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In-silico perturbation

Material

NCBI dataset: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE90546

Paper Adamson B, Norman TM, Jost M, Cho MY et al. A Multiplexed Single-Cell CRISPR Screening Platform Enables Systematic Dissection of the Unfolded Protein Response. Cell 2016 Dec 15;167(7):1867-1882.e21. PMID: 27984733

Methods

Training Process

All Catagory
{'3x_neg_ctrl_pMJ144-1',
'3x_neg_ctrl_pMJ144-2',
'ATF6_IRE1_pMJ152',
'ATF6_PERK_IRE1_pMJ158',

'ATF6_PERK_pMJ150',
'ATF6_only_pMJ145',
'IRE1_only_pMJ148',
'PERK_IRE1_pMJ154',
'PERK_only_pMJ146'}

Training Dataset
{'3x_neg_ctrl_pMJ144-1',
'ATF6_only_pMJ145',
'IRE1_only_pMJ148',
'PERK_only_pMJ146'}

Test Dataset
{'ATF6_IRE1_pMJ152',
'ATF6_PERK_IRE1_pMJ158',
'ATF6_PERK_pMJ150',
'PERK_IRE1_pMJ154',}

process the dataset

Use the original value of each type of cell type

```
def construct_test_dataset(cell_type):
    test_z_genes = adata[adata.obs['cell_type'].str.startswith(cell_type) ,:].X
    test_z =  adata[adata.obs['cell_type'].str.startswith(cell_type) ,tfs].X
    test_z_genes_mean_raw = np.mean(adata[adata.obs['cell_type'].str.startswith(cell_type) ,:].X
    return test_z_genes,test_z,test_z_genes_mean_raw
```

After get the prediction we used the mean value of original and predicted sc dastset to draw the plot.

The function for perturbation.

```
import matplotlib.pyplot as plt
def visualization(cell_type):
    _,test_z,test_z_genes_mean_raw = construct_test_dataset(cell_type)
    # plt.scatter(test_z_genes,pred.detach().numpy(),s=2)
    pred= model.tf12genes(torch.tensor(test_z))
    test_z_genes_mean_pred = np.mean(pred.detach().numpy(),axis=0)
    # plt.figure(1)
    plt.scatter(test_z_genes_mean_raw,test_z_genes_mean_pred,s=2)
def visualization_comparison_between_perturbation(cell_type1,cell_type2):
    _,test_z,test_z_genes_mean_raw = construct_test_dataset(cell_type1)
    _,_,test_z_genes_mean_raw2 = construct_test_dataset(cell_type2)
    # plt.scatter(test_z_genes,pred.detach().numpy(),s=2)
    pred= model.tf12genes(torch.tensor(test_z))
    test_z_genes_mean_pred = np.mean(pred.detach().numpy(),axis=0)
    # plt.figure(1)
    plt.scatter(test_z_genes_mean_raw2,test_z_genes_mean_raw,s=2)
```

Architecture

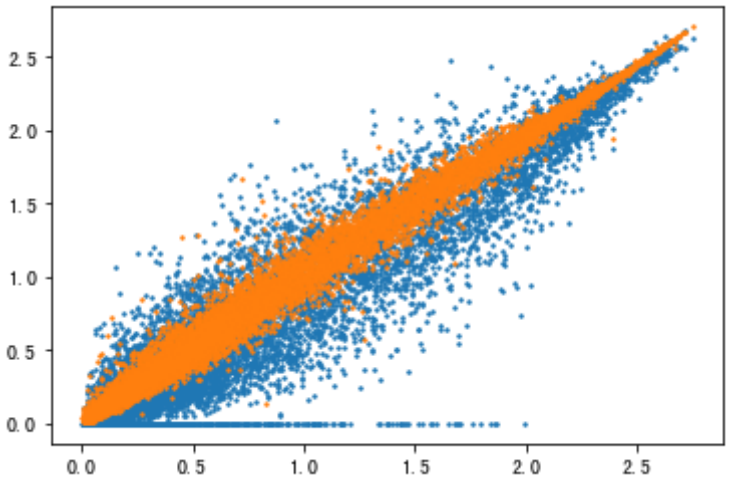
I got 2 layers of tf-layer, one is after the reparameterization, after the reparameterization there is a FCNN layer we construct another tf-layer, which shows after the preturbation how the tfs will be influenced.

