PROBABILISTIC CLASSIFIERS CAN PREDICT RADIATION EXPOSURE IN RODENTS FROM PERFORMANCE TESTS

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DATA DRIVEN MODELS CAN EXPLORE COMPLEXITIES OF CBS RISKS

- Sensorimotor, radiation, and stress can impact in-mission performance.
  - We here focus on radiation-induced performance decrements.
- Galactic cosmic radiation (GCR) exposure impairs cognitive performance.
  - Wistar rats exhibit discrimination impairment after GCR exposure [1].
- *A priori* modeling of radiation effects is difficult.
- Data driven models can capture data trends without modeling assumptions.
- Data driven models natively account for noise with sufficient training data.

[1] J.S. Jewel *et al*. Exposure to ≤ 15 cGy of 600 MeV/n ^{56}Fe Particles Impairs Rule Acquisition but not Long-Term Memory in the Attentional Set-Shifting Assay. Radiation Research, 190(1): 565-575, 2018.

DATA DRIVEN TREND MODELING USING RODENT ATTENTIONAL SET-SHIFTING ASSAY RESULTS

DATA DRIVEN MODELS ARE DEVELOPED FROM ANALOG STUDY DATA

- Data that relates human radiation to cognitive performance is limited.
- Rodent *medial-* and primate *lateral- pre-frontal cortex* functions are similar [2].
- Rodent "Attentional Set-Shifting" (ATSET) assay is therefore used as an analog study.
  - This test measures the ability to discern between cues to obtain a food reward.
- Tested rodents each received different radiation doses from single-ion beams [3].
  - None, Helium (^{4}He), Oxygen (^{16}O), Silicon (^{28}Si), Titanium (^{48}Ti), and Iron (^{56}Fe).
- **Goal:** Infer received radiation dose to make go/no-go mission decisions.

[2] J.M. Birrell and V.J Brown. Medial frontal cortex mediates perceptual attentional set shifting in the rat. Journal of Neuroscience, 20(11): 4320-4324, 2000.
[3] R.A. Britten. Personal communication, 2019.

THE DATA DRIVEN MODEL RELATES PERFORMANCE VS. ION DOSE

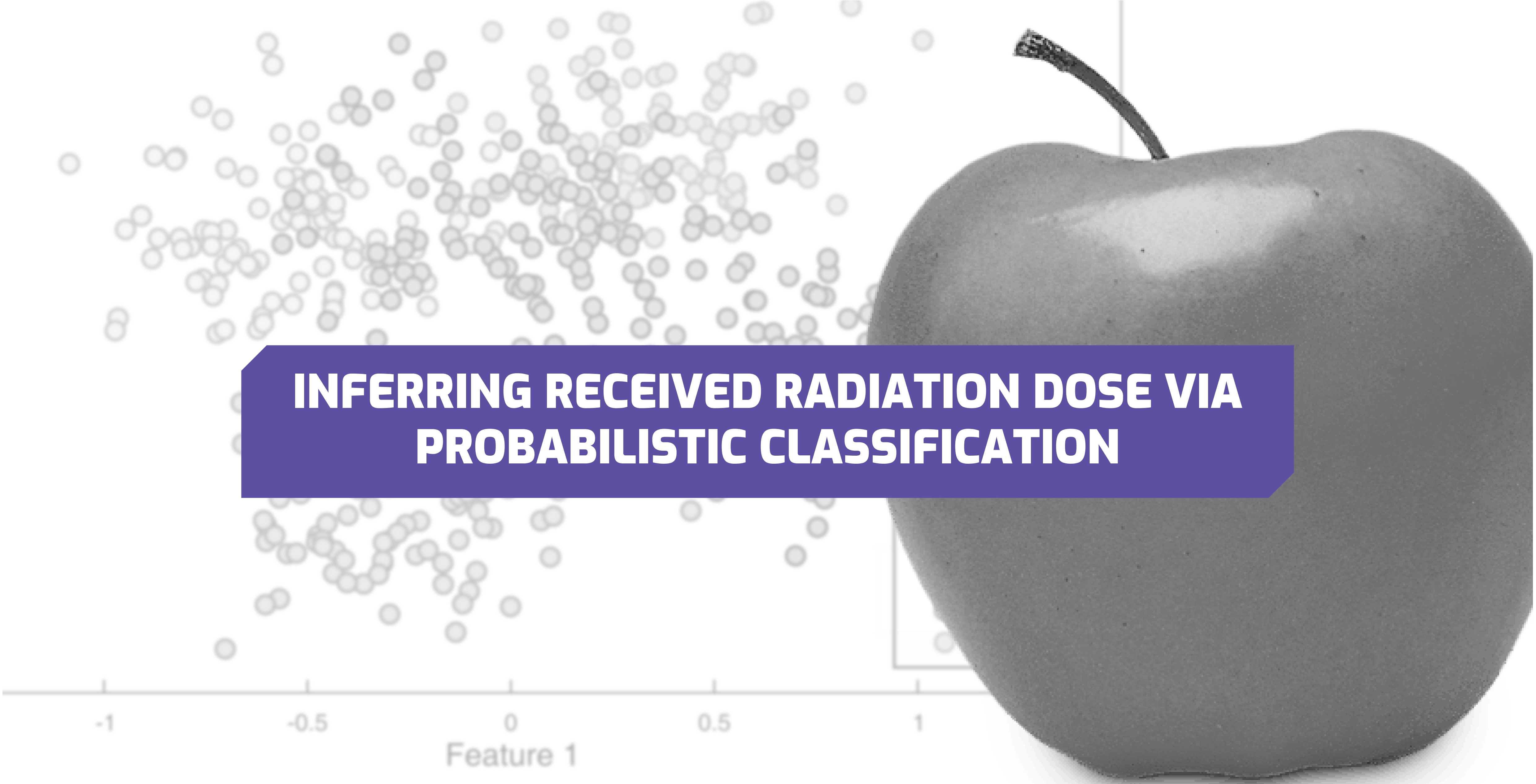
^{28}Si DATA		ATTEMPTS TO REACH CRITERION (ATRC)							MEAN CORRECT LATENCY TIME (MCL) [s]						
SUBJECT ID	DOSE [cGy]	SD	CD	CDR	IDS	IDR	EDS	EDR	SD	CD	CDR	IDS	IDR	EDS	EDR
2BCC	1	12	13	7	7	13	6	8	14.1	18.3	16.9	10.4	9.9	14.7	9.4
5976	1	12	6	10	6	6	6	6	9.0	14.8	18.2	20.0	9.8	9.8	8.3
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
A78A	15	8	36	6	6	6	16	17	15.6	11.2	11.2	16.8	18.5	13.1	8.1

Table II: Sample ATSET data for ^{28}Si. Performance decrements should manifest as larger ATRC and MCL for higher doses [1].

