Interpretable Deep Learning for Single-Cell Data Analysis

Introduction to Interpretable AI

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Why Explainable AI?

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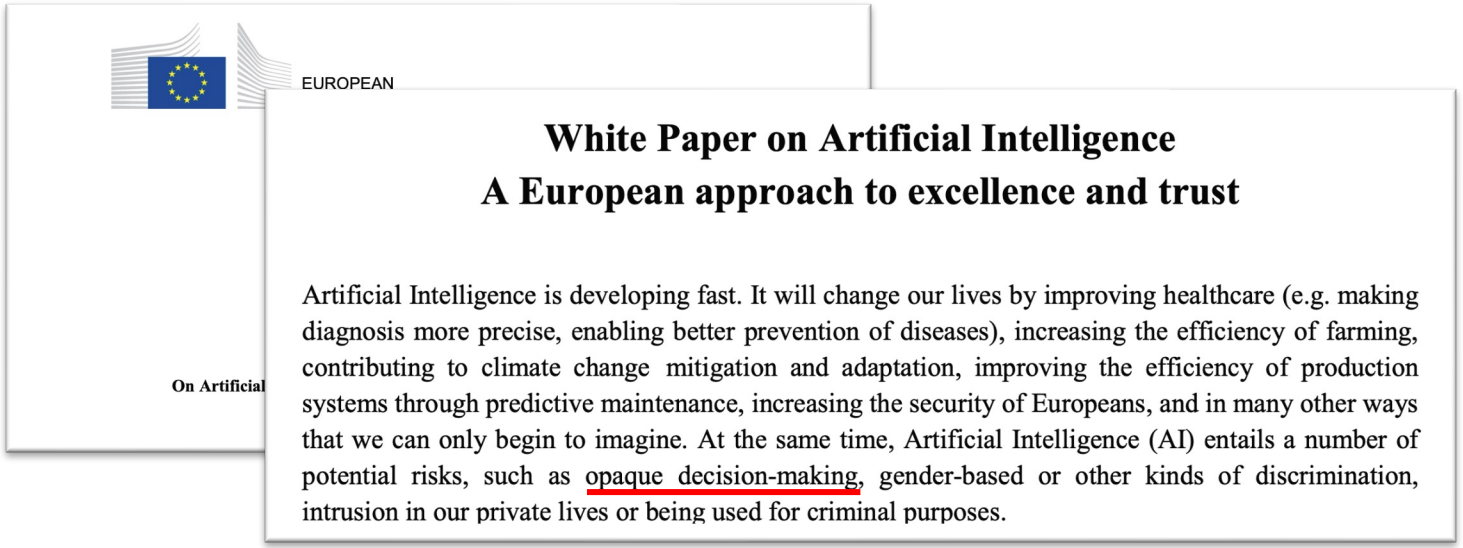
WHITE PAPER

On Artificial Intelligence - A European approach to excellence and trust

Why Explainable AI?


EUROPEAN

On Artificial

White Paper on Artificial Intelligence
A European approach to excellence and trust

Artificial Intelligence is developing fast. It will change our lives by improving healthcare (e.g. making diagnosis more precise, enabling better prevention of diseases), increasing the efficiency of farming, contributing to climate change mitigation and adaptation, improving the efficiency of production systems through predictive maintenance, increasing the security of Europeans, and in many other ways that we can only begin to imagine. At the same time, Artificial Intelligence (AI) entails a number of potential risks, such as opaque decision-making, gender-based or other kinds of discrimination, intrusion in our private lives or being used for criminal purposes.

Explainable AI Taxanomy:

Linardatos, P. et al. (2020). Explainable AI: A review of machine learning interpretability methods. *Entropy*.

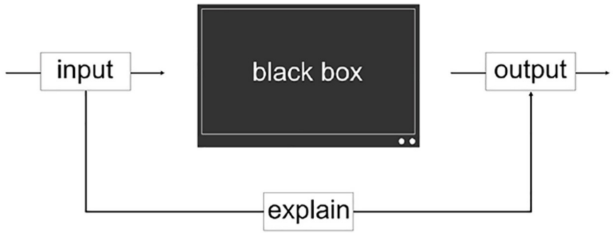
Post-hoc vs. Model-based interpretability

Treppner, M. et al. (2022) Interpretable generative deep learning: an illustration with single cell gene expression data. *Hum Gen*.

