Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης
Πολυτεχνική Σχολή
Τμήμα Ηλεκτρολόγων Μηχανικών και Μηχανικών Υπολογιστών
Τομέας Τηλεπικοινωνιών

Multi-task learning in perturbation modeling

Διπλωματική Εργασία
του
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Επιβλέπων: Όνομα Επίθετο
Καθηγητής Α.Π.Θ.

March 31, 2025

Abstract

abstract

Abstract

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Ευχαριστίες

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March 31, 2025

Περιεχόμενα

0.1 Abstract

With the recent advancements in single cell technology and the large scale perturbation datasets, the field of perturbation modeling [1] has created an opportunity for a wide variety of computational methods to be leveraged to harness its potential. Multi-task learning is one of the methods that has been left unexplored in this field. In this study we aim to bridge this gap unraveling the potential of multi-task learning in single cell perturbation modeling.

0.2 Literature review

Studying the effect of external stimuli to the cell level, a field named as perturbation modeling, has a significant impact to the biomedicine sector and drug discovery.

A review has been conducted to outline the methods and the datasets. One of the major tasks of perturbation modeling is the out of distribution prediction.

UnitedNet has followed a multi task approach in a multi-omics datasets, showed the promising results of the method. scButterfly followed a cross modal architecture has proporsed its potential to perturbation modeling.

scbutterfly, scgen, scvidr, unitednet

0.3 Method

the usage of film layers

0.4 Results and discussion

0.5 Conclusions

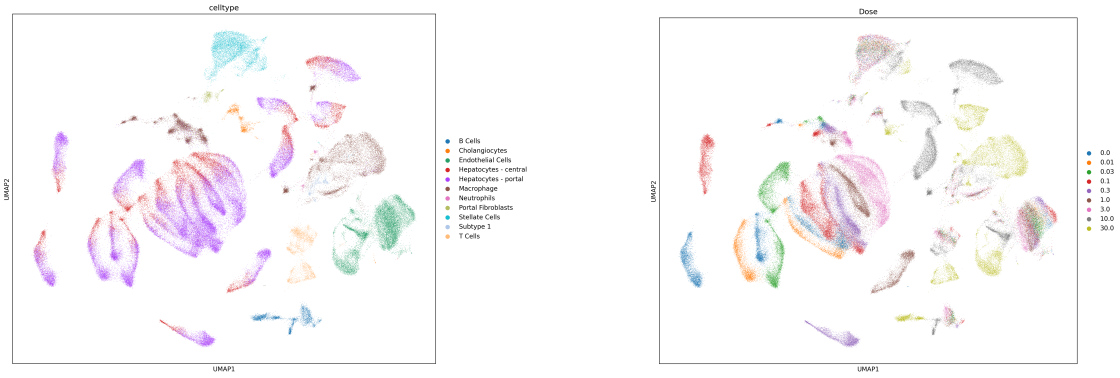
0.6 Future work

Chapter 1

Benchmarking

1.1 Datasets

1.1.1 Nault et al. 2022



(a) (b)

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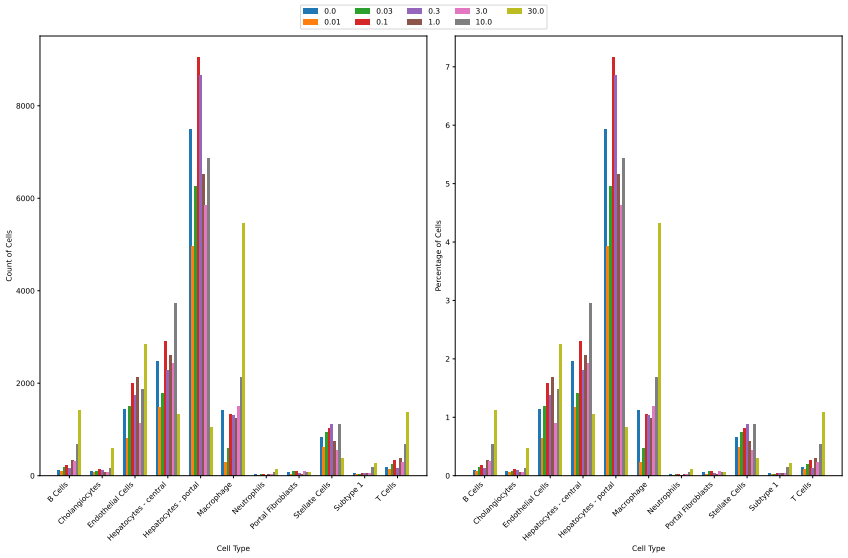

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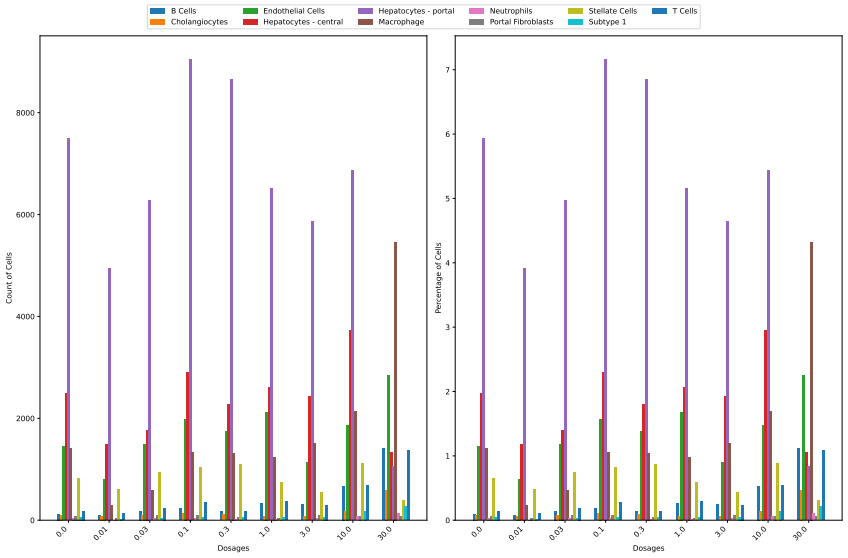


(d)

