PREDICTING TISSUE-SPECIFIC GENE EXPRESSION FROM BLOOD USING AI

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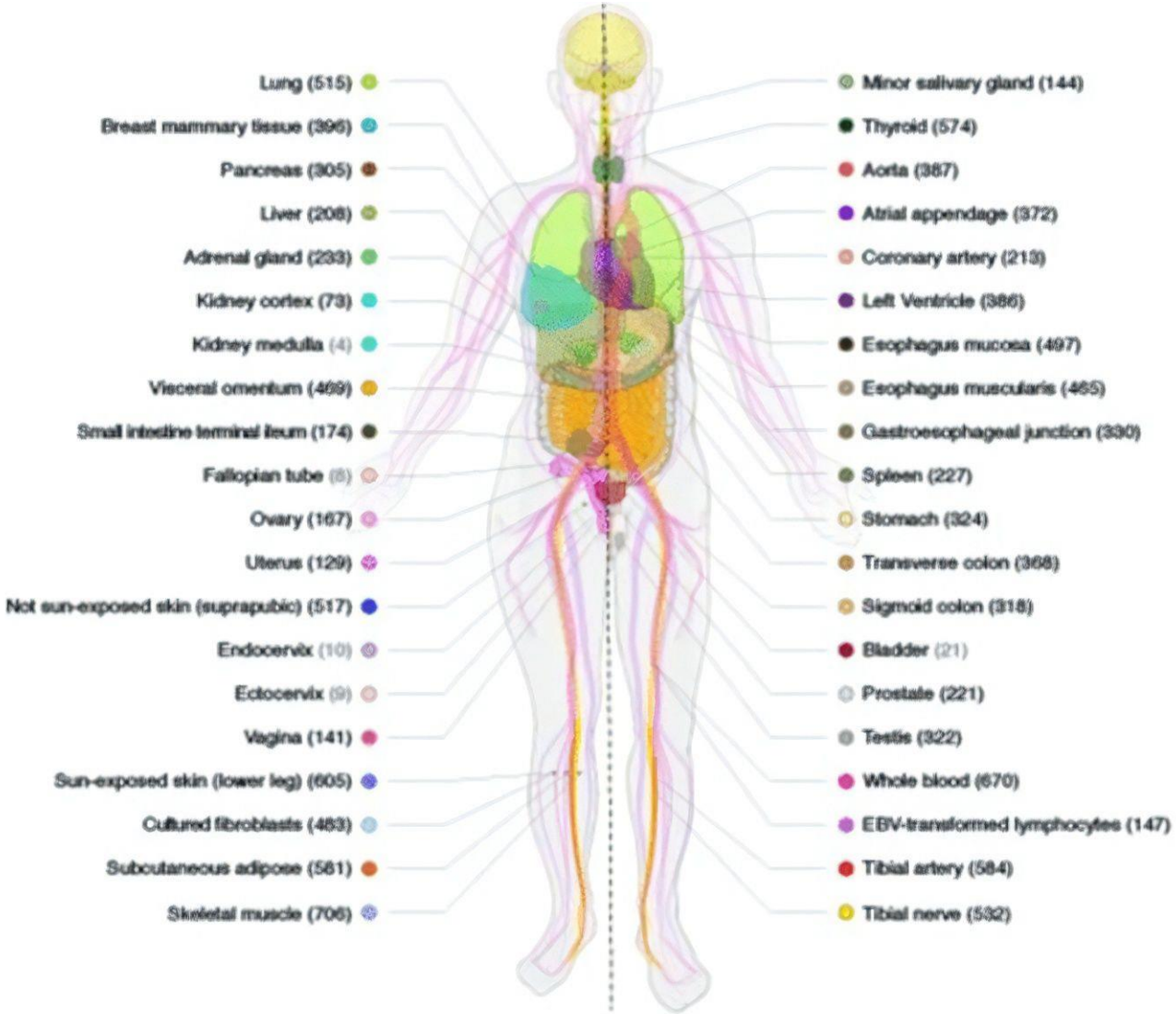


DATA

The Genotype-Tissue Expression (GTEx)

Publicly available dataset containing gene expression of 54 post-mortem tissues from almost 1,000 individuals

Website: https://www.gtexportal.org/home/

Image source: https://www.researchgate.net/figure/Sample-and-data-types-in-the-GTEx-v8-study-A-Illustration-of-the-54-tissue-types_fig1_336246636

PROBLEM

- Gene expression varies across tissues
- Obtaining samples from heart, lung, brain and other organs is often not possible

