Memorial Sloan Kettering Cancer Center

IMPACT annotator

November 5, 2018

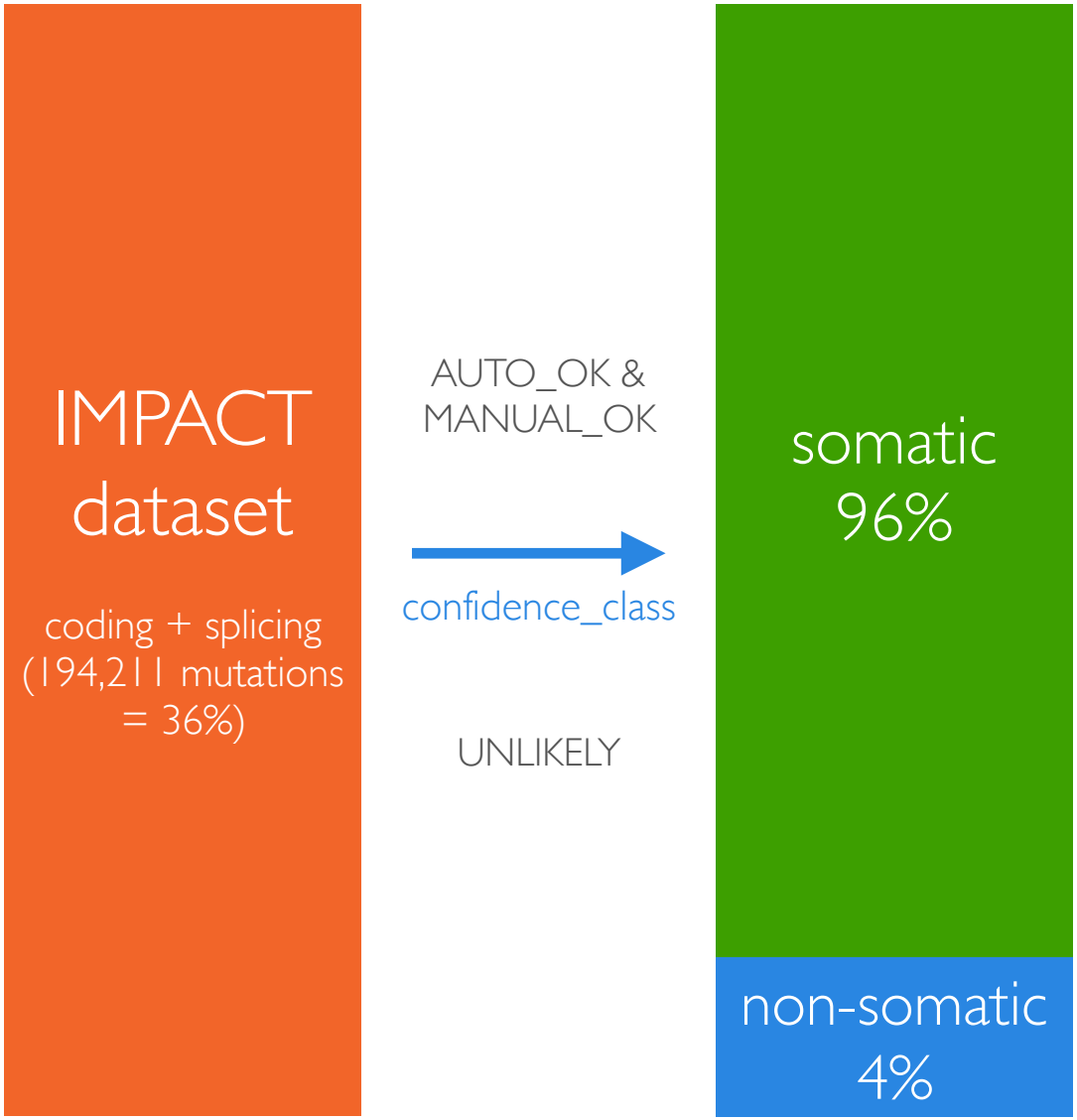
Pierre Guilmin
Elsa Bernard

Different classes

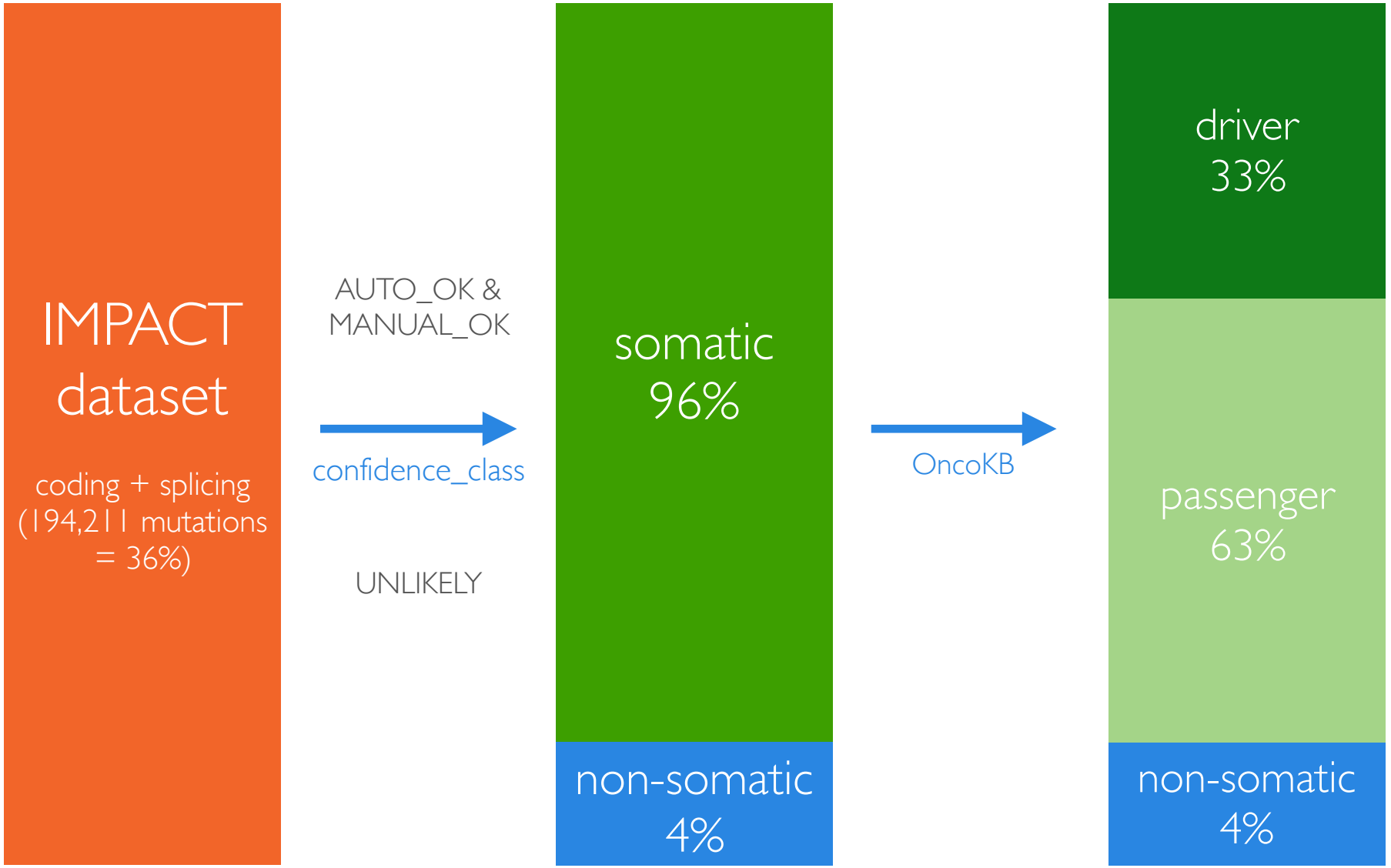
IMPACT dataset

coding + splicing
(194,211 mutations
= 36%)

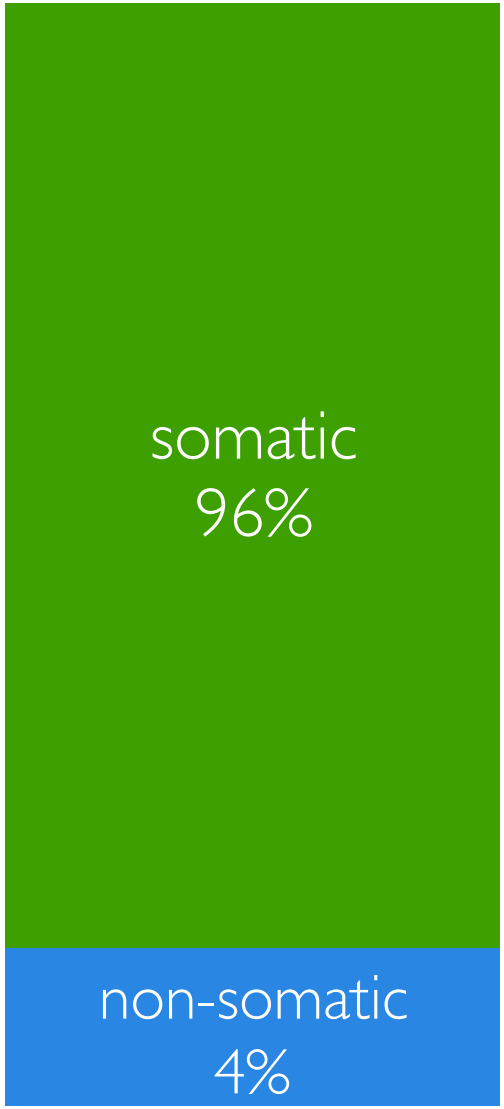
Different classes

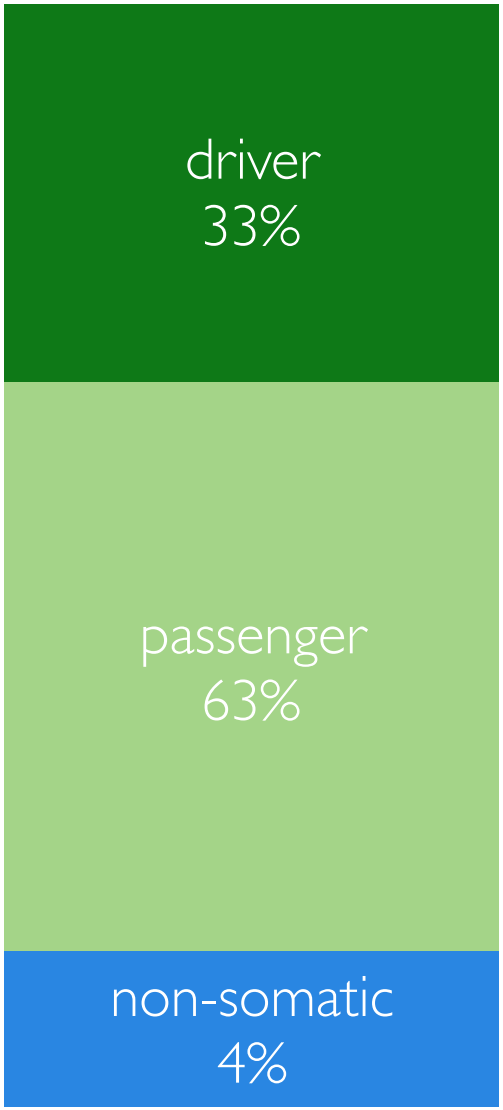


Different classes



Supervised learning





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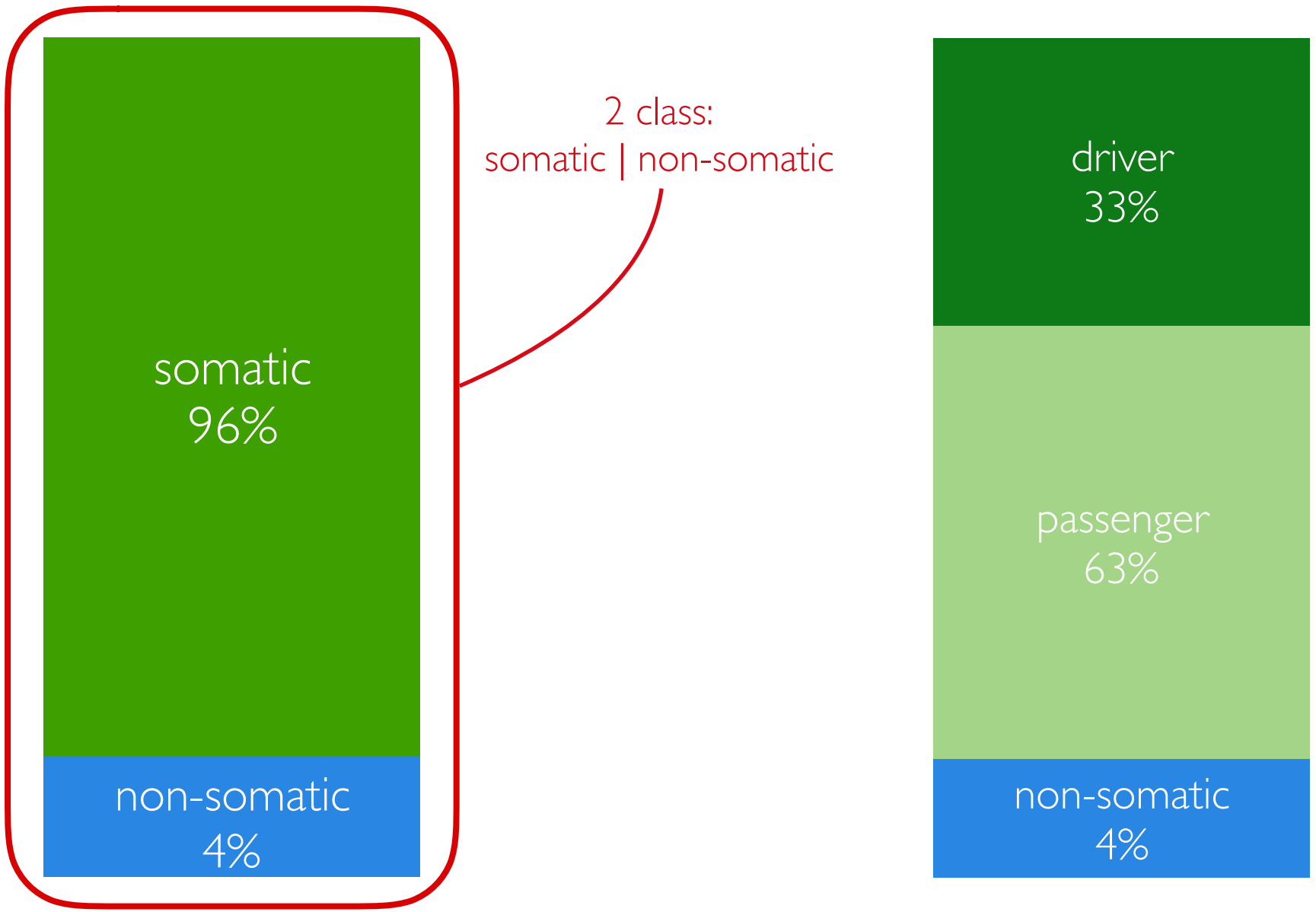