Figure 1.1: Nault overview

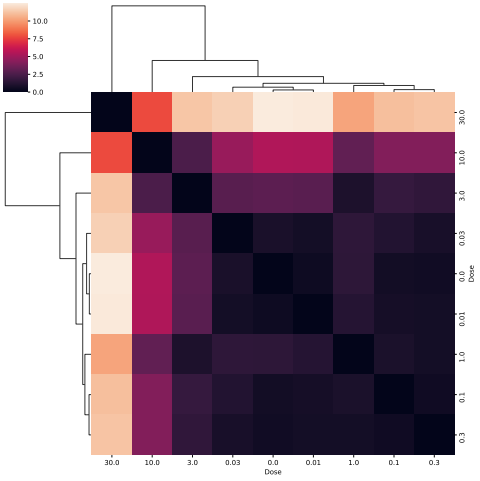


Figure 1.2: E-distance

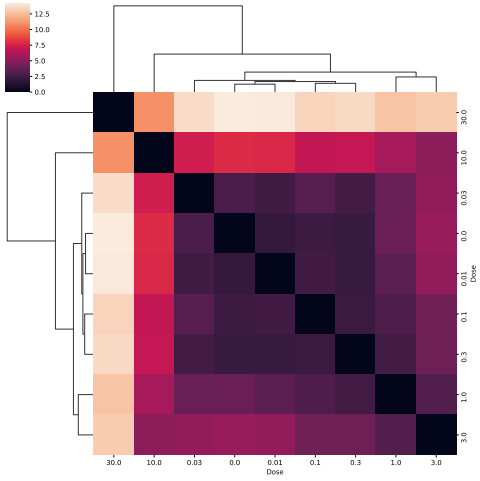


Figure 1.3: Euclidean

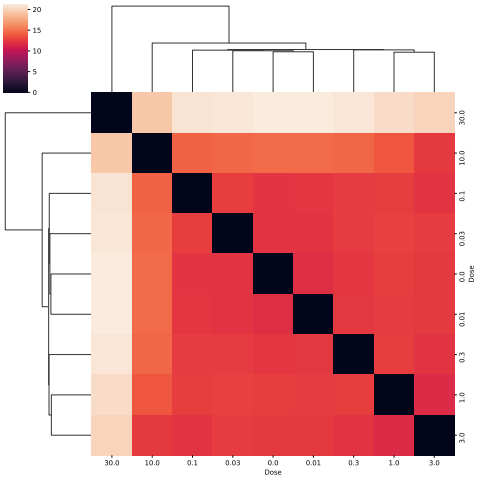


Figure 1.4: Mean pairwise

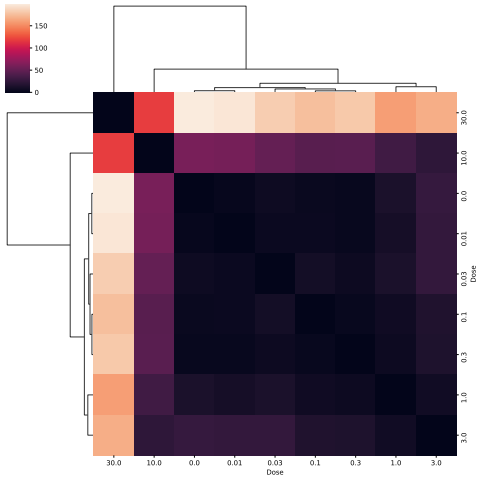


Figure 1.5: MMD

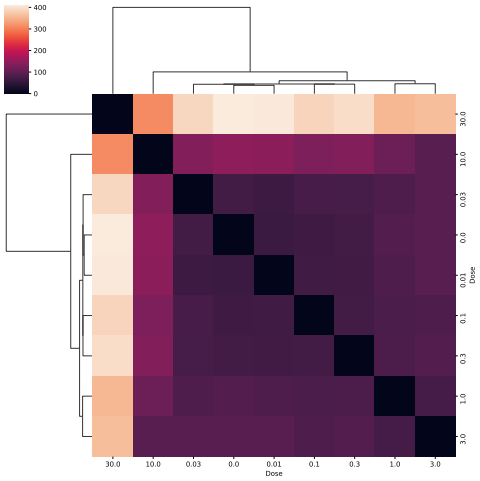


Figure 1.6: Wasserstein

Figure 1.7: Distance metrics across all cell types per dosage

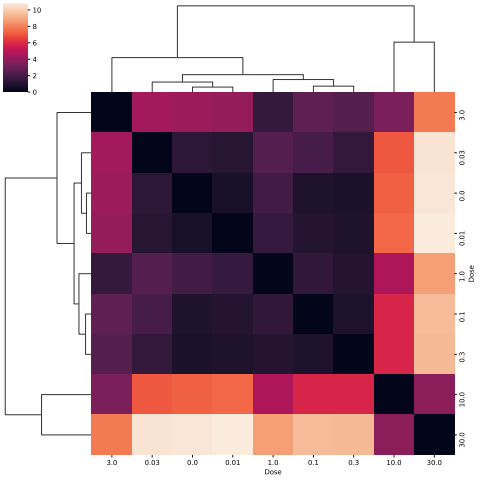


Figure 1.8: E-distance

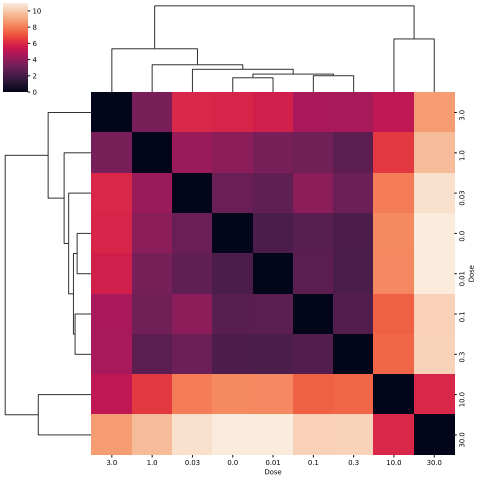


Figure 1.9: Euclidean

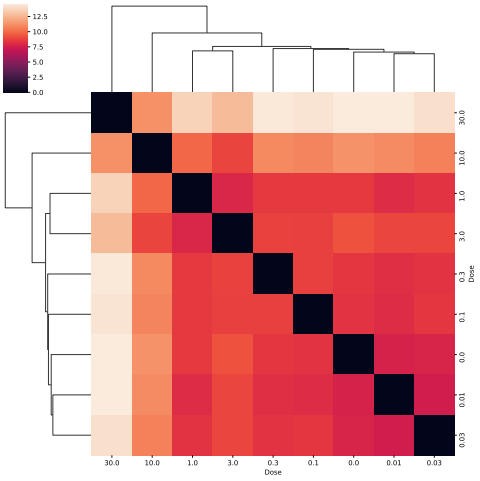


Figure 1.10: Mean pairwise

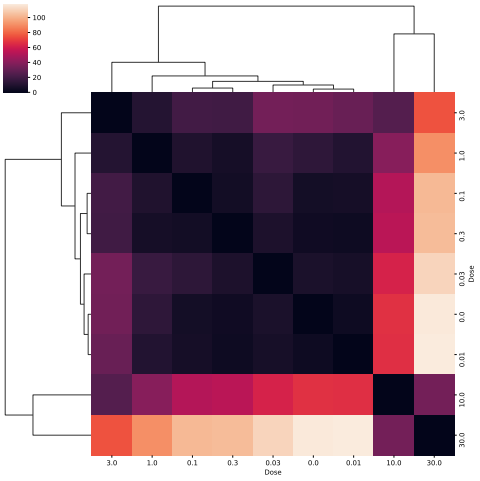


Figure 1.11: MMD

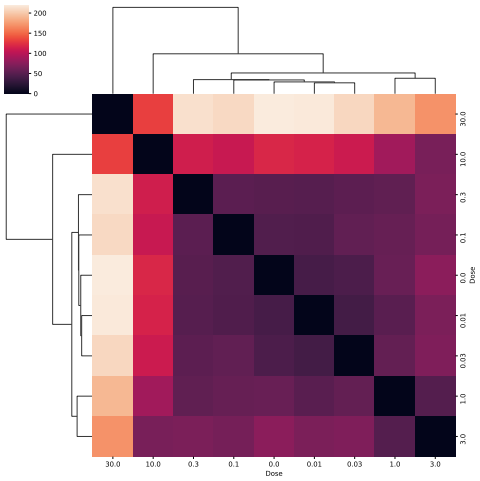


Figure 1.12: Wasserstein

Figure 1.13: Distance metrics for cell type Hepatocytes - portal per dosage

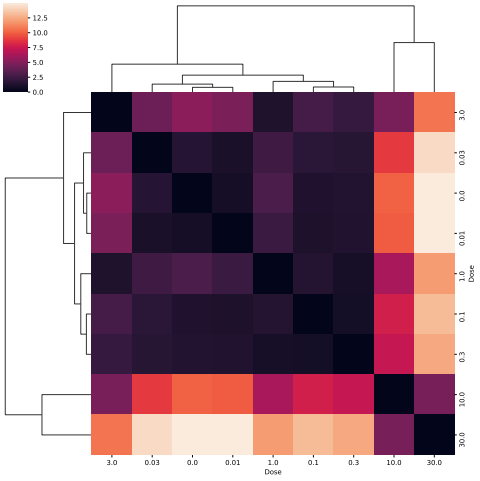


Figure 1.14: E-distance

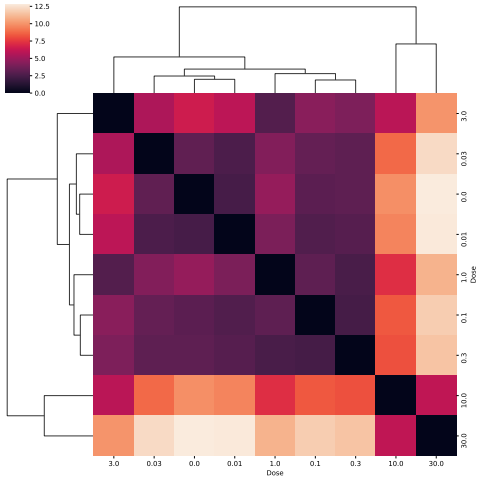


Figure 1.15: Euclidean

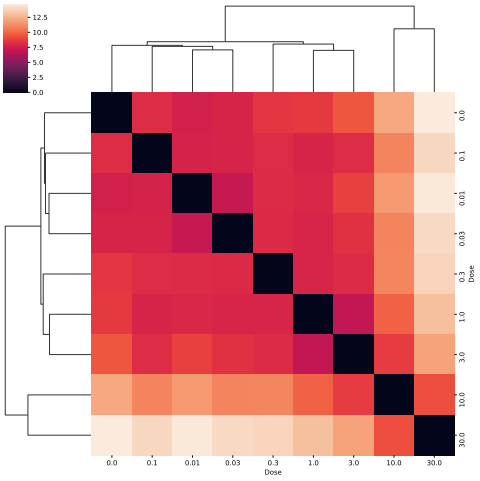


Figure 1.16: Mean pairwise

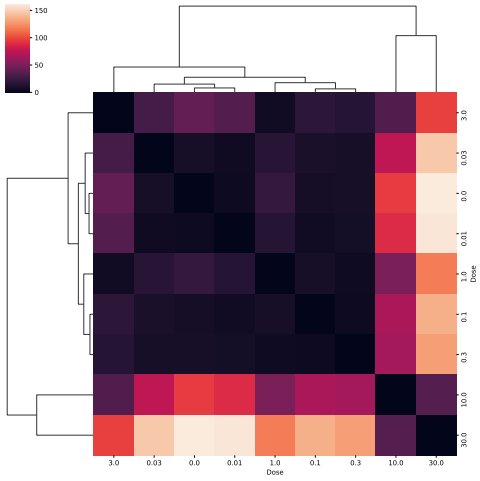


Figure 1.17: MMD

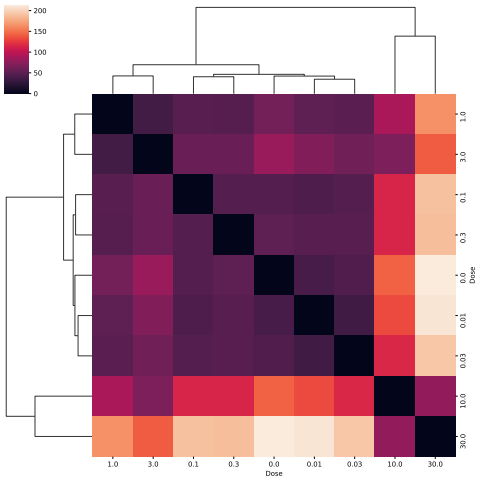


Figure 1.18: Wasserstein

Figure 1.19: Distance metrics for cell type Hepatocytes - central per dosage

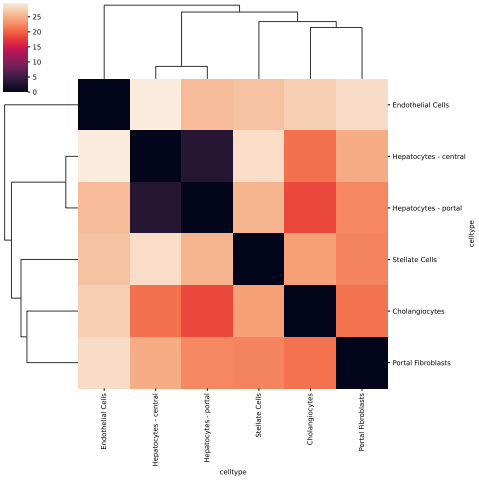


Figure 1.20: E-distance

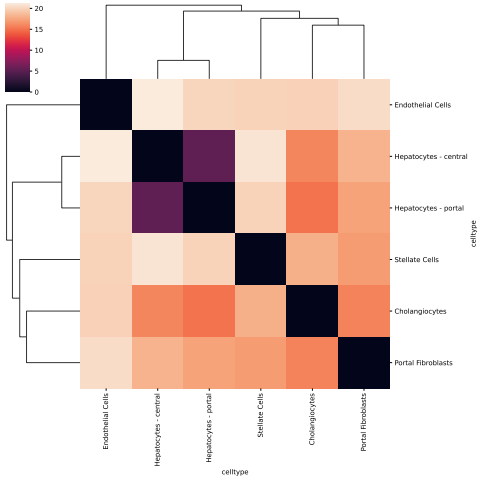


Figure 1.21: Euclidean

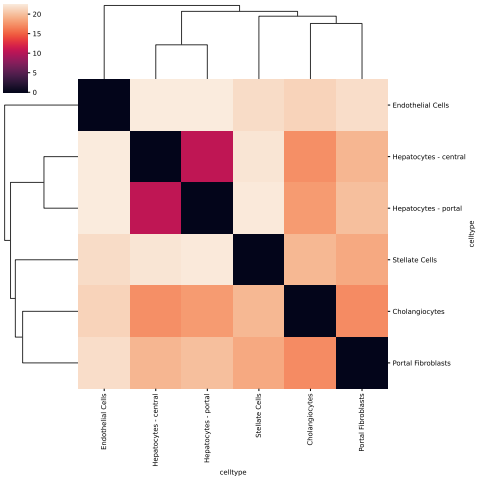


Figure 1.22: Mean pairwise

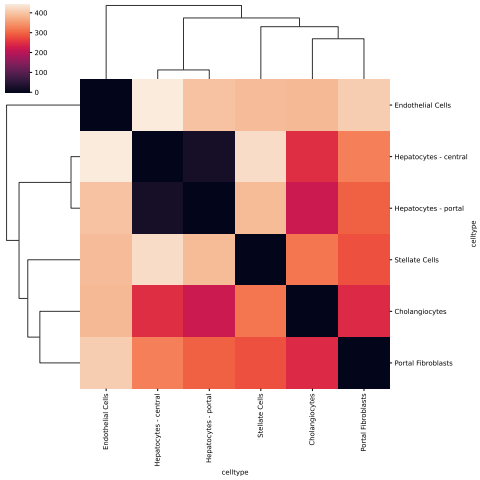


Figure 1.23: MMD

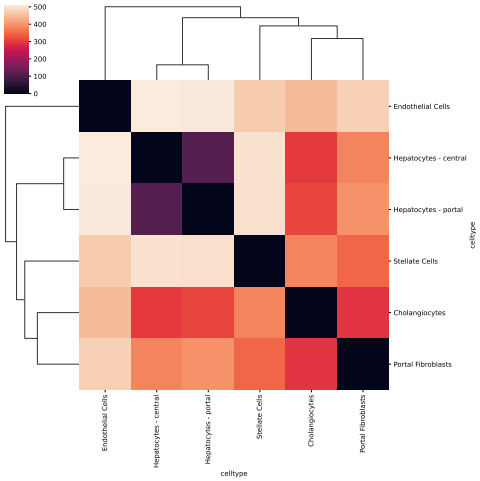


Figure 1.24: Wasserstein

Figure 1.25: Distance metrics for dosage highest 30 $\mu g/kg$ per cell type

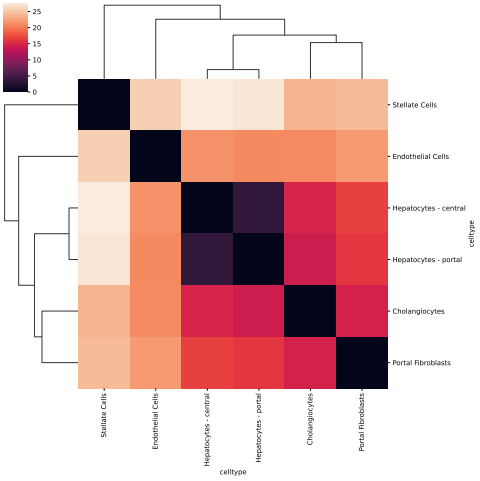


Figure 1.26: E-distance

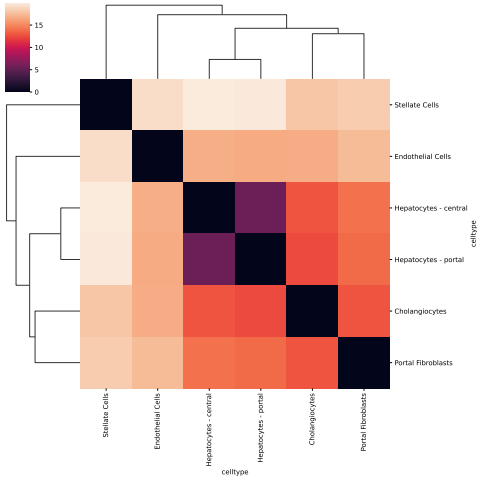


Figure 1.27: Euclidean

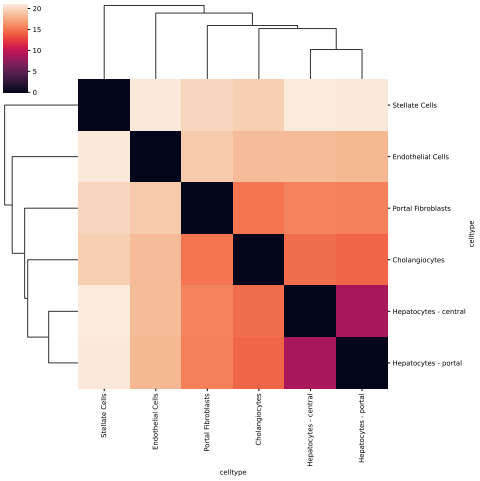


Figure 1.28: Mean pairwise

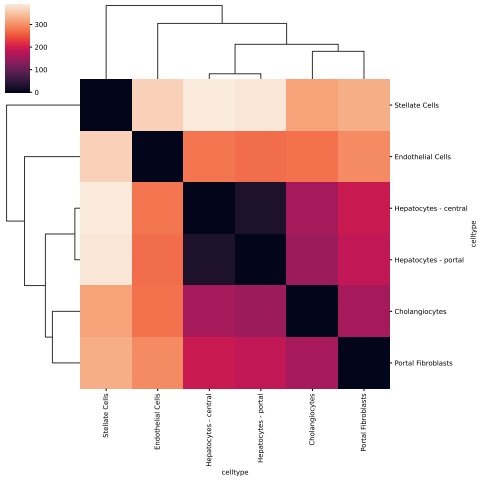


Figure 1.29: MMD

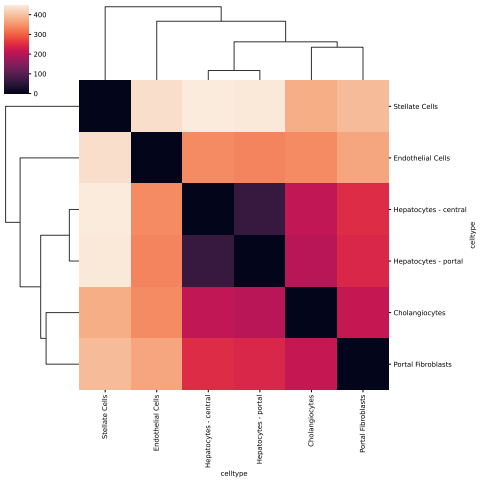
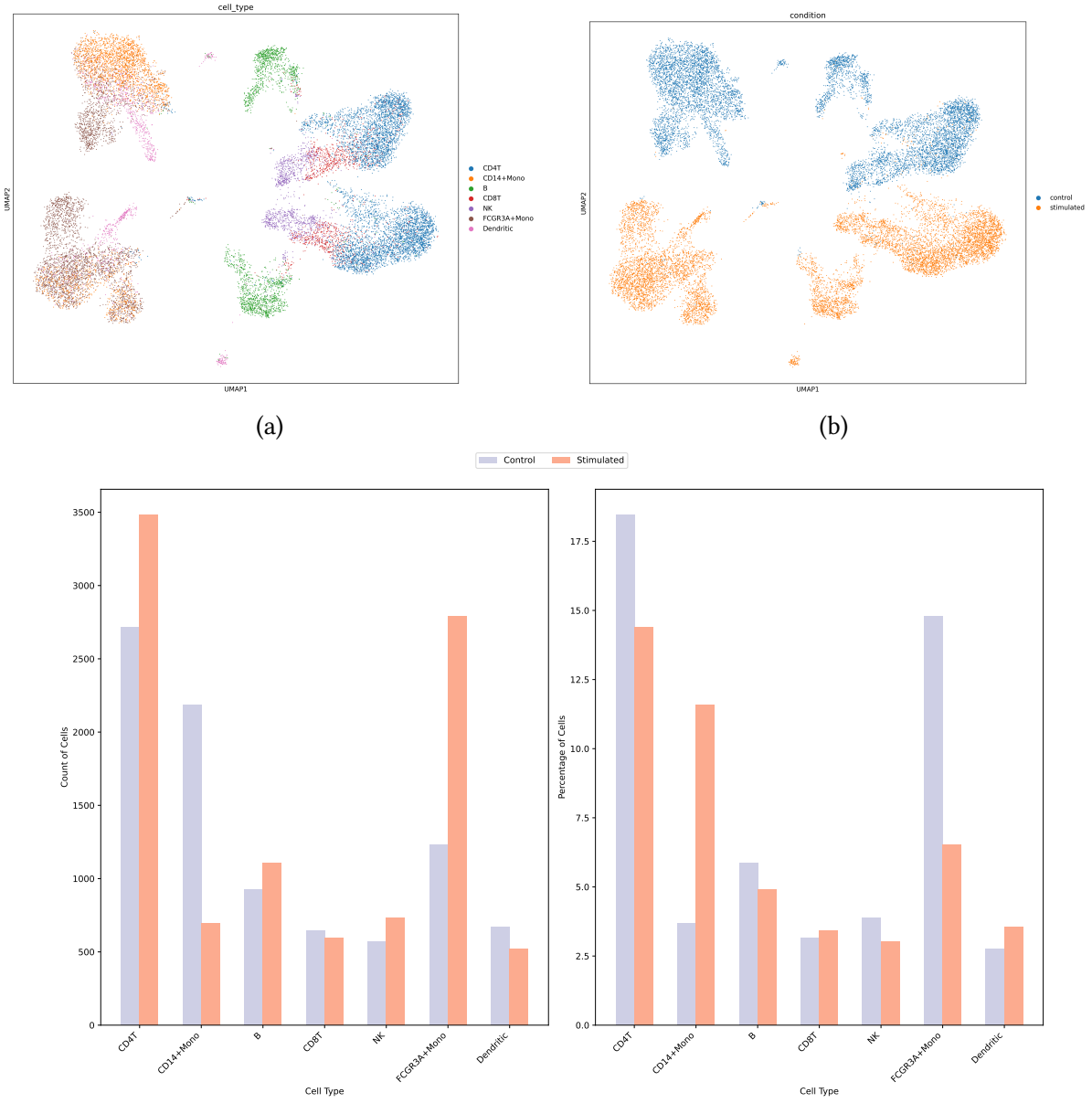


Figure 1.30: Wasserstein

Figure 1.31: Distance metrics for lowest dosage 0.01 $\mu g/kg$ per cell type

1.1.2 PBMC dataset



(a) (b)

(c)

Figure 1.32: PBMC overview

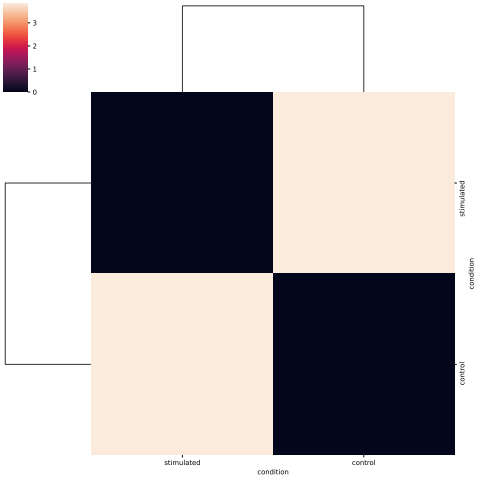


Figure 1.33: E-distance

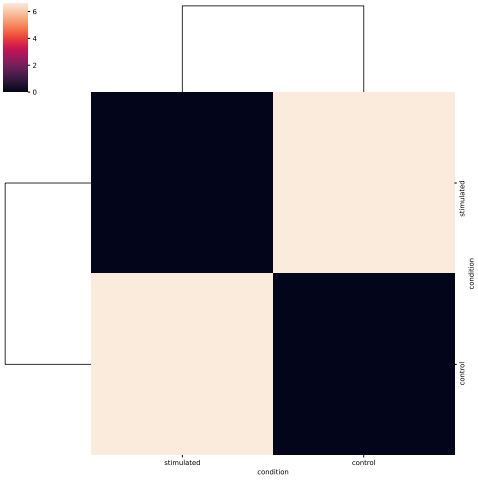


Figure 1.34: Euclidean

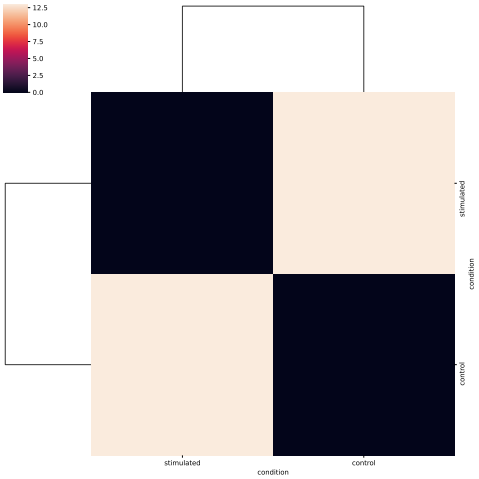


Figure 1.35: Mean pairwise

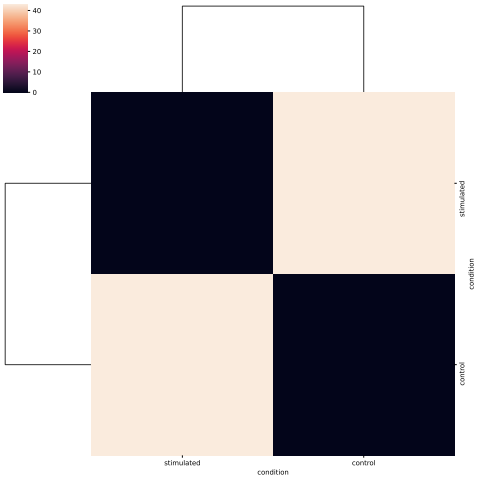


Figure 1.36: MMD

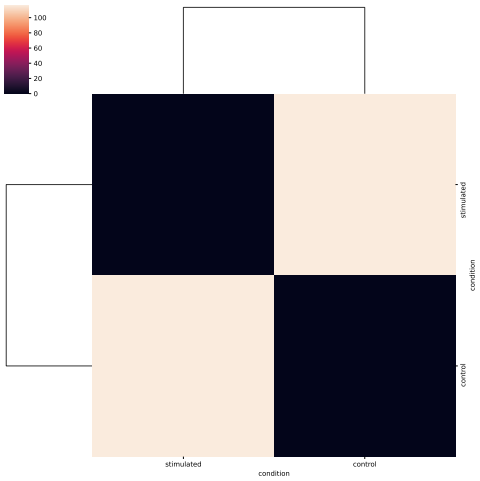


Figure 1.37: Wasserstein

Figure 1.38: Distance metrics per condition

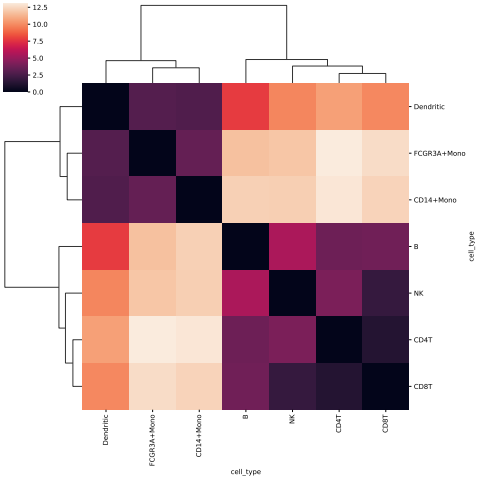


Figure 1.39: E-distance

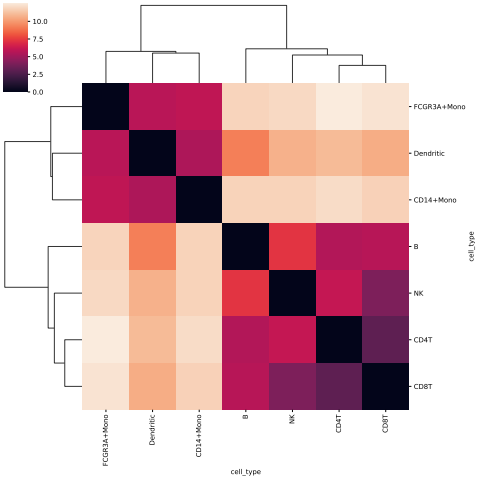


Figure 1.40: Euclidean

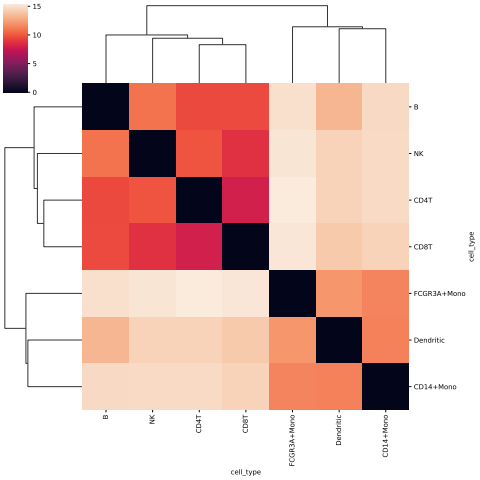


Figure 1.41: Mean pairwise

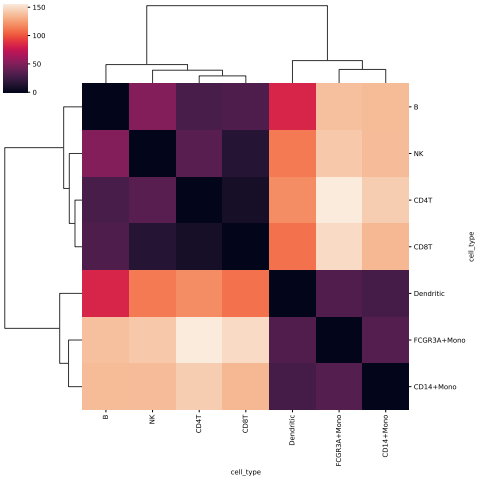


Figure 1.42: MMD

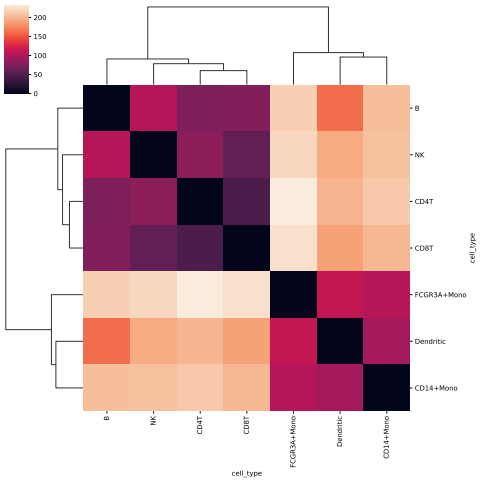
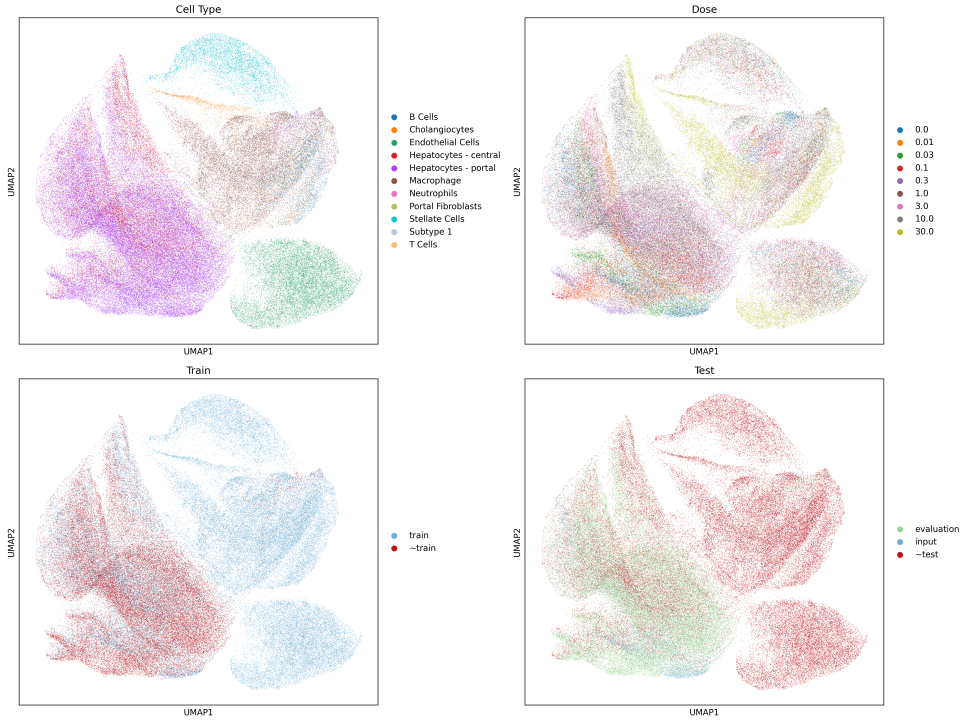


