CSI5180. Machine Learning for Bioinformatics Applications

Fundamentals of Machine Learning — Feature Engineering and Data Imputation

by

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Preamble

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Fundamentals of Machine Learning — Feature Engineering and Data Imputation

This lecture is all about the data. How the amount of data might affect the outcome of the project. How to encode the various data types encountered in bioinformatics. How to scale the data. Finally, how to handle situations where some values are missing.

General objective :

- **Describe** the fundamental concepts of machine learning

Learning objectives

- **Describe** the different ways to encode data, distinguishing the case of ordinal and categorical data.
- **Compare** the different ways to scale numerical values.
- **Explain** the approaches to handle missing values.

Reading:

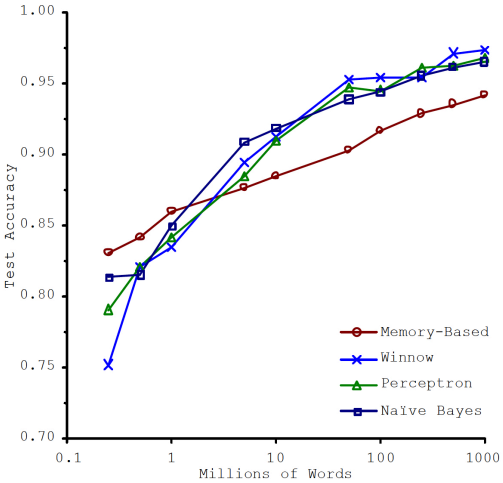
- Ernst, J. & Kellis, M. Large-scale imputation of epigenomic datasets for systematic annotation of diverse human tissues. *Nat Biotechnol* 33, 364376 (2015).
- Durham, T. J., Libbrecht, M. W., Howbert, J. J., Bilmes, J. & Noble, W. S. PREDICTD PaRallel Epigenomics Data Imputation with Cloud-based Tensor Decomposition. *Nature Communications* 9, (2018).

Plan

Data

Size does matter

- **"However, these results suggest that we may want to reconsider the trade-off between spending time and money on algorithm development versus spending it on corpus development algorithms themselves."**
- Banko, M. & Brill, E. Scaling to very very large corpora for natural language disambiguation. Association for Computational Linguistics, 2001.



The Unreasonable Effectiveness of Data

- Halevy, A., Norvig, P. & Pereira, F. The Unreasonable Effectiveness of Data. *IEEE Intelligent Systems* **24**, 812 (2009).
- `https://youtu.be/yvDCzhbjYWs` (01:02:56)

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- **Poor quality**: some experimental methods produce a high number of false positive (protein-protein interactions, ChIP-Seq, etc.).
- A large number of **irrelevant** features might confuse the learning algorithms.

Encoding

Feature Engineering

1. Get **enough** data
2. Extract **features** from the raw data
   - **Labour** intensive
   - Requires **creativity**
   - **Domain knowledge** is a plus!

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- The latter is called **one-hot encoding** and it should be preferred for **categorical** data.
- This increases the dimensionality of the feature vectors.
- The other encodings are introducing a **bias**. With the first two encodings, we are saying that **A** and **C** are somewhat similar, but **A** and **T** are not!

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- Compare **one-hot** and *l*-**words**.

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- From **assignment 1**, we have seen that sequences can be represented by *l*-**words** (grams) frequency vectors.
- Compare **one-hot** and *l*-**words**.
- Later in the semester, we will consider an additional encoding called **embedding**.

sklearn.preprocessing.OneHotEncoder

```
from numpy import array
from sklearn.preprocessing import OneHotEncoder

data = ['T','T','C','T','G','G','C','A','C','T','T','G']

values = array(data)
values = values.reshape(len(values),1)

onehot_encoder = OneHotEncoder()
onehot_encoder.fit(values)

values_encoded = onehot_encoder.transform(values)

print(values_encoded.toarray())
```

- **Save the encoding** and use on your validation set, test set, and production!

keras.utils.to_categorical

```
import numpy as np
from sklearn.preprocessing import LabelEncoder
from keras.utils import to_categorical

data = ['T','T','C','T','G','G','C','A','C','T','T','G']

values = array(data)
values = values.reshape(len(values),1)

label_encoder = LabelEncoder()
integer_encoded = label_encoder.fit_transform(values)

data_encoded = to_categorical(integer_encoded)

print(data_encoded)
```

pandas.get_dummies

```
import pandas as pd

data = list('TTCTGGCACTTGGTTGTTCT')

onehot_encoded = pd.get_dummies(pd.Series(data))

print(onehot_encoded)
```

```
   A  C  G  T
0  0  0  0  1
1  0  0  0  1
2  0  1  0  0
3  0  0  0  1
4  0  0  1  0
5  0  0  1  0
...
```

Feature engineering - ordinal

- **Categorical** data should not be encoded with ordered numbers.
- **Ordinal** data can be encoded with **ordered numbers**.
  - **Resolution:** Poor = 1, Average = 2, Good = 3, Excellent = 4

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  1 to 20 = **n-terminal**, -1 to -20 = **c-terminal**, otherwise = **core**.
- **Pros:** might allow the algorithm to learn using less training examples.
- **Cons:** could require domain expertise to create meaningful categories might fail to generalize, perhaps **n-terminal** should have been defined as 1 to 21, 1 to 22, etc.