GOAL

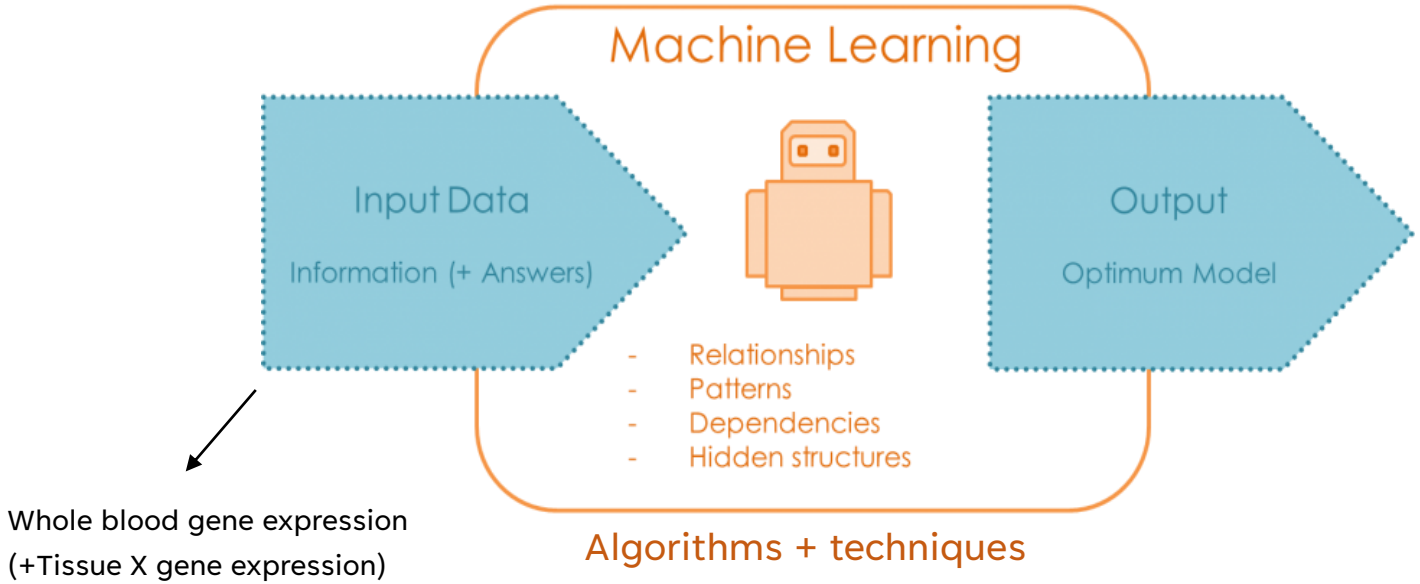


Image source: https://quantdare.com/

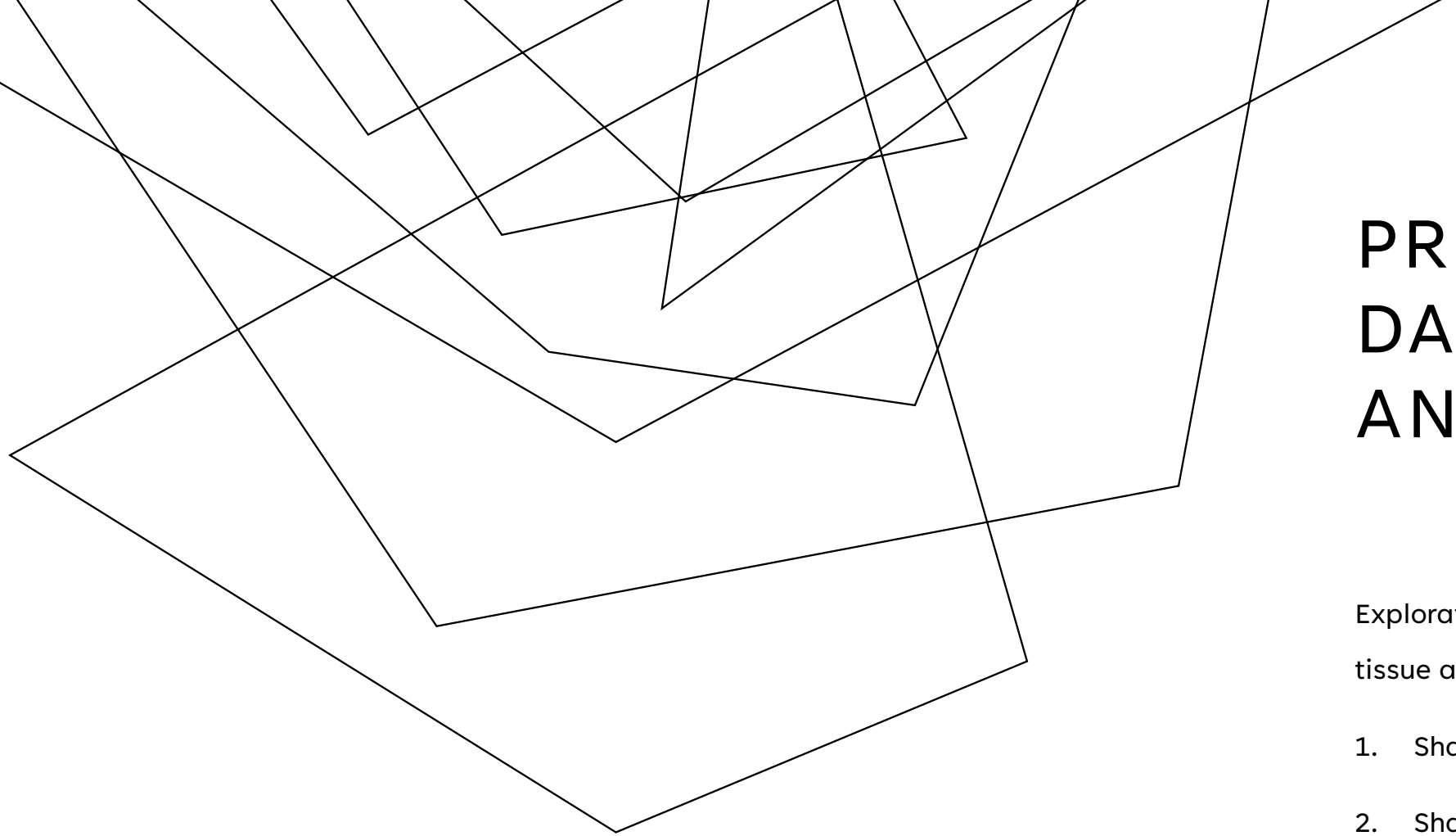
DATA PRE-PROCESSING

	GTEX-111YS	GTEX-1122O	GTEX-1128S	GTEX-117YW	GTEX-11DXX
ENSG00000188976	4.62364473	3.78253909	4.5133603	5.4527936	3.37519628
ENSG00000187961	1.93052342	1.27499967	3.5022390	3.5097032	1.82645735
ENSG00000187583	-0.75745530	-2.17811244	0.8867026	-0.3610409	-2.00195164
ENSG00000188290	-2.04196059	-0.37572051	-0.0725749	1.2067569	-3.55957777
ENSG00000187608	3.20267015	3.30039771	2.5859542	4.9613959	2.44112346

	GTEX-111YS	GTEX-1122O	GTEX-1128S	GTEX-117YW	GTEX-11DXX
ENSG00000188976	5.56460543	5.8744263	5.970547249	5.16622735	5.95836923
ENSG00000187961	3.60586511	3.9661503	4.392572536	4.02935543	4.00614281
ENSG00000187583	-0.26752148	0.5173860	1.411392148	1.74797744	0.23257945
ENSG00000188290	3.18410789	3.4222746	3.491766740	5.04511280	2.75391016
ENSG00000187608	3.87791649	4.2725832	4.466592815	5.18764207	3.90172955

	GTEX-1128S	GTEX-117XS	GTEX-1192X	GTEX-11DXW	GTEX-11DXY
ENSG00000188976	4.5133603	5.41962562	4.40573764	5.62804043	4.97935857
ENSG00000187961	3.5022390	2.86169747	3.54214773	3.29359001	3.82458092
ENSG00000188290	-0.0725749	0.70906184	0.88278386	1.70362024	-0.56079737
ENSG00000187608	2.5859542	5.66514689	5.17640485	4.86172548	4.24214853
ENSG00000188157	2.7483510	1.73139723	1.64804437	2.11621022	2.45405401

	GTEX-1128S	GTEX-117XS	GTEX-1192X	GTEX-11DXW	GTEX-11DXY
ENSG00000188976	6.36783476	6.2316949	6.46433195	6.3887099	6.2711988467
ENSG00000187961	5.56040664	4.9513539	6.16913252	5.3212697	5.0969189121
ENSG00000188290	1.61186294	1.4614192	2.71896260	2.4761530	1.4588005060
ENSG00000187608	0.70806198	1.5332473	1.69497304	0.6651525	1.6285311222
ENSG00000188157	4.52051422	4.8785337	5.12529845	4.8907246	5.1851027306