^{28}Si DATA		NORMALIZED ATRC							NORMALIZED MCL						
SUBJECT ID	DOSE [cGy]	SD	CD	CDR	IDS	IDR	EDS	EDR	SD	CD	CDR	IDS	IDR	EDS	EDR
2BCC	1	1	1.1	0.6	0.6	1.1	0.5	0.7	1.0	1.3	1.2	0.7	0.7	1.0	0.7
5976	1	1	0.5	0.8	0.5	0.5	0.5	0.5	1.0	1.7	2.0	2.2	1.1	1.1	0.9
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
A78A	15	1	4.5	0.8	0.8	0.8	2.0	2.1	1.0	0.7	0.8	1.1	1.2	0.8	0.5

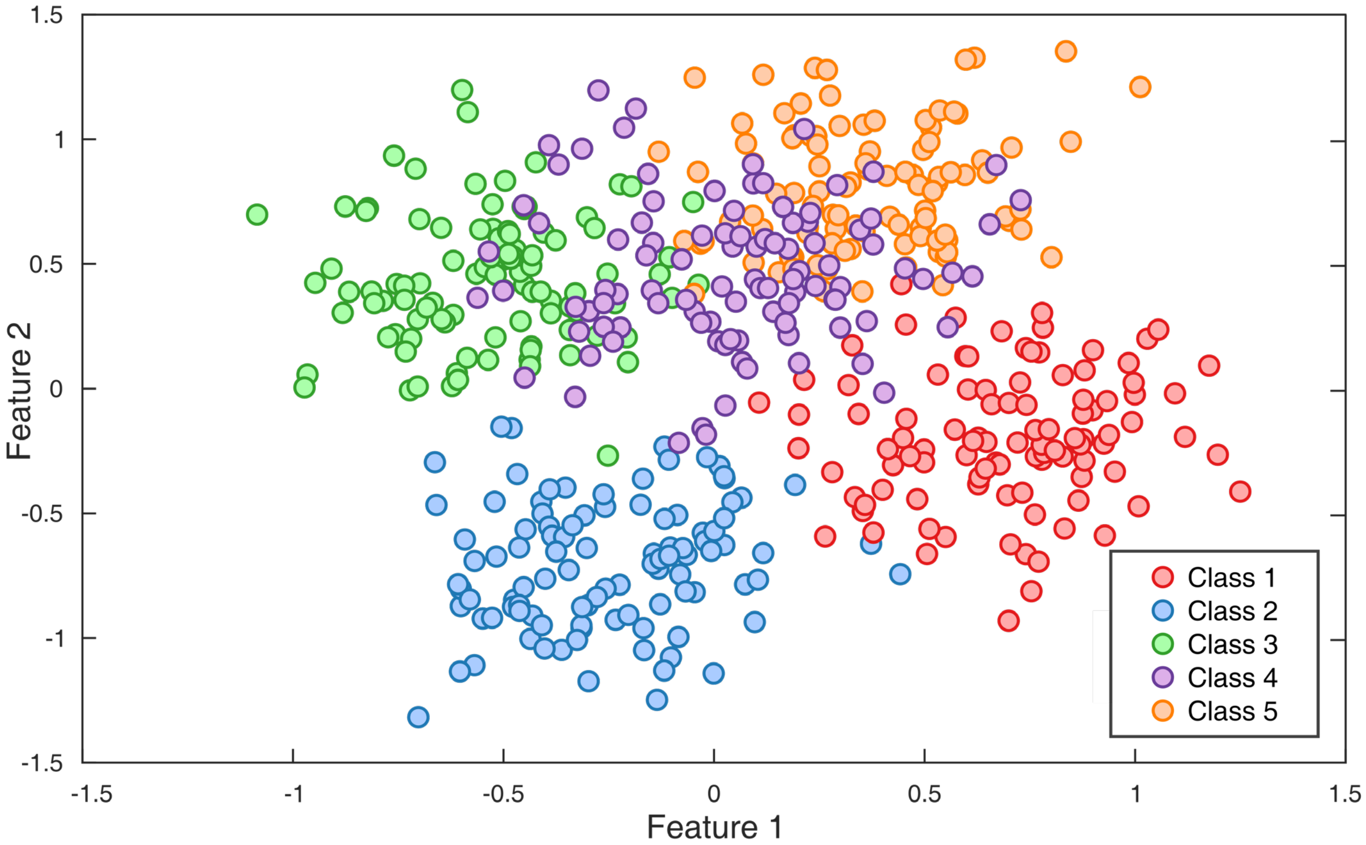
Table III: Normalized ATSET data for ^{28}Si. SD ATRC and MCL values used for respective normalization [4].

[1] J.S. Jewel *et al*. Exposure to ≤ 15 cGy of 600 MeV/n ^{56}Fe Particles Impairs Rule Acquisition but not Long-Term Memory in the Attentional Set-Shifting Assay. Radiation Research, 190(1): 565-575, 2018.
[4] J.M. Heisler *et al.* The attentional set shifting task: a measure of cognitive flexibility in mice. Journal of Visualized Experiments: JoVE, 96(1): 1-6, 2015



INFERRING RECEIVED RADIATION DOSE VIA PROBABILISTIC CLASSIFICATION
-1
-0.5
0
0.5
1
Feature 1

A CLASSIFICATION APPROACH YIELDS A MULTI INPUT, SINGLE OUTPUT MODEL



Classifying data based on clustering from two features.

PROBABILISTIC CLASSIFICATION VIA GAUSSIAN NAÏVE BAYES (GNB)

Given a set of features X^{new} *to describe a sample…*

$$X^{new} =< X_1, \dots, X_n >$$

$$\hat{y} = \underset{j \in \{1,\dots,J\}}{\operatorname{argmax}} \propto P(Y = y_j) \prod_{i=1}^{n} P(X_i^{new} | Y = y_j)$$

… the sample described by those features most likely came from group y_j …

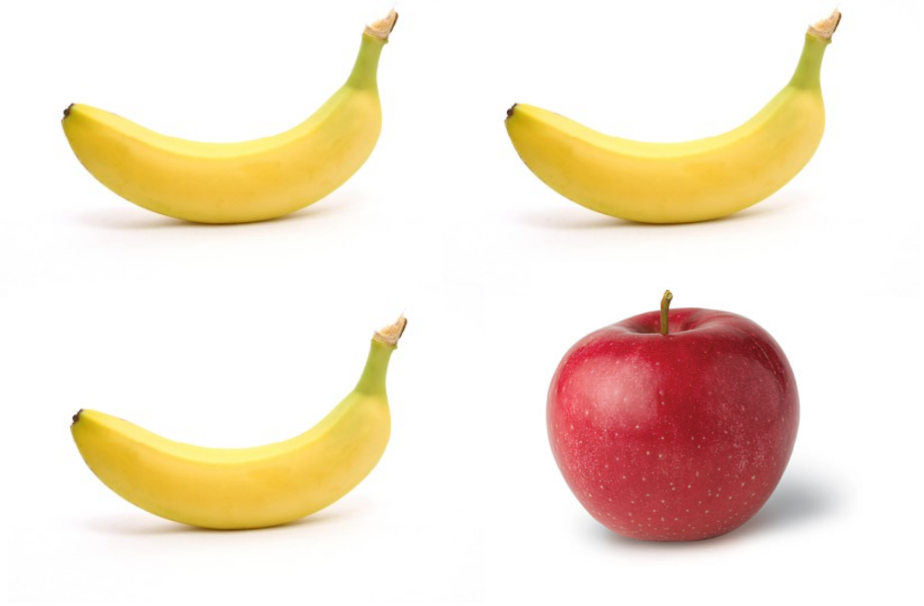
… based on other samples with the same features.

Naïve Bayes classifier using the maximum a posteriori decision rule.

