

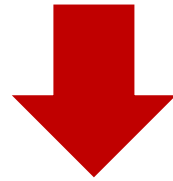
# Validation / Evaluation

Christian Salvatore  
Scuola Universitaria Superiore IUSS Pavia

# VALIDATION & PERFORMANCE EVALUATION

# How to test a machine-learning classifier?

A good validation process allows to obtain a **minimally biased estimate** of the true diagnostic performance of the classifier



- Correct quantification of the discriminatory power of a given model (model evaluation)
- Possibility to compare classification techniques based on different approaches (model selection)

# How to test a machine-learning classifier?

For example, if parameter selection, training of the predictive model and validation are performed using the same dataset, the generated classifier will show limited generalization ability when classifying unseen samples



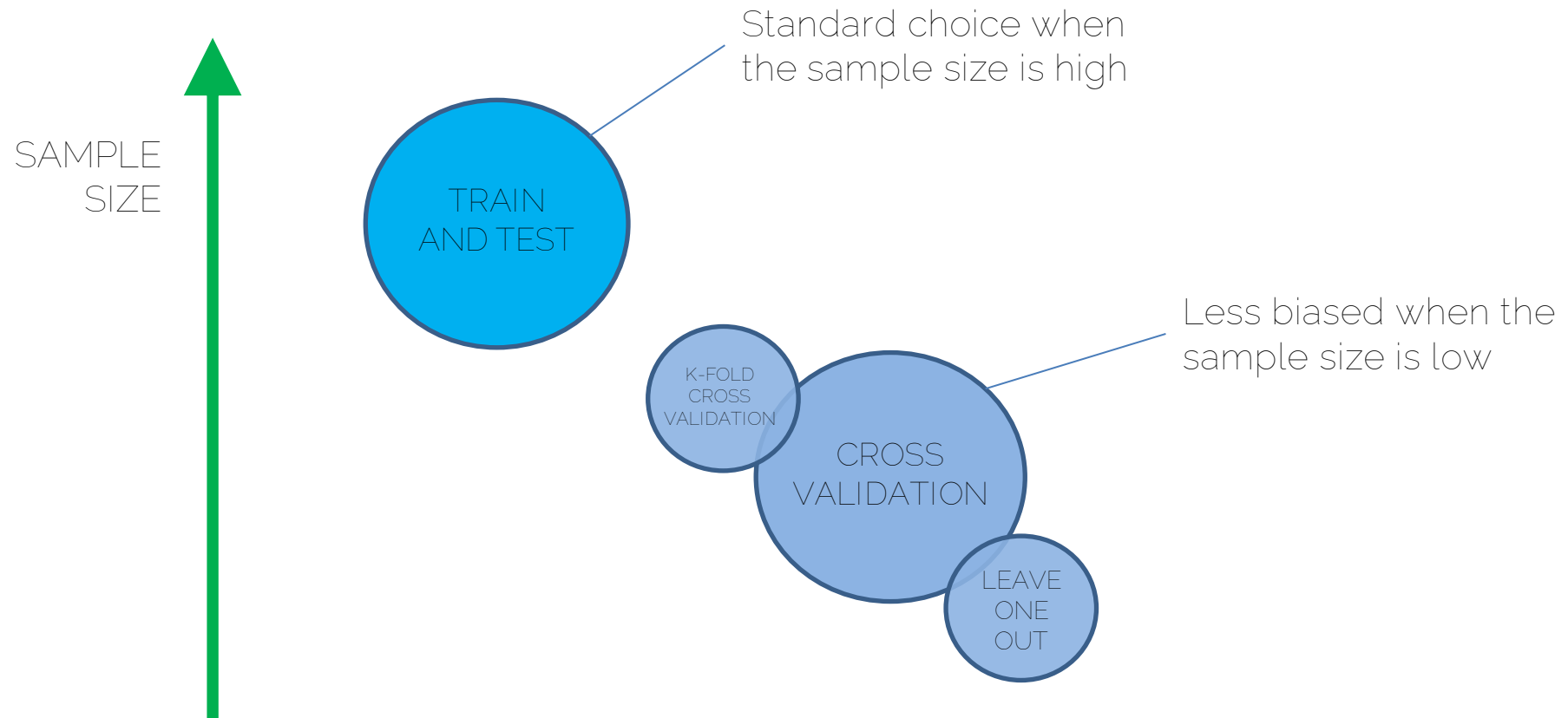
LOW  
TRAINING ERROR



HIGH  
TESTING ERROR  
(low generalization  
ability)

OVERFITTING

# Which validation approach?

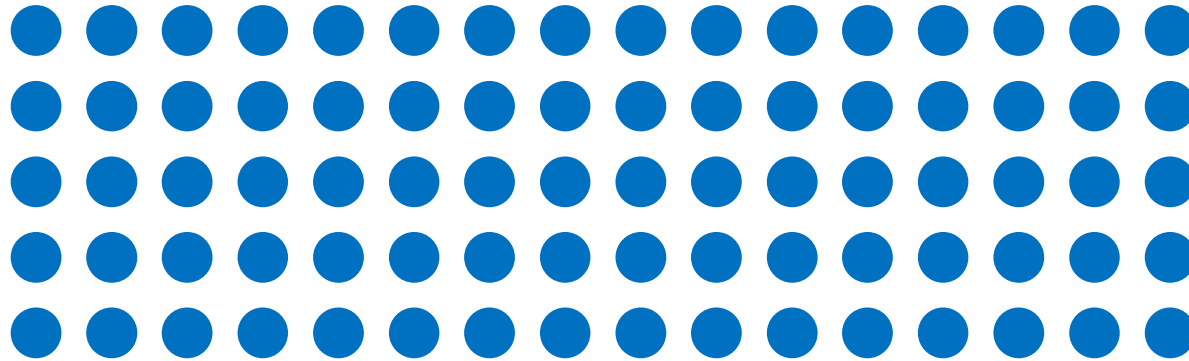


# Train-and-test

This kind of procedure is used when the number of samples in the original dataset is high enough to allow its splitting into two subsets including different samples, which can be used to train and test the classifier.

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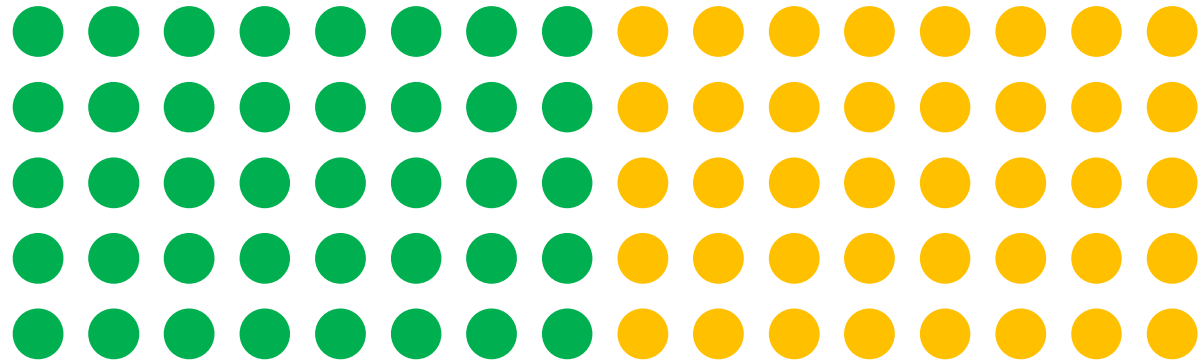


The original dataset is partitioned into 2 complementary subsets, the TRAINING set and the TESTING set.

The TRAINING set is used to train the classifier

The TESTING set is used for validation

# Train-and-test



● Training

● Testing



# Train-and-test

Advantages:

- Over-training problems are reduced, because the training and testing sets are completely independent

Drawbacks:

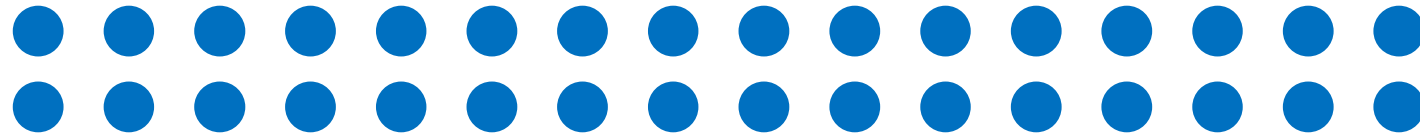
- Results could be related to the particular choice of the partition subsets

# Leave-one-out cross validation

Leave-One-Out (LOO) CV can be considered a particular form of k-fold CV in which

$k$  = number of samples in the original dataset

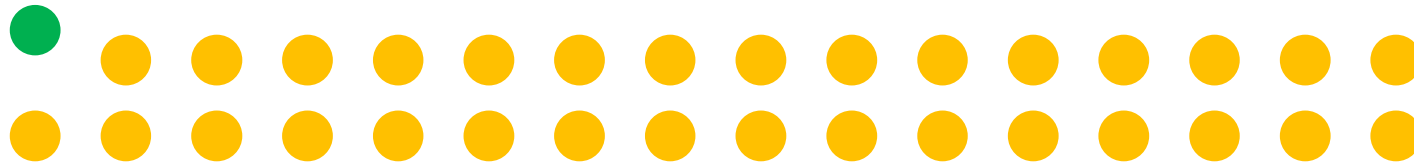
# Leave-one-out cross validation



TRAINING of the classifier is performed using  $n-1$  samples of the original dataset

TESTING is performed using the remaining sample ( $n$  being the total number of samples in the original dataset)

# Leave-one-out cross validation

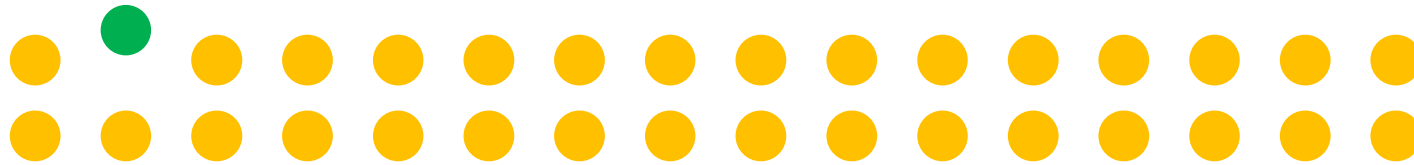


● Training

● Testing

The procedure is then repeated  $n$  times, until all samples are used once for validation.

# Leave-one-out cross validation

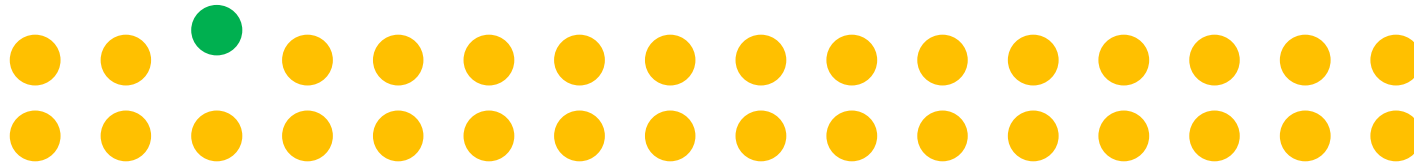


● Training

● Testing

The procedure is then repeated  $n$  times, until all samples are used once for validation.

# Leave-one-out cross validation

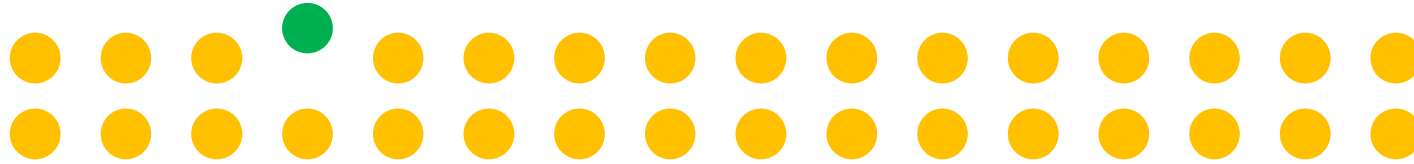


● Training

● Testing

The procedure is then repeated  $n$  times, until all samples are used once for validation.

# Leave-one-out cross validation



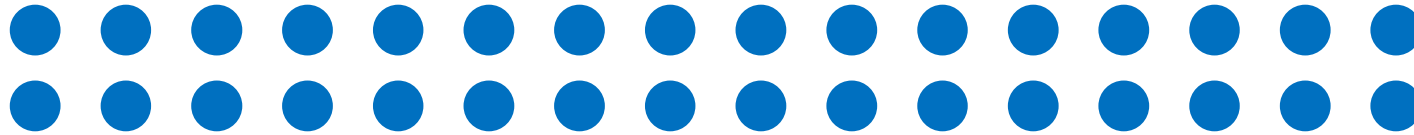
● Training

● Testing

and so on...

# Cross validation

Quantification of the discriminatory power of a predictive model even if the size of the dataset is small



CV involves partitioning the original dataset into complementary subsets, the training set and the testing set

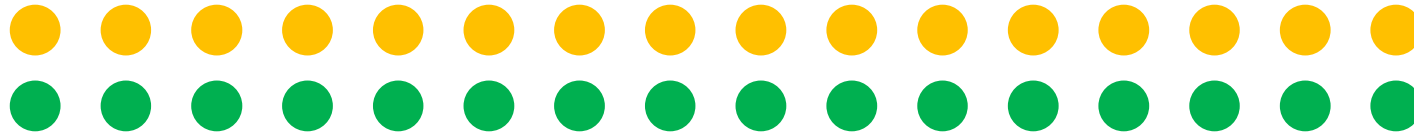
The TRAINING set is used to train the classifier

The TESTING set is used to validate the generated predictive model



# Cross validation

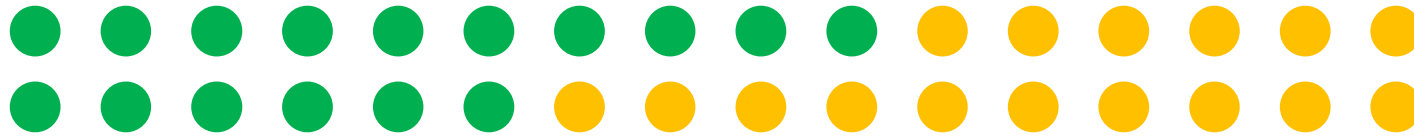
● Training  
● Testing



By using different partitions of the original dataset, multiple rounds of CV can be performed, which can aid reducing the variability of the partitioned subsets.

# Cross validation

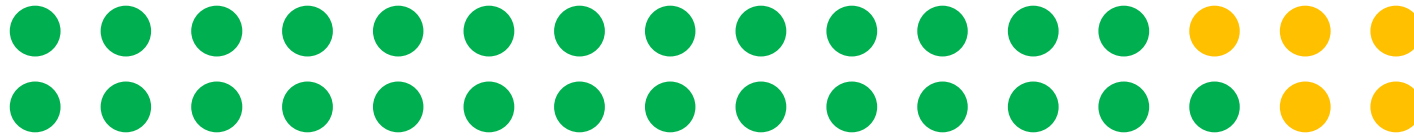
● Training  
● Testing



By using different partitions of the original dataset, multiple rounds of CV can be performed, which can aid reducing the variability of the partitioned subsets.

