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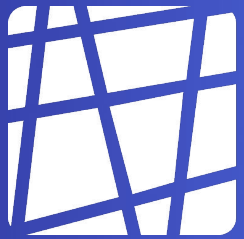

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Weekly Updates

- Please provide a quick update on either:
  - Something you did/saw this week that you thought was interesting
  - What you're looking forward to about this week's workshop

(Reminder - please have your cameras on if possible)

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Workshop 4 Featurization & Baseline Modeling

Recap

Sessions Overview

- Workshop 1 – Project Introduction & Setup
- Workshop 2 – Genomic Data (A2 Assignment)
- Workshop 3 – Data Analysis & Visualization (A3 Assignment)
- **Workshop 4 – Featurization & Baseline Modeling (A4 Assignment)**
- Workshop 5 – Model Training Approaches (Final Assignment Set)
- Workshop 6 – Model Tuning
- Workshop 7 – Performance Evaluation (Final Assignment Code/Testing Due)
- Workshop 8 – Results Presentation & Wrap up (Final Presentation Due)

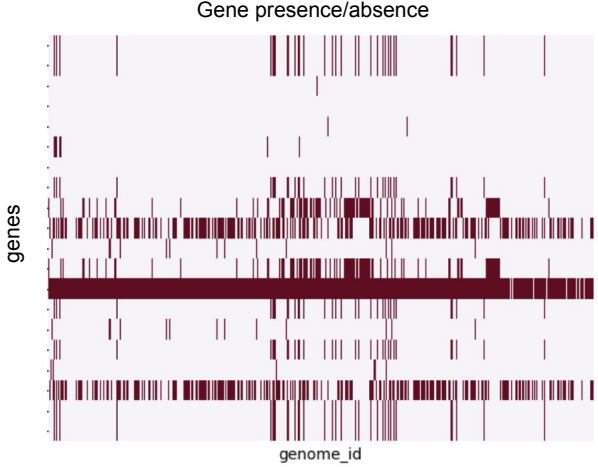
Exploratory Data Analysis

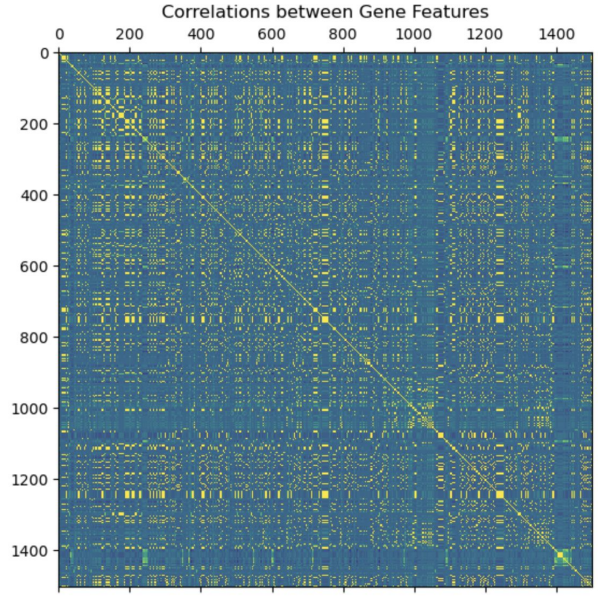
What did we achieve last week?

1. Took a look through our datasets, finding key information
2. Processed our targets (AMR) into clean binary S vs R
3. Identified a few suspicious E coli genomes
4. Reviewed gene presence/absence across samples
5. Started reviewing the nucleotide sequences and identified some mutations

Assignment (Optional):

