Dimension Reduction Methods:
From PCA to TSNE and UMAP

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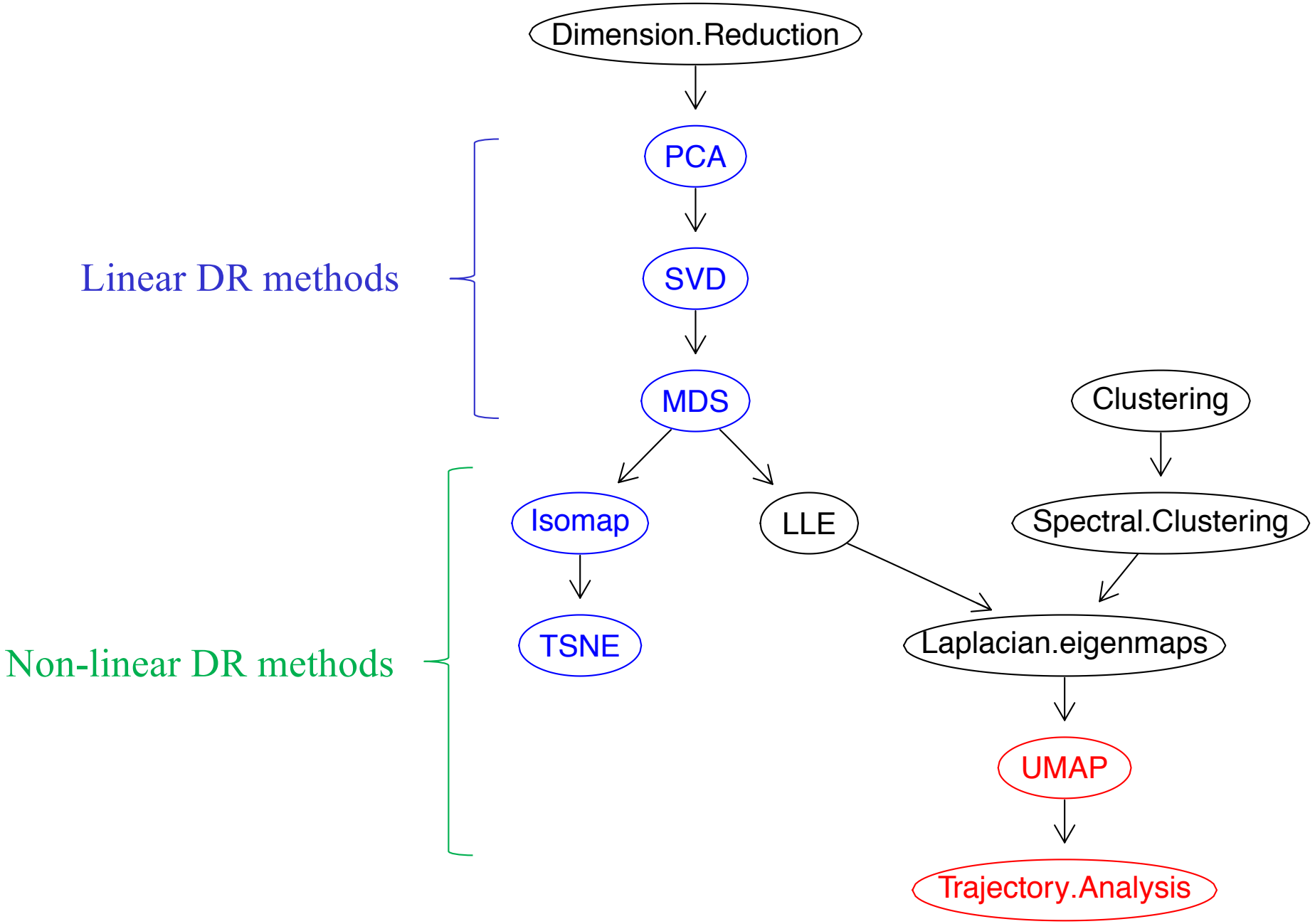
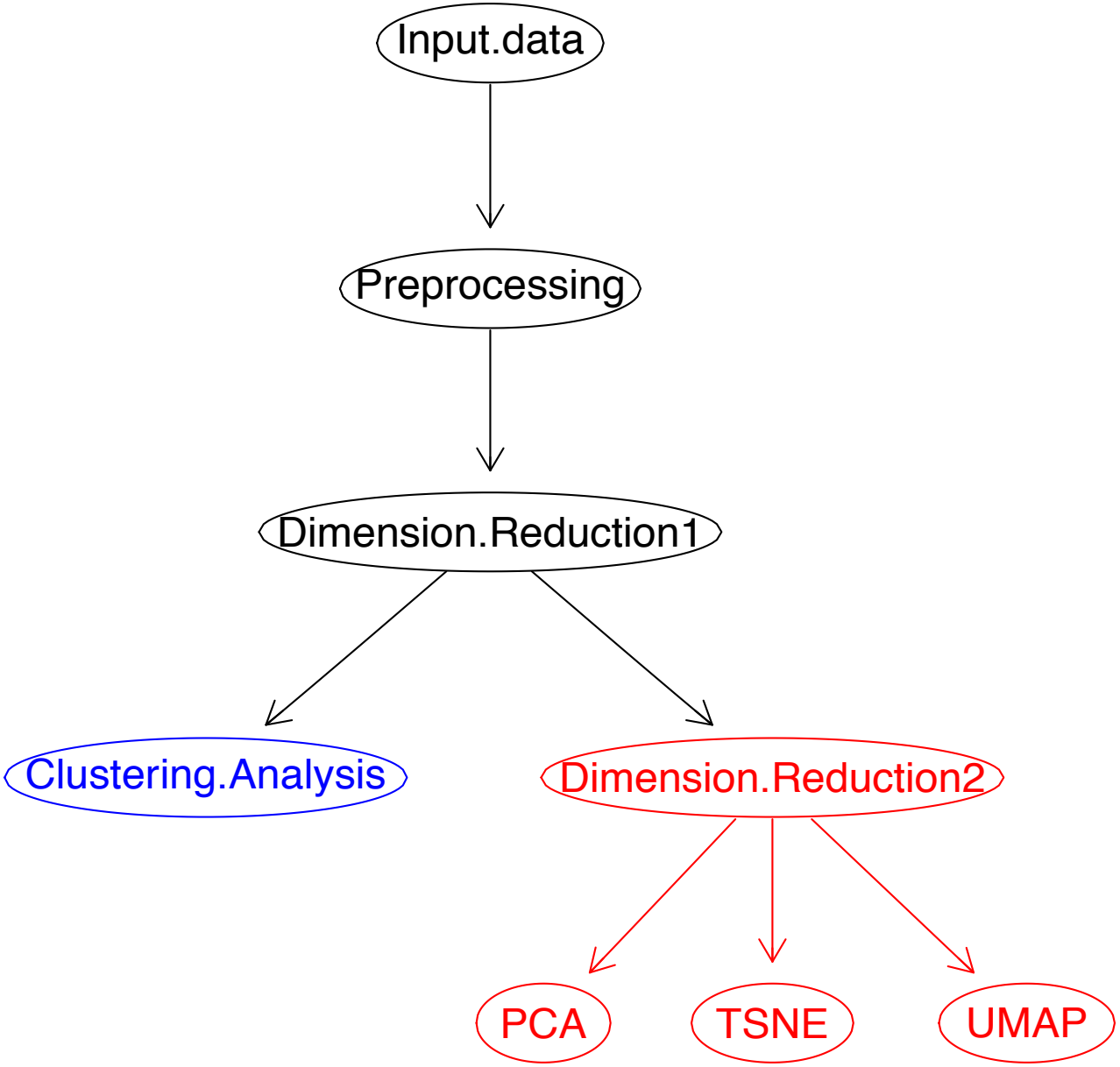
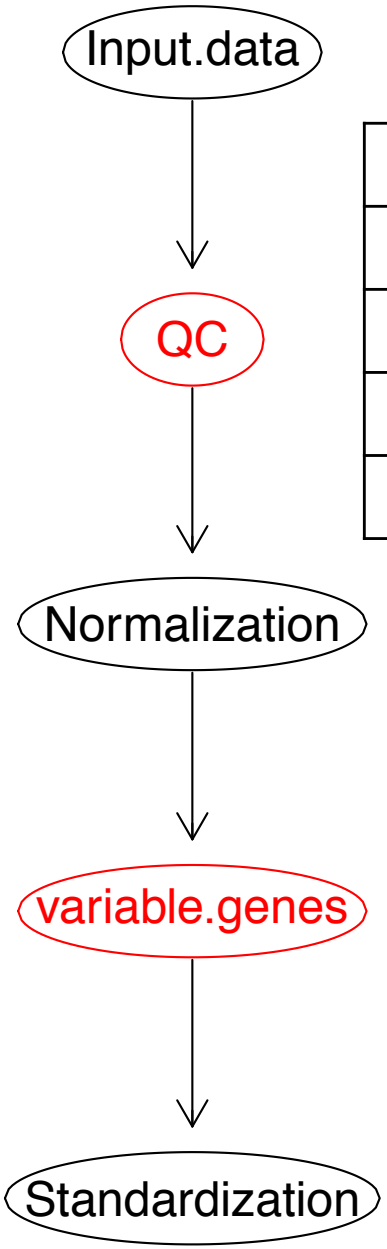
Road Map for Dimension Reduction Methods



