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Cell type determination of single cell transcriptomics via ML

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Philipp Trinh 11839949
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"C. elegans connectome in anatomy model ." From *Math Insight*. http://mathinsight.org/image/c_elegans_connectome_anatomy_model

Überblick

1. Background / Intro
2. Data exploration
3. Clustering
4. Machine learning Modelle
5. Neural Networks
6. Mögliche Fortsetzung

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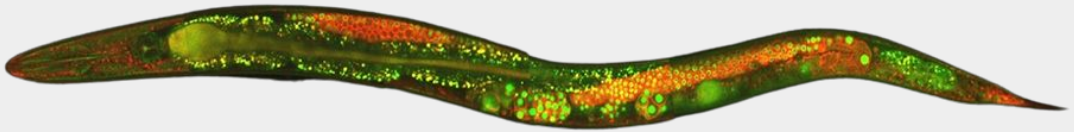
Background & Data preprocessing

Background

- Caenorhabditis elegans
  - Fadenwurm
  - 1 mm lang
  - Im Boden
  - Modellorganismus für viele Bereiche der Biologie

by Mark Leaver
https://hymanlab.org/hyman_lab/c-elegans/

- Single cell transcriptomics
  - Expression jeder Zelle für alle Gene
  - Gen-Expressions-Analyse

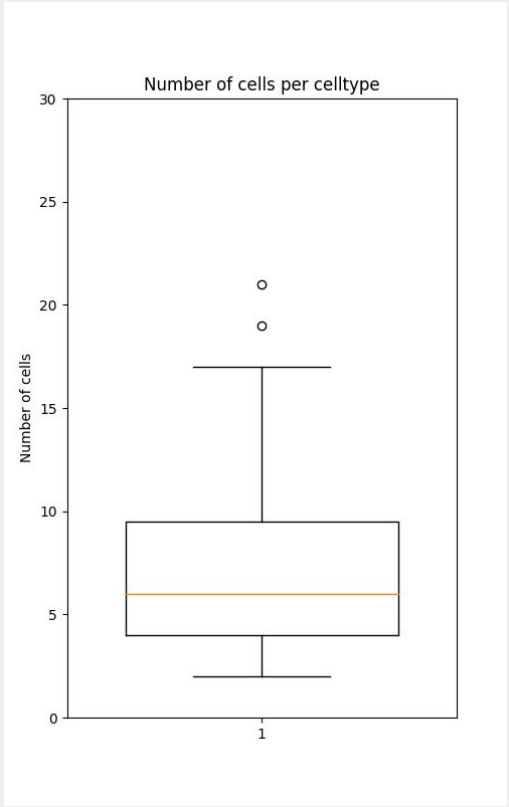


by Ian Chin-Sang,
Queens University, ON,
Canada

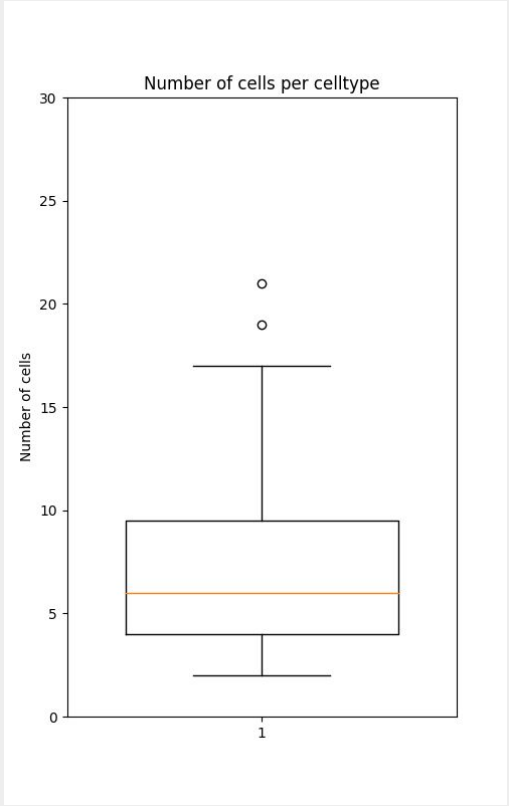
Data preprocessing

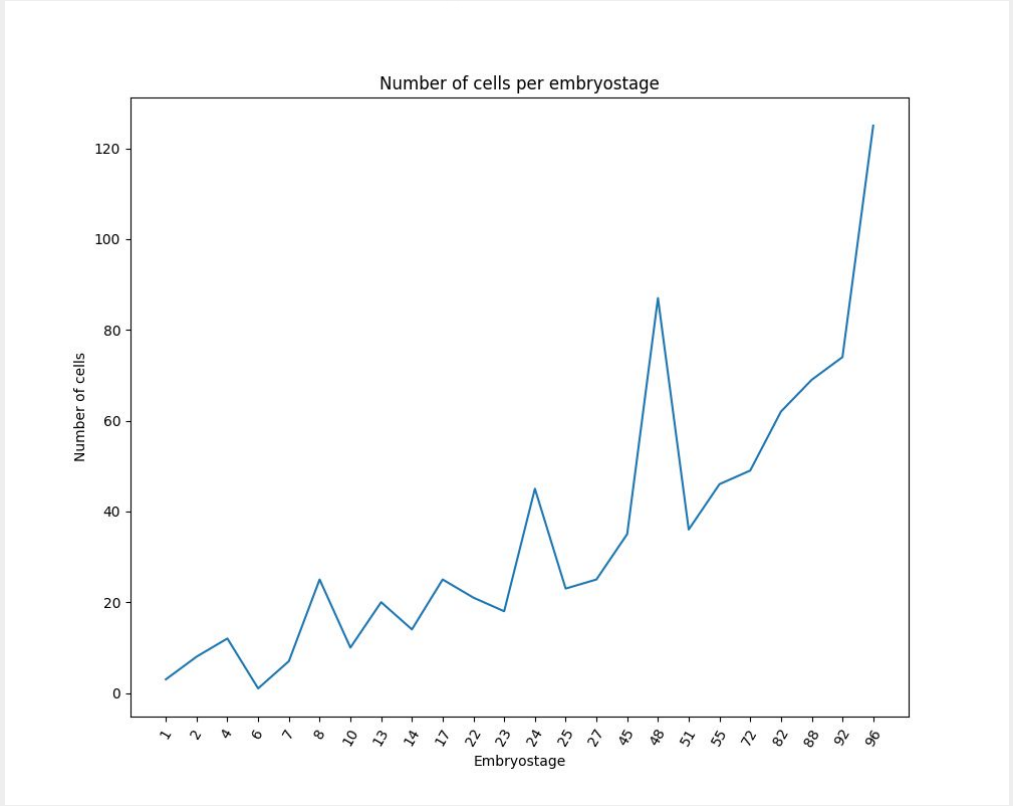
- Filtern via scanpy[2]:
  - Zellen: minimum 200 Gene exprimiert
  - Gene: minimum in 3 Zellen exprimiert
  - Normalisieren über Zellen
  - Variance stabilization: log1p
  - Selektion von den 2000 variabelsten Genen
- Batch effects[3]: z-transformation pro Embryo
- Selektion von bereits manuell annotierten Zellen[4]
- Expressionsmatrix: 840 Zellen x 2000 Gene

Data exploration



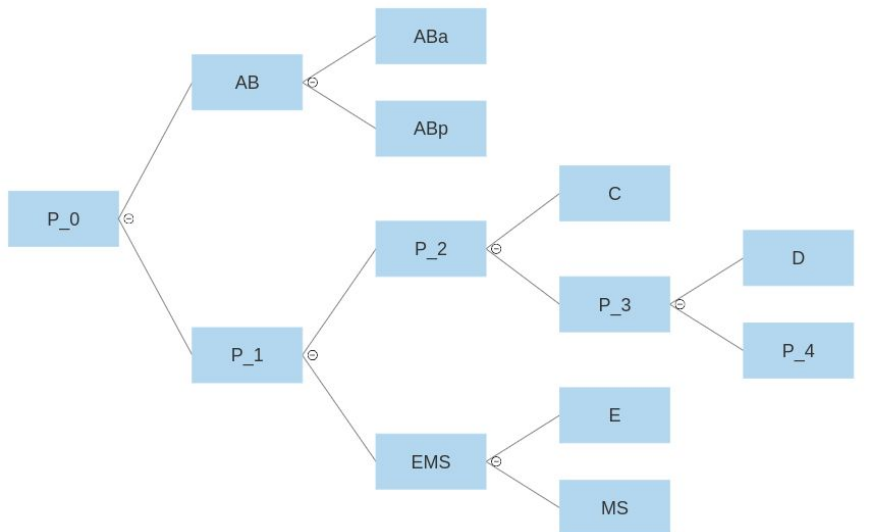
Data exploration

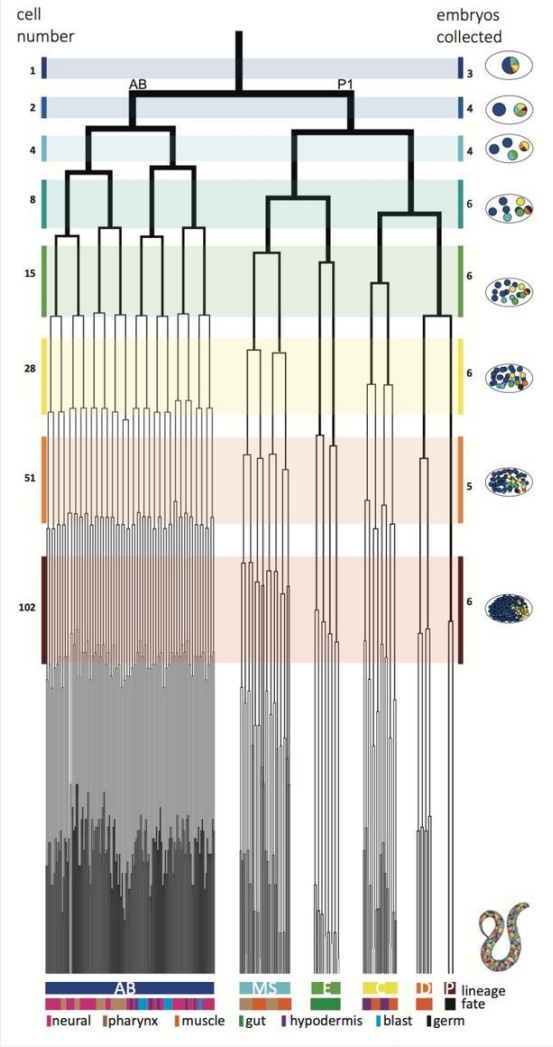




Data exploration II

- Equivalenzgruppen[4]:
- 119 Zelltypen
- Differenzierungsbaum[5]:





