batches. Default: 'inner'.
- **batch_key** – Add the batch annotation to obs using this key. Default: 'batch'.
- **batch_name** – Use this annotation in obs as batches for training model. Default: 'batch'.
- **min_features** – Filtered out cells that are detected in less than min_features. Default: 600.
- **min_cells** – Filtered out genes that are detected in less than min_cells. Default: 3.

- **n_top_features** – Number of highly-variable genes to keep. Default: 2000.
- **batch_size** – Number of samples per batch to load. Default: 64.
- **chunk_size** – Number of samples from the same batch to transform. Default: 20000.
- **log** – If log, record each operation in the log file. Default: None.

**Returns**

- *adata* – The AnnData object after combination and preprocessing.
- *trainloader* – An iterable over the given dataset for training.
- *testloader* – An iterable over the given dataset for testing

### scalex.data.concat_data

scalex.data.**concat_data**(*data_list*, *batch_categories=None*, *join='inner'*, *batch_key='batch'*, *index_unique=None*, *save=None*)

Concatenate multiple datasets along the observations axis with name `batch_key`.

**Parameters**

- **data_list** – A path list of AnnData matrices to concatenate with. Each matrix is referred to as a "batch".
- **batch_categories** – Categories for the batch annotation. By default, use increasing numbers.
- **join** – Use intersection ('inner') or union ('outer') of variables of different batches. Default: 'inner'.
- **batch_key** – Add the batch annotation to obs using this key. Default: 'batch'.
- **index_unique** – Make the index unique by joining the existing index names with the batch category, using index_unique='-', for instance. Provide None to keep existing indices.
- **save** – Path to save the new merged AnnData. Default: None.

**Return type**
New merged AnnData.

### scalex.data.load_files

scalex.data.**load_files**(*root*)

Load single cell dataset from files

**Parameters**
**root** – the root store the single-cell data files, each file represent one dataset

**Return type**
AnnData

### scalex.data.load_file

scalex.data.**load_file**(*path*, *backed=True*)

Load single cell dataset from file

**Parameters**
**path** – the path store the file

**Return type**
AnnData

### scalex.data.read_mtx

scalex.data.**read_mtx**(*path*)

Read mtx format data folder including:

- matrix file: e.g. count.mtx or matrix.mtx or their gz format
- barcode file: e.g. barcode.txt
- feature file: e.g. feature.txt

**Parameters**
**path** – the path store the mtx files

**Return type**
AnnData

## 4.2.2 Preprocessing

| | |
|---|---|
| *data.preprocessing*(adata[, profile, ...]) | Preprocessing single-cell data |
| *data.preprocessing_rna*(adata[, ...]) | Preprocessing single-cell RNA-seq data |
| *data.preprocessing_atac*(adata[, ...]) | Preprocessing single-cell ATAC-seq |
| *data.batch_scale*(adata[, chunk_size]) | Batch-specific scale data |
| *data.reindex*(adata, genes[, chunk_size]) | Reindex AnnData with gene list |

### scalex.data.preprocessing

scalex.data.**preprocessing**(*adata*, *profile='RNA'*, *min_features=600*, *min_cells=3*, *target_sum=None*, *n_top_features=None*, *backed=False*, *chunk_size=20000*, *log=None*)

Preprocessing single-cell data

**Parameters**

- **adata** (AnnData) – An AnnData matrice of shape n_obs x n_vars. Rows correspond to cells and columns to genes.
- **profile** (str) – Specify the single-cell profile type, RNA or ATAC, Default: RNA.
- **min_features** (int) – Filtered out cells that are detected in less than n genes. Default: 100.
- **min_cells** (int) – Filtered out genes that are detected in less than n cells. Default: 3.
- **target_sum** (Optional[int]) – After normalization, each cell has a total count equal to target_sum. If None, total count of each cell equal to the median of total counts for cells before normalization.

- **n_top_features** – Number of highly-variable genes to keep. Default: 2000.
- **chunk_size** (int) – Number of samples from the same batch to transform. Default: 20000.
- **log** – If log, record each operation in the log file. Default: None.

**Return type**
The AnnData object after preprocessing.

### scalex.data.preprocessing_rna

scalex.data.**preprocessing_rna**(*adata*, *min_features=600*, *min_cells=3*, *target_sum=10000*, *n_top_features=2000*, *chunk_size=20000*, *backed=False*, *log=None*)

Preprocessing single-cell RNA-seq data

**Parameters**

- **adata** (AnnData) – An AnnData matrice of shape n_obs x n_vars. Rows correspond to cells and columns to genes.
- **min_features** (int) – Filtered out cells that are detected in less than n genes. Default: 600.
- **min_cells** (int) – Filtered out genes that are detected in less than n cells. Default: 3.
- **target_sum** (int) – After normalization, each cell has a total count equal to target_sum. If None, total count of each cell equal to the median of total counts for cells before normalization.
- **n_top_features** – Number of highly-variable genes to keep. Default: 2000.
- **chunk_size** (int) – Number of samples from the same batch to transform. Default: 20000.
- **log** – If log, record each operation in the log file. Default: None.