Flow Chart of ScRNAseq Analyses with Seurat Package



Preprocessing Steps in Seurat Package

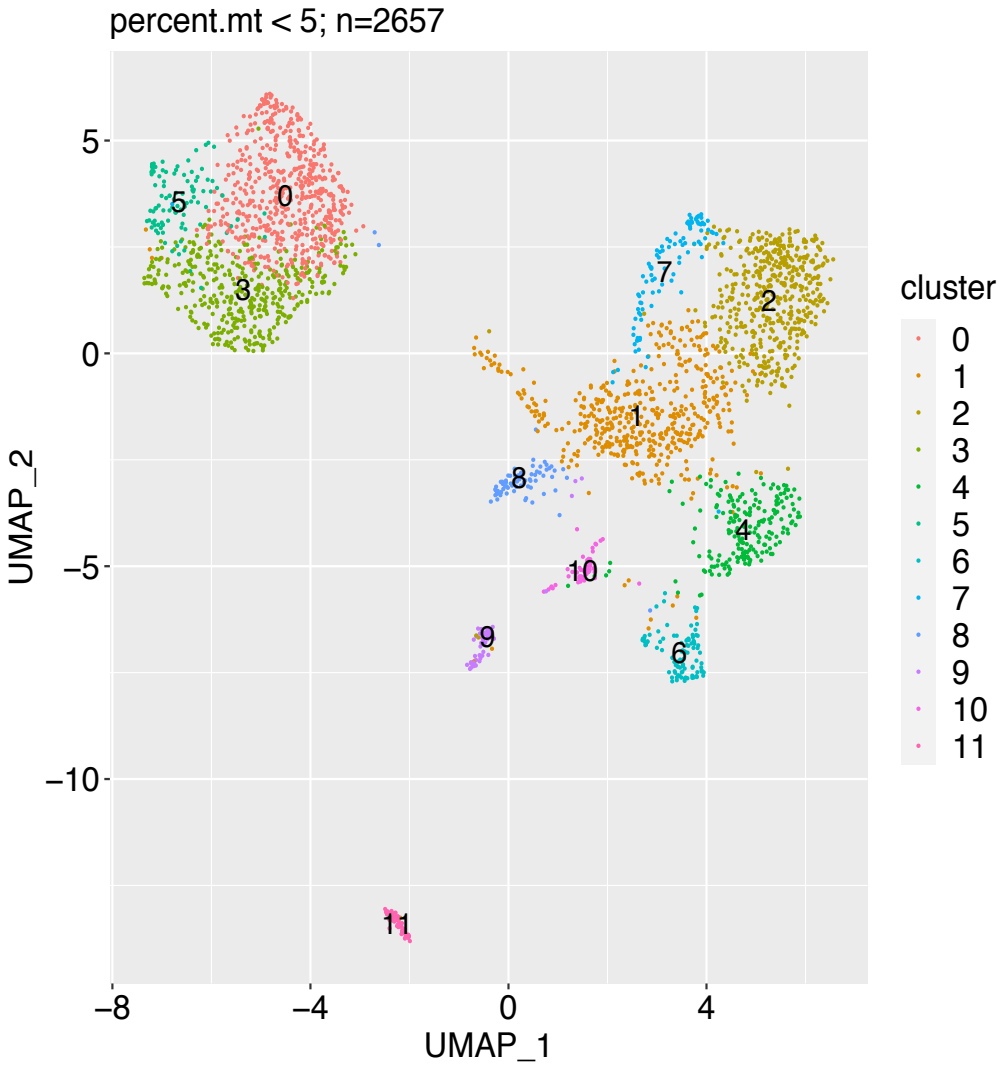


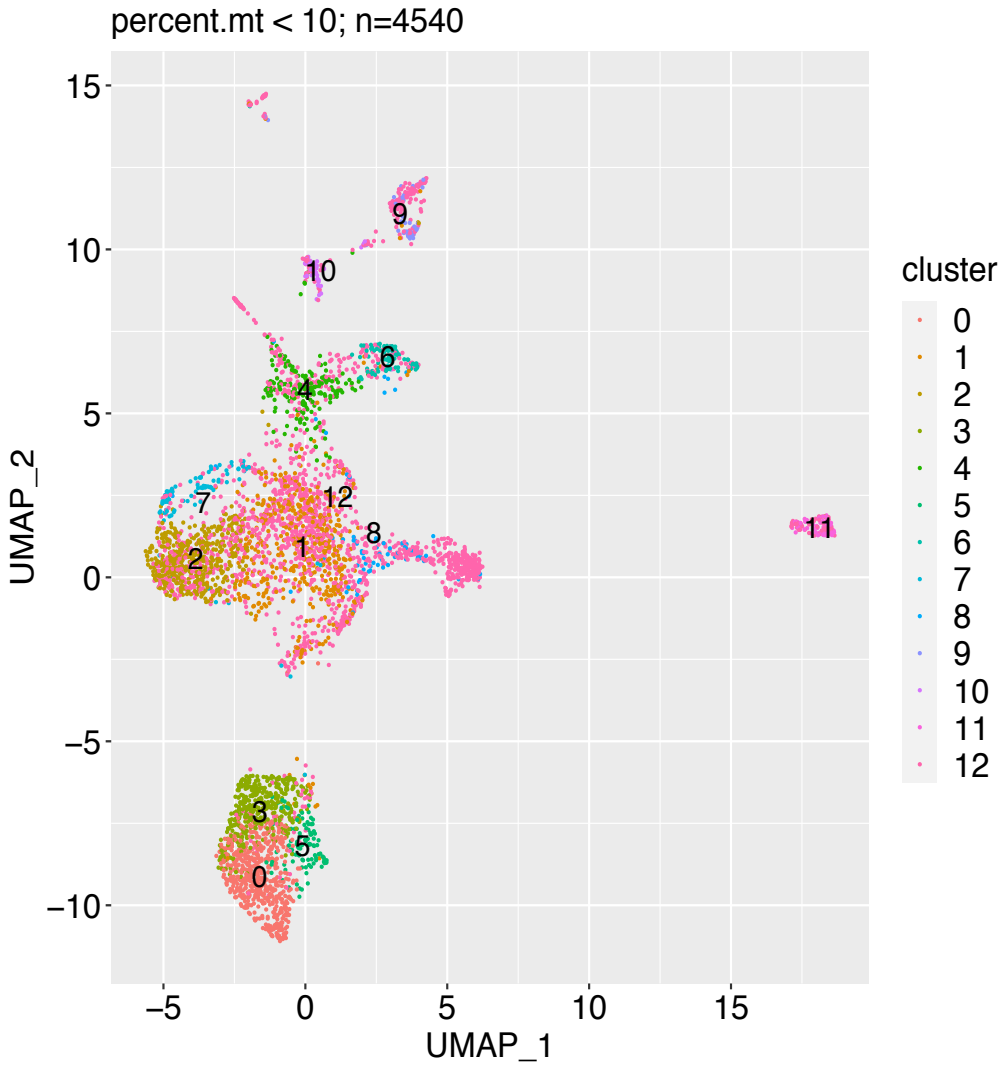
Preprocessing	function	Description
QC	Select cells	percent.mt < 5%
Normalization	Normalizing cells	TP10K
Variable genes	Most variable genes	nfeatures = 2000
Standardization	Standardization across cells	z score

Effects of Using Percent of Mitochondrial Gene Cutoff on UMAP

Clustering and Dimension Reduction 2

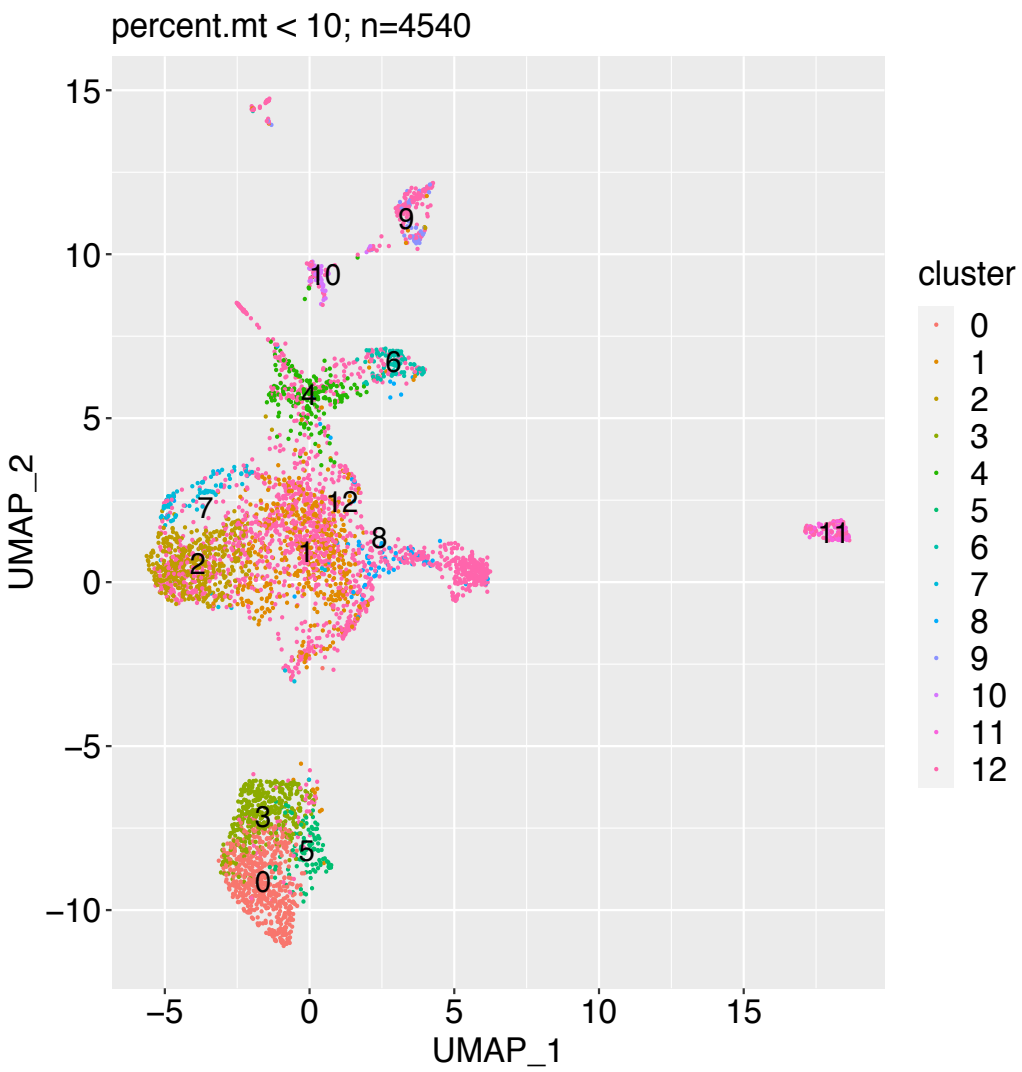
Dimension Reduction 2
Clusters 0-11 are identical to the left plot (percent.mt < 5)
Cluster 12 has the additional cells (percent.mt between 5 and 10)



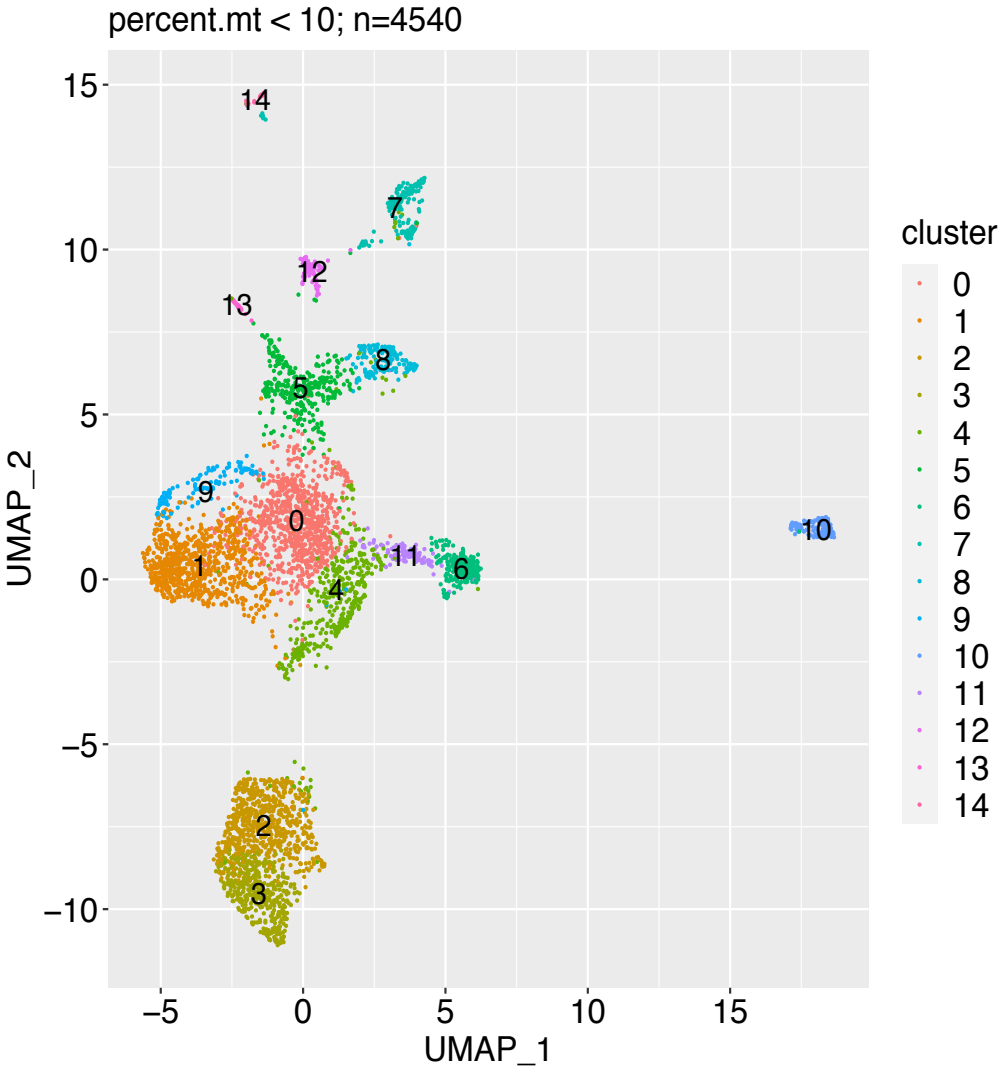


How Is UMAP Affected by New Clustering Analysis?