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Clustering

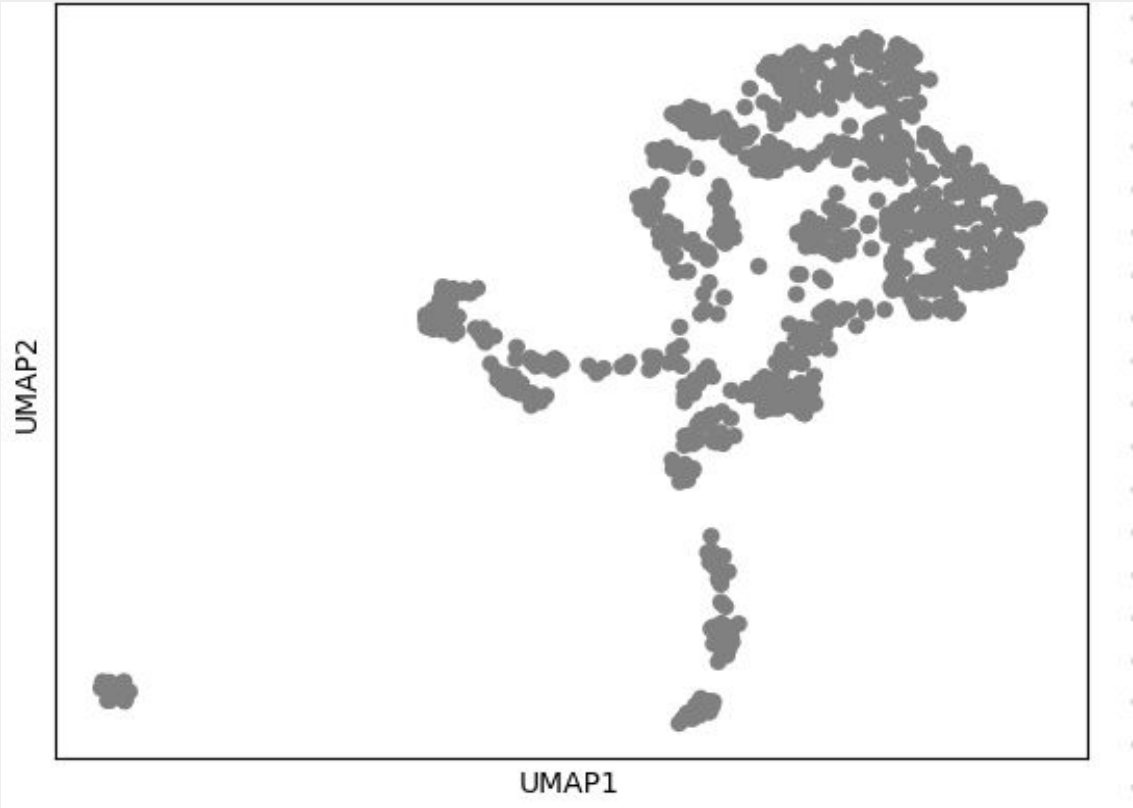
Clustering

UMAP[6]:

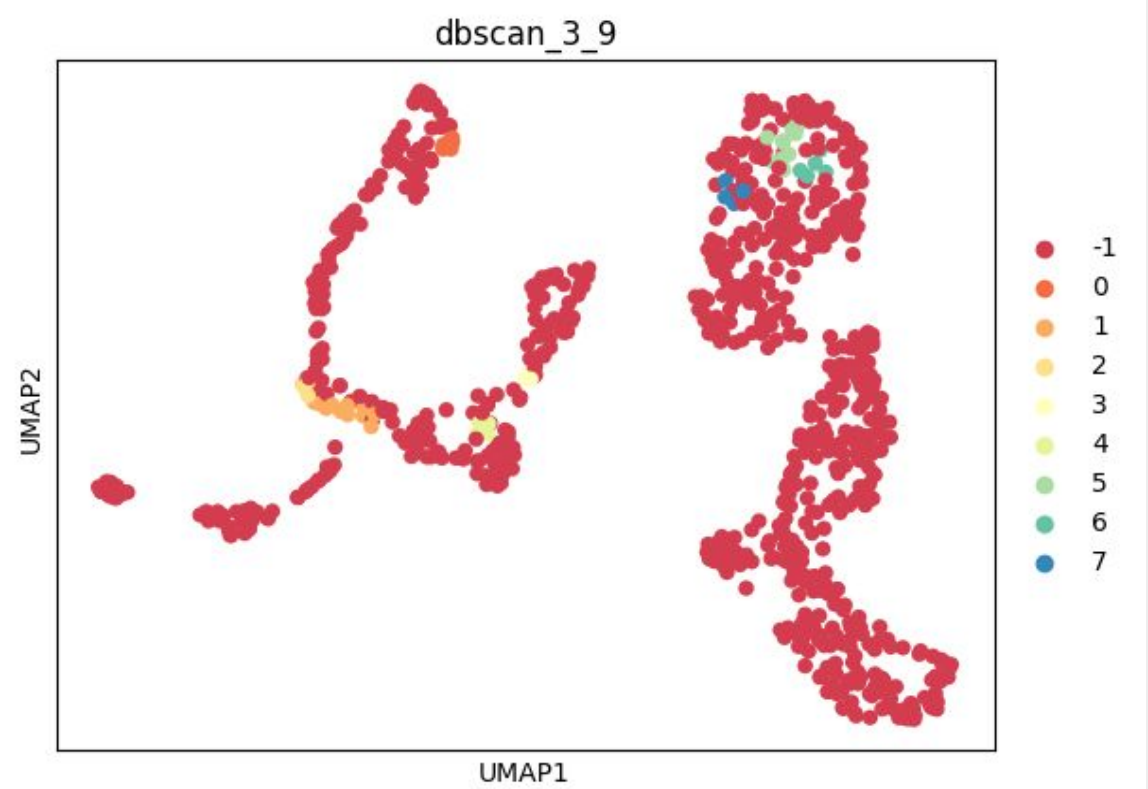
- Distance Measure zwischen Samples
- Lokale Struktur (k-nearest-neighbour -Graph) der Daten
- Reduktion der Raumdimension auf 2 bei Erhaltung der Distanzen