# Cross validation

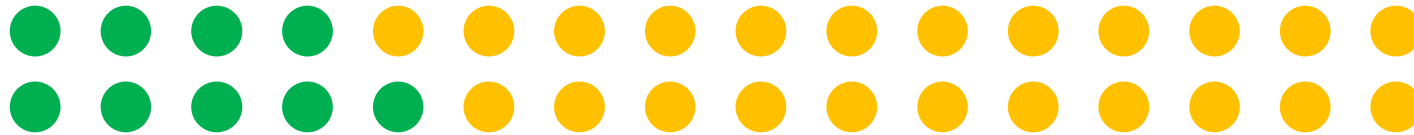
● Training  
● Testing



By using different partitions of the original dataset, multiple rounds of CV can be performed, which can aid reducing the variability of the partitioned subsets.

# Cross validation

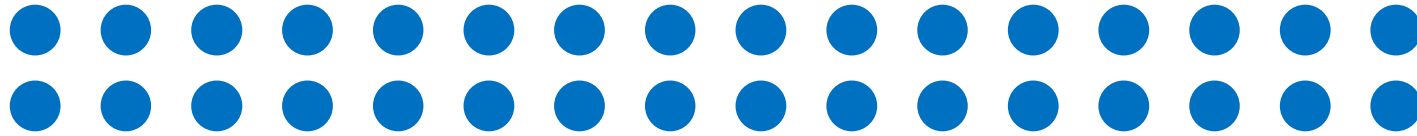
● Training  
● Testing



and so on...

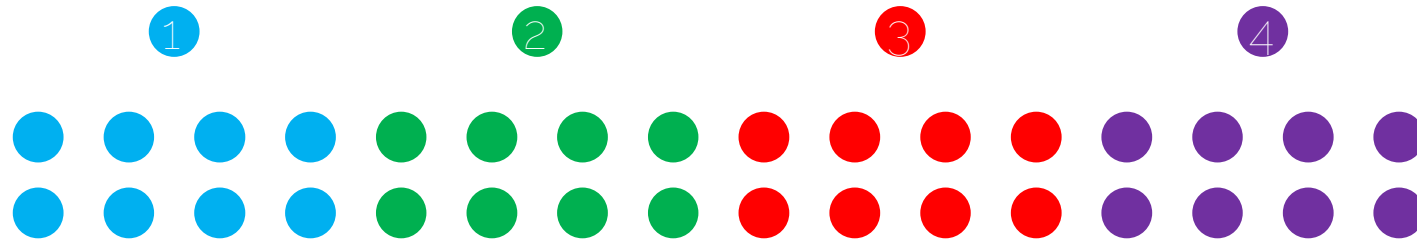
Results obtained from multiple rounds can be averaged in order to obtain a quantification of the performance of the classifier.

# K-fold cross validation



The original dataset is randomly partitioned into  $k$  subsets of equal size.

# K-fold cross validation

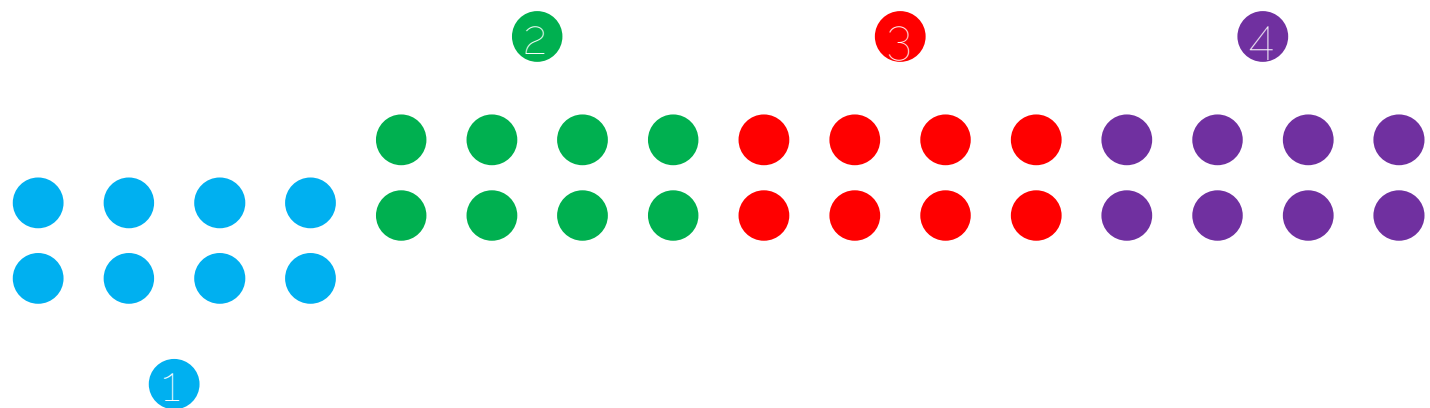


The original dataset is randomly partitioned into  $k$  subsets of equal size

TRAINING of the classifier is performed using  $k-1$  subsets

TESTING is performed using the remaining subset

# K-fold cross validation



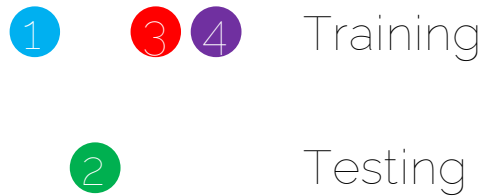
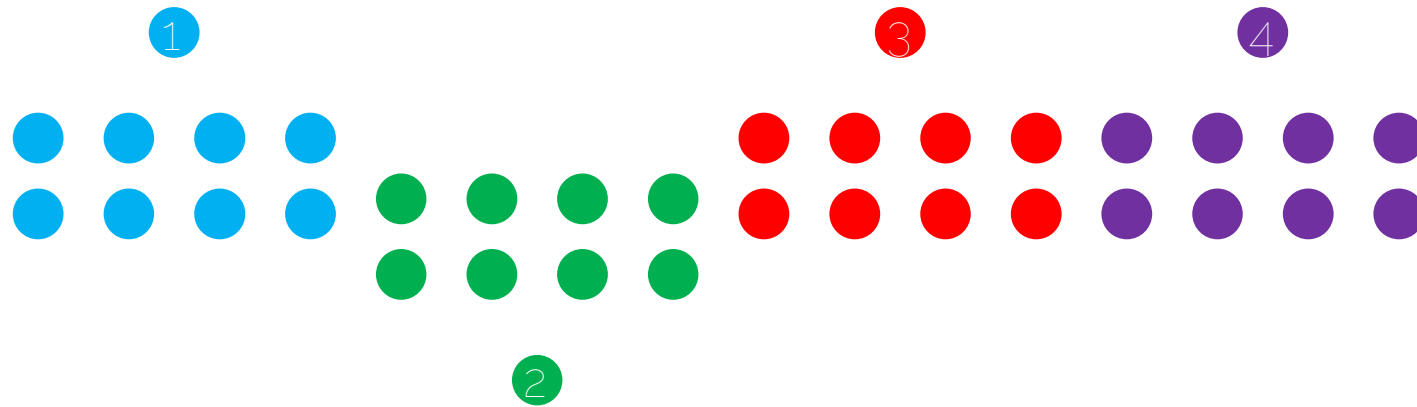
Training



Testing

The procedure is then repeated k times, until all subsets are used once as testing set.

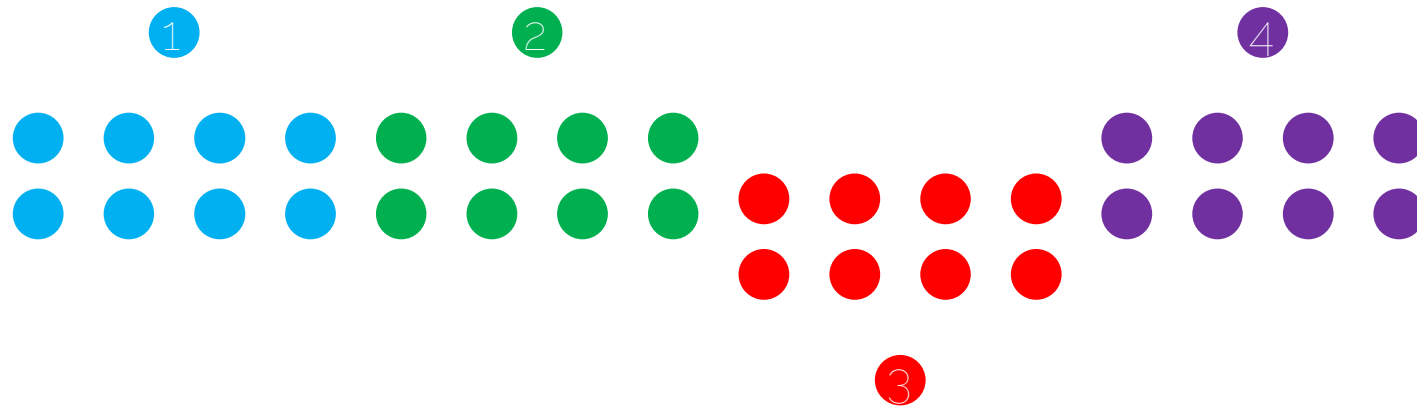
# K-fold cross validation



The procedure is then repeated k times, until all subsets are used once as testing set.



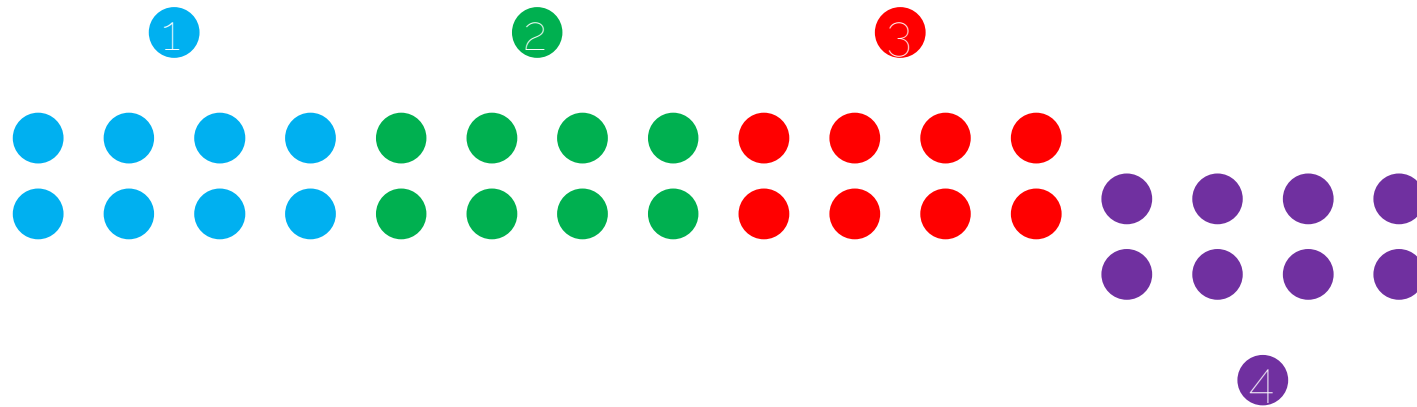
# K-fold cross validation



1 2 4 Training  
3 Testing

The procedure is then repeated k times, until all subsets are used once as testing set.

# K-fold cross validation



1 2 3

Training

4

Testing

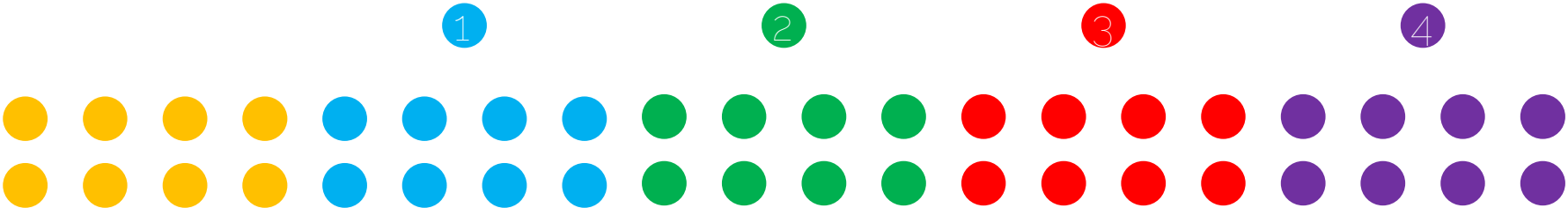
The procedure is then repeated k times, until all subsets are used once as testing set.

# K-fold cross validation

Advantages:

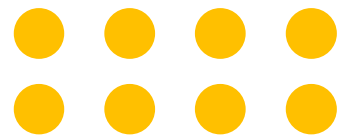
- each sample of the original dataset is used once for validation
- all samples being used for both training and testing phases

# Nested K-fold cross validation

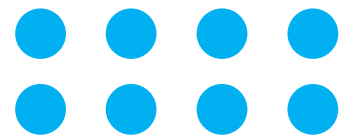


# Nested K-fold cross validation

TESTING  
(PERFORMANCE  
EVALUATION)

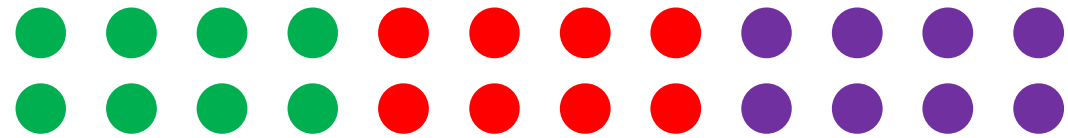


VALIDATION  
(HYPERPARAMETER  
ESTIMATION AND  
OPTIMIZATION)