Scaling

Normalization

- Many learning algorithms work best if the numerical values of the features have **similar range of values**, say [-1,1] or [0,1].
  - Namely, the optimization (say gradient descent) may converge more rapidly.

Normalization:

$$\frac{x_i^{(j)} - \min^{(j)}}{\max^{(j)} - \min^{(j)}}$$

See: sklearn.preprocessing.MinMaxScaler

Standardization (or z-score normalization)

With **standardization**, each feature has a **normal distribution**, with $\mu = 0$ and $\sigma = 1$.

$$\frac{x_i^{(j)} - \mu^{(j)}}{\sigma^{(j)}}$$

- Note that the range of values is not bounded!

See: sklearn.preprocessing.StandardScaler

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  - Else, use **normalization**

Pipeline

Recall

As discussed in **Essential Bioinformatics skills**, write scripts for everything!

- It **documents** your project
- This allows to **redo** the work
- With time, you will be building a reusable library of functions for your specific domain
- As **new data** become available, you will be able to retrain your learning algorithm

sklearn.pipeline.Pipeline

```
from sklearn.pipeline import Pipeline
from sklearn.preprocessing import StandardScaler

num_pipeline = Pipeline([
        ('imputer', SimpleImputer(strategy="median")),
        ('attribs_adder', CombinedAttributesAdder()),
        ('std_scaler', StandardScaler()),
        ])

training_num_tr = num_pipeline.fit_transform(training_num)

full_pipeline = ColumnTransformer([
        ("num", num_pipeline, num_attribs),
        ("cat", OneHotEncoder(), ["sequence"]),
    ])

training_prepared = full_pipeline.fit_transform(training)
```

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  - A related technique consists of replacing the missing values by the **most frequent value** for that feature, with the same drawback as above.

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    - Here, you are hoping that the **learning algorithm** will **learn how to handle** missing values.

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    - Say [0.25, 0.25, 0.25, 0.25] where you would have used [1, 0, 0, 0] for A, [0, 1, 0, 0] for C, [0, 0, 1, 0] for G, [0, 0, 0, 1] for T.

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  - The **hope** is that those intermediate values will not affect too negatively the results.
- In all the cases, you **cannot know in advance** which method works best, you will have compare several methods and use the one that works best.

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    - Let $\hat{x}_i$ be a new example, $[x_i^{(1)}, x_i^{(2)}, x_i^{(j-1)}, x_i^{(j+1)}, \ldots, x_i^{(D)}]$ and $\hat{y}_i = x_i^j$.

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    - Use all the examples x_i for which x_i^j is **not** missing as **training set**.

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    - Does this sound **familiar** to you?
    - Indeed, this can be seen as a **supervised learning** problem.
    - Let $\hat{x}_i$ be a new example, $[x_i^{(1)}, x_i^{(2)}, x_i^{(j-1)}, x_i^{(j+1)}, \ldots, x_i^{(D)}]$ and $\hat{y}_i = x_i^j$.
    - Use all the examples x_i for which x_i^j is **not** missing as **training set**.
    - Train a classifier, which you will use the predict (impute) the missing values.

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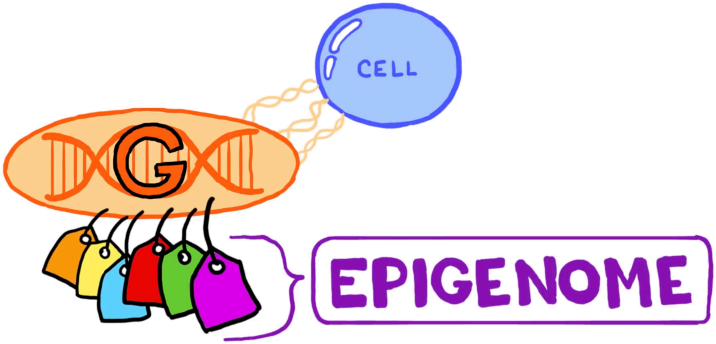
    - **However**, these approaches are cost intensive (labour, CPU time, memory, etc.).