=> Methode, mehrdimensionale Datenpunkte zweidimensional darzustellen

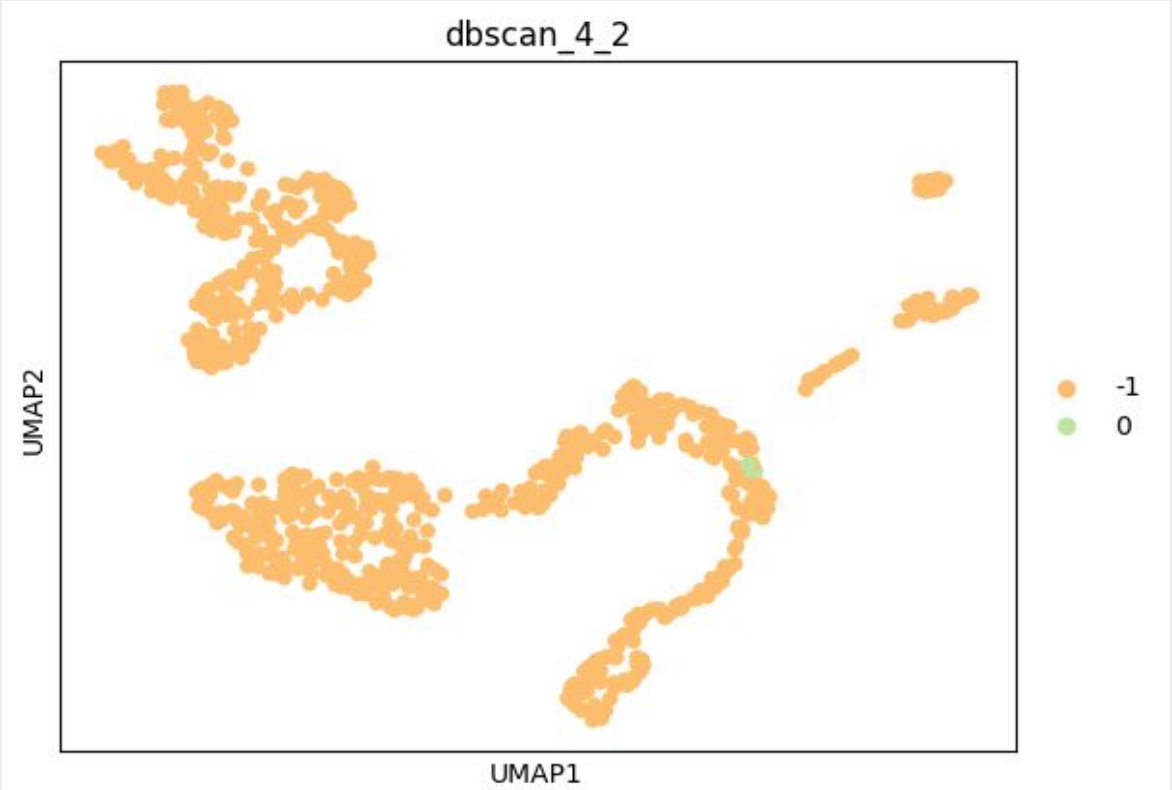
Clustering



Clustering



Clustering



Clustering

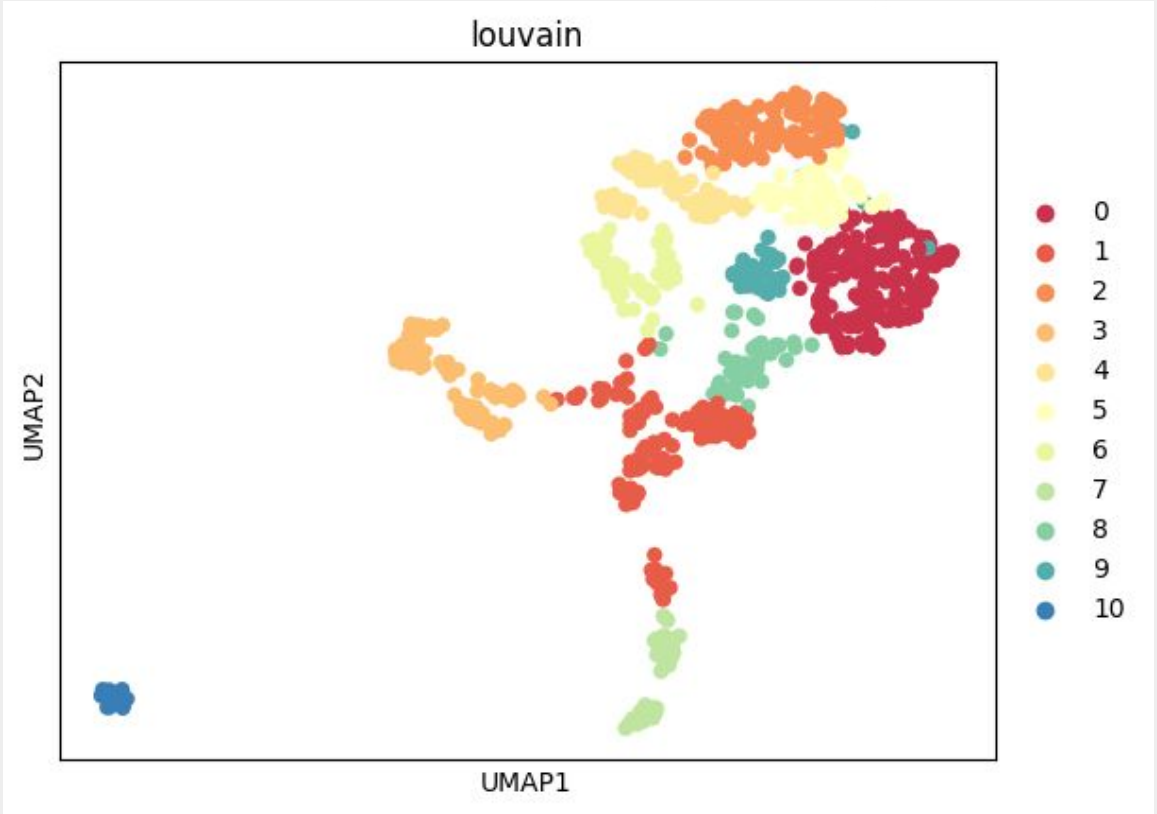
Louvain[7]:

- Distance Measure zwischen Samples
- k-nearest-neighbour-Graphen der Daten
- Zuweisung jedes Knotens zu einer “Gemeinschaft”
- Iterative Neuzuweisung basierend auf Clusterdichte (“Modularität”).

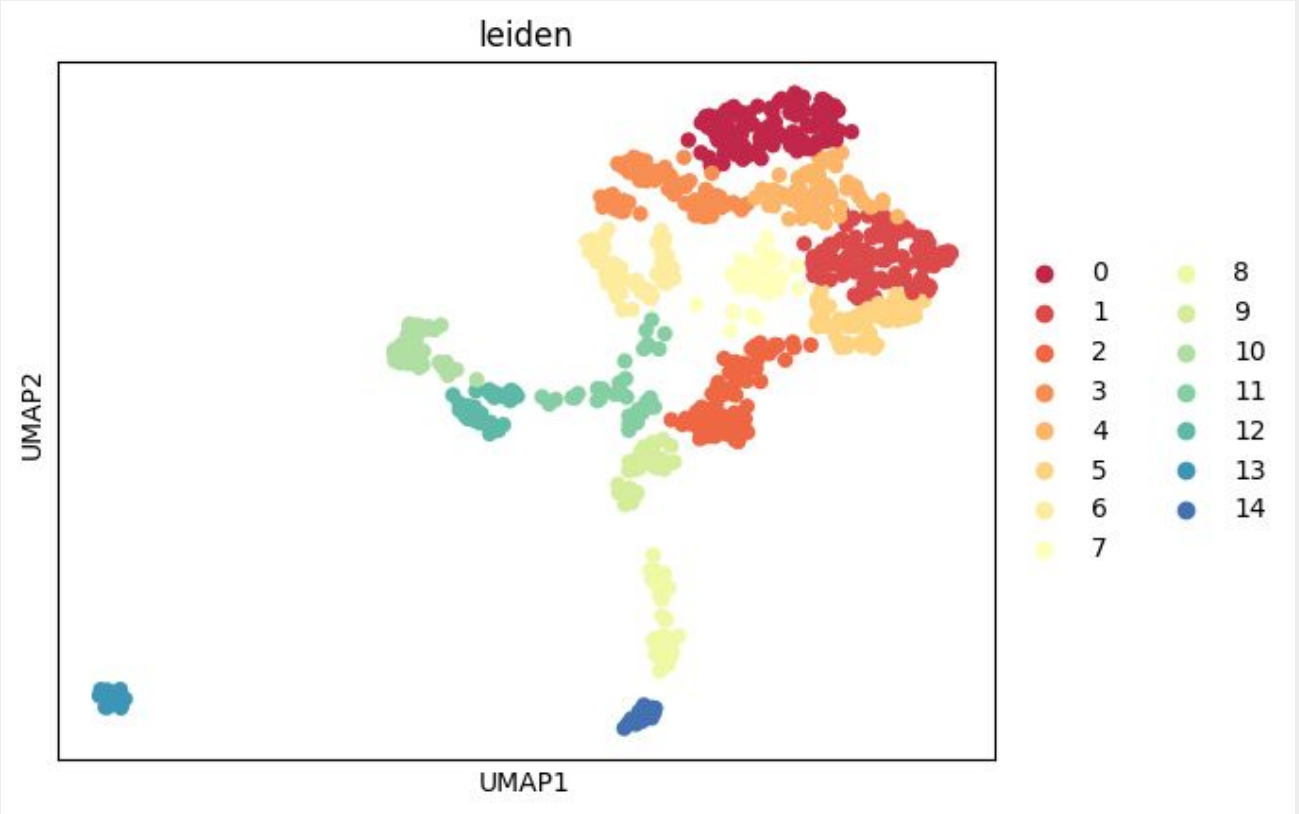
Leiden[7]: Verbesserte Version, robuster gegenüber Rauschen.

ScanPy: k-nearest-neighbour-Graphen basierend auf Genexpressionsdaten.