Dimension Reduction 2



Clustering and Dimension Reduction 2



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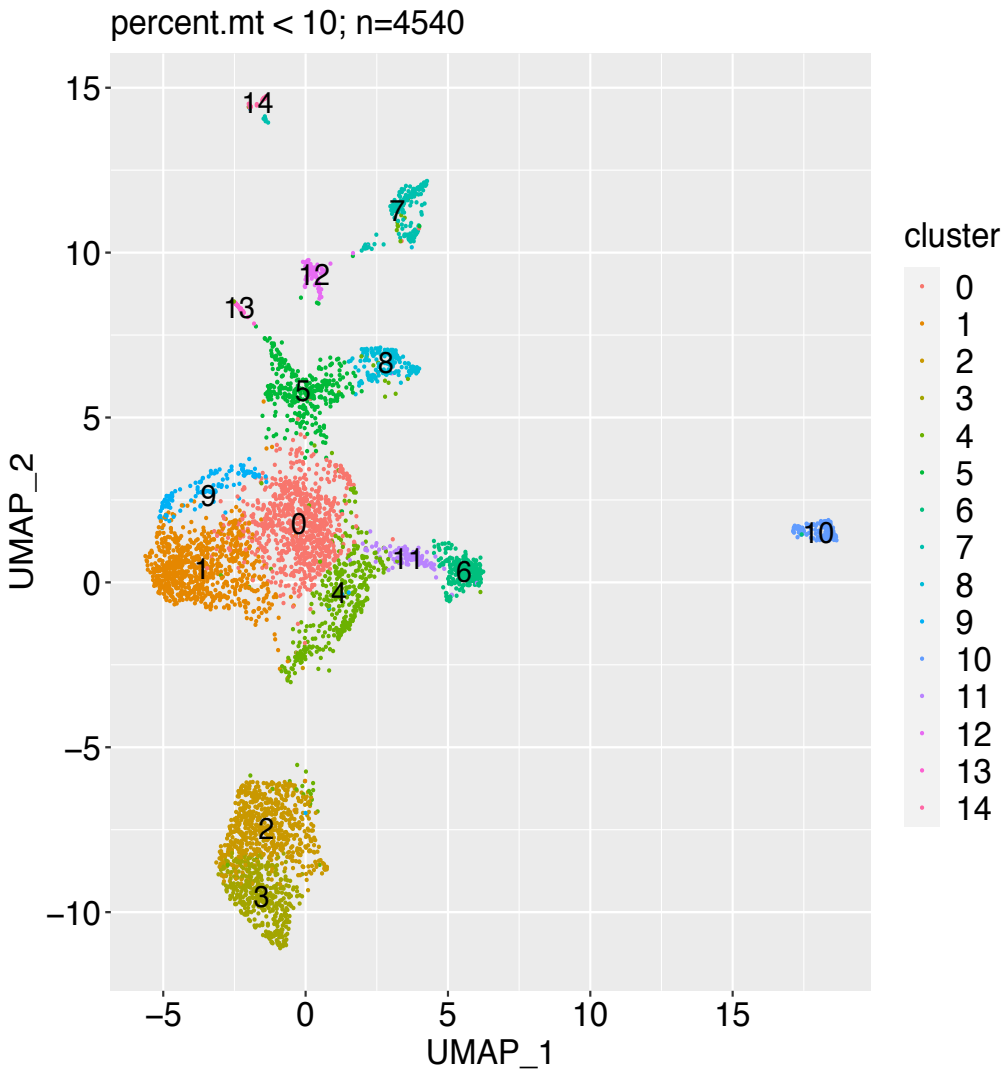
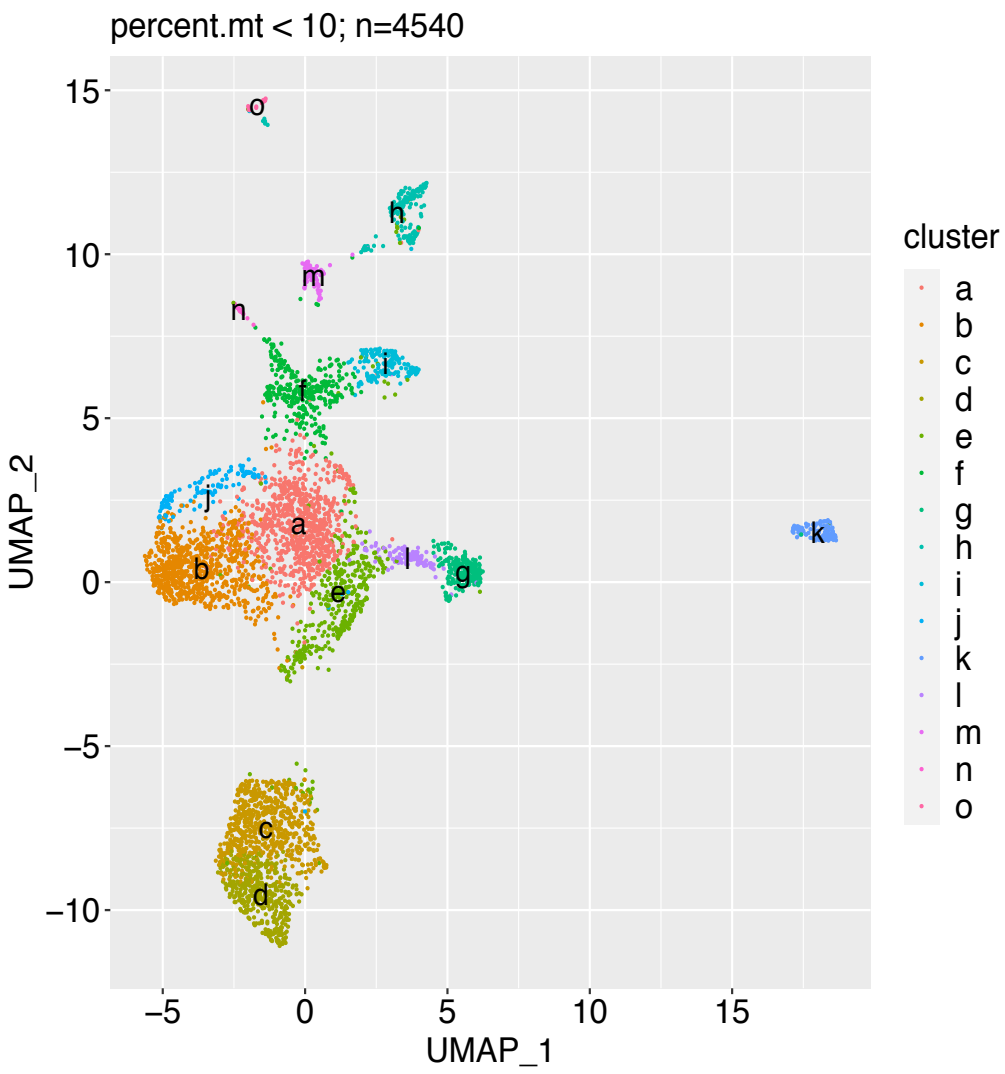
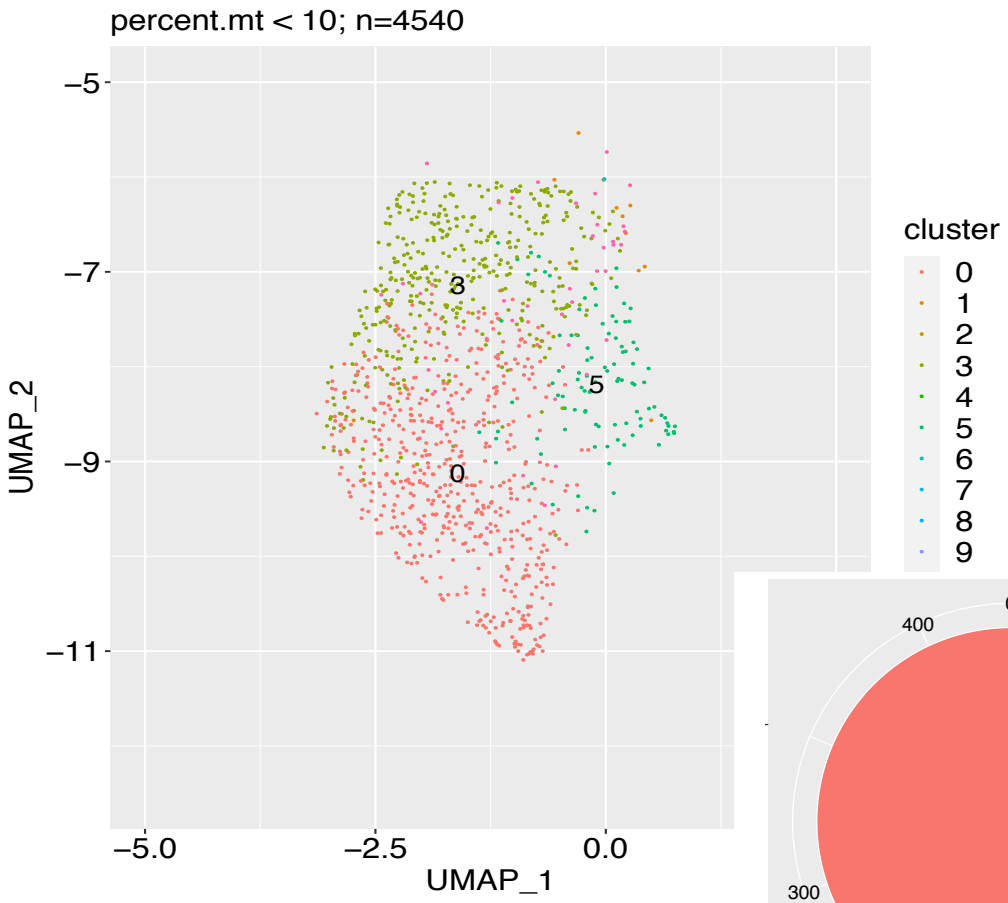


Clustering and Dimension Reduction 2

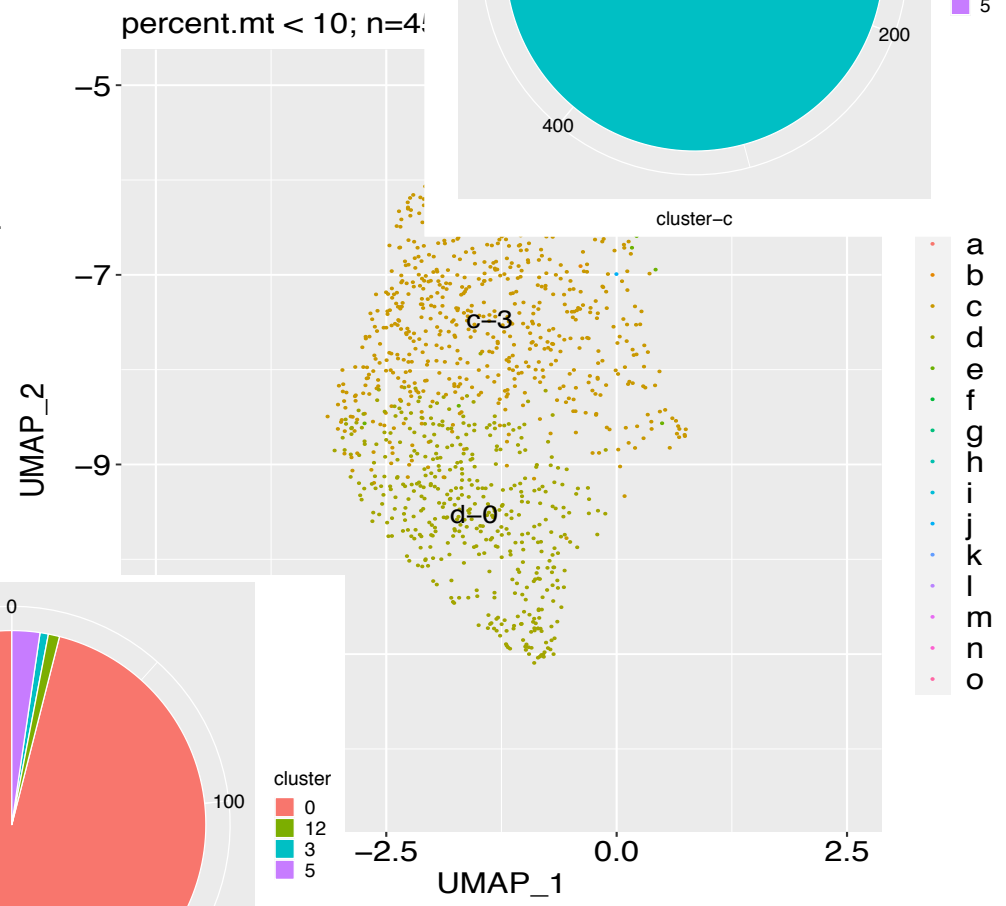


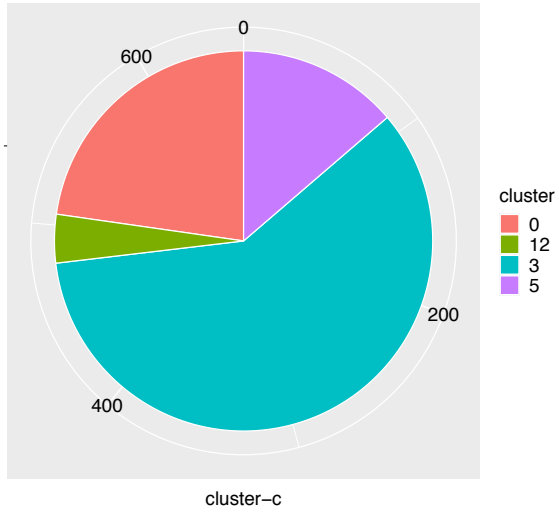
How Is UMAP Affected by New Clustering Analysis?