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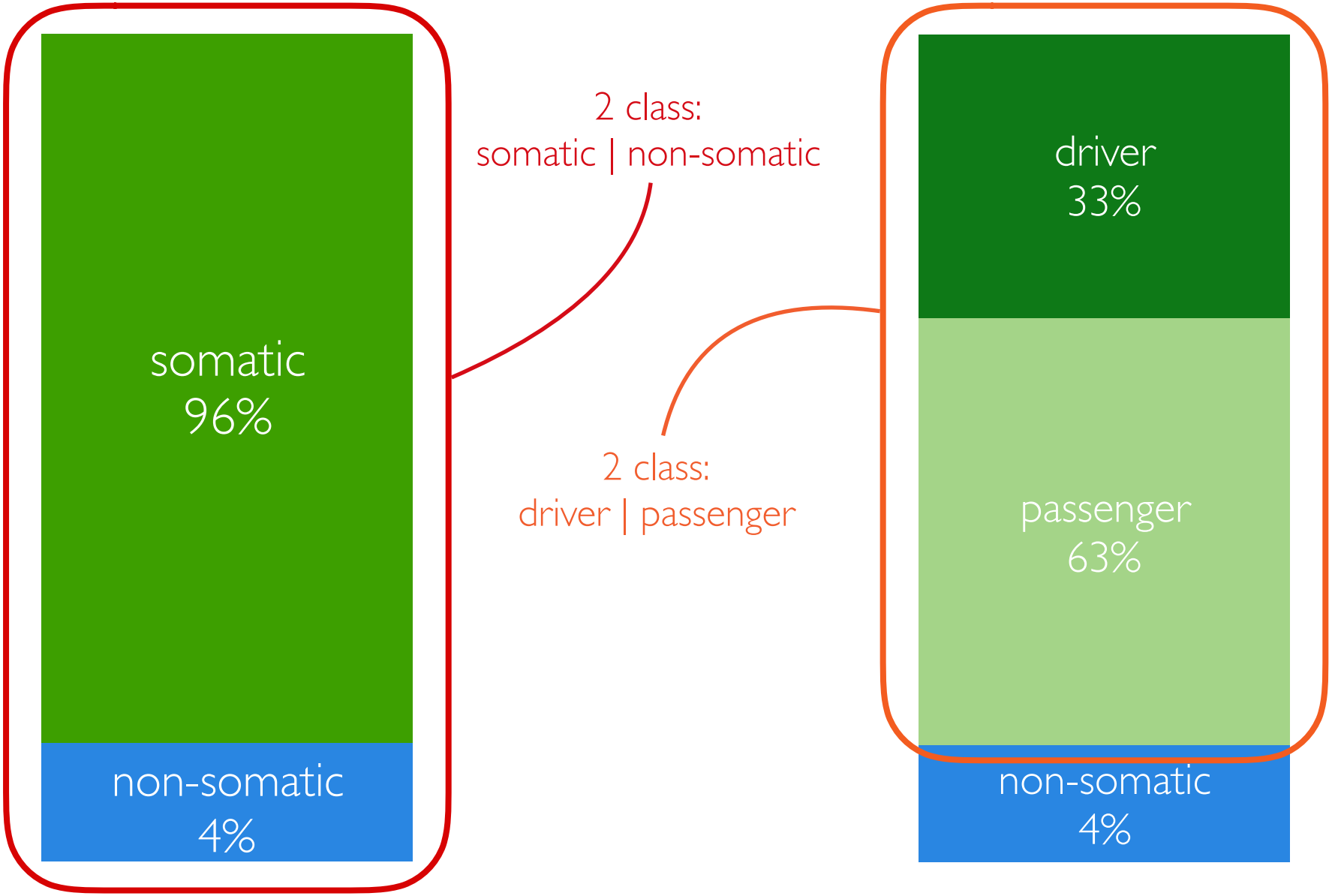

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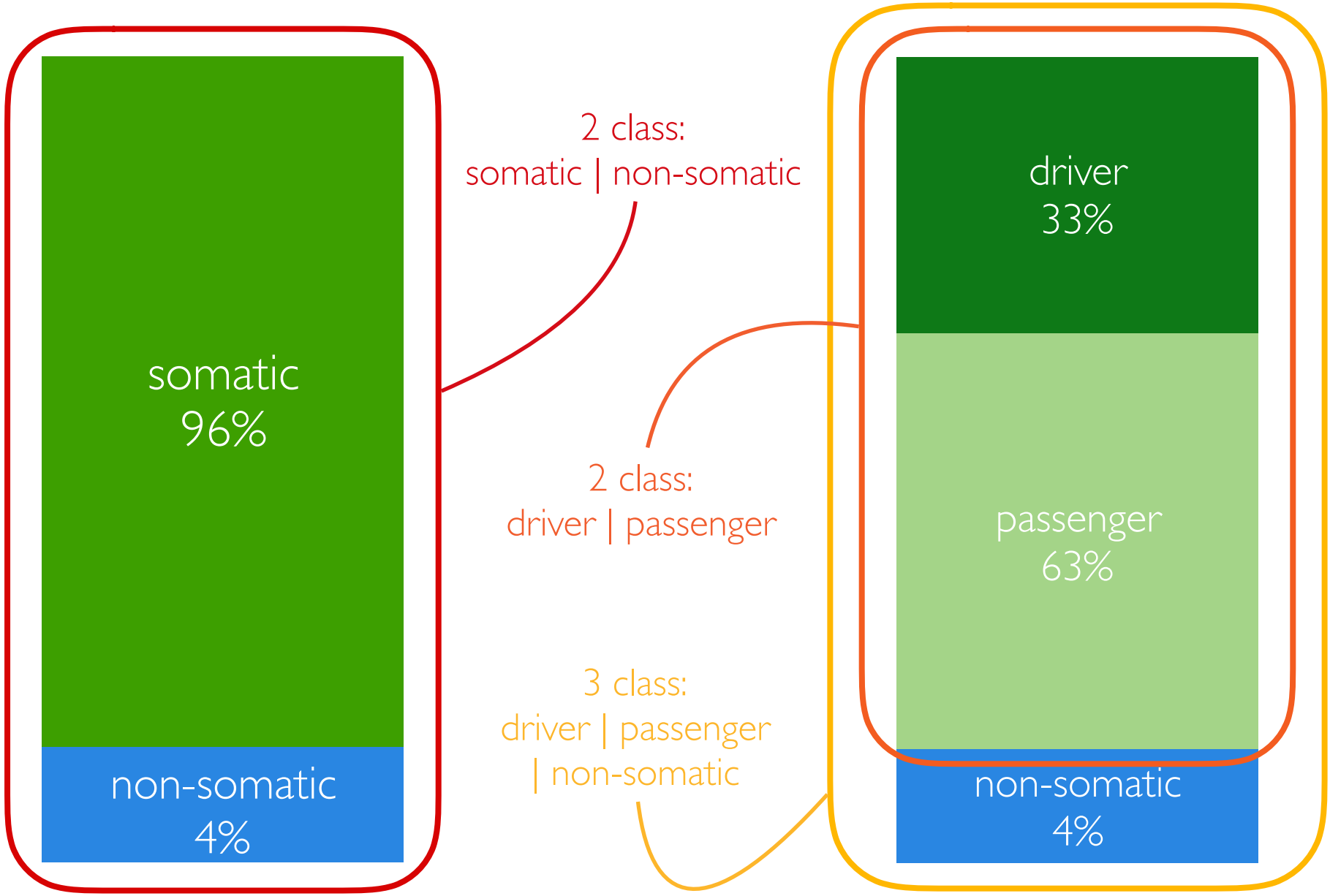
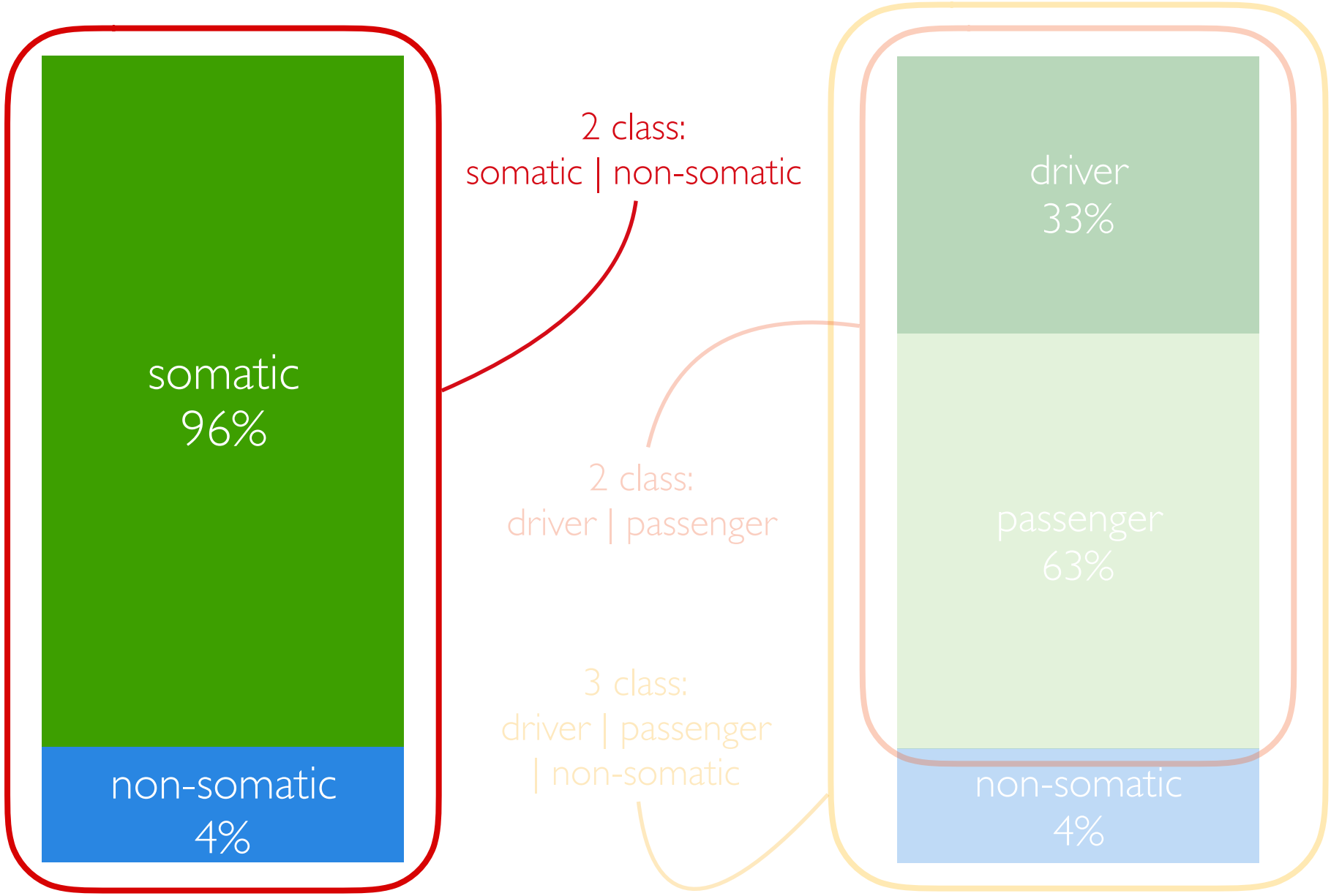
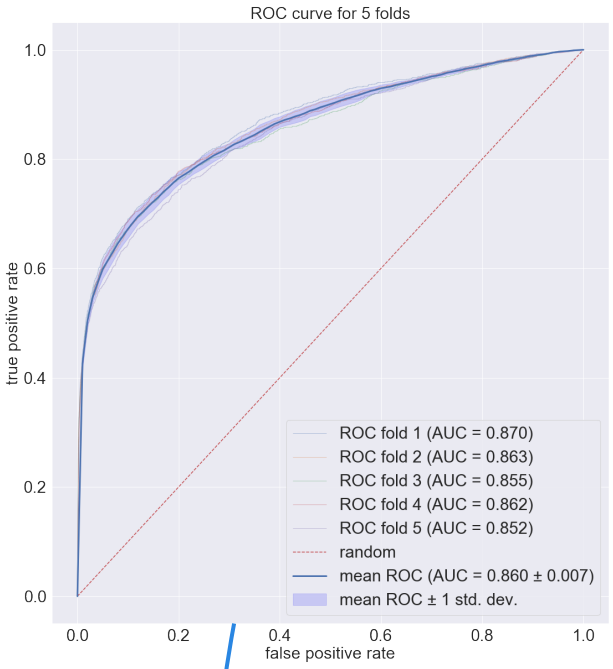
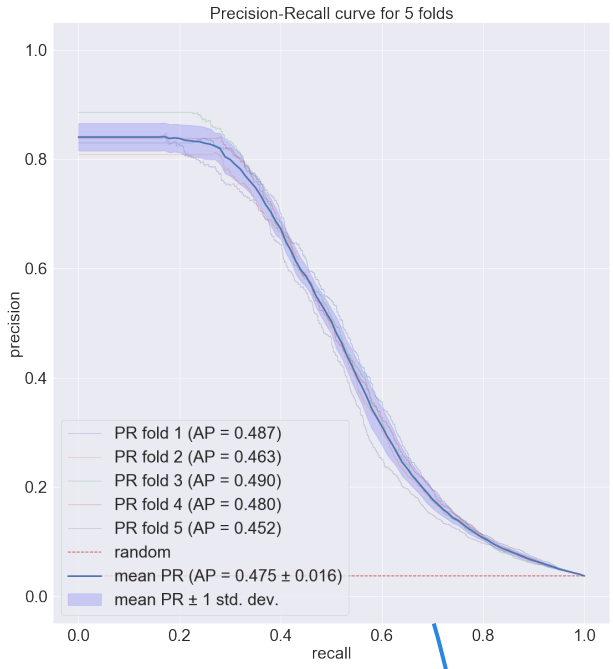