Clustering



Clustering



Clustering

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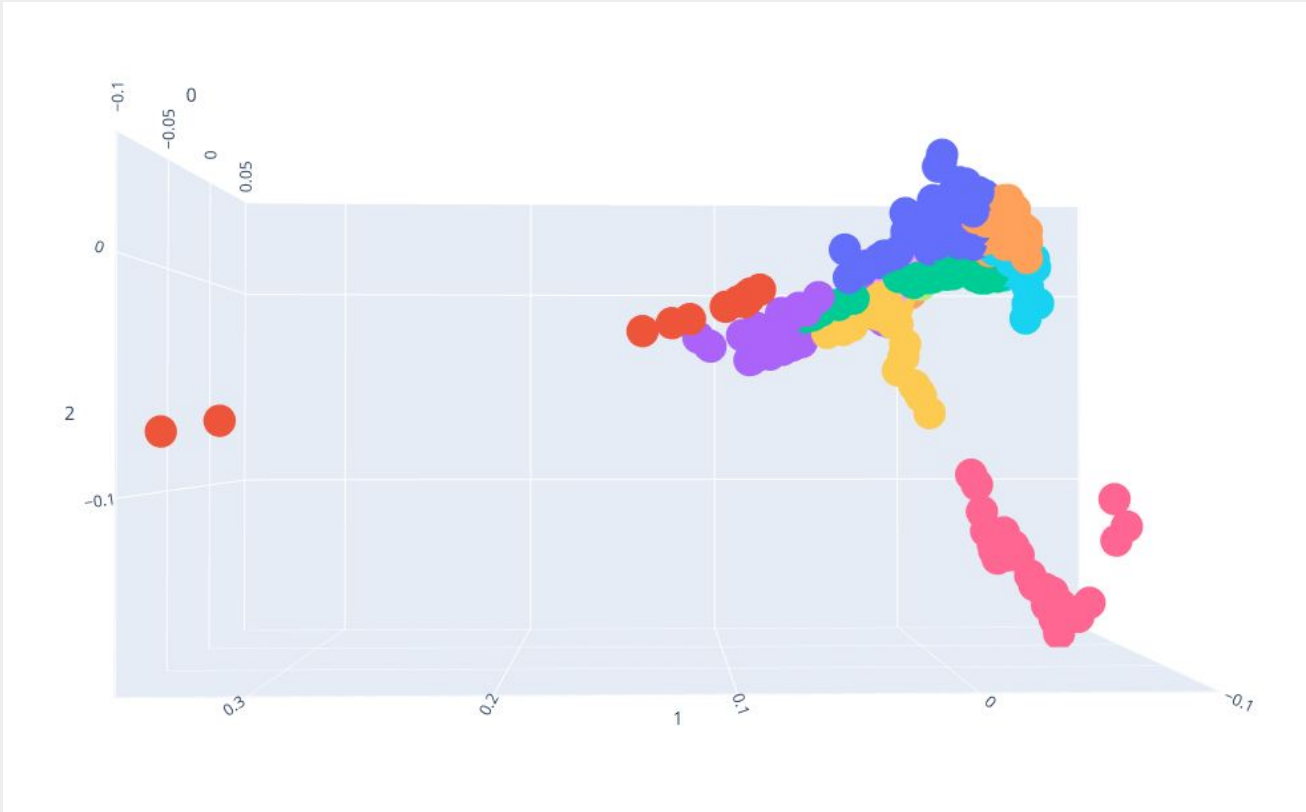
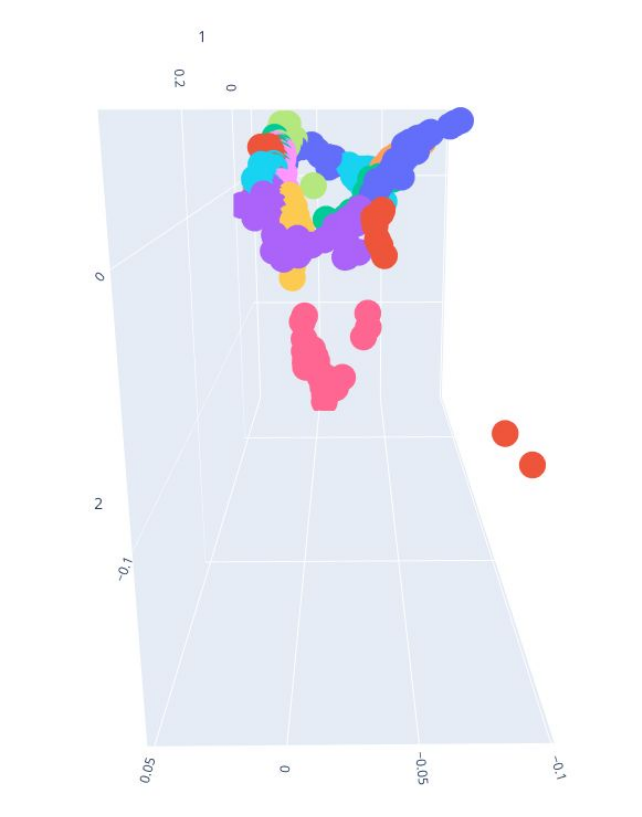
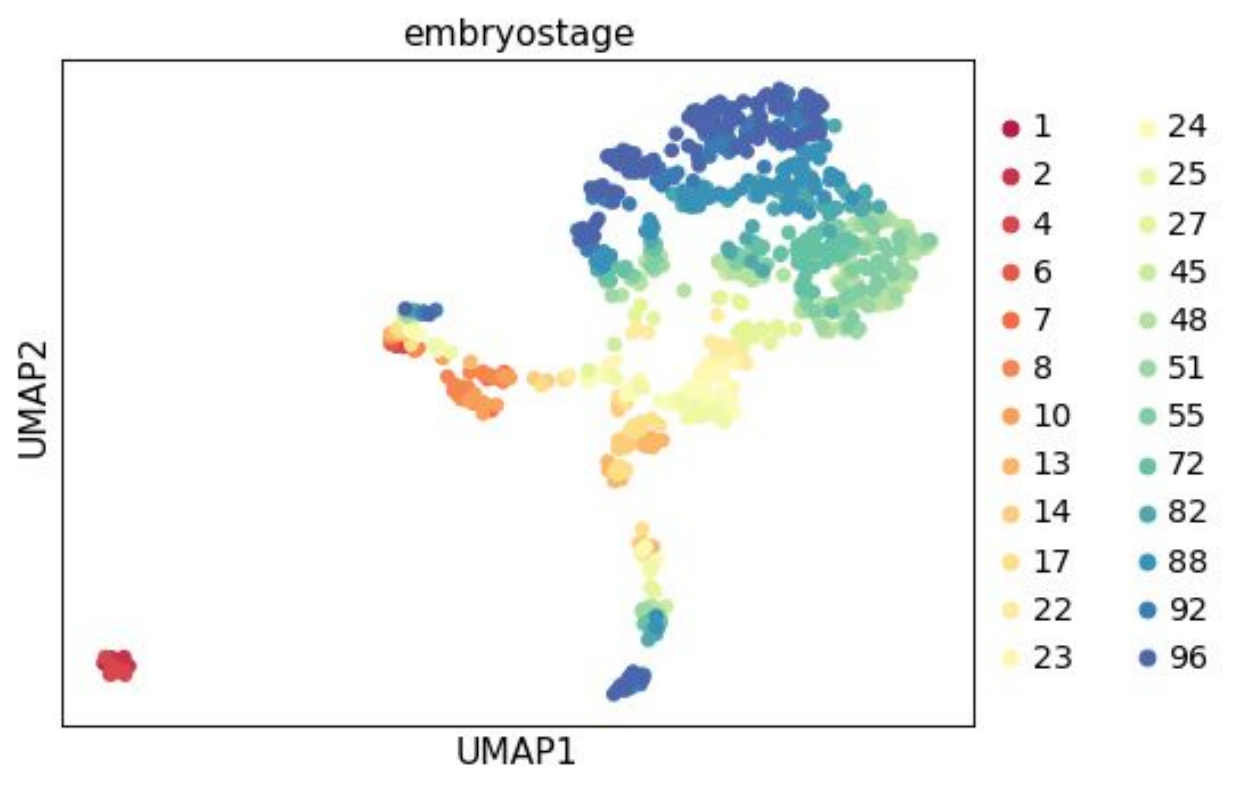


Clustering



Clustering


embryostage
UMAP2
UMAP1
1
2
4
6
7
8
10
13
14
17
22
23
24
25
27
45
48
51
55
72
82
88
92
96

Hierarchical Clustering

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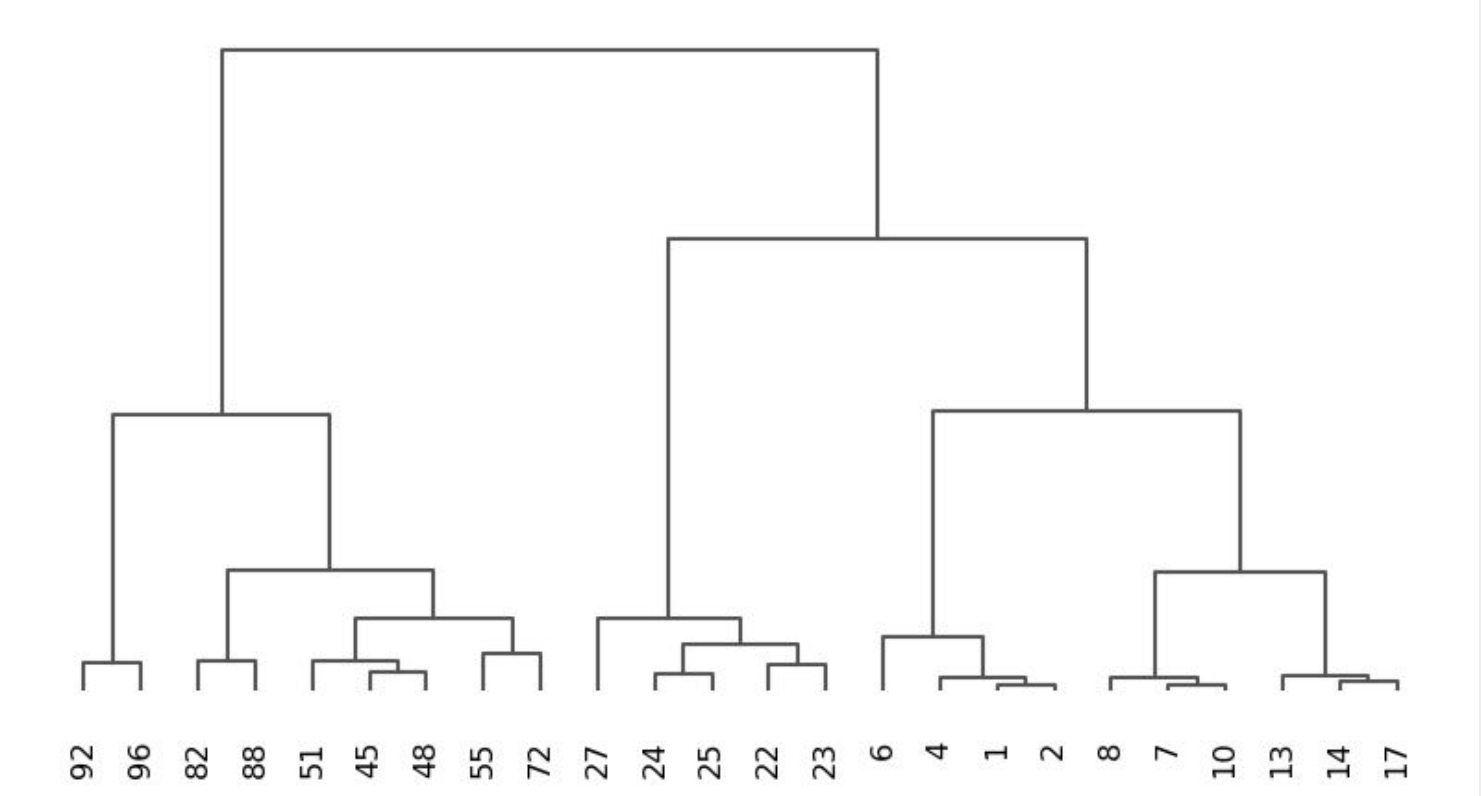
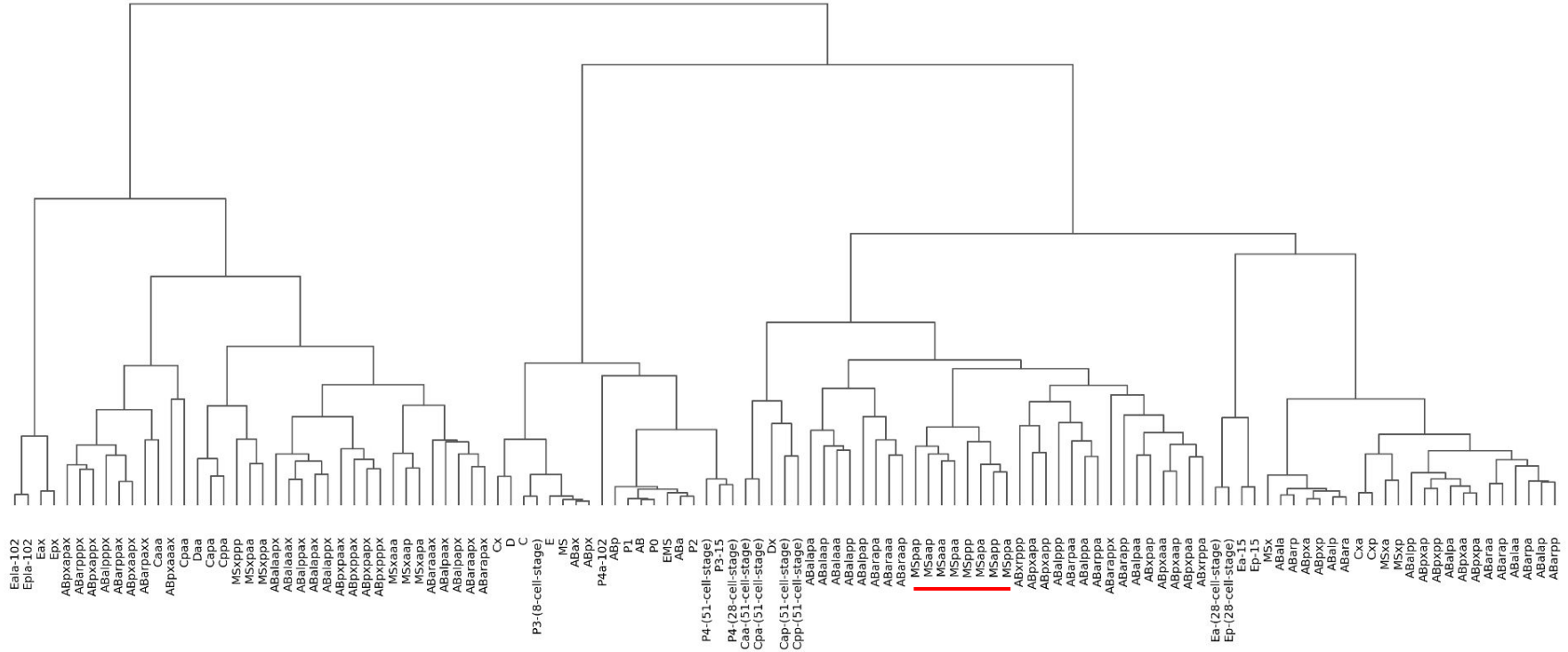