Post-hoc vs. Model-based interpretability

Post-hoc:

- Infer feature importance by approximating the non-interpretable model with simpler models



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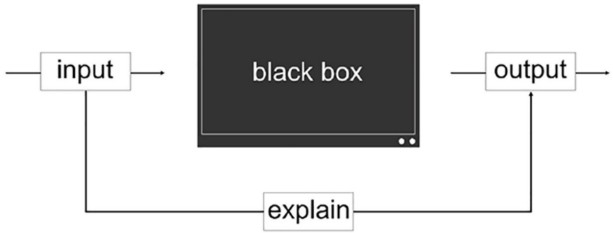

Model-based:

- Refers to models that incorporate mechanisms that allow direct interpretation of learned relationships

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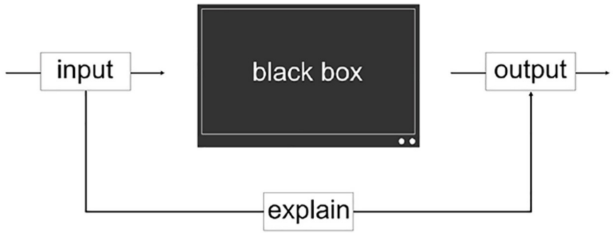

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Local explainability:

- Local interpretability relates to the determination of features that explain the predictions made for a given observational unit, e.g., a patient

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Global explainability:

- Global interpretability relates to the features (variables) that are overall important

Local explainability

Gradient-based or perturbation-based

Ancona, M. et al. (2017) Towards better understanding of gradient-based attribution methods for deep neural networks. *arXiv*.

Local explainability

Gradient-based or perturbation-based

- **Gradient-based methods** compute the attributions for all input features in a single forward and backward pass through the network

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Local explainability

Gradient-based or perturbation-based

- **Gradient-based methods** compute the attributions for all input features in a single forward and backward pass through the network

- **Perturbation-based methods** directly compute the attribution of an input feature (or set of features) by removing, masking or altering them, and running a forward pass on the new input, measuring the difference with the original output.

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Gradient-based methods – Integrated Gradients

Importance value for the ith feature:

$$\phi_i^{IG}(f, x, x') = \overbrace{(x_i - x'_i)}^{\text{Difference from baseline}} \times \underbrace{\int_{\alpha=0}^{1}}_{\text{From baseline to input...}} \overbrace{\frac{\delta f(x' + \alpha(x - x'))}{\delta x_i} d\alpha}^{\text{...accumulate local gradients}}$$

Sundararajan et al. (2017) Axiomatic attribution for deep networks. *PMLR*.

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where x is the current input, f is the model function and x' is some baseline input that is meant to represent "absence" of feature input. α is the interpolation constant.

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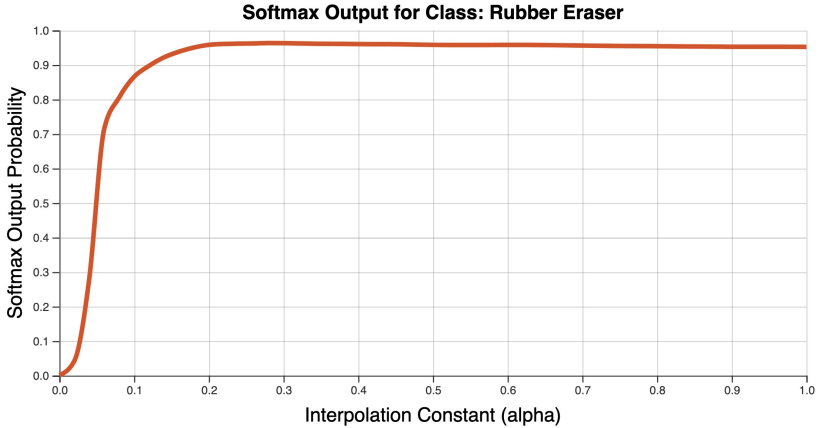
Problem with taking gradients

Saturation

Gradients of input features may have small magnitudes around a sample even if the network depends heavily on those features.

This can happen if the network function flattens after those features reach a certain magnitude.

By integrating over a path, integrated gradients avoids problems with local gradients being saturated.



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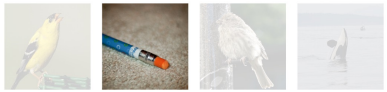

A plot of network outputs at $x' + \alpha(x - x')$. Notice that the network output saturates the correct class at small values of α. By the time $\alpha = 1$, the network output barely changes.

https://distill.pub/2020/attribution-baselines/

Global methods – Pattern extractor

Investigating the joint distribution of discretized synthetic observations

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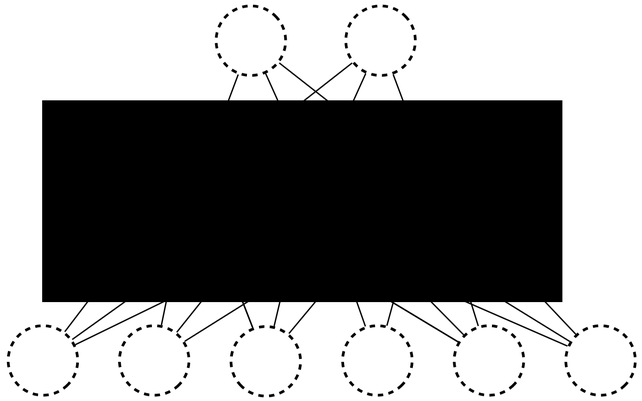