**Return type**
The AnnData object after preprocessing.

### scalex.data.preprocessing_atac

scalex.data.**preprocessing_atac**(*adata*, *min_features=100*, *min_cells=3*, *target_sum=None*, *n_top_features=100000*, *chunk_size=20000*, *backed=False*, *log=None*)

Preprocessing single-cell ATAC-seq

**Parameters**

- **adata** (AnnData) – An AnnData matrice of shape n_obs x n_vars. Rows correspond to cells and columns to genes.
- **min_features** (int) – Filtered out cells that are detected in less than n genes. Default: 100.
- **min_cells** (int) – Filtered out genes that are detected in less than n cells. Default: 3.
- **target_sum** – After normalization, each cell has a total count equal to target_sum. If None, total count of each cell equal to the median of total counts for cells before normalization. Default: None.
- **n_top_features** – Number of highly-variable features to keep. Default: 30000.
- **chunk_size** (int) – Number of samples from the same batch to transform. Default: 20000.
- **log** – If log, record each operation in the log file. Default: None.

**Return type**
The AnnData object after preprocessing.

#### scalex.data.batch_scale

scalex.data.**batch_scale**(*adata*, *chunk_size=20000*)

Batch-specific scale data

**Parameters**

- **adata** – AnnData
- **chunk_size** – chunk large data into small chunks

**Return type**
AnnData

#### scalex.data.reindex

scalex.data.**reindex**(*adata*, *genes*, *chunk_size=20000*)

Reindex AnnData with gene list

**Parameters**

- **adata** – AnnData
- **genes** – gene list for indexing
- **chunk_size** – chunk large data into small chunks

**Return type**
AnnData

### 4.2.3 DataLoader

| | |
|---|---|
| *data.SingleCellDataset*(adata[, use_layer]) | Dataloader of single-cell data |
| *data.BatchSampler*(batch_size, batch_id[, ...]) | Batch-specific Sampler sampled data of each batch is from the same dataset. |

#### scalex.data.SingleCellDataset

**class** scalex.data.**SingleCellDataset**(*adata*, *use_layer='X'*)

Dataloader of single-cell data

**__init__**(*adata*, *use_layer='X'*)

create a SingleCellDataset object

**Parameters**
**adata** – AnnData object wrapping the single-cell data matrix

#### Methods

| | |
|---|---|
| *__init__*(adata[, use_layer]) | create a SingleCellDataset object |

### scalex.data.BatchSampler

**class** scalex.data.**BatchSampler**(*batch_size*, *batch_id*, *drop_last=False*)

Batch-specific Sampler sampled data of each batch is from the same dataset.

**__init__**(*batch_size*, *batch_id*, *drop_last=False*)

create a BatchSampler object

**Parameters**

- **batch_size** – batch size for each sampling
- **batch_id** – batch id of all samples
- **drop_last** – drop the last samples that not up to one batch

#### Methods

| | |
|---|---|
| *__init__*(batch_size, batch_id[, drop_last]) | create a BatchSampler object |

## 4.3 Net

### 4.3.1 Model

| | |
|---|---|
| *net.vae.VAE*(enc, dec[, n_domain]) | VAE framework |

### scalex.net.vae.VAE

**class** scalex.net.vae.**VAE**(*enc*, *dec*, *n_domain=1*)

VAE framework

**__init__**(*enc*, *dec*, *n_domain=1*)

**Parameters**

- **enc** – Encoder structure config
- **dec** – Decoder structure config
- **n_domain** – The number of different domains

### Methods

| | |
|---|---|
| *__init__*(enc, dec[, n_domain]) | **type enc** |
| add_module(name, module) | Adds a child module to the current module. |
| apply(fn) | Applies fn recursively to every submodule (as returned by .children()) as well as self. |
| bfloat16() | Casts all floating point parameters and buffers to bfloat16 datatype. |
| buffers([recurse]) | Returns an iterator over module buffers. |
| children() | Returns an iterator over immediate children modules. |
| cpu() | Moves all model parameters and buffers to the CPU. |
| cuda([device]) | Moves all model parameters and buffers to the GPU. |
| double() | Casts all floating point parameters and buffers to double datatype. |
| encodeBatch(dataloader[, device, out, ...]) | Inference |
| eval() | Sets the module in evaluation mode. |
| extra_repr() | Set the extra representation of the module |
| fit(dataloader[, lr, max_iteration, beta, ...]) | Fit model |
| float() | Casts all floating point parameters and buffers to float datatype. |
| forward(*input) | Defines the computation performed at every call. |
| get_buffer(target) | Returns the buffer given by target if it exists, otherwise throws an error. |
| get_extra_state() | Returns any extra state to include in the module's state_dict. |
| get_parameter(target) | Returns the parameter given by target if it exists, otherwise throws an error. |
| get_submodule(target) | Returns the submodule given by target if it exists, otherwise throws an error. |
| half() | Casts all floating point parameters and buffers to half datatype. |
| ipu([device]) | Moves all model parameters and buffers to the IPU. |
| load_model(path) | Load trained model parameters dictionary. |
| load_state_dict(state_dict[, strict]) | Copies parameters and buffers from state_dict into this module and its descendants. |
| modules() | Returns an iterator over all modules in the network. |
| named_buffers([prefix, recurse]) | Returns an iterator over module buffers, yielding both the name of the buffer as well as the buffer itself. |
| named_children() | Returns an iterator over immediate children modules, yielding both the name of the module as well as the module itself. |
| named_modules([memo, prefix, remove_duplicate]) | Returns an iterator over all modules in the network, yielding both the name of the module as well as the module itself. |
| named_parameters([prefix, recurse]) | Returns an iterator over module parameters, yielding both the name of the parameter as well as the parameter itself. |
| parameters([recurse]) | Returns an iterator over module parameters. |
| register_backward_hook(hook) | Registers a backward hook on the module. |