Result Visualization

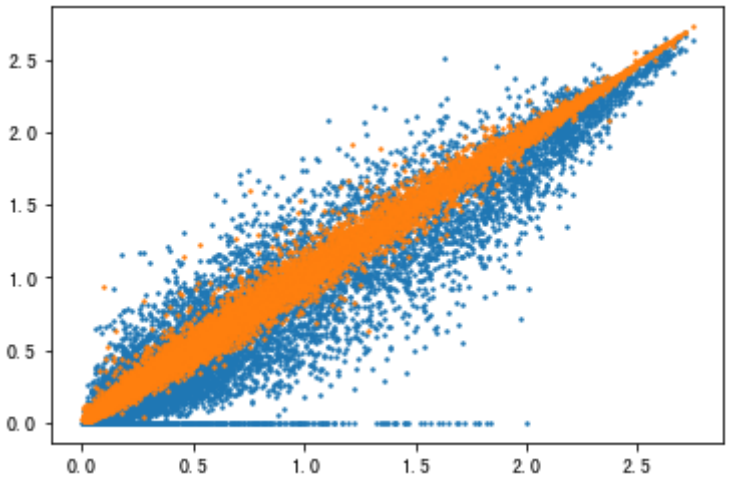
> Test Dataset
> {'ATF6_IRE1_pMJ152',
> 'ATF6_PERK_IRE1_pMJ158',
> 'ATF6_PERK_pMJ150',
> 'PERK_IRE1_pMJ154'}

We show the reconstruction of genes by transcription factors in an in-silico perturbation dataset. Two visualizations are included, one comparing predicted genes with real genes (blue), and the other comparing other processed genes with real genes (orange).

