CoDON: a learning framework for linking genomics and transcriptomics data to protein expression

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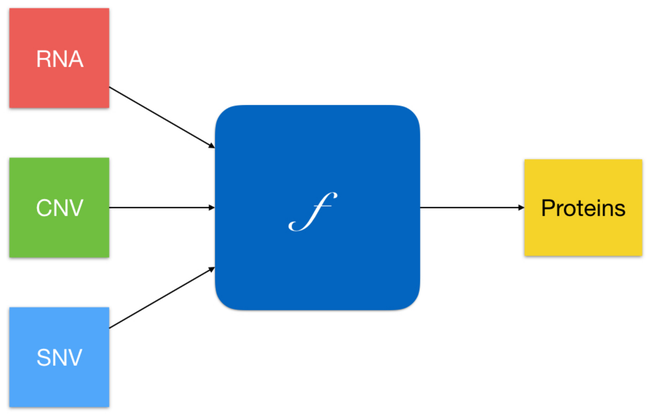
Outline

Motivation

- **Explain** the **protein expression profiles** through the integration of genomic and transcriptomic data
- **Link different data types** in the context of **complex diseases**
- Wide range of applications (e.g.: multi-omics perturbation analysis)

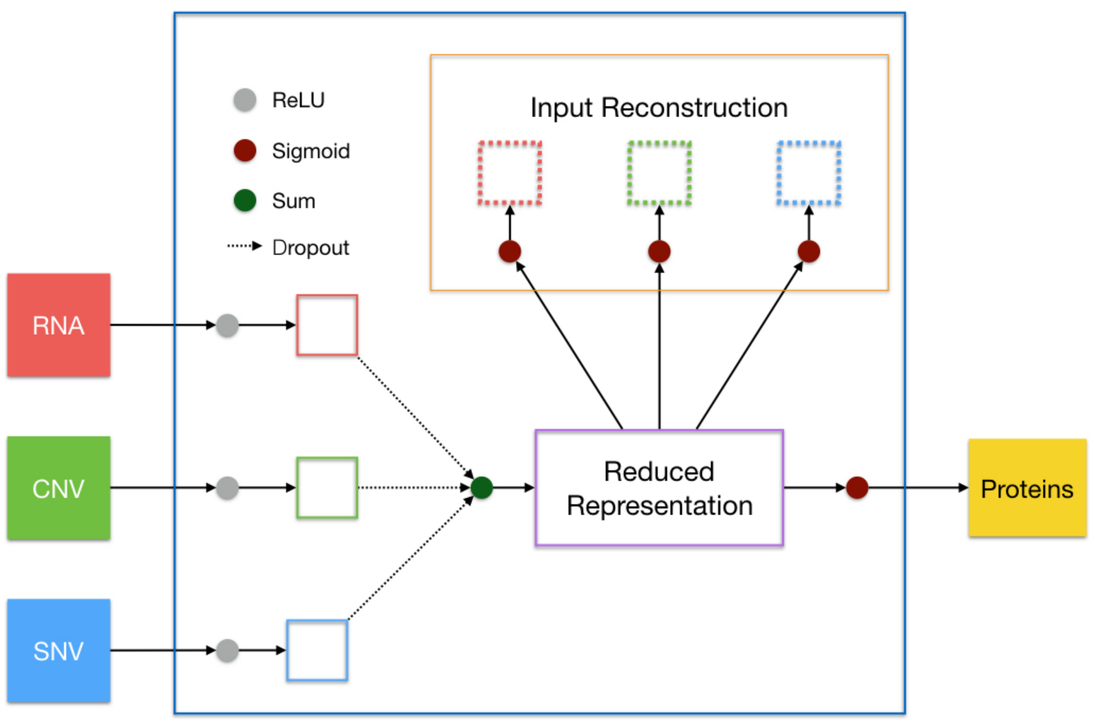


Aims

- **Reconstruct proteins profiles** from different data layers using a **common learning framework**
- **Understand** how different omic datasets can be combined in a **common reduced representation**
- **Decipher** highly **non-linear molecular interactions**

Model

Learning Architecture



CoDON is based on a **neural network architecture**.
A **joint training procedure** is performed, where a lower dimensional representation is built and used to **infer proteomic profiles**, while optimizing the reconstruction on the genomic and transcriptomic level.

Main features:

- Shallow architecture allows to **use weights to analyze complex molecular interactions** within and between different data levels
- **Reconstructing the input datasets** improves the common reduced representation and the reconstruction of the protein profiles[1]
- **Dropout regularization**[1] in merging of the input activation units is used to avoid overfitting

Learning Algorithm

$$\min_{w} \sum_{t \in \mathcal{T}} \|X_t - \mathcal{F}_t(w, X_{RNA}, X_{CNV}, X_{SNV})\|_{L^2}$$

$$\mathcal{T} = \{RNA,\ CNV,\ SNV,\ proteins\}$$

$\mathcal{F}_t(w, X_{RNA}, X_{CNV}, X_{SNV})$ is the non-linear transformation for the reconstruction of dataset t using the learned weights and the input data.