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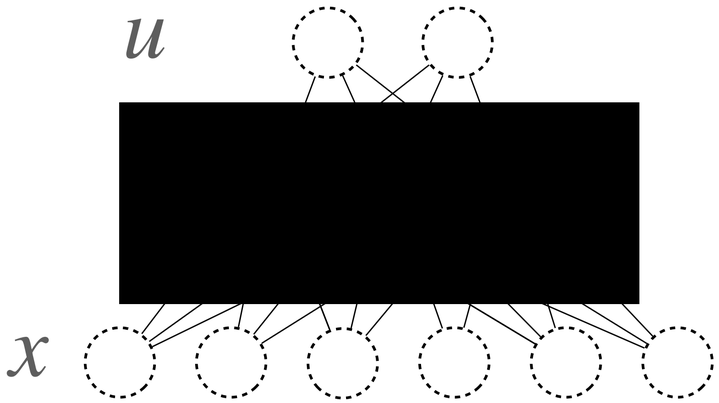

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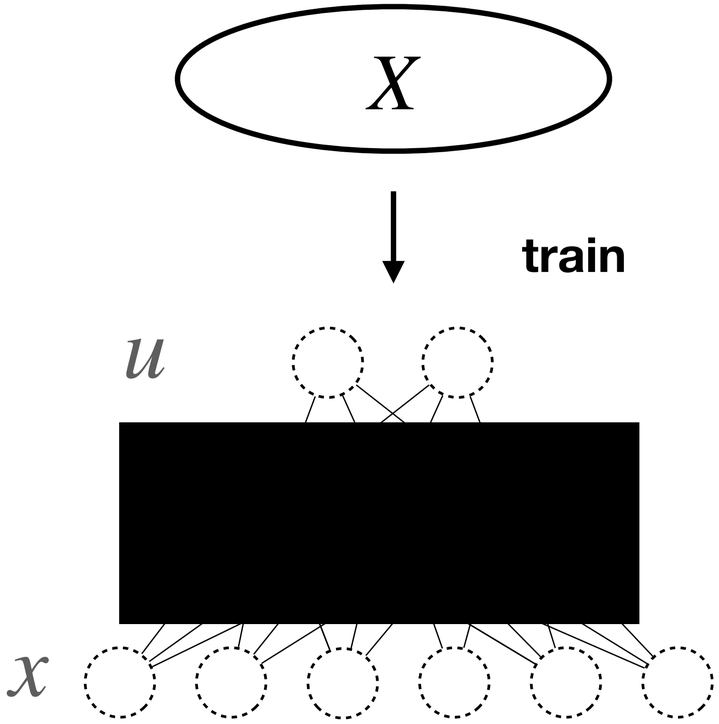