6. Identified highly correlated genes





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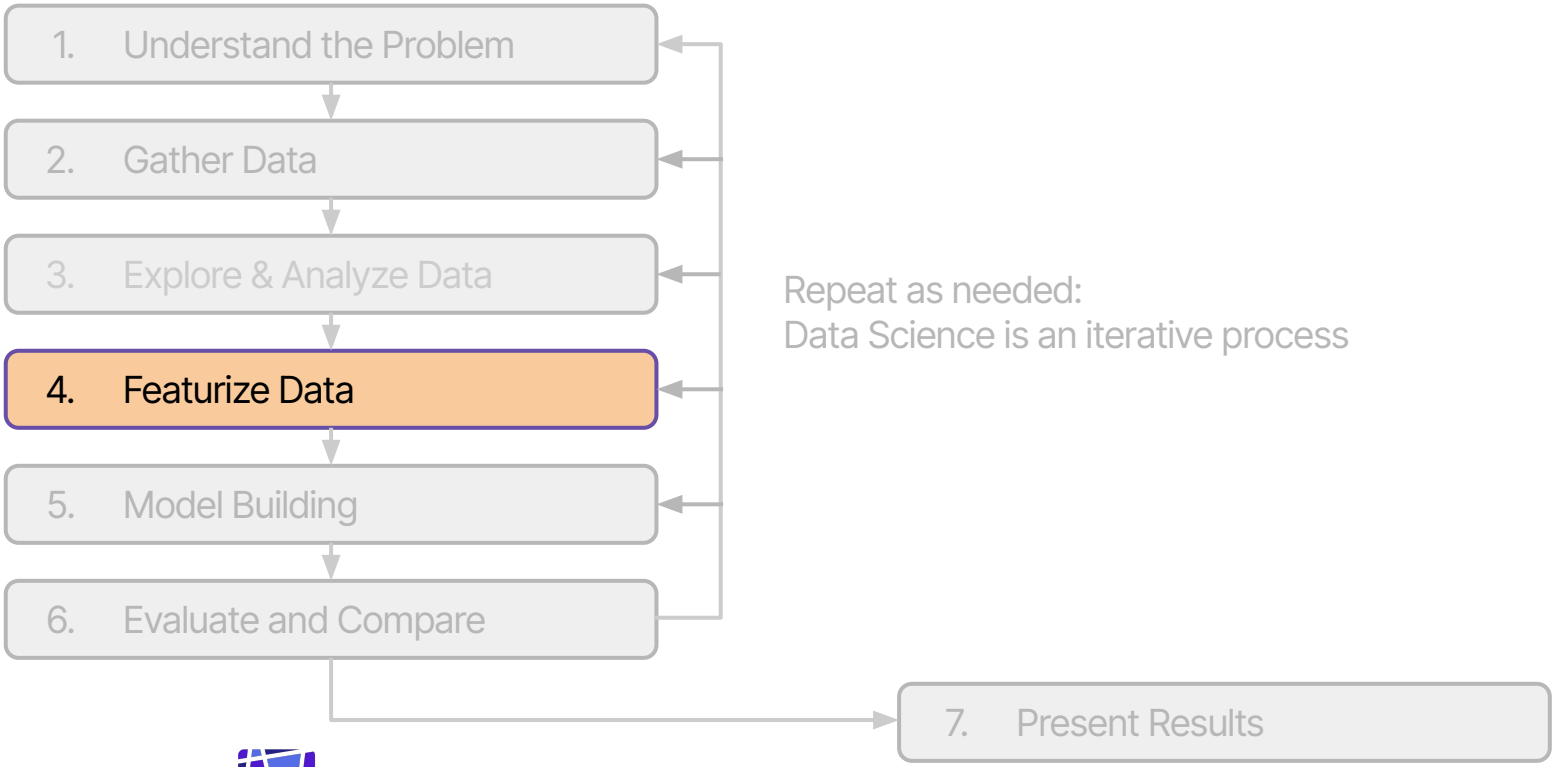
The Data Science Process



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What is Featurization?

Gene Alignment to Sequence Input

CGTATAACTGA GGAACAGCGGT

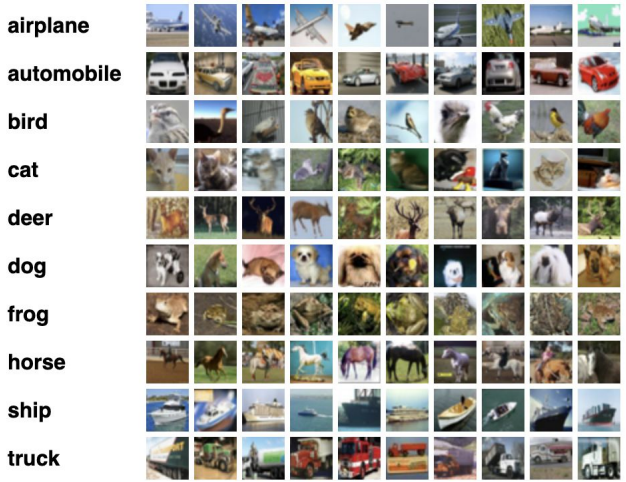
AACGTATAACTGATCGGAACAGCGGTA

- Tightly coupled with model building
- How do we go from raw data to predictions?
- Different ML models expect different data types
  - Tabular (Matrix)
  - Sequences
  - Images
  - Graphs
- Data formats & shapes need to be **consistent**
- We can't expect to pass raw data directly into our model
- Usually need to Encode our data into a numeric format