GNB CLASSIFICATION EXAMPLE: CLASSIFYING FRUIT USING ONE FEATURE

$$P(Y = \text{🍎} \mid X = \square) \propto P(X = \square \mid Y = \text{🍎})P(Y = \text{🍎})$$
$$\propto 0 * 0.25 = 0$$

$$P(Y = \text{🍌} \mid X = \square) \propto P(X = \square \mid Y = \text{🍌})P(Y = \text{🍌})$$
$$\propto 1 * 0.75 = 0.75$$

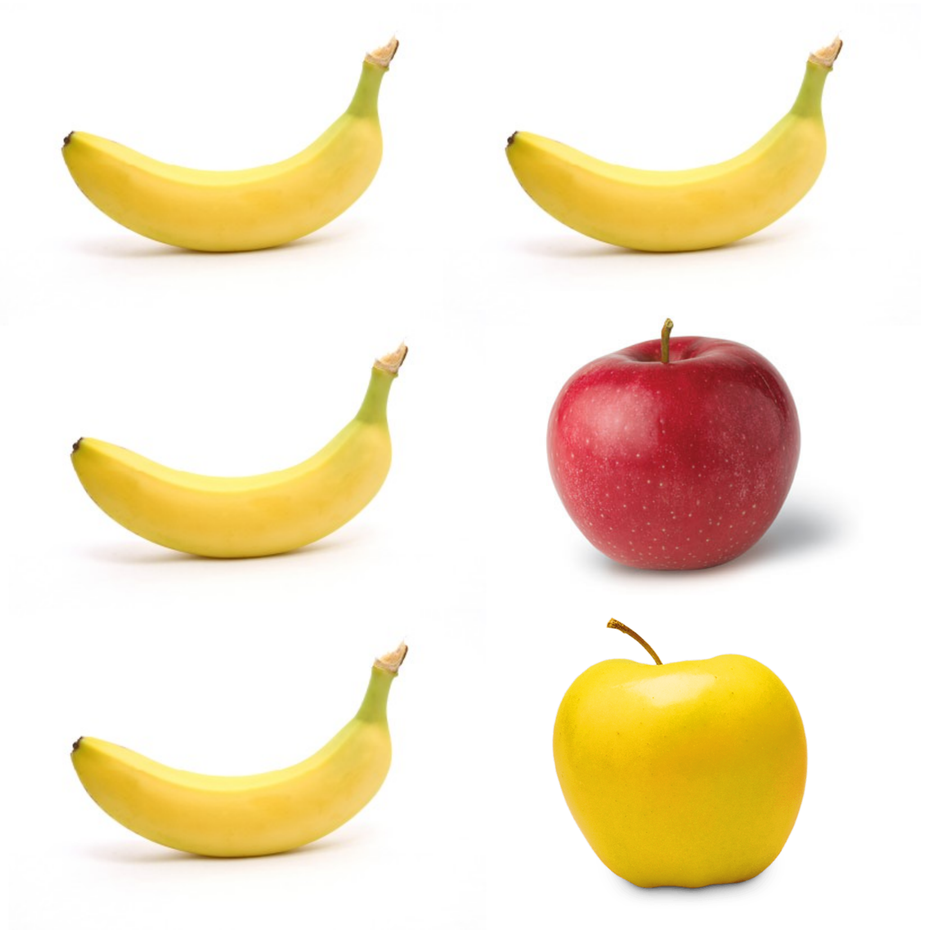


The banana-apple universe, where 75% of all fruit are bananas.

GNB EXAMPLE: CLASSIFYING APPLES WITH INSUFFICIENT FEATURES

$$P(Y = \text{🍎} | X = \boxed{}) \propto P(X = \boxed{} | Y = \text{🍎}) P(Y = \text{🍎})$$
$$\propto 0.2 * 0.33 = 0.07$$

$$P(Y = \text{🍌} | X = \boxed{}) \propto P(X = \boxed{} | Y = \text{🍌}) P(Y = \text{🍌})$$
$$\propto 0.8 * 0.66 = 0.53$$



The banana-apple universe, where 66% of all fruit are bananas and yellow apples exist.

GNB EXAMPLE: CLASSIFYING APPLES WITH MULTIPLE FEATURES

$$P(Y = \,|X = \square, round)$$

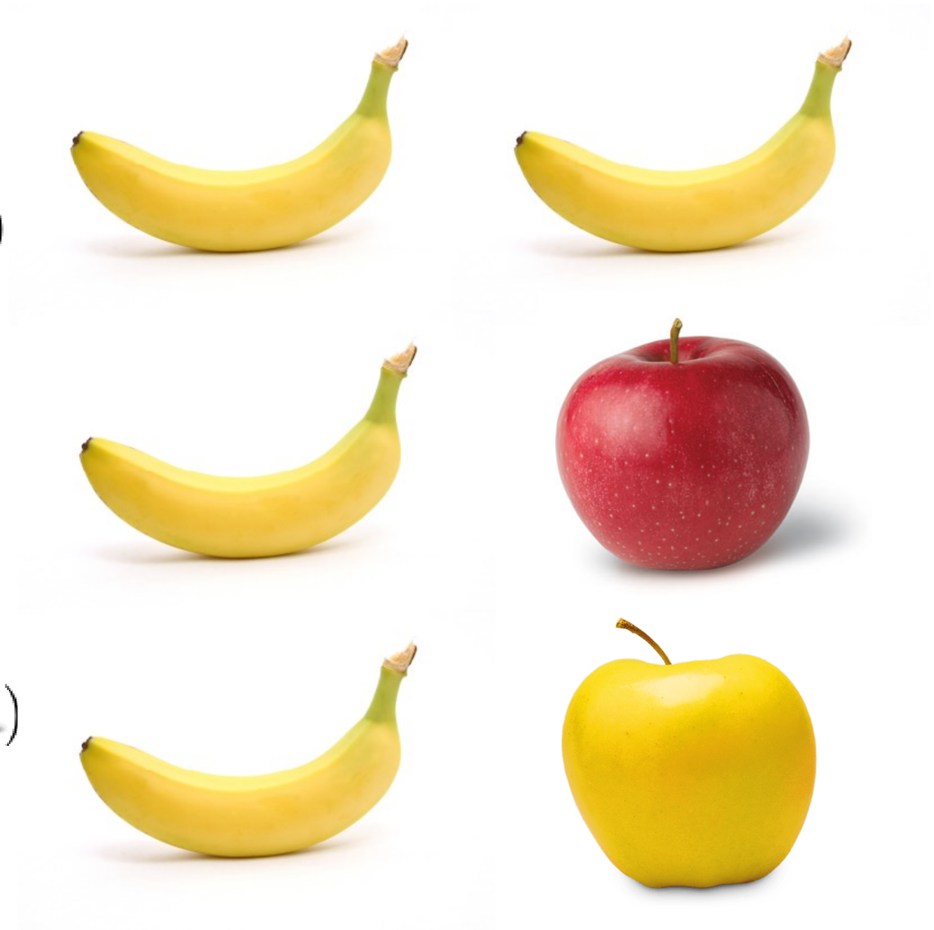
$$\propto P(Y = \,) * P(X = \square|Y = \,)P(X = round|Y = \,)$$

$$\propto 0.66 * 0.8 * 0 = 0$$

$$P(Y = \,|X = \square, round)$$

$$\propto P(Y = \,) * P(X = \square|Y = \,)P(X = round|Y = \,)$$

$$\propto 0.33 * 0.2 * 1 = 0.07$$



The banana-apple universe, but fruits are described by color <u>and</u> shape.