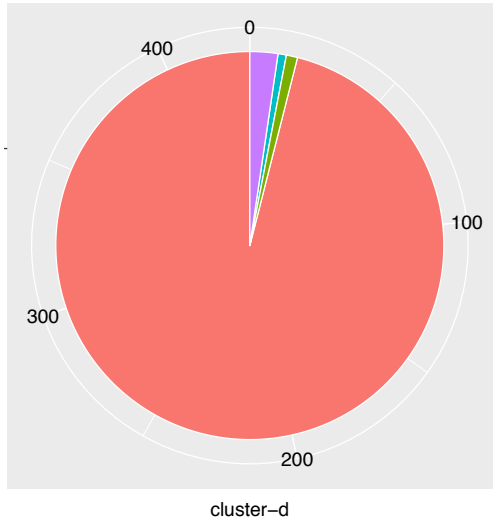
Clustering and Dimension Reduction 2



Clustering and D
Label with alphal



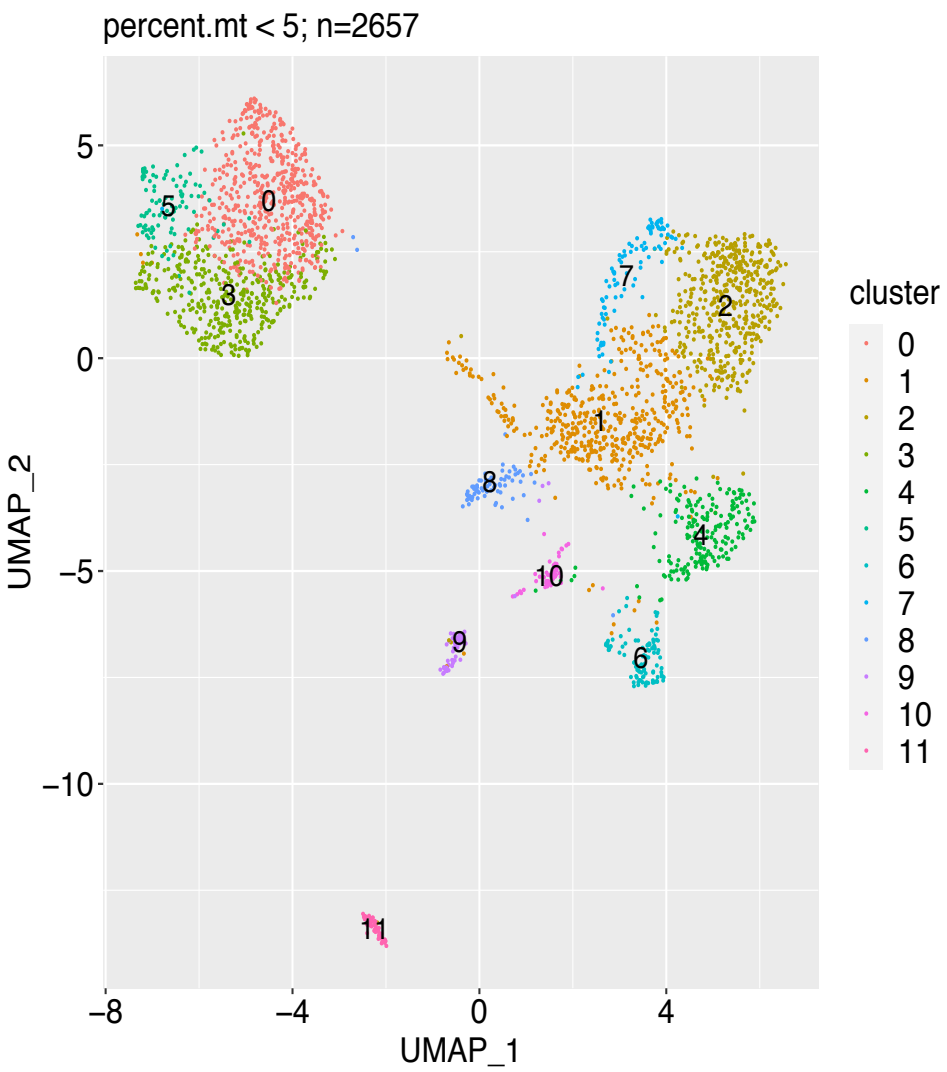




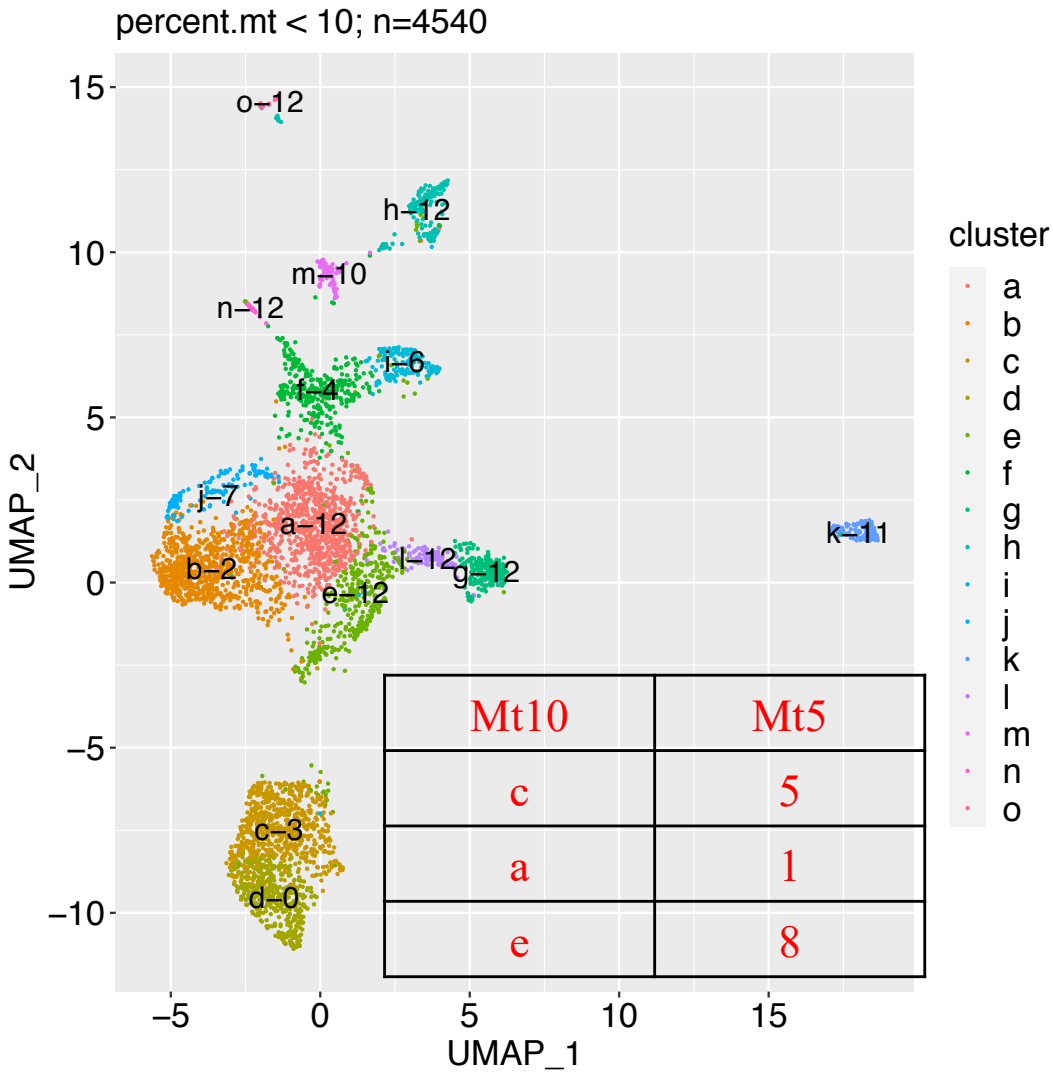
Numbers outside of the pie chart are numbers of cells

How Is UMAP Affected by New Clustering Analysis?

Clustering and Dimension Reduction 2

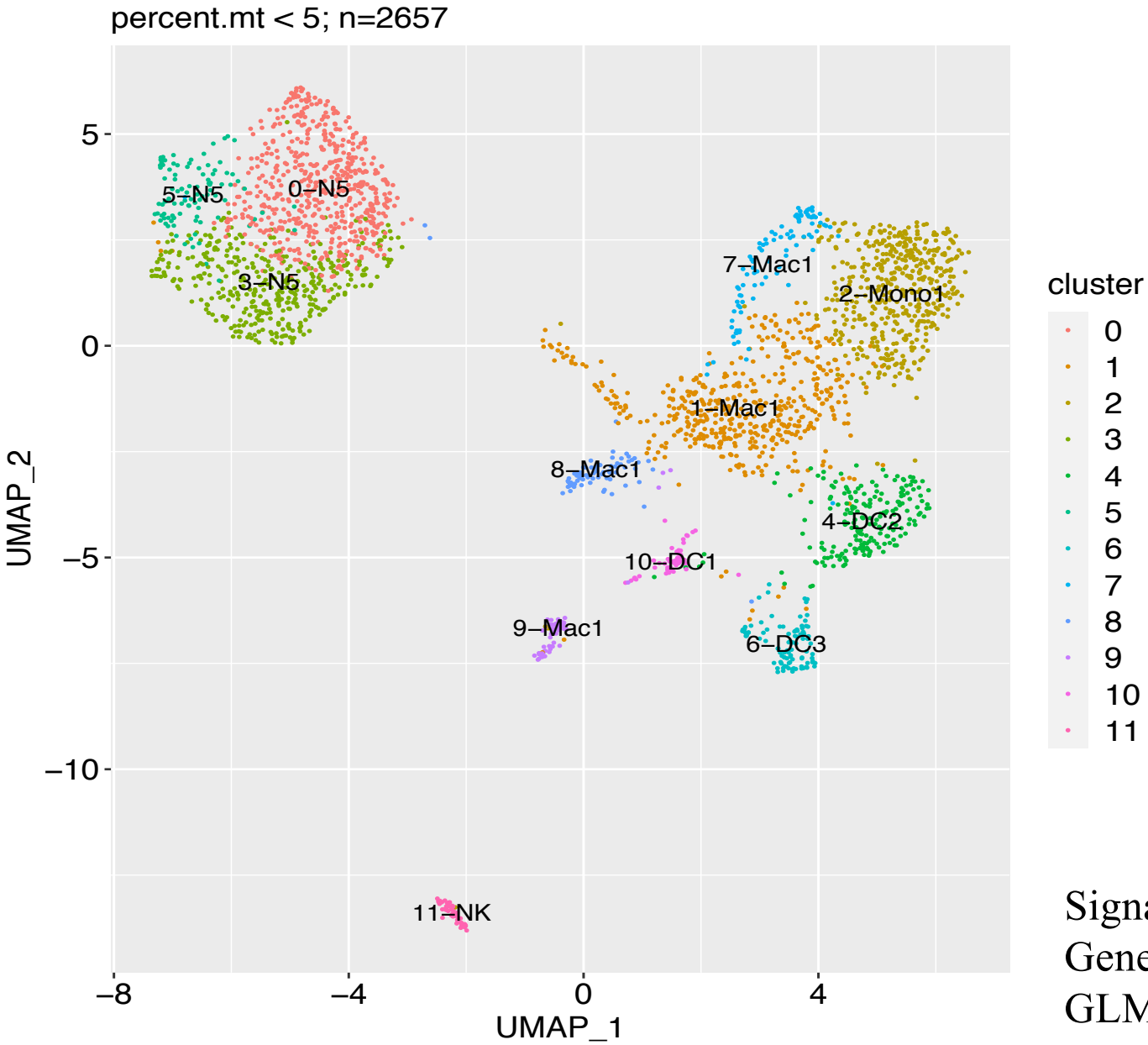


Clustering and Dimension Reduction 2
Label with alphabet and its mapping

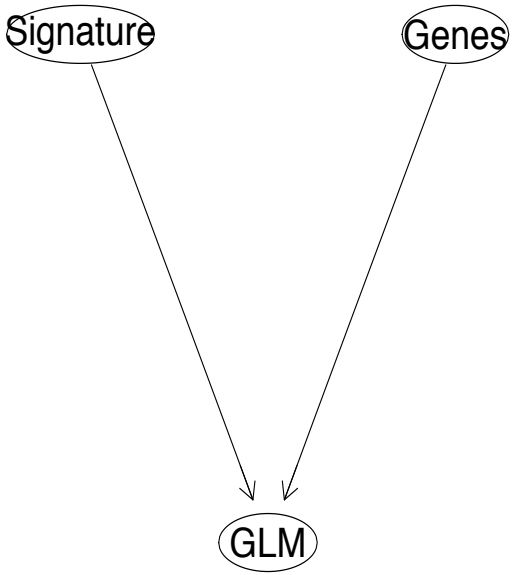


Mt10	Mt5
c	5
a	1
e	8

Tissue Subtype of Clusters with Percent.mt5



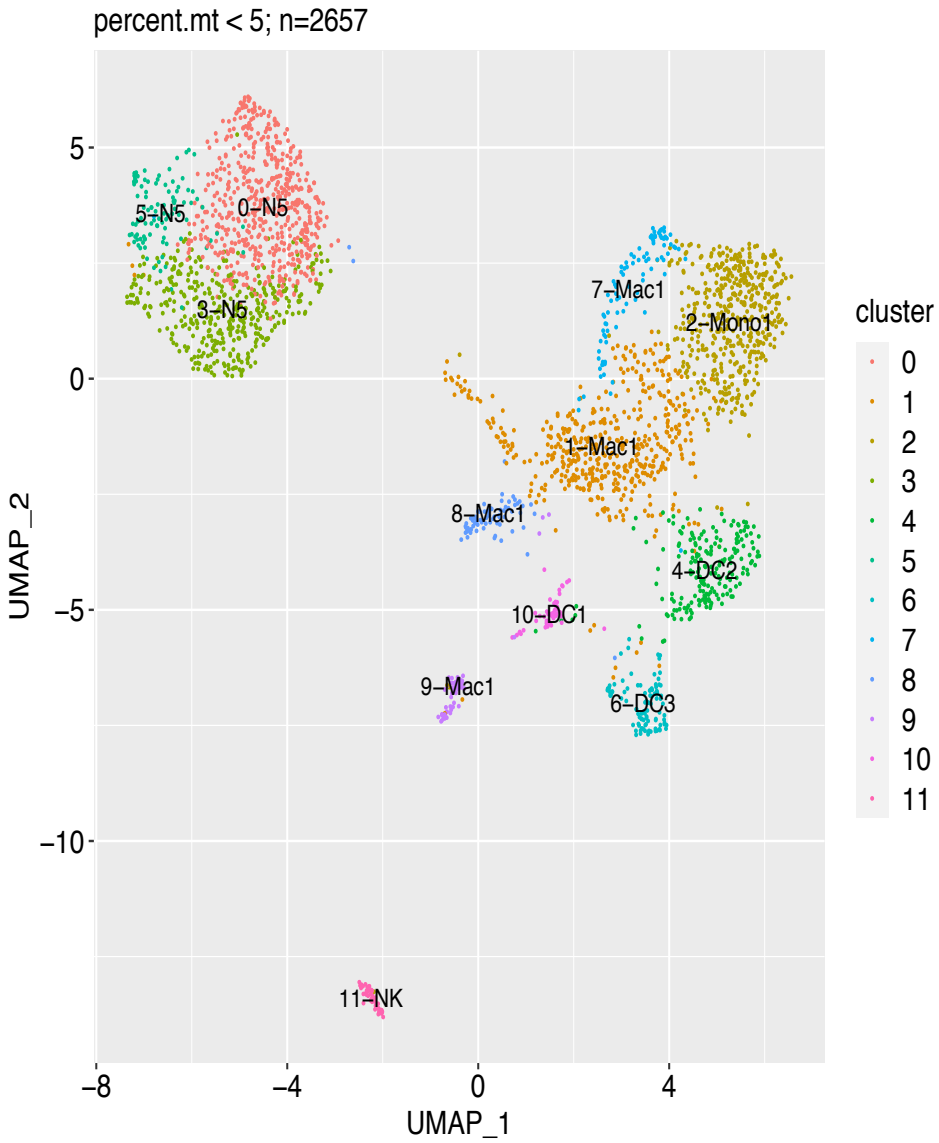
DC: dendritic cells
Mac: macrophage
Mono: monocyte
N: neutrophils
NK: natural killer cells