Batch optimization performed using Adam[2] with a fixed learning rate.

Preliminary Results

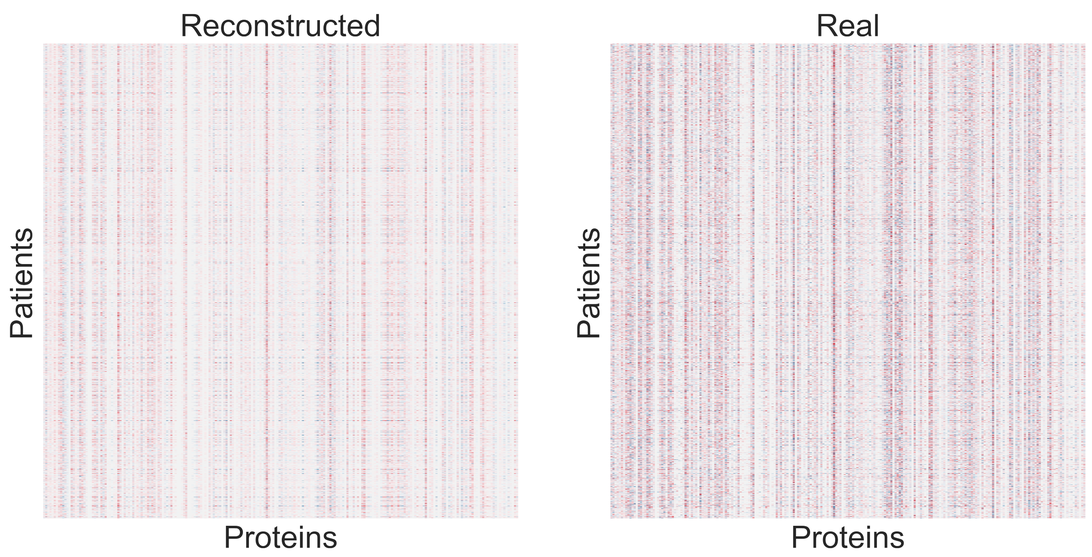
Data

The results were obtained using public data from TCGA[3] for different cancer types:

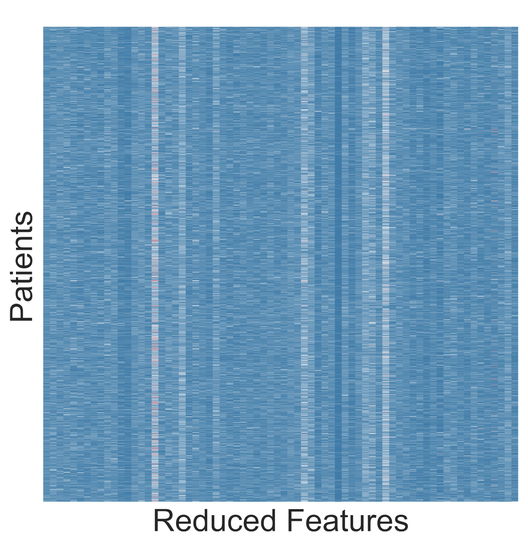
- **RNA-Seq** Version 2 data processed with RSEM[4]
- Gene-wise **CNV** data processed with GISTIC2.0[5]
- Mutation data processed to obtain gene-wise count of **SNV**
- **RPPA** proteins expression data annotated with genes

Patients and genes sets given by the intersection of available datasets were considered (4609 patients and 224 genes).

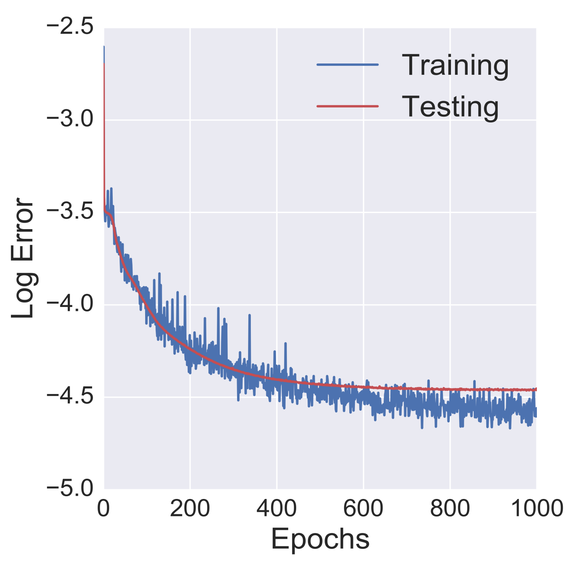
Proteins Profiles Reconstruction



Reduced Representation



Learning Diagnostic



References

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Acknowledgments

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