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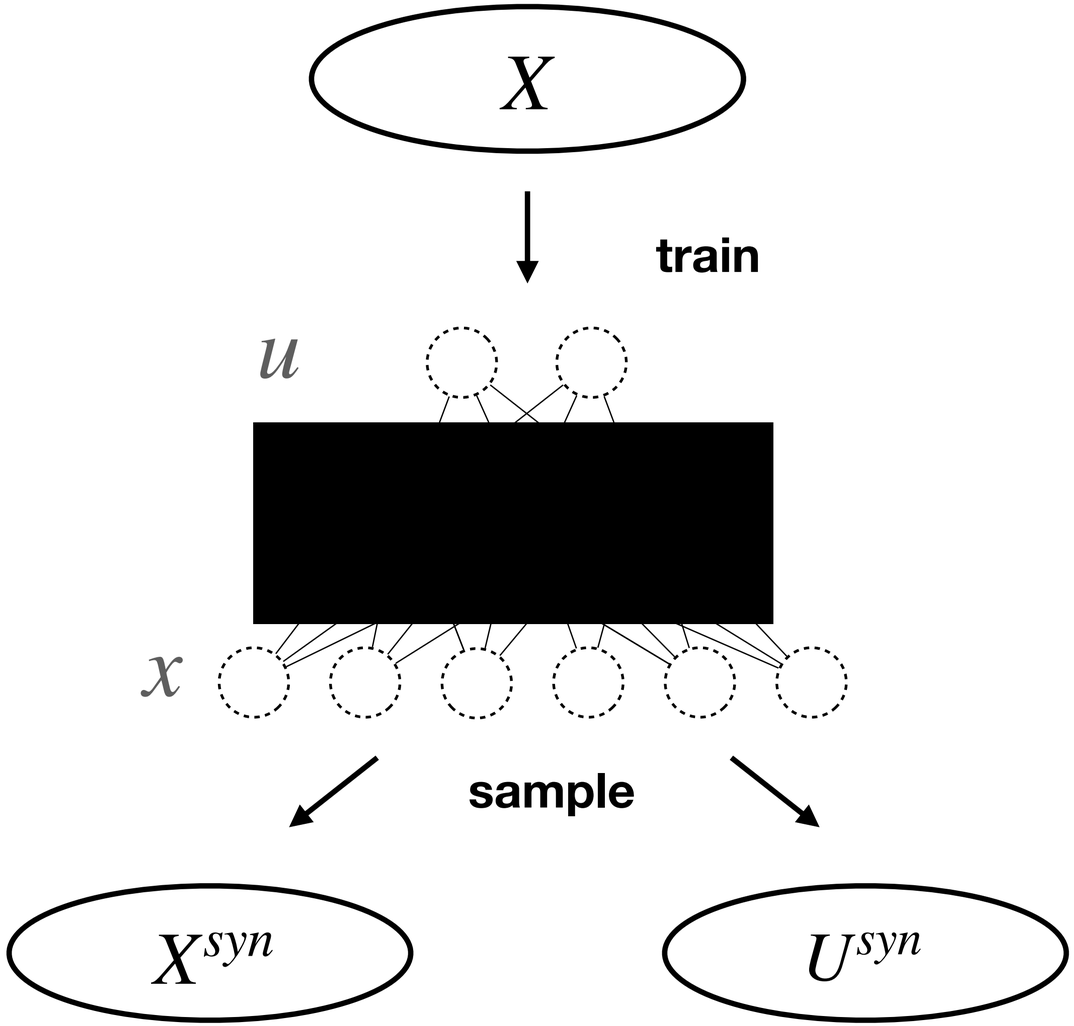

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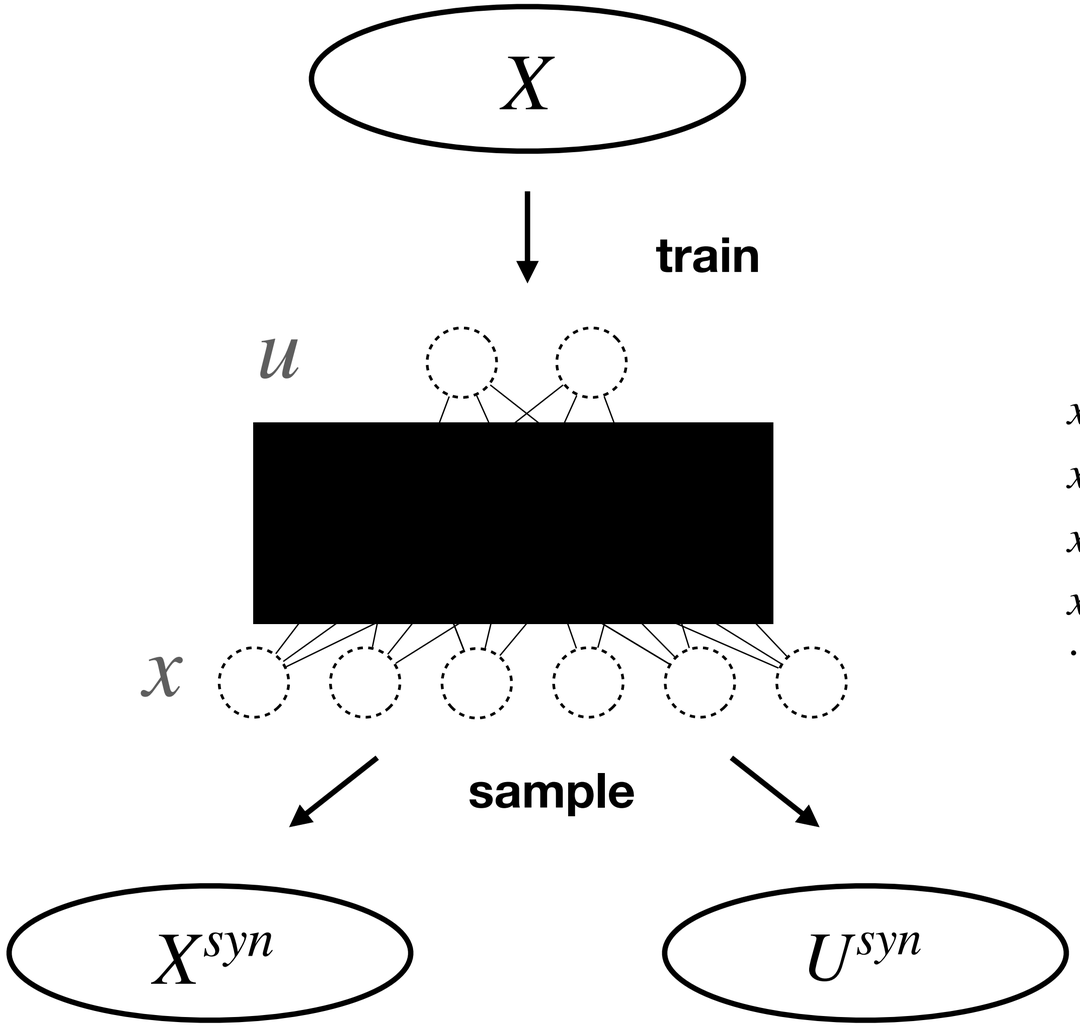