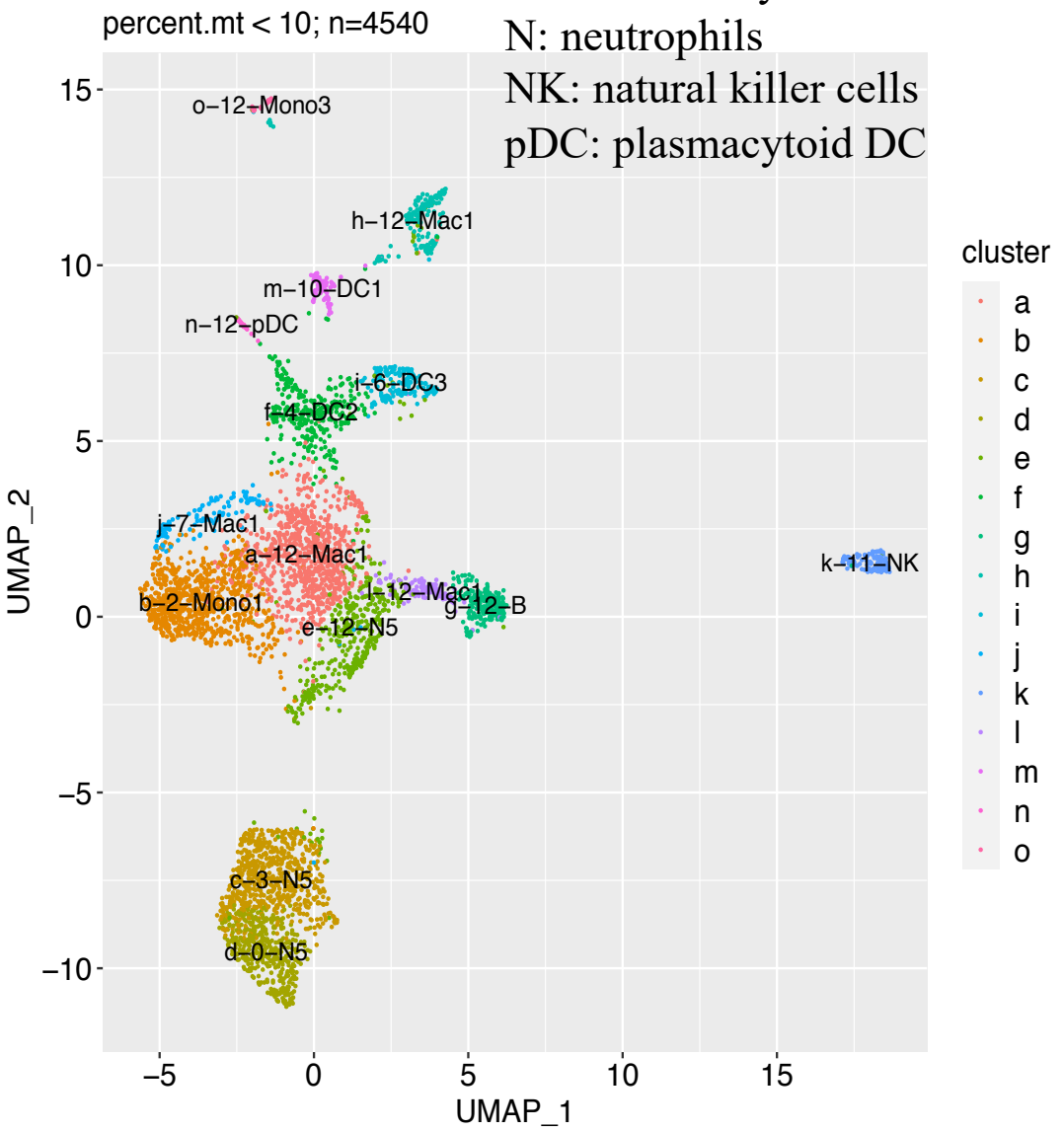


Signature: gene signatures
Genes: genes from Cibersort
GLM: generalized linear model

Rapolas Zilionis..Allon Klein 2019 Immunity 50, 1317-1334

Tissue Subtype of Clusters: Percent.mt5 vs Percent.mt10



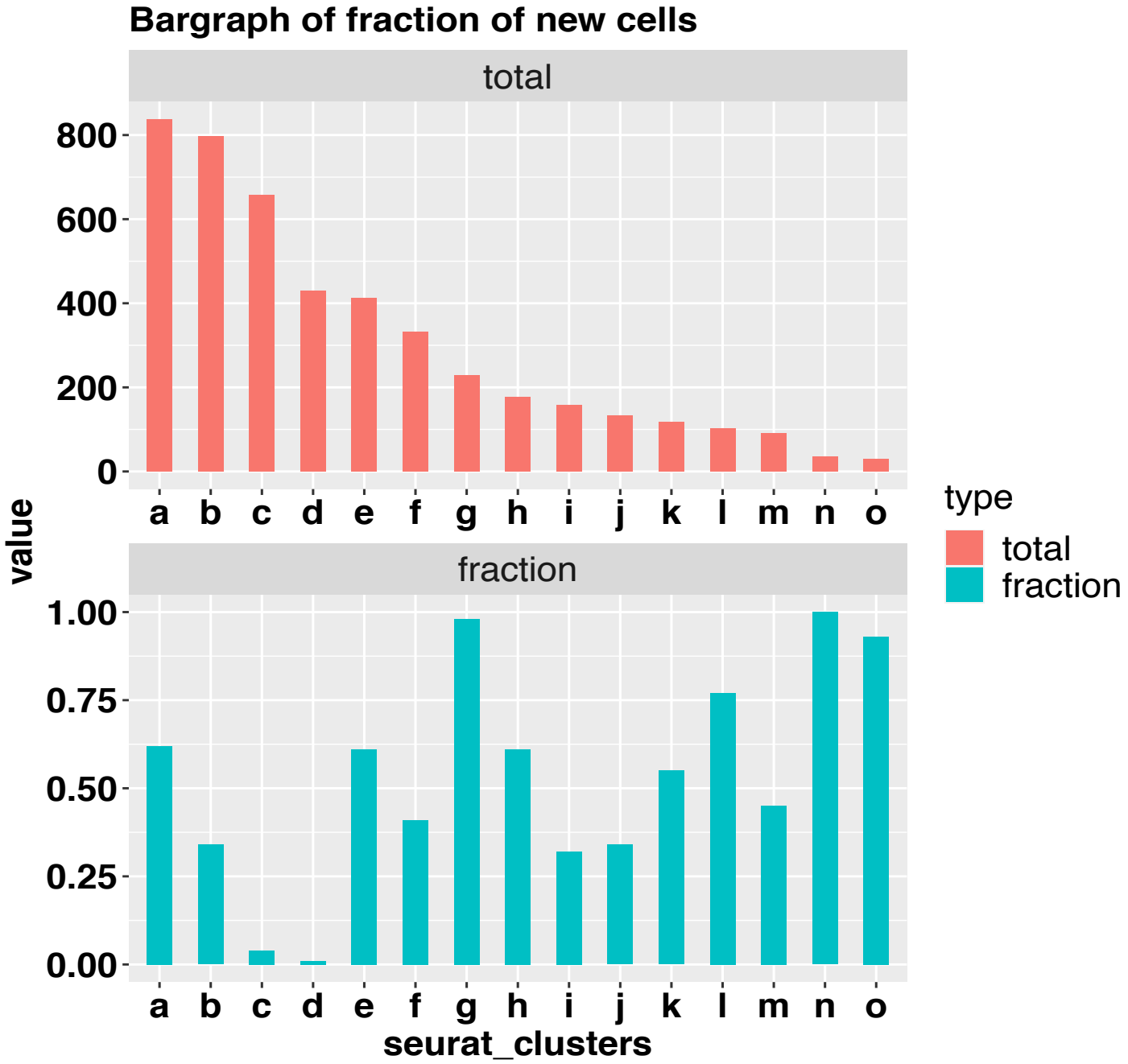


B: B cells
DC: dendritic cells
Mac: macrophage
Mono: monocyte
N: neutrophils
NK: natural killer cells
pDC: plasmacytoid DC

Comparison of Cluster Tissue Subtypes

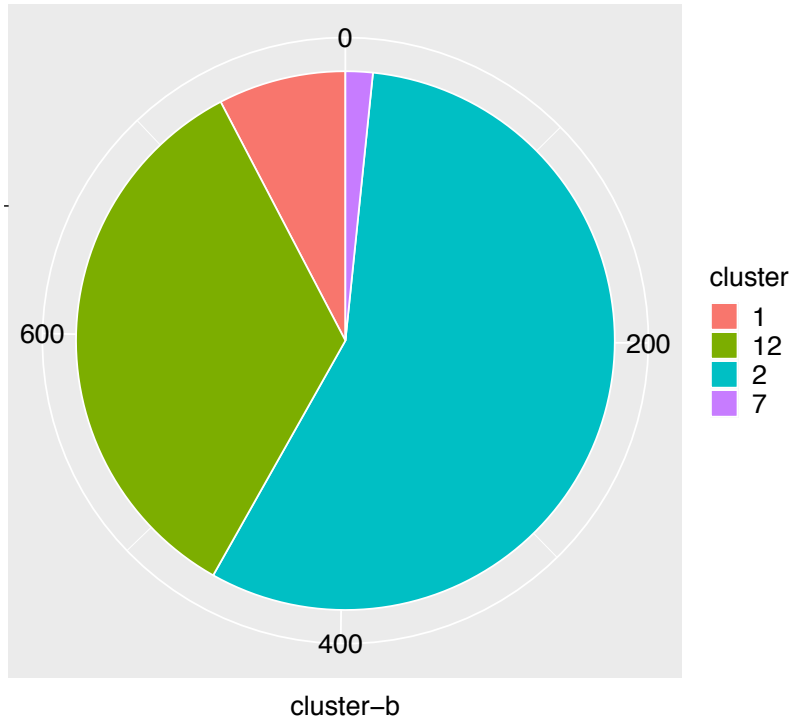
mt10.tissue	cluster	mt5.tissue
Mac1	a-12	
Mono1	b-2	Mono1
N5	c-3	N5
N5	d-0	N5
N5	e-12	
DC2	f-4	DC2
B	g-12	
Mac1	h-12	
DC3	i-6	DC3
Mac1	j-7	Mac1
NK	k-11	NK
Mac1	l-12	
DC1	m-10	DC1
pDC	n-12	
Mono3	o-12	