continues on next page

Table 1 – continued from previous page

| | |
|---|---|
| register_buffer(name, tensor[, persistent]) | Adds a buffer to the module. |
| register_forward_hook(hook) | Registers a forward hook on the module. |
| register_forward_pre_hook(hook) | Registers a forward pre-hook on the module. |
| register_full_backward_hook(hook) | Registers a backward hook on the module. |
| register_load_state_dict_post_hook(hook) | Registers a post hook to be run after module's load_state_dict is called. |
| register_module(name, module) | Alias for add_module(). |
| register_parameter(name, param) | Adds a parameter to the module. |
| requires_grad_([requires_grad]) | Change if autograd should record operations on parameters in this module. |
| set_extra_state(state) | This function is called from load_state_dict() to handle any extra state found within the *state_dict*. |
| share_memory() | See torch.Tensor.share_memory_() |
| state_dict(*args[, destination, prefix, ...]) | Returns a dictionary containing references to the whole state of the module. |
| to(*args, **kwargs) | Moves and/or casts the parameters and buffers. |
| to_empty(*, device) | Moves the parameters and buffers to the specified device without copying storage. |
| train([mode]) | Sets the module in training mode. |
| type(dst_type) | Casts all parameters and buffers to dst_type. |
| xpu([device]) | Moves all model parameters and buffers to the XPU. |
| zero_grad([set_to_none]) | Sets gradients of all model parameters to zero. |

#### Attributes

| | |
|---|---|
| T_destination | alias of TypeVar('T_destination', bound=Dict[str, Any]) |
| dump_patches | |

### 4.3.2 Layer

| | |
|---|---|
| *net.layer.DSBatchNorm*(num_features, n_domain) | Domain-specific Batch Normalization |
| *net.layer.Block*(input_dim, output_dim[, ...]) | Basic block consist of: |
| *net.layer.NN*(input_dim, cfg) | Neural network consist of multi Blocks |
| *net.layer.Encoder*(input_dim, cfg) | VAE Encoder |

#### scalex.net.layer.DSBatchNorm

**class** scalex.net.layer.**DSBatchNorm**(*num_features*, *n_domain*, *eps=1e-05*, *momentum=0.1*)

Domain-specific Batch Normalization

**__init__**(*num_features*, *n_domain*, *eps=1e-05*, *momentum=0.1*)

**Parameters**

- **num_features** – dimension of the features
- **n_domain** – domain number

### Methods

| | |
|---|---|
| *__init__*(num_features, n_domain[, eps, momentum]) | **type num_features** |
| add_module(name, module) | Adds a child module to the current module. |
| apply(fn) | Applies `fn` recursively to every submodule (as returned by `.children()`) as well as self. |
| bfloat16() | Casts all floating point parameters and buffers to `bfloat16` datatype. |
| buffers([recurse]) | Returns an iterator over module buffers. |
| children() | Returns an iterator over immediate children modules. |
| cpu() | Moves all model parameters and buffers to the CPU. |
| cuda([device]) | Moves all model parameters and buffers to the GPU. |
| double() | Casts all floating point parameters and buffers to `double` datatype. |
| eval() | Sets the module in evaluation mode. |
| extra_repr() | Set the extra representation of the module |
| float() | Casts all floating point parameters and buffers to `float` datatype. |
| forward(x, y) | Defines the computation performed at every call. |
| get_buffer(target) | Returns the buffer given by `target` if it exists, otherwise throws an error. |
| get_extra_state() | Returns any extra state to include in the module's state_dict. |
| get_parameter(target) | Returns the parameter given by `target` if it exists, otherwise throws an error. |
| get_submodule(target) | Returns the submodule given by `target` if it exists, otherwise throws an error. |
| half() | Casts all floating point parameters and buffers to `half` datatype. |
| ipu([device]) | Moves all model parameters and buffers to the IPU. |
| load_state_dict(state_dict[, strict]) | Copies parameters and buffers from `state_dict` into this module and its descendants. |
| modules() | Returns an iterator over all modules in the network. |
| named_buffers([prefix, recurse]) | Returns an iterator over module buffers, yielding both the name of the buffer as well as the buffer itself. |
| named_children() | Returns an iterator over immediate children modules, yielding both the name of the module as well as the module itself. |
| named_modules([memo, prefix, remove_duplicate]) | Returns an iterator over all modules in the network, yielding both the name of the module as well as the module itself. |
| named_parameters([prefix, recurse]) | Returns an iterator over module parameters, yielding both the name of the parameter as well as the parameter itself. |
| parameters([recurse]) | Returns an iterator over module parameters. |
| register_backward_hook(hook) | Registers a backward hook on the module. |
| register_buffer(name, tensor[, persistent]) | Adds a buffer to the module. |
| register_forward_hook(hook) | Registers a forward hook on the module. |
| register_forward_pre_hook(hook) | Registers a forward pre-hook on the module. |