$$x^{syn}_{1.} = 12\ 32\ 4\ 5\ 13\ 5 \qquad u^{syn}_{1.} = -3.2\ 2.8$$
$$x^{syn}_{2.} = 68\ 90\ 8\ 44\ 31\ 9 \qquad u^{syn}_{2.} = -1.2\ 1.4$$
$$x^{syn}_{3.} = 6\ 5\ 78\ 12\ 24\ 36 \qquad u^{syn}_{3.} = 1.2\ -1.2$$
$$x^{syn}_{4.} = 98\ 5\ 6\ 76\ 47\ 67 \qquad u^{syn}_{4.} = 4.2\ -2.0$$
$$\cdots \qquad \cdots$$

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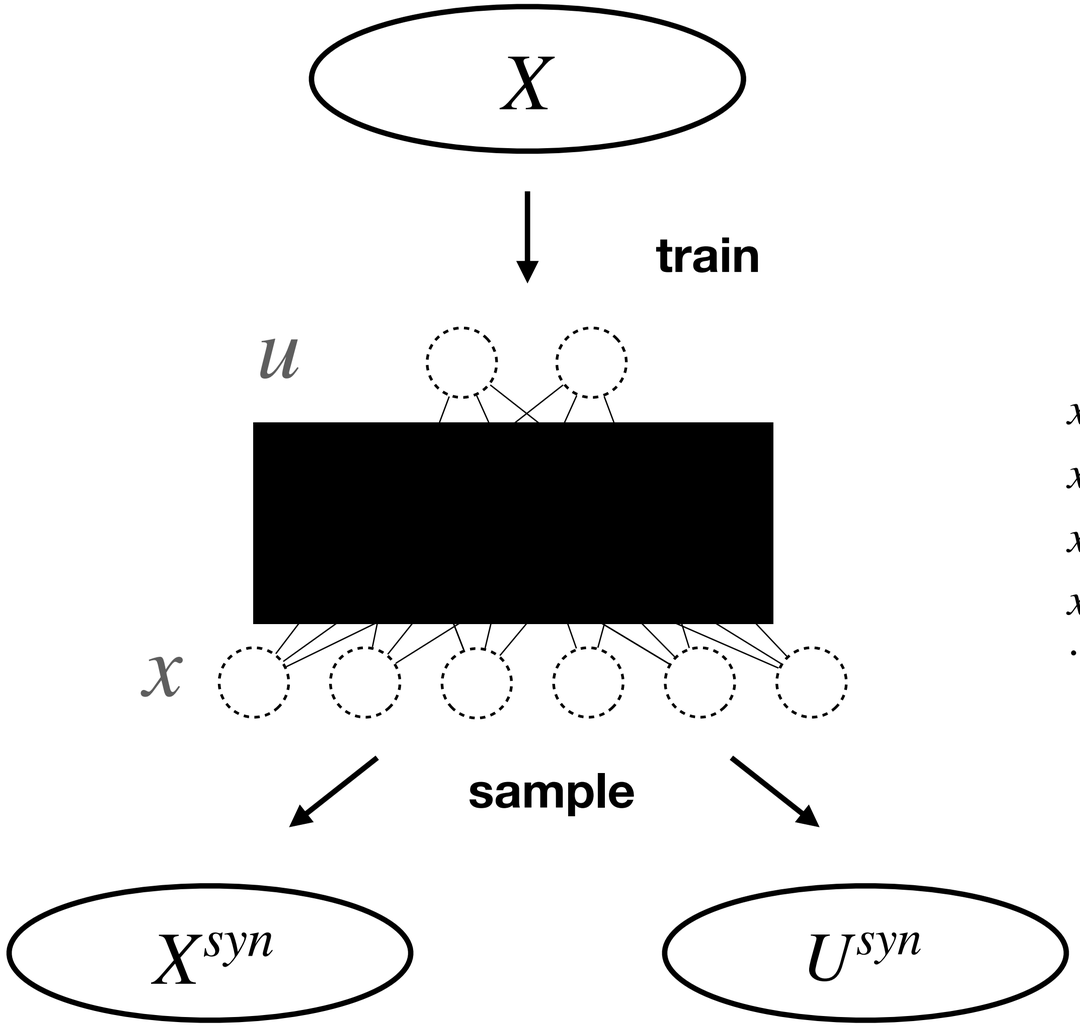