1

TRAINING



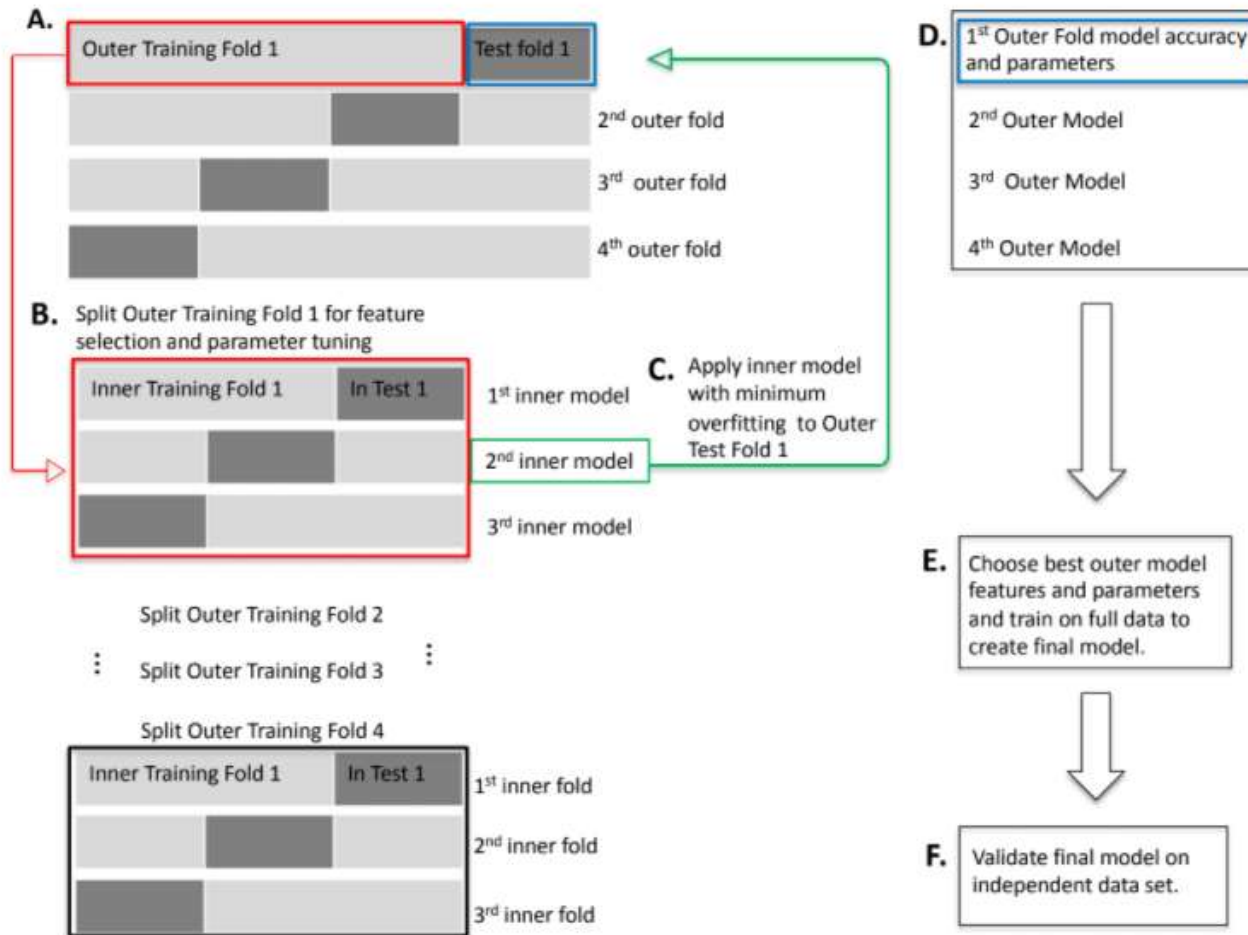
2

3

4

# Nested K-fold cross validation

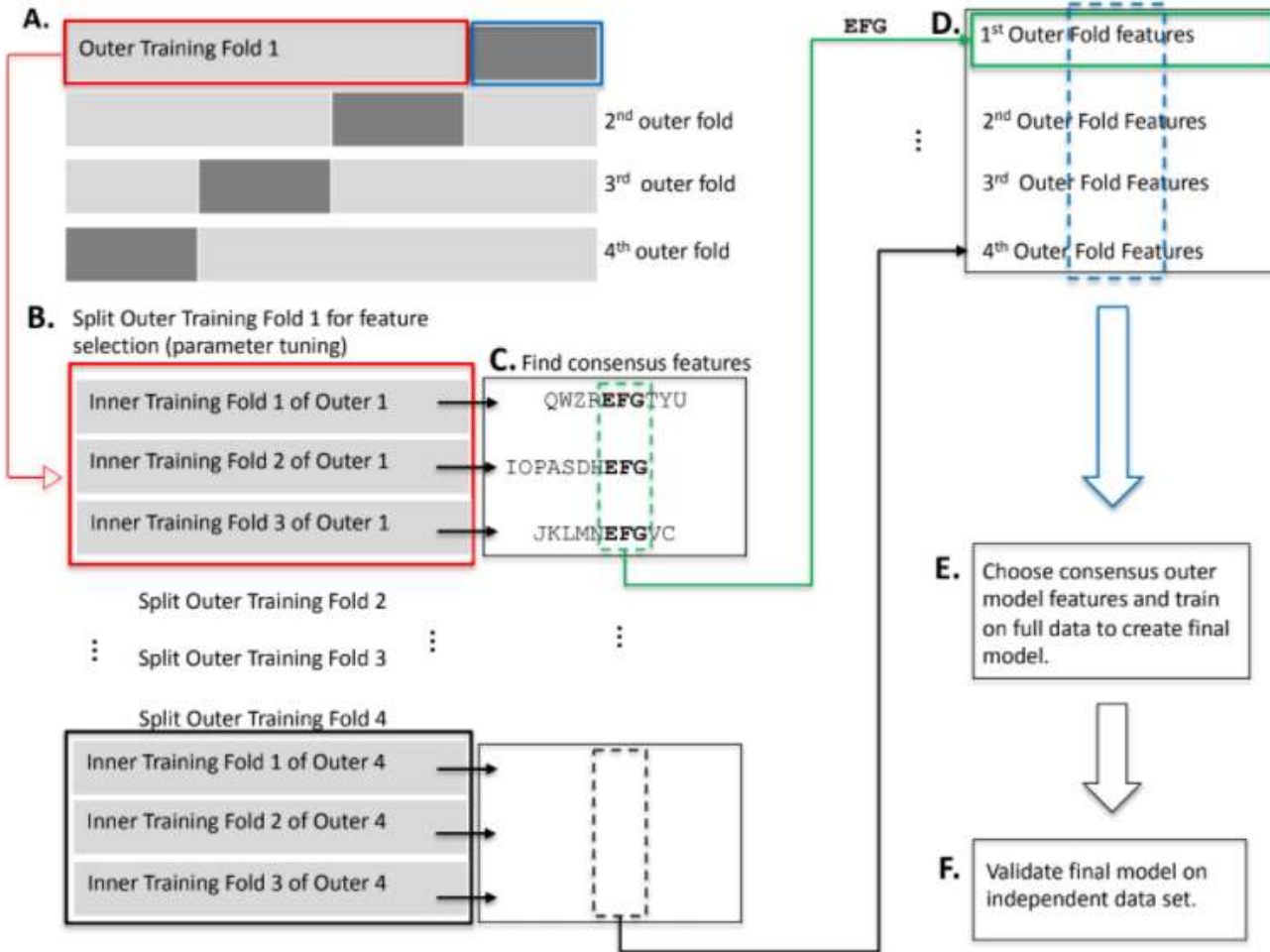
## Standard Nested Cross Validation (nCV)



**Fig. 1. Standard nested Cross-Validation (nCV).** A. Split the data into outer folds of training and testing data pairs (4 outer folds in this illustration). Then do the following for each outer training fold (illustration starting with Outer Training Fold 1 (red box, A)). B. Split outer training fold into inner folds for feature selection and possible hyperparameter tuning by grid search. C. Use the best inner training model including features and parameters (2nd inner model, green box, for illustration) based on minimum overfitting (difference between training and test accuracies) in the inner folds to test on the outer test fold (green arrow to blue box, Test Fold 1). D. Save the best model for this outer fold including the features and test accuracies. Repeat B-D for the remaining outer folds. E. Choose the best outer model with its features based on minimum overfitting. Train on the full data to create the final model. F. Validate the final model on independent data.

# Nested K-fold cross validation

## Consensus Nested Cross Validation (cnCV)



**Fig. 2. Consensus Nested Cross-Validation (cnCV).** **A.** Split the data into outer folds (4 outer folds in this illustration). Then do the following for each outer training fold (illustration starting with Outer Training Fold 1 (red box, A)). **B.** Split outer training fold into inner folds for feature selection and optional hyperparameter tuning by grid search. **C.** Find consensus features. For each fold, features with positive Relief scores are collected (e.g., "QWZREFGTYU" for fold 1). Negative Relief scores have high probability of being irrelevant to classification. The implementation allows for different feature importance methods and tuning the number of input features. Consensus features (found in all folds) are used as the best features in the corresponding outer fold. For example, features "EFG" are shared across the three inner folds. This procedure is used in the inner and outer folds of cnCV. Classification is not needed to select consensus features. **D.** The best outer fold features (green arrow to green box) are found for each fold (i.e., Repeat B-D for all outer folds). **E.** Choose the consensus features across all the outer folds to train the final model on full data. Consensus features are selected based on training data only. Classification is not performed until the outer consensus features are selected (A-D). **F.** Validate the final model on independent data.

# Performance metrics

A brief overview. . .

1. Accuracy
2. Sensitivity and Specificity
3. Precision and Recall
4. Positive and Negative Predictive Value
5. False/True Positive/Negative Rates
6. Imbalanced datasets
7. ROC-AUC



# Accuracy

Accuracy is the most used metric in classification problems

Accuracy of classification =

# correctly classified  
samples (for both  
classes)



# classified samples

If the error rate is defined as the number of misclassified samples (both classes) divided by the total number of classified samples, it is evident that accuracy and error rate are complementary measures.

# Sensitivity and Specificity

Two metrics of great importance in medicine are sensitivity and specificity, as they measure the rate of correctly classified samples in the positive (pathological) and negative (normal) class, respectively.

Sensitivity (also known as True Positive Rate) is given by the number of correctly classified samples belonging to the positive class (true positives) divided by the total number of samples belonging to the positive class (true positives plus false negatives).

Sensitivity =

# correctly classified  
samples in the positive  
class



# positive samples

# Sensitivity and Specificity

Specificity (also known as True Negative Rate) is given by the number of correctly classified samples belonging to the negative class (true negatives) divided by the total number of samples belonging to the negative class (true negatives plus false positives).

Specificity =

# correctly classified  
samples in the negative  
class



# negative samples

Here, true positive (negative) gives the number of correctly classified samples belonging to the positive (negative) class, while false positive (negative) gives the number of misclassified samples belonging to the negative (positive) class.

# Precision and Recall

Precision is the number of correctly classified samples belonging to the positive class (true positives) divided by the total number of samples predicted as positive by the classifier (true positives plus false positives).

Precision =

# correctly classified  
samples in the positive  
class

/

# predicted-as-  
positive samples

# Precision and Recall

Recall is the number of correctly classified samples belonging to the positive class (true positives) divided by the total number of samples in the positive class (true positives plus false negatives = positive samples).

Recall =

# correctly classified  
samples in the positive  
class



# actually-positive  
samples

# Positive and Negative Predictive Value

Positive Predictive Value is the number of correctly classified samples belonging to the positive class (true positives) divided by the total number of samples predicted as positive by the classifier (true positives plus false positives).

PPV =

# correctly classified  
samples in the positive  
class

/

# predicted-as-  
positive samples

# Positive and Negative Predictive Value

Negative Predictive Value is the number of correctly classified samples belonging to the negative class (true negatives) divided by the total number of samples predicted as negative by the classifier (true negatives plus false negatives).

NPV =

# correctly classified  
samples in the negative  
class



# predicted-as-  
negative samples

# False/True Positive/Negative Rates

TPR =

# correctly classified  
samples in the positive  
class / # positive samples

FPR =

# incorrectly classified  
samples in the positive  
class / # negative samples

TNR =

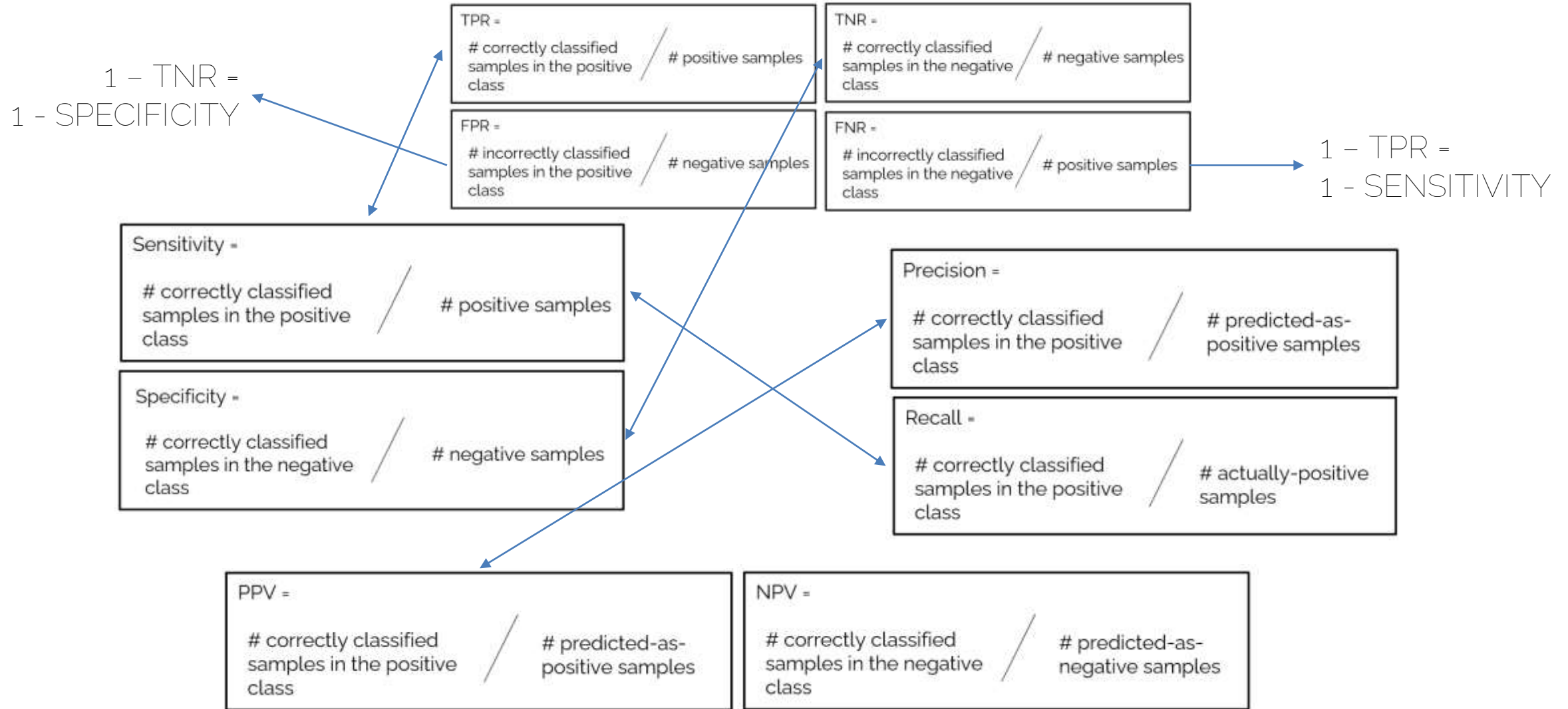
# correctly classified  
samples in the negative  
class / # negative samples

FNR =

# incorrectly classified  
samples in the negative  
class / # positive samples



# Precision and Recall



# Confusion matrix

		Predicted condition	
Total population = P + N		Positive (PP)	Negative (PN)
Actual condition	Positive (P)	True positive (TP)	False negative (FN)
	Negative (N)	False positive (FP)	True negative (TN)

Positive	95/100
Negative	75/100



	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	25	75

# Confusion matrix



Positive	95/100
Negative	75/100



	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	25	75



# Confusion matrix

P 1	95/100
P 2	55/100
P 3	90/100
N	75/100

CLASS-X ACCURACY

	P 1 PREDICTED	P 2 PREDICTED	P 3 PREDICTED	N PREDICTED
P 1 ACTUAL	95	0	1	4
P 2 ACTUAL	5	55	5	35
P 3 ACTUAL	2	1	90	7
N ACTUAL	5	15	5	75