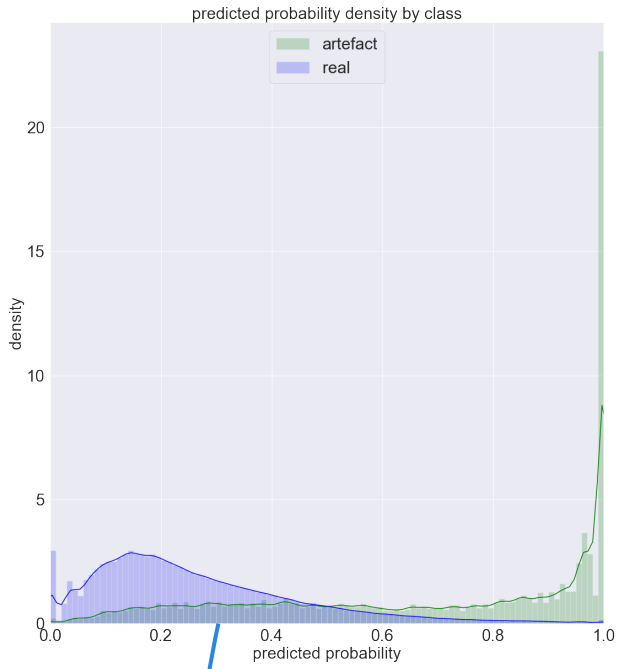
Supervised learning



Main metrics used







ROC AUC

area under the ROC curve

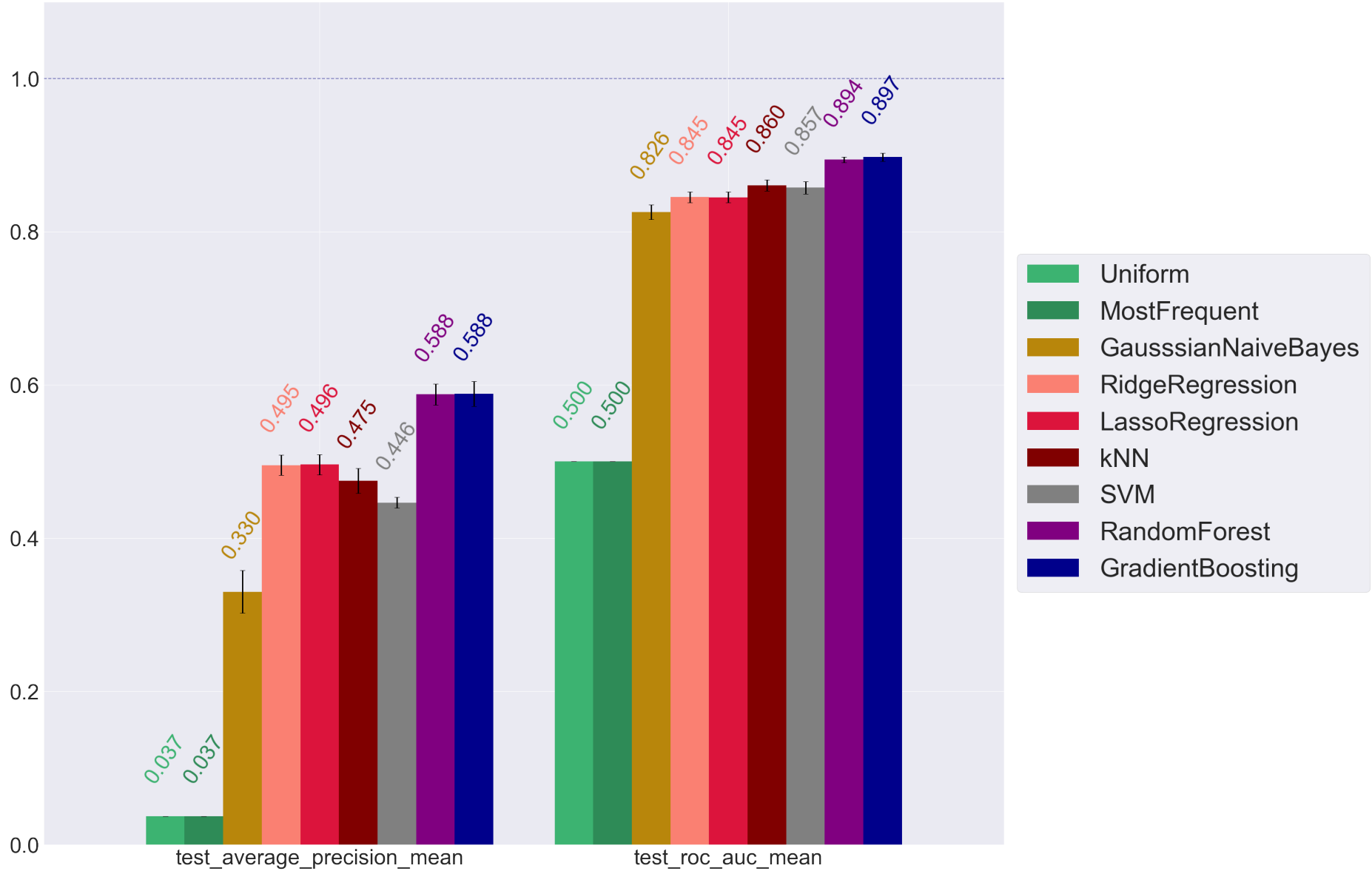
average precision

area under the precision-recall curve

Probability distribution

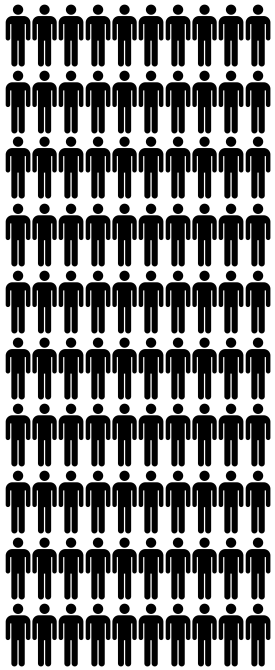
probability predicted by the classifier for each class

Algorithm comparison



IMPACT annotator

100 patients



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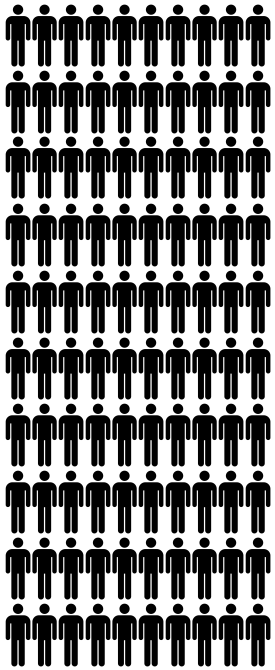
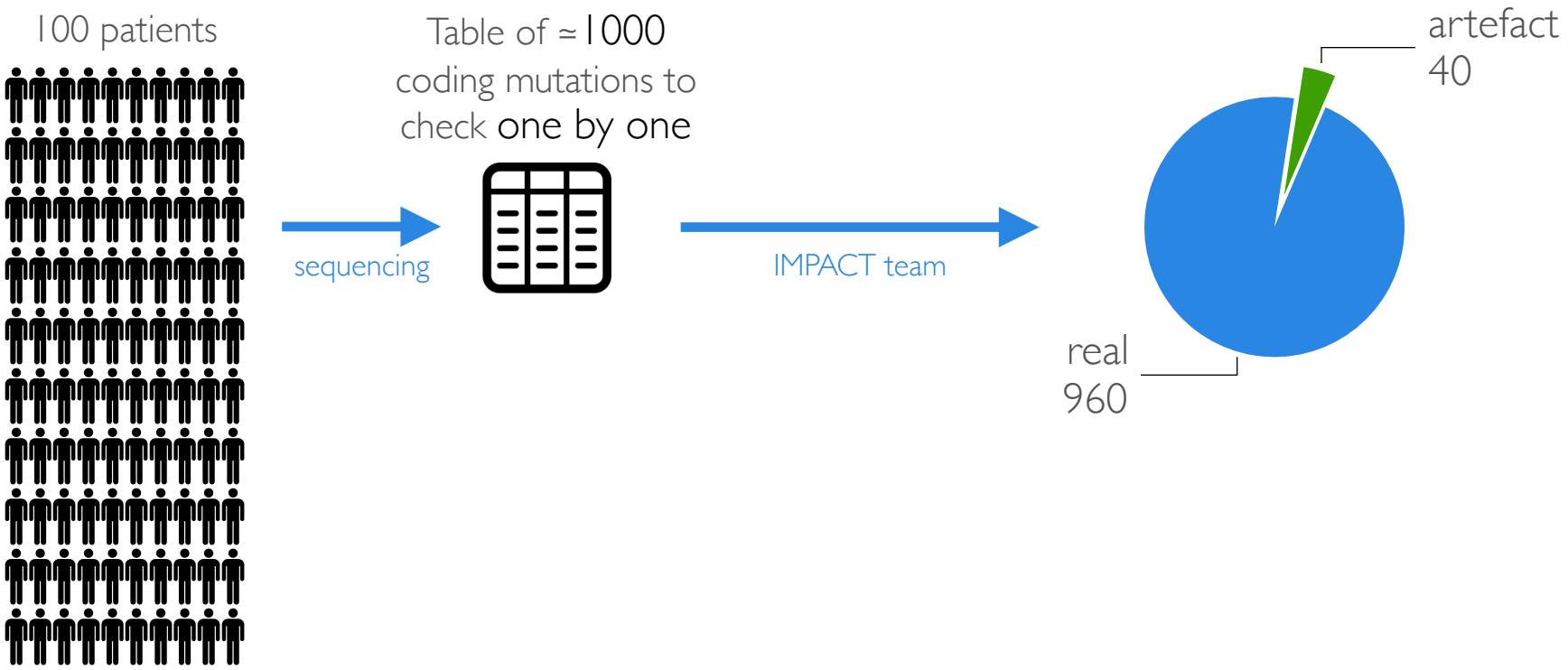