$$x^{syn}_{1.} = 0\ 1\ 0\ 0\ 1\ 0 \qquad u^{syn}_{1.} = 0\ 1$$
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$$i, j, k \in \{1,2\}$$

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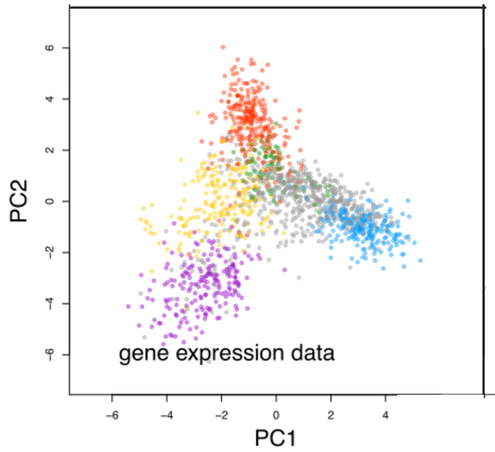
Patterns in selected genes allow to assign synthetic data to their overall most similar training example

Synthetic data matched to training data based on patterns in ...



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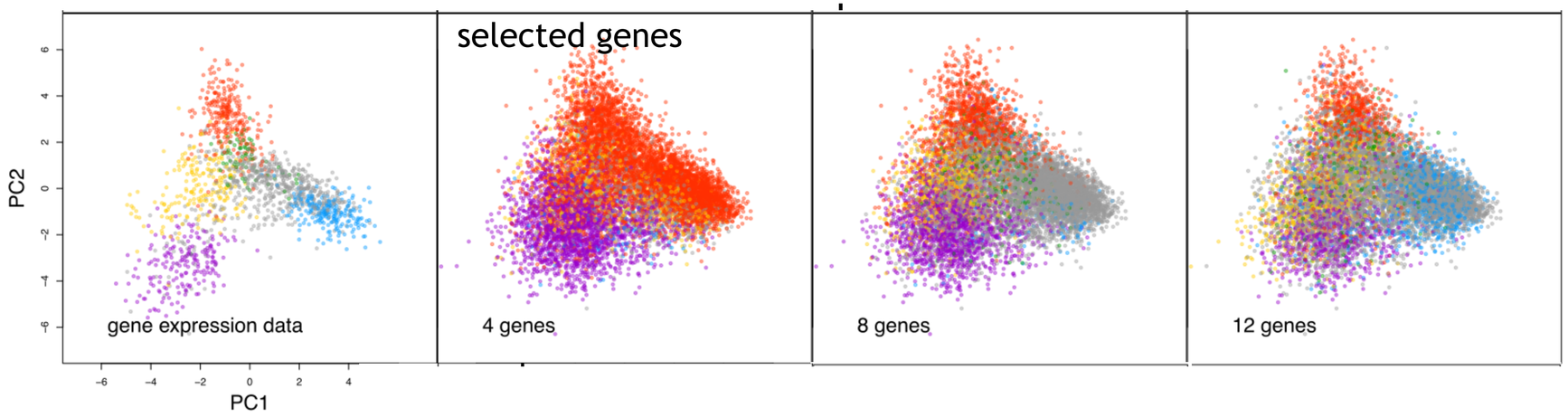