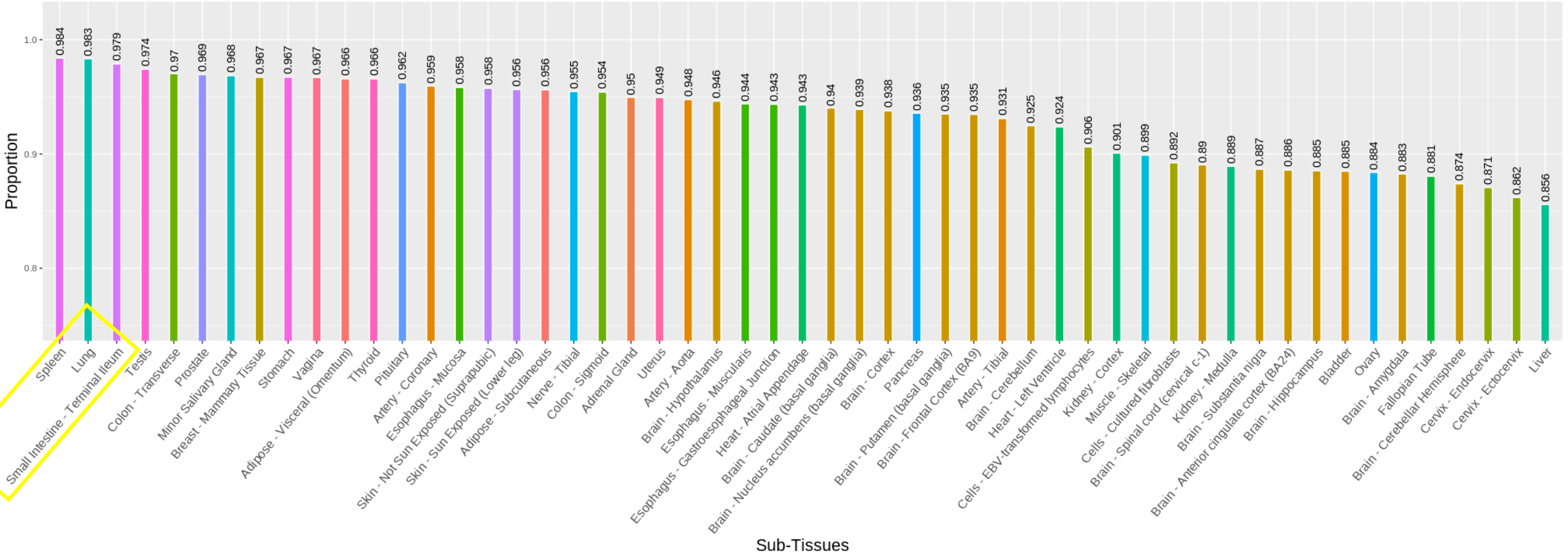


PRELIMINARY DATA ANALYSIS

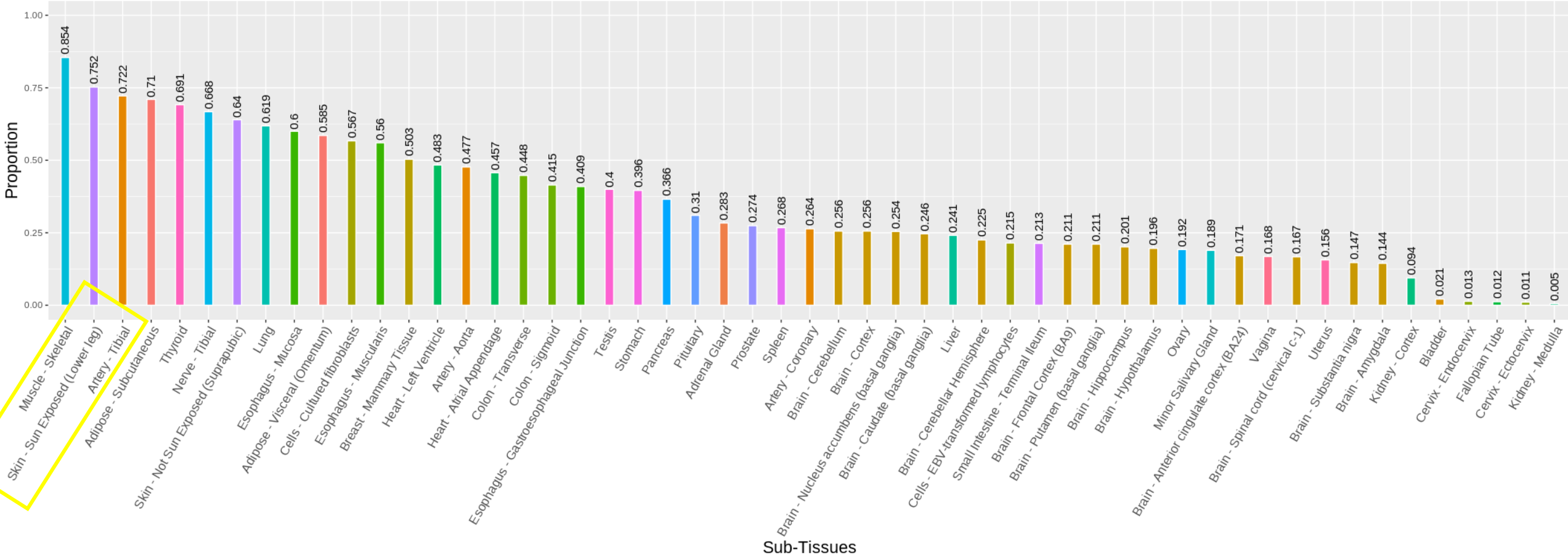
Exploration of **similarities** between each tissue and whole blood

1. Shared expressed **genes**
2. Shared **donors**
3. Gene expression **correlation**

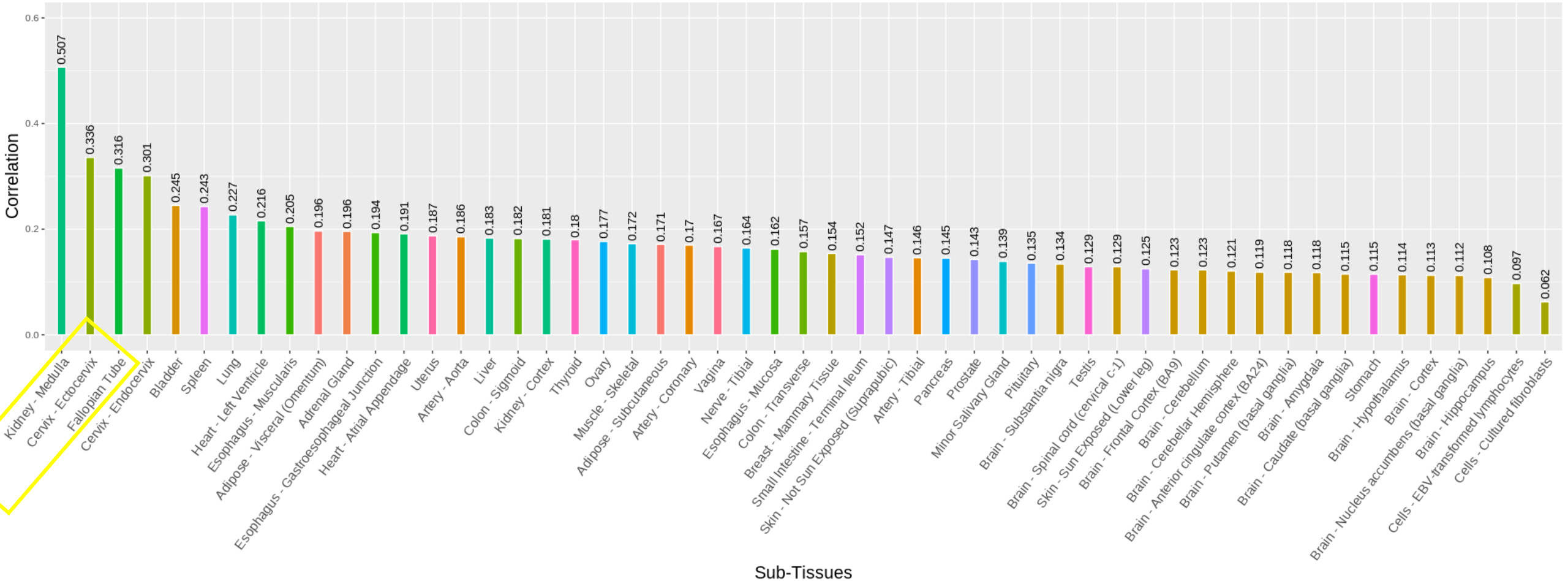
Proportion of Overlapping Genes of Whole Blood with all other Tissues



Proportion of Overlapping Donors of Whole Blood with all other Tissues



Mean of Absolute Correlation of a Tissue and Whole Blood, based on their Shared Genes



TISSUE SELECTION

Rank tissues based on the previously observed measures

Subtissue	Donor Proportion	Donor Rank	Gene Proportion	Gene Rank	Mean Absolute Correlation	Correlation Rank	Average Rank
Lung	0.619	8	0.983	2	0.227	7	5.67
Adipose - Visceral (Omentum)	0.585	10	0.966	11	0.196	10	10.33
Spleen	0.268	26	0.984	1	0.243	6	11
Thyroid	0.691	5	0.966	12	0.18	19	12
Adipose - Subcutaneous	0.71	4	0.956	18	0.171	22	14.67
Esophagus - Muscularis	0.56	12	0.944	25	0.205	9	15.33
Breast - Mammary Tissue	0.503	13	0.967	8	0.154	28	16.33
Colon - Transverse	0.448	17	0.97	5	0.157	27	16.33
Esophagus - Mucosa	0.6	9	0.958	15	0.162	26	16.67
Nerve - Tibial	0.668	6	0.955	19	0.164	25	16.67
Artery - Aorta	0.477	15	0.948	23	0.186	15	17.67
Skin - Not Sun Exposed (Suprapubic)	0.64	7	0.958	16	0.147	30	17.67
Colon - Sigmoid	0.415	18	0.954	20	0.182	17	18.33
Adrenal Gland	0.283	24	0.95	21	0.196	11	18.67
Heart - Atrial Appendage	0.457	16	0.943	27	0.191	13	18.67
Esophagus - Gastroesophageal Junction	0.409	19	0.943	26	0.194	12	19