sequencing

Table of ≃1000 coding mutations to check one by one

IMPACT annotator



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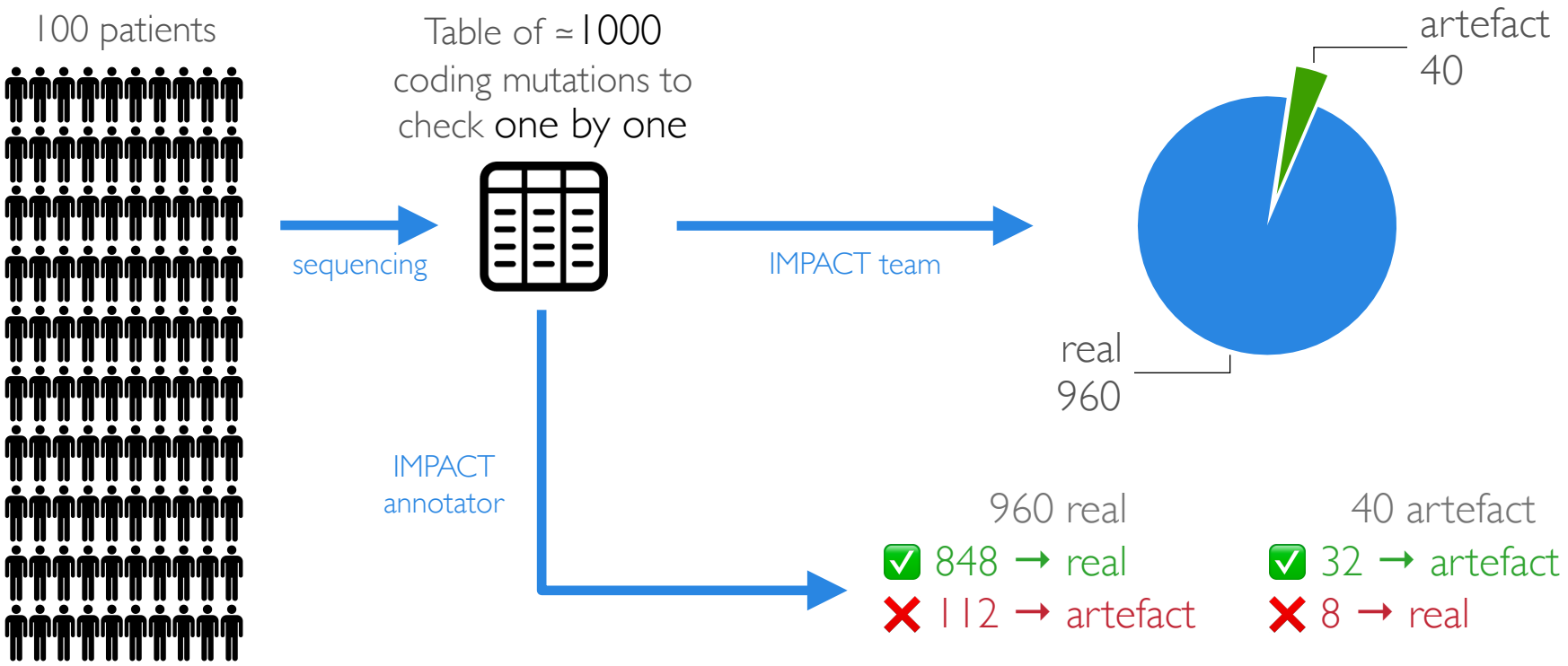

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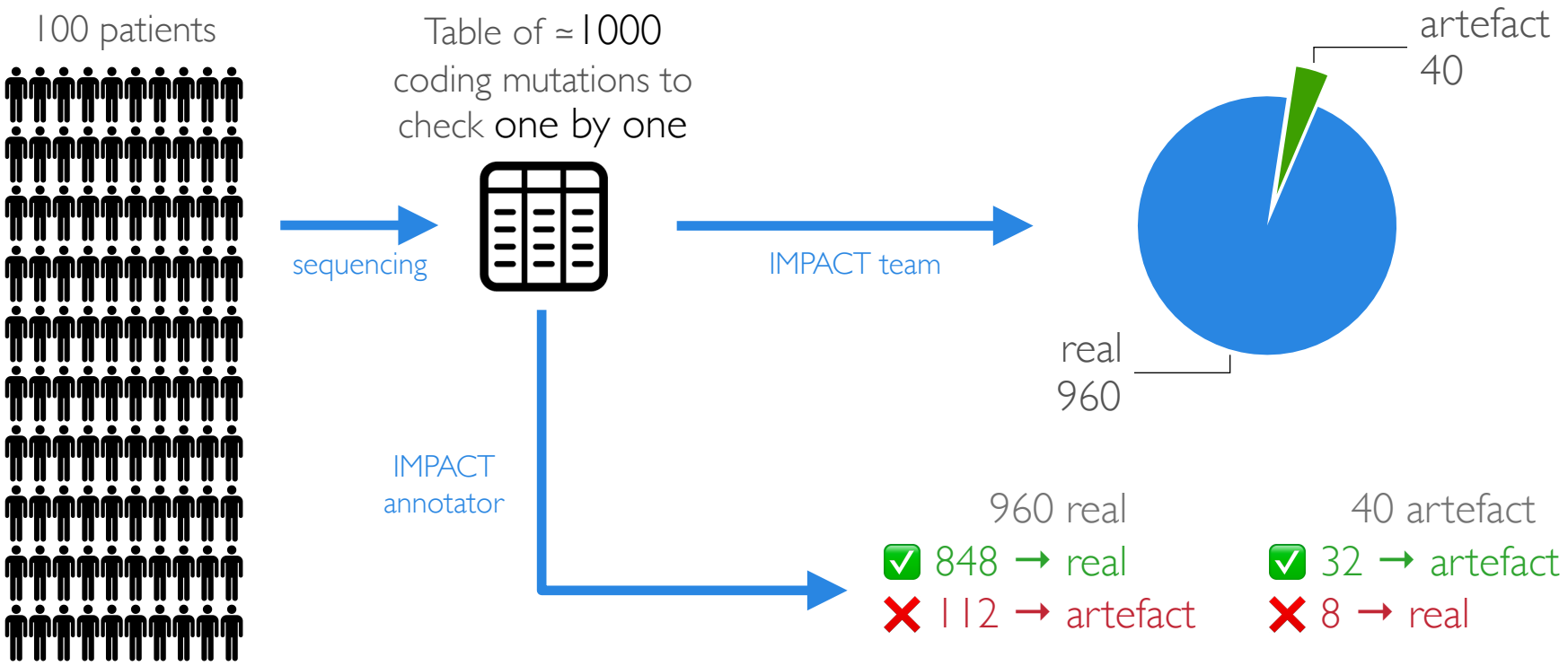