95%

55%

90%

75%

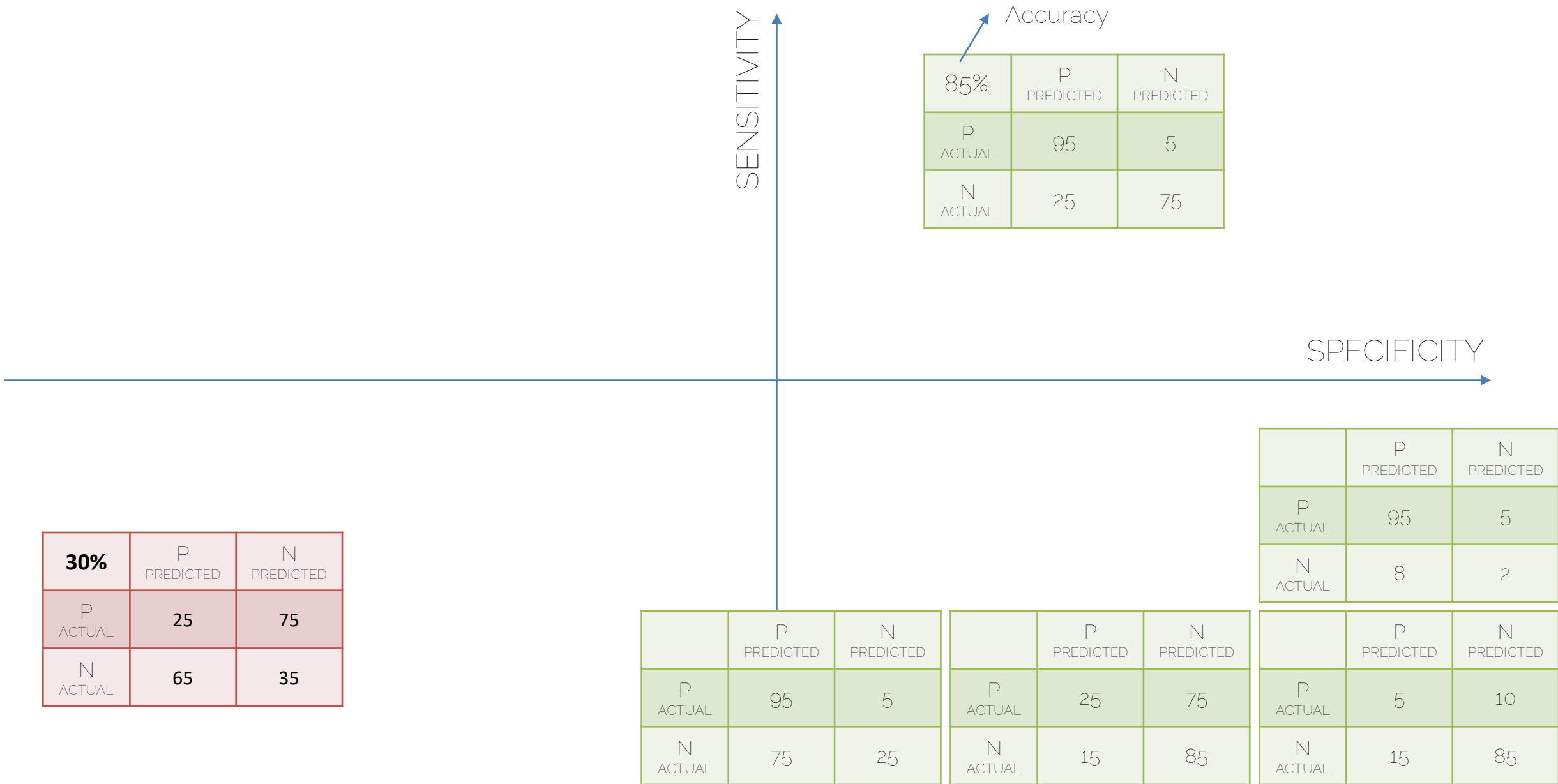
# Confusion matrix



# Confusion matrix



# Confusion matrix



# Confusion matrix

<b>60%</b>	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	75	25

<b>30%</b>	P PREDICTED	N PREDICTED
P ACTUAL	25	75
N ACTUAL	65	35

SENSITIVITY

Accuracy

85%	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	25	75

SPECIFICITY

	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	8	2

	P PREDICTED	N PREDICTED
P ACTUAL	25	75
N ACTUAL	15	85

	P PREDICTED	N PREDICTED
P ACTUAL	5	10
N ACTUAL	15	85



# Confusion matrix

<b>60%</b>	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	75	25

Accuracy

85%	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	25	75

<b>30%</b>	P PREDICTED	N PREDICTED
P ACTUAL	25	75
N ACTUAL	65	35

<b>55%</b>	P PREDICTED	N PREDICTED
P ACTUAL	25	75
N ACTUAL	15	85

	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	8	2

	P PREDICTED	N PREDICTED
P ACTUAL	5	10
N ACTUAL	15	85

# Confusion matrix

<b>60%</b>	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	75	25

<b>30%</b>	P PREDICTED	N PREDICTED
P ACTUAL	25	75
N ACTUAL	65	35

SENSITIVITY

Accuracy

85%	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	25	75

SPECIFICITY

<b>55%</b>	P PREDICTED	N PREDICTED
P ACTUAL	25	75
N ACTUAL	15	85

78%	P PREDICTED	N PREDICTED
P ACTUAL	5	10
N ACTUAL	15	85

	P PREDICTED	N PREDICTED
P ACTUAL	95	5
N ACTUAL	8	2

# Confusion matrix

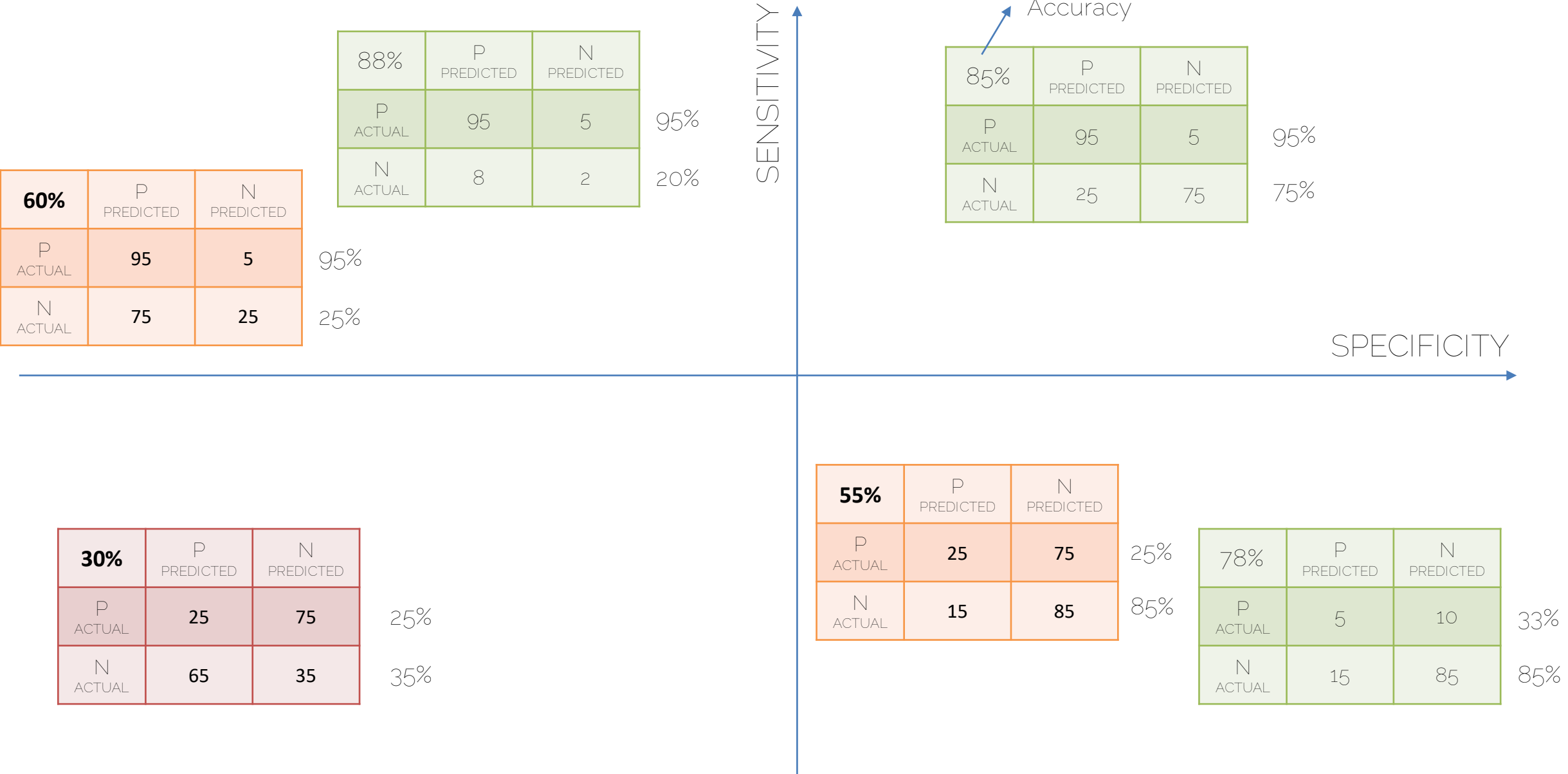
60%			88%		
	P PREDICTED	N PREDICTED	P ACTUAL	P PREDICTED	N PREDICTED
P ACTUAL	95	5	P ACTUAL	95	5
N ACTUAL	75	25	N ACTUAL	8	2

85%			Accuracy		
	P PREDICTED	N PREDICTED	P ACTUAL	P PREDICTED	N PREDICTED
P ACTUAL	95	5	P ACTUAL	95	5
N ACTUAL	25	75	N ACTUAL	25	75

30%					
	P PREDICTED	N PREDICTED	P ACTUAL	P PREDICTED	N PREDICTED
P ACTUAL	25	75	P ACTUAL	25	75
N ACTUAL	65	35	N ACTUAL	65	35

55%					
	P PREDICTED	N PREDICTED	P ACTUAL	P PREDICTED	N PREDICTED
P ACTUAL	25	75	P ACTUAL	5	10
N ACTUAL	15	85	N ACTUAL	15	85

# Confusion matrix



# Performance metrics for imbalanced datasets

Prevalence is "the proportion of a particular population with a given condition".

In our case, it is the ratio between the number of actually-positive samples and the entire-sample size

Prevalence =

# samples in the positive  
class (actual)



# samples  
(actual positives +  
negatives)

# Performance metrics for imbalanced datasets

Geometric Mean of the true rates is the geometric mean between sensitivity and specificity

GM =

$$(\text{Sensitivity} \times \text{Specificity})^{1/2}$$

Which values does it span?

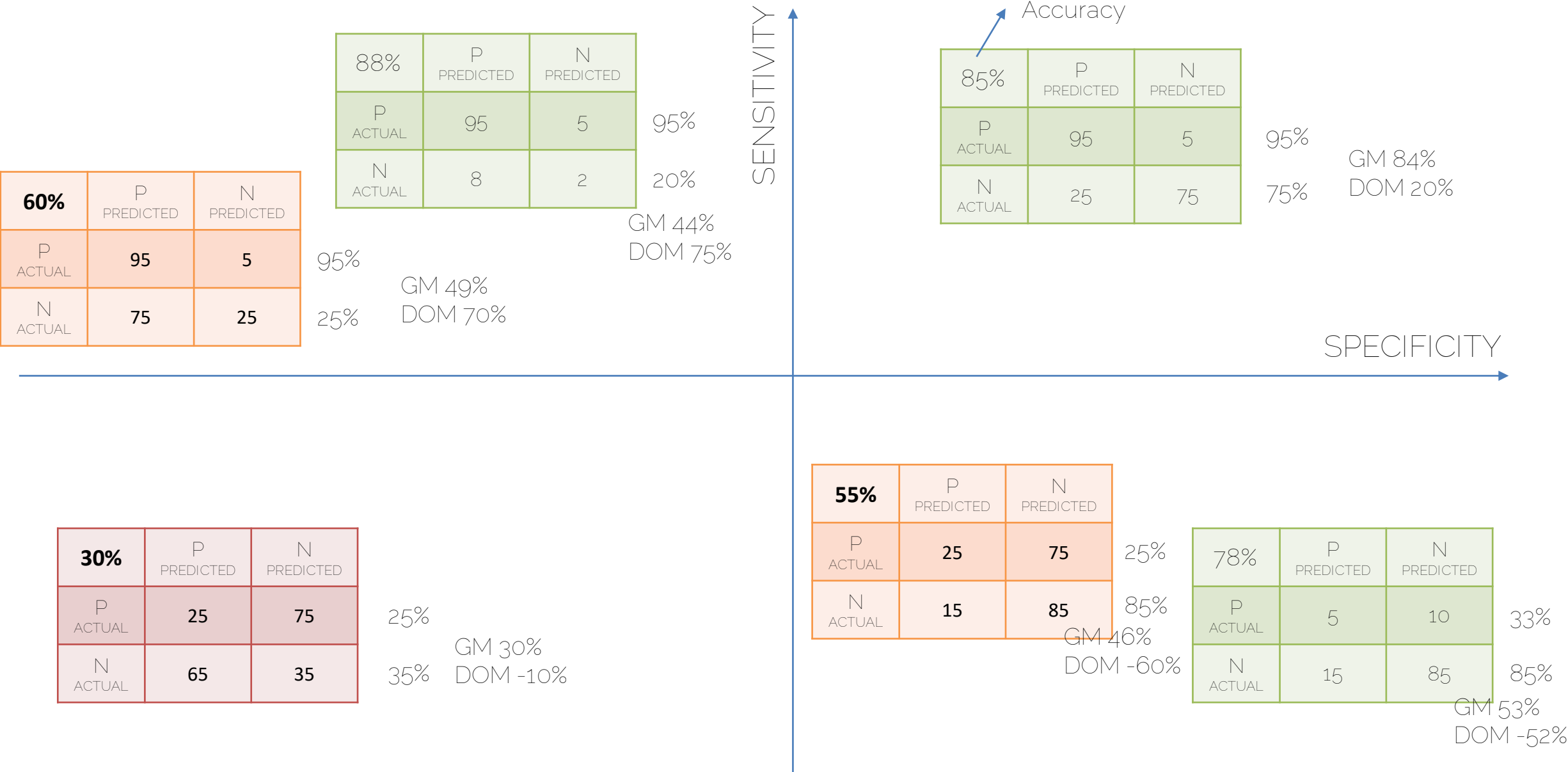
# Performance metrics for imbalanced datasets

Dominance is the difference between sensitivity and specificity

$$\text{Dominance} = \text{Sensitivity} - \text{Specificity}$$

Which values does it span?

# Confusion matrix





# F1 Score

F1 score is an harmonic mean of precision (PPV) and recall (= sensitivity)

$$F_1 = \frac{2}{\text{recall}^{-1} + \text{precision}^{-1}} = 2 \frac{\text{precision} \cdot \text{recall}}{\text{precision} + \text{recall}} = \frac{2\text{tp}}{2\text{tp} + \text{fp} + \text{fn}}$$

Why useful?