CGTATAACTGA + GGAACAGCGGT

= CGTATAACTGAGGAACAGCGGT

Cifar10 - Common ML Image Dataset



Model Options

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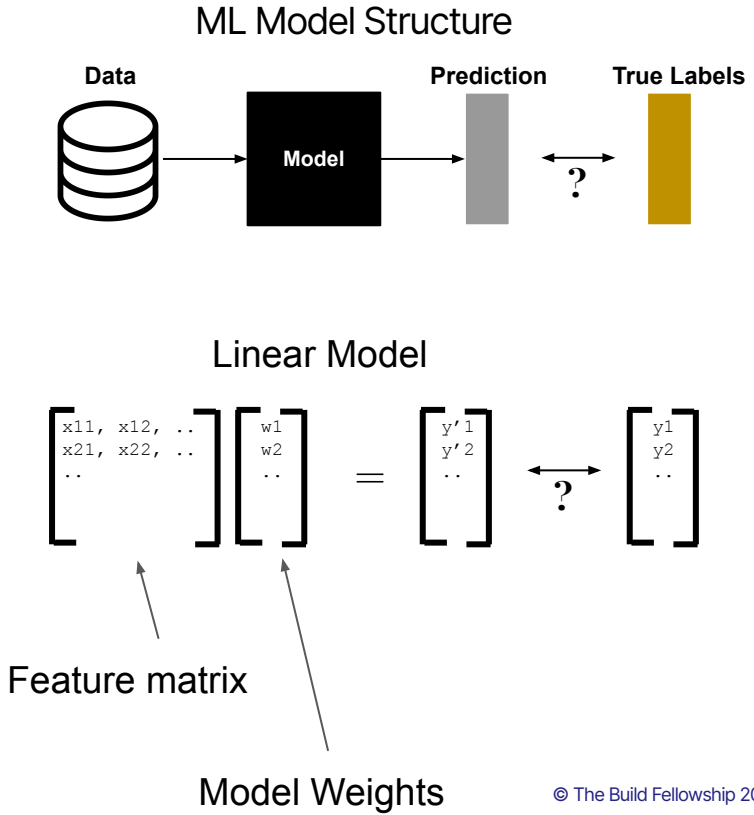
What model types can we use?

What sort of models can we leverage?

- Linear models (Tabular)
- Tree based models (Tabular)
- Neural networks (Tabular + Sequence)

Tabular
- Resistance genes
- Kmers

Sequence
- Gene sequences (mutations)



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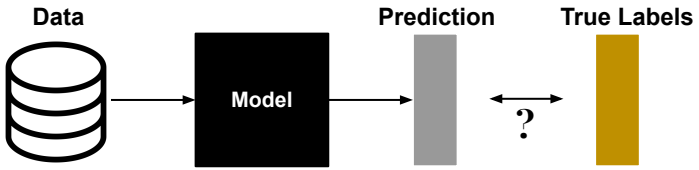
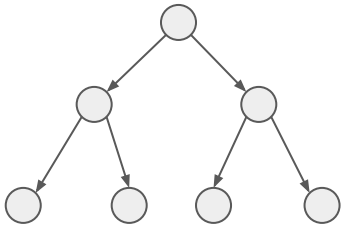
ML Model Structure



Tree Based Models



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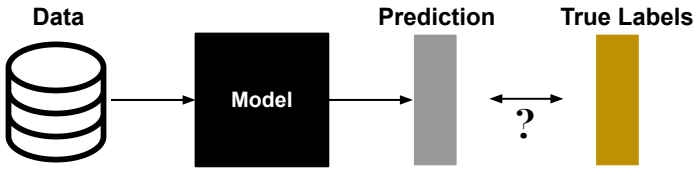
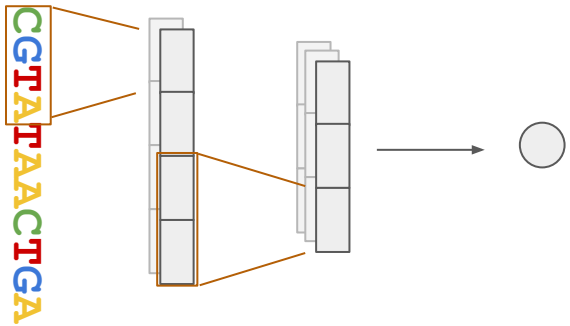


Sequence Based Model



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QUIZ TIME !?