IMPACT team

1000/1000 mutations to check one by one

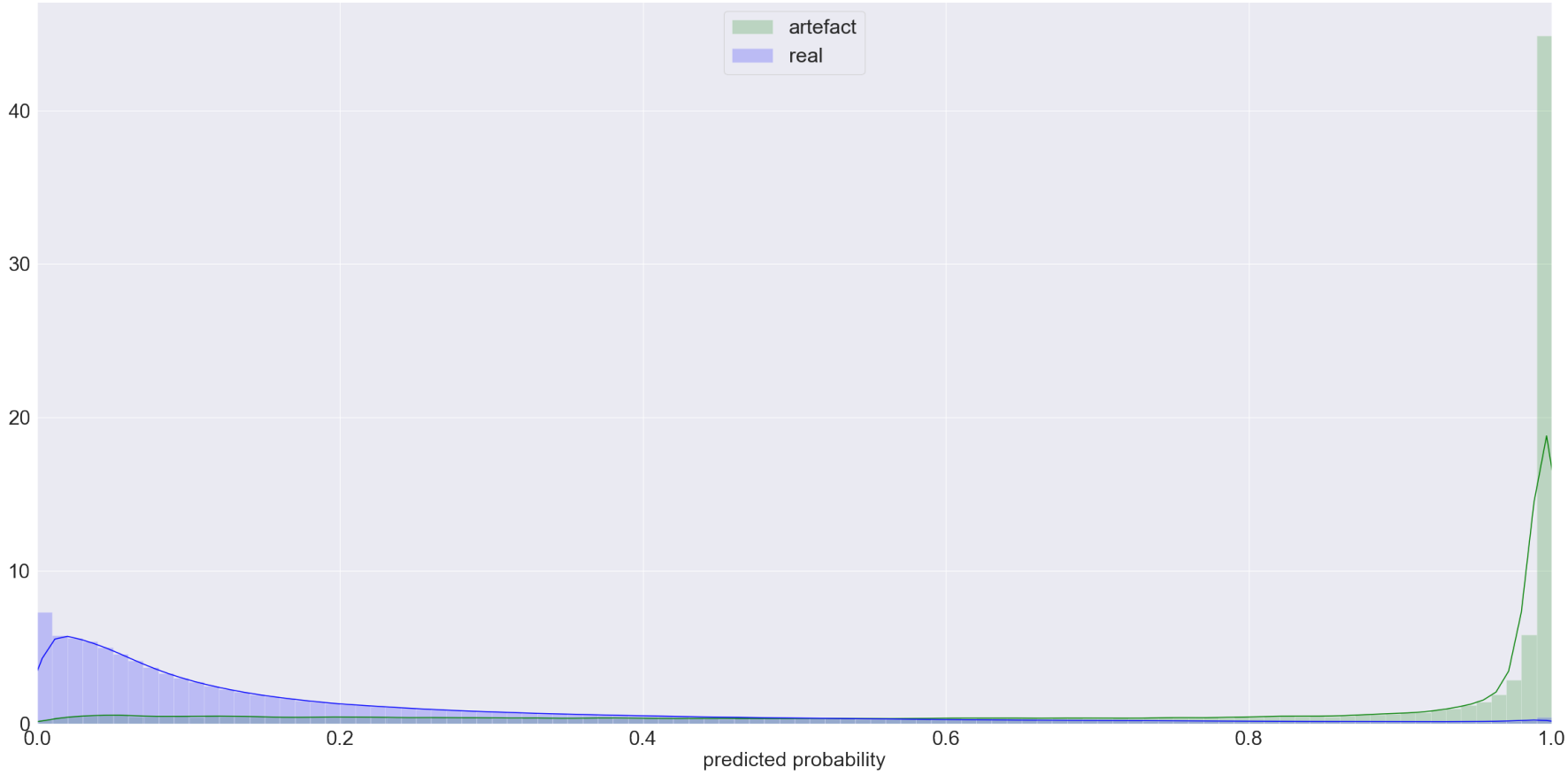
❌ 0/40 artefacts considered as real

IMPACT annotator

144/1000 mutations to check one by one

❌ 8/40 artefacts considered as real

Threshold choice

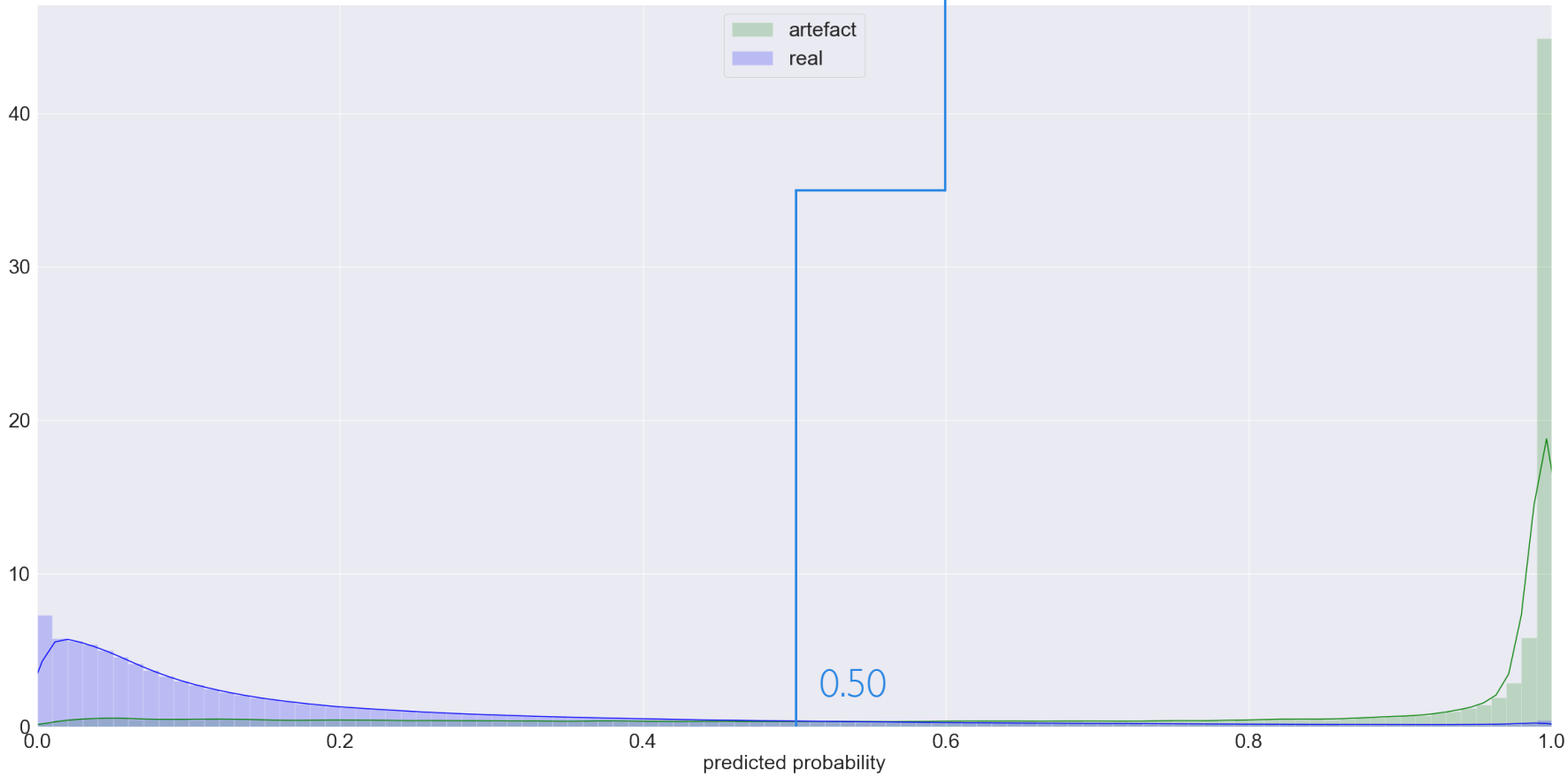


Threshold choice

threshold = 0.5

📝 144 mutations to check

960 real	40 artefact
✅ 848 → real	✅ 32 → artefact
❌ 112 → artefact	❌ 8 → real



Threshold choice

threshold = 0.25

296

960 real	40 artefact
✅ 699	✅ 35
❌ 261	❌ 5

threshold = 0.5

144 mutations to check

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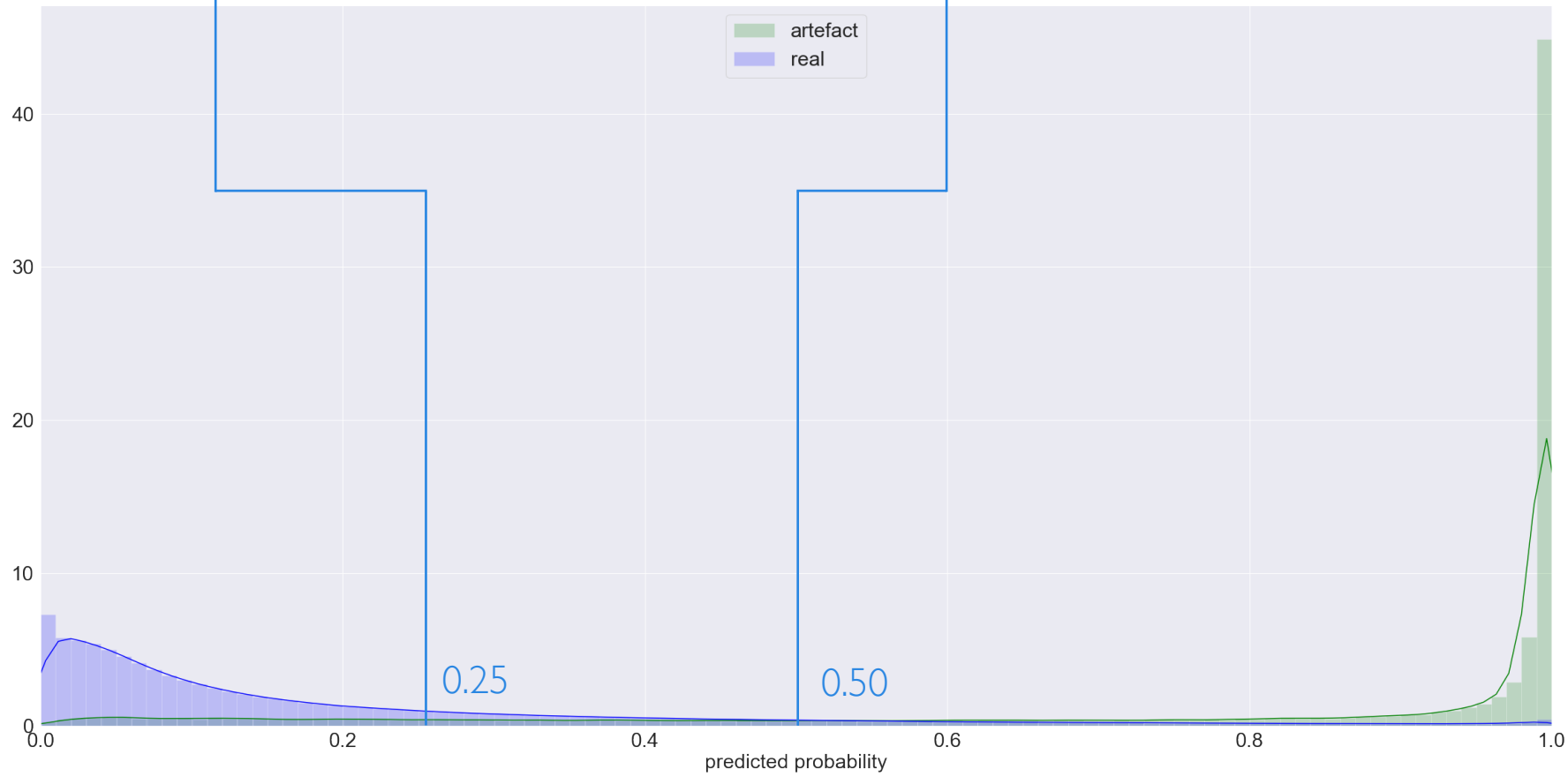
✅ 848 → real	✅ 32 → artefact
❌ 112 → artefact	❌ 8 → real



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144 mutations to check

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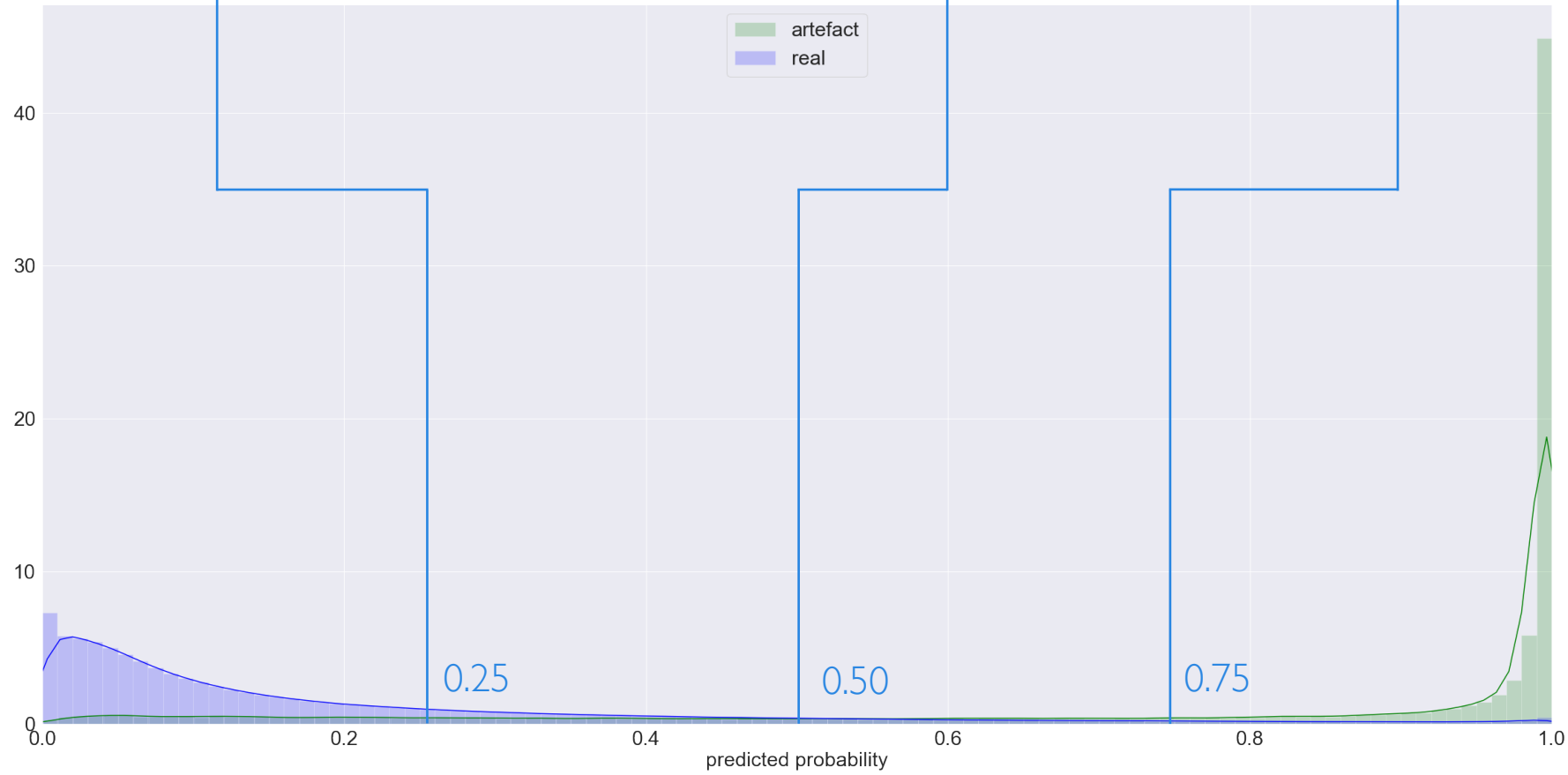
threshold = 0.75
72

960 real	40 artefact
✅ 916	✅ 28
❌ 44	❌ 12



The features group

NGS (x 11)

- tumor & normal depth, vaf and count
- tumor +/- strand count
- sample_coverage

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somatic driver (x 4)

- COSMIC count
- is a hotspot, is a 3d hotspot
- OncoKB oncogenic

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AF (x 12)

- in dbSNP
- gnomAD total AF and AF by population (AFR, AMR, ASJ, …)

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Consequence (x 6)

- gene type
- mutation consequence (stopgain, frameshift, …)
- VEP_IMPACT, VEP_CLIN_SIG
- SIFT and PolyPhen class

The features group

AF (x 12)

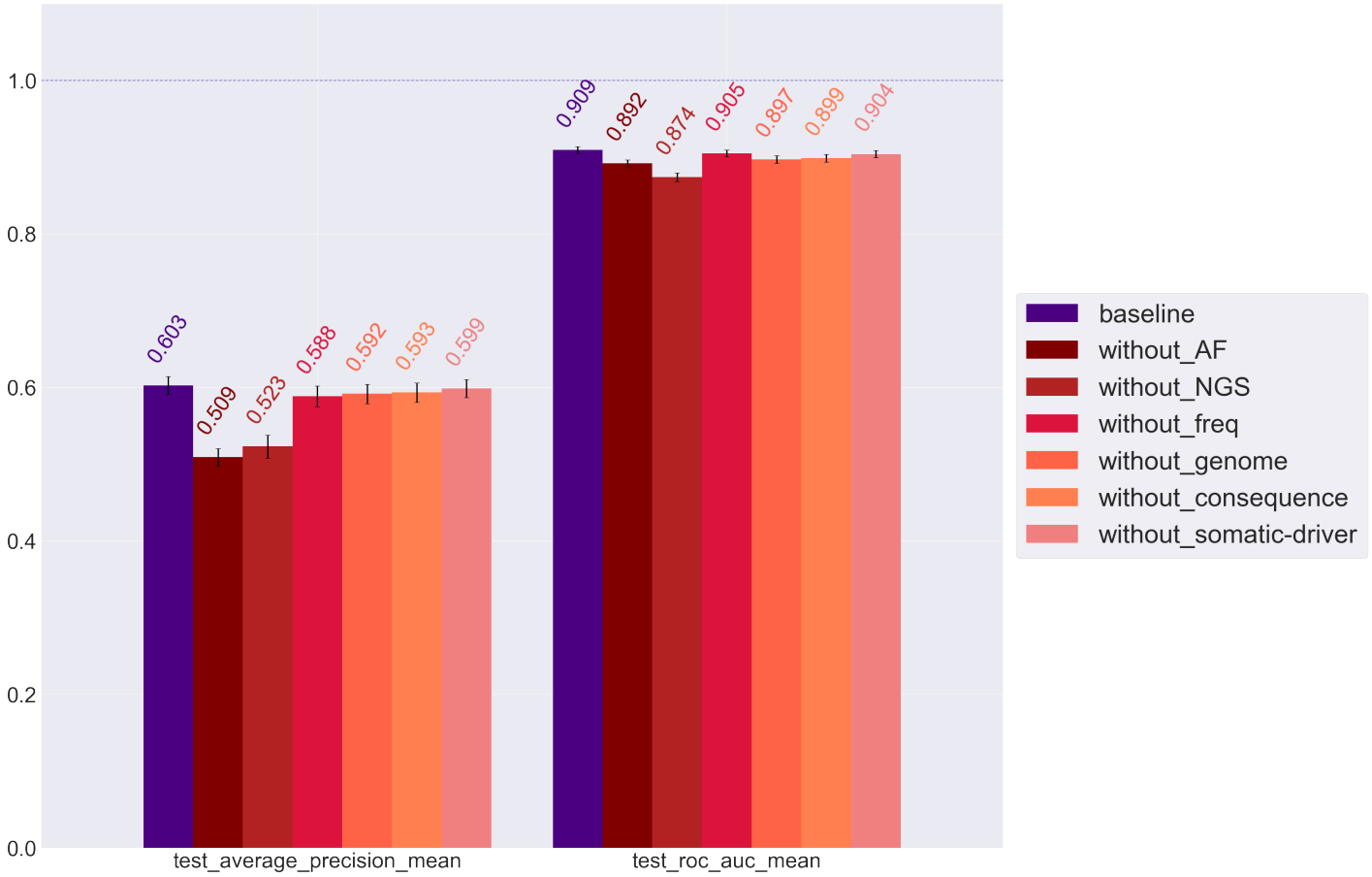
- in dbSNP
- gnomAD total AF and AF by population (AFR, AMR, ASJ, …)

NGS (x 11)

- tumor & normal depth, vaf and count
- tumor positive and negative count
- sample_coverage

freq (x 1)