CROSS-VALIDATION

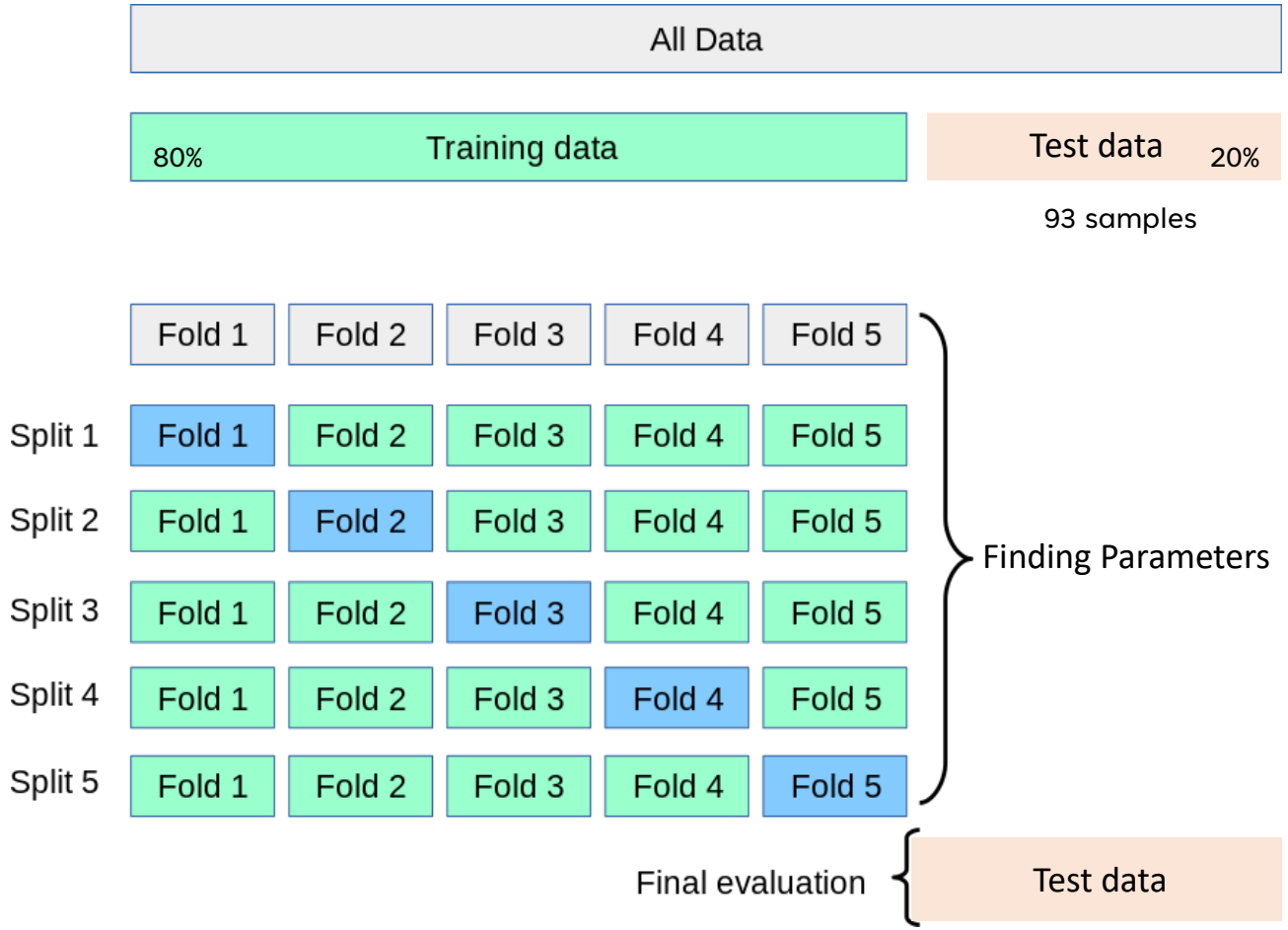
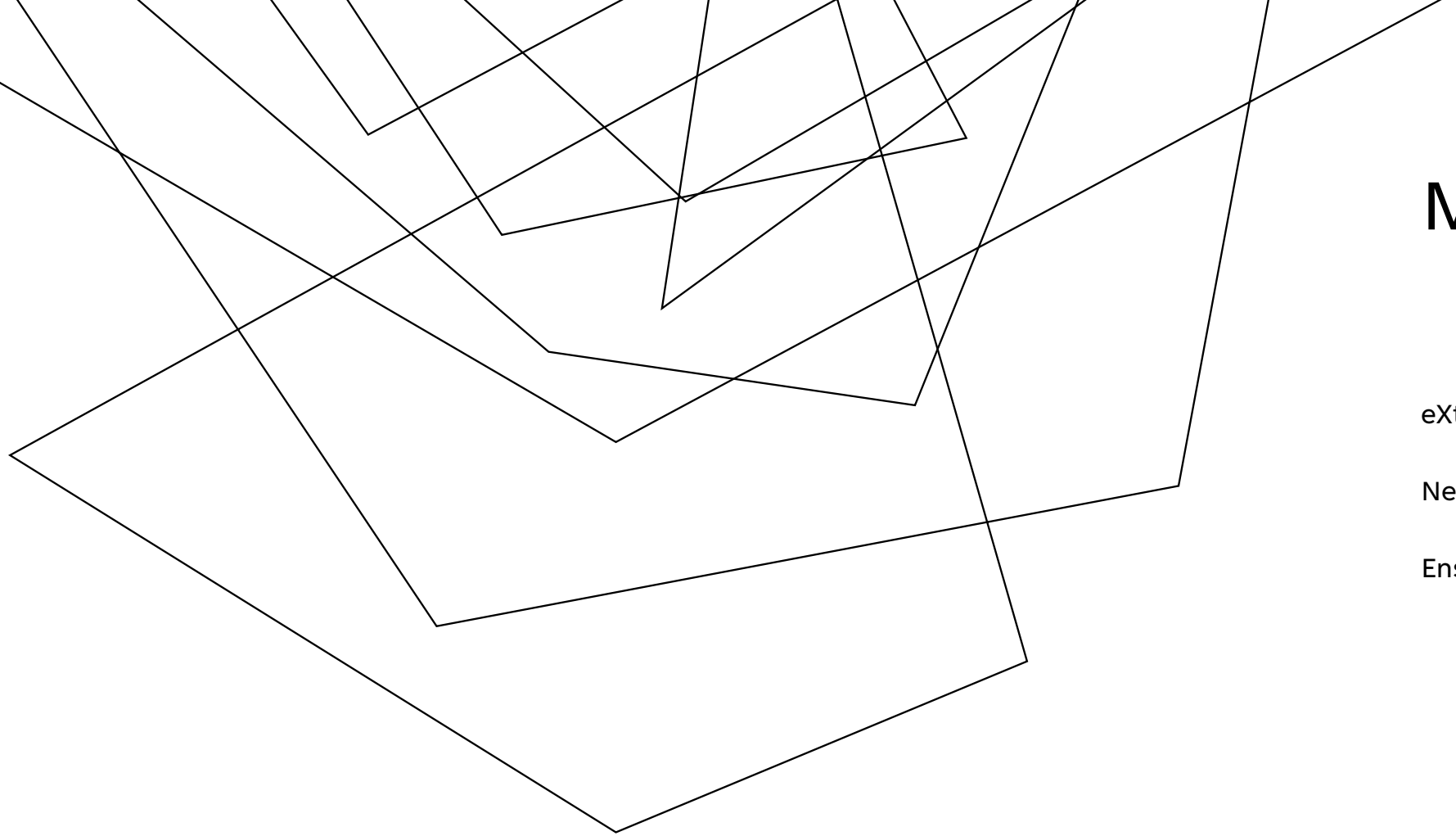