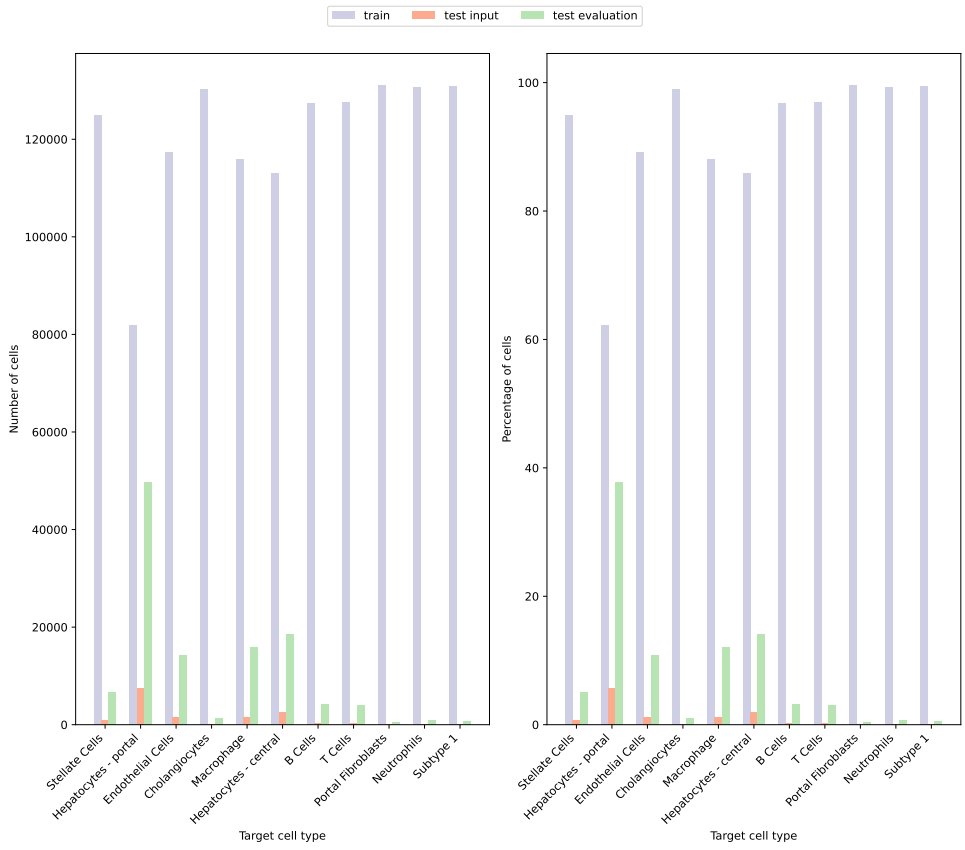
Figure 1.43: Wasserstein

Figure 1.44: Distance metrics per cell type

1.2 Nault all cell types evaluation

1.2.1 Multiple doses





1.2.2 Single dose

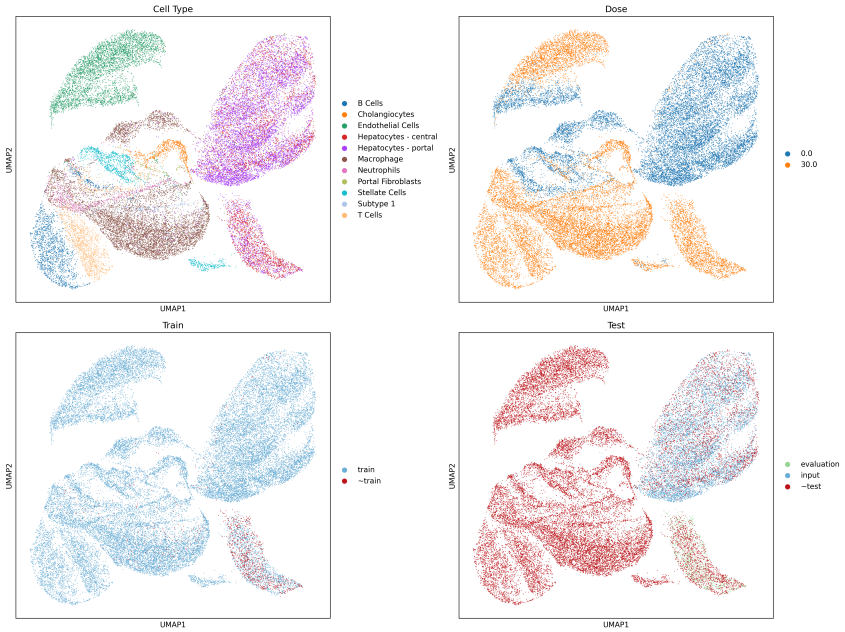


Figure 1.45: Example of $30\mu g/kg$

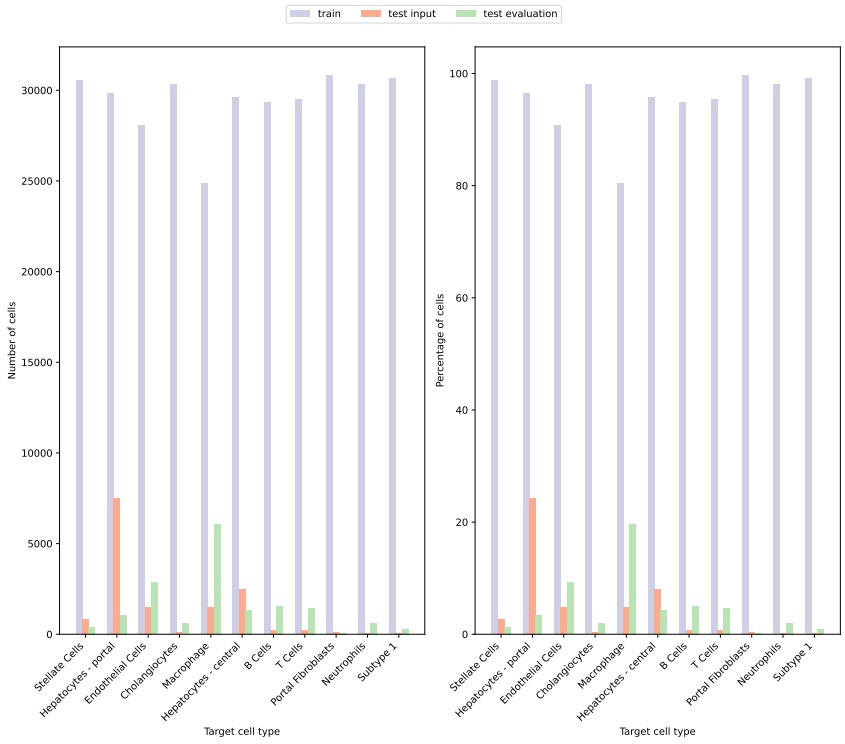


Figure 1.46: Number of cells per cell type for $30\mu g/kg$

1.2.3 Comparison

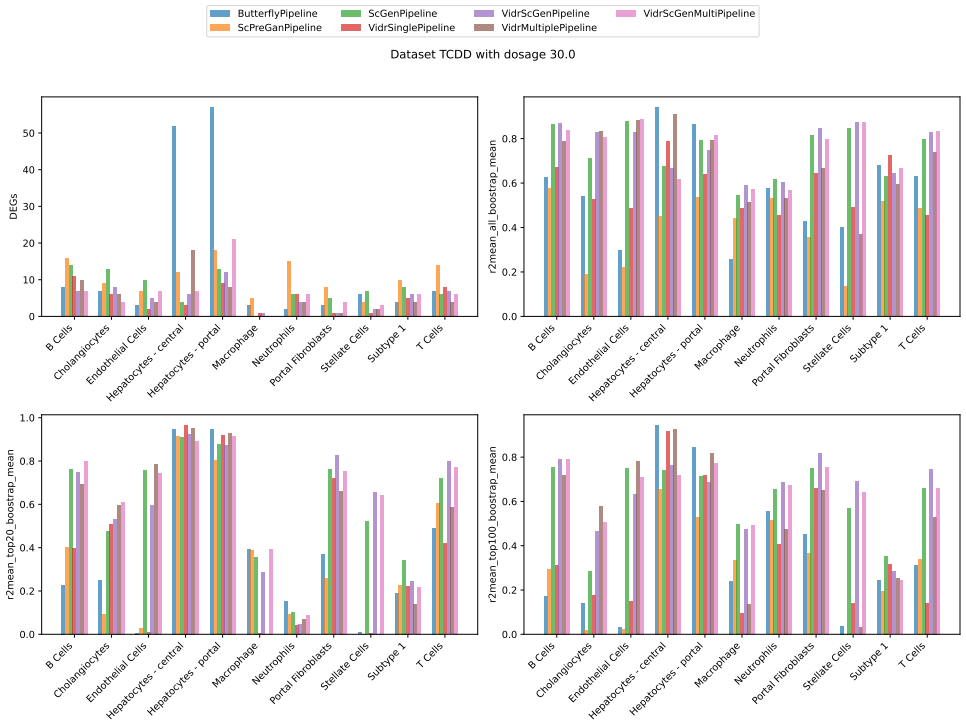


Figure 1.47: Baseline metrics for highest dosage $30\mu g/kg$ across cell types

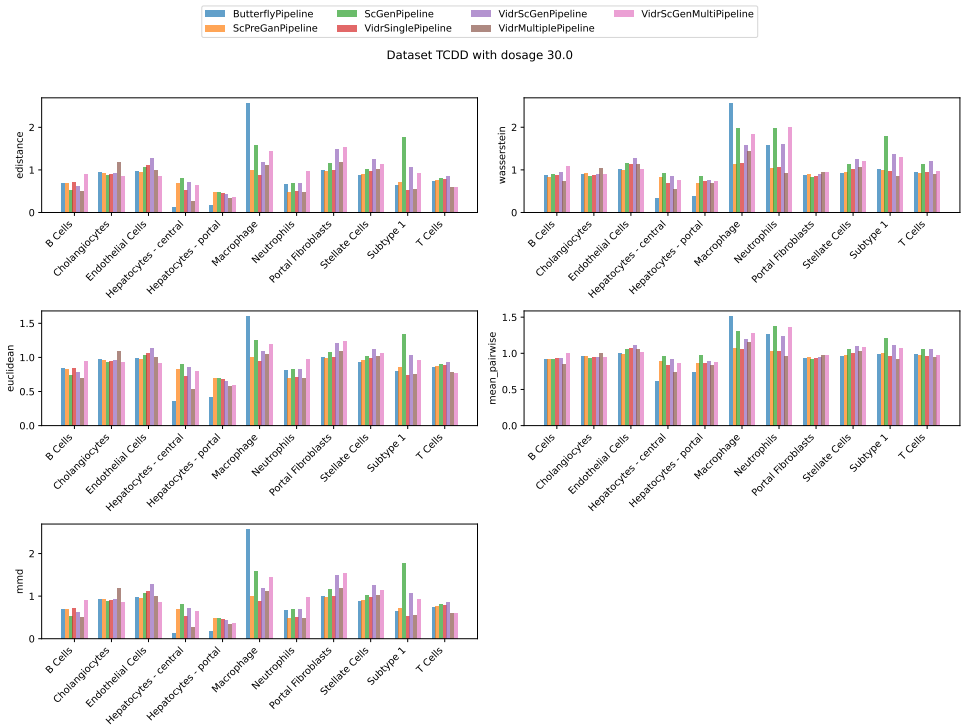


Figure 1.48: Distance metrics for highest dosage $30\mu g/kg$ across cell types

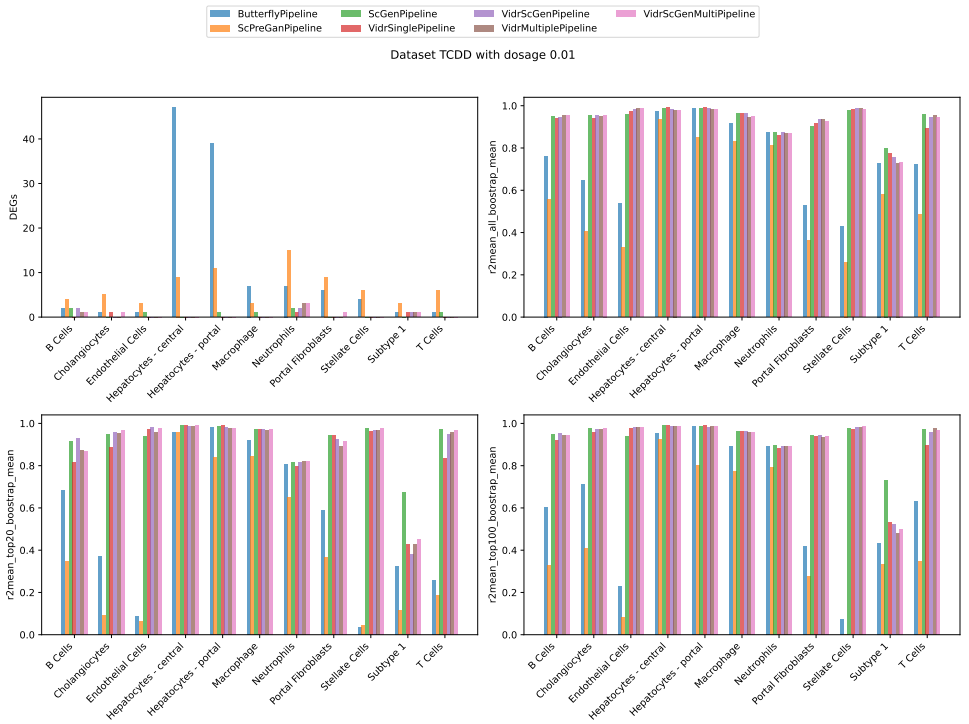


Figure 1.49: Baseline metrics for lowest dosage $0.01\mu g/kg$ across cell types

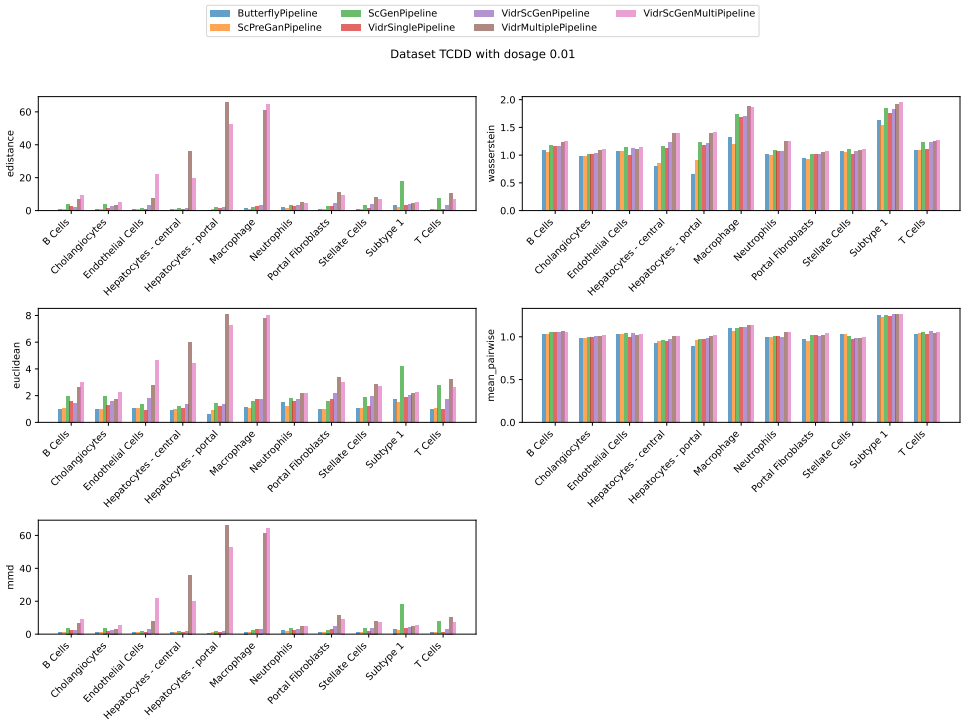


Figure 1.50: Distance metrics for lowest dosage $0.01\mu g/kg$ across cell types

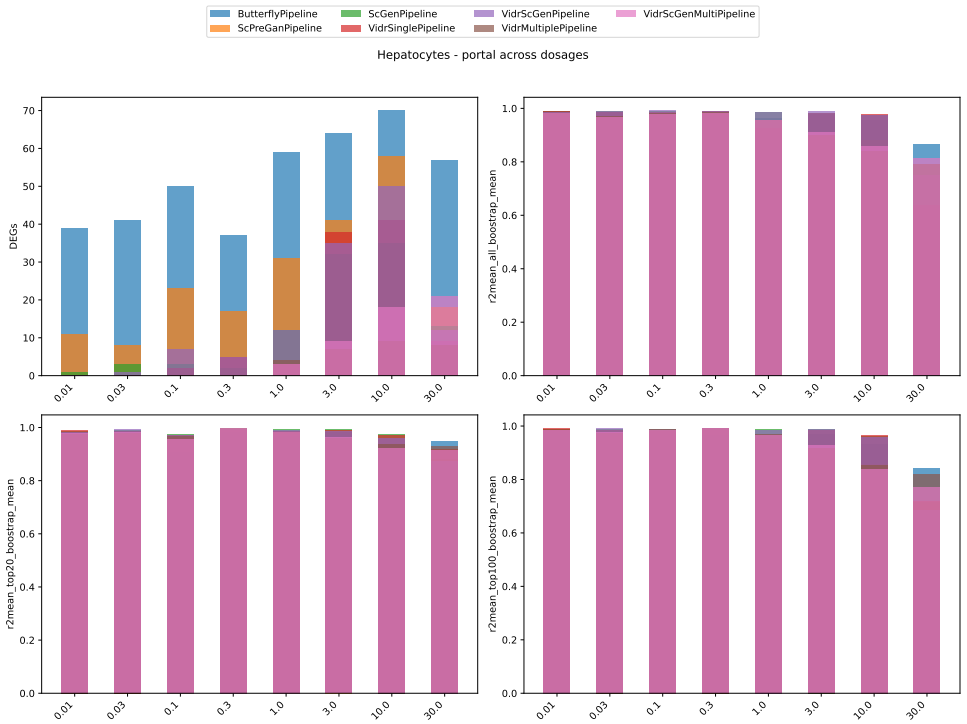


Figure 1.51: Baseline metrics for Hepatocytes - portal across dosages

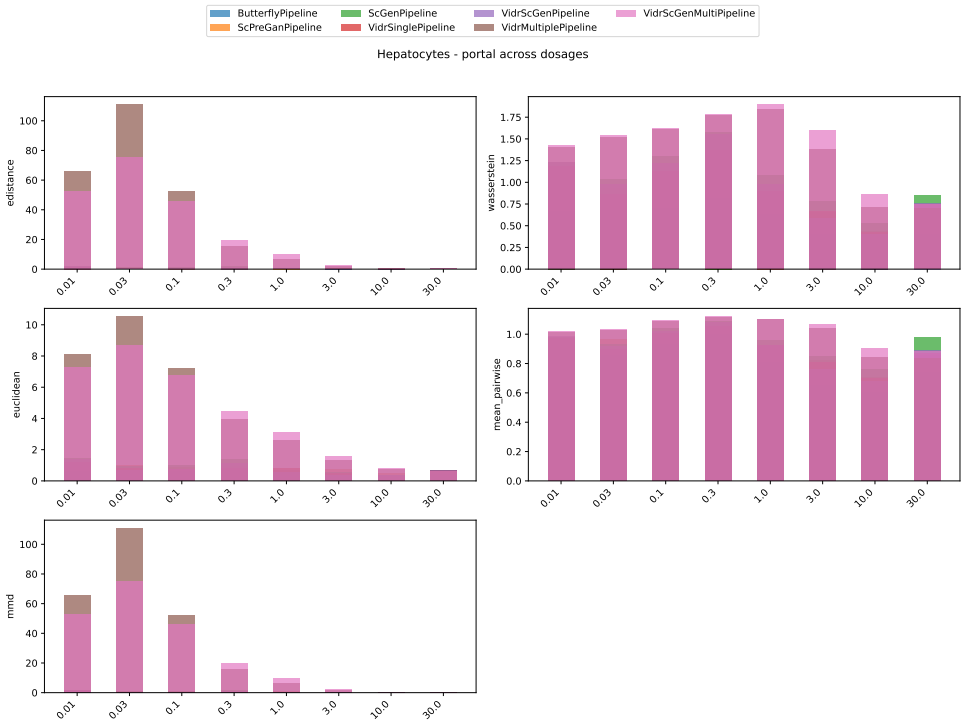


Figure 1.52: Distance metrics for Hepatocytes - portal across dosages

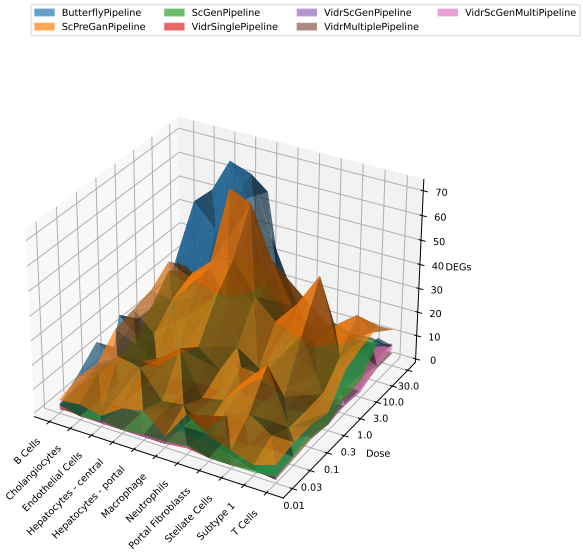


Figure 1.53

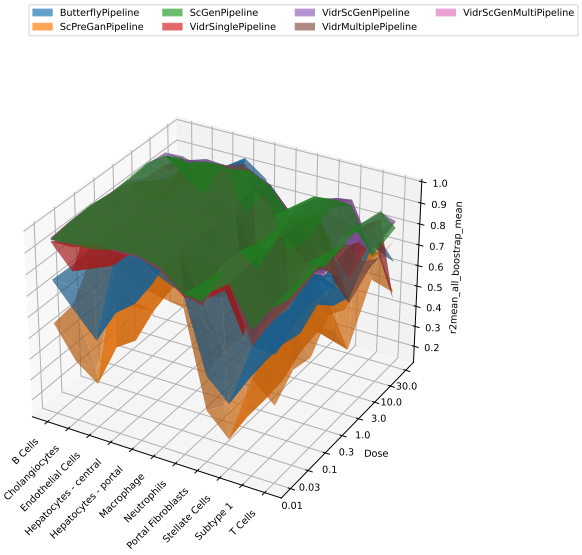
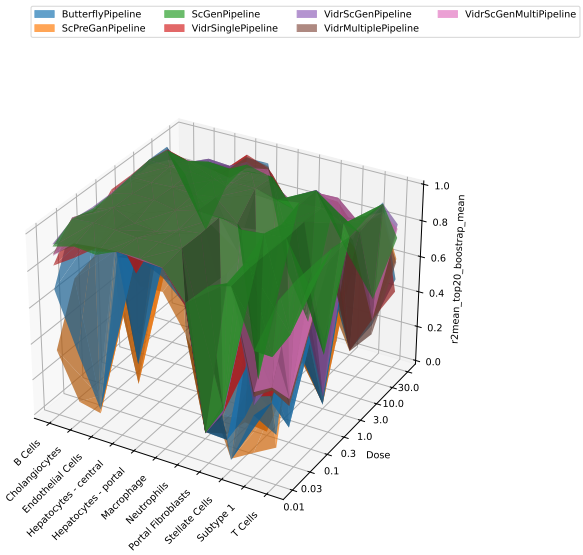


Figure 1.54



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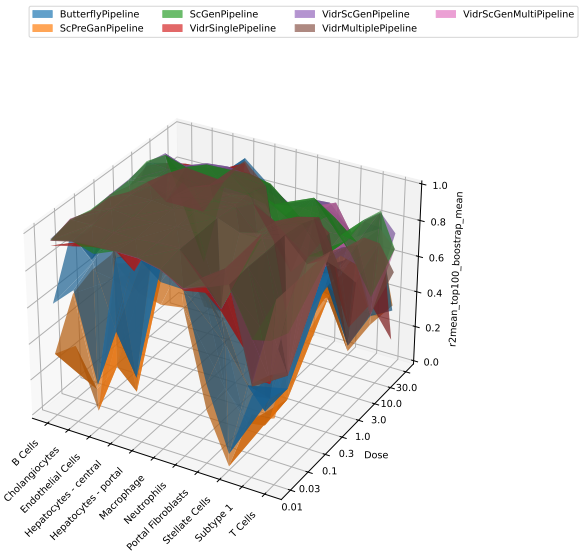

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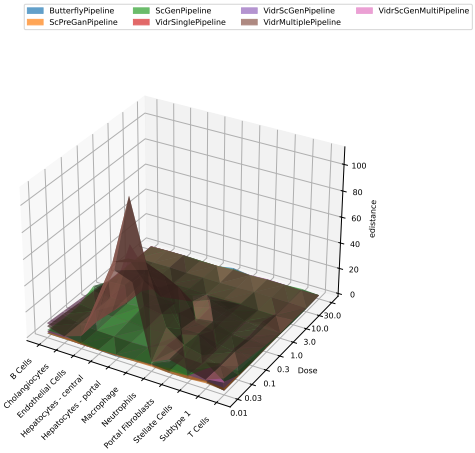


Figure 1.57: E-distance

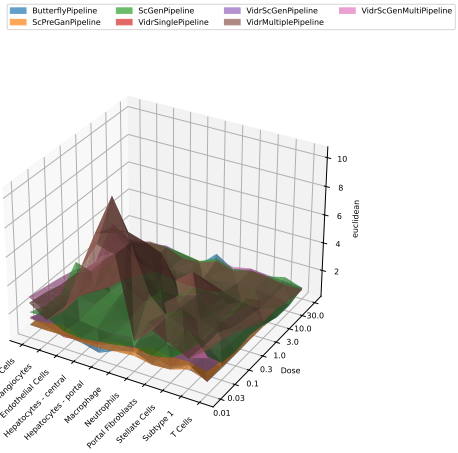


Figure 1.58: Euclidean

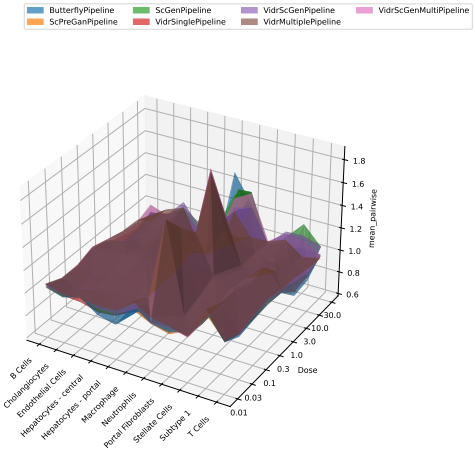


Figure 1.59: Mean pairwise

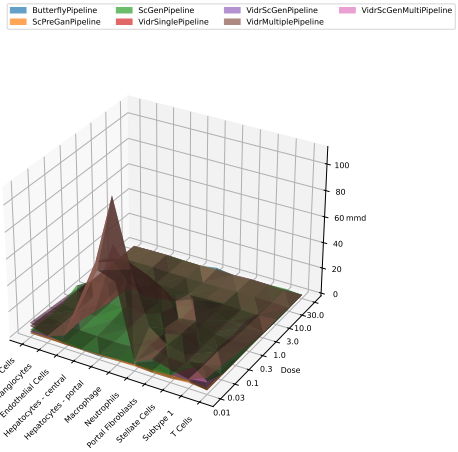


Figure 1.60: MMD

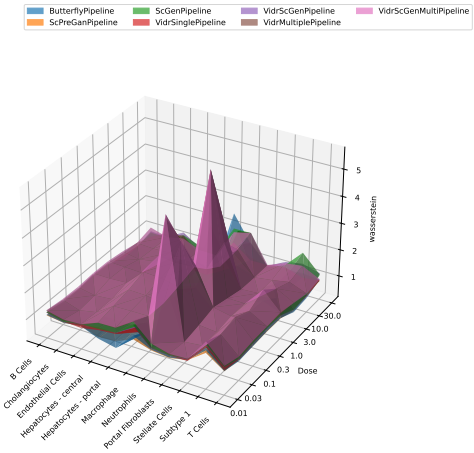
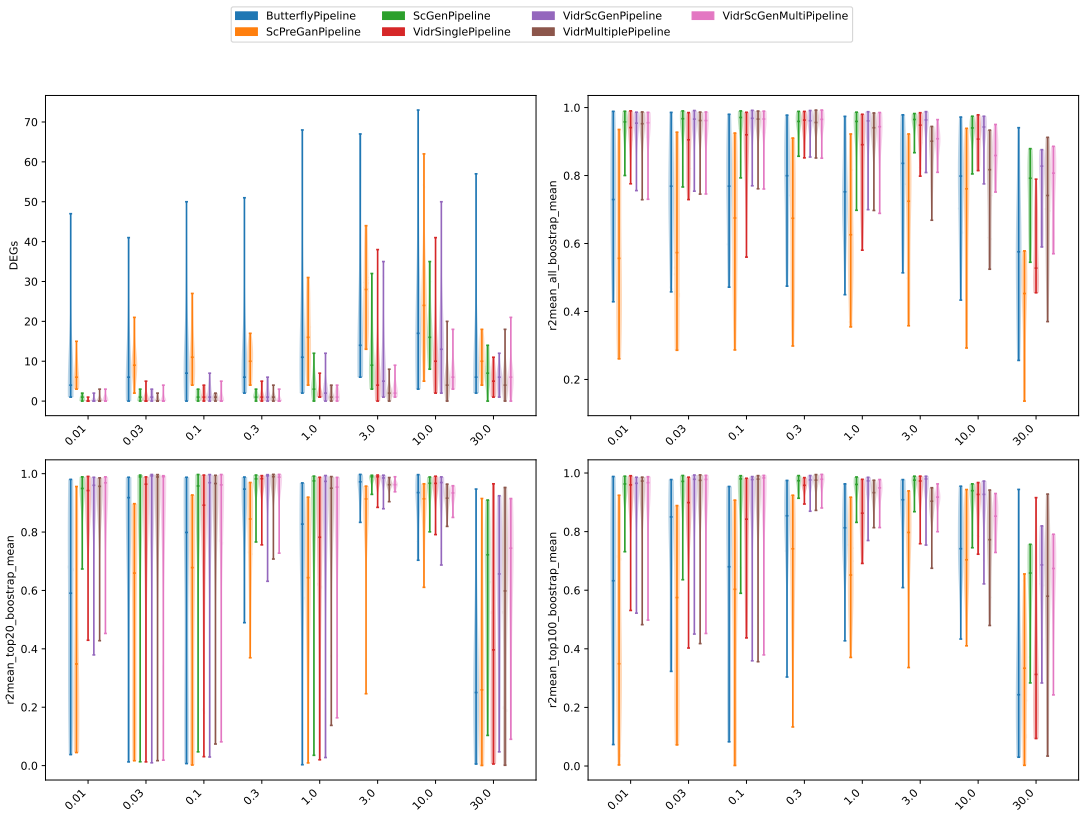