As above, it is convenient to have one single metric to compare classification performance (not both sensitivity/specificity or precision/recall)

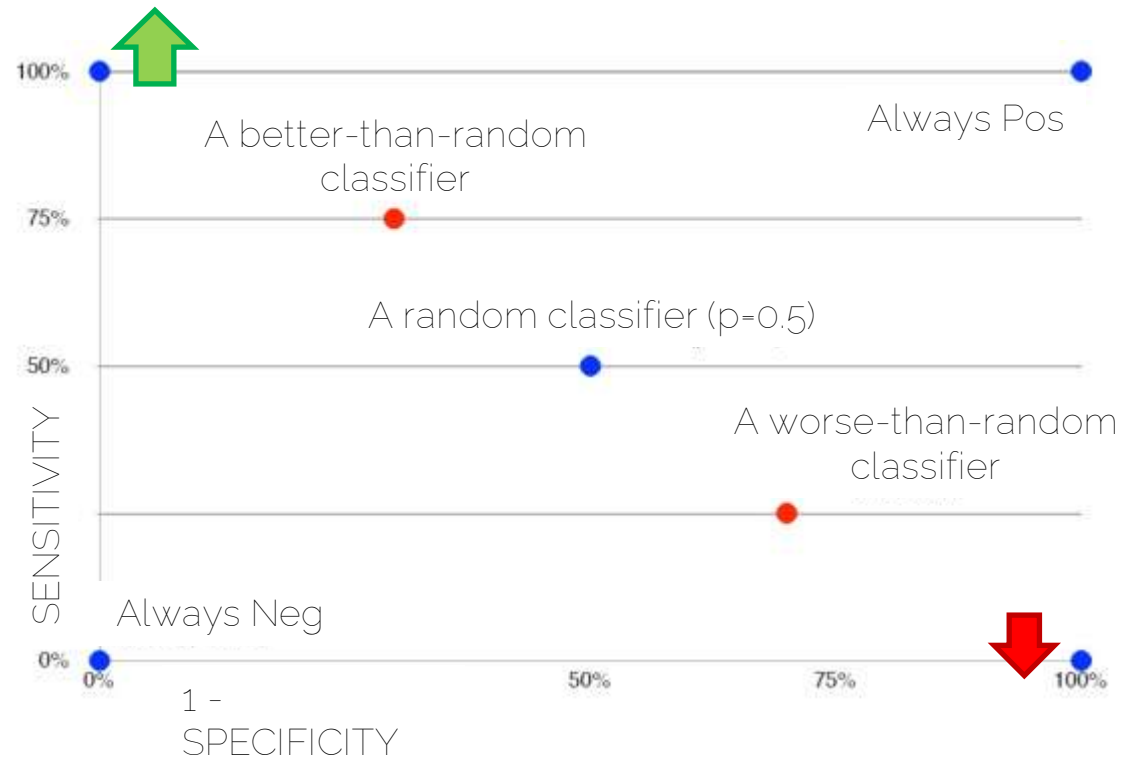
Standard average is not always a good measure  $\frac{P + R}{2}$

F1 score behaves better (what happens when precision = 0? when recall = 0? when is F1 score = 1?)

# ROC analysis and Area Under the (ROC) Curve

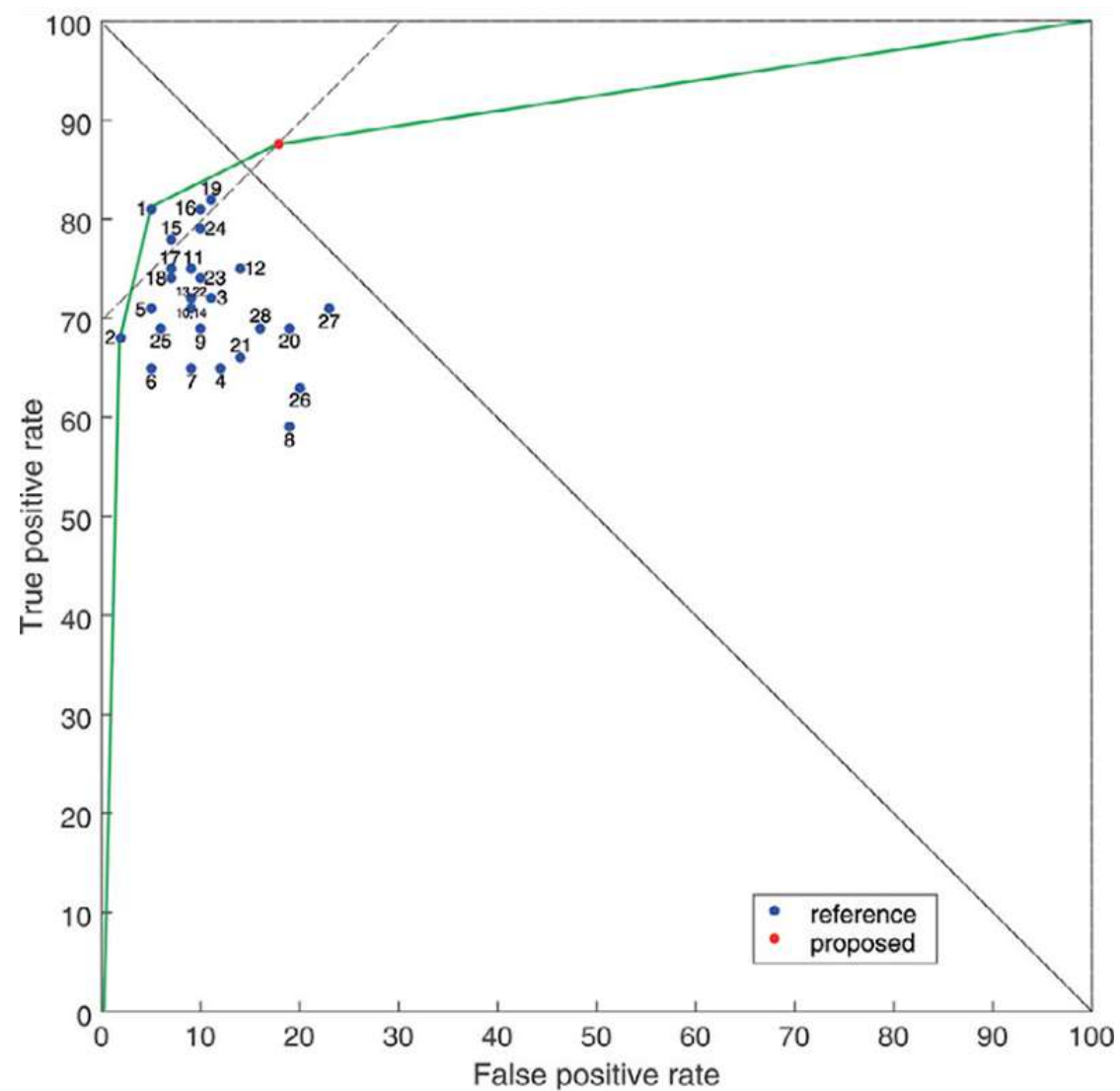
Another important metric in classification problems is given by the study of the Receiver Operating Characteristic (ROC) curve.

For a binary classifier, A ROC curve is a plot of the TPR (sensitivity) against the FPR (1 – specificity), which can be obtained at different setting thresholds.

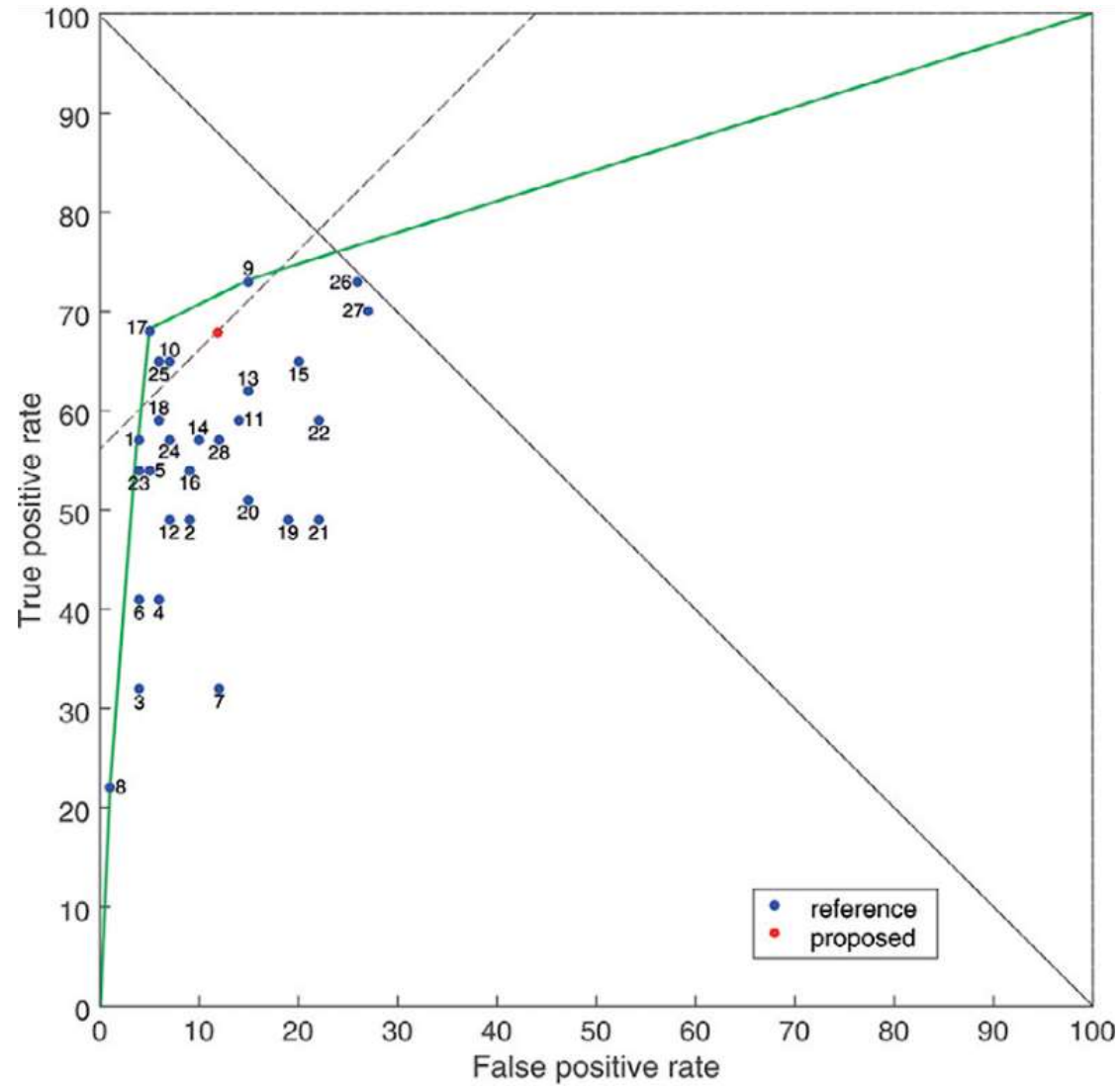


The Area Under the ROC Curve (AUC) gives a quantification of the classifier performance, with a higher statistical consistency than accuracy.

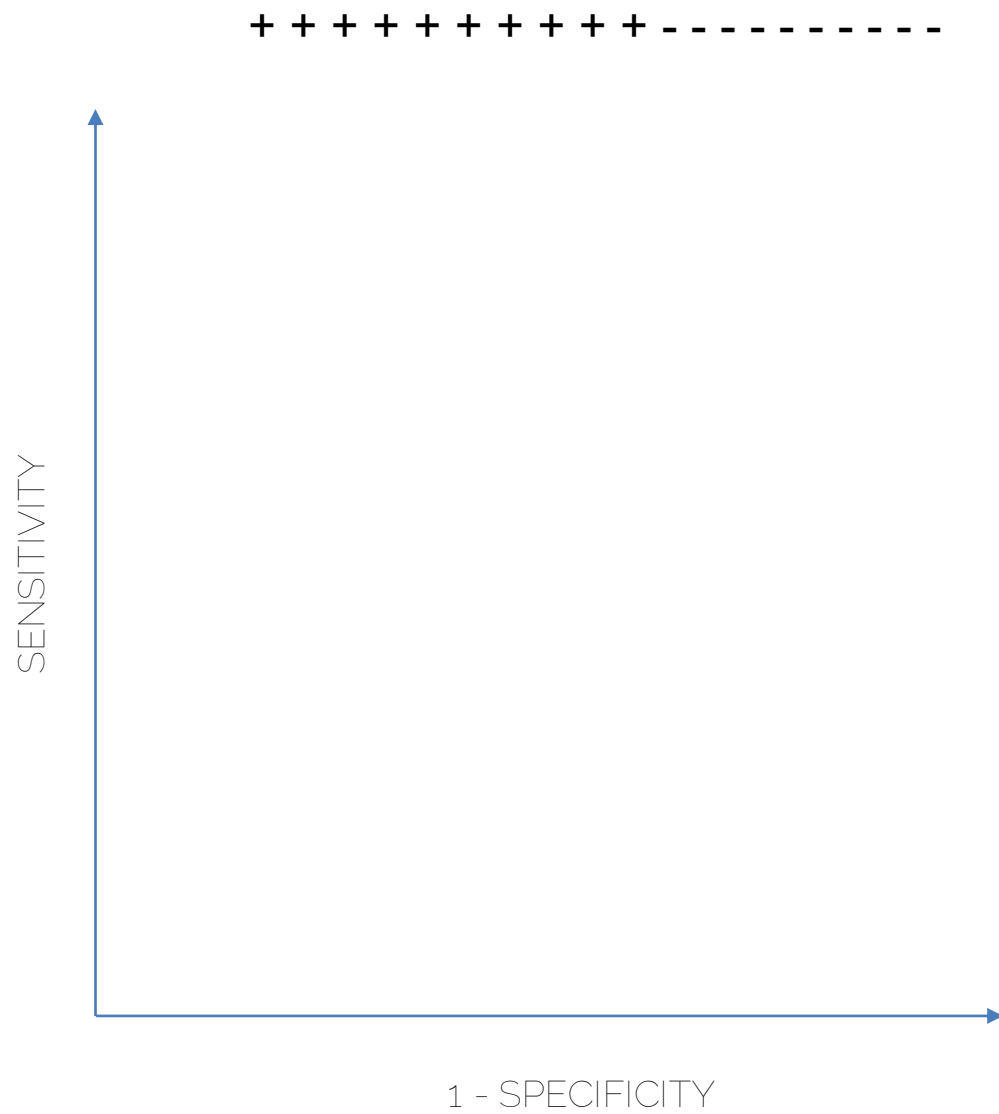
# ROC analysis and Area Under the (ROC) Curve



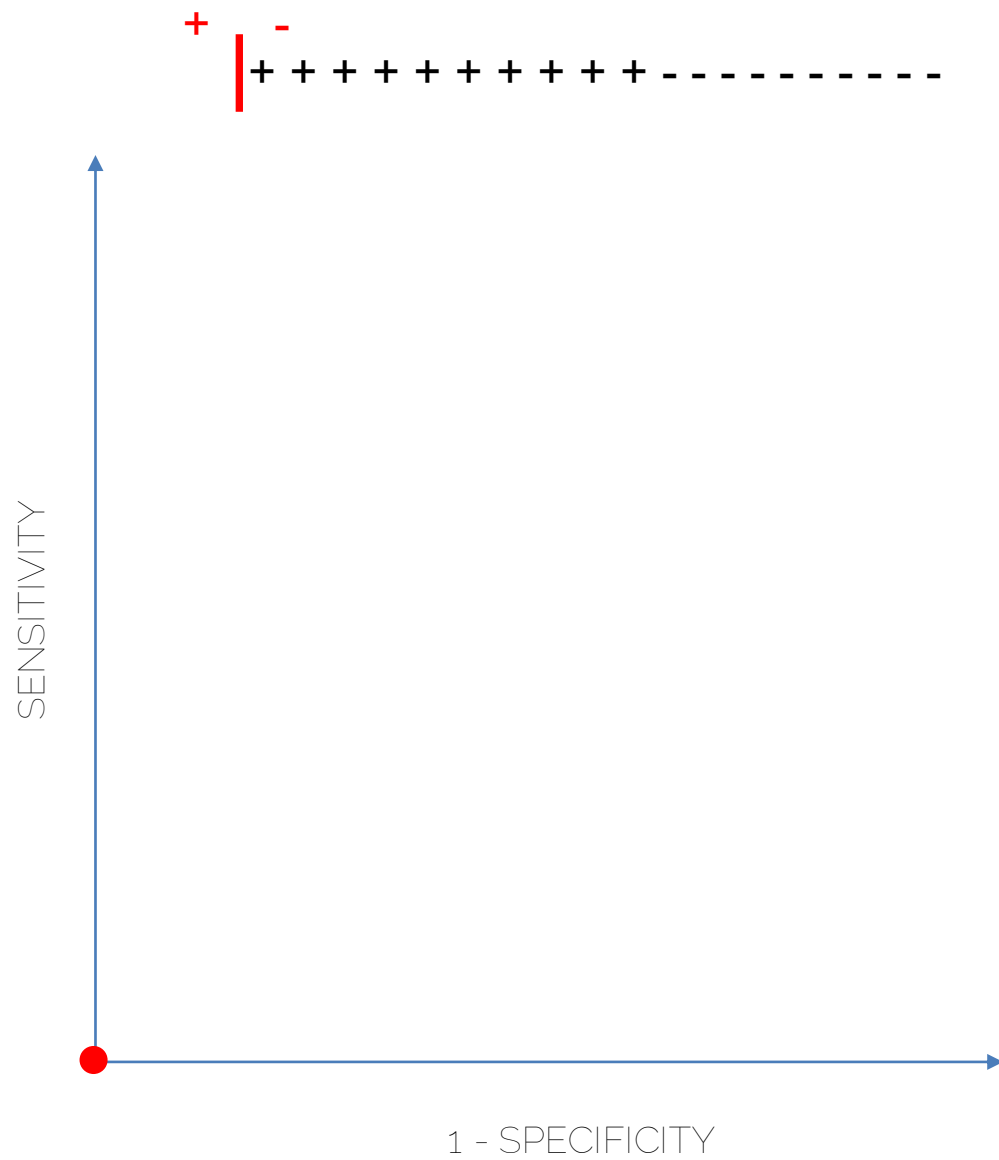
# ROC analysis and Area Under the (ROC) Curve