Image source: https://scikit-learn.org/stable/modules/cross_validation.html



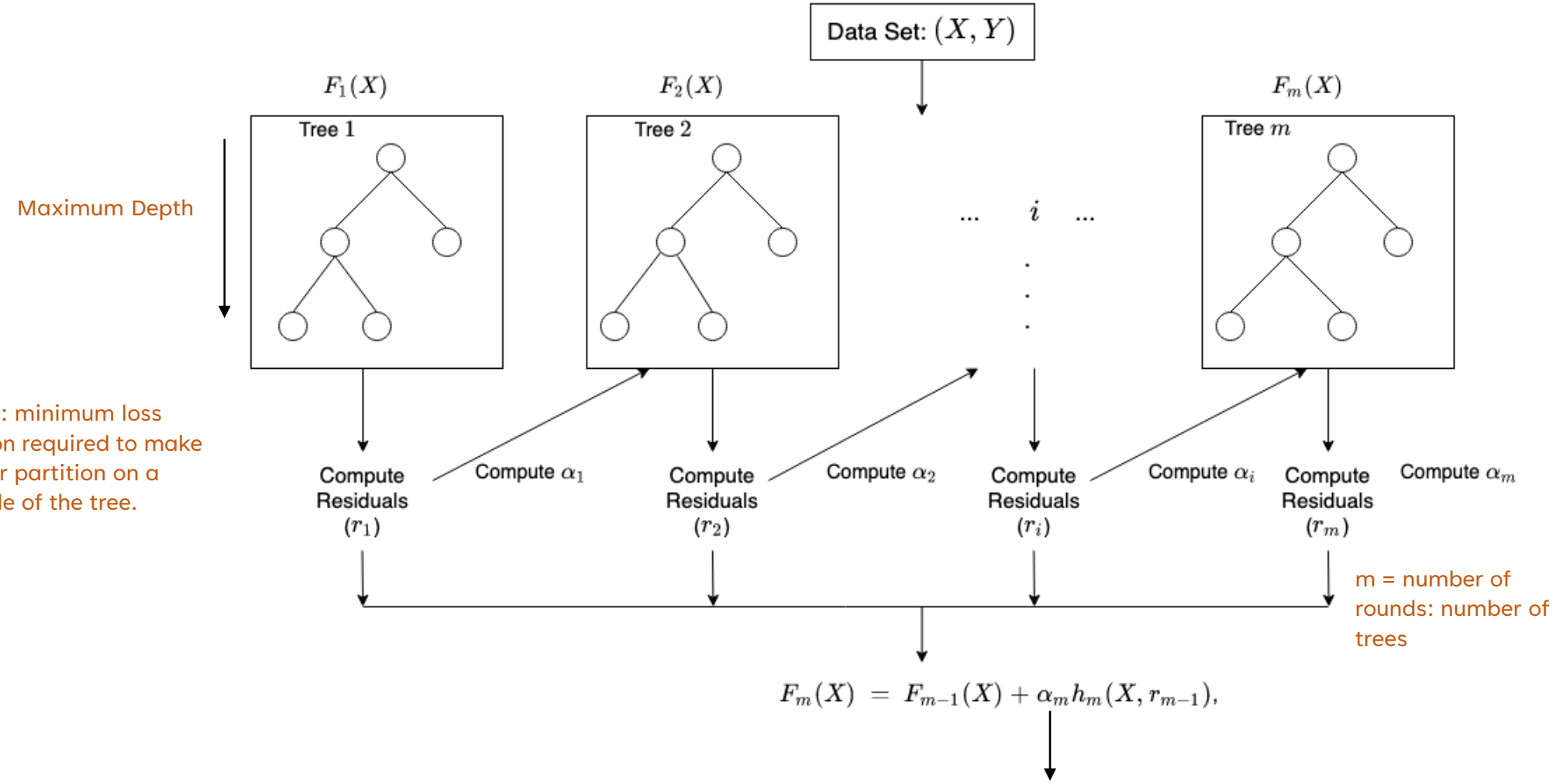
MODELS

eXtreme Gradient Boosting

Neural Network

Ensemble Model

EXTREME GRADIENT BOOSTING (XGBOOST)



Gamma: minimum loss reduction required to make a further partition on a leaf node of the tree.

m = number of rounds: number of trees

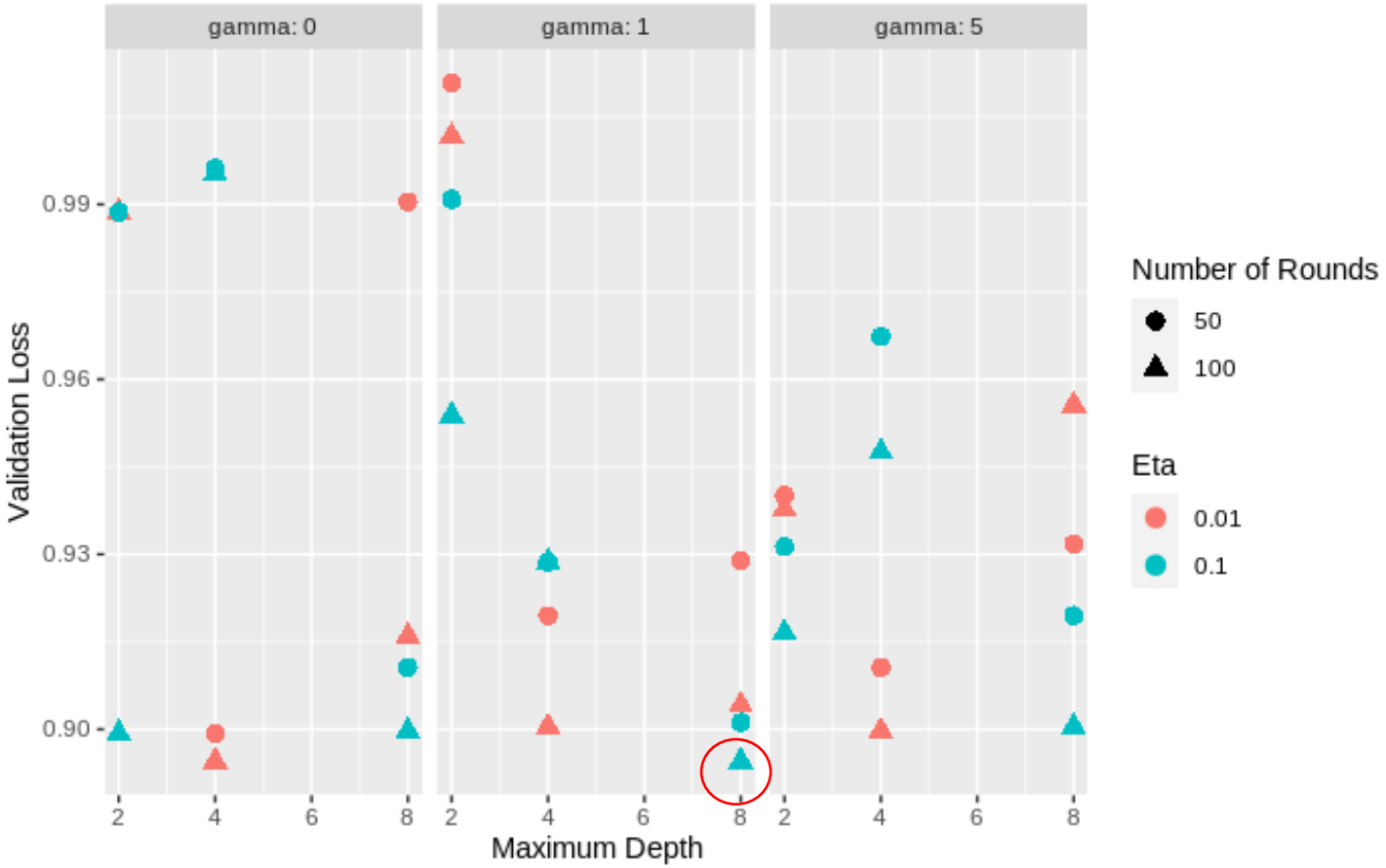
Eta: learning rate

Image source: https://docs.aws.amazon.com/sagemaker/latest/dg/xgboost-HowItWorks.html

HYPERPARAMETER TUNING

On 50 random genes

On gamma, maximum depth, eta, and number of rounds



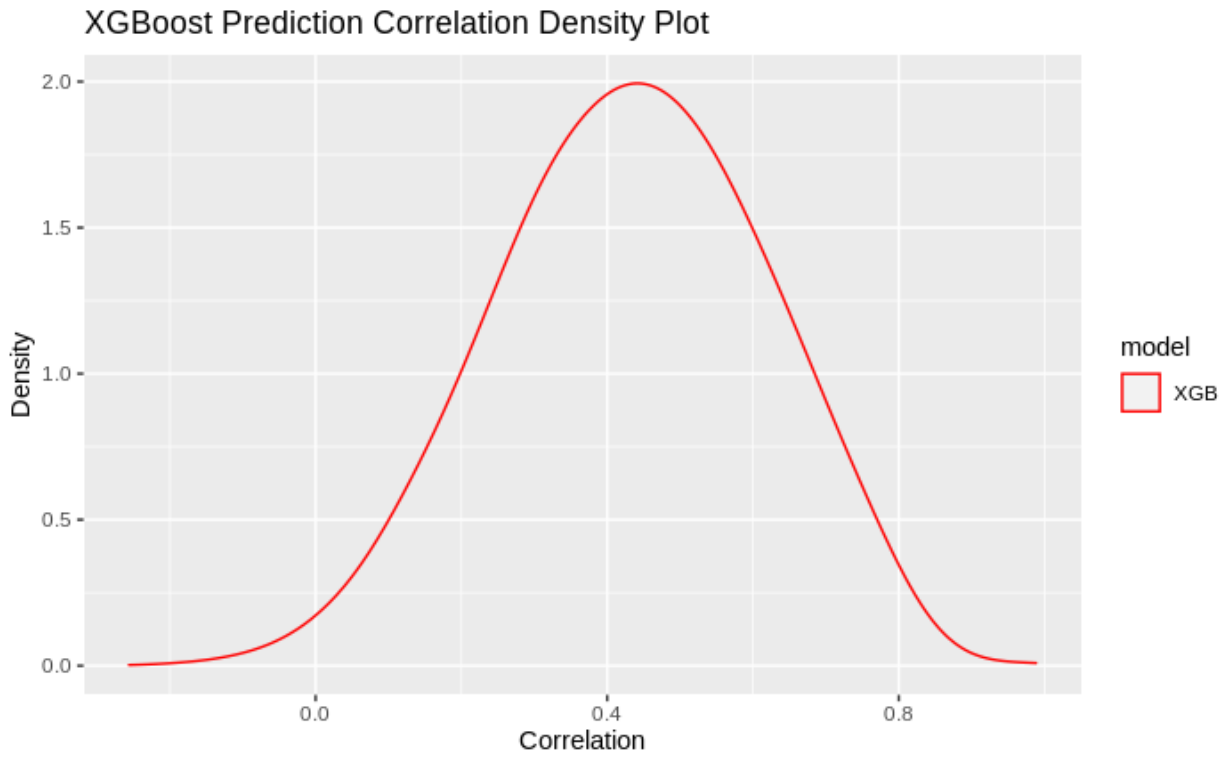
Loss Function

$$\text{MSE} = \frac{1}{n}\sum_{i=1}^{n}(y_i - \tilde{y}_i)^2$$

Best hyperparameter combination:
Gamma = 1
Maximum depth = 8
Eta = 0.1
Number of rounds = 100