Figure 1.61: Wasserstein

Figure 1.62: Distance metrics per cell type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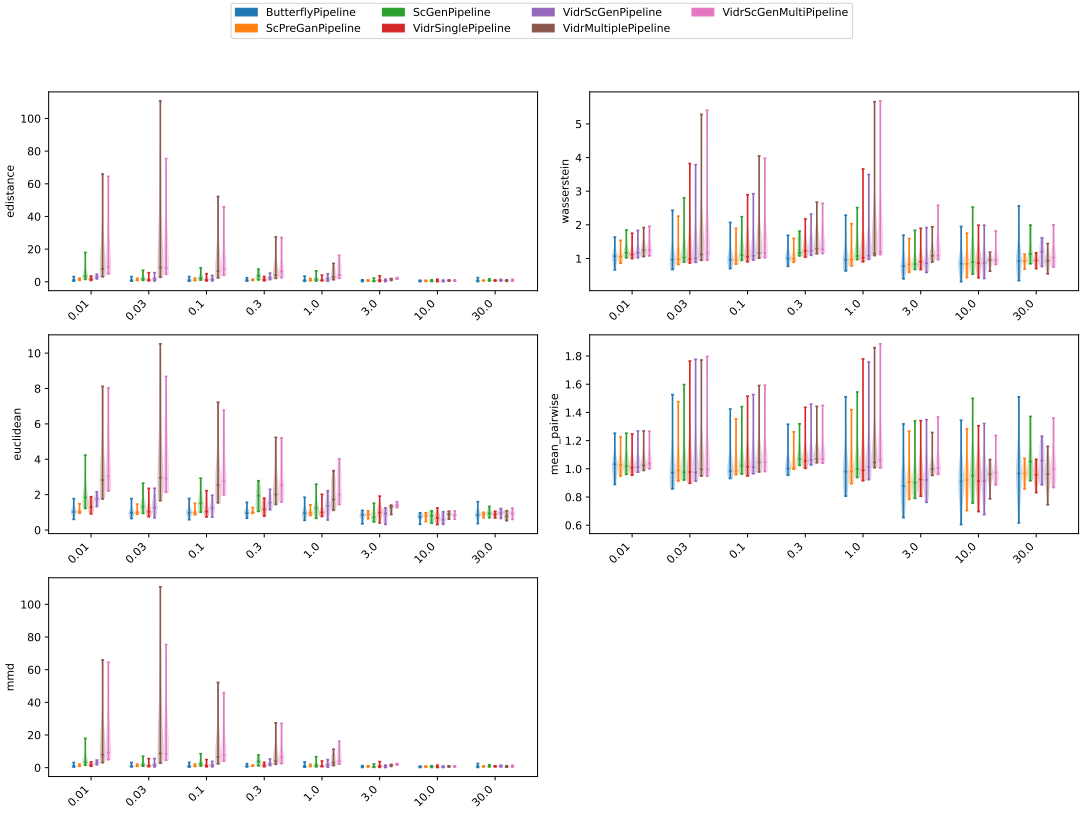
ScGenPipeline
VidrSinglePipeline
VidrScGenPipeline
VidrMultiplePipeline
VidrScGenMultiPipeline
DEGs
r2mean_all_boostrap_mean
r2mean_top20_boostrap_mean
r2mean_top100_boostrap_mean
0.01
0.03
0.1
0.3
1.0
3.0
10.0
30.0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ScGenPipeline
VidrSinglePipeline
VidrScGenPipeline
VidrMultiplePipeline
VidrScGenMultiPipeline
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wasserstein
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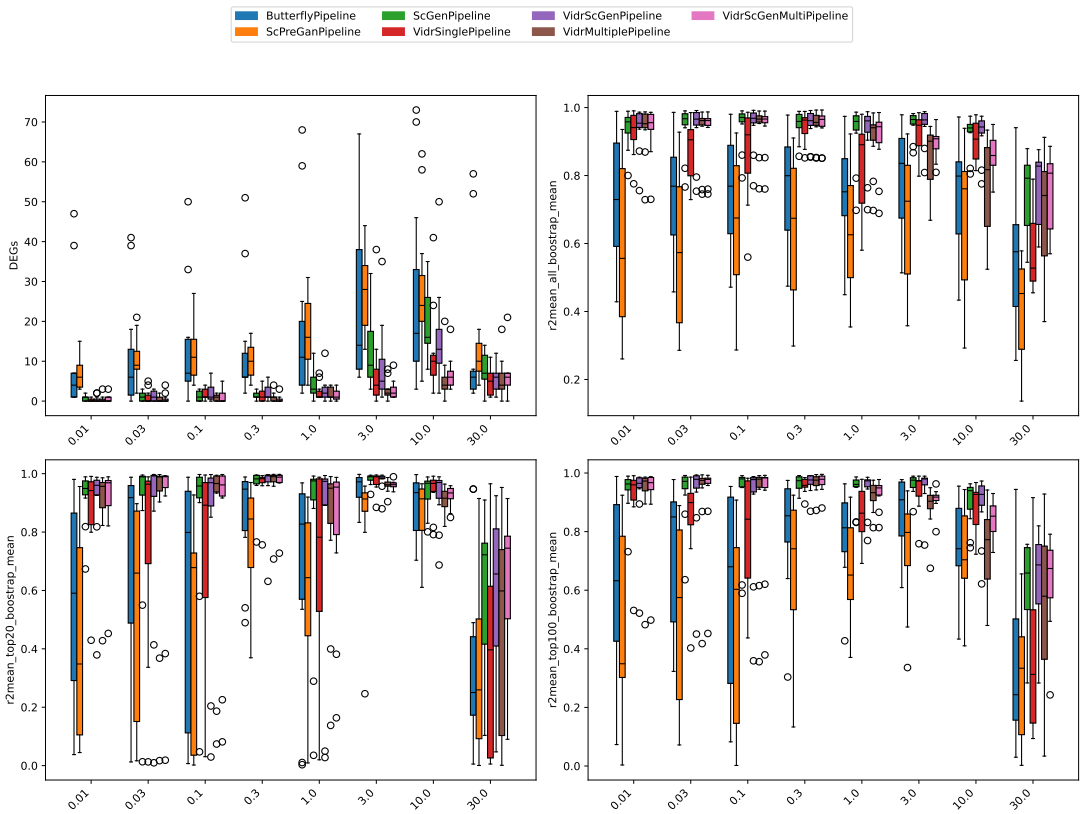
mean_pairwise
mmd
0.01
0.03
0.1
0.3
1.0
3.0
10.0
30.0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VidrScGenPipeline
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DEGs
r2mean_all_boostrap_mean
r2mean_top20_boostrap_mean
r2mean_top100_boostrap_mean
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0.03
0.1
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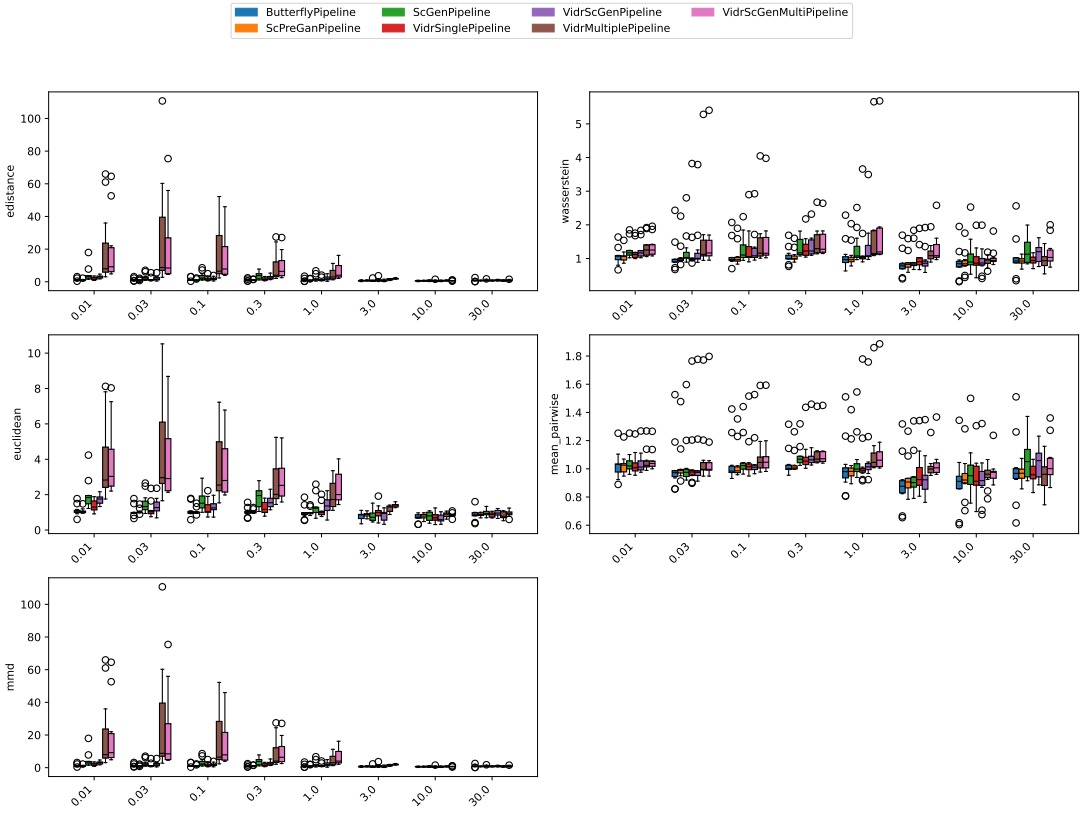
10.0
30.0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ScGenPipeline
VidrSinglePipeline
VidrScGenPipeline
VidrMultiplePipeline
VidrScGenMultiPipeline
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0.1
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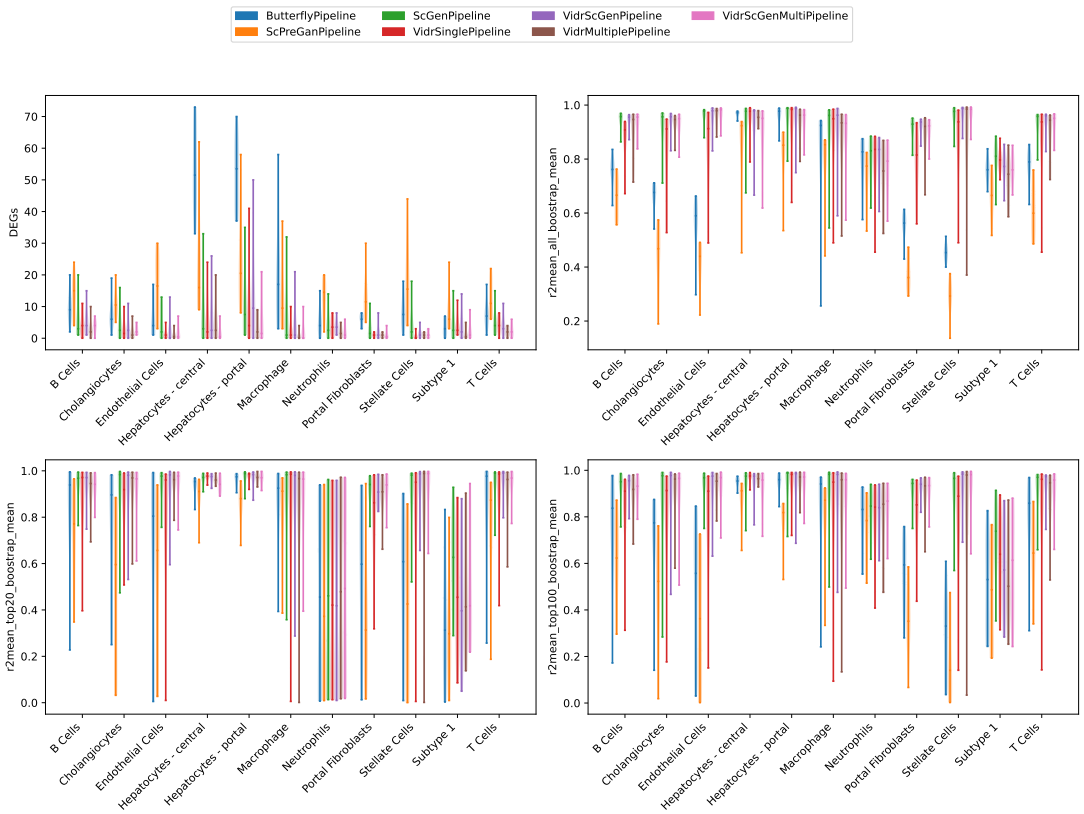
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VidrScGenPipeline
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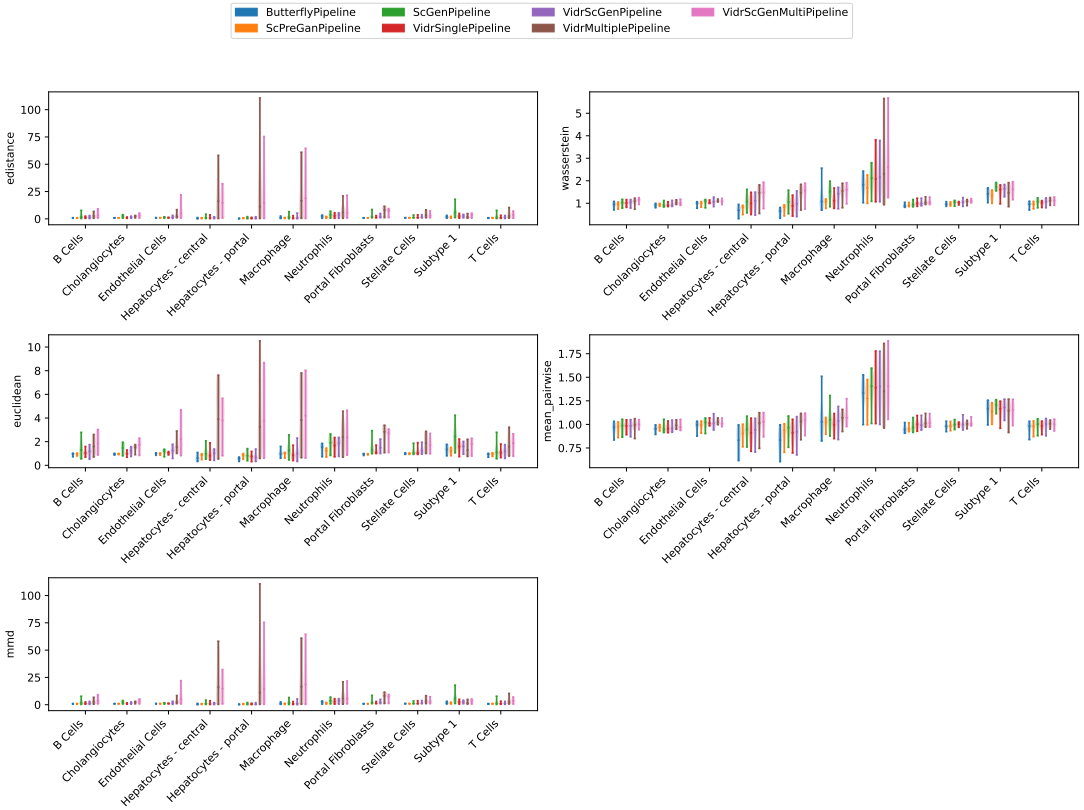
DEGs
r2mean_all_boostrap_mean
r2mean_top20_boostrap_mean
r2mean_top100_boostrap_mean
B Cells
Cholangiocytes
Endothelial Cells
Hepatocytes - central
Hepatocytes - portal
Macrophage
Neutrophils
Portal Fibroblasts
Stellate Cells
Subtype 1
T Cells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ScGenPipeline
VidrSingleCellPipeline
VidrScGenPipeline
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euclidean
mean_pairwise
mmd
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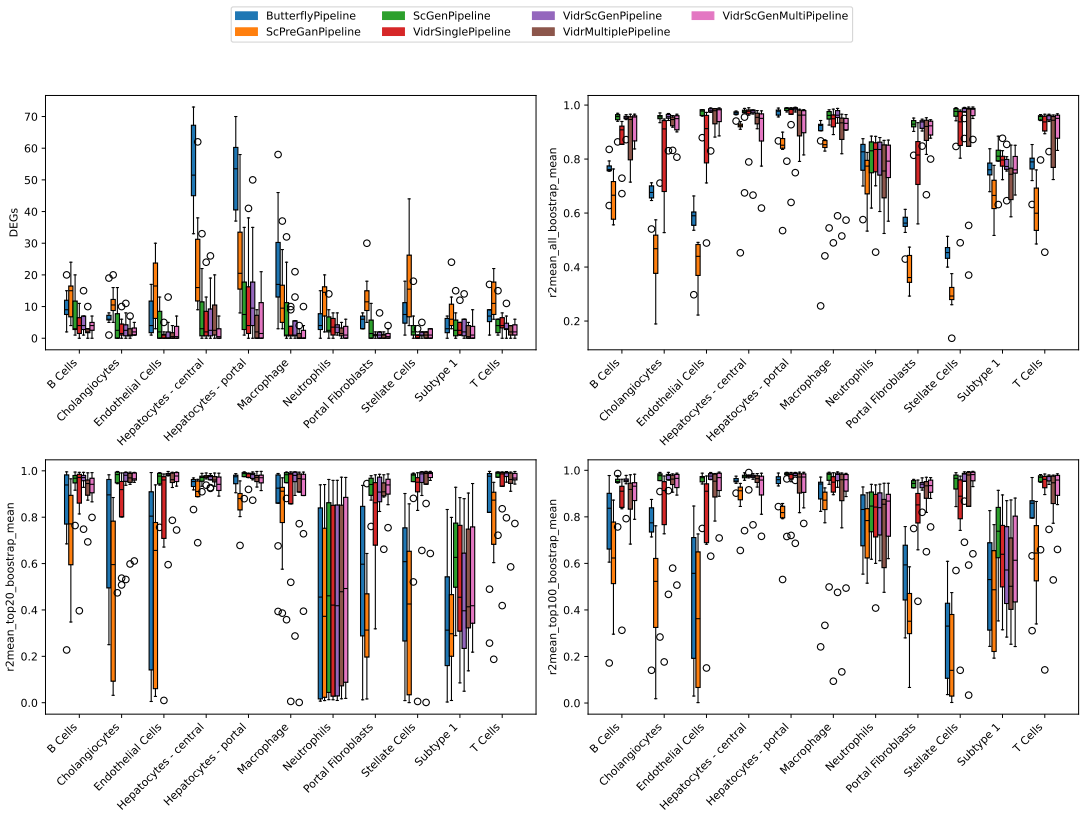
Cholangiocytes
Endothelial Cells
Hepatocytes - central
Hepatocytes - portal
Macrophage
Neutrophils
Portal Fibroblasts
Stellate Cells
Subtype 1
T Cells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VidrScGenPipeline
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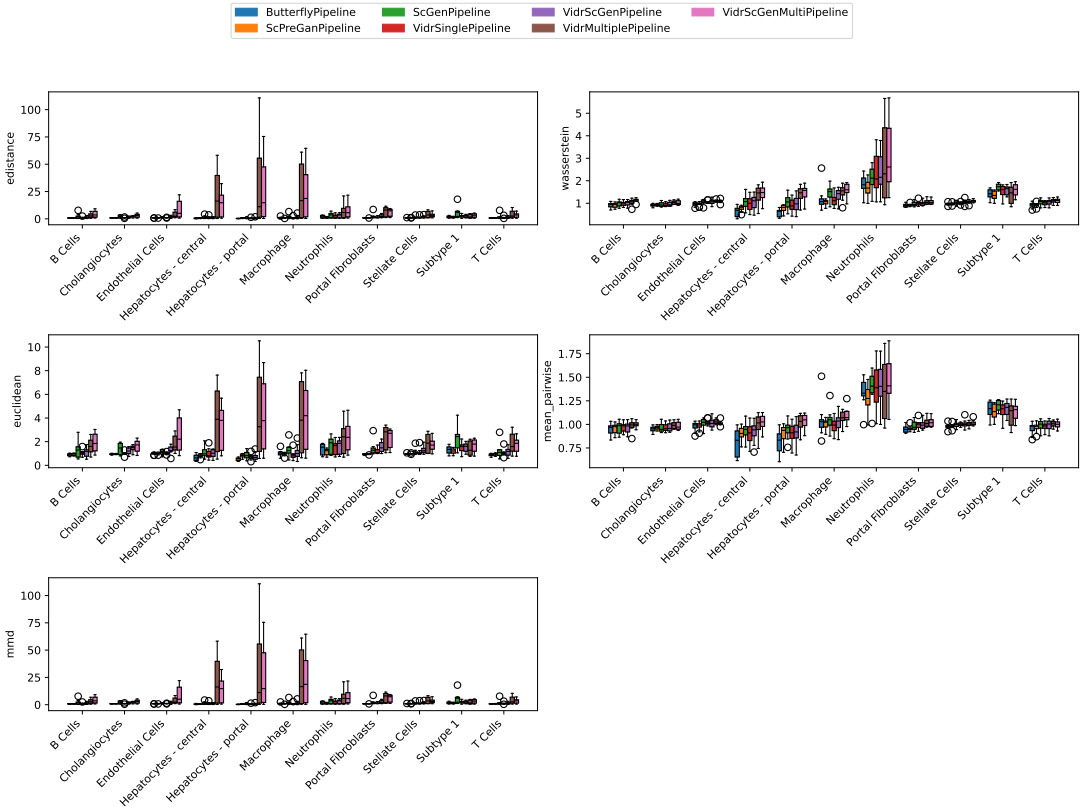
DEGs
r2mean_all_boostrap_mean
r2mean_top20_boostrap_mean
r2mean_top100_boostrap_mean
B Cells
Cholangiocytes
Endothelial Cells
Hepatocytes - central
Hepatocytes - portal
Macrophage
Neutrophils
Portal Fibroblasts
Stellate Cells
Subtype 1
T Cells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euclidean
mean_pairwise
mmd
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Cholangiocytes
Endothelial Cells
Hepatocytes - central
Hepatocytes - portal
Macrophage
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Portal Fibroblasts
Stellate Cells
Subtype 1
T Cells