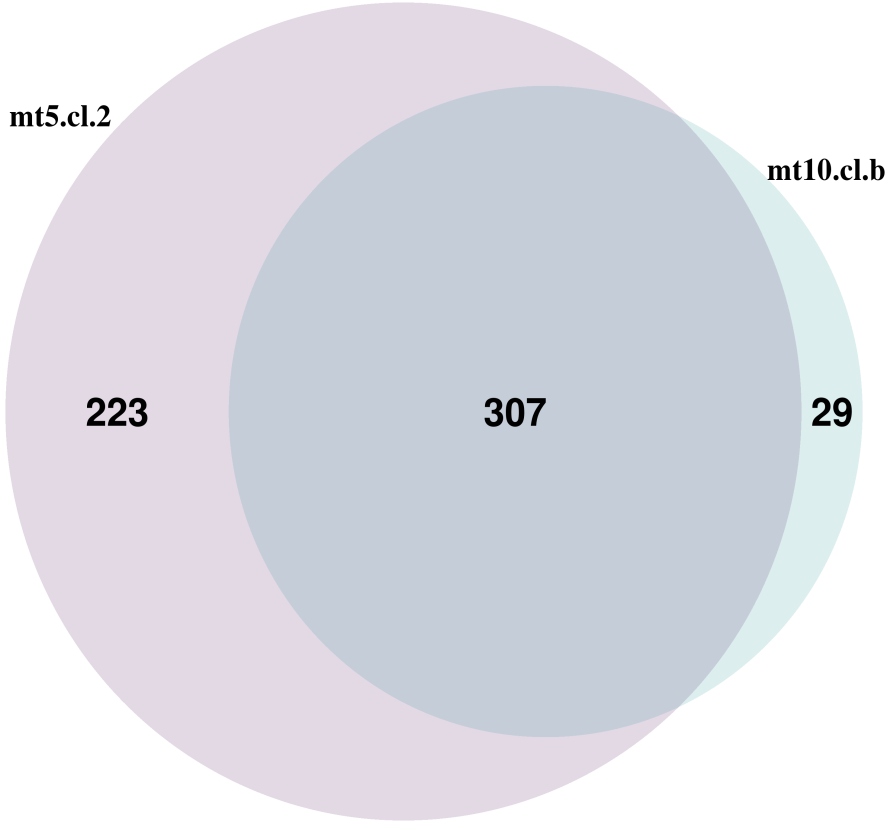
Fraction of the Cells with Percent.mt Larger Than 5



Mono1: Cluster b (Mt10) vs Cluster 2 (Mt5) Specific Genes

mt5.cl.2: mt5 cluster 2
mt10.cl.b: mt10 cluster b

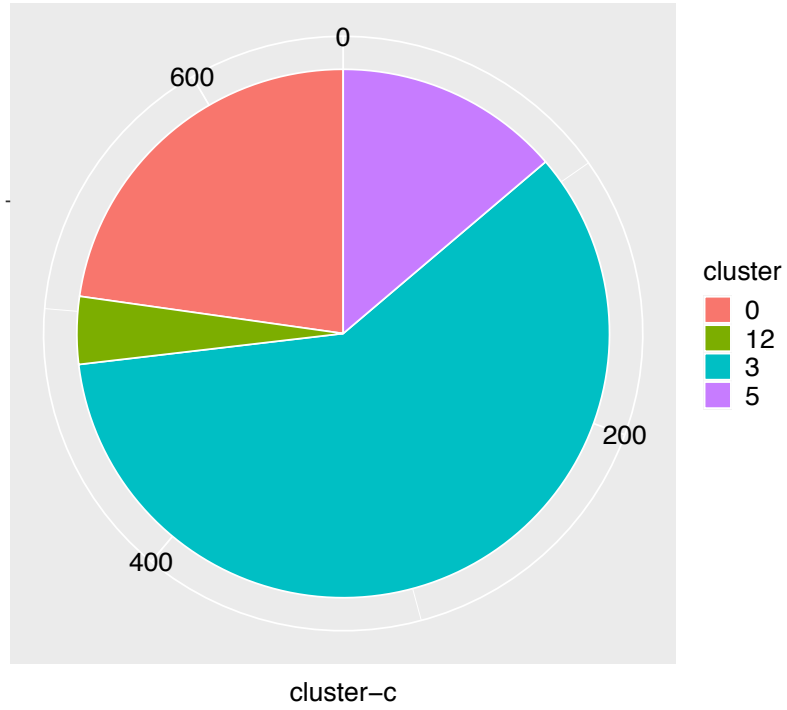


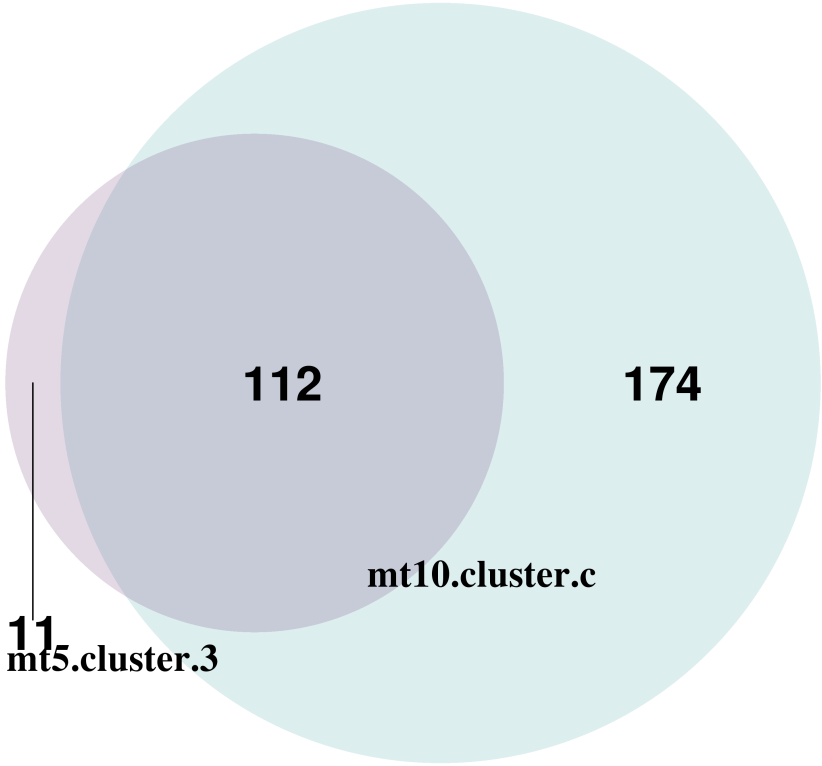


Numbers outside of the pie chart
are numbers of cells

Cluster-specific genes
Common: 307 genes
Unique to mt5 cluster 2: 223 genes
Unique to mt10 cluster b: 29 genes

N5: Cluster c (Mt10) vs Cluster 3 (Mt5) Specific Genes

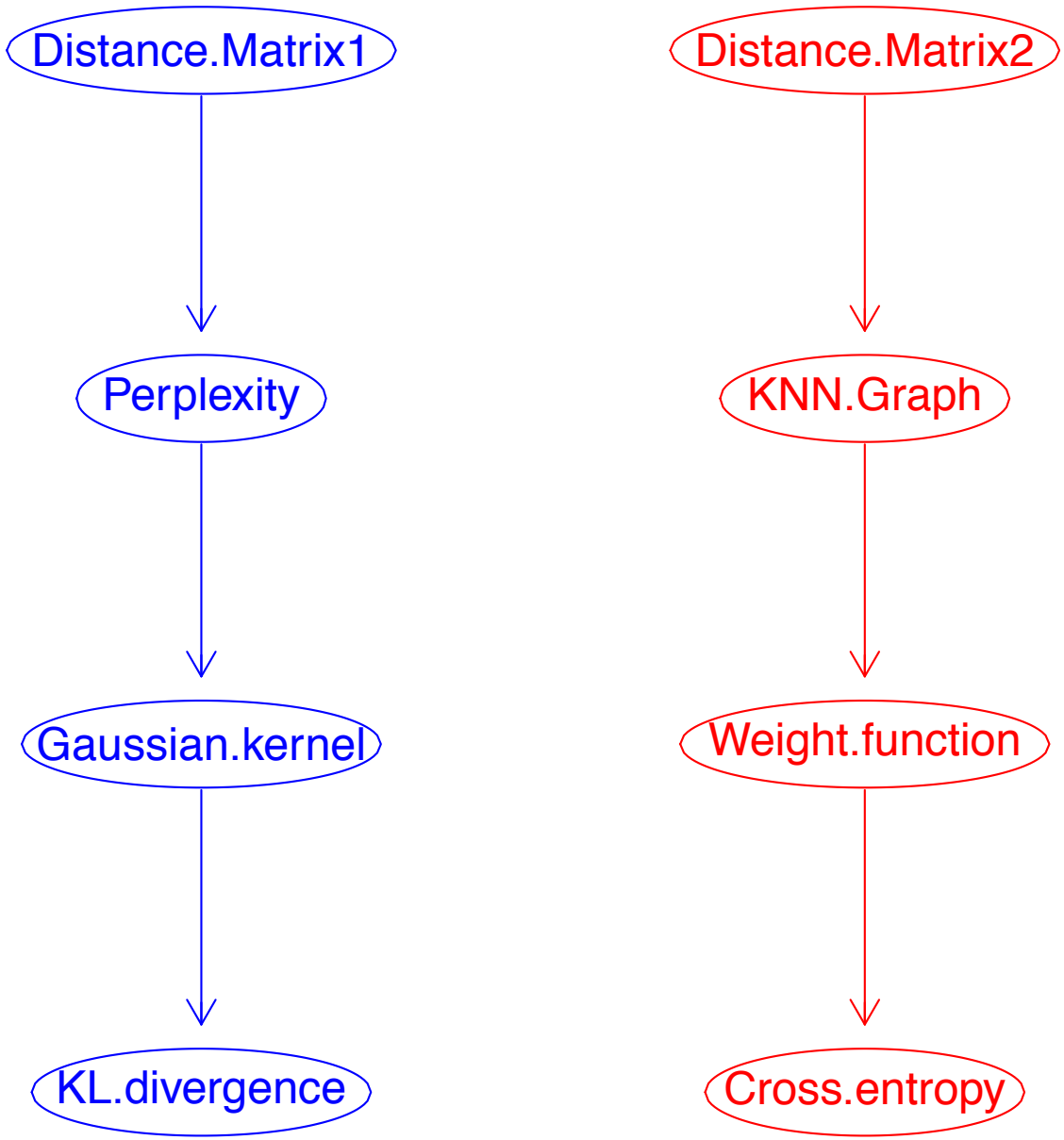




Numbers outside of the pie chart are numbers of cells

Cluster-specific genes
Common: 112 genes
Unique to mt5 cluster 0: 11 genes
Unique to mt10 cluster d: 174 genes

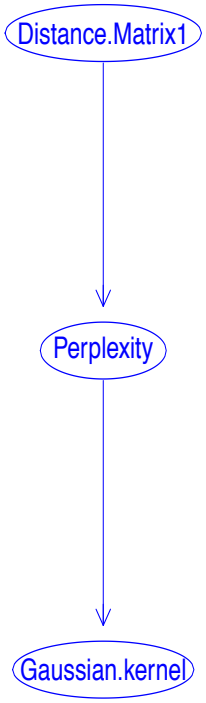
TSNE vs. UMAP


Distance.Matrix1
Perplexity
Gaussian.kernel
KL.divergence
Distance.Matrix2
KNN.Graph
Weight.function
Cross.entropy

TSNE vs. UMAP

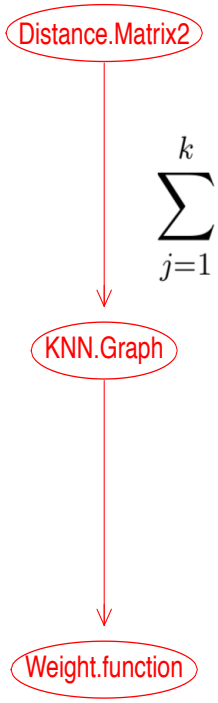
$$Perp(P_i) = 2^{H(P_i)}$$

$$H(P_i) = -\sum_j p_{j|i} \log_2 p_{j|i}$$



$$p_{j|i} = \frac{\exp\left(-\|x_i - x_j\|^2 / 2\sigma_i^2\right)}{\sum_{k \neq i} \exp\left(-\|x_i - x_k\|^2 / 2\sigma_i^2\right)}$$

$$p_{ij} = \frac{p_{j|i} + p_{i|j}}{2n}$$



$$\sum_{j=1}^{k} \exp\left(\frac{-\max(0, d(x_i, x_{i_j}) - \rho_i)}{\sigma_i}\right) = \log_2(k)$$

$$w((x_i, x_{i_j})) = \exp\left(\frac{-\max(0, d(x_i, x_{i_j}) - \rho_i)}{\sigma_i}\right)$$

$$B = A + A^\top - A \circ A^\top$$

ρ_i: shortest distance of x_i neighbors

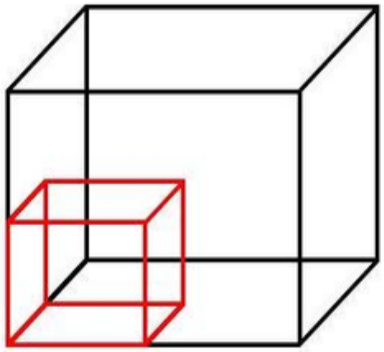
Euclidean Distance and Other Distance Metrics