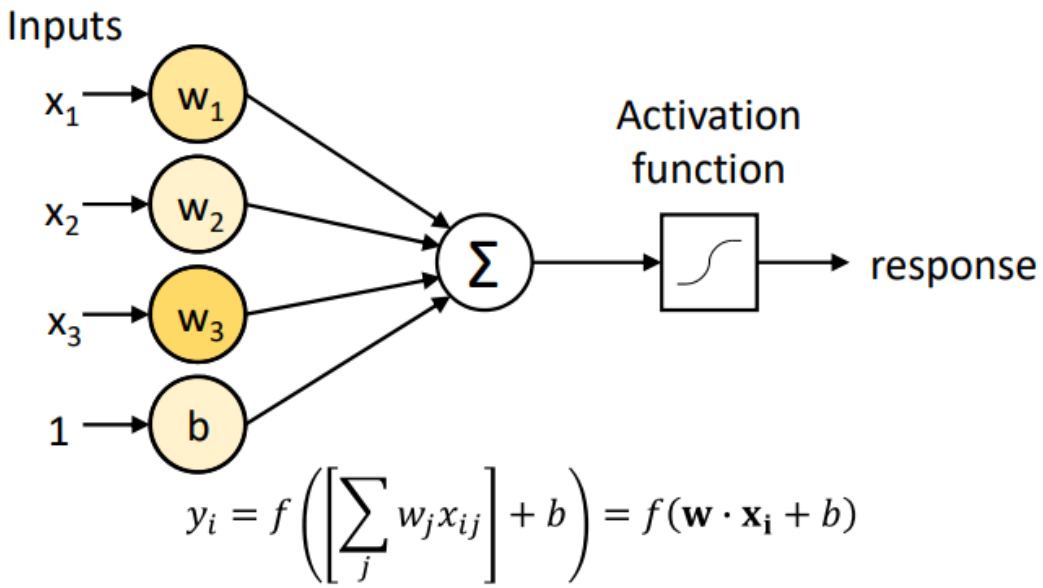
EVALUATION

Compute the correlation between each gene in the prediction and its true value



Model	Median Correlation	
	Training	Test
XGBoost	0.990975	0.4364047
Neural Network		
Ensemble		

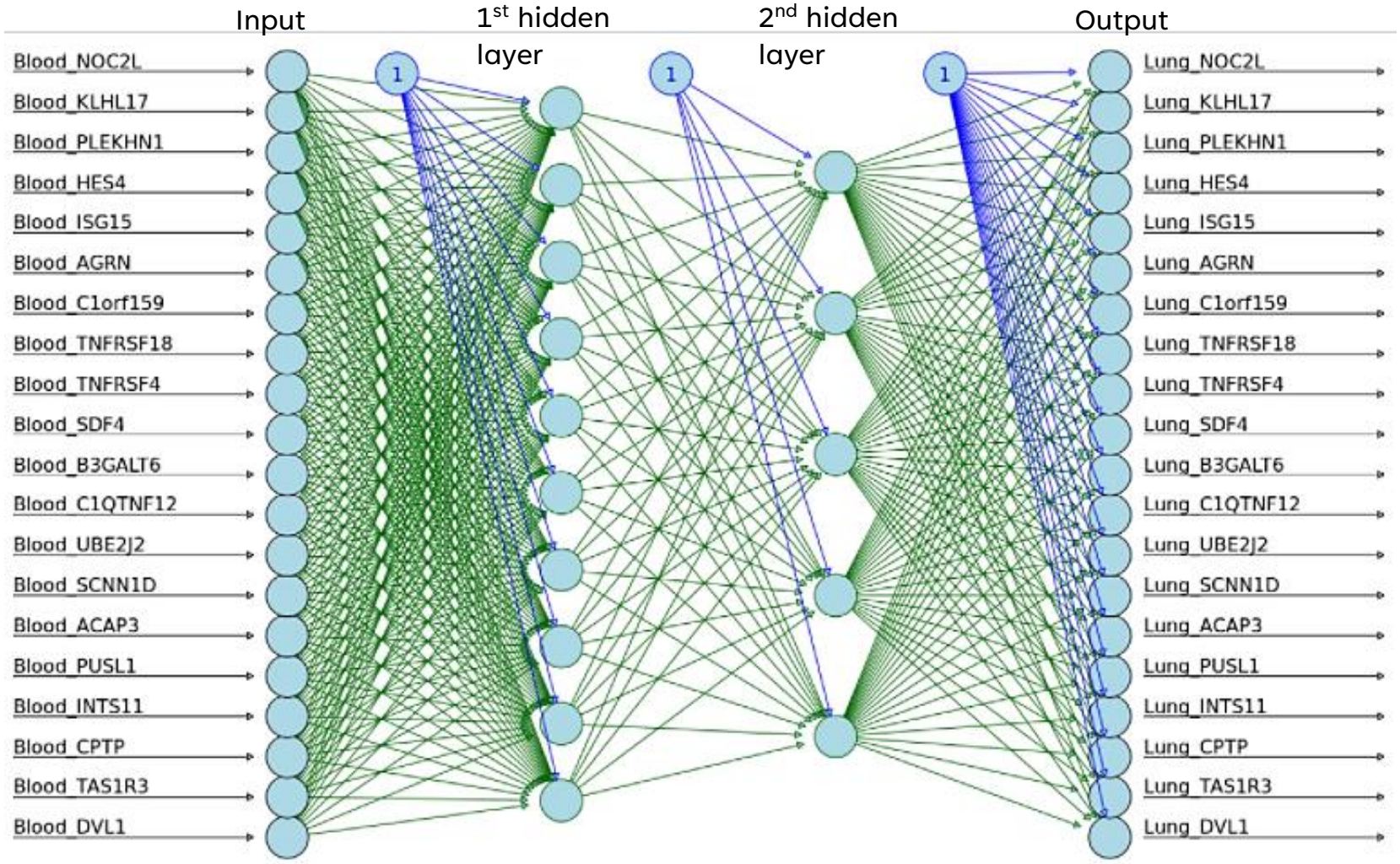
NEURAL NETWORK



$$y_i = f\left(\left[\sum_j w_j x_{ij}\right] + b\right) = f(\mathbf{w} \cdot \mathbf{x_i} + b)$$