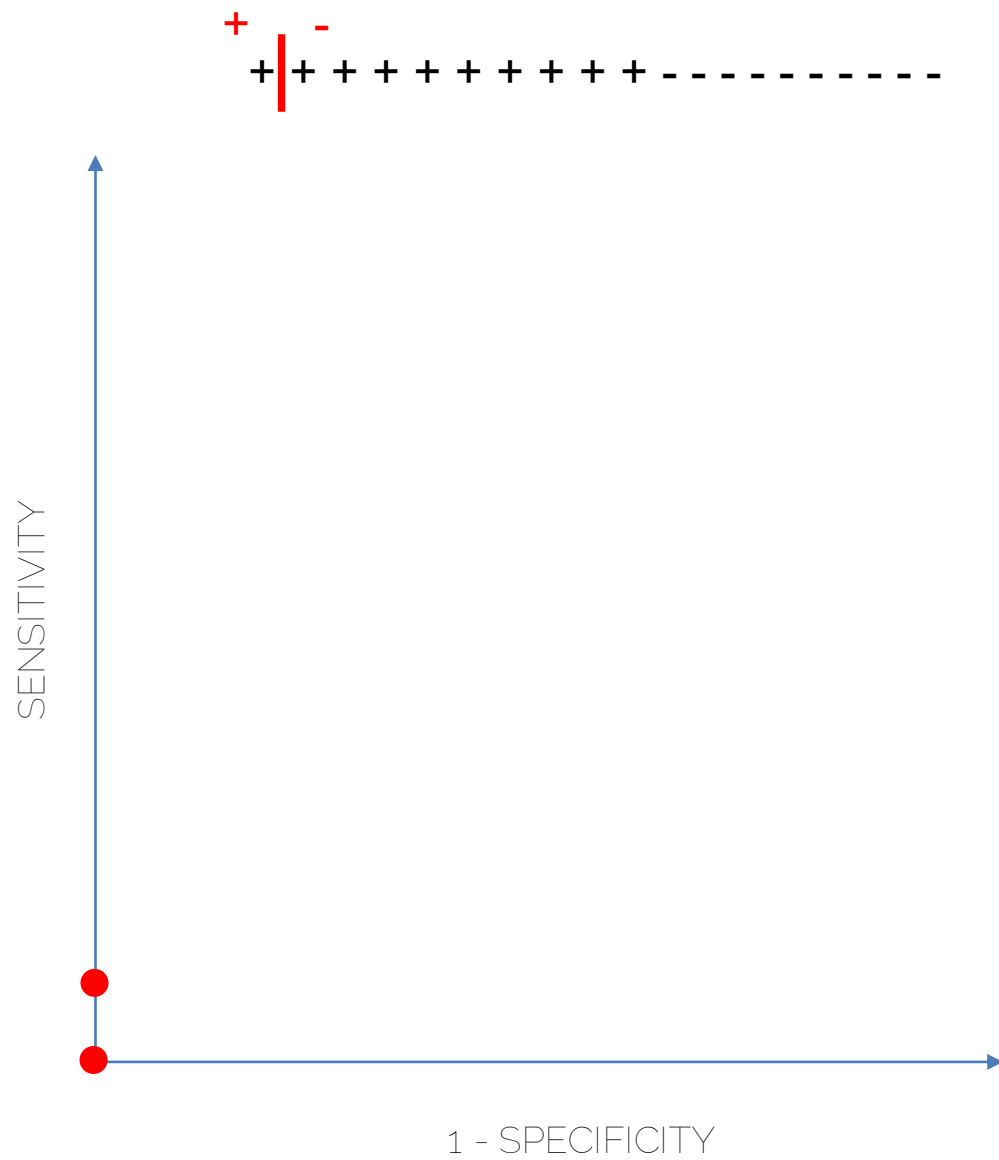
# ROC analysis and Area Under the (ROC) Curve



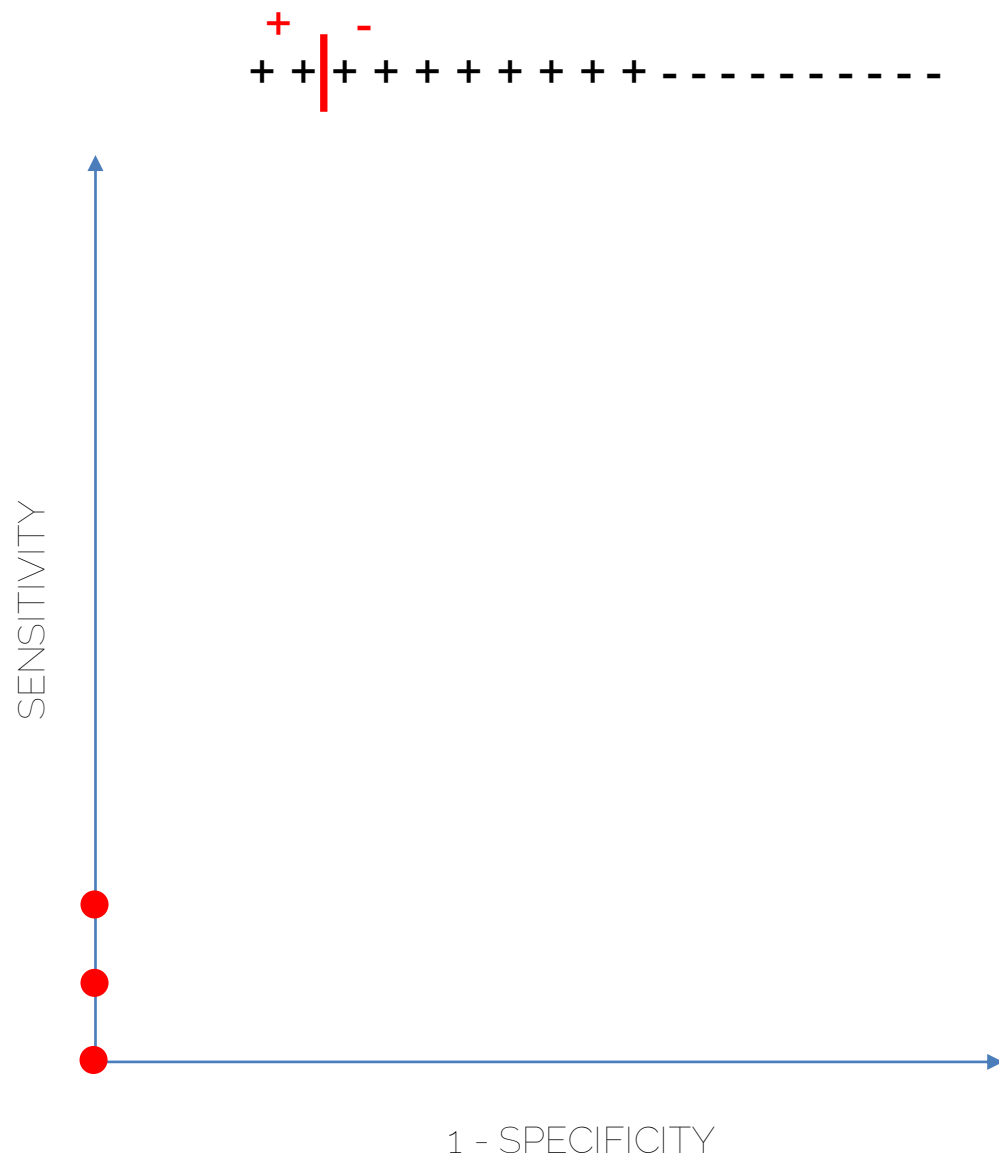
# ROC analysis and Area Under the (ROC) Curve