Hierarchical Clustering



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Machine Learning Modelle

ML Modelle

via scikitlearn[8]:

1. SVM
2. Random forest
3. KNeighborsClassifier
4. Multinomial Logistic Regression
5. MLP Classifier
6. Neural Networks

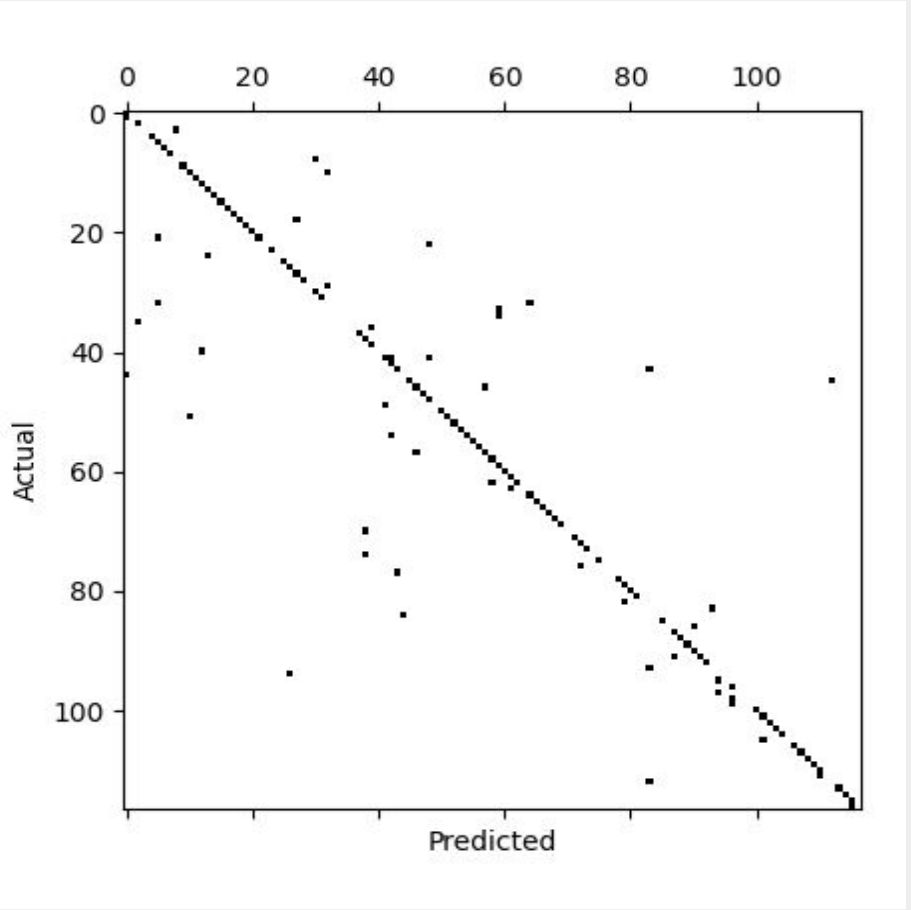
Support Vektor Maschine

1.

- 72 % true positives
- hyperparameters:

C	100
kernel	linear

tested param grid =
{"C": [0.1, 0.8, 4, 10, 30, 100],
"kernel": ["linear"]}



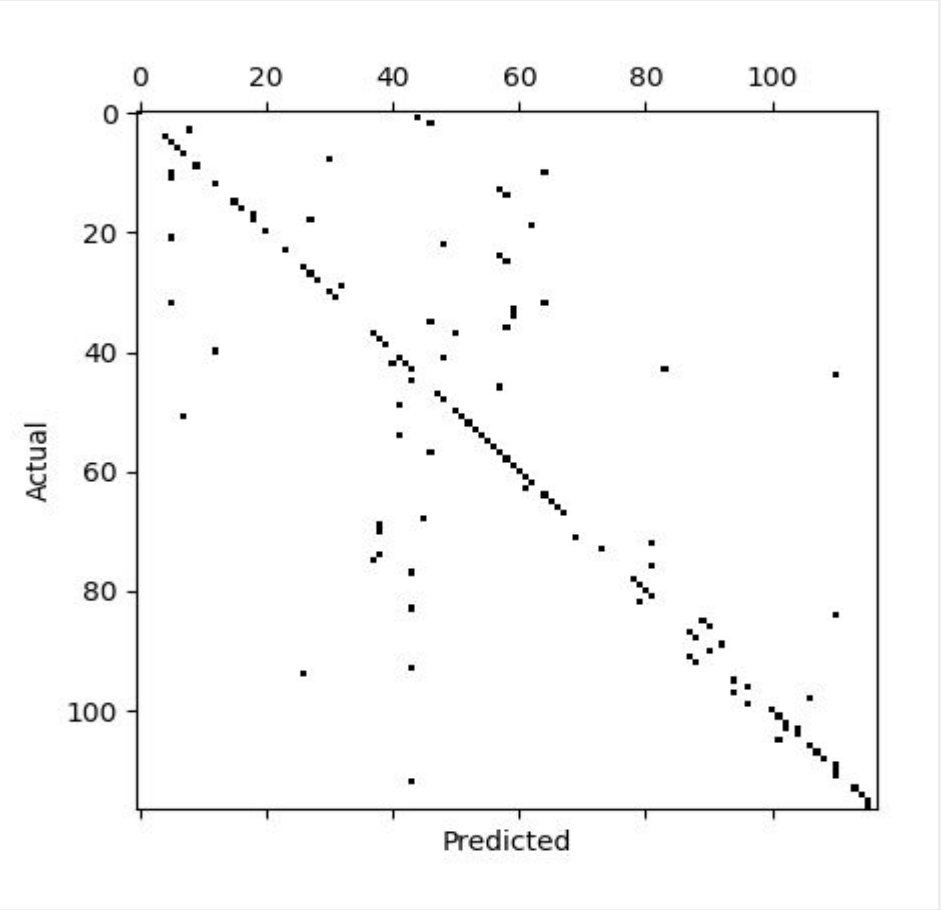
Random Forest

2.

- 58 % true positives
- hyperparameters:

n_estimators	1000
max_depth	None

tested param grid =
{"n_estimators": [10, 100, 1000],
"max_depth": [None, 10, 100]}



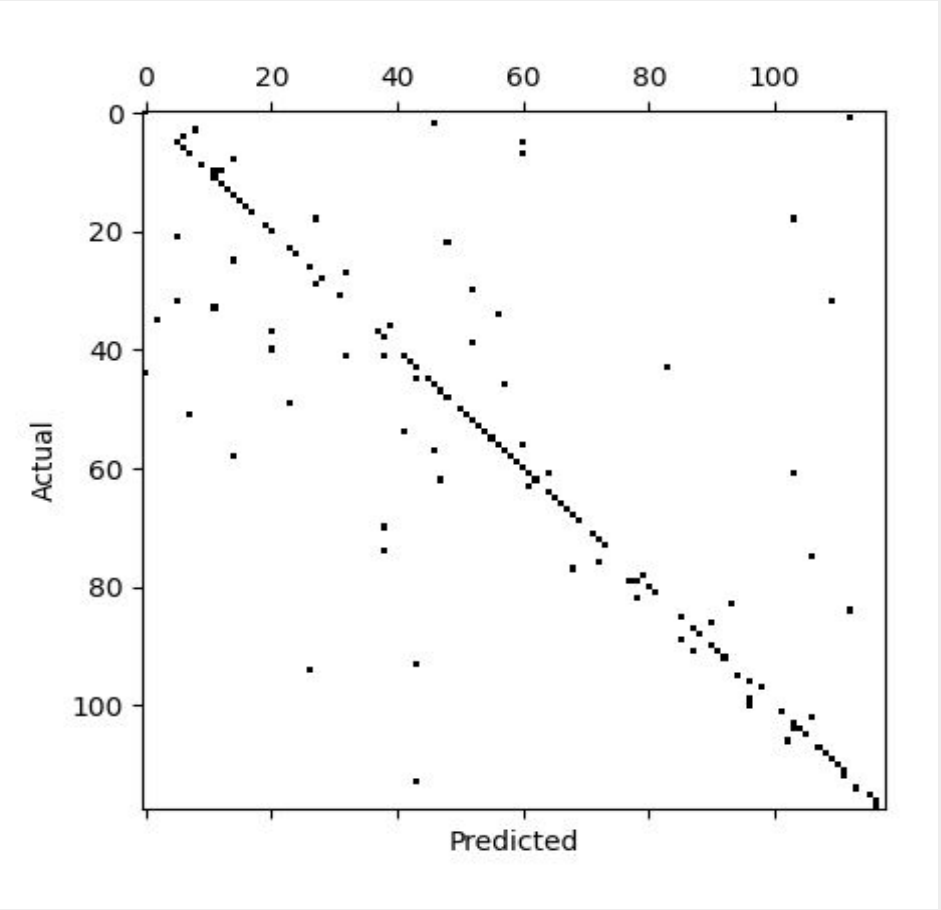
Kneighbors Classifier

3.