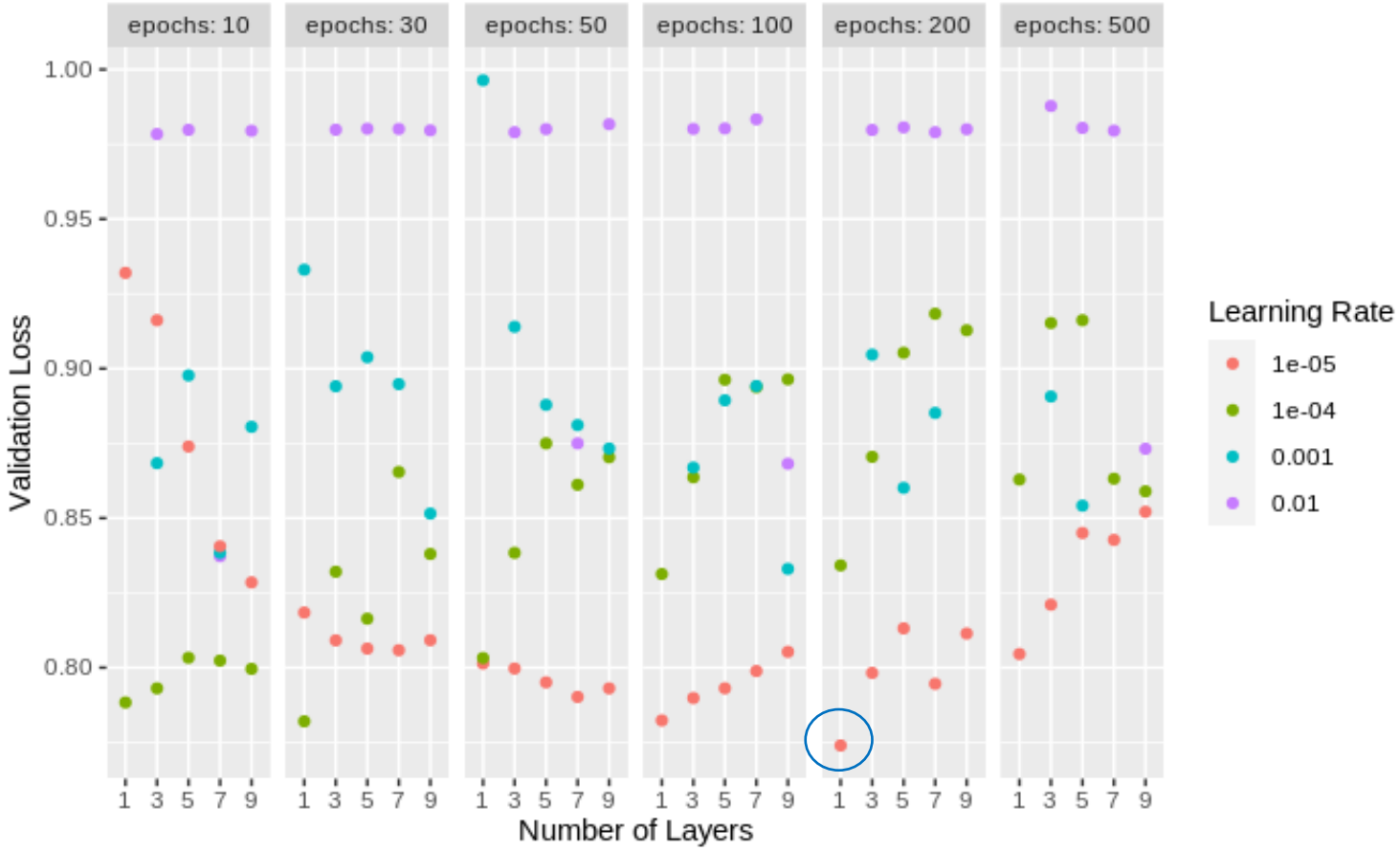
Image Source: The University of Melbourne COMP30027 Machine Learning Lecture, by Kris Ehinger

NEURAL NETWORK ILLUSTRATION



HYPERPARAMETER TUNING

On number of layers, learning rate, and number of epochs



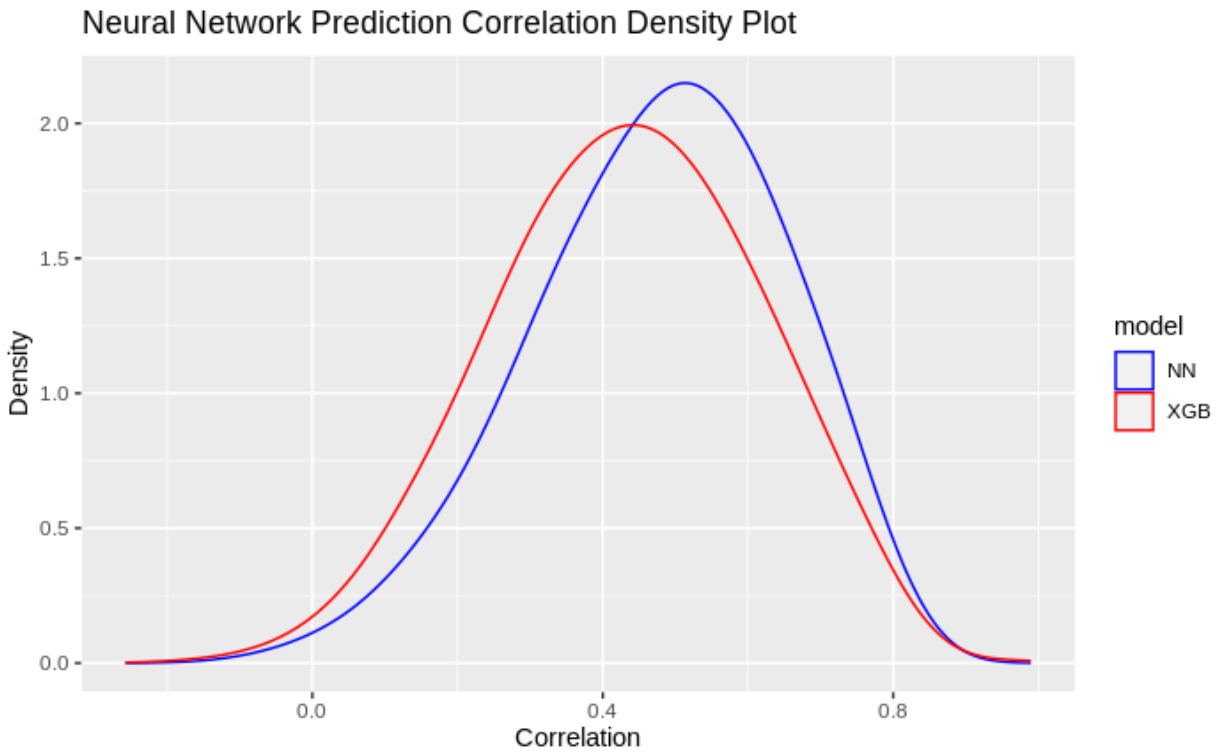
Loss Function

$$\text{MSE} = \frac{1}{n}\sum_{i=1}^{n}(y_i - \tilde{y}_i)^2$$

Best hyperparameter combination:
1 hidden layer of 100 units
Learning rate = e^{-5}
Epochs = 200

EVALUATION

Compute the correlation between each gene in the prediction and its true value



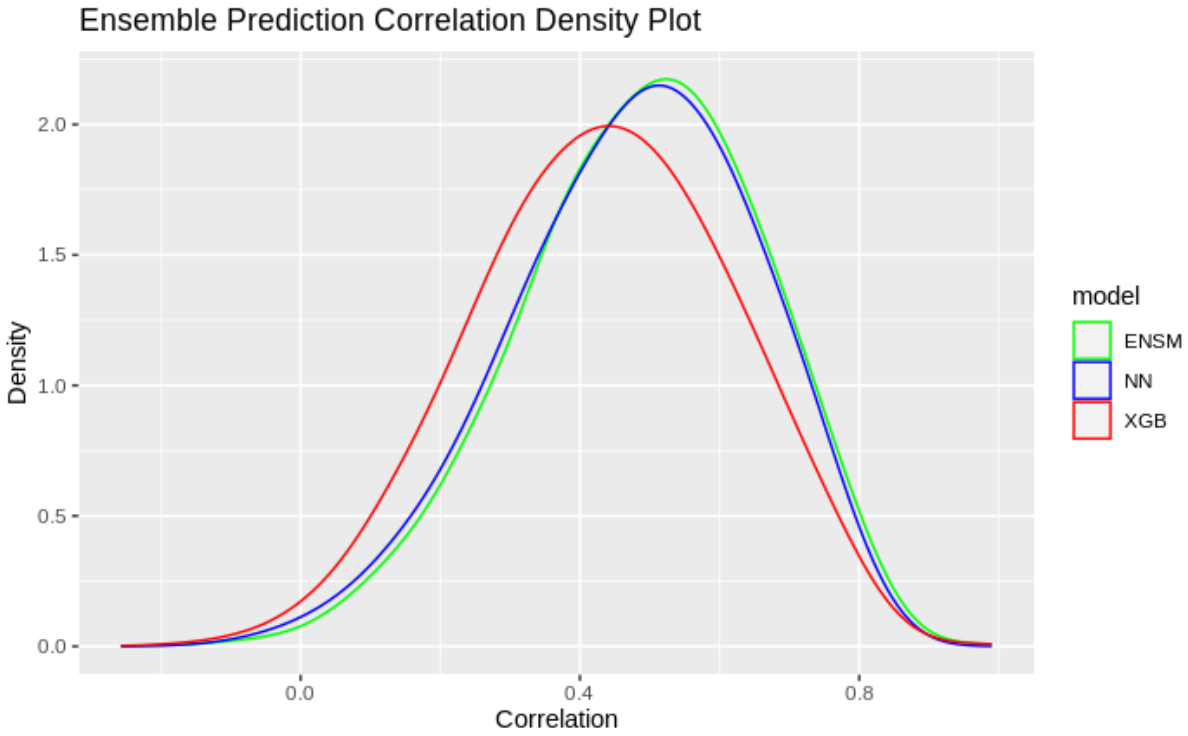
Model	Median Correlation	
	Training	Test
XGBoost	0.990975	0.4364047
Neural Network	0.6278658	0.4887672
Ensemble		