continues on next page

Table 2 – continued from previous page

| | |
|---|---|
| register_full_backward_hook(hook) | Registers a backward hook on the module. |
| register_load_state_dict_post_hook(hook) | Registers a post hook to be run after module's load_state_dict is called. |
| register_module(name, module) | Alias for add_module(). |
| register_parameter(name, param) | Adds a parameter to the module. |
| requires_grad_([requires_grad]) | Change if autograd should record operations on parameters in this module. |
| reset_parameters() | |
| reset_running_stats() | |
| set_extra_state(state) | This function is called from load_state_dict() to handle any extra state found within the *state_dict*. |
| share_memory() | See torch.Tensor.share_memory_() |
| state_dict(*args[, destination, prefix, ...]) | Returns a dictionary containing references to the whole state of the module. |
| to(*args, **kwargs) | Moves and/or casts the parameters and buffers. |
| to_empty(*, device) | Moves the parameters and buffers to the specified device without copying storage. |
| train([mode]) | Sets the module in training mode. |
| type(dst_type) | Casts all parameters and buffers to dst_type. |
| xpu([device]) | Moves all model parameters and buffers to the XPU. |
| zero_grad([set_to_none]) | Sets gradients of all model parameters to zero. |

#### Attributes

| | |
|---|---|
| T_destination | alias of TypeVar('T_destination', bound=Dict[str, Any]) |
| dump_patches | |

### scalex.net.layer.Block

**class** scalex.net.layer.**Block**(*input_dim*, *output_dim*, *norm=''*, *act=''*, *dropout=0*)

**Basic block consist of:**

fc -> bn -> act -> dropout

**__init__**(*input_dim*, *output_dim*, *norm=''*, *act=''*, *dropout=0*)

**Parameters**

- **input_dim** – dimension of input
- **output_dim** – dimension of output
- **norm** –

  **batch normalization,**

  – '' represent no batch normalization

  – 1 represent regular batch normalization

- int>1 represent domain-specific batch normalization of n domain

- **act** –

  **activation function,**

  - relu -> nn.ReLU
  - rrelu -> nn.RReLU
  - sigmoid -> nn.Sigmoid()
  - leaky_relu -> nn.LeakyReLU()
  - tanh -> nn.Tanh()
  - ” -> None

- **dropout** – dropout rate

### Methods

| | |
|---|---|
| *__init__*(input_dim, output_dim[, norm, act, ...]) | **type input_dim** |
| add_module(name, module) | Adds a child module to the current module. |
| apply(fn) | Applies fn recursively to every submodule (as returned by .children()) as well as self. |
| bfloat16() | Casts all floating point parameters and buffers to bfloat16 datatype. |
| buffers([recurse]) | Returns an iterator over module buffers. |
| children() | Returns an iterator over immediate children modules. |
| cpu() | Moves all model parameters and buffers to the CPU. |
| cuda([device]) | Moves all model parameters and buffers to the GPU. |
| double() | Casts all floating point parameters and buffers to double datatype. |
| eval() | Sets the module in evaluation mode. |
| extra_repr() | Set the extra representation of the module |
| float() | Casts all floating point parameters and buffers to float datatype. |
| forward(x[, y]) | Defines the computation performed at every call. |
| get_buffer(target) | Returns the buffer given by target if it exists, otherwise throws an error. |
| get_extra_state() | Returns any extra state to include in the module's state_dict. |
| get_parameter(target) | Returns the parameter given by target if it exists, otherwise throws an error. |
| get_submodule(target) | Returns the submodule given by target if it exists, otherwise throws an error. |
| half() | Casts all floating point parameters and buffers to half datatype. |
| ipu([device]) | Moves all model parameters and buffers to the IPU. |
| load_state_dict(state_dict[, strict]) | Copies parameters and buffers from state_dict into this module and its descendants. |
| modules() | Returns an iterator over all modules in the network. |