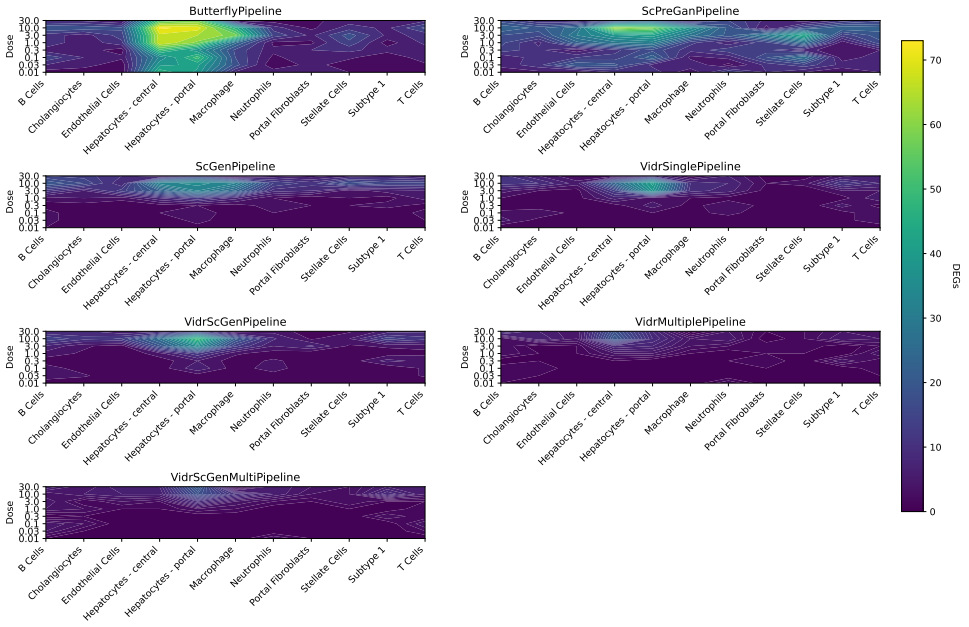


Figure 1.63: DEGs

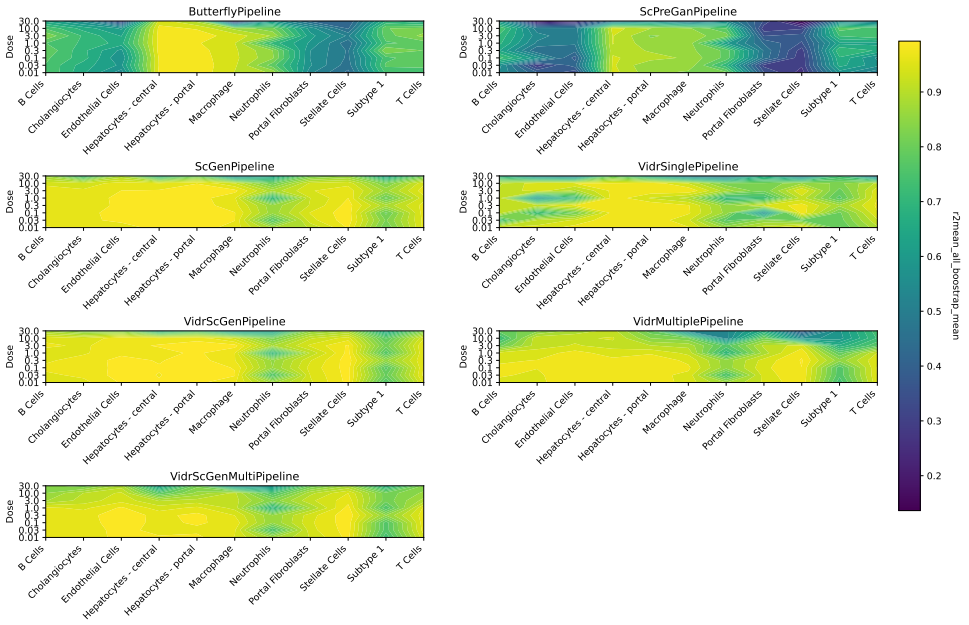


Figure 1.64: r2 HVGs

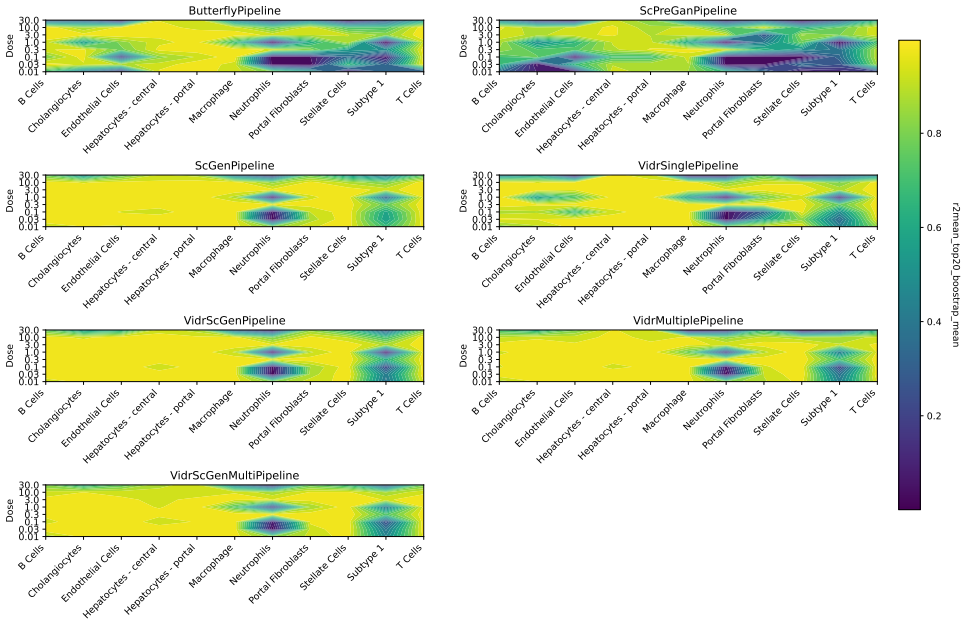


Figure 1.65: r2 top 20

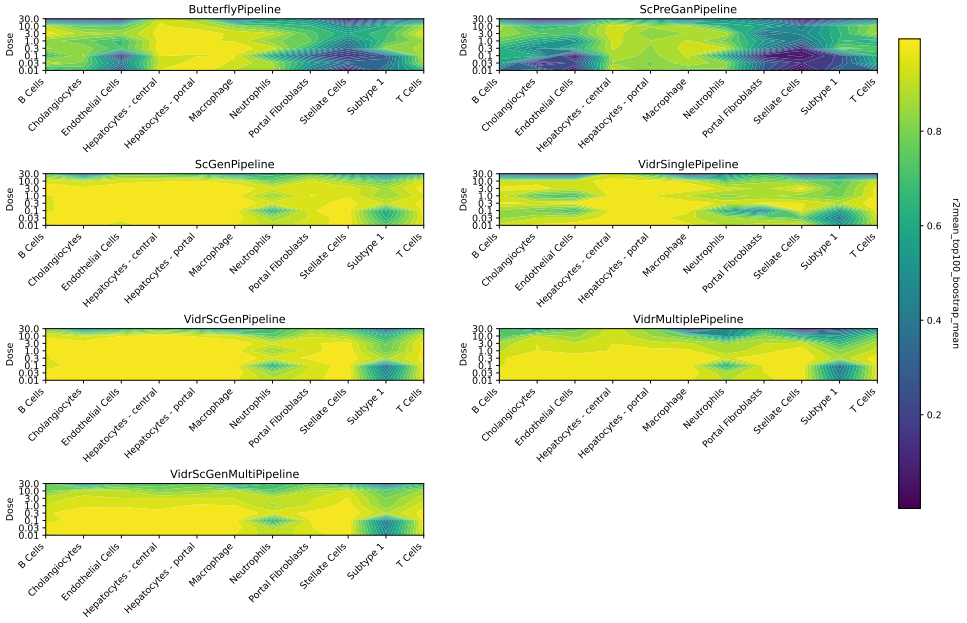


Figure 1.66: r2 top 100

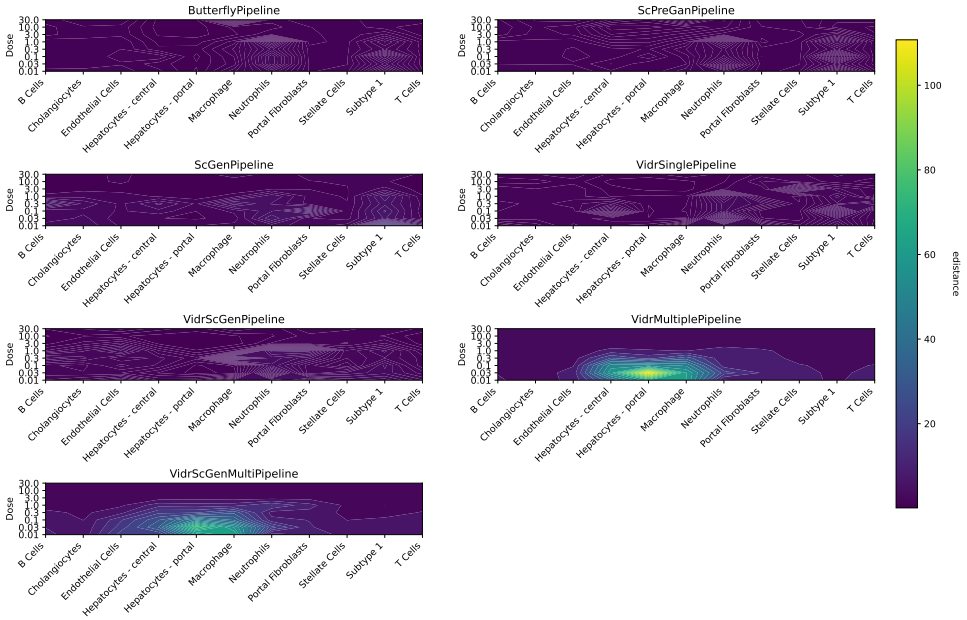


Figure 1.67: E-distance

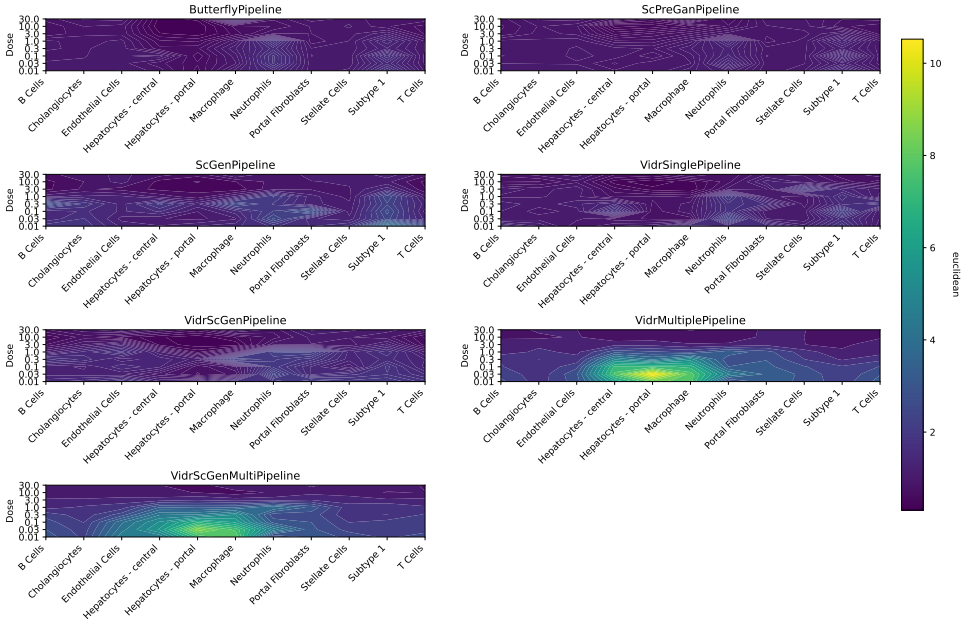


Figure 1.68: Euclidean

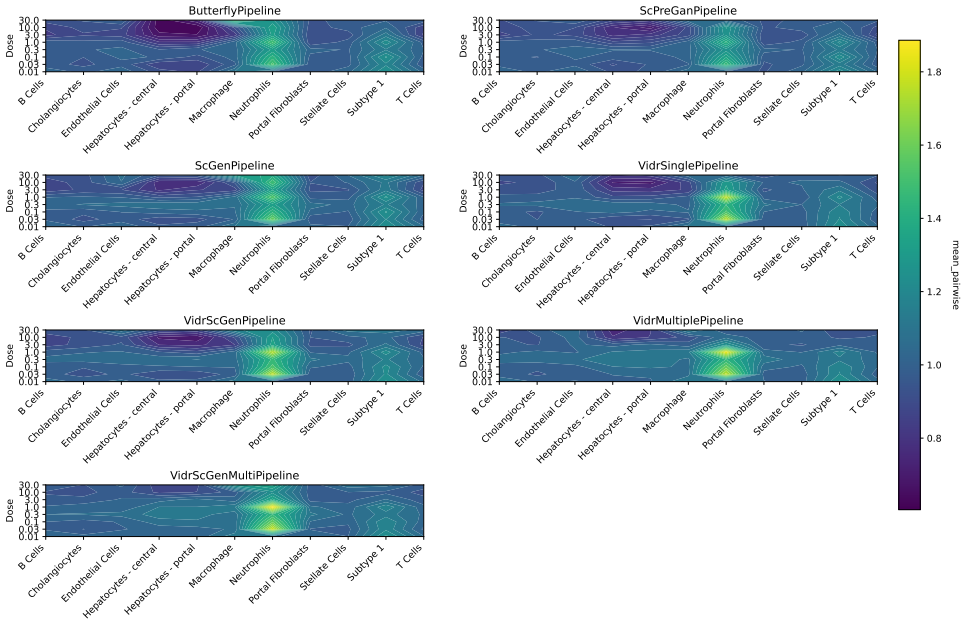


Figure 1.69: Mean pairwise

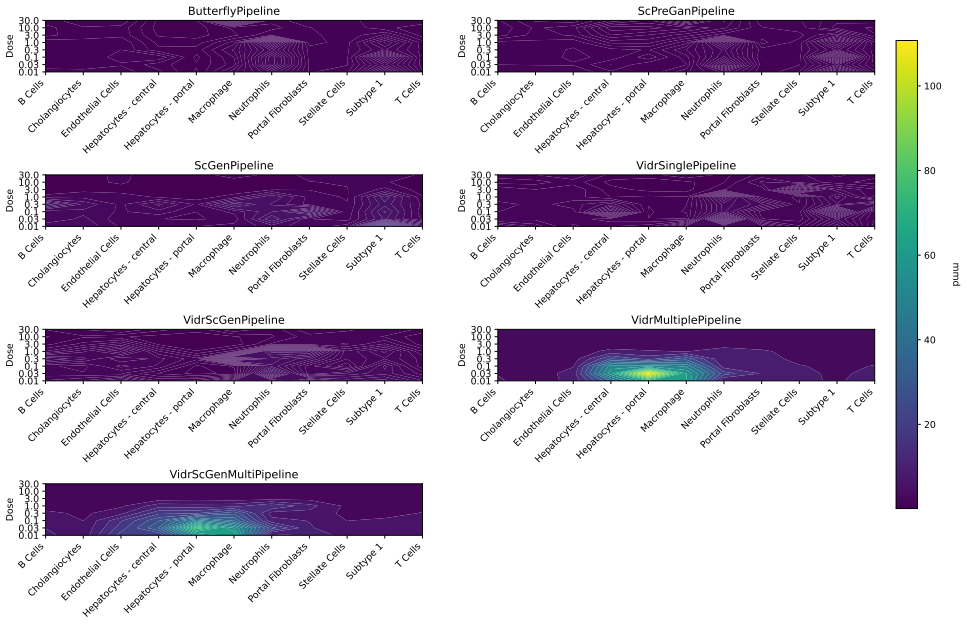


Figure 1.70: MMD

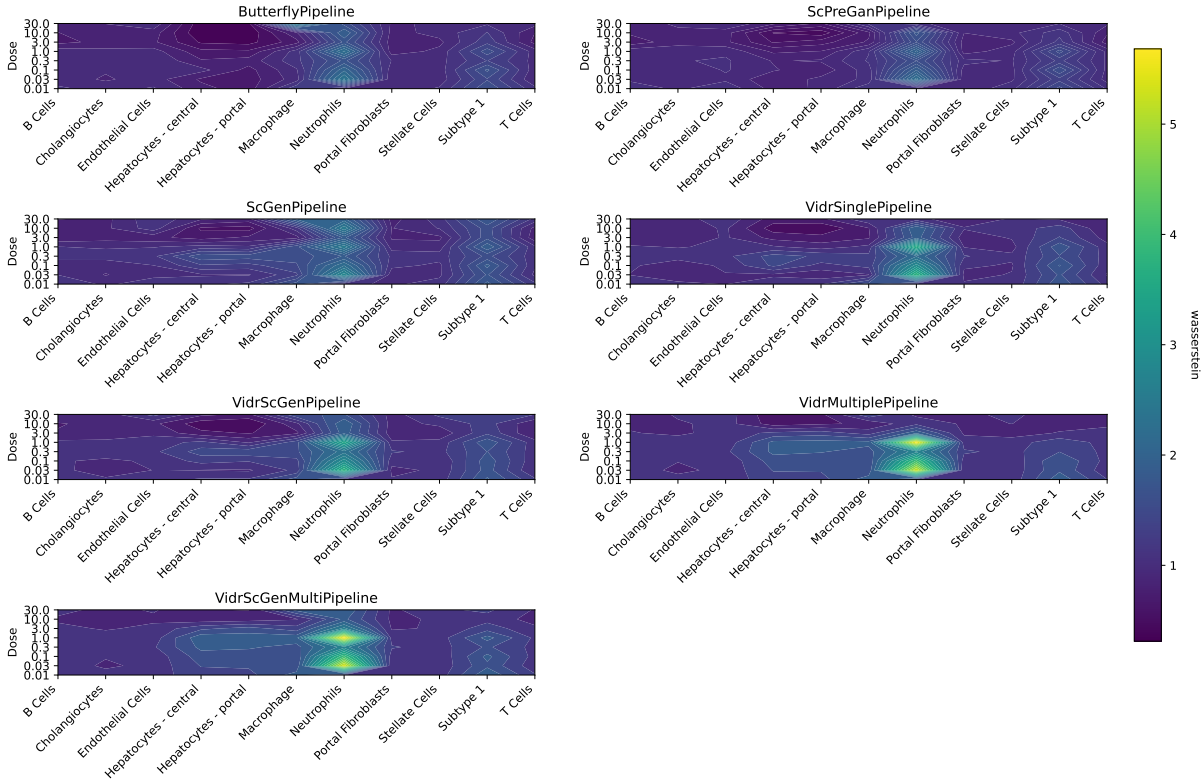
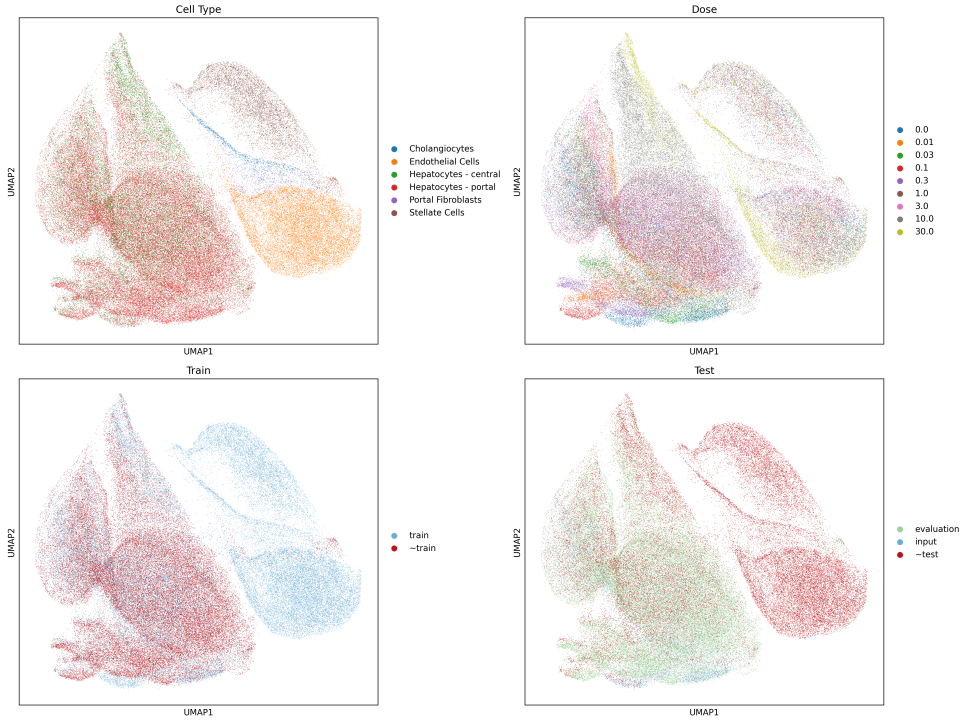
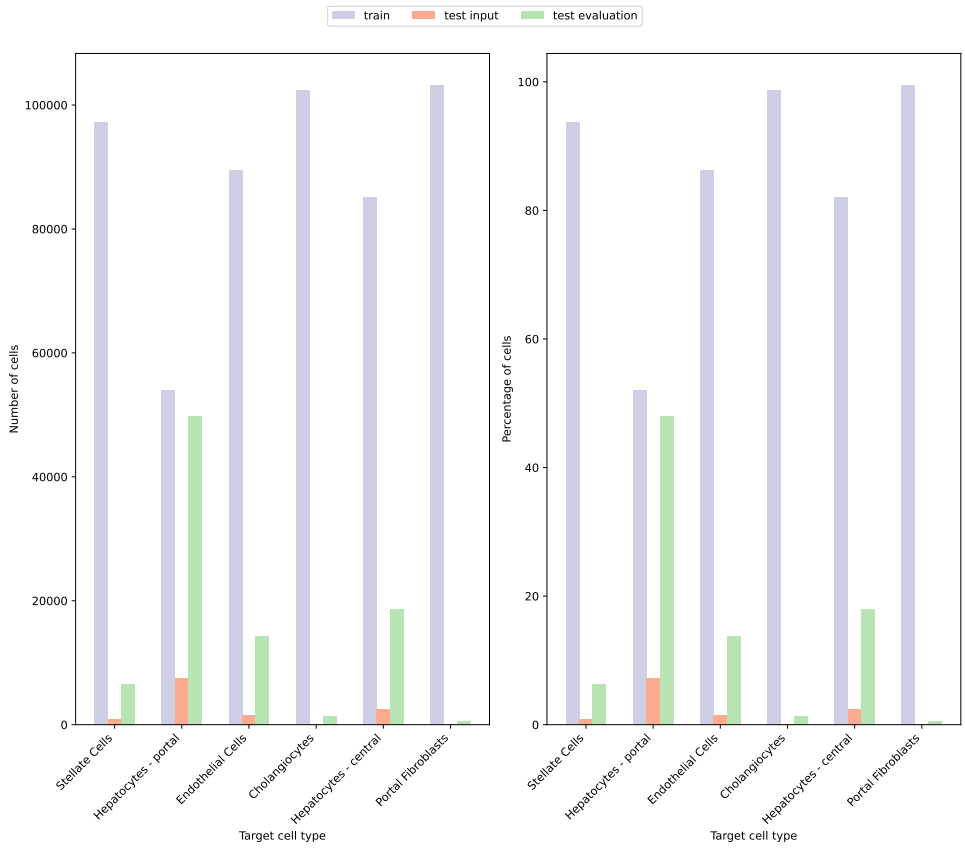