ESTIMATING THE CONDITIONAL PROBABILITY OF CONTINUOUS VALUES

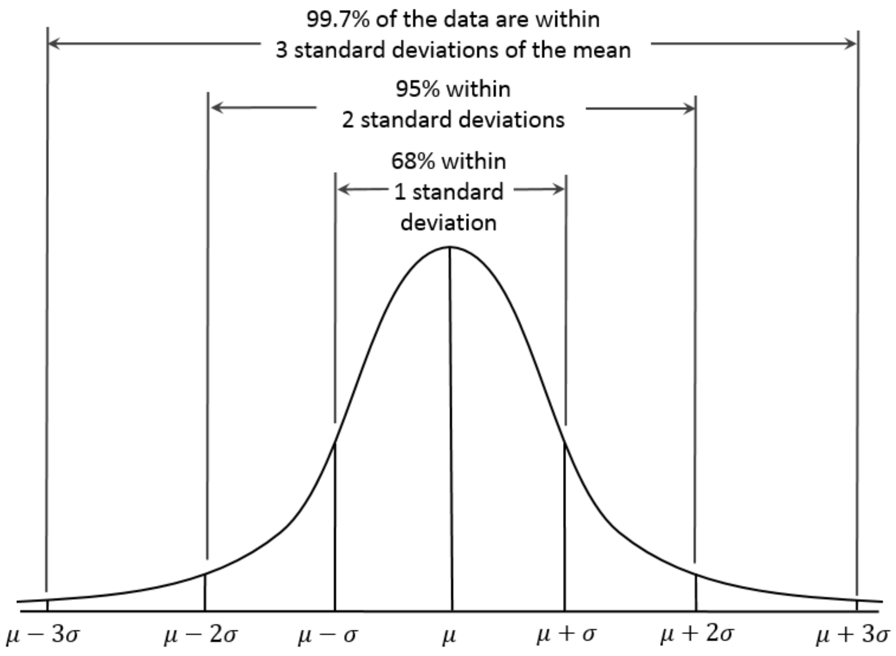
$$P(Y = y_j) \prod_{i=1}^{n} P(X_i | Y = y_j)$$

Calculated as (n_{class} / n_{tot})

Feature mean of class

$$P(X = x_i | Y = y_j) = \frac{1}{\sqrt{2\pi\sigma_{y_j}^2}} e^{-(x_i - \mu_{y_j})^2 / (2\sigma_{y_j}^2)}$$

Feature standard deviation of class



The probability density function of a Gaussian distribution [5].

[5] Normal Distribution. Wikipedia, https://en.wikipedia.org/wiki/Normal_distribution. Accessed 2019.

DATA INVERSION + CLASSIFICATION APPROACH YIELDS A QUERYABLE MODEL

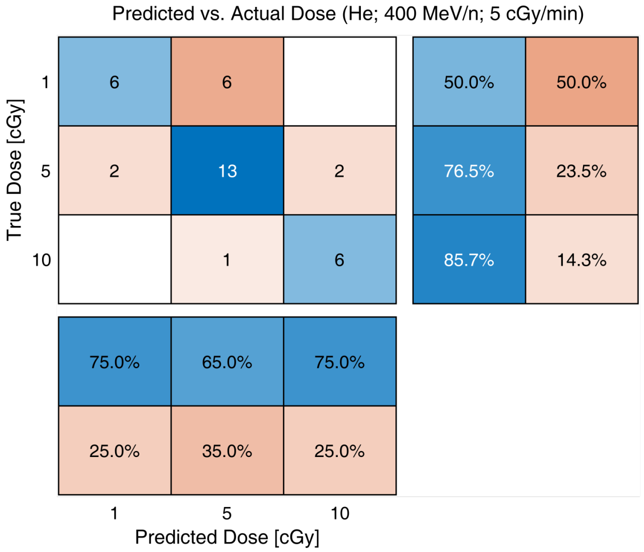
- GNB enables multi-feature prediction about exposure dose/type from ATSET values.
  - Naïve Bayes probabilistically combines multiple features/measurements.
- Data-driven classification model requires little data given representative statistics.
- **Caveat:** Due to data availability, we are training and testing on the same data set.
  - **This analysis therefore represents the best possible classification scenario.**

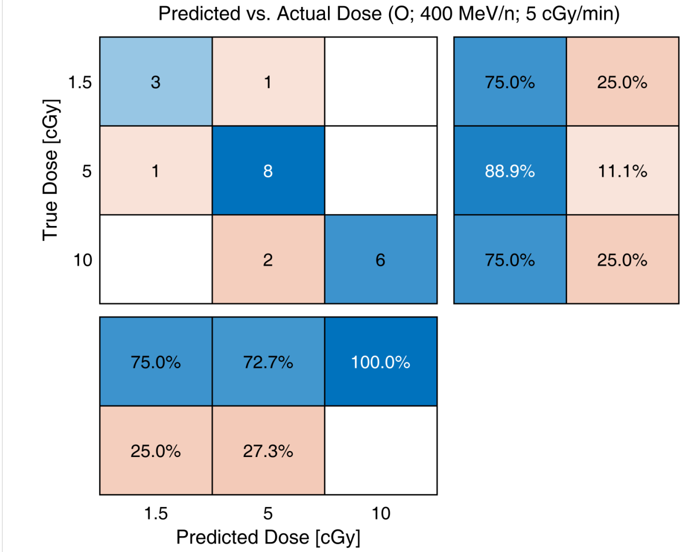
DATA DRIVEN PRIOR OF CONTROL DATA DOMINATES DUE TO SAMPLE SIZE

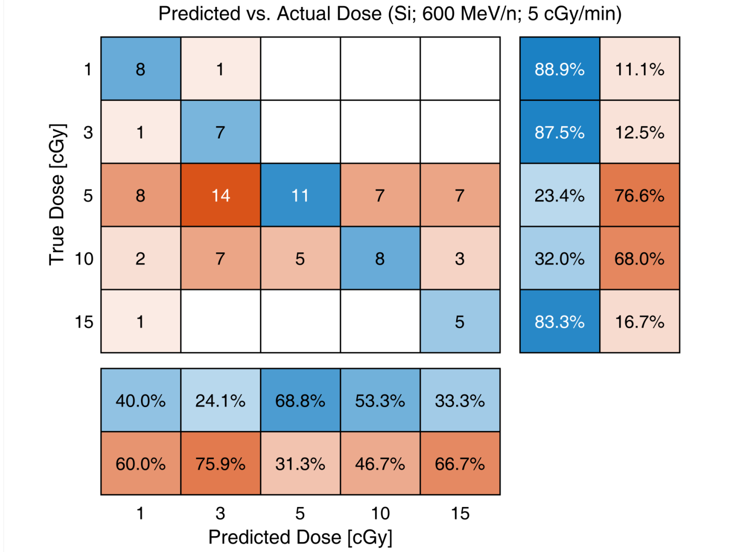
	0 cGy	1 cGy	1.5 cGy	3 cGy	5 cGy	9.1 cGy	10 cGy	15 cGy
^{4}He	0.47	0.18	-	-	0.25	-	0.10	-
^{16}O	0.71	-	0.09	-	0.2	-	-	-
^{28}Si	0.25	0.07	-	0.06	0.37	-	0.20	0.05
^{48}Ti	0.50	-	-	0.11	0.16	0.06	0.09	0.08
^{56}Fe	0.48	0.03	-	0.07	0.14	-	0.12	0.15