How can we featurize DNA sequences?

a) Convert sequences to tabular counts
b) Don’t bother, just take it as is
c) Stitch all the sequences together into a single length
d) Consult experts to take only the important information

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Feature Options

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Gene Presence Absence

- Simplest and most approachable feature
- Minimal processing required
- Saw an example of this last week

Tabular approach
- Standardize the data into a fixed shape
- Need to have a consistent size per sample

Binary
- Outcomes will be present vs absent for every possible gene

Input Data - Gene Alignment

genome_id	contig	res_gene	match_start	match_end	match_qual
562.11346	FLKS01000064	gb|U00096.3|-|3324062-3324911|ARO:3003386|Ecol...	96835	97684	849M
562.11346	FLKS01000044	gb|AP009048.1|+|3760295-3762710|ARO:3003303|Ec...	61096	63511	2415M
562.11346	FLKS01000070	gb|BA000007.3|+|4990267-4994296|ARO:3003288|Ec...	22038	26067	4029M
562.11346	FLKS01000068	gb|U00096.3|-|2336792-2339420|ARO:3003294|Ecol...	755765	758393	2628M
562.11346	FLKS01000064	gb|AP009048.1|-|3172159-3174052|ARO:3003316|Ec...	241841	243734	1893M

query_str	ref_gene_str
ATGAAACTCTTTGCCCAGGGTACTTCACTGGACCTTAGCCATCCTC...	ATGAAACTCTTTGCCCAGGGTACTTCACTGGACCTTAGCCATCCTC...
ATGTCGAATTCTTATGACTCCTCCAGTATCAAAGTCCTGAAAGGGC...	ATGTCGAATTCTTATGACTCCTCCAGTATCAAAGTCCTGAAAGGGC...
TTACTCGTCTTCCAGTTCGATGTTGATACCCAGCGAACGAATCTCT...	TTACTCGTCTTCCAGTTCGATGTTGATACCCAGCGAACGAATCTCT...
TTATTCTTCTTCTGGCTCGTCGTCAACGTCCACTTCCGGAGCGATT...	TTATTCTTCTTCTGGtTCGTCGTCAACaTCCACTTCCGGAGCGATT...
ATGACGCAAACTTATAACGCTGATGCCATTGAGGTACTCACCGGGC...	ATGACGCAAACTTATAACGCTGATGCCATTGAGGTACTCACCGGGC...

Gene Presence Absence

Format
- Reshape to a clean binary matrix
- Predicting AMR from genes directly
- Loss of a lot of information (sequences, counts)

Correlations
- Genes can be very similar
- Some genes can appear in all samples

Clustering
- Naive subsetting (throw away genes)
- Clustering can be used to group genes hierarchically

Presence/Absence Feature Matrix

	Gene A	Gene B	Gene C	Gene D	…
Sample A	1	1	1	0	
Sample B	0	1	0	1	
Sample C	1	0	1	0	
Sample D	0	1	0	0	
Sample E	1	0	1	1	
	↑	…	↑		

Identical Presence Absence

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Gene Presence Absence

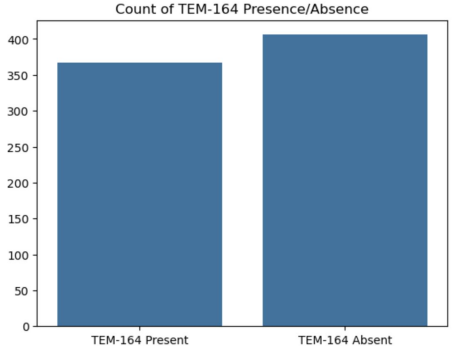
Why might Gene presence absence not always work?