Case study

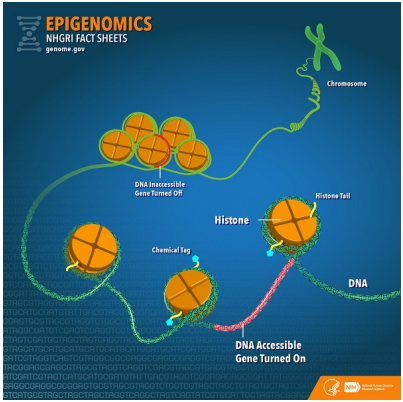
What is epigenetics?



https://youtu.be/_aAhcNjmvhc

What is epigenetics?

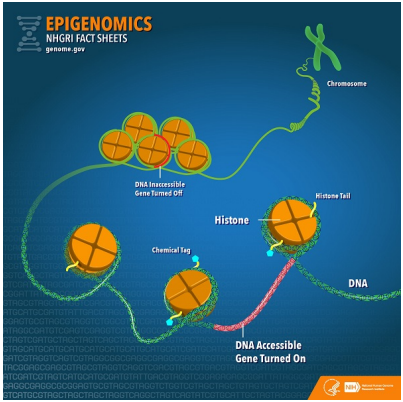
- "Chemical compounds that are **added to single genes** can regulate their activity; these modifications are known as epigenetic changes."



Source: `https://ghr.nlm.nih.gov/primer/howgeneswork/epigenome`

What is epigenetics?

- "Chemical compounds that are **added to single genes** can regulate their activity; these modifications are known as epigenetic changes."
- "The **epigenome** comprises all of the chemical compounds that have been added to the entirety of ones DNA (genome) as a way to regulate the activity (expression) of all the genes within the genome."



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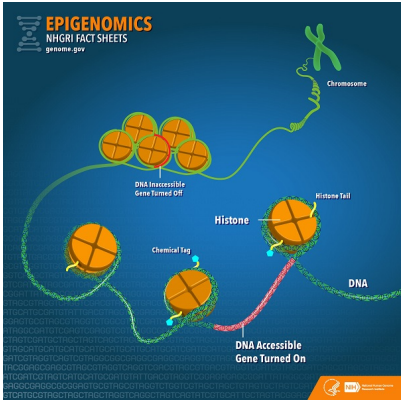
- "The **epigenome** comprises all of the chemical compounds that have been added to the entirety of ones DNA (genome) as a way to regulate the activity (expression) of all the genes within the genome."
- "The chemical compounds of the epigenome are **not** part of the DNA sequence, but are on or attached to DNA (epi- means above in Greek)."



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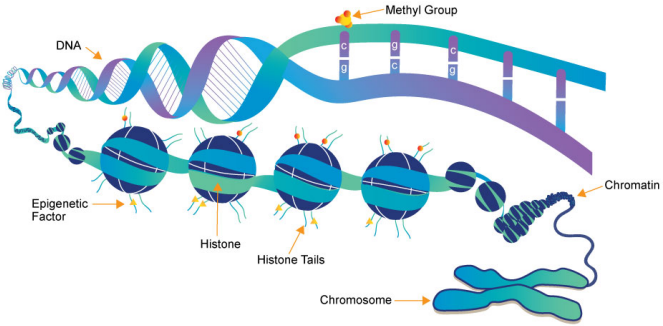
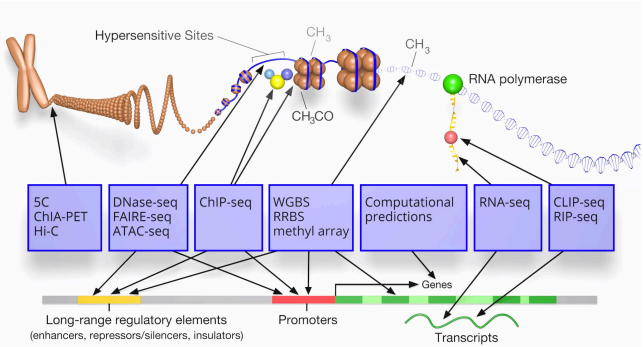


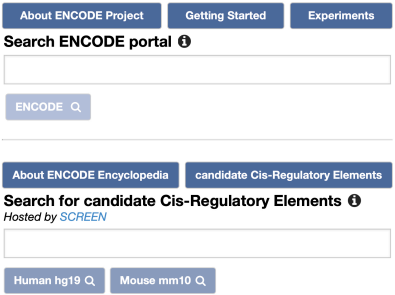
"(...) a change in **phenotype** without a change in **genotype** (...)"