Figure 1.71: Wasserstein

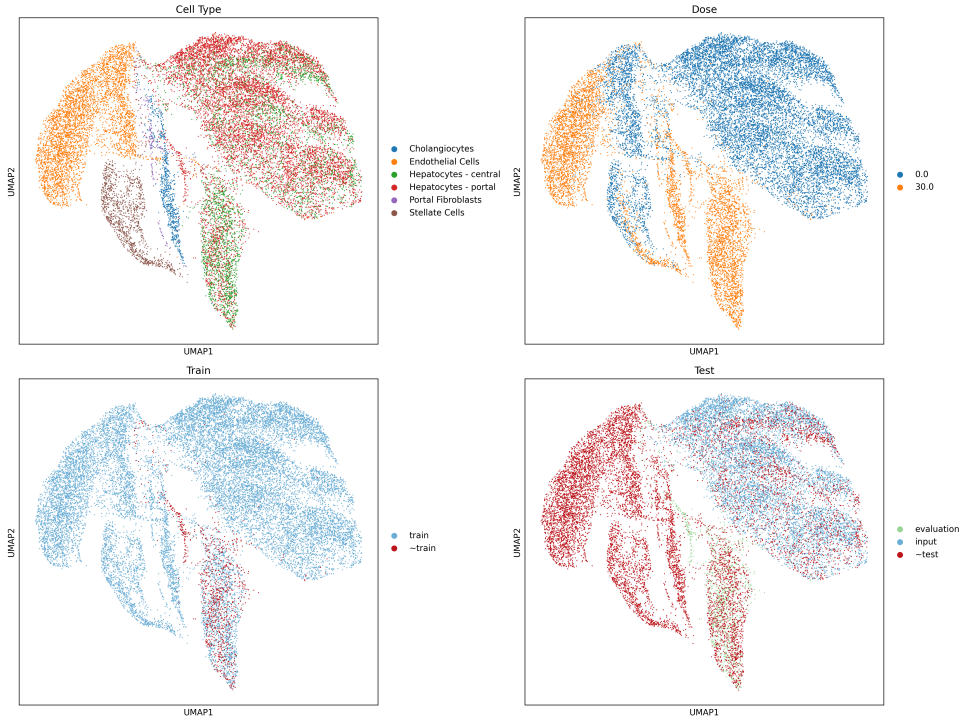
1.3 Nault liver cell types evaluation

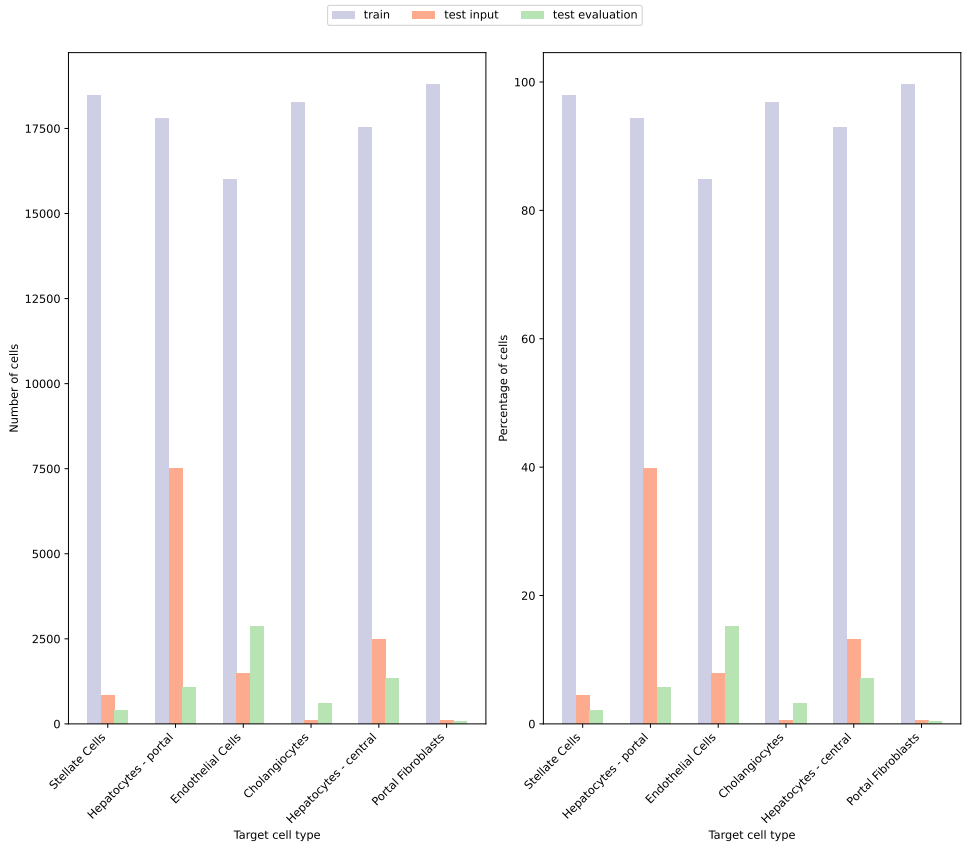
1.3.1 Multiple doses





1.3.2 Single dose 30 $\mu g/kg$





1.3.3 Comparison

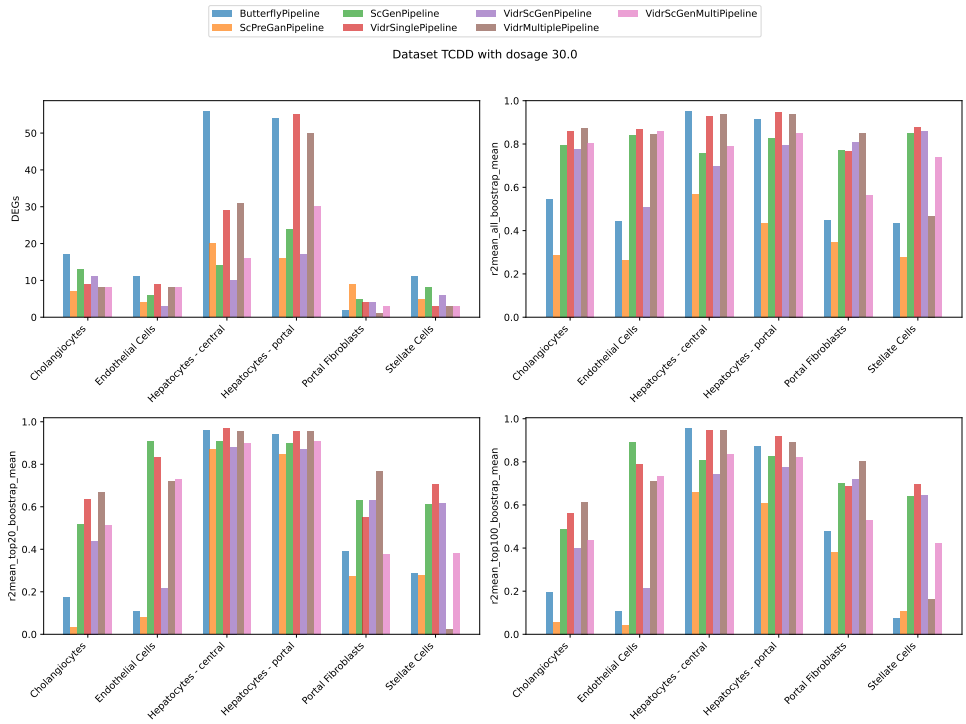


Figure 1.72: Baseline metrics for highest dosage $30\mu g/kg$ across cell types

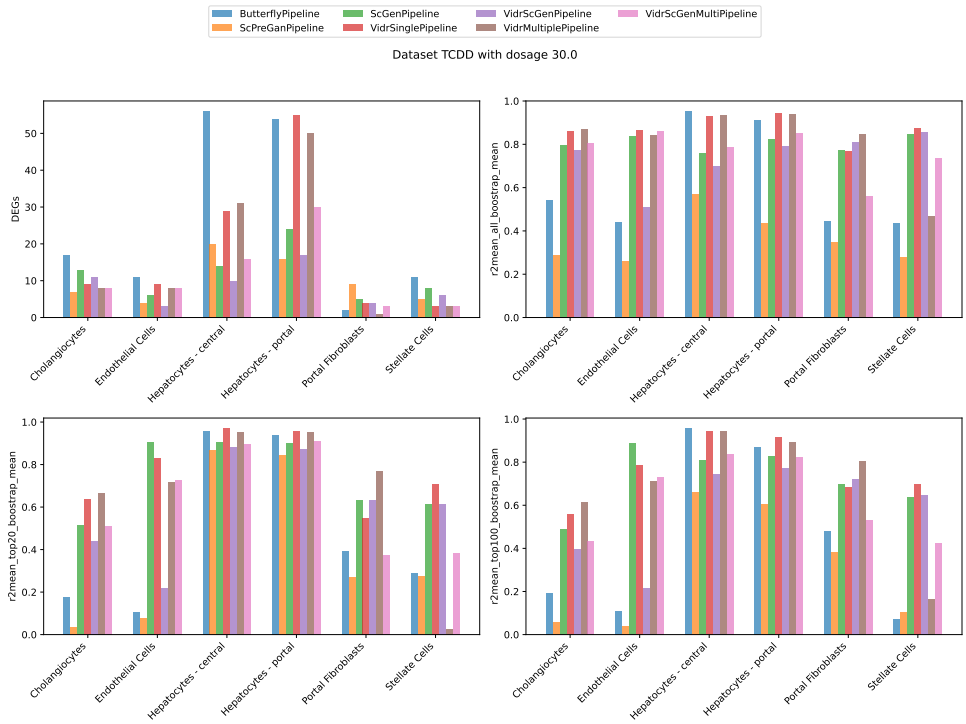


Figure 1.73: Distance metrics for highest dosage $30\mu g/kg$ across cell types

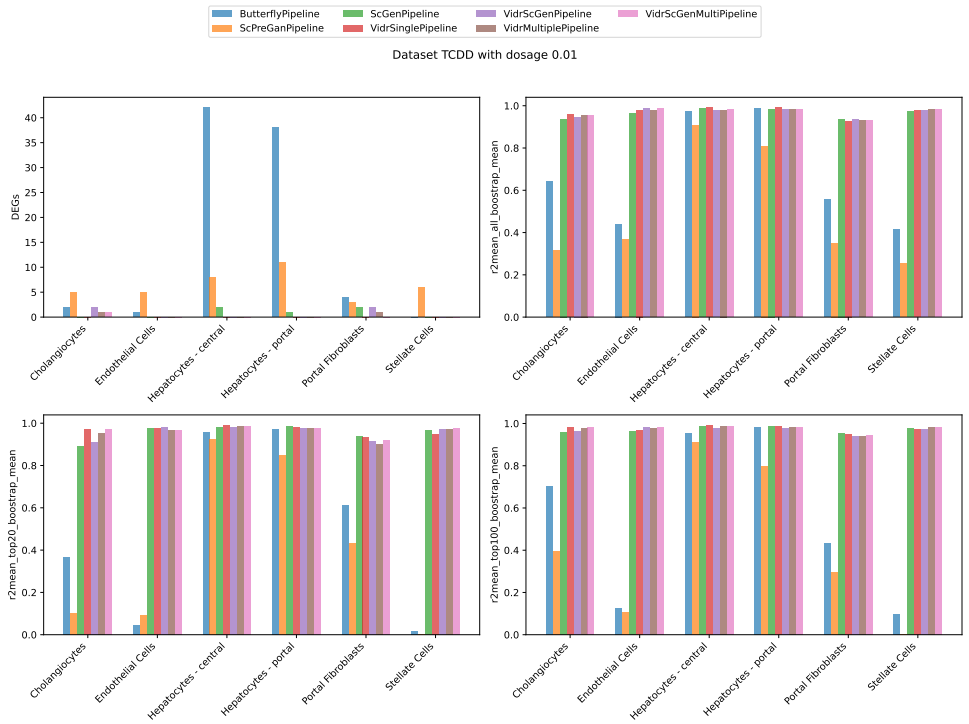


Figure 1.74: Baseline metrics for highest dosage $0.1\mu g/kg$ across cell types

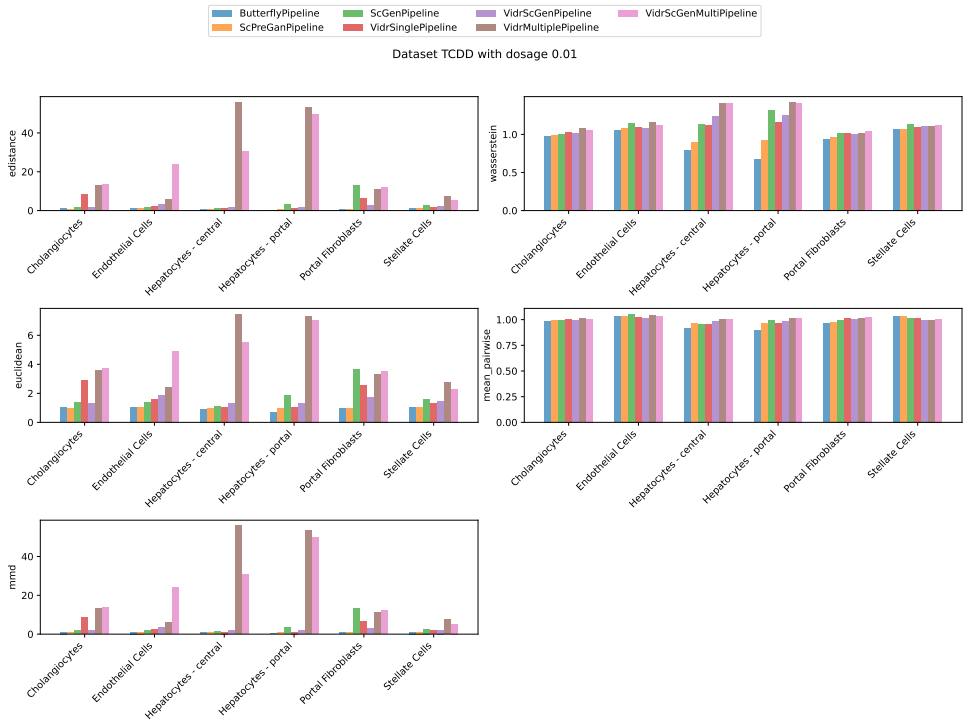


Figure 1.75: Distance metrics for highest dosage $0.1\mu g/kg$ across cell types

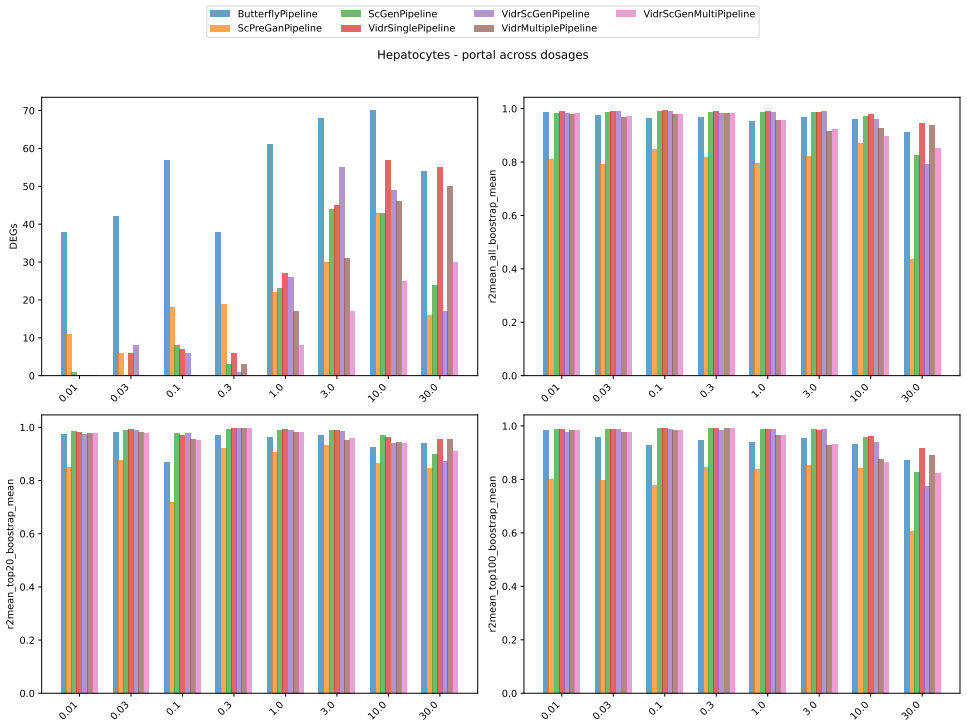


Figure 1.76: Baseline metrics for Hepatocytes - portal across dosages

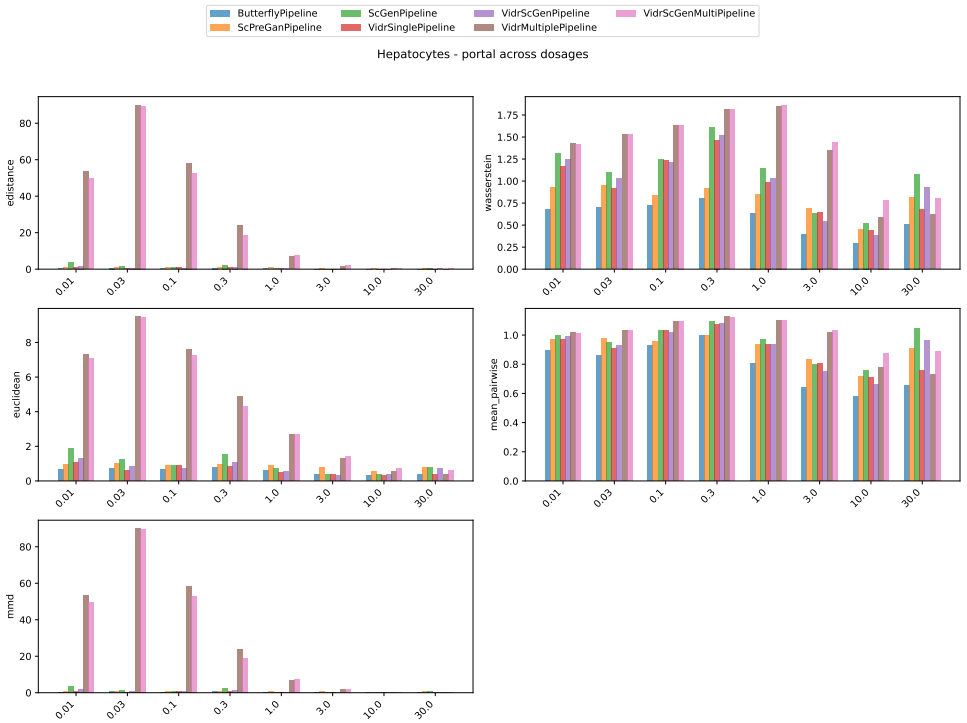


Figure 1.77: Distance metrics for Hepatocytes - portal across dosages

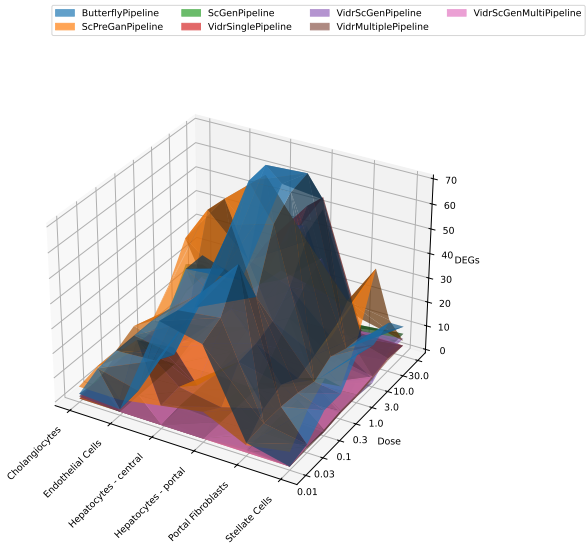


Figure 1.78

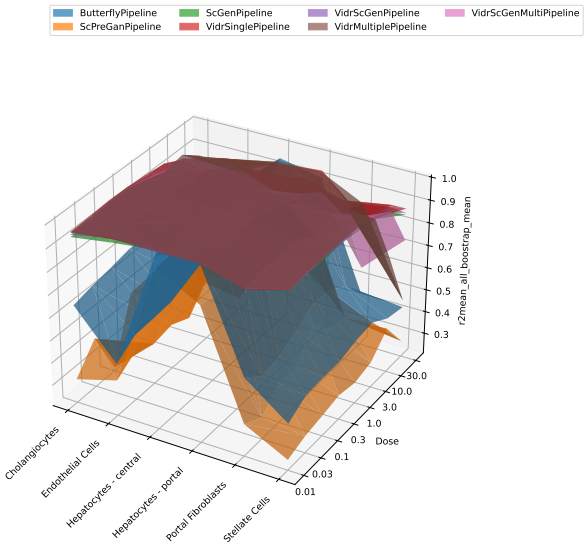


Figure 1.79

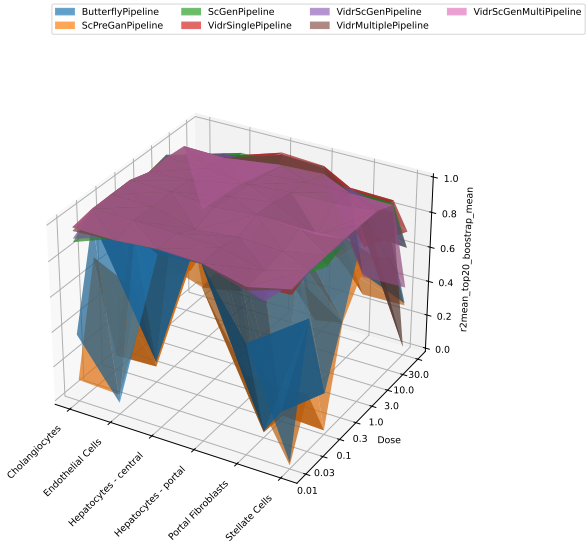


Figure 1.80

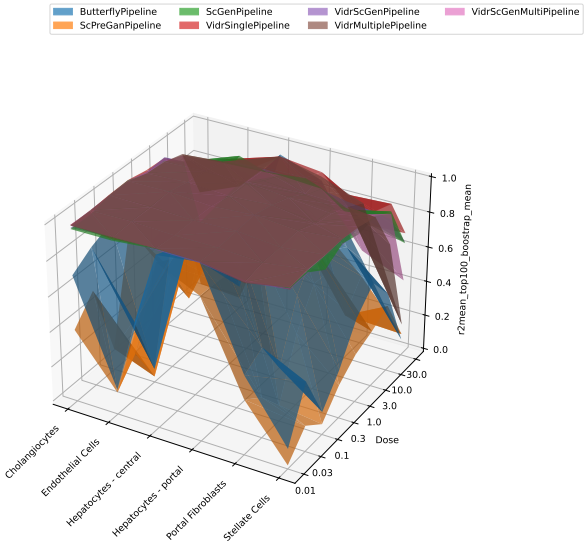


Figure 1.81

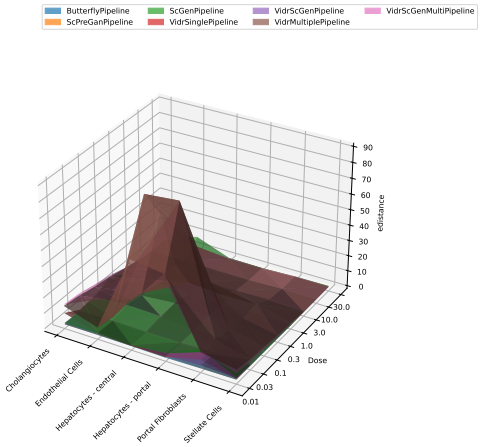


Figure 1.82: E-distance

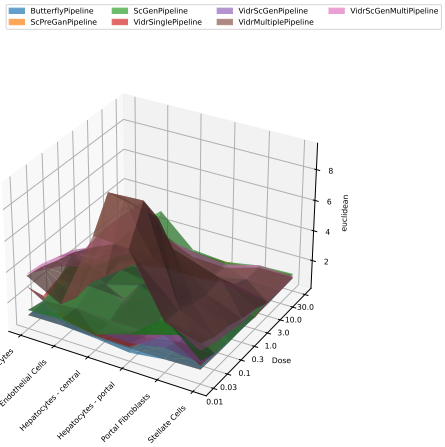


Figure 1.83: Euclidean

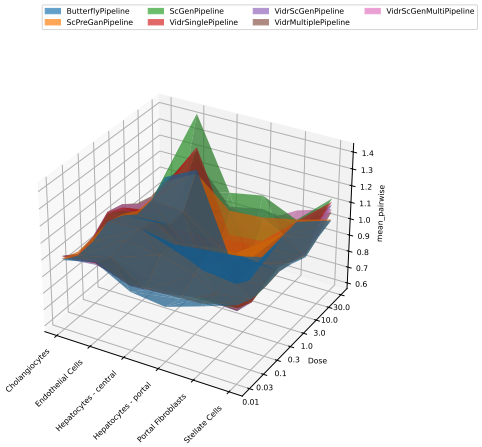


Figure 1.84: Mean pairwise

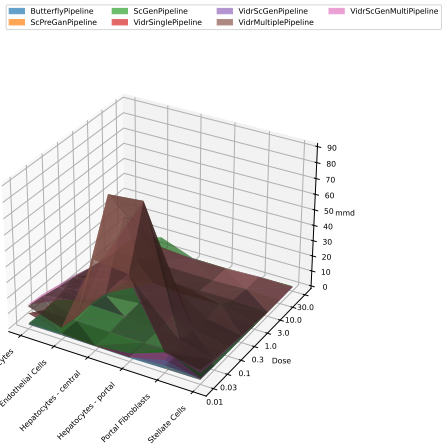


Figure 1.85: MMD

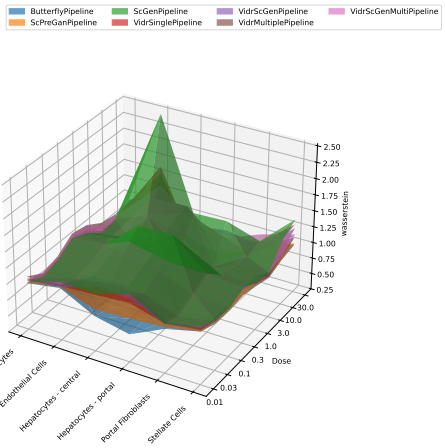
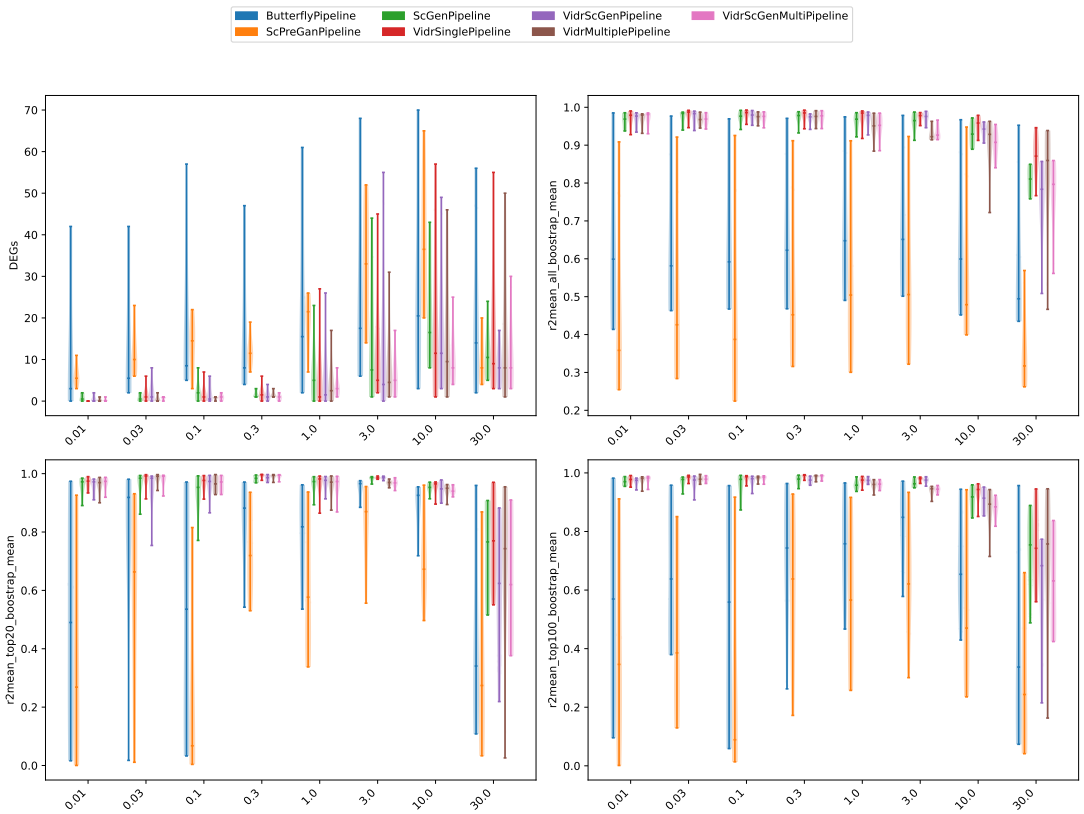