ENSEMBLE MODEL

$$ENSpred = \frac{1}{2}NNpred + \frac{1}{2}XGBpred = \frac{1}{2}\begin{bmatrix} \hat{y}_{11} & \cdots & \hat{y}_{1p} \\ \vdots & \ddots & \\ \hat{y}_{n1} & \cdots & \hat{y}_{np} \end{bmatrix} + \frac{1}{2}\begin{bmatrix} \hat{z}_{11} & \cdots & \hat{z}_{1p} \\ \vdots & \ddots & \\ \hat{z}_{n1} & \cdots & \hat{z}_{np} \end{bmatrix}$$

EVALUATION

Compute the correlation for each gene in the prediction and the true value



Model	Median Correlation	
	Training	Test
XGBoost	0.990975	0.4364047
Neural Network	0.6278658	0.4887672
Ensemble	0.9205496	0.4976427

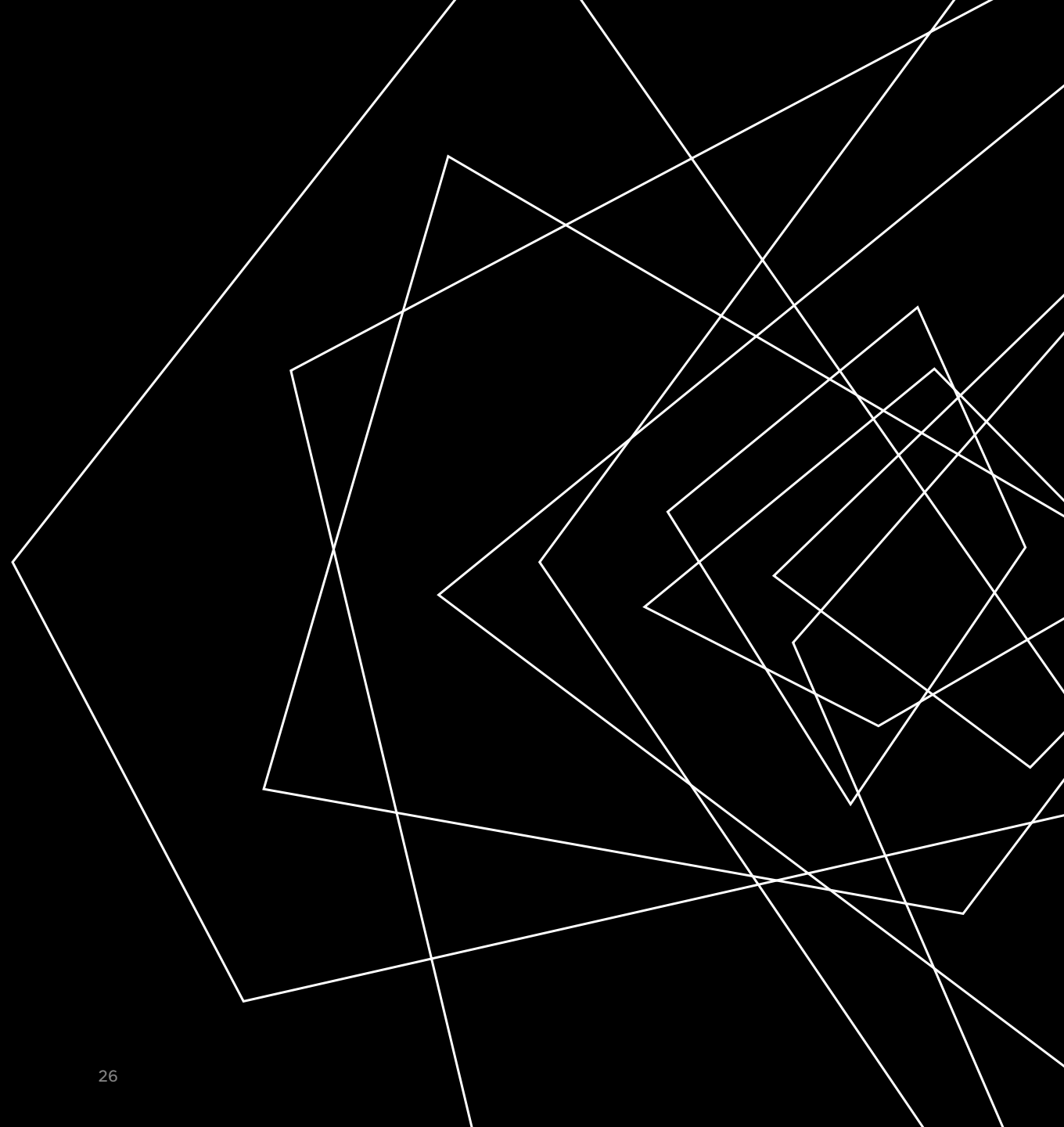
FUTURE DIRECTIONS

Training the models on all other tissues, on the entire dataset

Stacking ensemble for improved prediction

Biological validation

Implementation of the web application



WE WOULD LIKE TO EXTEND A HEARTFELT THANK YOU TO ALL OUR MENTORS INVOLVED IN THIS PROJECT!

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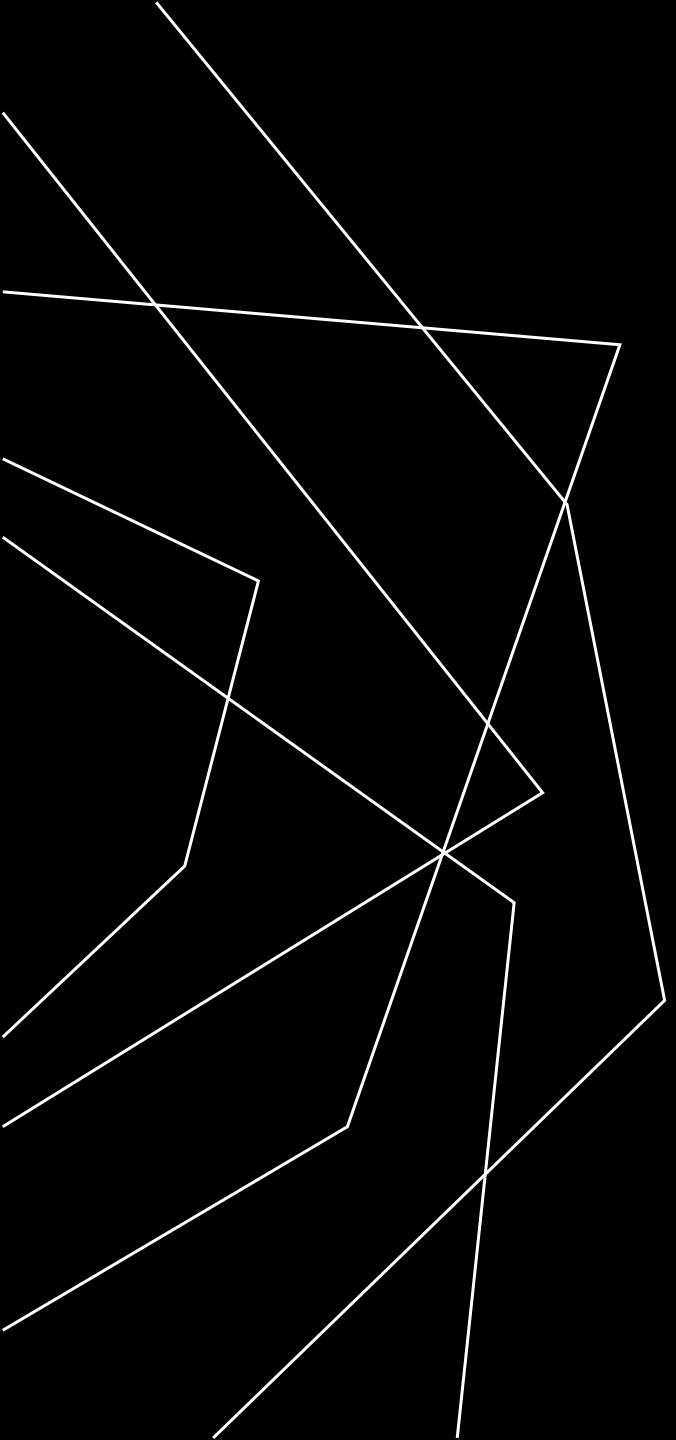

THANK YOU