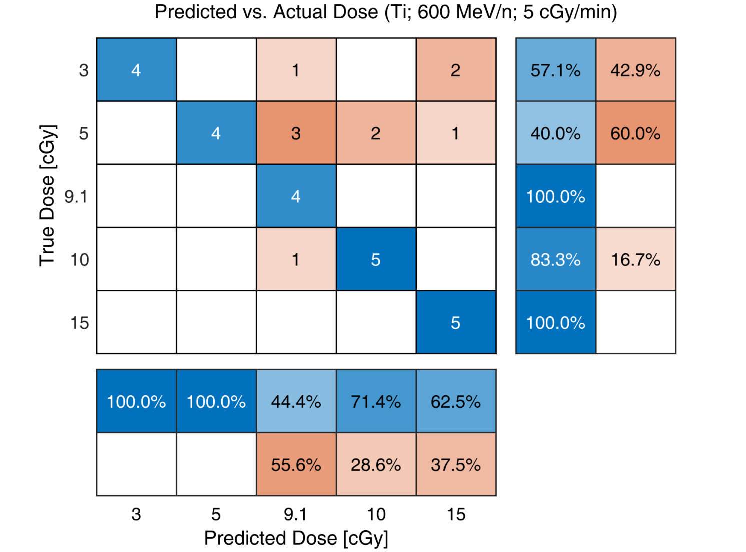
Prior probability based on data. Subsequent analyses will assume a uniform prior and additionally use MCL data as classification features.

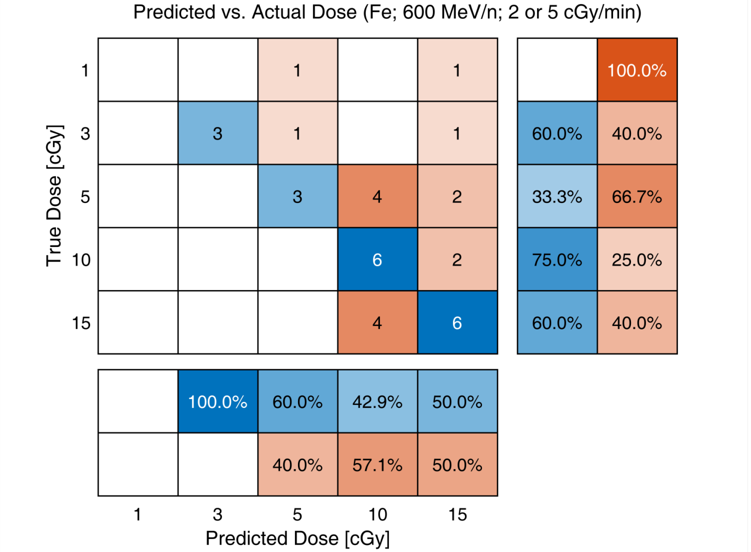
PREDICTING DOSE FROM ATRC AND MCL VALUES WITH A UNIFORM PRIOR











NAÏVE BAYES CLASSIFICATION CAN DIFFERENTIATE BETWEEN DOSES

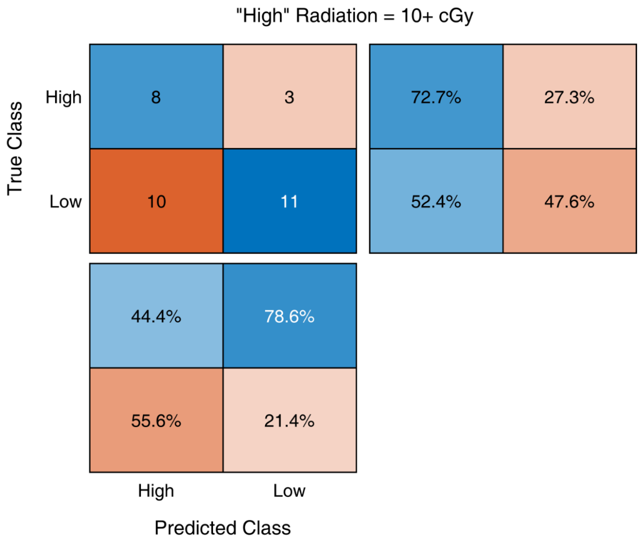
- Naïve Bayes classifier is able to distinguish between doses with mixed success.
  - Many doses are correctly identified with a probability greater than chance.
  - Sparse data with large variance may lead to unrepresentative statistics.
- GNB classification suggests that trends exist in the data.
  - This result highlights the benefits of using multiple features in a model.

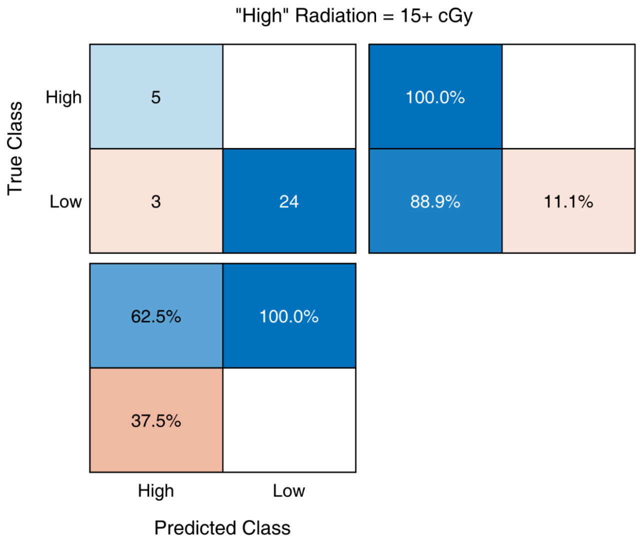
INVESTIGATING CLASSIFICATION ACCURACY WITH LARGER DATA POOLS

- Naïve Bayes can distinguish between doses, but can its accuracy be improved?
- Depending on the application, is knowing an exact exposure dose necessary?
  - Would a binary [impaired, not impaired] output be sufficient?
  - Pooling data could improve classification accuracy.
- The following analysis investigates effects of data pooling on classification accuracy.
  - This analysis bins data into variable “high” and “low” exposure categories.
  - “High” radiation threshold increases with subsequent analyses.