- frequency in normals



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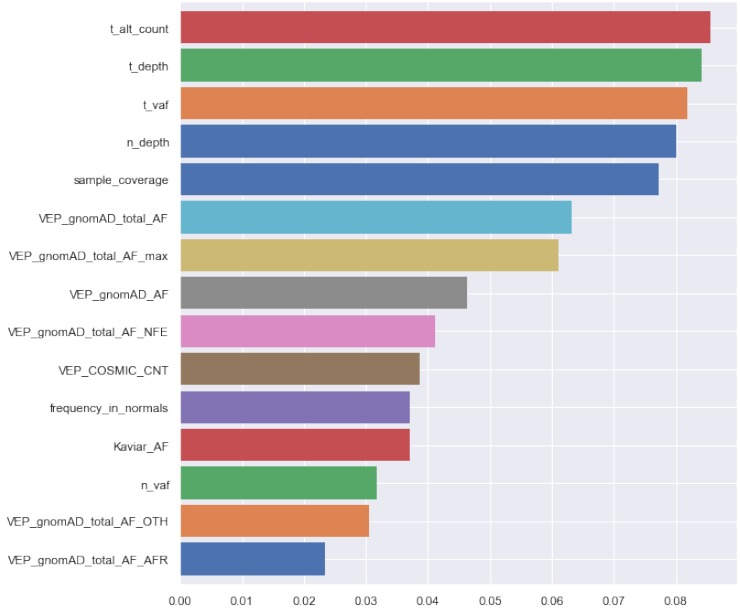
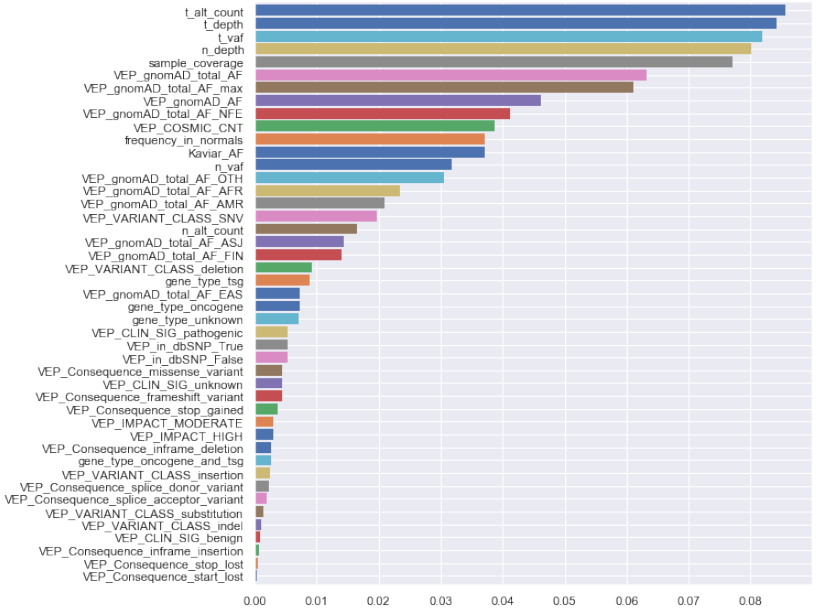
Individual features importance

Random Forest (1000 trees)





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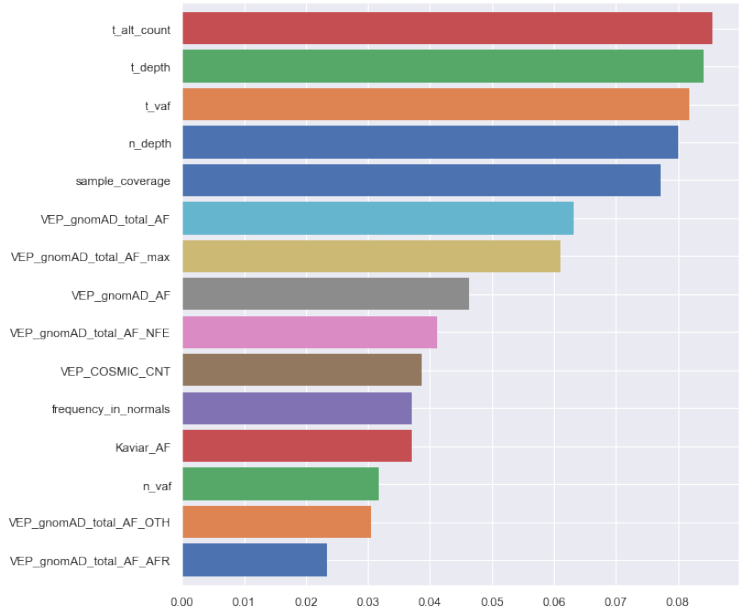
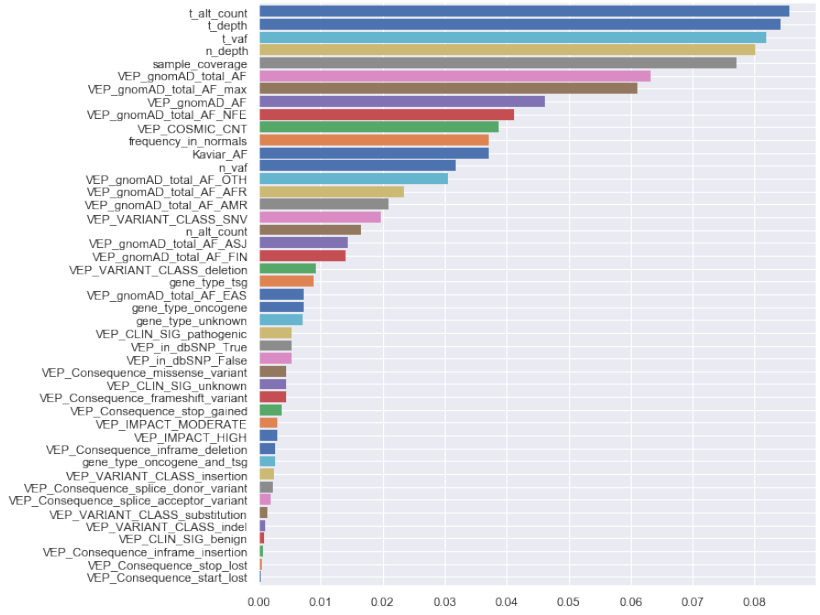
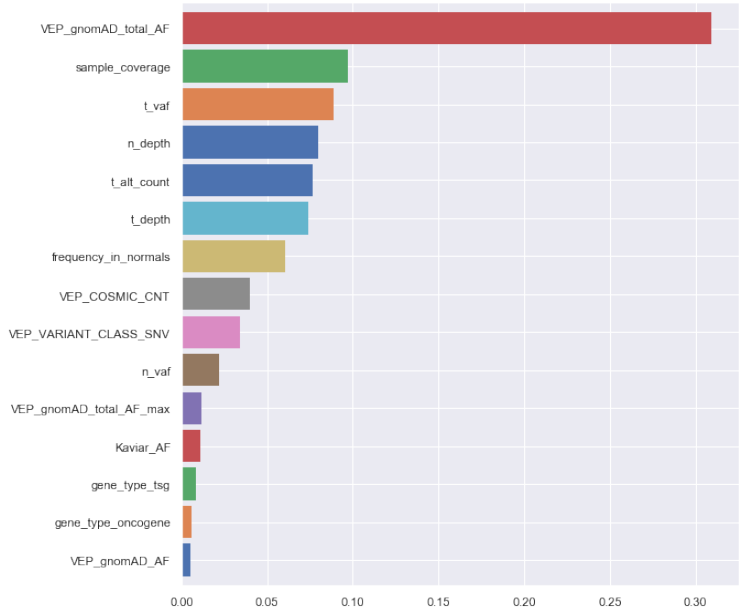
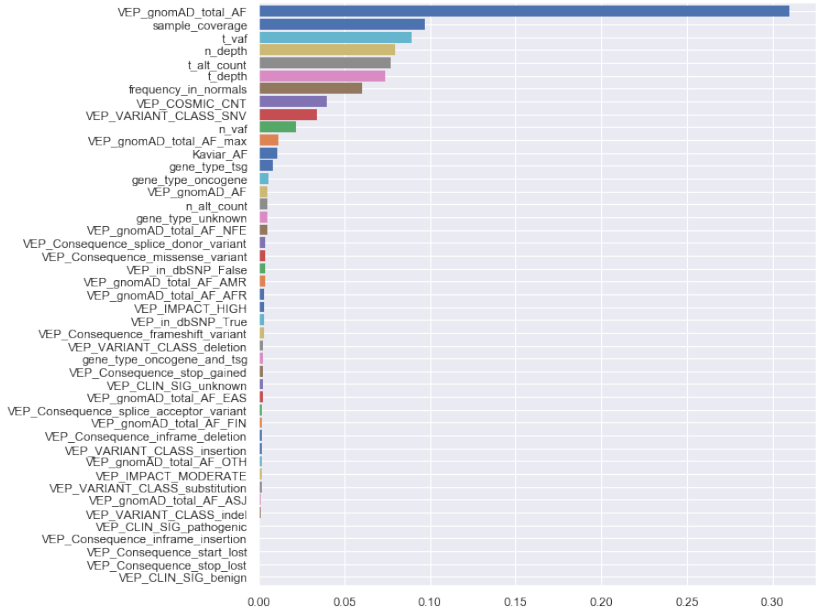


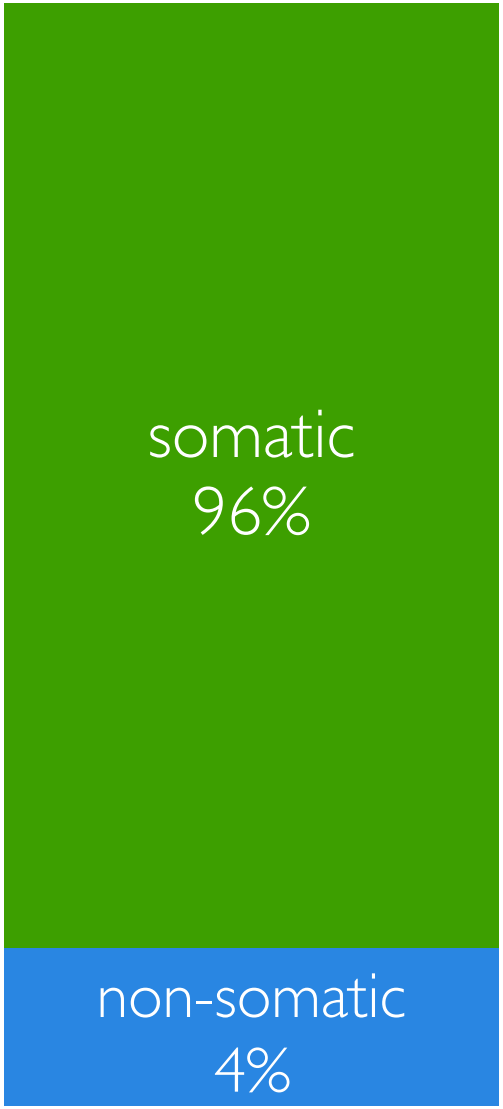


Gradient Boosting (1000 trees)





Imbalanced learning



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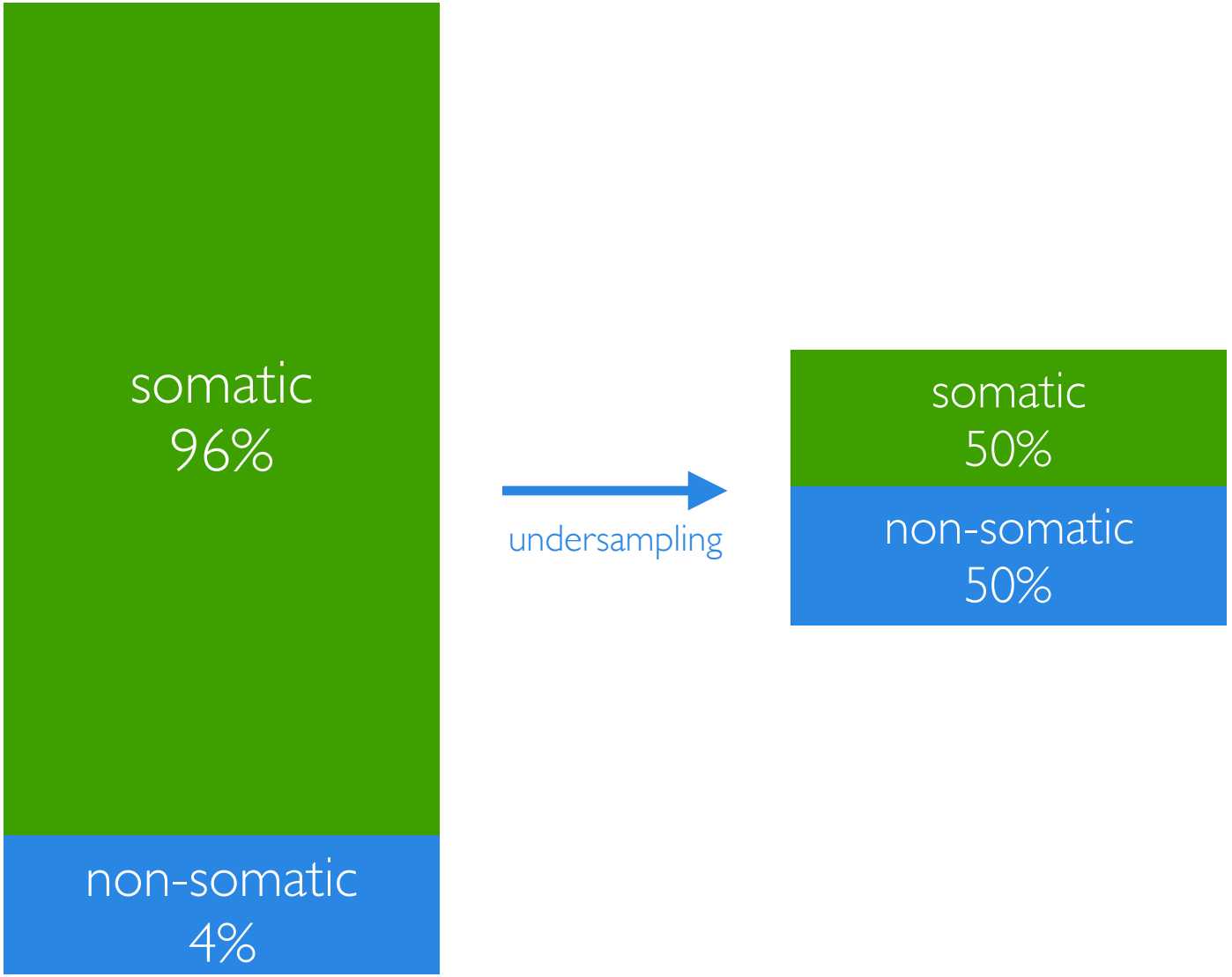