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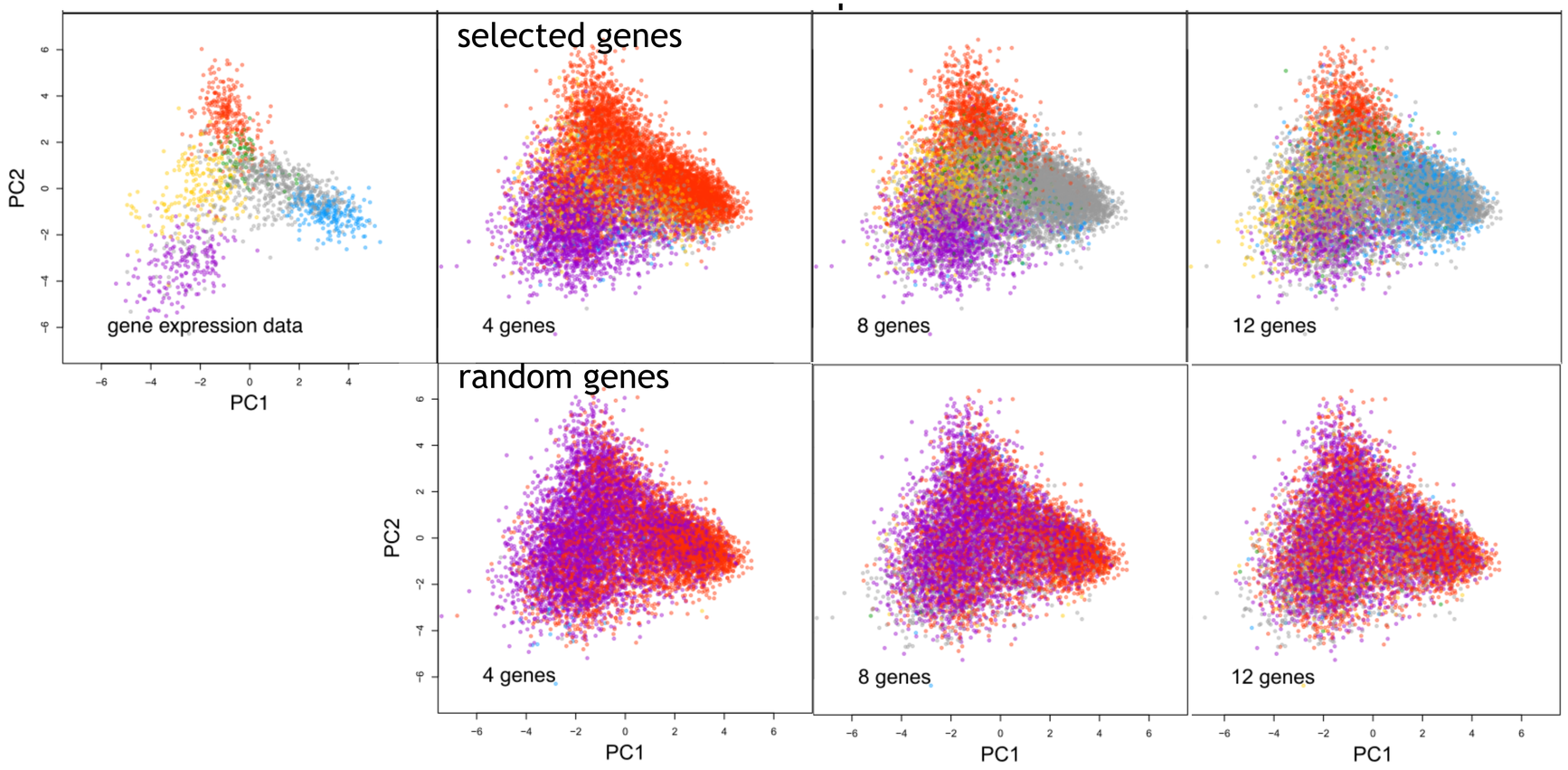

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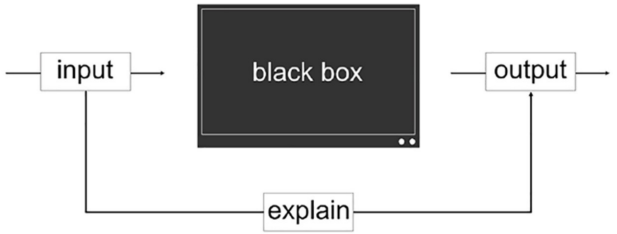

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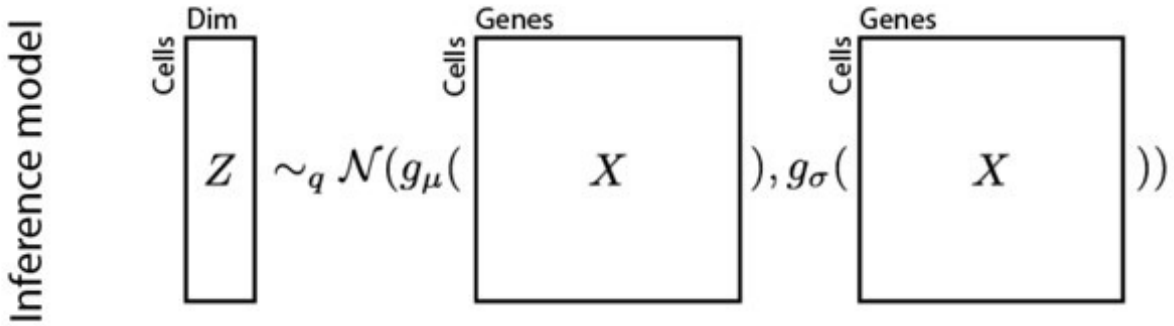
- Disentanglement strategies, deep learning approaches are modifed to enforce, e.g., linearity or monotonicity