https://www.whatisepigenetics.com/fundamentals/

ENCODE

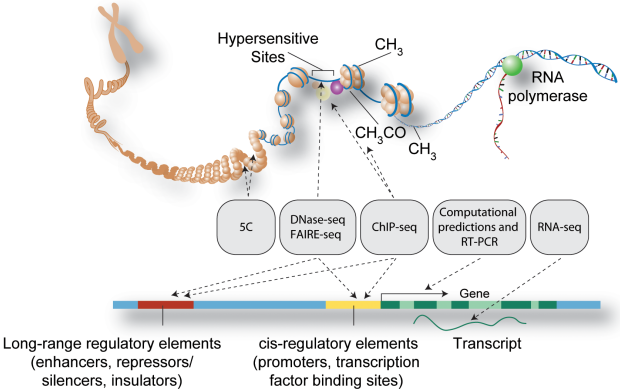
ENCODE: Encyclopedia of DNA Elements





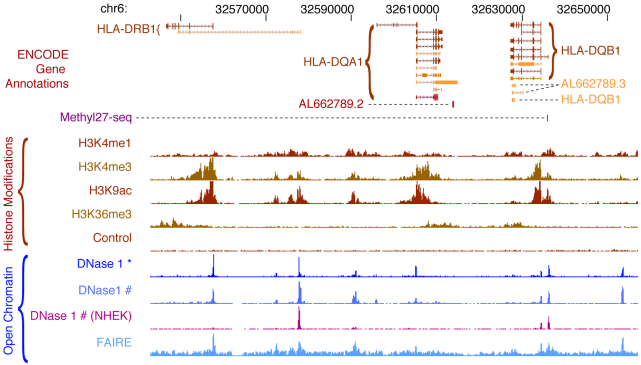
https://www.encodeproject.org

ENCODE - Assays



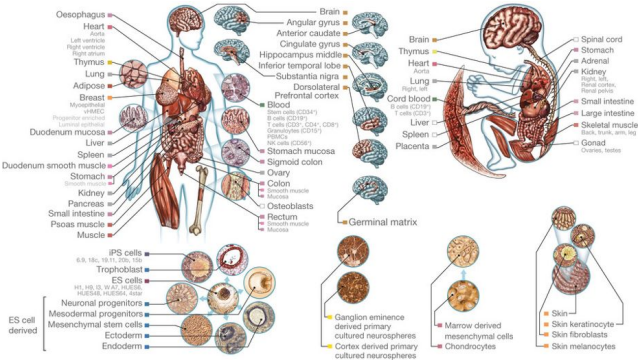
https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1001046

ENCODE - Conceptually



https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1001046

ENCODE - Cell types/lines

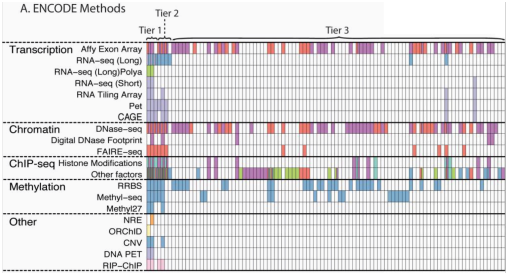


https://www.nature.com/articles/nature14248

ENCODE - Matrix

From W. S. Noble' talk:

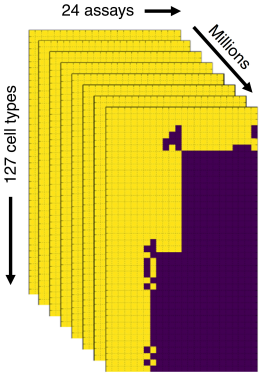
- 359 assay types
- 583 cell types
- Theoretically: 209,297 pairs!
- 5,707 experiments have been done
- The matrix is less than 5 % complete



https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1001046

ENCODE - 3D Matrix

- For every assay (359)
  - For every cell line (583)
    - For every position (3.2 Gbp)



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ENCODE - Data imputation

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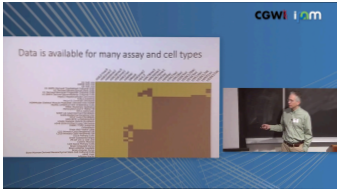
William Noble - IPAM 2018



https://youtu.be/JzSf5AU9VVc (46:13)

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Prologue

Summary

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Summary

- The **amount of data** might be more important than the learning algorithm itself.
- **Categorical data** can be encoded using the **one-hot encoding**.
- Consider **scaling** the data
- Write **scripts**
- We have seen several approaches for handling **missing values**

Next module

- **Dimensionality reduction**, **feature selection** and **unsupervised learning**.

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