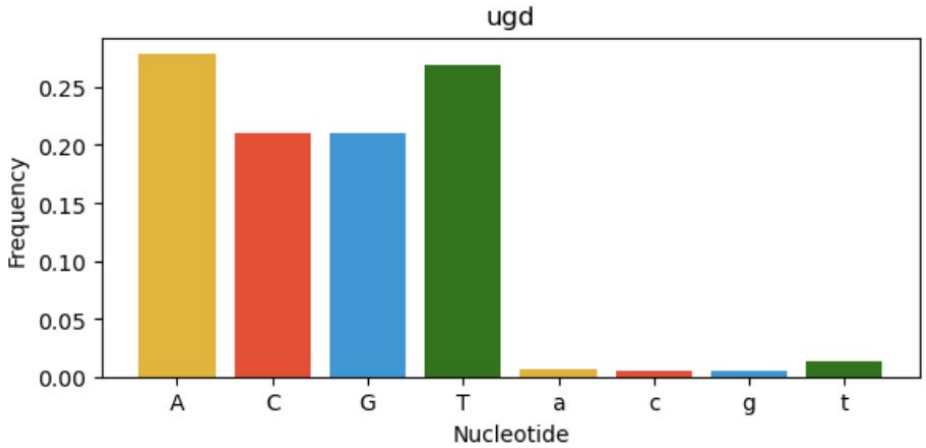
- Weak correlations
- Genes can be always present (mutations matter)
- Losing information

Query vs Ref Gene String

- Raw data has both query & reference
- Query = CARD sequencing
- Reference = Sample genomes
- Lower case = difference in nucleotides

Can we capture these sequence differences?





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Kmers

Kmers is one of the most common approaches for featurizing genomic data

Core concepts:

1. K = Fixed length representation (parameter)
2. Wish to capture the nucleotide information
3. Convert from arbitrary sequences to a fixed shape representation

High K = huge feature space, high chance of uniqueness

Low K = small feature space, high chance of repetition within genomes

K is a parameter

2-mers: AA AC AT AG CA CC CT CG
TA TC TT TG GA GC GT GG

16 unique combinations

5-mers: AAAAA AAAAC AAAAT AAAAG
AAACA AAACC AAACT AAACG

1,024 unique combinations

10-mers AAAAAAAAAA AAAAAAAAAG
AAAAAAAAAC AAAAAAAAAT

1,048,576 unique combinations

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Kmers

How to generate Kmers?

- Want unique occurrences of each kmer
- High K's = millions/billions of sequences
- Sliding window approach
- Scan the whole sequence one step at a time
- Keep track of counts

Using 5-mers:

Slide a window of size K across the genome

Kmers

How to generate Kmers?

- Want unique occurrences of each kmer
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Using 5-mers:

CGTAT = 1
GTATA = 1

Count each occurrence

Kmers

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Using 5-mers:

CGTAT = 1
GTATA = 1
TATAA = 1

Count each occurrence

Kmers

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Using 5-mers:

CGTAT = 1
GTATA = 1
TATAA = 1
ATAAC = 1

Count each occurrence

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Kmers

Kmer Count Matrix

	CGTAT	GTATA	TATAA	ATAAC
Sample A	10	1	34	0
Sample B	0	3	30	0
Sample C	3	1	54	0
Sample D	8	2	21	0
Sample E	0	1	24	1

…

…

Using 5-mers:

CGTAT = 1
GTATA = 1
TATAA = 1
ATAAC = 1
…

Count each occurrence

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Sequences

- Sequences are the most raw format of data
- Most difficult to work with
- Convolutional/Recurrent Neural Networks
- Few proven working examples in literature

Challenges:

- Data size (full sequences are millions of characters)
- Complexity vs Training data

Working with Sequence models is an **optional extension**

- Computationally complex
- Possible option for final project
- See paper for reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8722762/

Sample A

```
GeneA: GTATCTGAGGAAC
GeneB: GAGGAGATTCGCT
GeneC: TGAAACGTATGCC
```

Sample B

```
GeneA: GTATCTGAGGAAC
GeneC: TGAAACGTATGCC
GeneD: GAGGAGATTCGCT
```

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Sequences

Simple sequence featurization scheme:

- Randomly concatenate genes
- Find all genes and stack together
- Require a consistent length
- Truncate or Pad ends
- One hot encode to numeric

Sample A

```
GeneA: GTATC
GeneB: GAGGA
GeneC: TGAA
```

↓

```
GTATC-GAGGA-TGAA
```

Sample B

```
GeneA: GTATC
GeneC: TGAAA
GeneD: TATGCA
```

↓

```
GTATC-TGAAA-TATGCA
```

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Sequences

A=1 C=2 G=3 T=4 Pad=0

Simple sequence featurization scheme:

- Randomly concatenate genes
- Find all genes and stack together
- Require a consistent length
- Truncate or Pad ends
- One hot encode to numeric