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Table 3 – continued from previous page

| | |
|---|---|
| named_buffers([prefix, recurse]) | Returns an iterator over module buffers, yielding both the name of the buffer as well as the buffer itself. |
| named_children() | Returns an iterator over immediate children modules, yielding both the name of the module as well as the module itself. |
| named_modules([memo, prefix, remove_duplicate]) | Returns an iterator over all modules in the network, yielding both the name of the module as well as the module itself. |
| named_parameters([prefix, recurse]) | Returns an iterator over module parameters, yielding both the name of the parameter as well as the parameter itself. |
| parameters([recurse]) | Returns an iterator over module parameters. |
| register_backward_hook(hook) | Registers a backward hook on the module. |
| register_buffer(name, tensor[, persistent]) | Adds a buffer to the module. |
| register_forward_hook(hook) | Registers a forward hook on the module. |
| register_forward_pre_hook(hook) | Registers a forward pre-hook on the module. |
| register_full_backward_hook(hook) | Registers a backward hook on the module. |
| register_load_state_dict_post_hook(hook) | Registers a post hook to be run after module's load_state_dict is called. |
| register_module(name, module) | Alias for add_module(). |
| register_parameter(name, param) | Adds a parameter to the module. |
| requires_grad_([requires_grad]) | Change if autograd should record operations on parameters in this module. |
| set_extra_state(state) | This function is called from load_state_dict() to handle any extra state found within the *state_dict*. |
| share_memory() | See torch.Tensor.share_memory_() |
| state_dict(*args[, destination, prefix, ...]) | Returns a dictionary containing references to the whole state of the module. |
| to(*args, **kwargs) | Moves and/or casts the parameters and buffers. |
| to_empty(*, device) | Moves the parameters and buffers to the specified device without copying storage. |
| train([mode]) | Sets the module in training mode. |
| type(dst_type) | Casts all parameters and buffers to dst_type. |
| xpu([device]) | Moves all model parameters and buffers to the XPU. |
| zero_grad([set_to_none]) | Sets gradients of all model parameters to zero. |

### Attributes

| | |
|---|---|
| T_destination | alias of TypeVar('T_destination', bound=Dict[str, Any]) |
| dump_patches | |

### scalex.net.layer.NN

**class** scalex.net.layer.**NN**(*input_dim*, *cfg*)

Neural network consist of multi Blocks

**__init__**(*input_dim*, *cfg*)

**Parameters**

- **input_dim** – input dimension
- **cfg** – model structure configuration, 'fc' -> fully connected layer

#### Example

```
>>> latent_dim = 10
>>> dec_cfg = [['fc', x_dim, n_domain, 'sigmoid']]
>>> decoder = NN(latent_dim, dec_cfg)
```

#### Methods

| | |
|---|---|
| *__init__*(input_dim, cfg) | **type input_dim** |
| add_module(name, module) | Adds a child module to the current module. |
| apply(fn) | Applies fn recursively to every submodule (as returned by .children()) as well as self. |
| bfloat16() | Casts all floating point parameters and buffers to bfloat16 datatype. |
| buffers([recurse]) | Returns an iterator over module buffers. |
| children() | Returns an iterator over immediate children modules. |
| cpu() | Moves all model parameters and buffers to the CPU. |
| cuda([device]) | Moves all model parameters and buffers to the GPU. |
| double() | Casts all floating point parameters and buffers to double datatype. |
| eval() | Sets the module in evaluation mode. |
| extra_repr() | Set the extra representation of the module |
| float() | Casts all floating point parameters and buffers to float datatype. |
| forward(x[, y]) | Defines the computation performed at every call. |
| get_buffer(target) | Returns the buffer given by target if it exists, otherwise throws an error. |
| get_extra_state() | Returns any extra state to include in the module's state_dict. |
| get_parameter(target) | Returns the parameter given by target if it exists, otherwise throws an error. |
| get_submodule(target) | Returns the submodule given by target if it exists, otherwise throws an error. |
| half() | Casts all floating point parameters and buffers to half datatype. |
| ipu([device]) | Moves all model parameters and buffers to the IPU. |

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| | |
|---|---|
| load_state_dict(state_dict[, strict]) | Copies parameters and buffers from state_dict into this module and its descendants. |
| modules() | Returns an iterator over all modules in the network. |
| named_buffers([prefix, recurse]) | Returns an iterator over module buffers, yielding both the name of the buffer as well as the buffer itself. |
| named_children() | Returns an iterator over immediate children modules, yielding both the name of the module as well as the module itself. |
| named_modules([memo, prefix, remove_duplicate]) | Returns an iterator over all modules in the network, yielding both the name of the module as well as the module itself. |
| named_parameters([prefix, recurse]) | Returns an iterator over module parameters, yielding both the name of the parameter as well as the parameter itself. |
| parameters([recurse]) | Returns an iterator over module parameters. |
| register_backward_hook(hook) | Registers a backward hook on the module. |
| register_buffer(name, tensor[, persistent]) | Adds a buffer to the module. |
| register_forward_hook(hook) | Registers a forward hook on the module. |
| register_forward_pre_hook(hook) | Registers a forward pre-hook on the module. |
| register_full_backward_hook(hook) | Registers a backward hook on the module. |
| register_load_state_dict_post_hook(hook) | Registers a post hook to be run after module's load_state_dict is called. |
| register_module(name, module) | Alias for add_module(). |
| register_parameter(name, param) | Adds a parameter to the module. |
| requires_grad_([requires_grad]) | Change if autograd should record operations on parameters in this module. |
| set_extra_state(state) | This function is called from load_state_dict() to handle any extra state found within the *state_dict*. |
| share_memory() | See torch.Tensor.share_memory_() |
| state_dict(*args[, destination, prefix, ...]) | Returns a dictionary containing references to the whole state of the module. |
| to(*args, **kwargs) | Moves and/or casts the parameters and buffers. |
| to_empty(*, device) | Moves the parameters and buffers to the specified device without copying storage. |
| train([mode]) | Sets the module in training mode. |
| type(dst_type) | Casts all parameters and buffers to dst_type. |
| xpu([device]) | Moves all model parameters and buffers to the XPU. |
| zero_grad([set_to_none]) | Sets gradients of all model parameters to zero. |