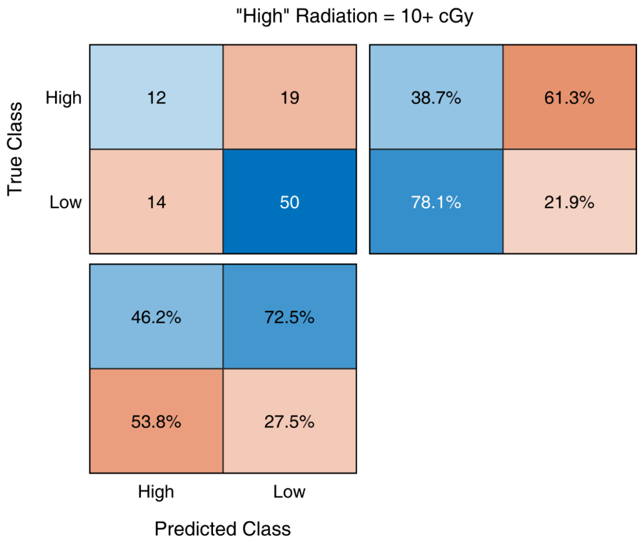
RADIATION THRESHOLD PREDICTION (ATRC & MCL, UNIFORM PRIOR)

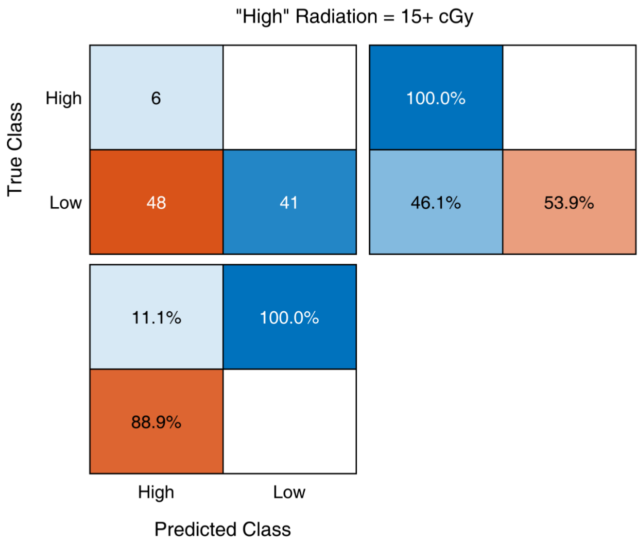
^{48}Ti:





^{28}Si:





NAÏVE BAYES HIGH/LOW EXPOSURE PREDICTION ACCURACY IS MIXED

- Prediction accuracy of pooled high and low exposure data is mixed.
  - Underlying data may be too broad to capture with single descriptor values.
  - Predicting exposures and then thresholding appears to be a better method.


CONCLUSIONS

GNB WITH ATSET DATA ENABLES PROBABILISTIC EXPOSURE PREDICTION

- GNB classifiers correctly identify doses with a probability greater than chance.
- The performed classification analysis:
  - Suggests that trends exist in the data.
  - Highlights the importance of additional data.
- For pooled data, classification accuracy is mixed.

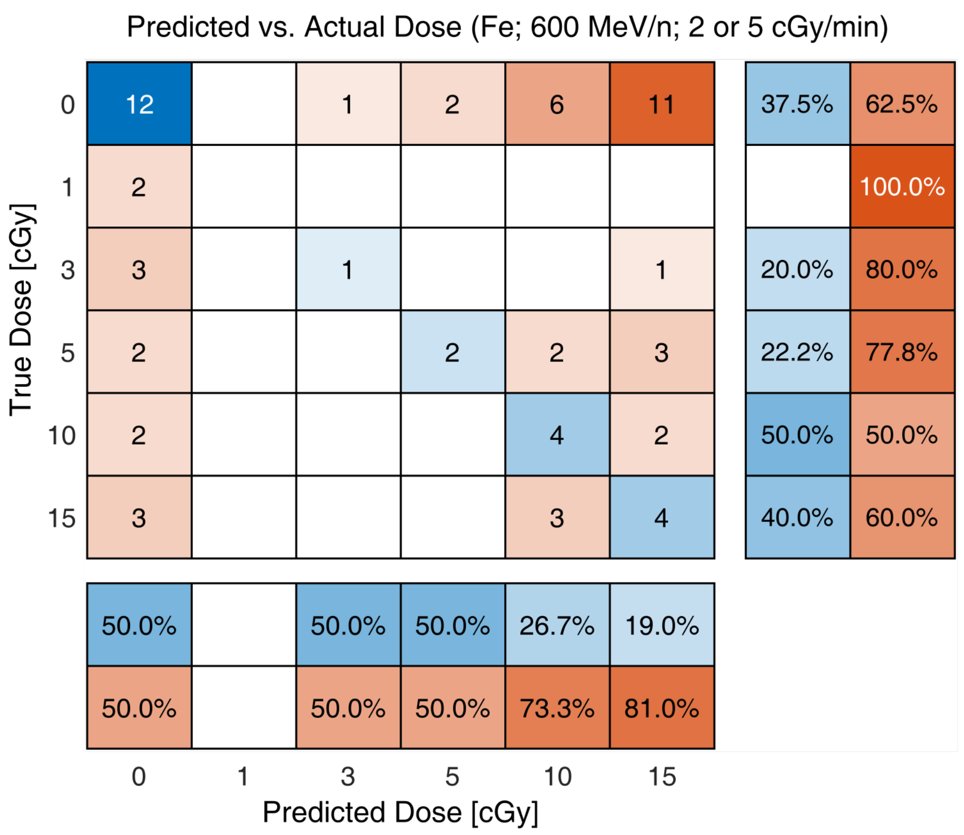
THE PERFORMED ANALYSIS POSES SEVERAL QUESTIONS

- Is having a continuous model that maps exposure to impairment necessary?
  - Is the exposure-impairment relationship cumulative?
- Is being able to predict the existence of cognitive impairments sufficient?
  - For this determination, discriminative models like GNB are sufficient.
- Pre-screening performance normalization could reveal underlying data trends.

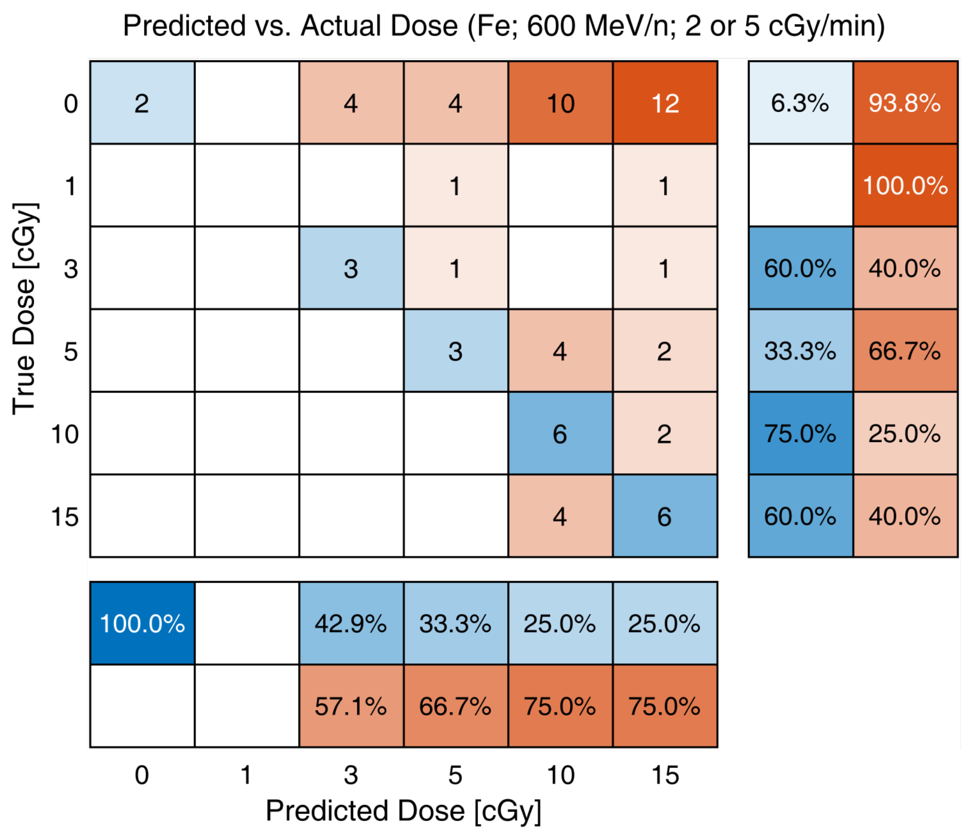
THANK YOU FOR YOUR ATTENTION.
ADDITIONAL COMMENTS OR QUESTIONS?