- 58.3 % true positives
- hyperparameters:

n_neighbors	1

tested param grid = {"n_neighbors": [1, 5, 10, 20, 50]}



Multinomial Logistic Regression

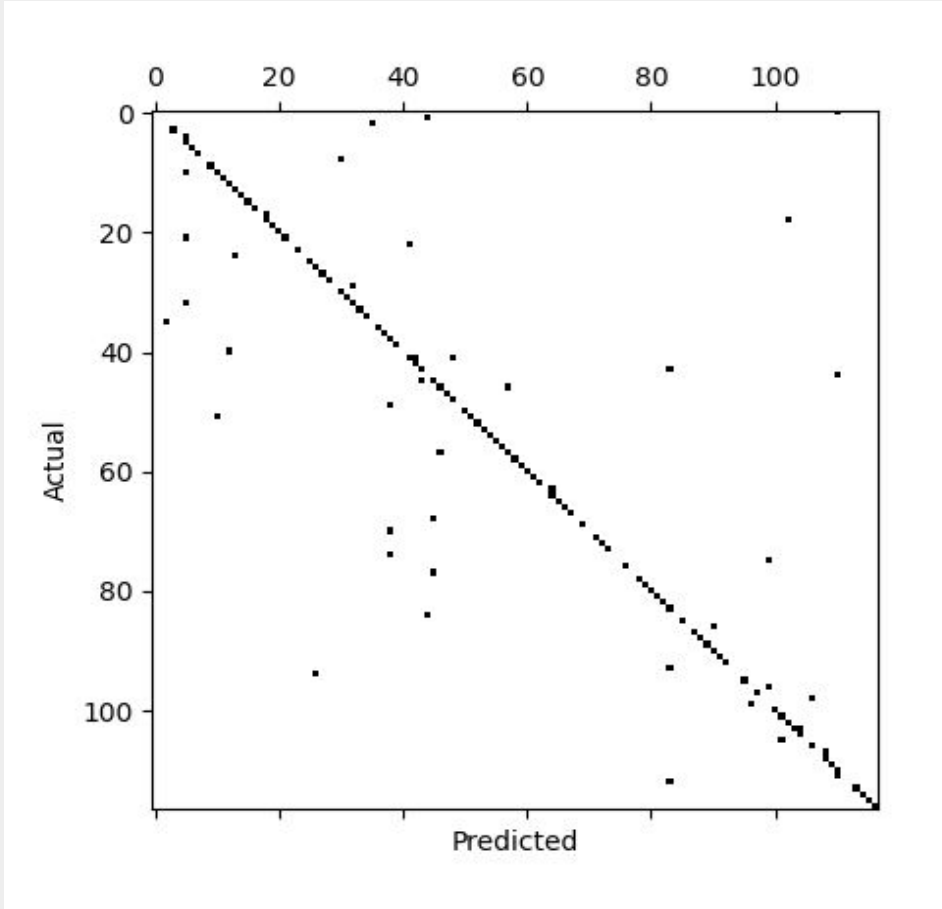
4.

- 75 % true positives
- hyperparameters:

C:	100
penalty	L1
solver	saga
multi_class	multinomial
max iteration	1000

tested param grid =

{'penalty': ['l1', 'l2'],
'solver': ['newton-cg', 'lbfgs', 'saga'],
'C': [0.1, 1, 10, 100]}
'multi_class': ['multinomial'],}



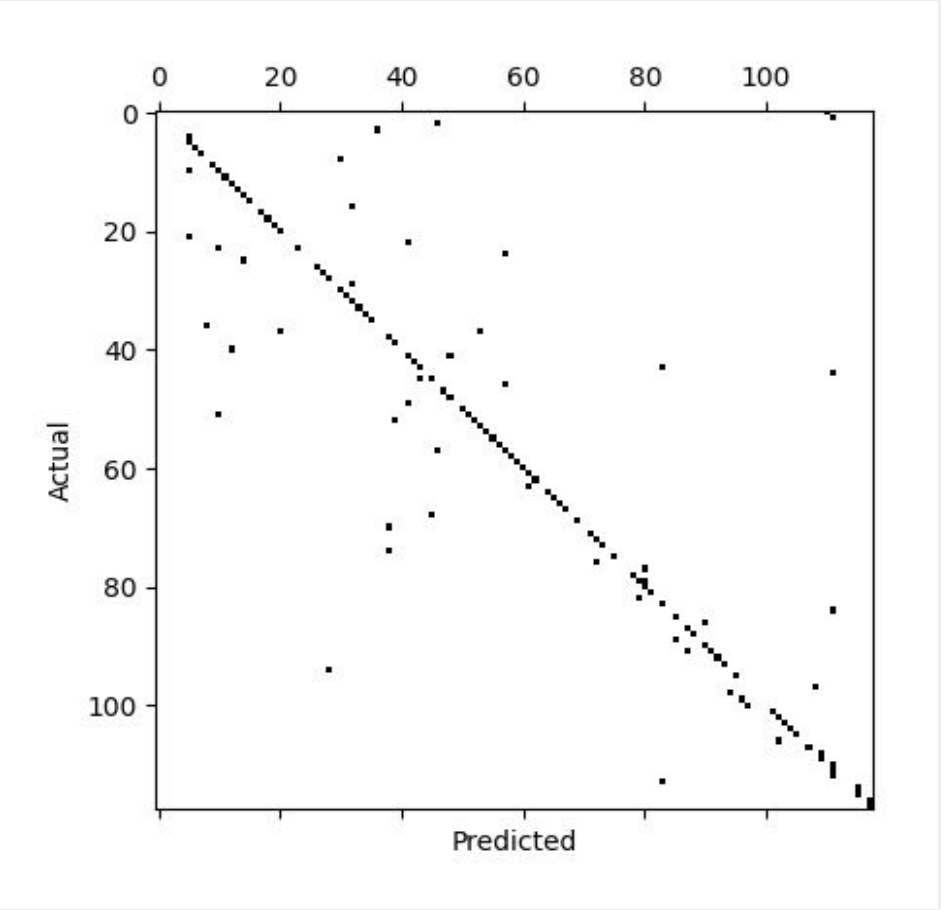
MLP Classifier

5.

- 68.45 % true positives
- hyperparameters:

activation:	relu
alpha:	1.00
hidden layer sizes:	(100)
max iteration:	1000

tested param grid =
{"hidden_layer_sizes": [(100,), (100, 100), (100, 100, 100)],
"activation": ["relu", "logistic", "tanh"],
'alpha': [0.001, 0.1, 0.01, 1]}



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Neuronale Netzwerke

6.

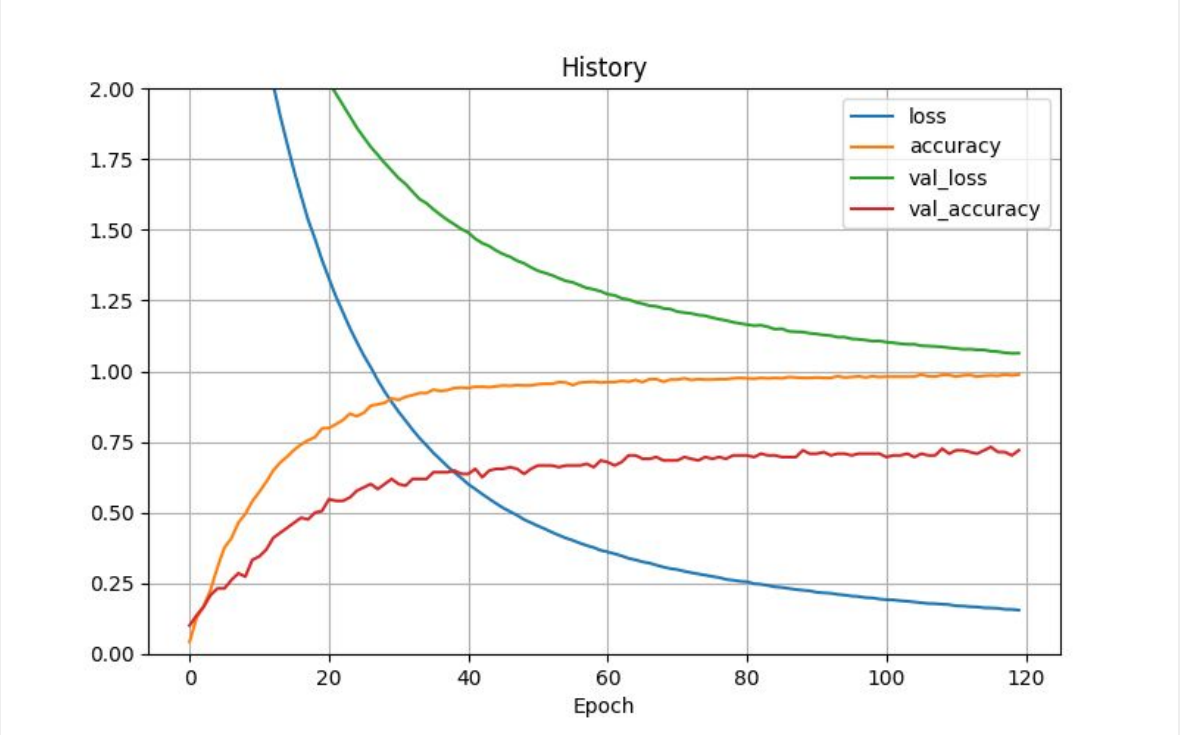
via tensorflow.keras[9]