# ROC analysis and Area Under the (ROC) Curve

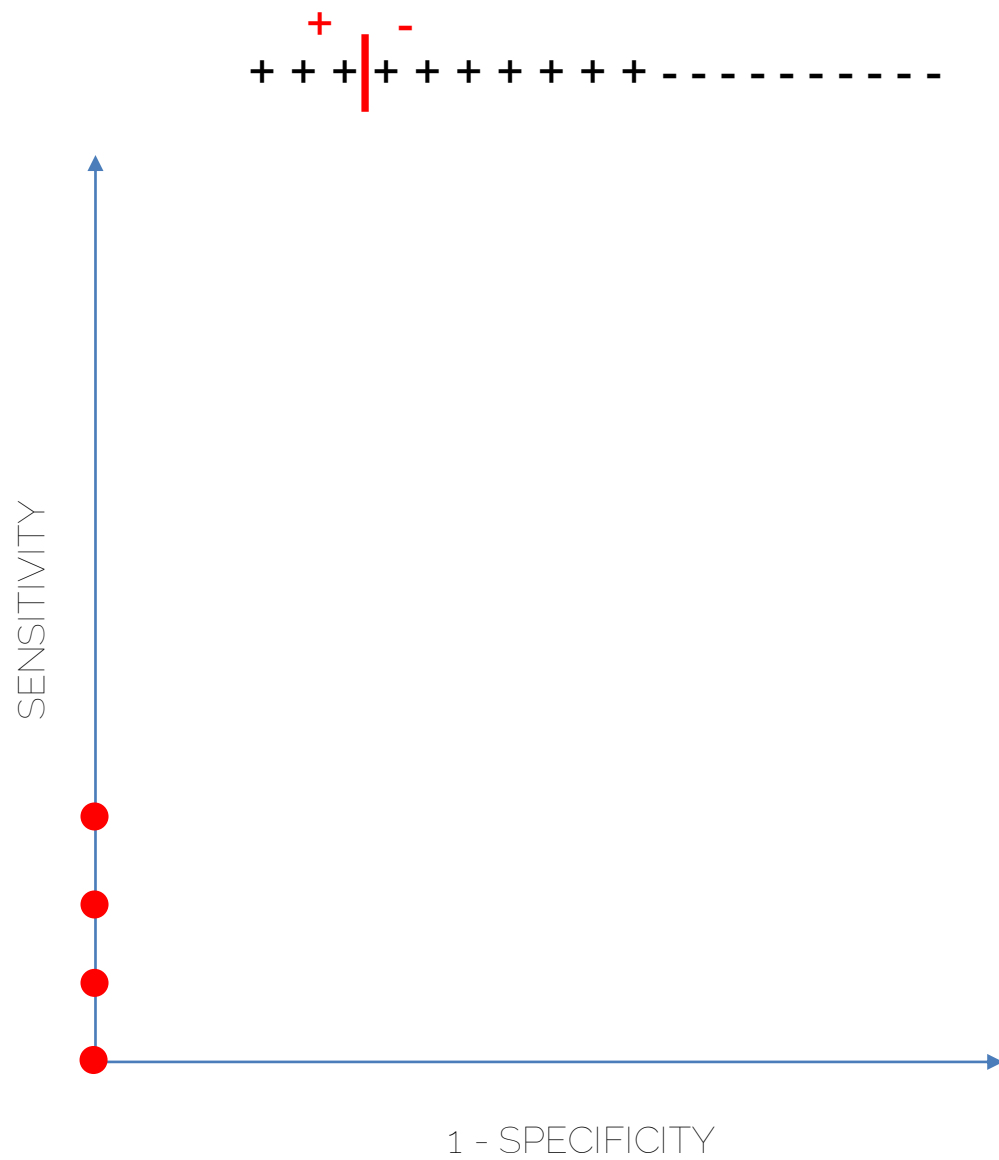


# ROC analysis and Area Under the (ROC) Curve

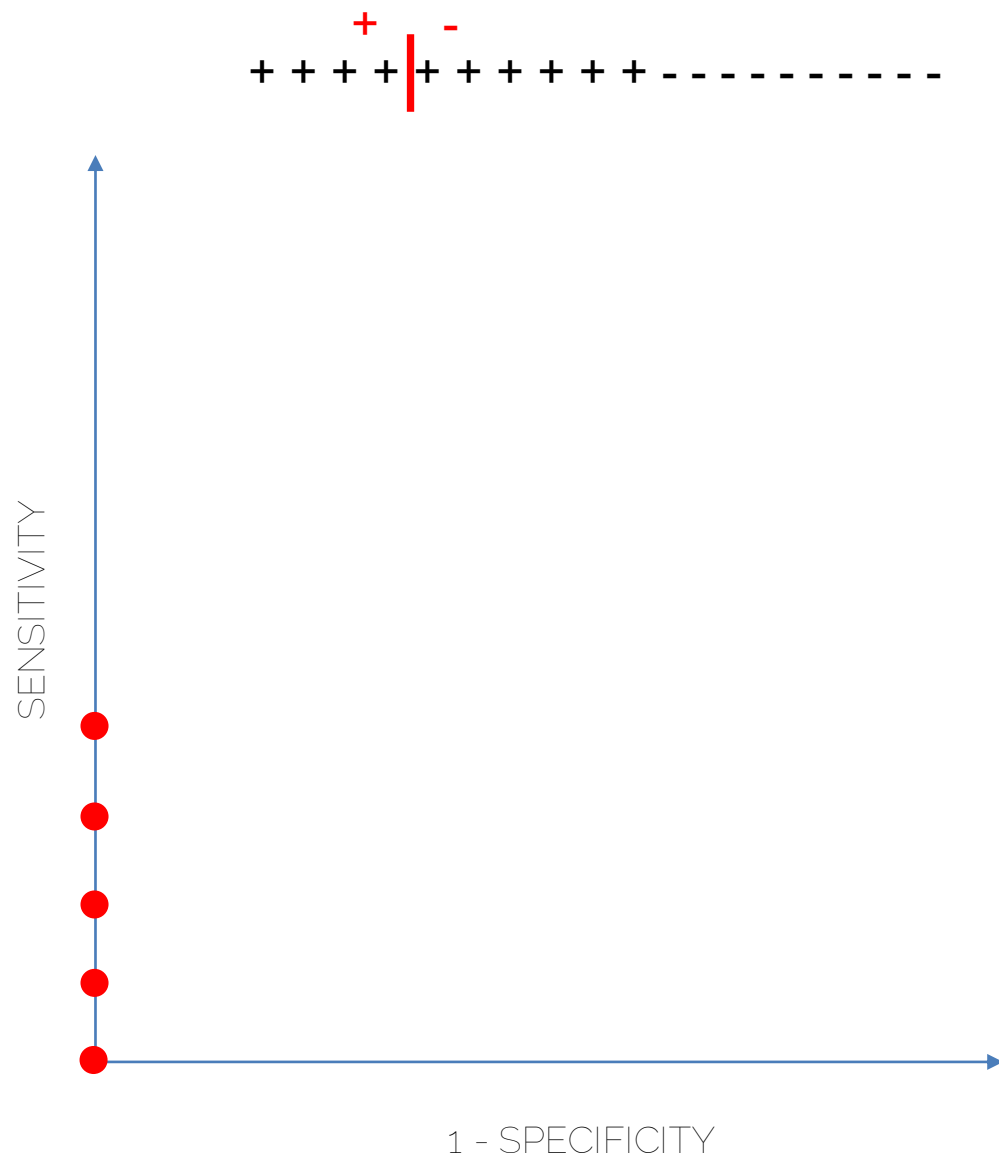




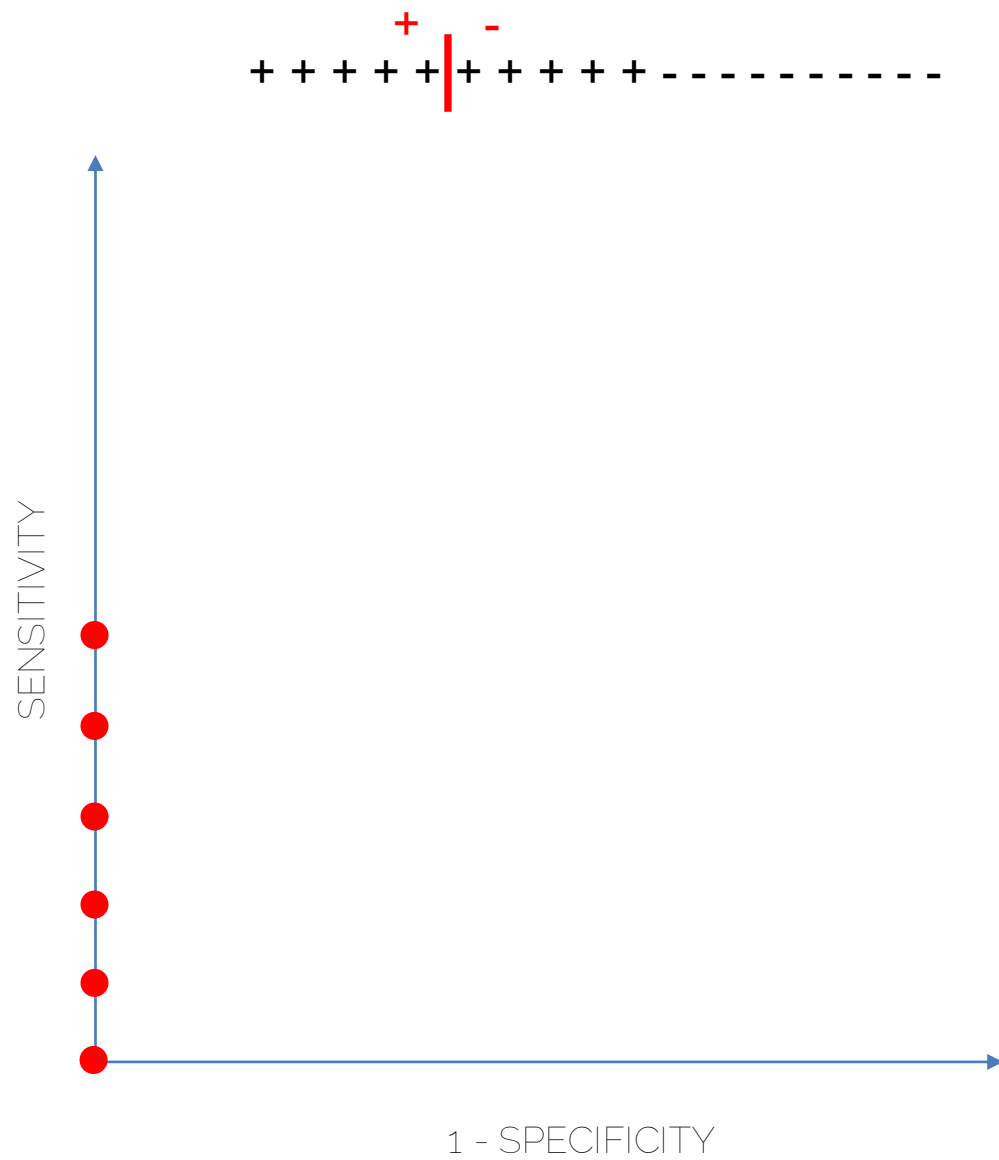
# ROC analysis and Area Under the (ROC) Curve

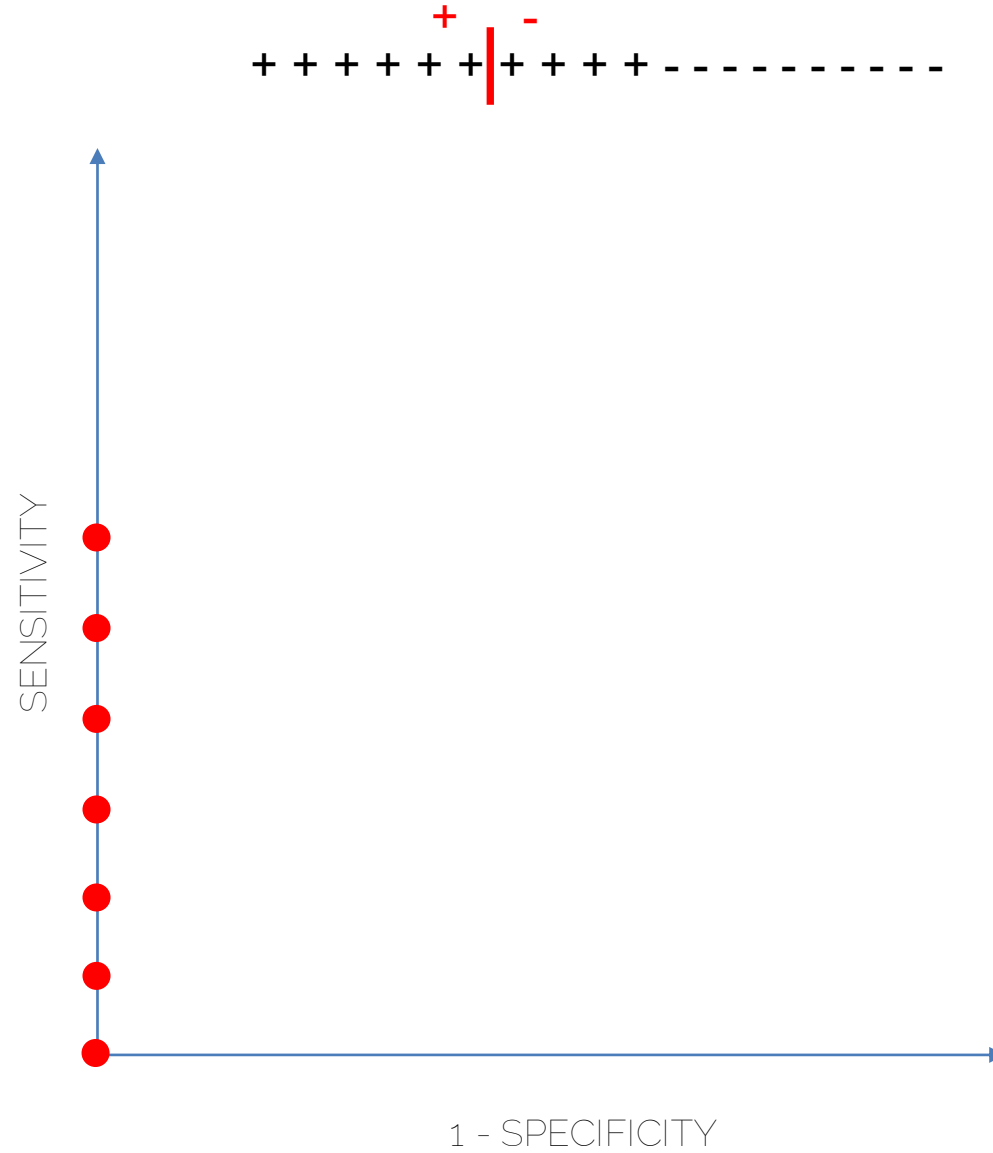


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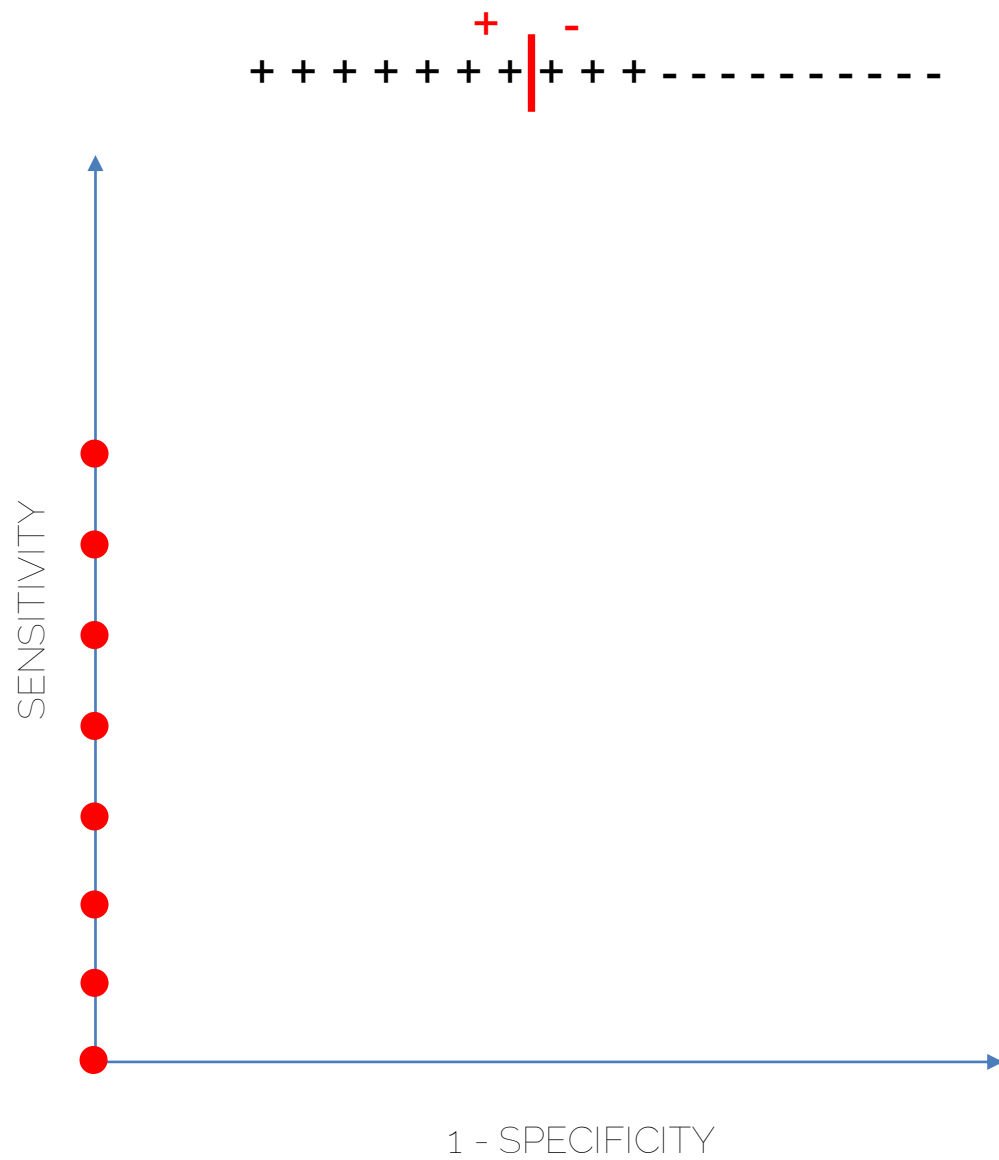