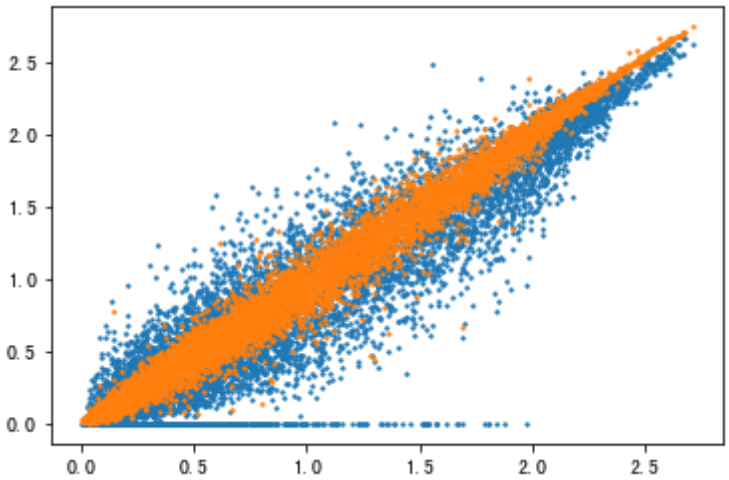
PERK_IRE1_pMJ154



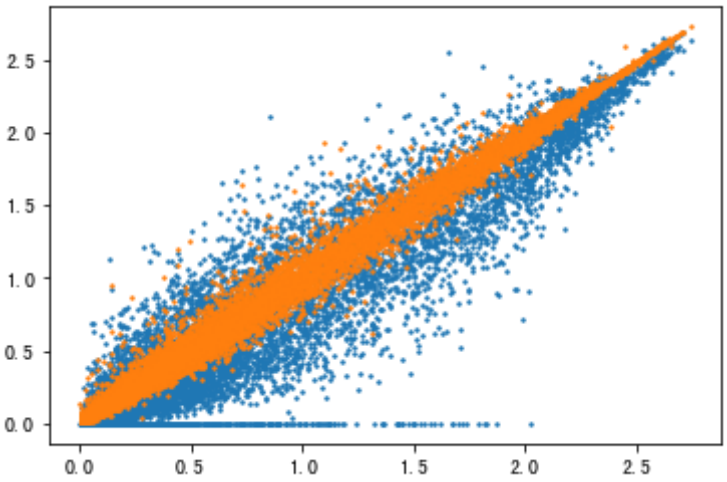
ATF6_PERK_pMJ150



ATF6_IRE1_pMJ152



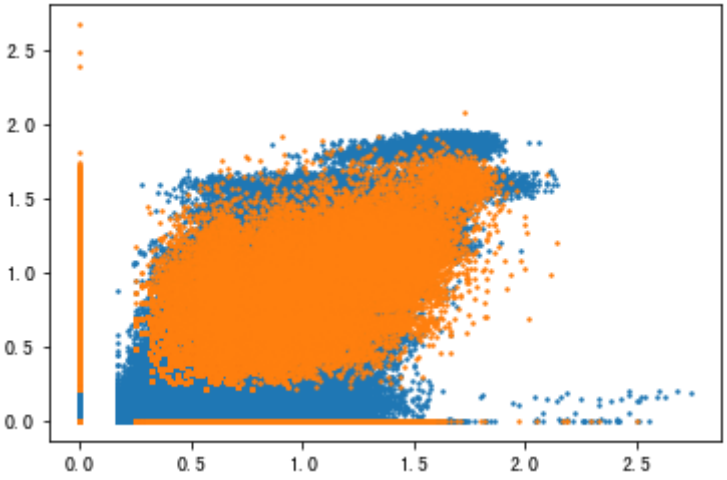
ATF6_PERK_IRE1_pMJ158



pbmc

I selected any two groups of PBMC for drawing. Due to the small number of PBMC genes, I randomly selected 1000 cells and plotted their expression.

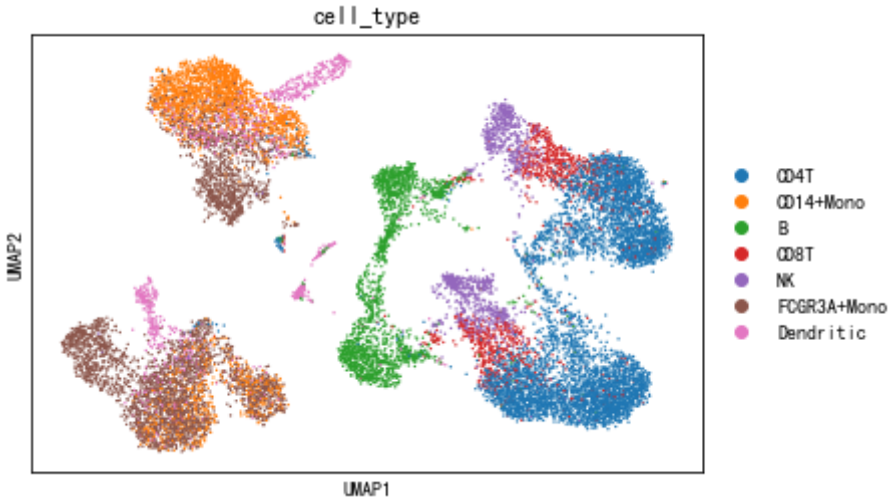
1000-cell *X AXIS* CD4T gene expression *Y AXIS* K gene expression