Modell 1

2 Dense layers:	600, 800 Neuronen
Aktivierungsfunktion	tanh
1 Softmax	119 Neuronen (entsprechend den 119 Zelltypen)
optimizer	Standard “Sgd” von keras

Ergebnis Modell 1

Richtig erkannte Samples:
~68-75%

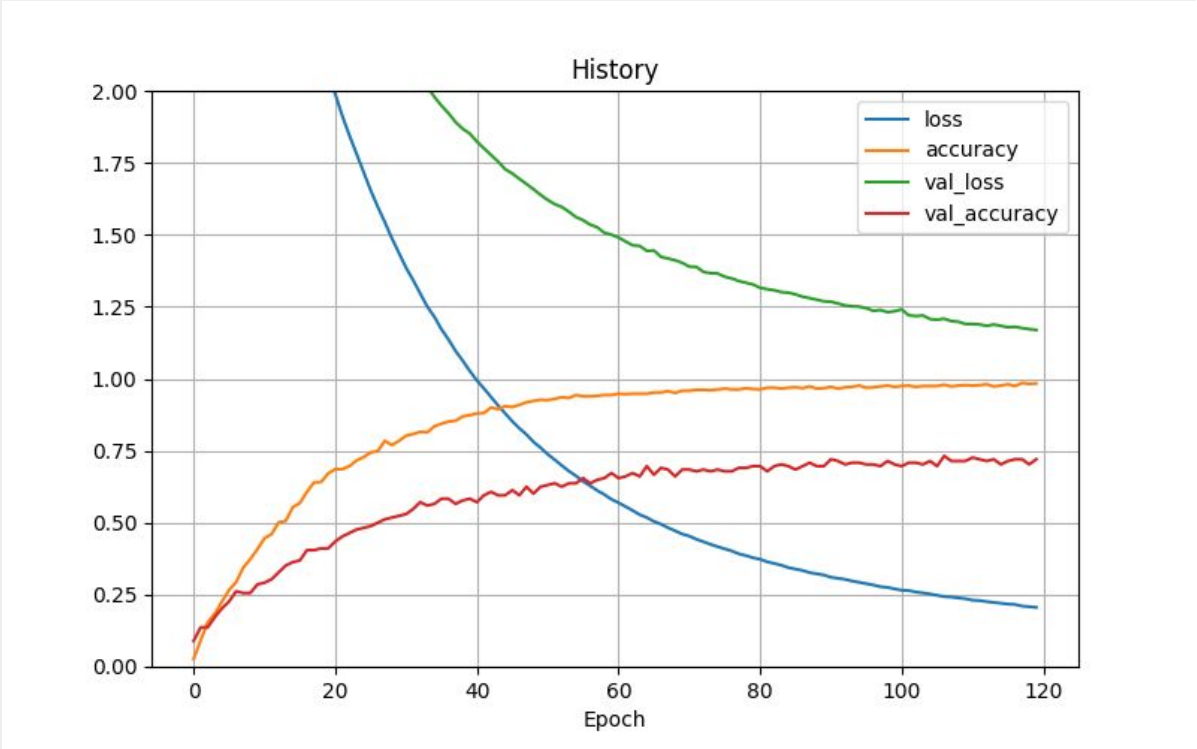


Modell 2

4 Dense layers	500,400,300,200 Neuronen
Aktivierungsfunktion	tanh
1 Softmax	119 Neuronen (entsprechend den 119 Zelltypen)
optimizer	Standard “Sgd” von keras

Ergebnis Modell 2

Richtig erkannte Samples:
~67-73%

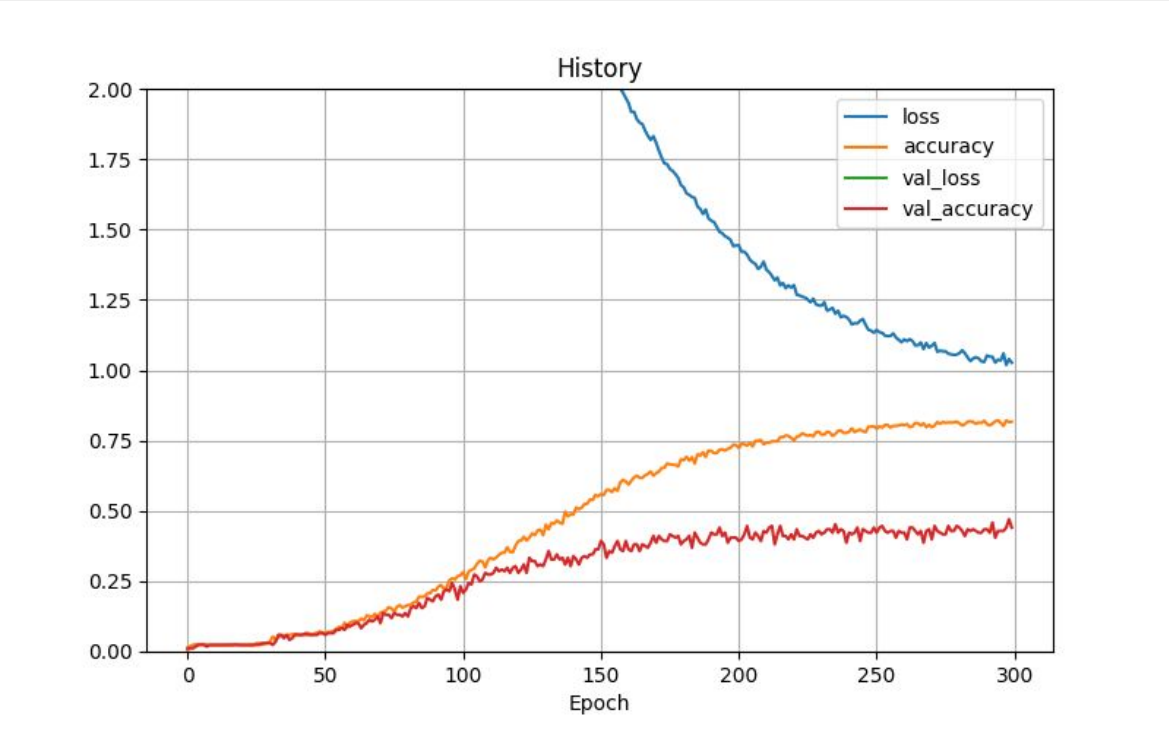


NN with Multihead attention

- Multihead Attention ist Basis für Transformer -> GPT[10]
- Hat drei inputs (query, key, value)
- Input is zu jedem der inputs jeweils durch einen dense layer verbunden
- Nachher noch ein dense und ein softmax layer
- Scheint nicht so geeignet zu sein für unsere Daten