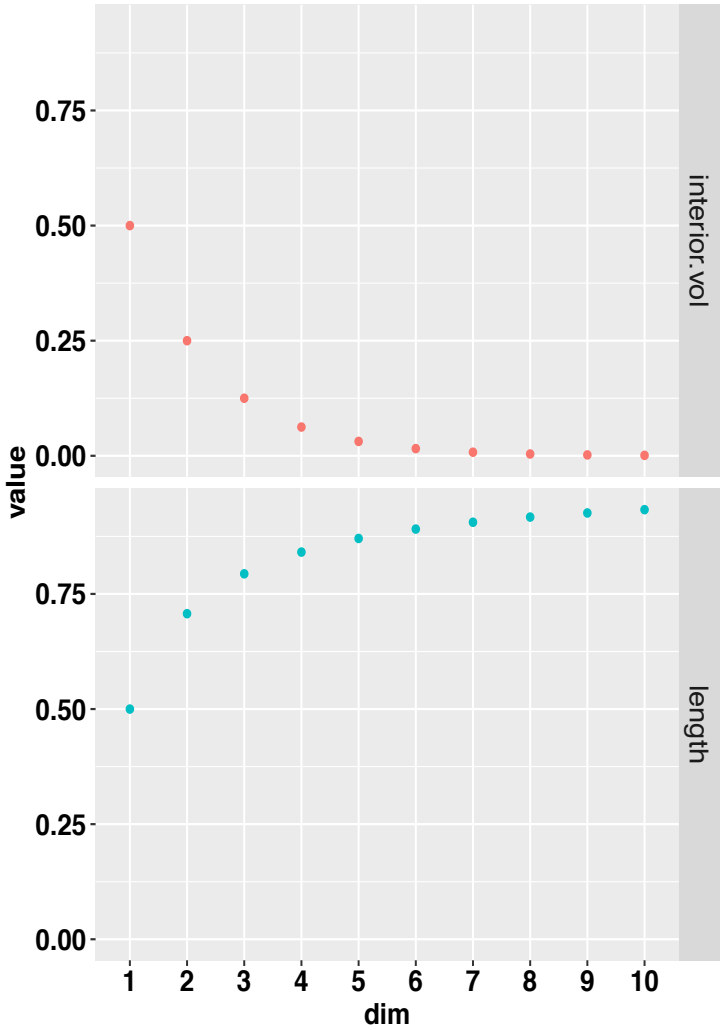
- Euclidean distance vs geodesic distance
- Euclidean distance vs Mahalanobis distance
- Curse of dimensionality

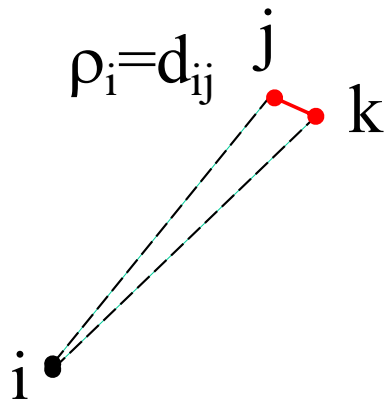
Curse of Dimensionality

(I) 50% of each dimension is sufficient to cover 25% of a 2-dimensional space

(II) 50% of each dimension is only sufficient to cover 12.5% of a 3-dimensional space







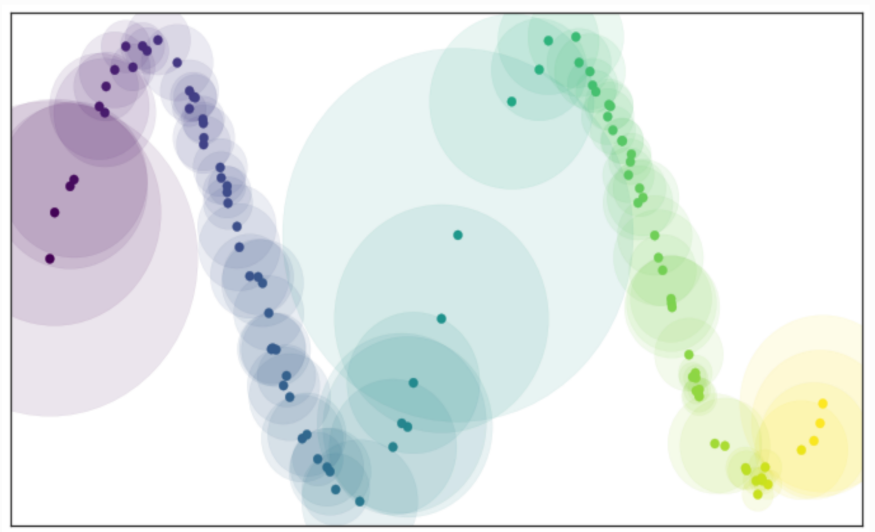
type
- interior.vol
- length

Uniform Manifold Approximation and Projection (UMAP)

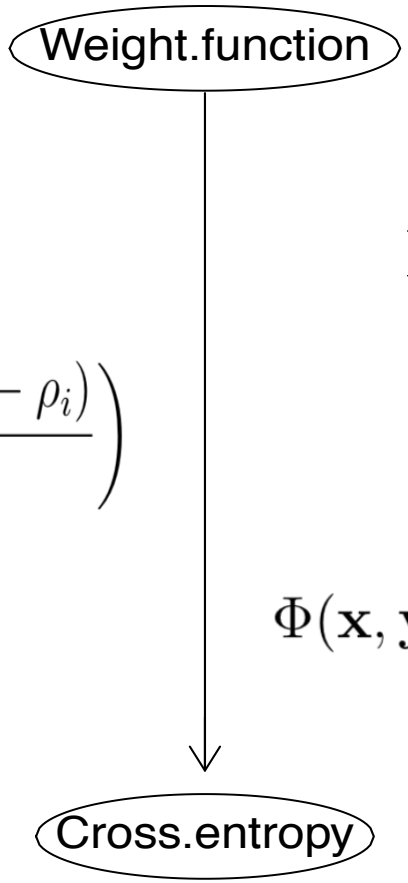
$$w((x_i, x_{i_j})) = \exp\left(\frac{-\max(0, d(x_i, x_{i_j}) - \rho_i)}{\sigma_i}\right)$$

$$B = A + A^\top - A \circ A^\top$$

$$\sum_{j=1}^{k} \exp\left(\frac{-\max(0, d(x_i, x_{i_j}) - \rho_i)}{\sigma_i}\right) = \log_2(k)$$



Uniform Manifold Approximation and Projection (UMAP)



High-dimension

$$w((x_i, x_{i_j})) = \exp\left(\frac{-\max(0, d(x_i, x_{i_j}) - \rho_i)}{\sigma_i}\right)$$

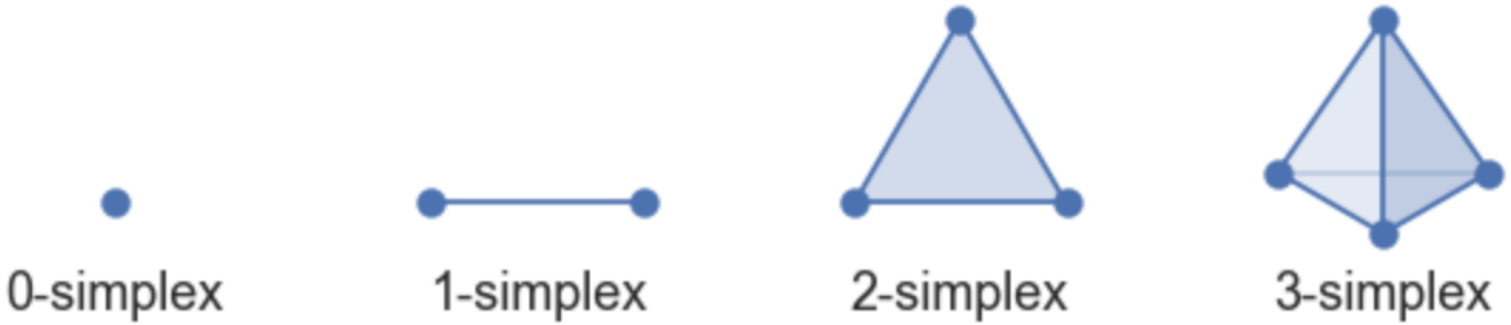
$$B = A + A^\top - A \circ A^\top$$

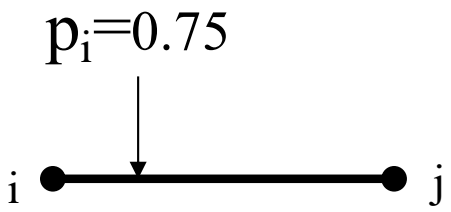
Low-dimension

Laplacian Eigenmaps

$$\Phi(\mathbf{x}, \mathbf{y}) = \left(1 + a(\|\mathbf{x} - \mathbf{y}\|_2^2)^b\right)^{-1}$$

Fuzzy Simplicial Sets





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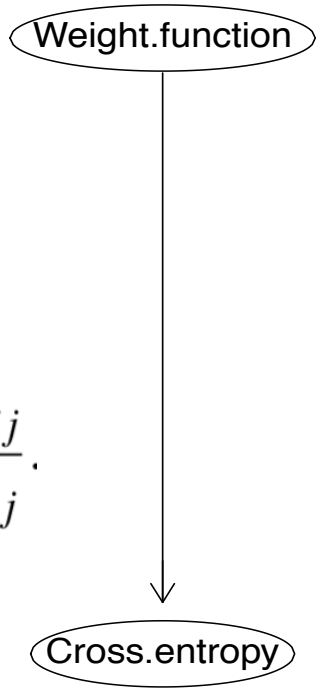