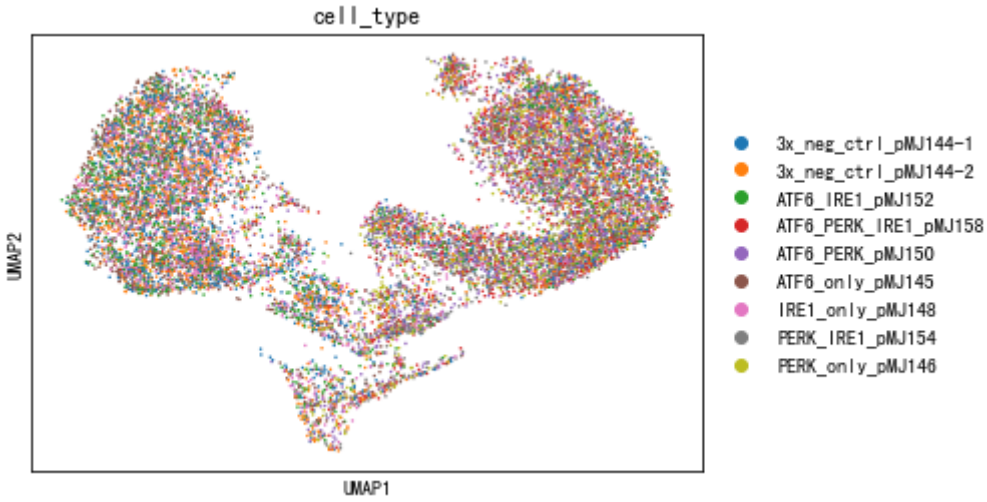
Problems

UMAP

pbmc umap plot



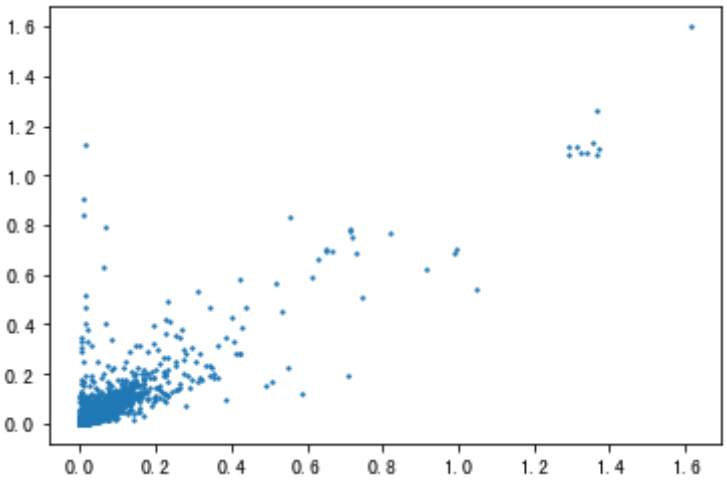
CRISPR-perturbation umap plot



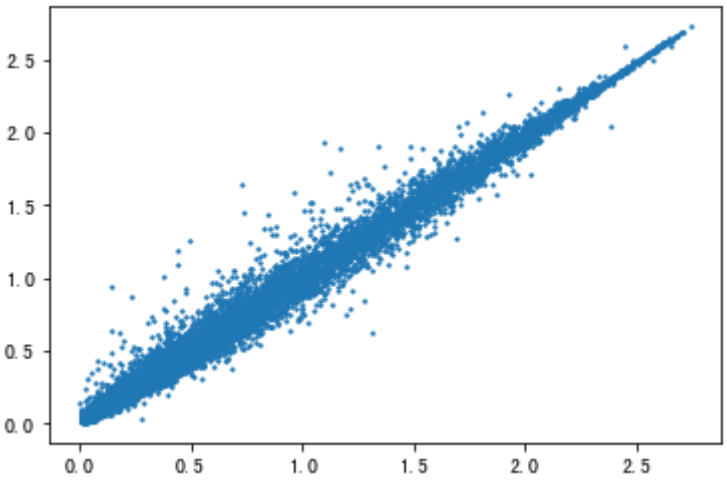
mean vs mean plot

I plot the mean gene expression of two types of single cells with different treatments, in the PBMC and in the CRISPR perturbation dataset.

X AXIS CD4T mean gene expression *Y AXIS* K mean gene expression



X AXIS ATF6_PERK_IRE1 perturbation mean gene expression *Y AXIS* control group mean gene expression



It can be seen that under different treatments in PBMC, cell expression is not very similar, while in the CRISPR-perturbation group, gene expression is very similar.

This result is validated by the umap plot.