Sample A

GTATCGAGGATGAA

341423133143100

Sample B

GTATCTGAAATATGCA

341424311141432 1

Baseline Models

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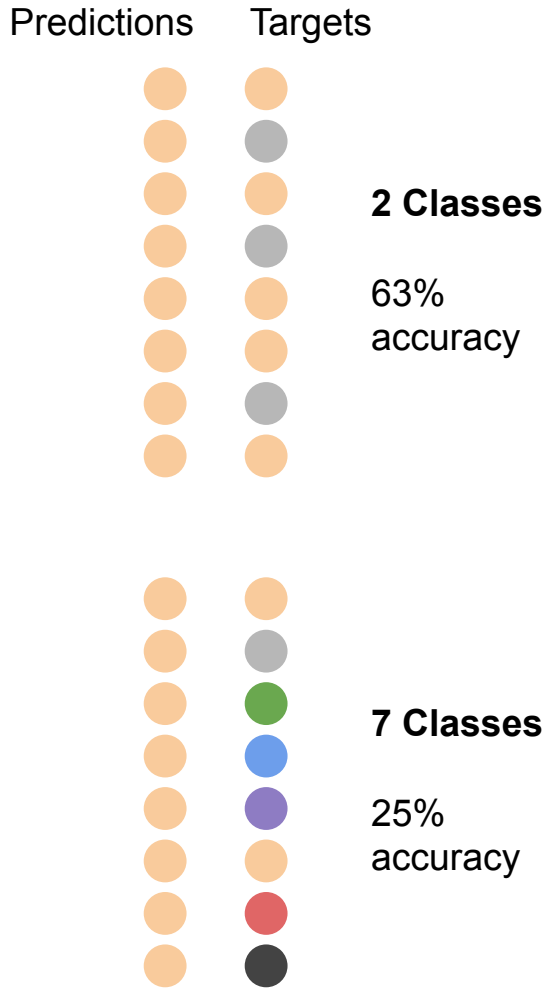
What is a Baseline Model?

- In any ML task: set ourselves a target to beat
- Understand how well we're performing
- Performance statistics out of context can be misleading
- Is 80% accuracy good? What about 20% accuracy?
- If we have two targets? If we have 50 targets?
- Baselines should be **interpretable**



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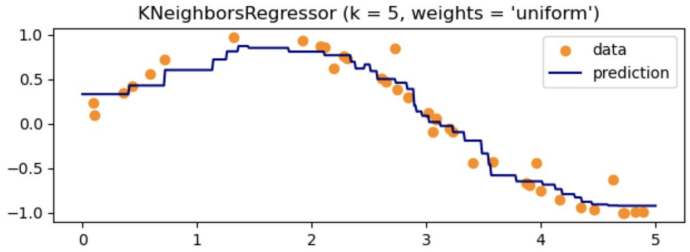
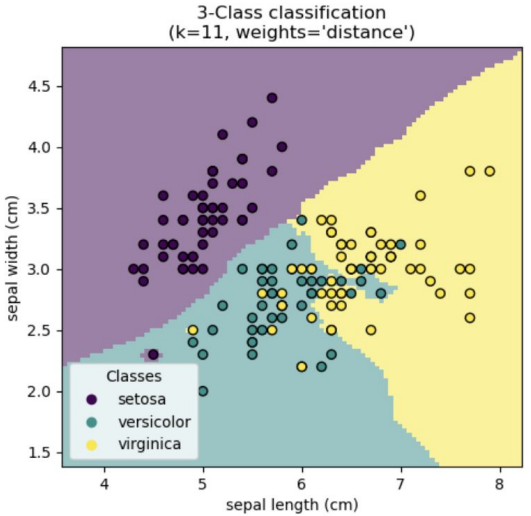
Common Baselines

- Completely Random
  - Nonsense worst case model
  - Useful to flag if data processing has failed
  - E.g. accidentally mixed up targets
- Predict the majority class
  - True “baseline”
  - Simplest way to get maximum performance
- KNN (K-nearest neighbor)
  - Doesn’t require training
  - Directly learn based on neighbors
  - Simple and interpretable

Examples: KNN Regression & Classification



[1]



[2]

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References

[1]:https://scikit-learn.org/stable/auto_examples/neighbors/plot_regression.html#sphx-glr-auto-examples-neighbors-plot-regression-py

[2]:https://scikit-learn.org/stable/auto_examples/neighbors/plot_classification.html#sphx-glr-auto-examples-neighbors-plot-classification-py