Figure 1.86: Wasserstein

Figure 1.87: Distance metrics per cell type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ScGenPipeline
VidrSingle Pipeline
VidrScGenPipeline
VidrMultiplePipeline
VidrScGenMultiPipeline
DEGs
r2mean_all_boostrap_mean
r2mean_top20_boostrap_mean
r2mean_top100_boostrap_mean
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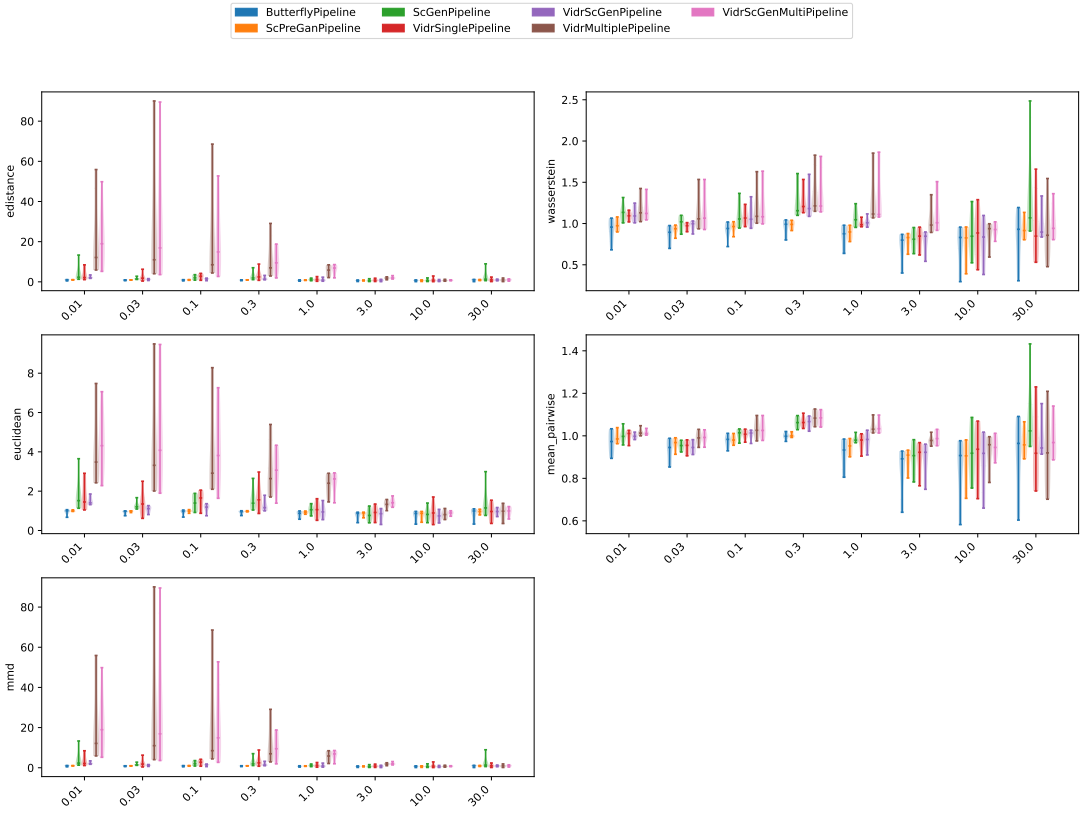
0.03
0.1
0.3
1.0
3.0
10.0
30.0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ScGenPipeline
VidrSinglePipeline
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VidrScGenMultiPipeline
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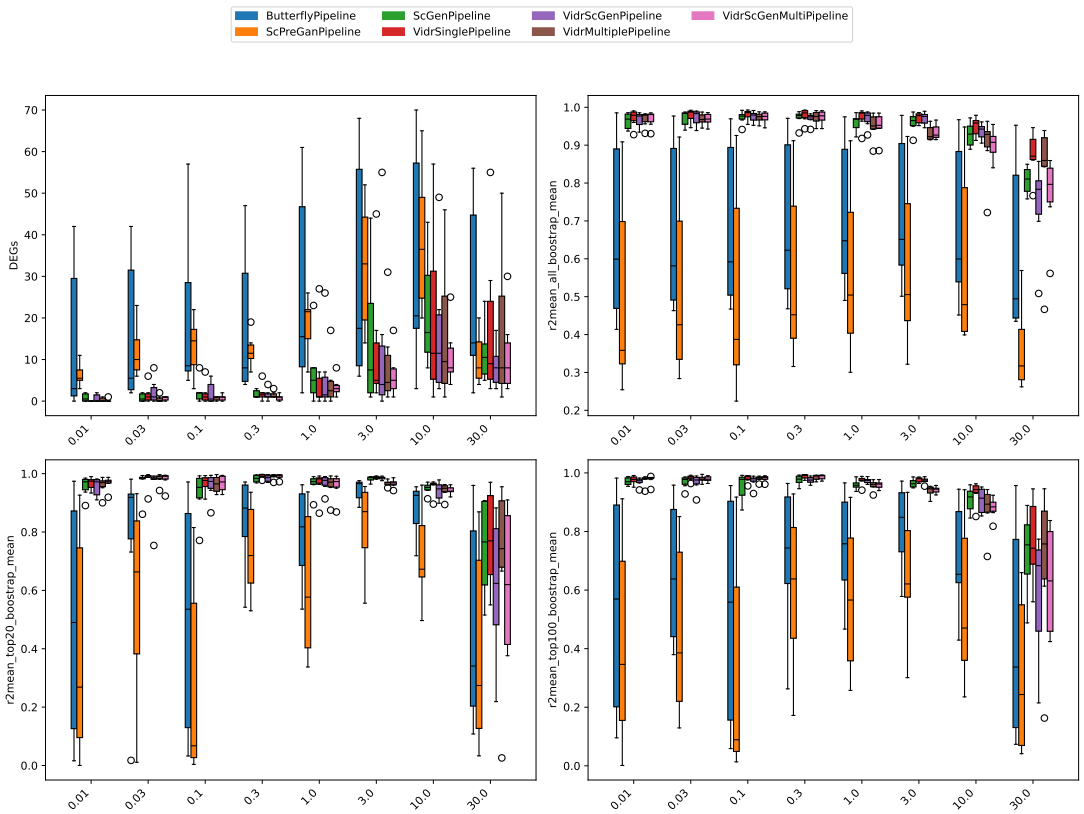
wasserstein
euclidean
mean_pairwise
mmd
0.01
0.03
0.1
0.3
1.0
3.0
10.0
30.0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ScGenPipeline
VidrSinglePipeline
VidrScGenPipeline
VidrMultiplePipeline
VidrScGenMultiPipeline
DEGs
r2mean_all_boostrap_mean
r2mean_top20_boostrap_mean
r2mean_top100_boostrap_mean
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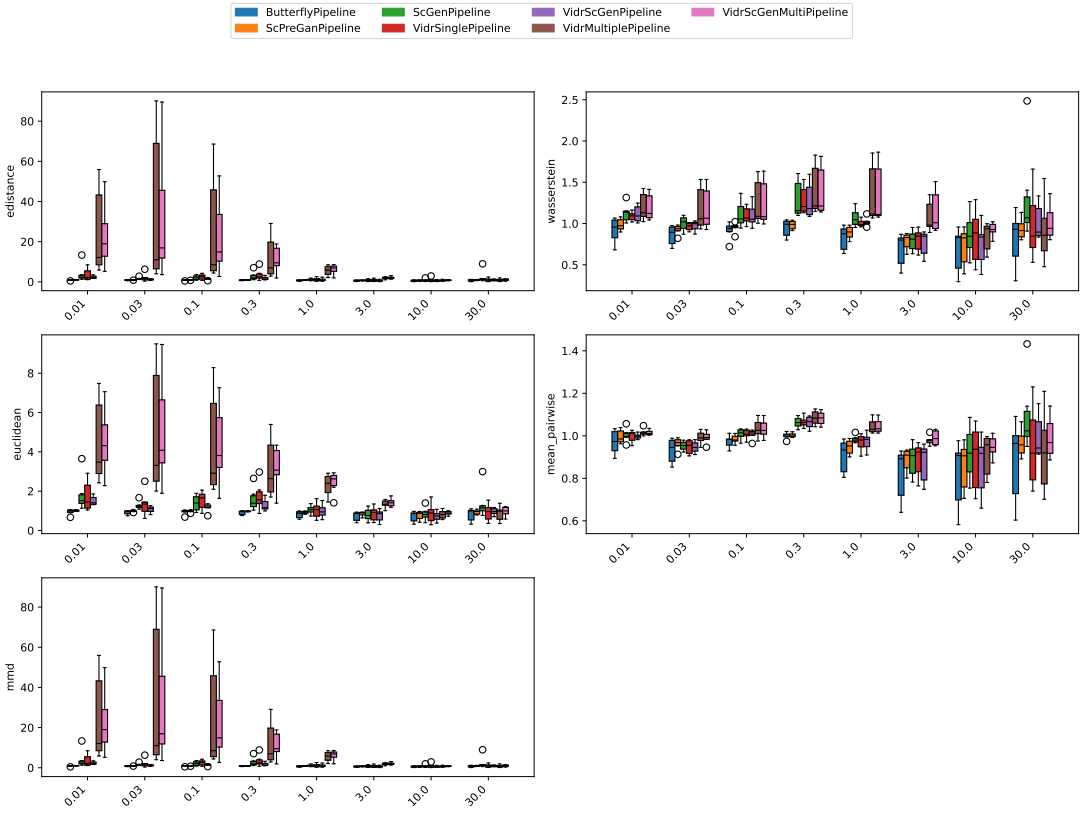
0.3
1.0
3.0
10.0
30.0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ScGenPipeline
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euclidean
mean_pairwise
mmd
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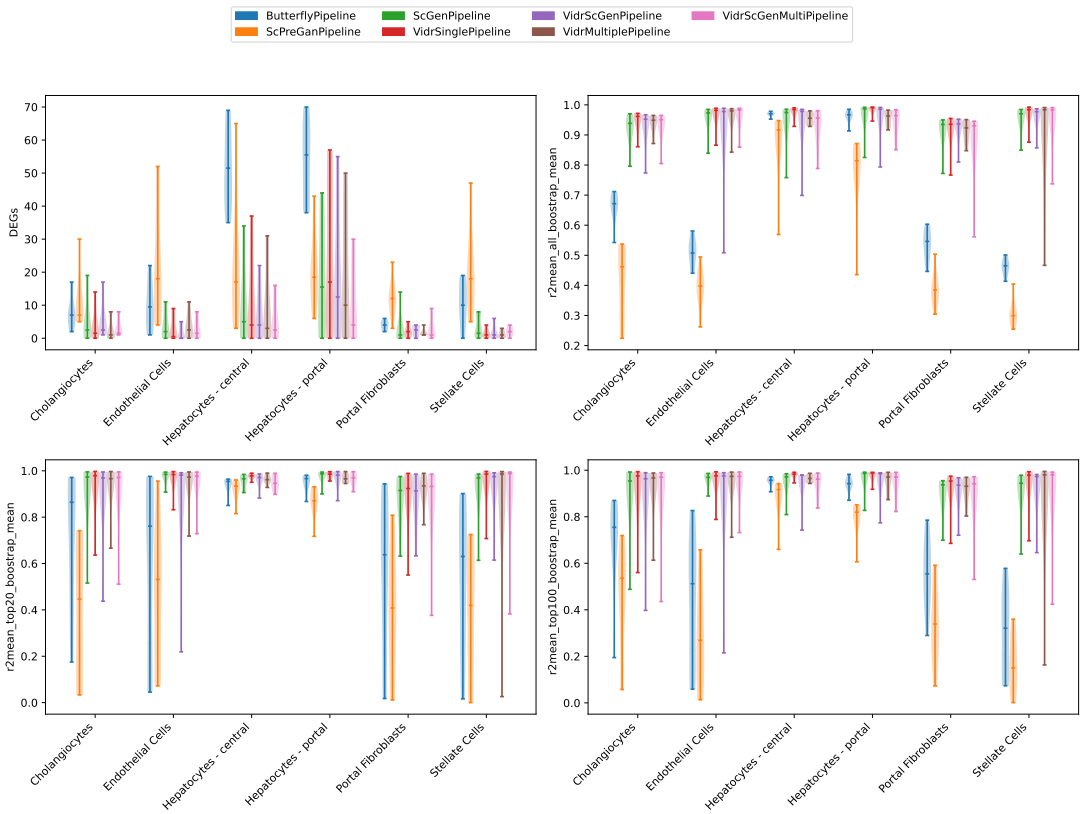
0.03
0.1
0.3
1.0
3.0
10.0
30.0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ScGenPipeline
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VidrMultiplePipeline
VidrScGenMultiPipeline
DEGs
r2mean_all_boostrap_mean
r2mean_top20_boostrap_mean
r2mean_top100_boostrap_mean
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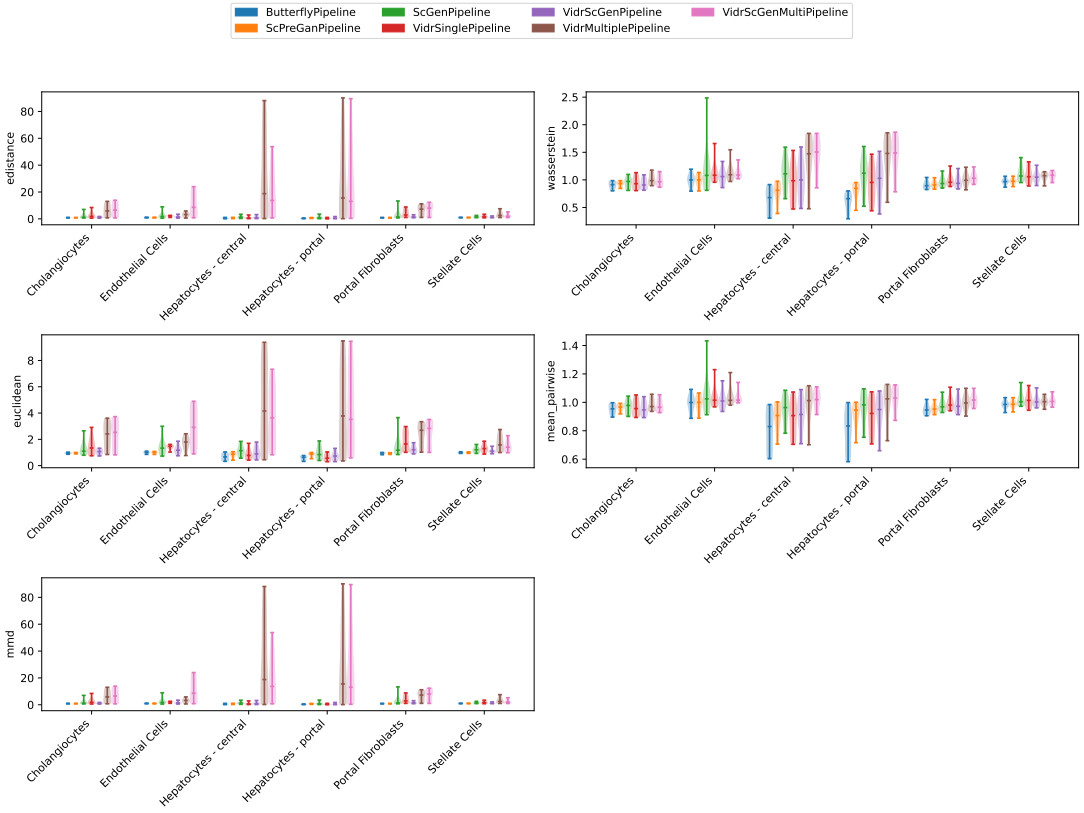
Endothelial Cells
Hepatocytes - central
Hepatocytes - portal
Portal Fibroblasts
Stellate Cells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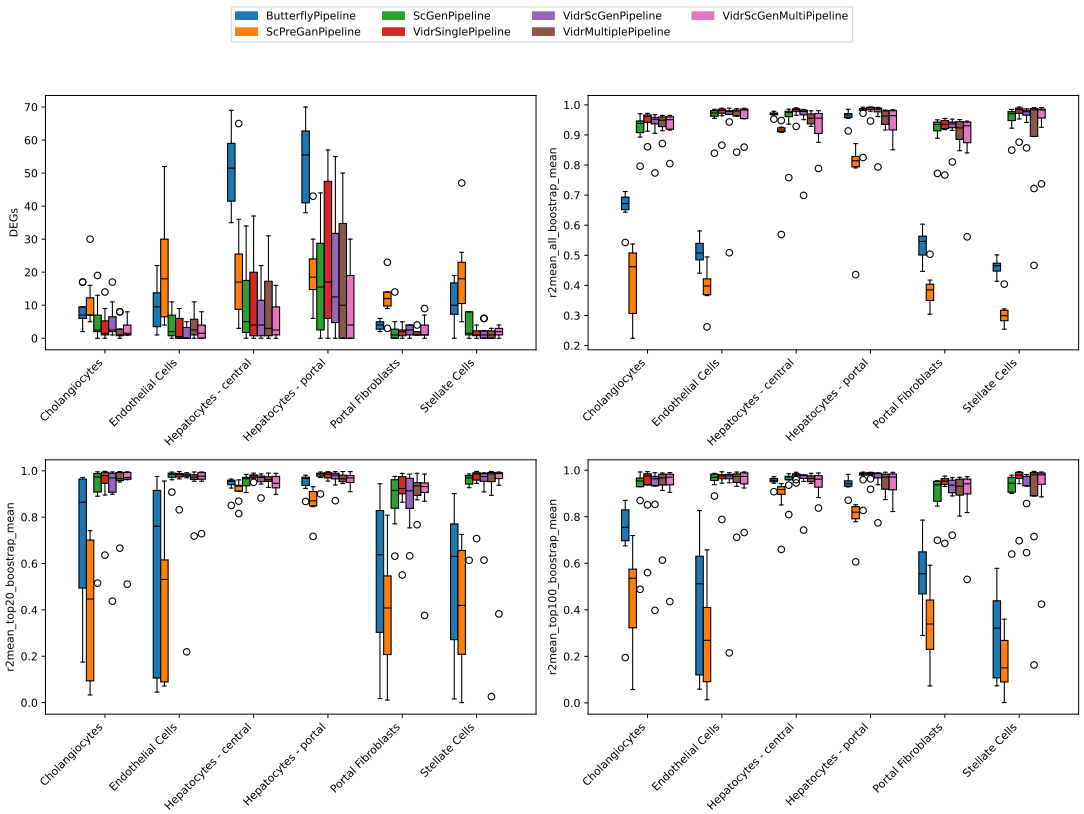
mean_pairwise
mmd
Cholangiocytes
Endothelial Cells
Hepatocytes - central
Hepatocytes - portal
Portal Fibroblasts
Stellate Cells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DEGs
r2mean_all_boostrap_mean
r2mean_top20_boostrap_mean
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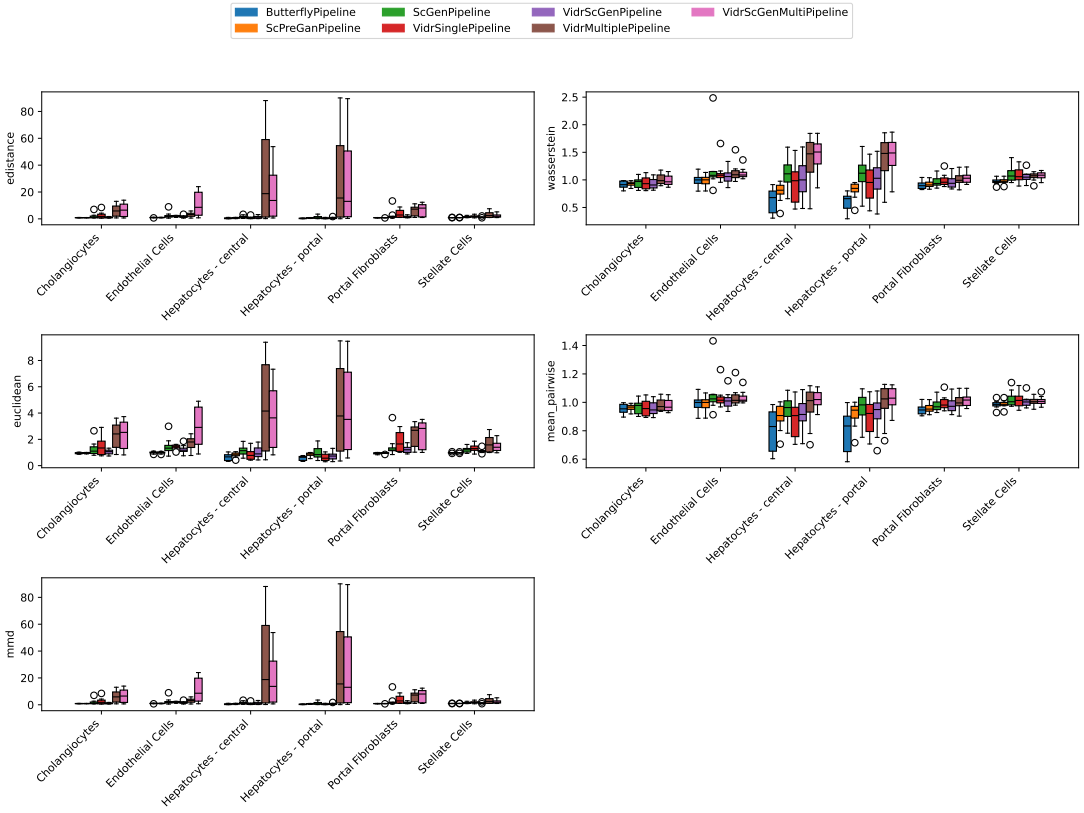
Cholangiocytes
Endothelial Cells
Hepatocytes - central
Hepatocytes - portal
Portal Fibroblasts
Stellate Cells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ScGenPipeline
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euclidean
mean_pairwise
mmd
Cholangiocytes
Endothelial Cells
Hepatocytes - central
Hepatocytes - portal
Portal Fibroblasts
Stellate Cells