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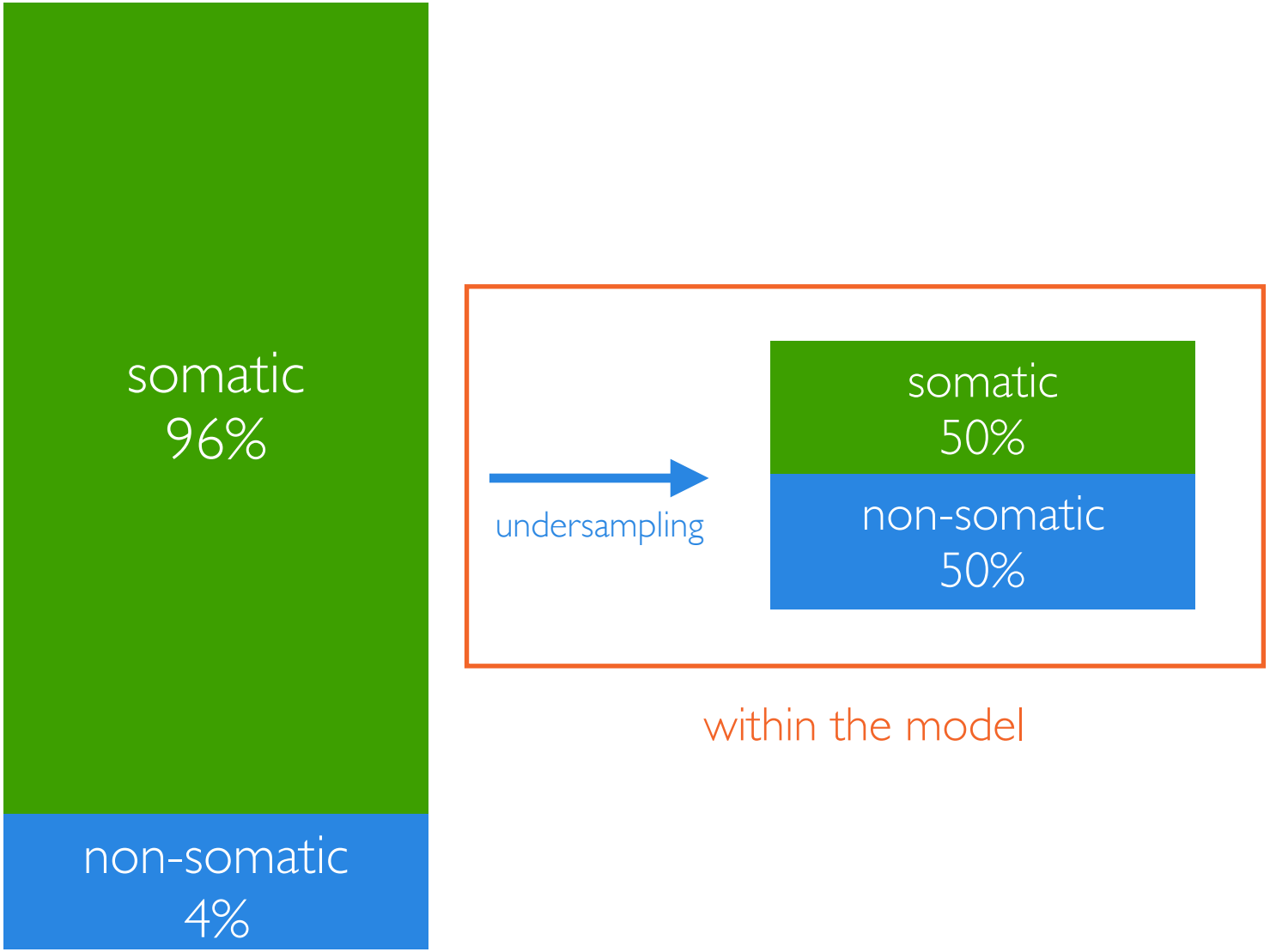

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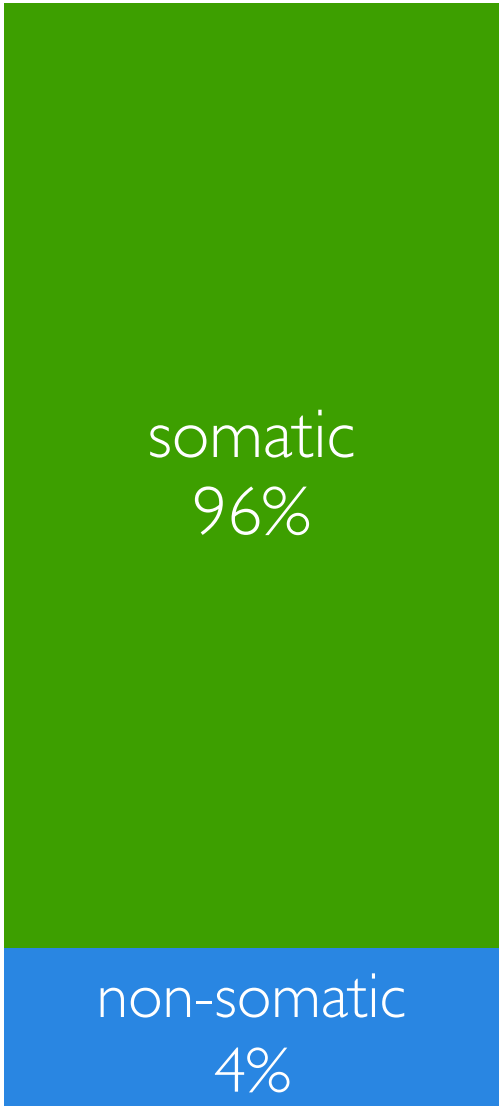
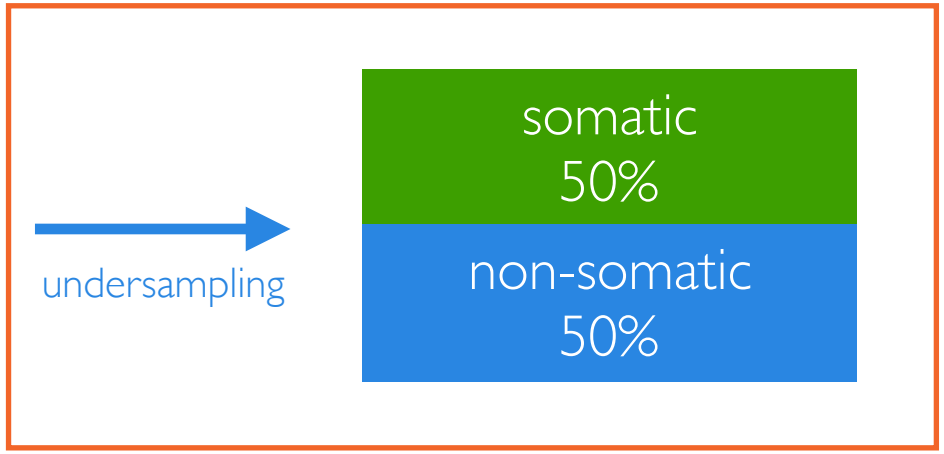
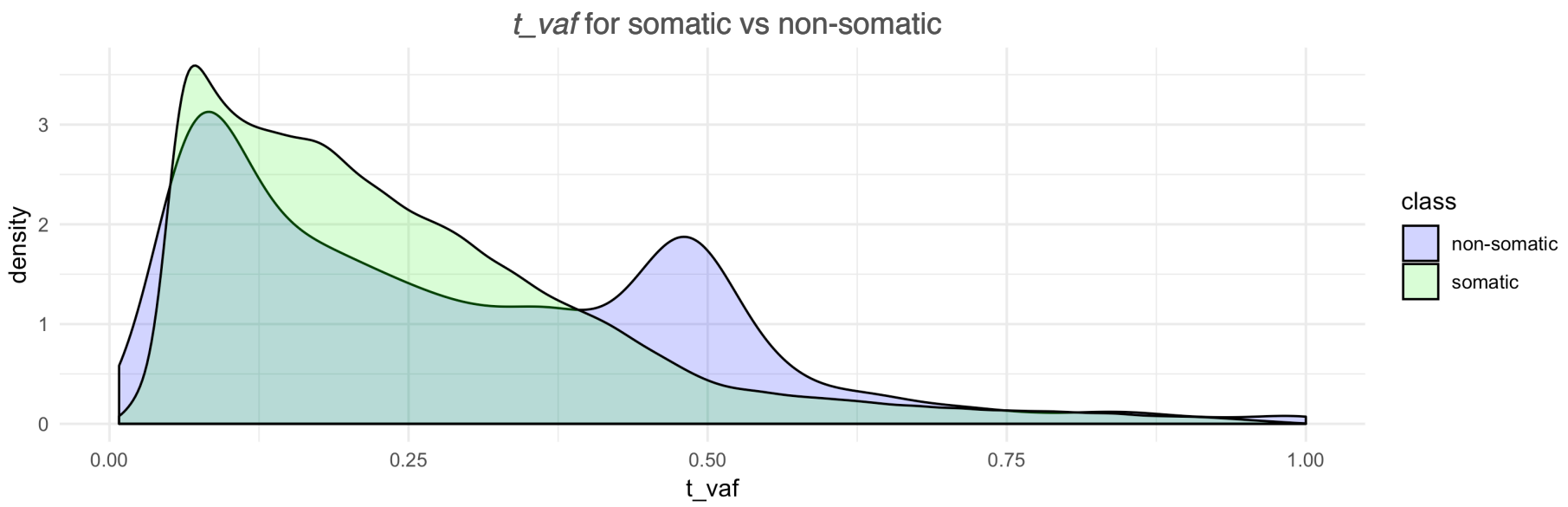




within the model

So the dataset used to train the model is only 8% of the whole dataset (7,199 real and 7,199 artefact mutations)

Removing the unmatched samples



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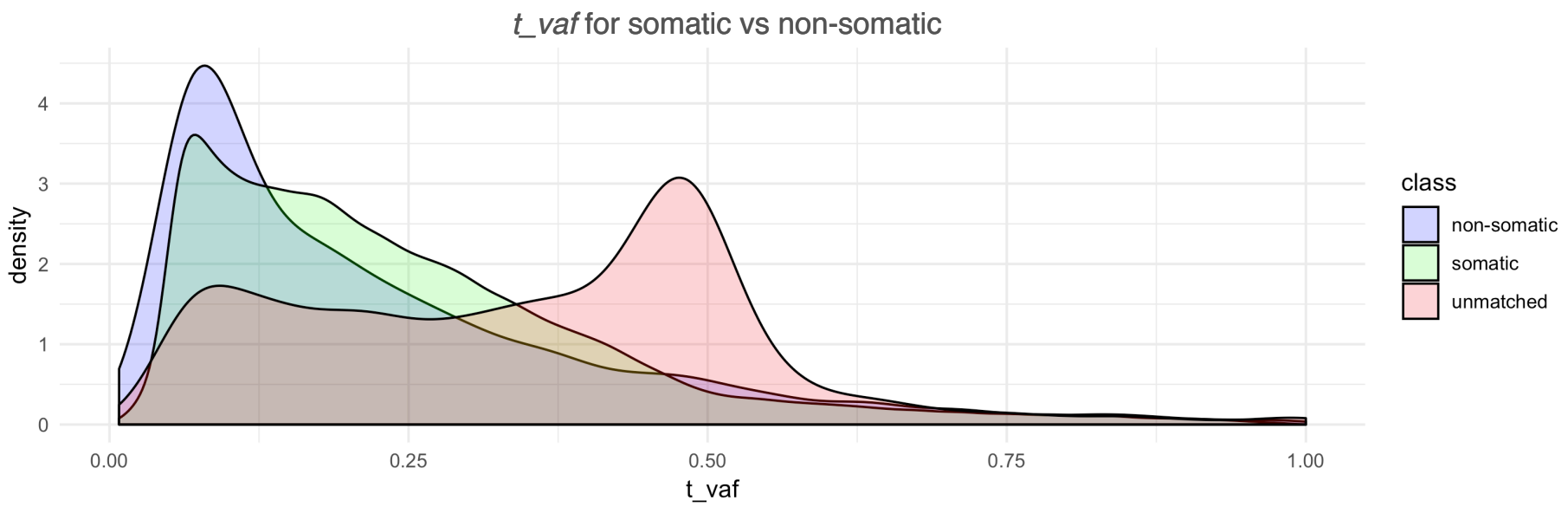