Multihead Attention Model Ergebnis

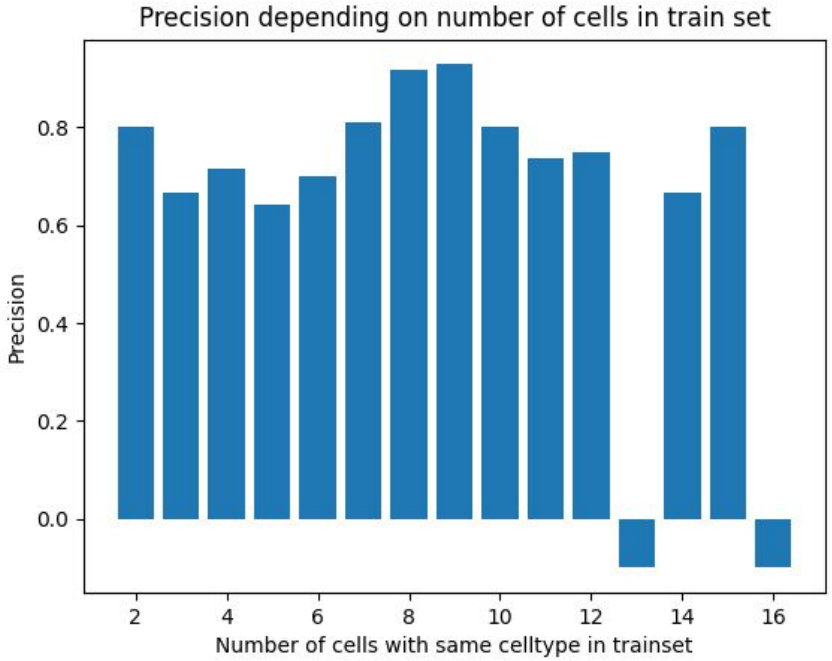
Richtig erkannte Samples:
~40-50%

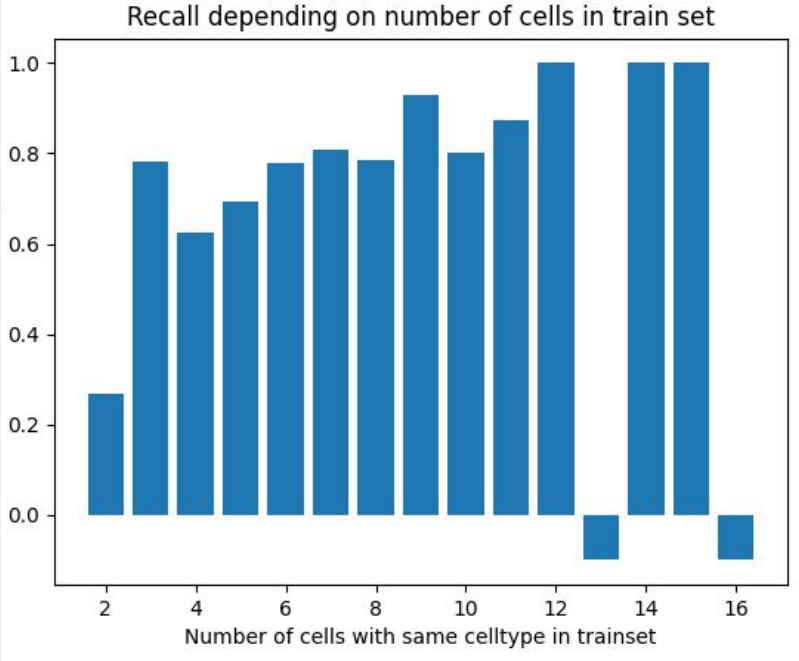


Auswirkung der Anzahl an Samples im Trainingsset

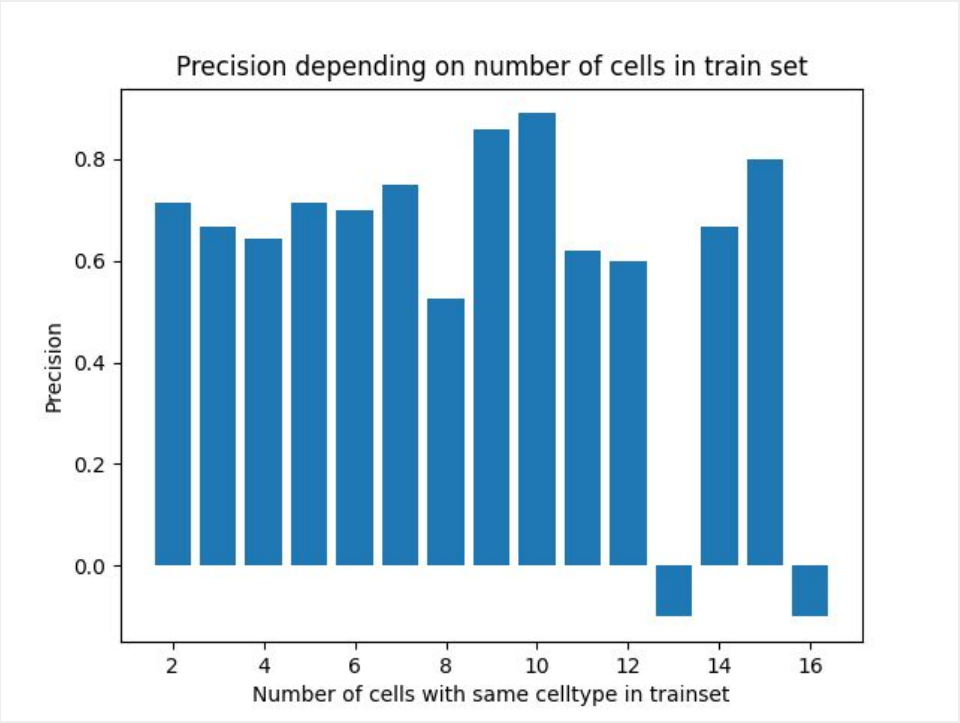
- Recall: Anzahl richtig erkannter Samples von Zelltypen, die n mal im Trainingsset vorkommen/Anzahl Samples der entsprechenden Zelltypen im Testset
- Precision: Anzahl richtig erkannter Samples von Zelltypen, die n mal im Trainingsset vorkommen/Anzahl Samples im Testset, die als der entsprechende Zelltyp klassifiziert wurden

Modell 1


Precision depending on number of cells in train set
Precision
0.0
0.2
0.4
0.6
0.8
2
4
6
8
10
12
14
16
Number of cells with same celltype in trainset


Recall depending on number of cells in train set
0.0
0.2
0.4
0.6
0.8
1.0
2
4
6
8
10
12
14
16
Number of cells with same celltype in trainset

Modell 2


Precision depending on number of cells in train set
Precision
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0.2
0.4
0.6
0.8
2
4
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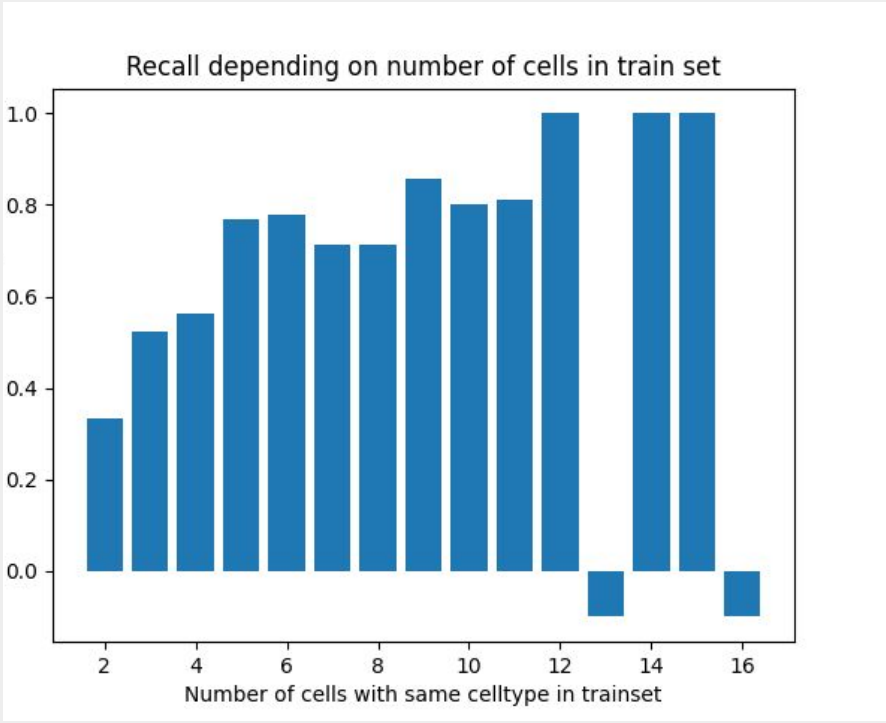
8
10
12
14
16
Number of cells with same celltype in trainset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0.8
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4
6
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10
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14
16
Number of cells with same celltype in trainset

Multihead Attention

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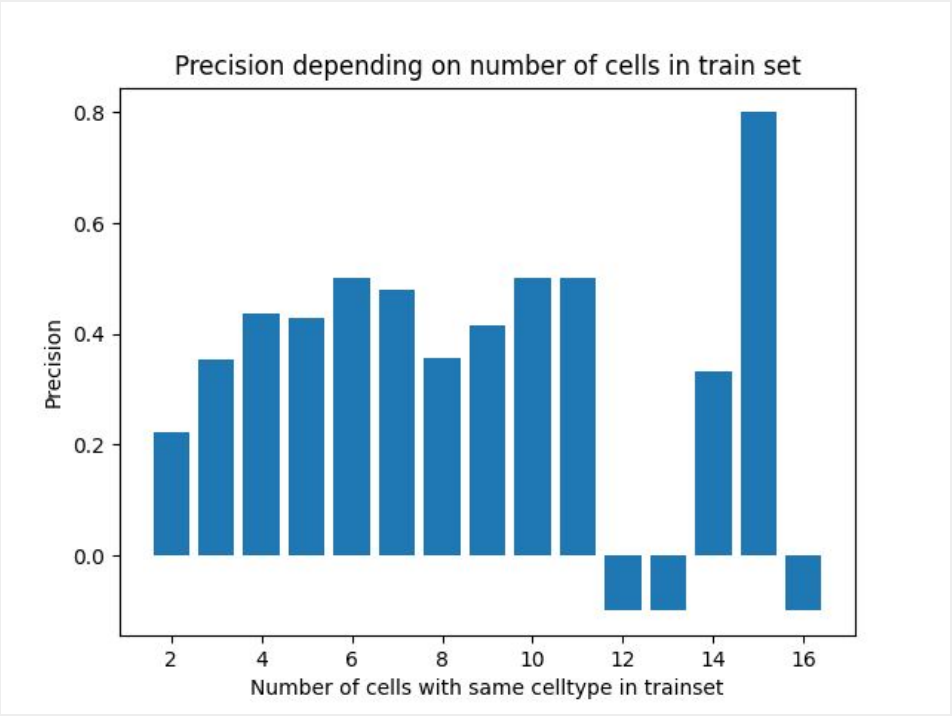

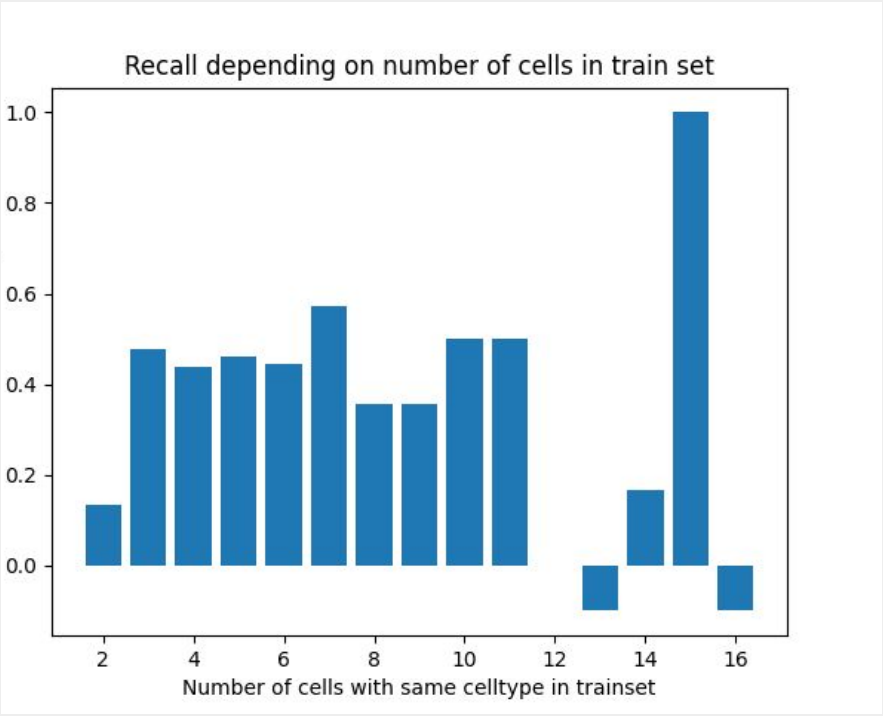

Modellen-vergleich

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Modellname	SVM	Random Forest	Kneighbor Classifier	Multinomial Logistic Regression	MLP	Neural Networks
Test-genauigkeit	72 %	58 %	58.3 %	**75 %**	68.45 %	**75 %**

Mögliche Fortsetzung

- Semi-supervised learning
- Andere Dimension-Reduktionsmethoden
- Andere Resolutions für Clustering-Algorithmen
- Rohe Daten

Danke!

Quellenangabe

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