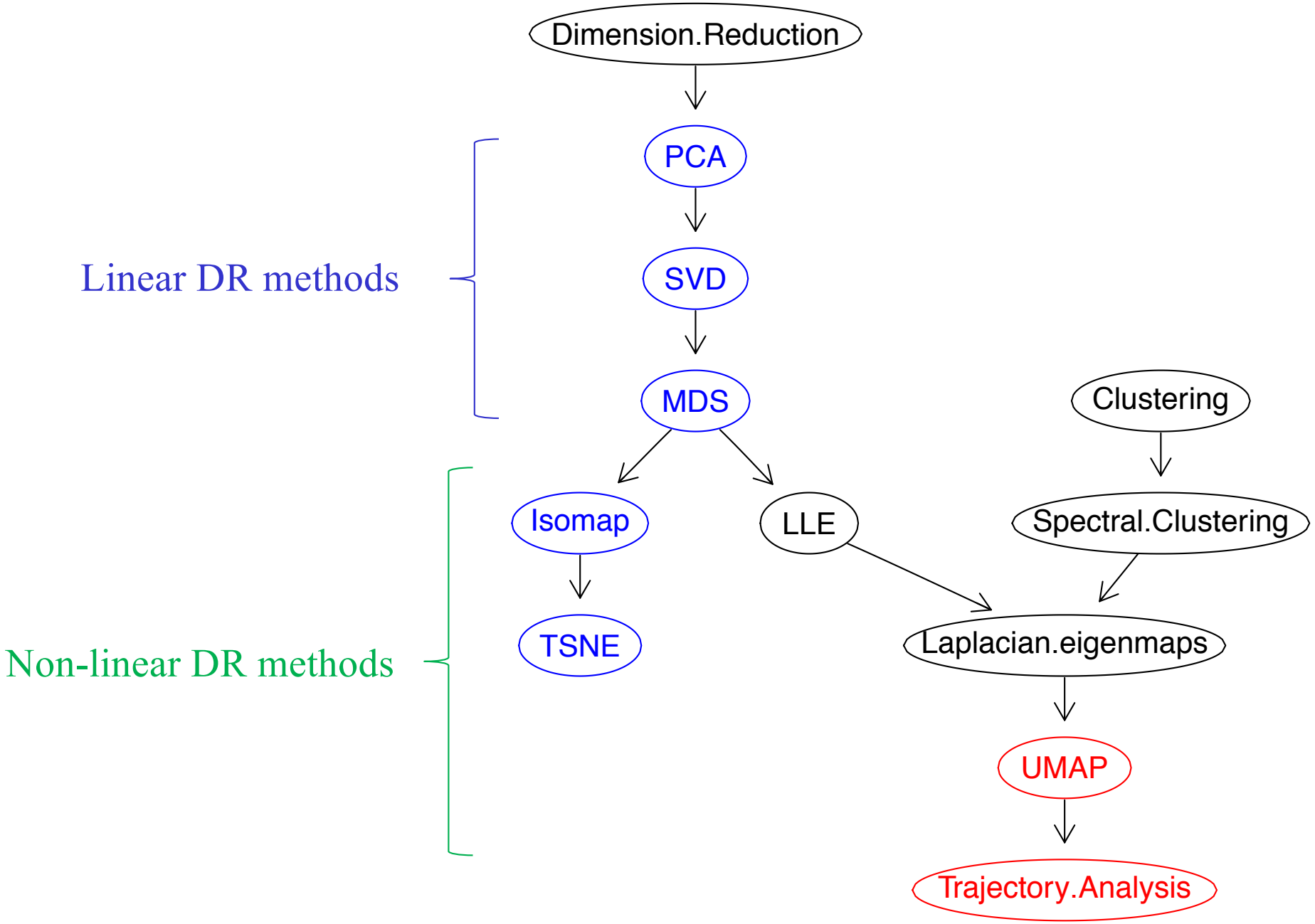
TSNE cost function

$$C = KL(P||Q) = \sum_i \sum_j p_{ij} \log \frac{p_{ij}}{q_{ij}}.$$

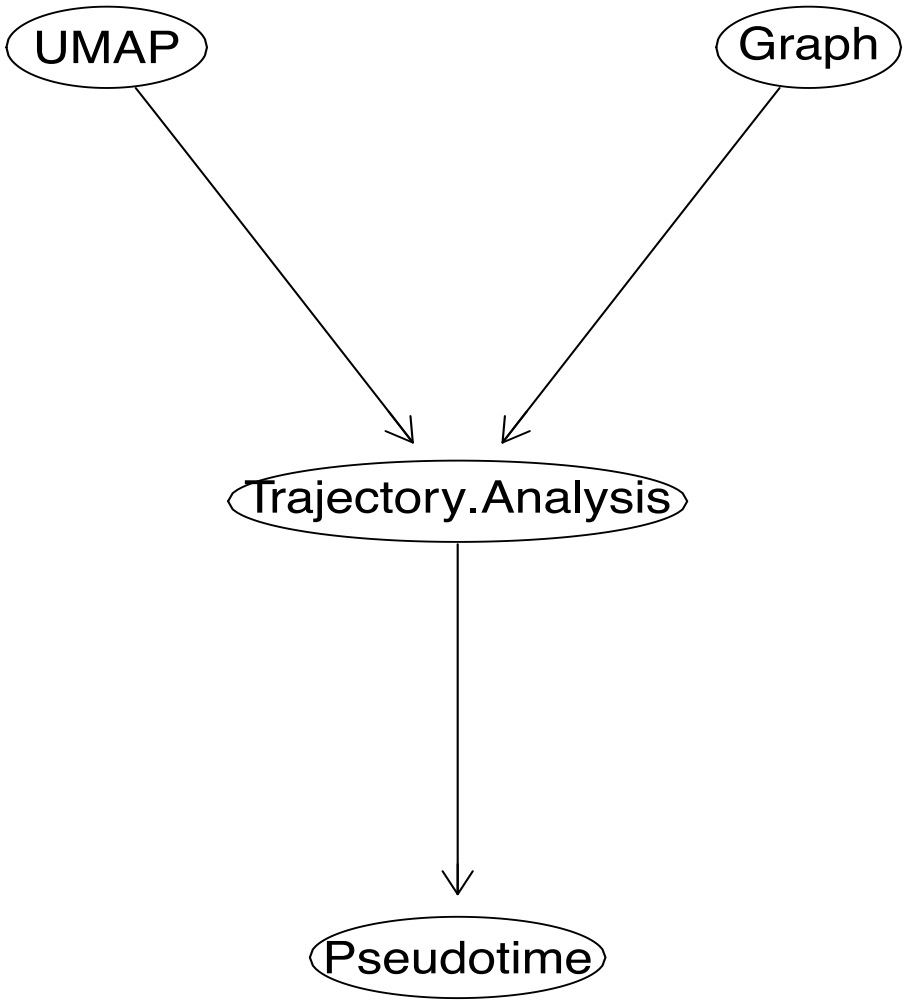
UMAP cost function

$$C((A,\mu),(A,\nu)) = \sum_{a \in A} \mu(a) \log \left(\frac{\mu(a)}{\nu(a)} \right) + (1-\mu(a)) \log \left(\frac{1-\mu(a)}{1-\nu(a)} \right)$$

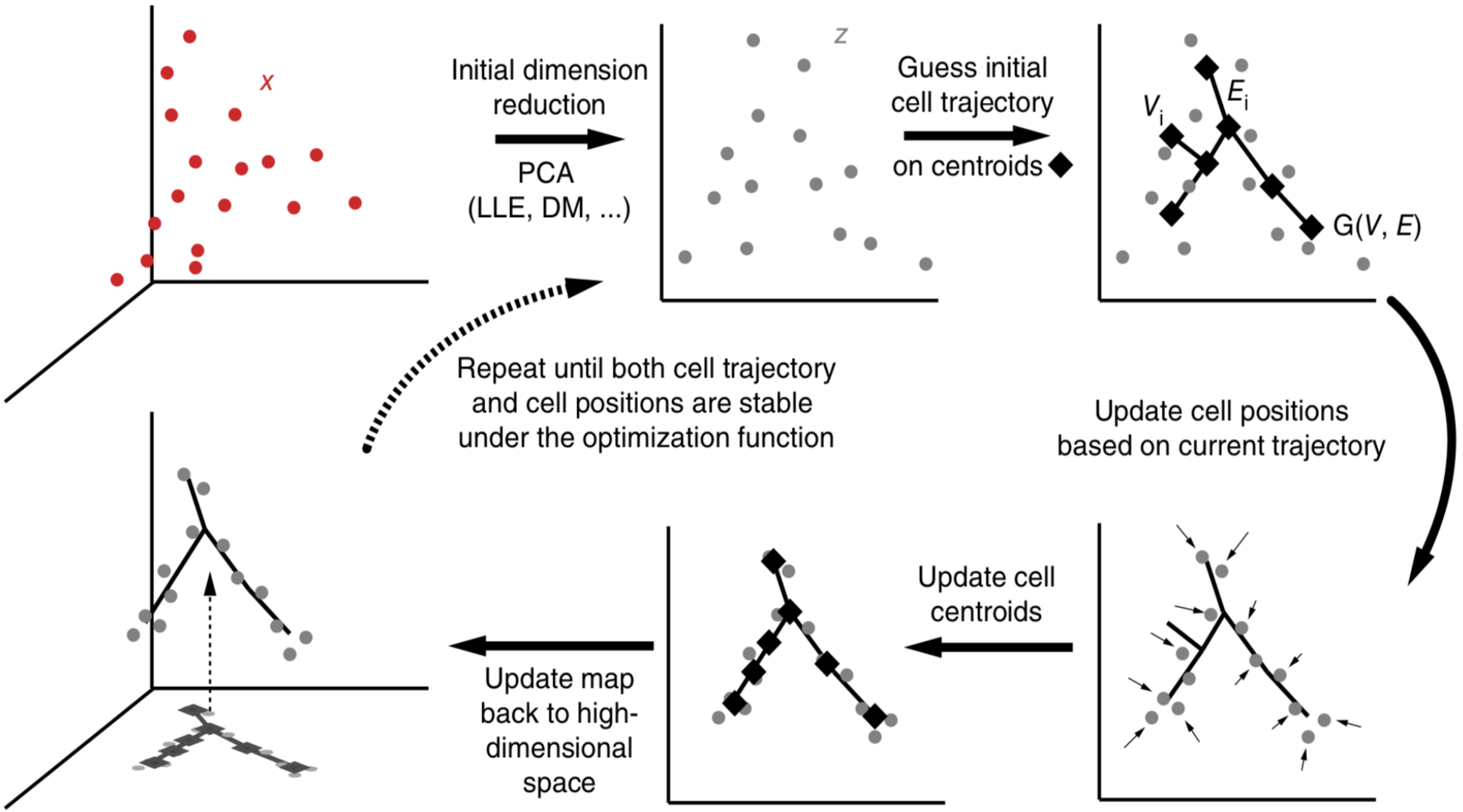
Road Map for Dimension Reduction Methods



Outline of Trajectory Analysis

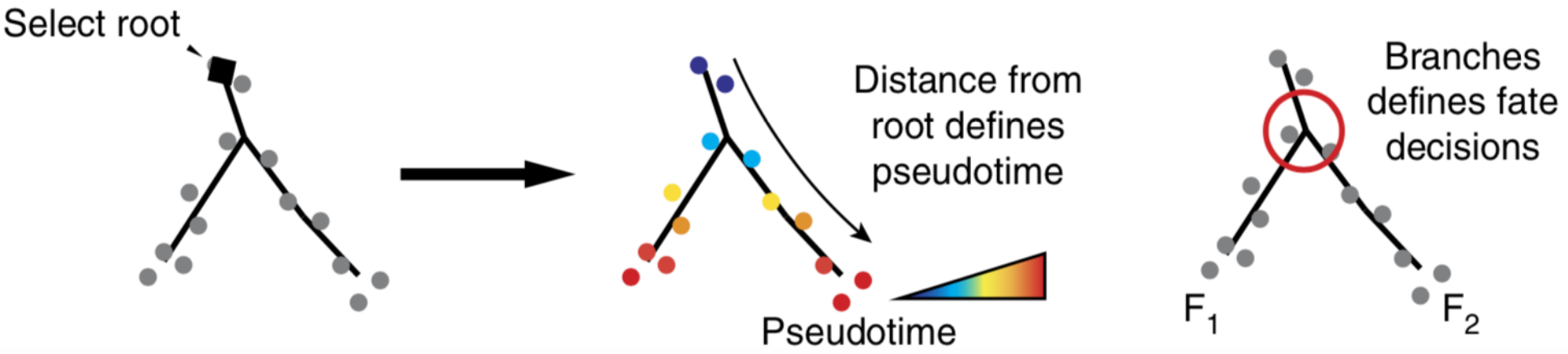


Trajectory Analysis (Monocle II)



Xiaojie Qiu..Cole Trapnell Nat Methods 14:979-982 2017

Pseudotime (Monocle II)



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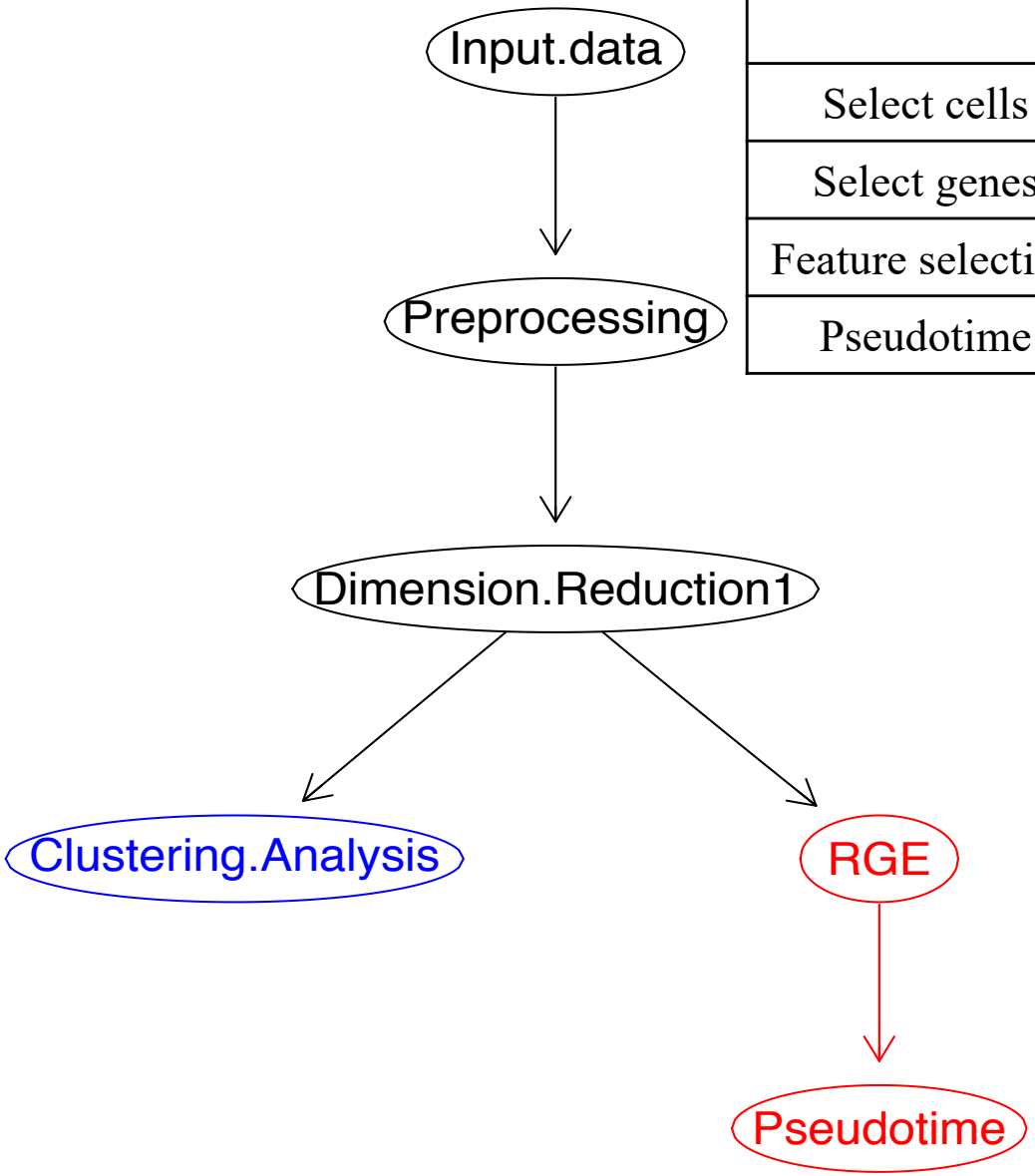
Flowchart of Trajectory Analysis with Monocle Package



	function	Description
Select cells	Remove low quality cells	
Select genes	Most variable genes	
Feature selection	Tree topology	Select subspace
Pseudotime	Select root	

RGE: reversed graph embedding

Road Map for Dimension Reduction Methods