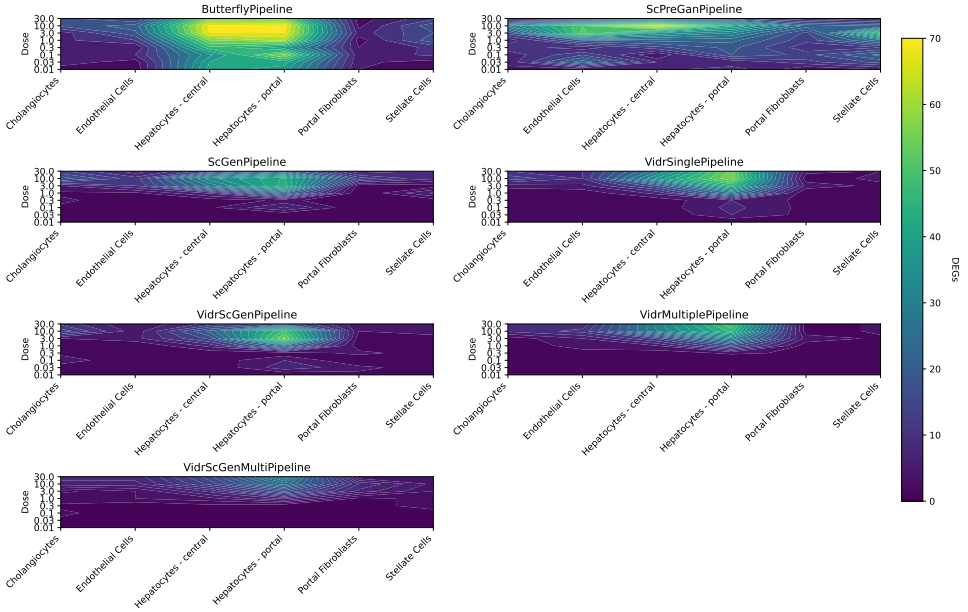


Figure 1.88: DEGs

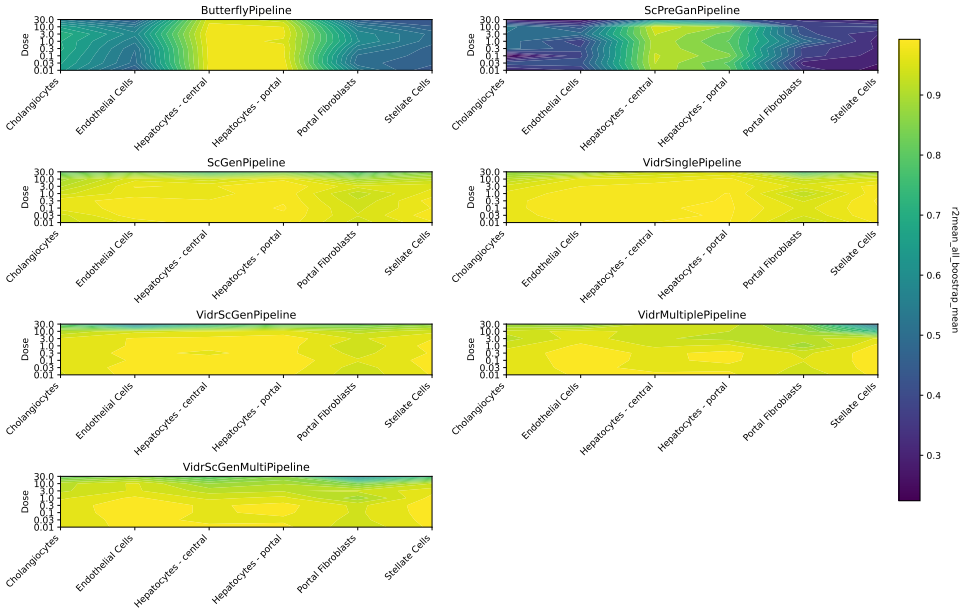


Figure 1.89: r2 HVGs

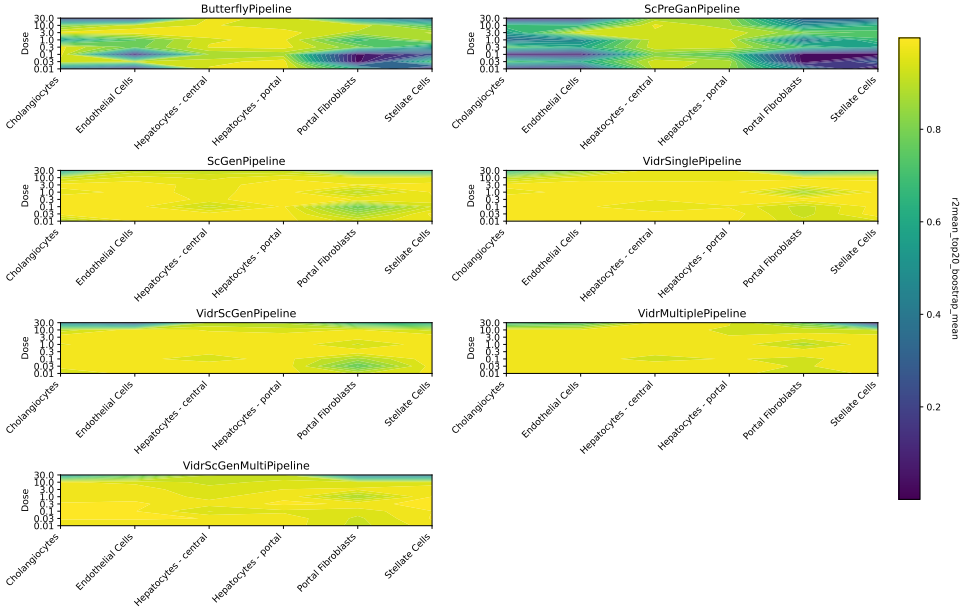


Figure 1.90: r2 top 20

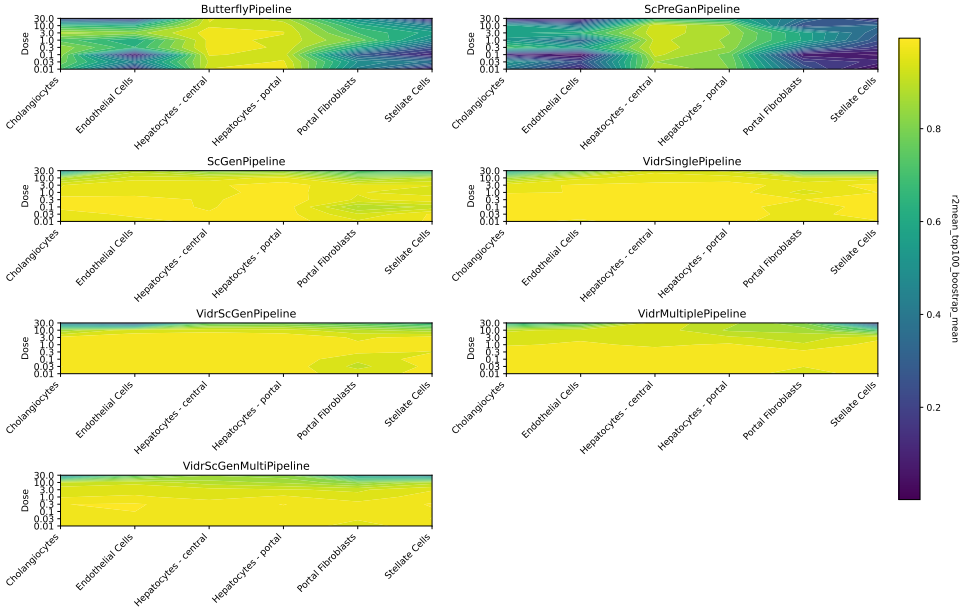


Figure 1.91: r2 top 100

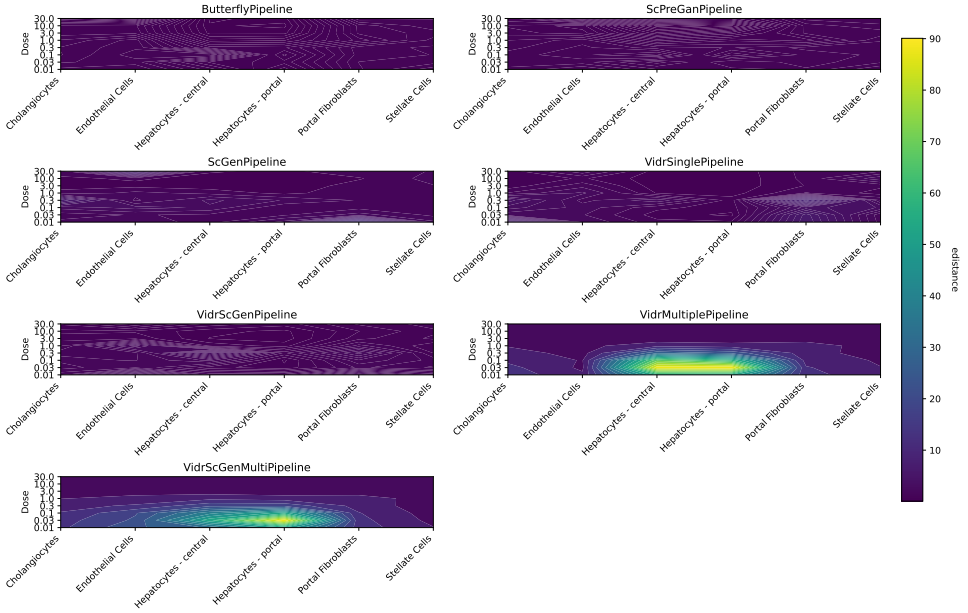
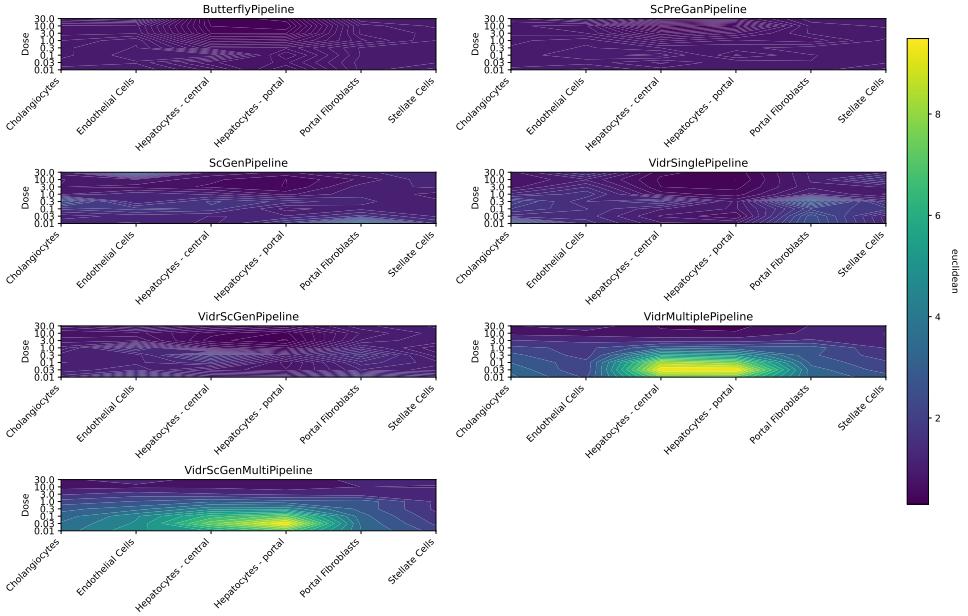


Figure 1.92: E-distance



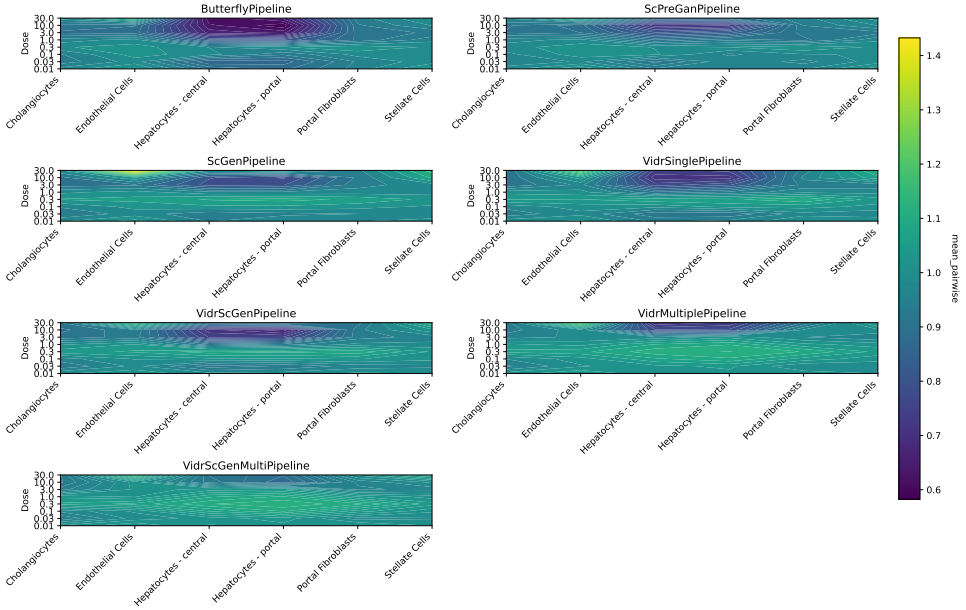


Figure 1.93: Mean pairwise

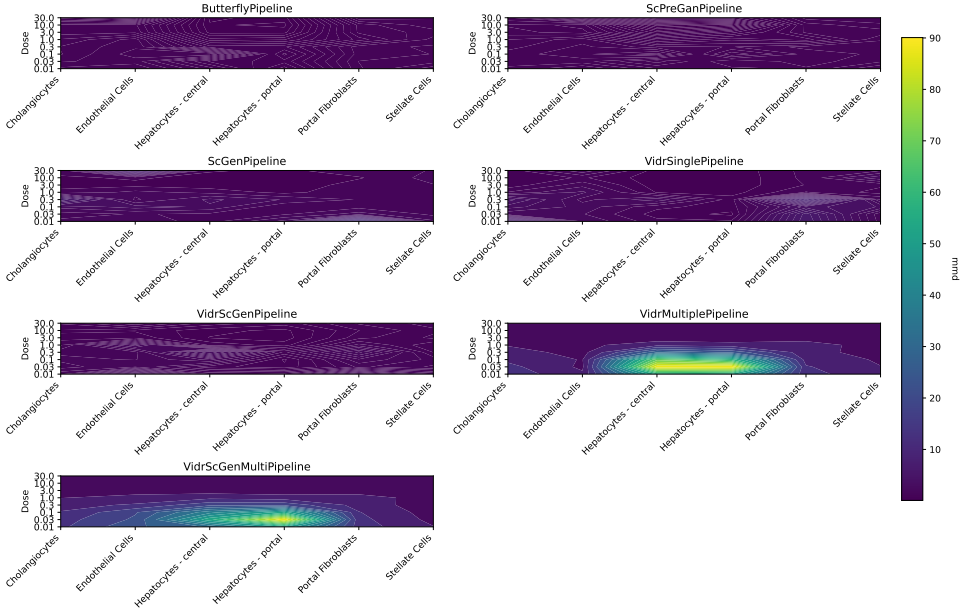


Figure 1.94: MMD

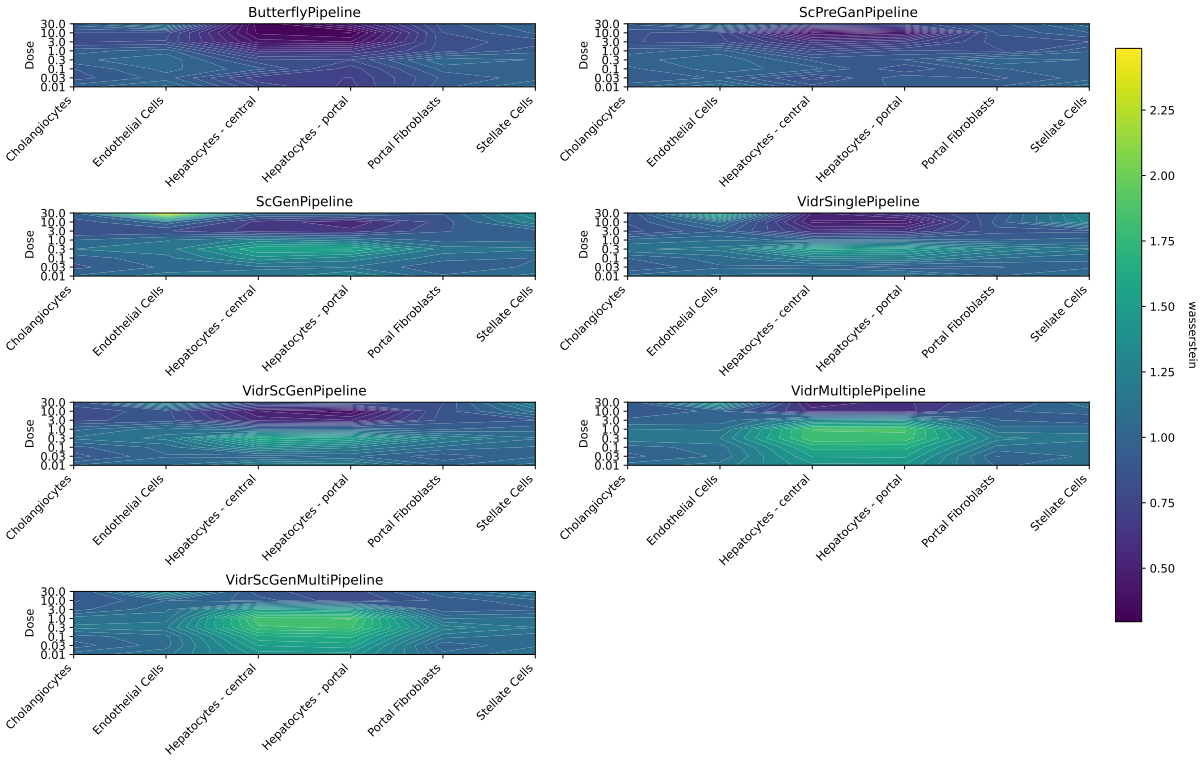
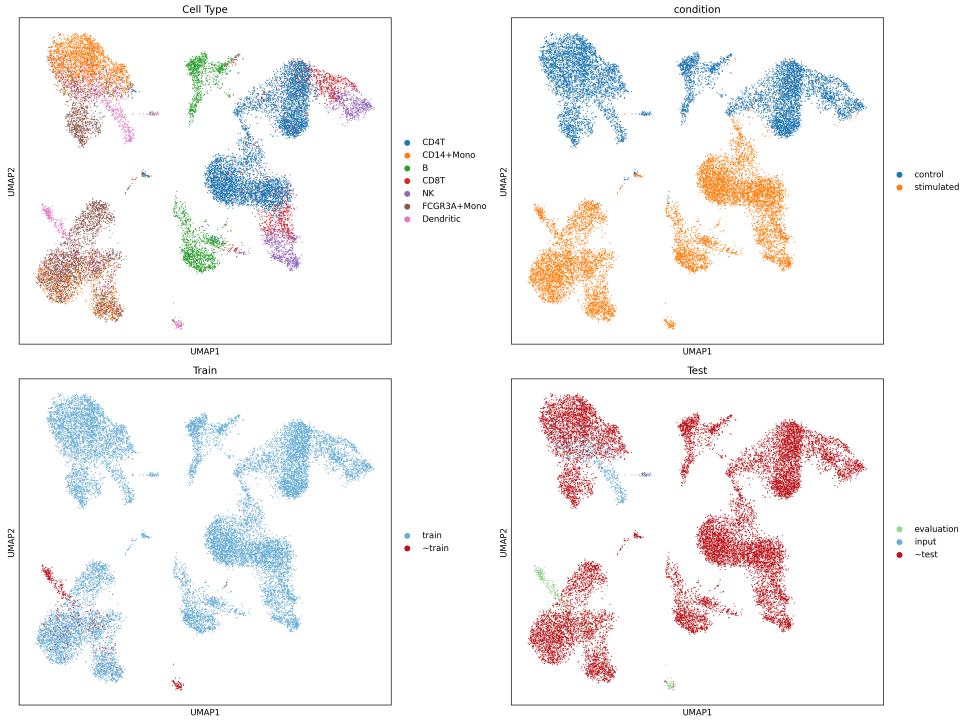


Figure 1.95: Wasserstein

1.3.4 Παρατηρήσεις

- Το scButterfly και το scPreGan έχουν παρόμοια συμπεριφορά στις μετρικές και εμφανίζουν μεγάλη διακύμανση κατά μήκος των τύπων των κυττάρων και των δόσεων.
- Τα μοντέλα που έχουν ως βάση την αρχιτεκτονική του scGen (scVIDR, και οι παραλλαγές του), VAR και post-processing στο latent space, έχουν την υψηλότερη και πιο σταθερή απόδοση σε μετρικές του R^2, ωστόσο υστερούν στην καταμέτρηση των κοινών διαφοροποιήσιμων γονιδίων έκφρασης (DEGs).

1.4 PBMC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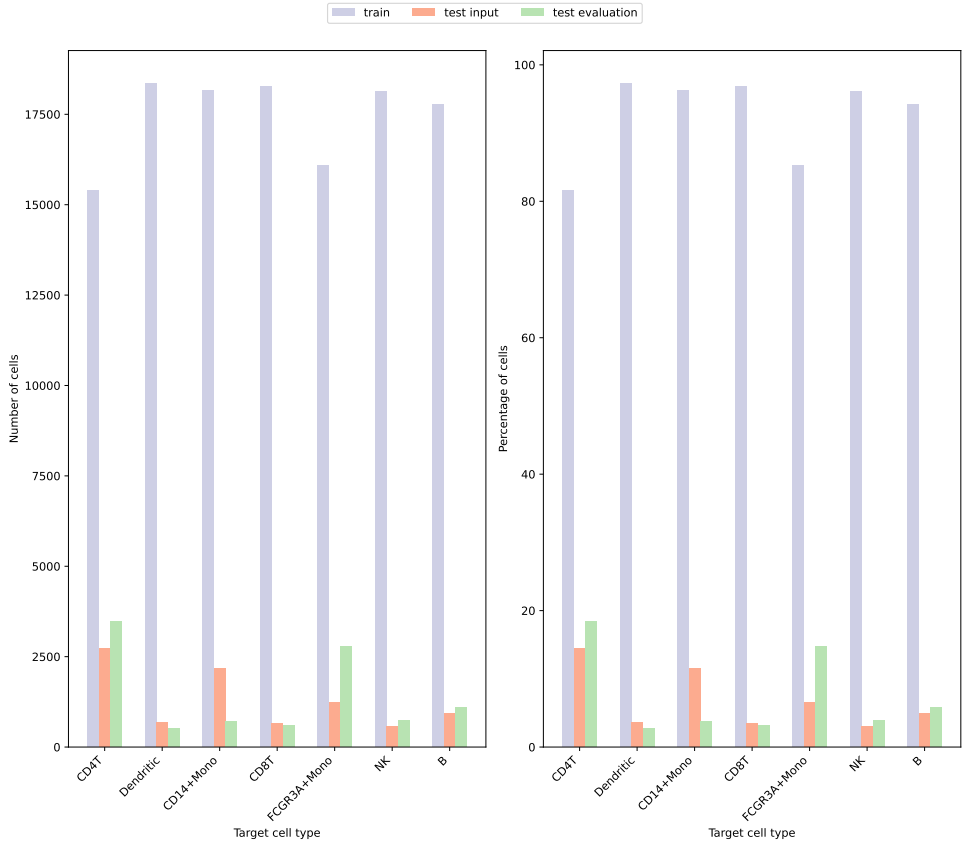
CD4T
CD14+Mono
B
CD8T
NK
FCGR3A+Mono
Dendritic
condition
control
stimulated
Train
train
~train
Test
evaluation
input
~test
UMAP1
UMAP2


train
test input
test evaluation
Number of cells
Percentage of cells
Target cell type
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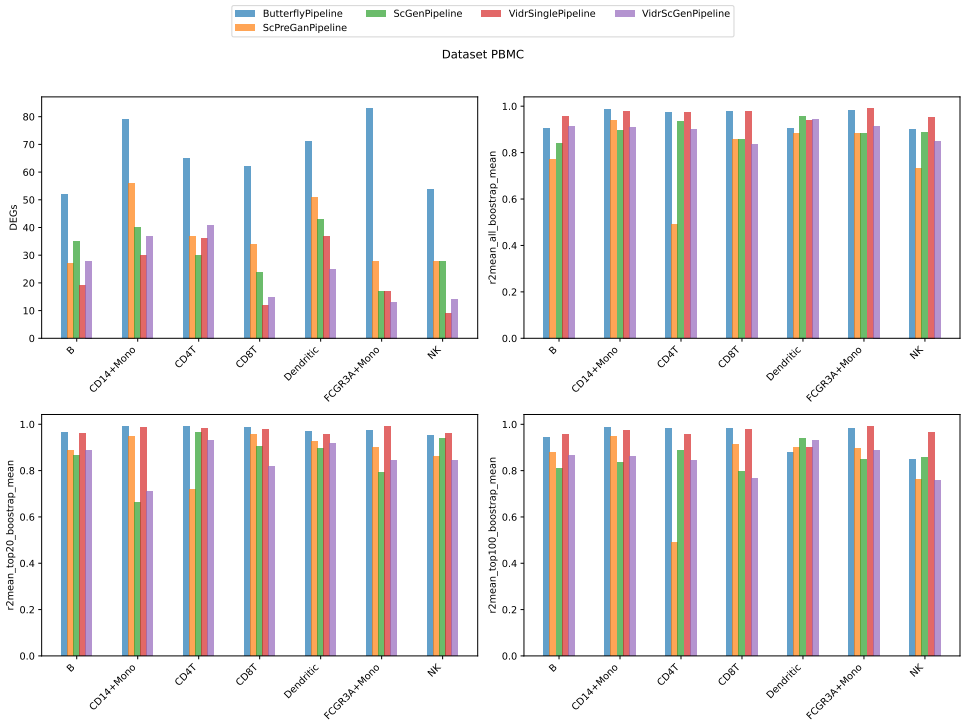
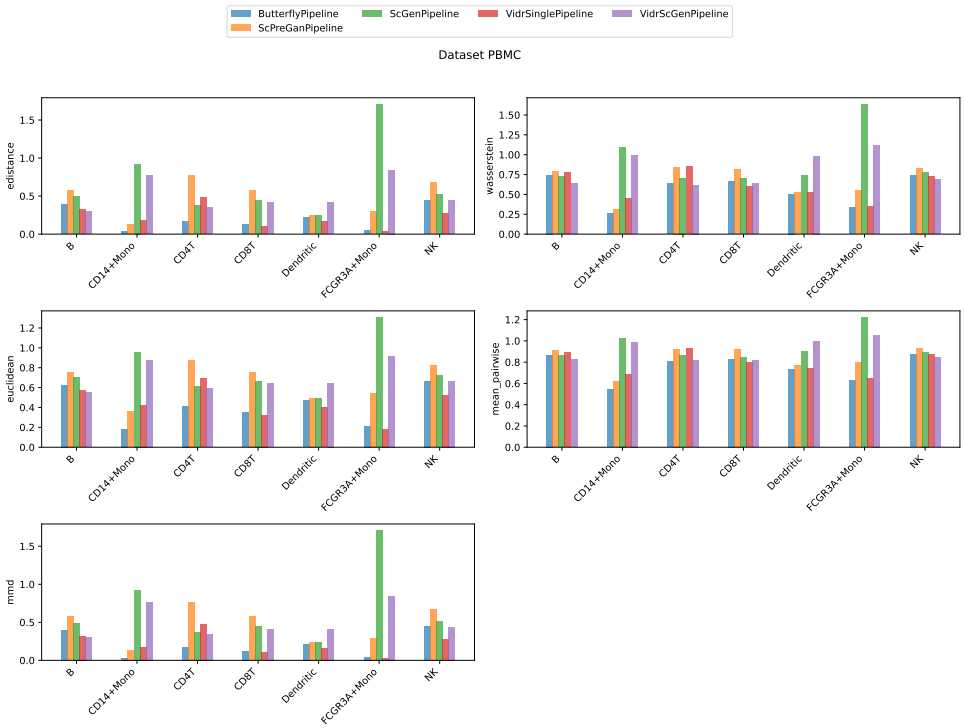
Dendritic
CD14+Mono
CD8T
FCGR3A+Mono
NK
B

1.4.1 Comparison





Appendix A

Ακρωνύμια και συντομογραφίες

LAN Local Area Network

Bibliography

[1] Yuge Ji, Mohammad Lotfollahi, F. Alexander Wolf, and Fabian J. Theis. Machine learning for perturbational single-cell omics. *Cell Systems*, 12(6):522–537, June 2021.