### Attributes

| | |
|---|---|
| T_destination | alias of TypeVar('T_destination', bound=Dict[str, Any]) |
| dump_patches | |

### scalex.net.layer.Encoder

class scalex.net.layer.**Encoder**(*input_dim*, *cfg*)

VAE Encoder

**__init__**(*input_dim*, *cfg*)

**Parameters**

- **input_dim** – input dimension
- **cfg** – encoder configuration, e.g. enc_cfg = [[‘fc’, 1024, 1, ‘relu’],[‘fc’, 10, ‘’, ‘’]]

#### Methods

| | |
|---|---|
| *__init__*(input_dim, cfg) | **type input_dim** |
| add_module(name, module) | Adds a child module to the current module. |
| apply(fn) | Applies `fn` recursively to every submodule (as returned by `.children()`) as well as self. |
| bfloat16() | Casts all floating point parameters and buffers to `bfloat16` datatype. |
| buffers([recurse]) | Returns an iterator over module buffers. |
| children() | Returns an iterator over immediate children modules. |
| cpu() | Moves all model parameters and buffers to the CPU. |
| cuda([device]) | Moves all model parameters and buffers to the GPU. |
| double() | Casts all floating point parameters and buffers to `double` datatype. |
| eval() | Sets the module in evaluation mode. |
| extra_repr() | Set the extra representation of the module |
| float() | Casts all floating point parameters and buffers to `float` datatype. |
| forward(x[, y]) | |
| get_buffer(target) | Returns the buffer given by `target` if it exists, otherwise throws an error. |
| get_extra_state() | Returns any extra state to include in the module's state_dict. |
| get_parameter(target) | Returns the parameter given by `target` if it exists, otherwise throws an error. |
| get_submodule(target) | Returns the submodule given by `target` if it exists, otherwise throws an error. |
| half() | Casts all floating point parameters and buffers to `half` datatype. |
| ipu([device]) | Moves all model parameters and buffers to the IPU. |
| load_state_dict(state_dict[, strict]) | Copies parameters and buffers from `state_dict` into this module and its descendants. |
| modules() | Returns an iterator over all modules in the network. |
| named_buffers([prefix, recurse]) | Returns an iterator over module buffers, yielding both the name of the buffer as well as the buffer itself. |

continues on next page

Table 5 – continued from previous page

| | |
|---|---|
| named_children() | Returns an iterator over immediate children modules, yielding both the name of the module as well as the module itself. |
| named_modules([memo, prefix, remove_duplicate]) | Returns an iterator over all modules in the network, yielding both the name of the module as well as the module itself. |
| named_parameters([prefix, recurse]) | Returns an iterator over module parameters, yielding both the name of the parameter as well as the parameter itself. |
| parameters([recurse]) | Returns an iterator over module parameters. |
| register_backward_hook(hook) | Registers a backward hook on the module. |
| register_buffer(name, tensor[, persistent]) | Adds a buffer to the module. |
| register_forward_hook(hook) | Registers a forward hook on the module. |
| register_forward_pre_hook(hook) | Registers a forward pre-hook on the module. |
| register_full_backward_hook(hook) | Registers a backward hook on the module. |
| register_load_state_dict_post_hook(hook) | Registers a post hook to be run after module's load_state_dict is called. |
| register_module(name, module) | Alias for add_module(). |
| register_parameter(name, param) | Adds a parameter to the module. |
| reparameterize(mu, var) | |
| requires_grad_([requires_grad]) | Change if autograd should record operations on parameters in this module. |
| set_extra_state(state) | This function is called from load_state_dict() to handle any extra state found within the *state_dict*. |
| share_memory() | See torch.Tensor.share_memory_() |
| state_dict(*args[, destination, prefix, ...]) | Returns a dictionary containing references to the whole state of the module. |
| to(*args, **kwargs) | Moves and/or casts the parameters and buffers. |
| to_empty(*, device) | Moves the parameters and buffers to the specified device without copying storage. |
| train([mode]) | Sets the module in training mode. |
| type(dst_type) | Casts all parameters and buffers to dst_type. |
| xpu([device]) | Moves all model parameters and buffers to the XPU. |
| zero_grad([set_to_none]) | Sets gradients of all model parameters to zero. |