SUPPLEMENTAL SLIDES

PREDICTING DOSE WITH A UNIFORM PRIOR IMPROVES ACCURACY



^{56}Fe classification with a data driven prior.



^{56}Fe classification with a uniform prior.

RADIATION THRESHOLD PREDICTION (ATRC & MCL, UNIFORM PRIOR): ^{48}Ti

"High" Radiation = 5+ cGy

True Class \ Predicted Class	High	Low		
High	22	3	88.0%	12.0%
Low	1	6	85.7%	14.3%
	95.7%	66.7%		
	4.3%	33.3%		

"High" Radiation = 9.1+ cGy

True Class \ Predicted Class	High	Low		
High	13	2	86.7%	13.3%
Low	6	11	64.7%	35.3%
	68.4%	84.6%		
	31.6%	15.4%		

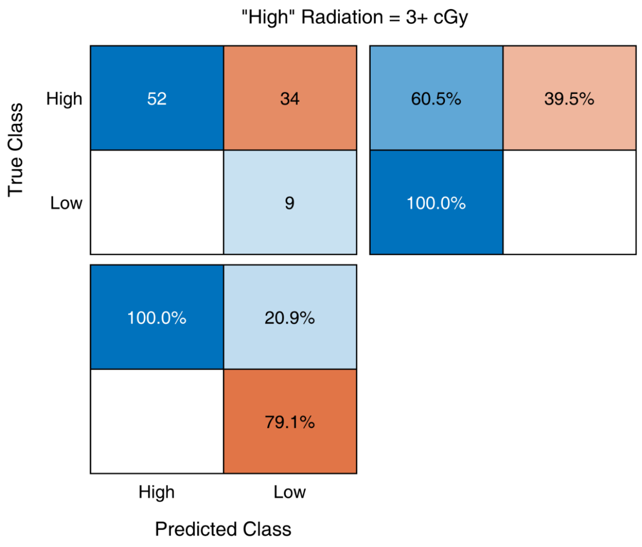
"High" Radiation = 10+ cGy

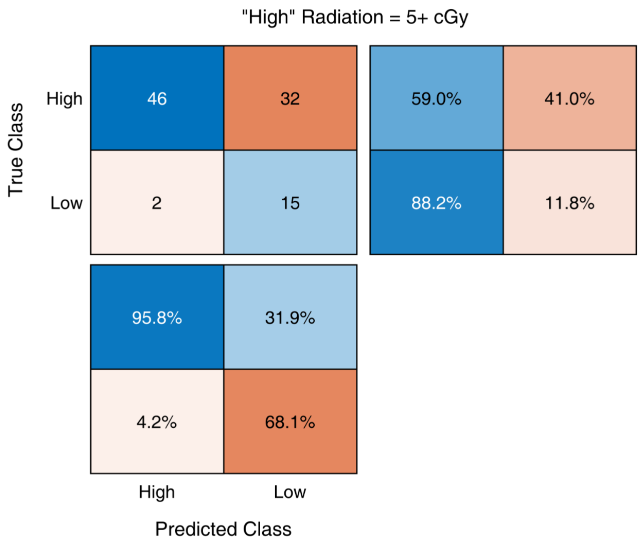
True Class \ Predicted Class	High	Low		
High	8	3	72.7%	27.3%
Low	10	11	52.4%	47.6%
	44.4%	78.6%		
	55.6%	21.4%		

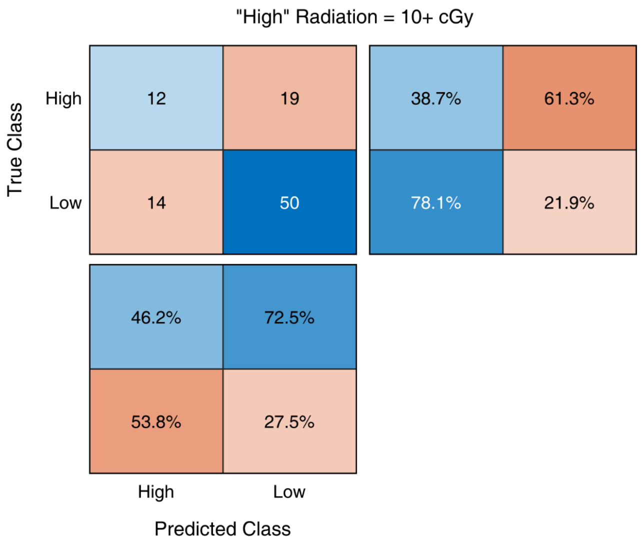
"High" Radiation = 15+ cGy

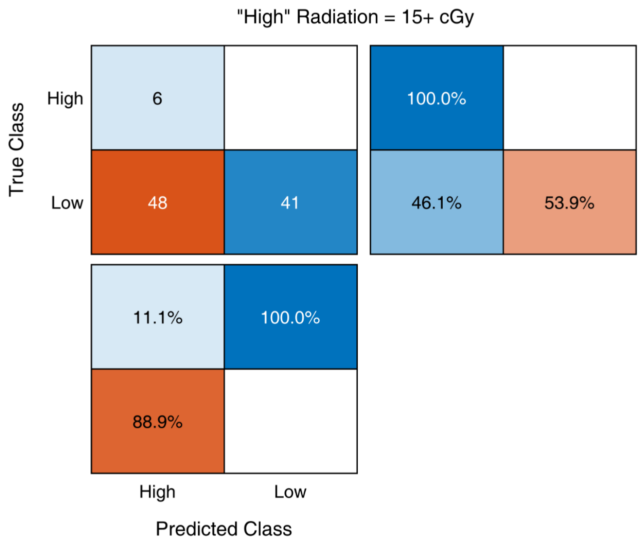
True Class \ Predicted Class	High	Low		
High	5		100.0%	
Low	3	24	88.9%	11.1%
	62.5%	100.0%		
	37.5%			