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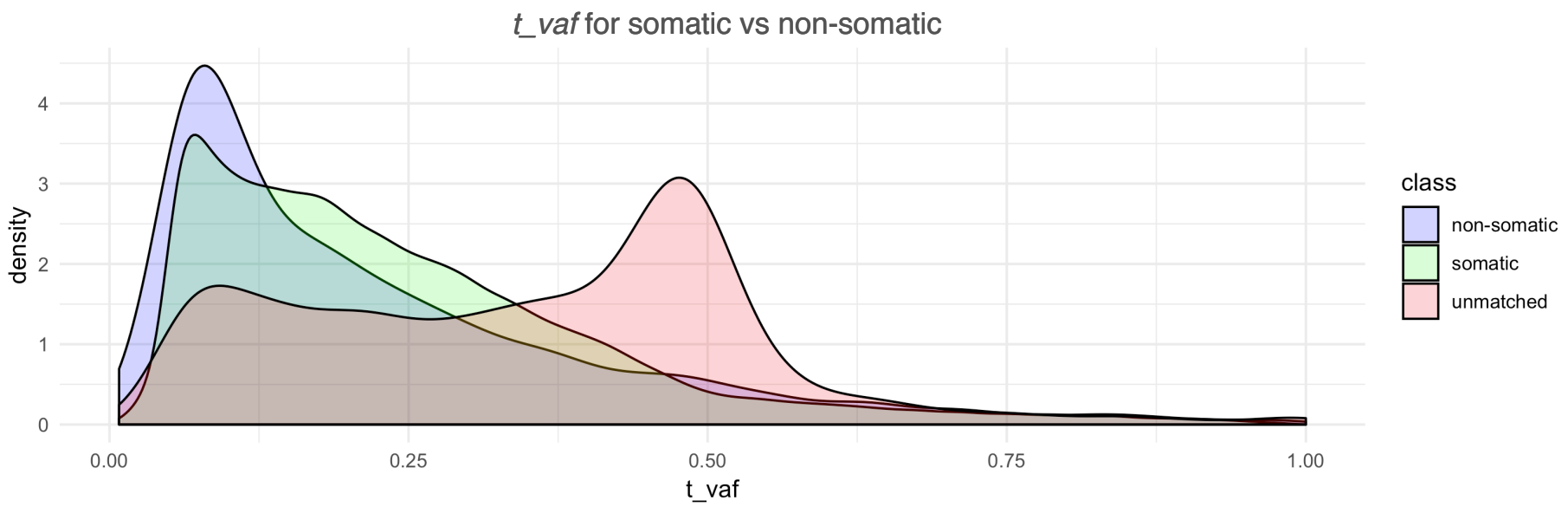
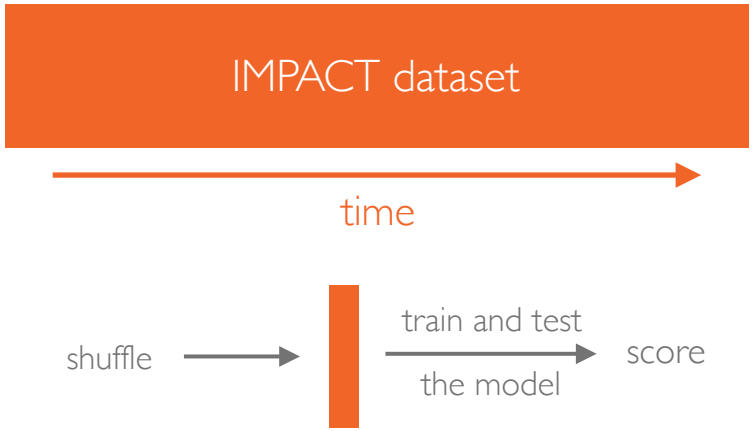


Without the unmatched artefacts (and missing rows):
4,477 artefacts (instead of 7,199)

The sorted dataset phenomenon

The sorted dataset phenomenon



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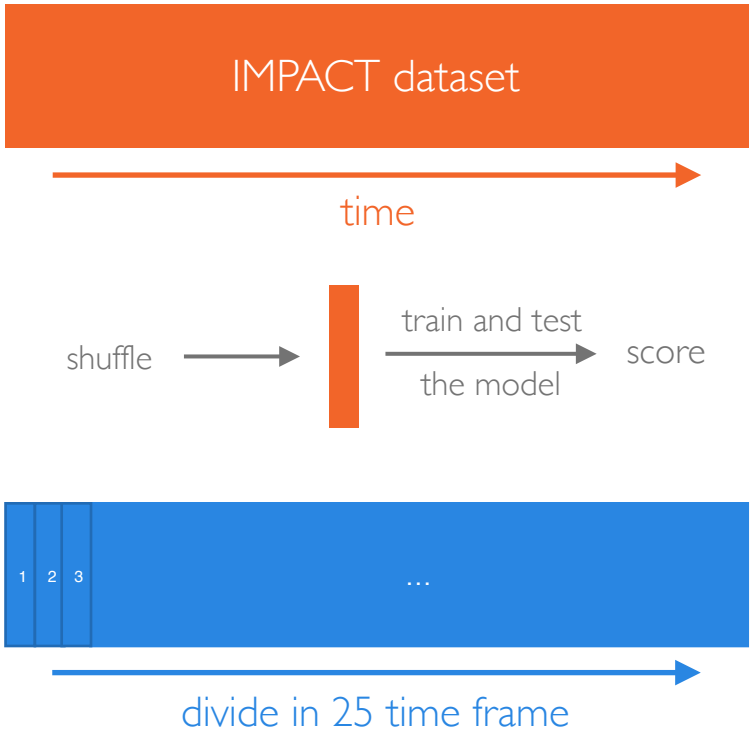

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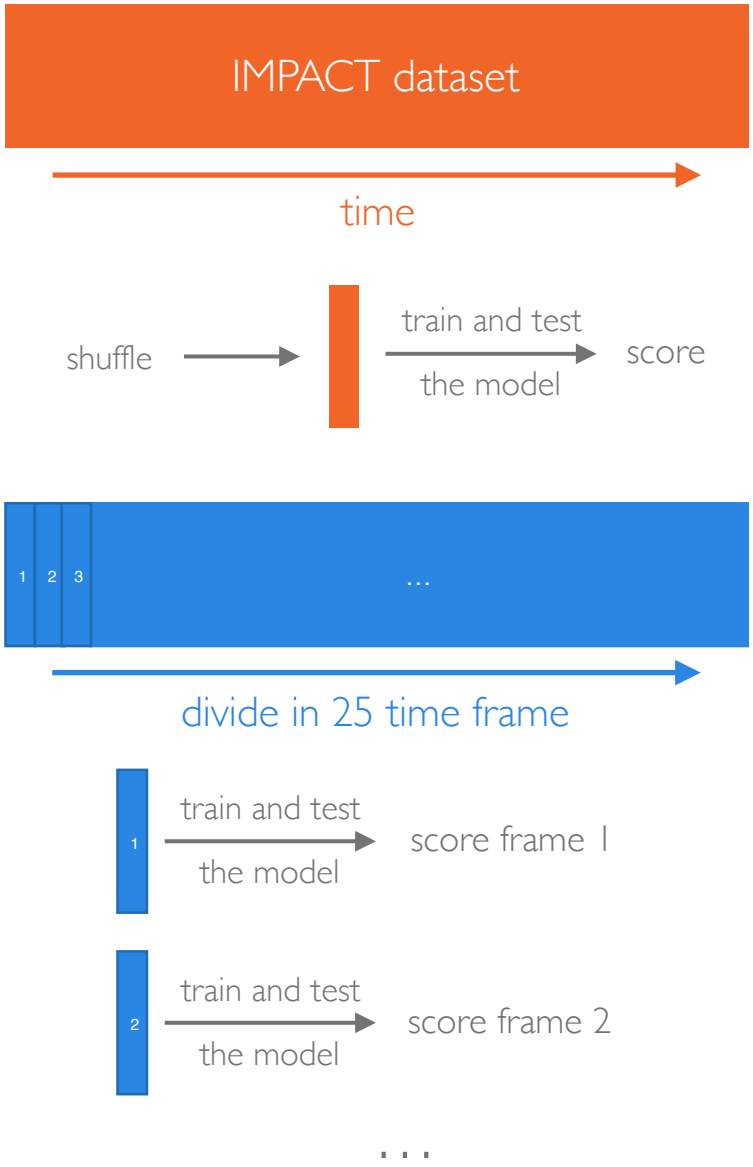

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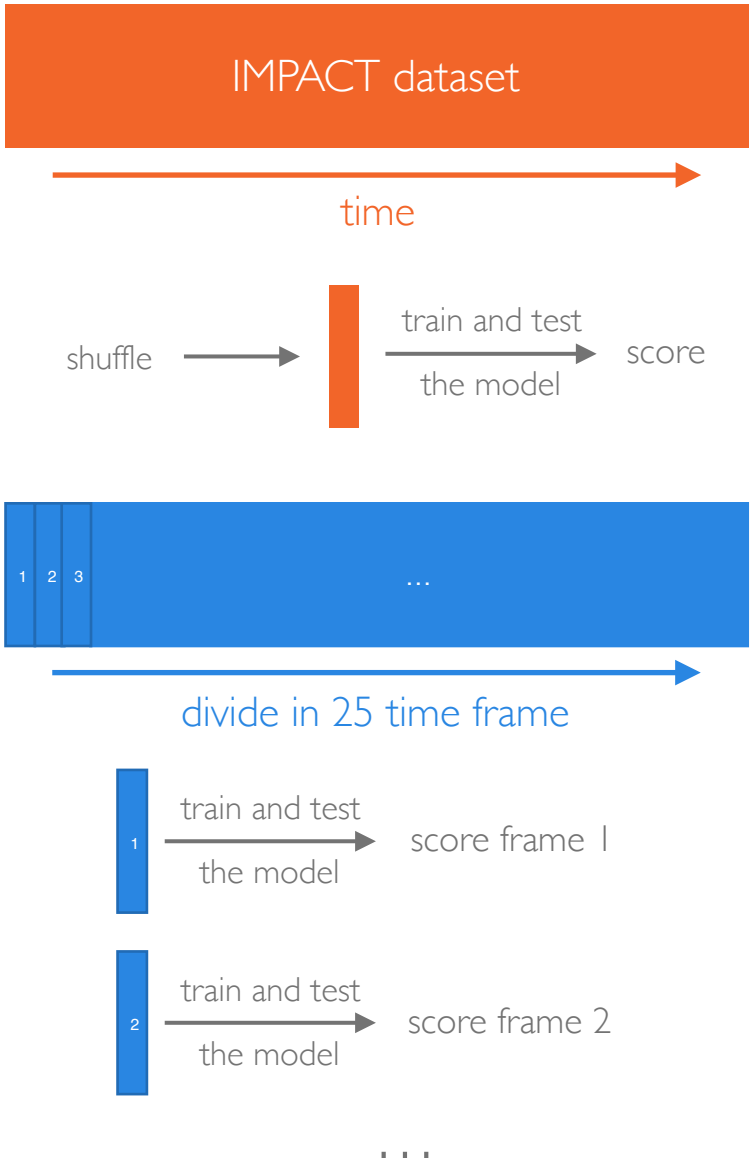

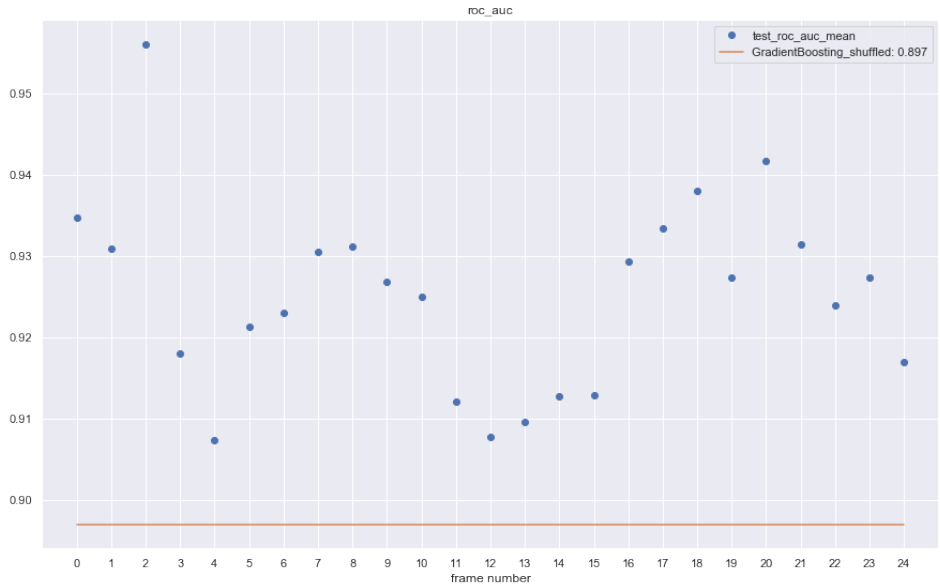

The sorted dataset phenomenon