Linearization: LDVAE

Linearly Decoded Variational Autoencoder



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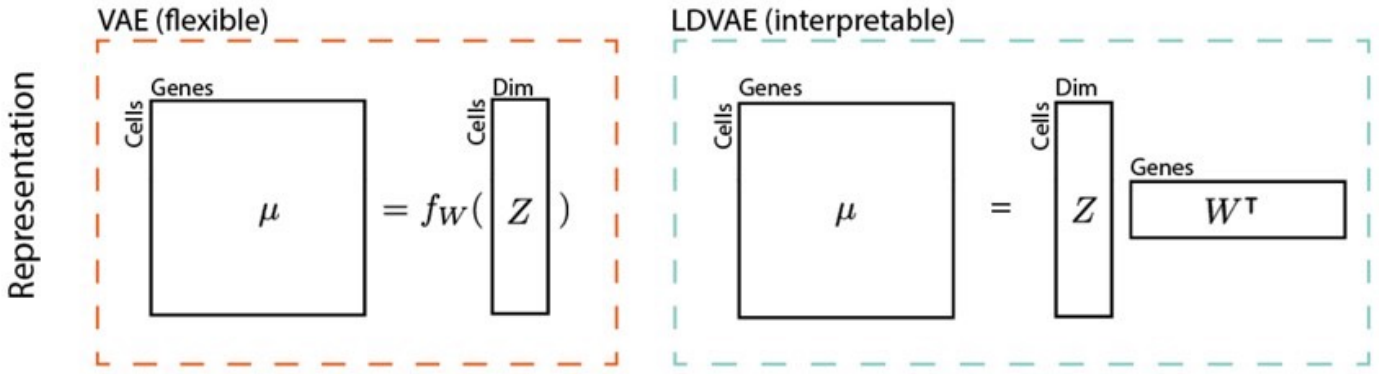

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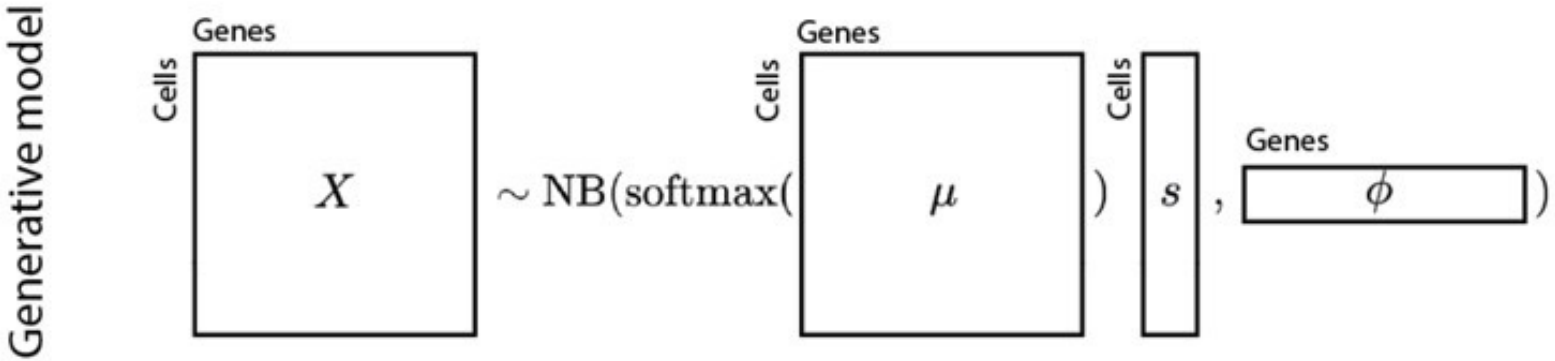

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Pros and cons – Post-hoc vs. model-based

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- Risk in post-hoc approaches is that the model, due to uncontrollable noise, focuses on artifacts
- Model-based interpretability approaches are adapted to a specific model class and thus cannot be used flexibly
- Additionally, model-based interpretability often leads to reduced predictive performance or increased reconstruction errors

Thanks to:

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DFG Deutsche Forschungsgemeinschaft

MEDIZIN INFORMATIK BIOLOGIE

NEPH GENOS

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Nice overview: https://christophm.github.io/interpretable-ml-book/index.html

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