### Attributes

| | |
|---|---|
| T_destination | alias of TypeVar('T_destination', bound=Dict[str, Any]) |
| dump_patches | |

### 4.3.3 Loss

| | |
|---|---|
| *net.loss.kl_div*(mu, var) | |
| *net.loss.binary_cross_entropy*(recon_x, x) | |

#### scalex.net.loss.kl_div

scalex.net.loss.**kl_div**(*mu*, *var*)

#### scalex.net.loss.binary_cross_entropy

scalex.net.loss.**binary_cross_entropy**(*recon_x*, *x*)

### 4.3.4 Utils

| | |
|---|---|
| *net.utils.onehot*(y, n) | Make the input tensor one hot tensors |
| *net.utils.EarlyStopping*([patience, verbose, ...]) | Early stops the training if loss doesn't improve after a given patience. |

#### scalex.net.utils.onehot

scalex.net.utils.**onehot**(*y*, *n*)

Make the input tensor one hot tensors

**Parameters**

- **y** – input tensors
- **n** – number of classes

**Return type**
Tensor

#### scalex.net.utils.EarlyStopping

**class** scalex.net.utils.**EarlyStopping**(*patience=10*, *verbose=False*, *checkpoint_file=''*)

Early stops the training if loss doesn't improve after a given patience.

**__init__**(*patience=10*, *verbose=False*, *checkpoint_file=''*)

**Parameters**

- **patience** – How long to wait after last time loss improved. Default: 10
- **verbose** – If True, prints a message for each loss improvement. Default: False

#### Methods

| | |
|---|---|
| *__init__*([patience, verbose, checkpoint_file]) | **type patience** |
| save_checkpoint(loss, model) | Saves model when loss decrease. |

## 4.4 Plot

| | |
|---|---|
| *plot.embedding*(adata[, color, color_map, ...]) | plot separated embeddings with others as background |
| *plot.plot_meta*(adata[, use_rep, color, ...]) | Plot meta correlations among batches |
| *plot.plot_meta2*(adata[, use_rep, color, ...]) | Plot meta correlations between two batches |
| *plot.plot_confusion*(y, y_pred[, save, cmap]) | Plot confusion matrix |

### 4.4.1 scalex.plot.embedding

scalex.plot.**embedding**(*adata*, *color='celltype'*, *color_map=None*, *groupby='batch'*, *groups=None*, *cond2=None*, *v2=None*, *save=None*, *legend_loc='right margin'*, *legend_fontsize=None*, *legend_fontweight='bold'*, *sep='_'*, *basis='X_umap'*, *size=10*, *show=True*)

plot separated embeddings with others as background

**Parameters**

- **adata** – AnnData
- **color** – meta information to be shown
- **color_map** – specific color map
- **groupby** – condition which is based-on to separate
- **groups** – specific groups to be shown
- **cond2** – another targeted condition
- **v2** – another targeted values of another condition
- **basis** – embeddings used to visualize, default is X_umap for UMAP
- **size** – dot size on the embedding

### 4.4.2 scalex.plot.plot_meta

scalex.plot.**plot_meta**(*adata*, *use_rep=None*, *color='celltype'*, *batch='batch'*, *colors=None*, *cmap='Blues'*, *vmax=1*, *vmin=0*, *mask=True*, *annot=False*, *save=None*, *fontsize=8*)

Plot meta correlations among batches

**Parameters**

- **adata** – AnnData
- **use_rep** – the cell representations or embeddings used to calculate the correlations, default is *latent* generated by *SCALE v2*

- **batch** – the meta information based-on, default is batch
- **colors** – colors for each batch
- **cmap** – color map for information to be shown
- **vmax** – max value
- **vmin** – min value
- **mask** – value to be masked
- **annot** – show specific values
- **save** – save the figure
- **fontsize** – font size

### 4.4.3 scalex.plot.plot_meta2

scalex.plot.**plot_meta2**(*adata*, *use_rep='latent'*, *color='celltype'*, *batch='batch'*, *color_map=None*, *figsize=(10, 10)*, *cmap='Blues'*, *batches=None*, *annot=False*, *save=None*, *cbar=True*, *keep=False*, *fontsize=8*, *vmin=0*, *vmax=1*)

Plot meta correlations between two batches

**Parameters**

- **adata** – AnnData
- **use_rep** – the cell representations or embeddings used to calculate the correlations, default is *latent* generated by *SCALE v2*
- **batch** – the meta information based-on, default is batch
- **colors** – colors for each batch
- **cmap** – color map for information to be shown
- **vmax** – max value
- **vmin** – min value
- **mask** – value to be masked
- **annot** – show specific values
- **save** – save the figure
- **fontsize** – font size