RADIATION THRESHOLD PREDICTION (ATRC & MCL, UNIFORM PRIOR): ^{28}Si

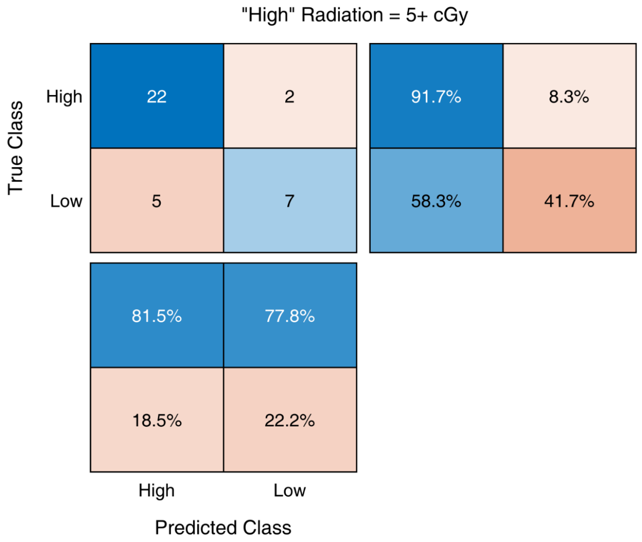


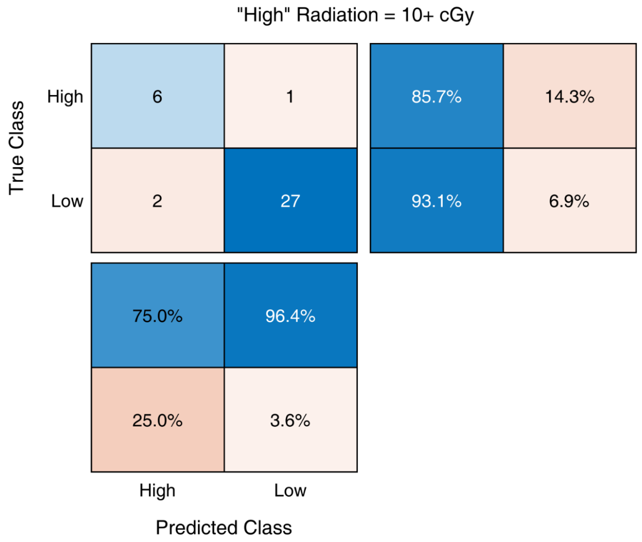




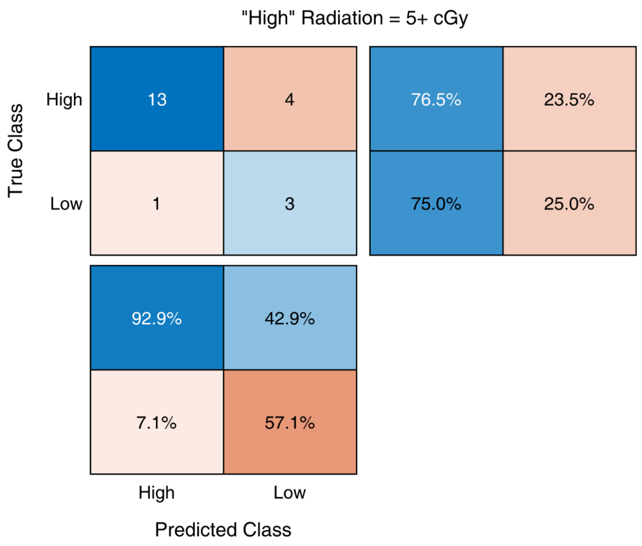


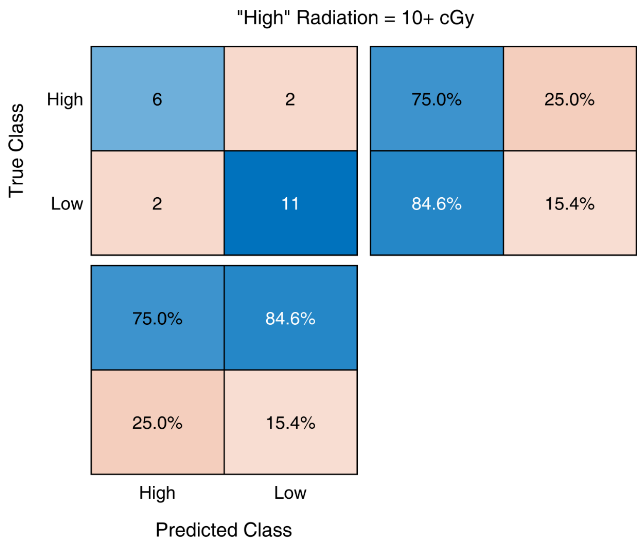
RADIATION THRESHOLD PREDICTION (ATRC & MCL, UNIFORM PRIOR): ^4He





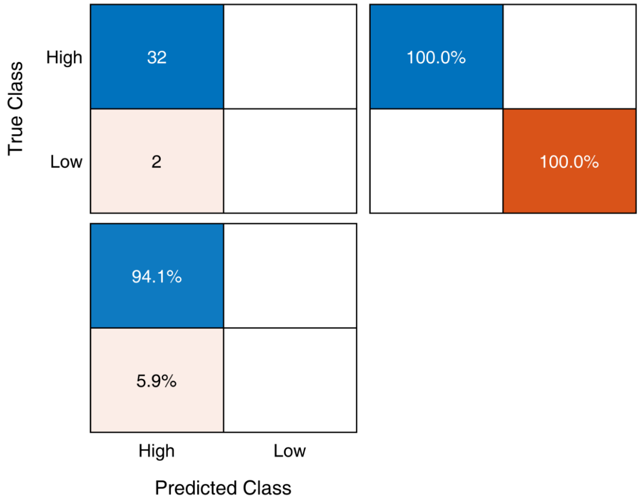
RADIATION THRESHOLD PREDICTION (ATRC & MCL, UNIFORM PRIOR): ^{16}O



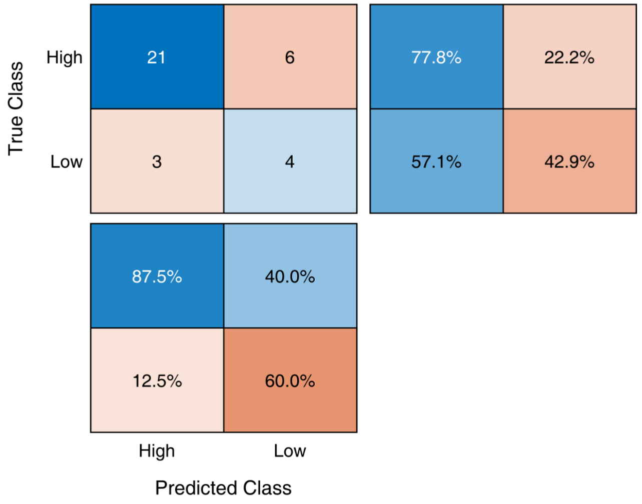


RADIATION THRESHOLD PREDICTION (ATRC ONLY, UNIFORM PRIOR): ^{56}Fe

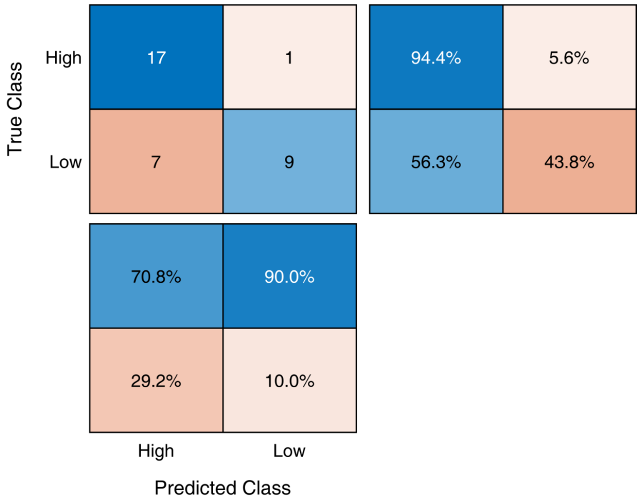
"High" Radiation = 3+ cGy



"High" Radiation = 5+ cGy



"High" Radiation = 10+ cGy



"High" Radiation = 15+ cGy