### 4.4.4 scalex.plot.plot_confusion

scalex.plot.**plot_confusion**(*y*, *y_pred*, *save=None*, *cmap='Blues'*)

Plot confusion matrix

**Parameters**

- **y** – ground truth labels
- **y_pred** – predicted labels
- **save** – save the figure
- **cmap** – color map

**Returns**

- *F1 score*
- *NMI score*
- *ARI score*

## 4.5 Metric

Collections of useful measurements for evaluating results.

| | |
|---|---|
| *metrics.batch_entropy_mixing_score*(data, batches) | Calculate batch entropy mixing score |
| *metrics.silhouette_score*(X, labels, *[, ...]) | Compute the mean Silhouette Coefficient of all samples. |

### 4.5.1 scalex.metrics.batch_entropy_mixing_score

scalex.metrics.**batch_entropy_mixing_score**(*data*, *batches*, *n_neighbors=100*, *n_pools=100*, *n_samples_per_pool=100*)

Calculate batch entropy mixing score

#### Algorithm

- 1. Calculate the regional mixing entropies at the location of 100 randomly chosen cells from all batches
- 2. Define 100 nearest neighbors for each randomly chosen cell
- 3. Calculate the mean mixing entropy as the mean of the regional entropies
- 4. Repeat above procedure for 100 iterations with different randomly chosen cells.

**type data**
**param data**
np.array of shape nsamples x nfeatures.

**type batches**
**param batches**
batch labels of nsamples.

**type n_neighbors**
**param n_neighbors**
The number of nearest neighbors for each randomly chosen cell. By default, n_neighbors=100.

**type n_samples_per_pool**
**param n_samples_per_pool**
The number of randomly chosen cells from all batches per iteration. By default, n_samples_per_pool=100.

**type n_pools**
**param n_pools**
The number of iterations with different randomly chosen cells. By default, n_pools=100.

**rtype**
Batch entropy mixing score

### 4.5.2 scalex.metrics.silhouette_score

scalex.metrics.**silhouette_score**(*X*, *labels*, ***, *metric='euclidean'*, *sample_size=None*, *random_state=None*, ***kwds*)

Compute the mean Silhouette Coefficient of all samples.

The Silhouette Coefficient is calculated using the mean intra-cluster distance (`a`) and the mean nearest-cluster distance (`b`) for each sample. The Silhouette Coefficient for a sample is `(b - a) / max(a, b)`. To clarify, `b` is the distance between a sample and the nearest cluster that the sample is not a part of. Note that Silhouette Coefficient is only defined if number of labels is `2 <= n_labels <= n_samples - 1`.

This function returns the mean Silhouette Coefficient over all samples. To obtain the values for each sample, use `silhouette_samples()`.

The best value is 1 and the worst value is -1. Values near 0 indicate overlapping clusters. Negative values generally indicate that a sample has been assigned to the wrong cluster, as a different cluster is more similar.

Read more in the User Guide.

**Parameters**

- **X** (*array-like of shape (n_samples_a, n_samples_a) if metric == "precomputed" or (n_samples_a, n_features) otherwise*) – An array of pairwise distances between samples, or a feature array.
- **labels** (*array-like of shape (n_samples,)*) – Predicted labels for each sample.
- **metric** (*str or callable, default='euclidean'*) – The metric to use when calculating distance between instances in a feature array. If metric is a string, it must be one of the options allowed by `metrics.pairwise.pairwise_distances`. If `X` is the distance array itself, use `metric="precomputed"`.
- **sample_size** (*int, default=None*) – The size of the sample to use when computing the Silhouette Coefficient on a random subset of the data. If `sample_size is None`, no sampling is used.
- **random_state** (*int, RandomState instance or None, default=None*) – Determines random number generation for selecting a subset of samples. Used when `sample_size is not None`. Pass an int for reproducible results across multiple function calls. See Glossary.
- ****kwds** (*optional keyword parameters*) – Any further parameters are passed directly to the distance function. If using a scipy.spatial.distance metric, the parameters are still metric dependent. See the scipy docs for usage examples.

**Returns**

**silhouette** – Mean Silhouette Coefficient for all samples.

**Return type**

float

### References

## 4.6 Logger

| | |
|---|---|
| *logger.create_logger*([name, ch, fh, ...]) | |

### 4.6.1 scalex.logger.create_logger

scalex.logger.**create_logger**(*name=''*, *ch=True*, *fh=False*, *levelname=20*, *overwrite=False*)

CHAPTER

FIVE

# NEWS

SCALEX is online on Nature Communications 2022-10-17 SCALEX is available on bioRxiv 2021-04-09

CHAPTER

SIX

# RELEASE

## 6.1 Version 1.0

### 6.1.1 1.0.0 2022-08-29

Online single-cell data integration through projecting heterogeneous datasets into a common cell-embedding space

CHAPTER

SEVEN

# NEWS

SCALEX is online on Nature Communications 2022-10-17 SCALEX is available on bioRxiv 2021-04-09

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