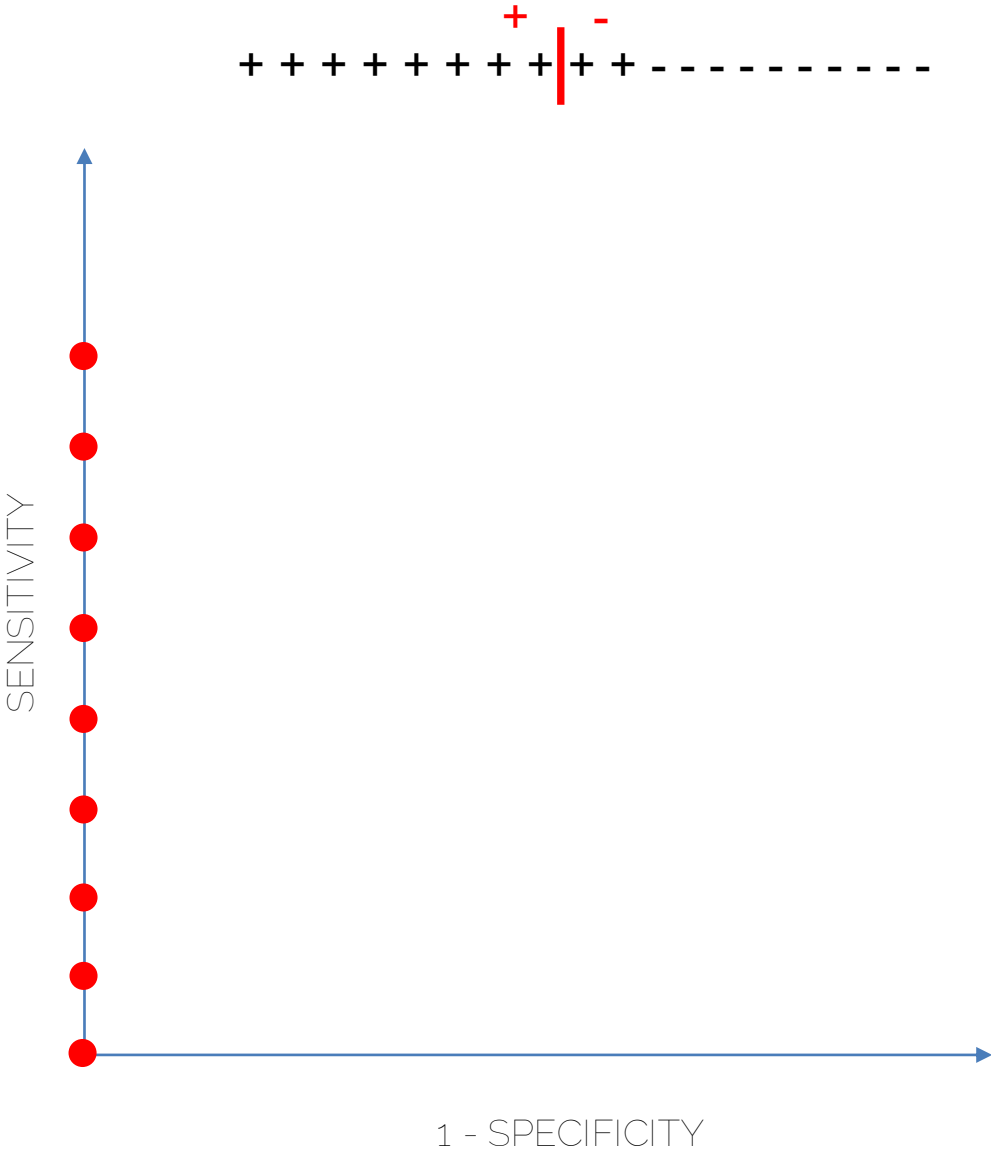
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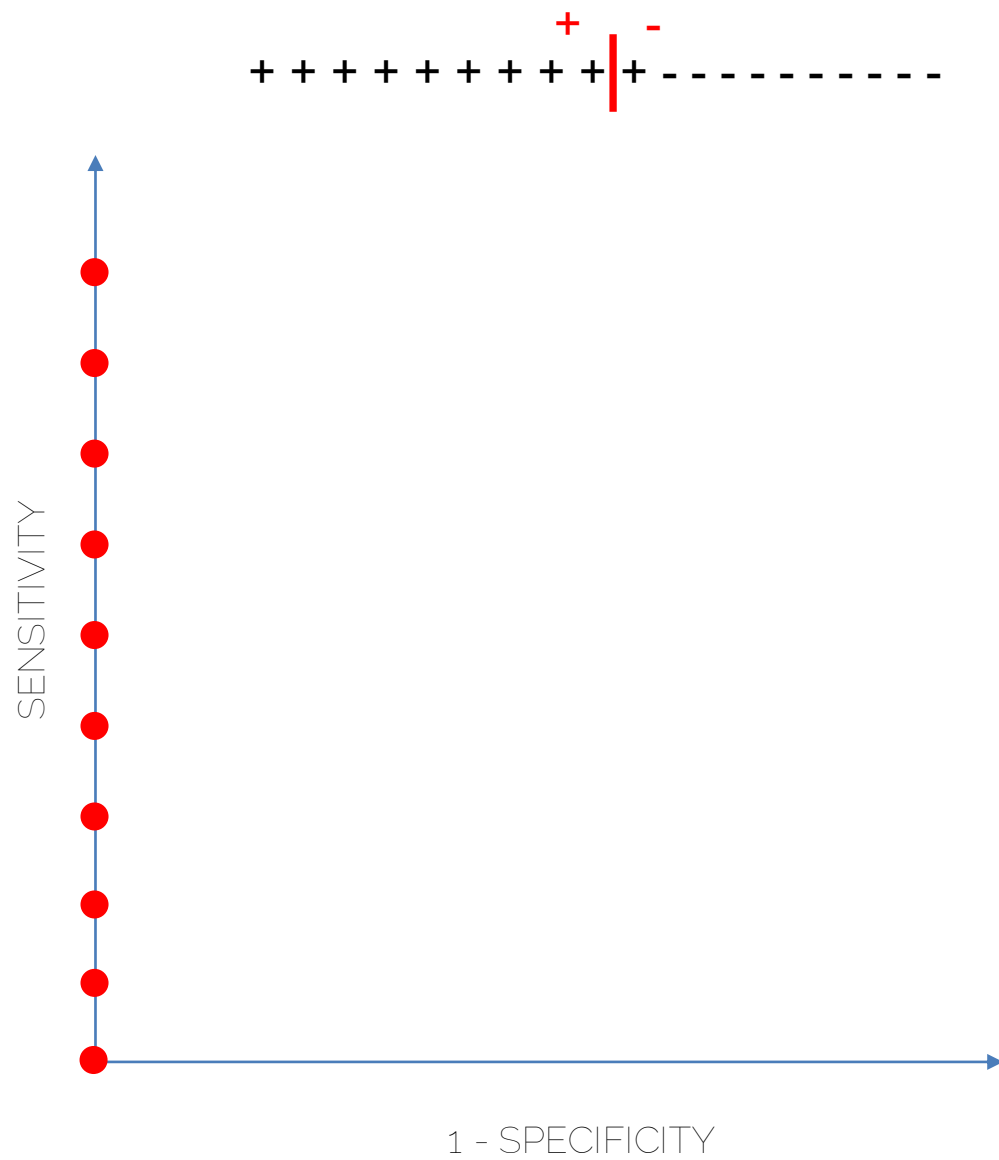


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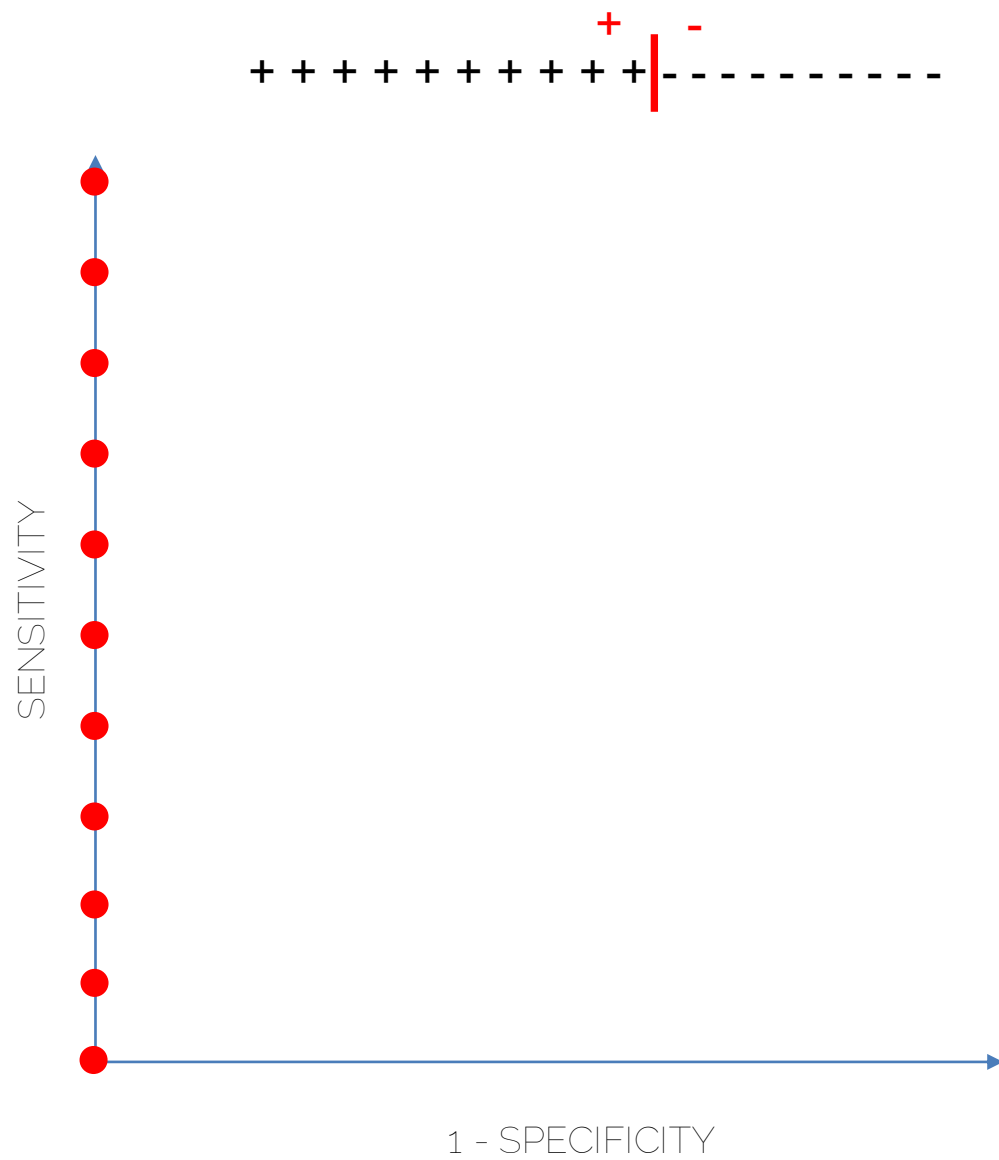




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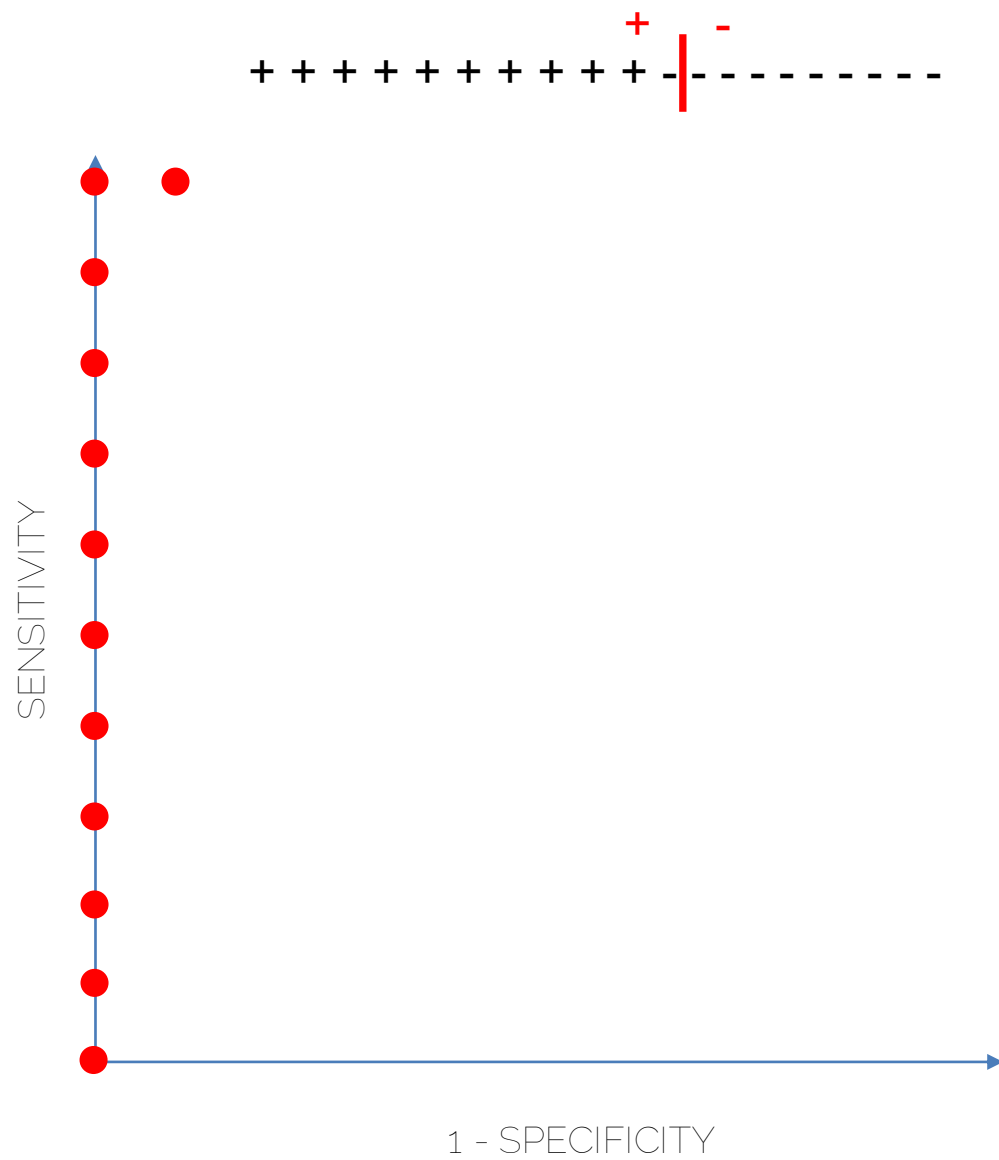


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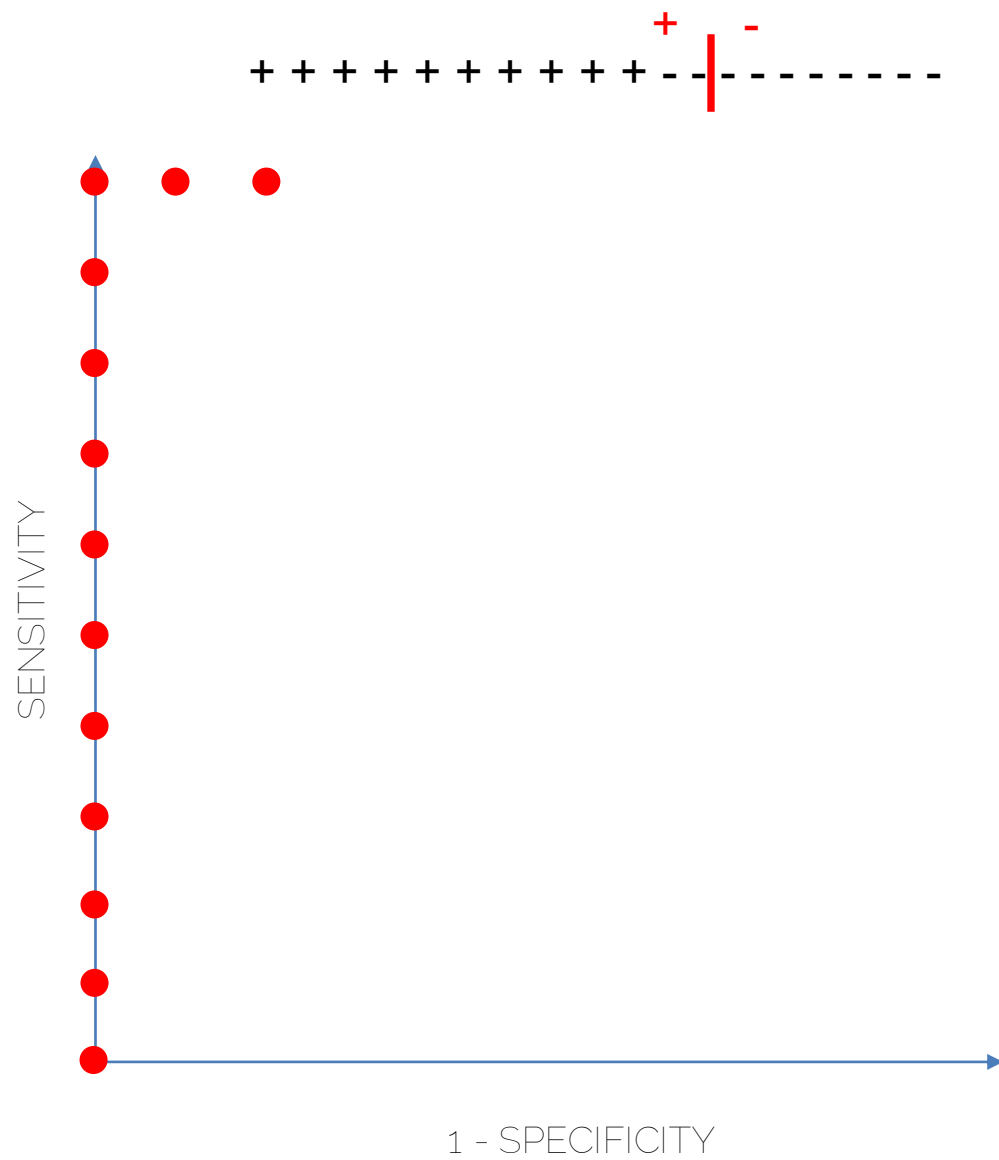




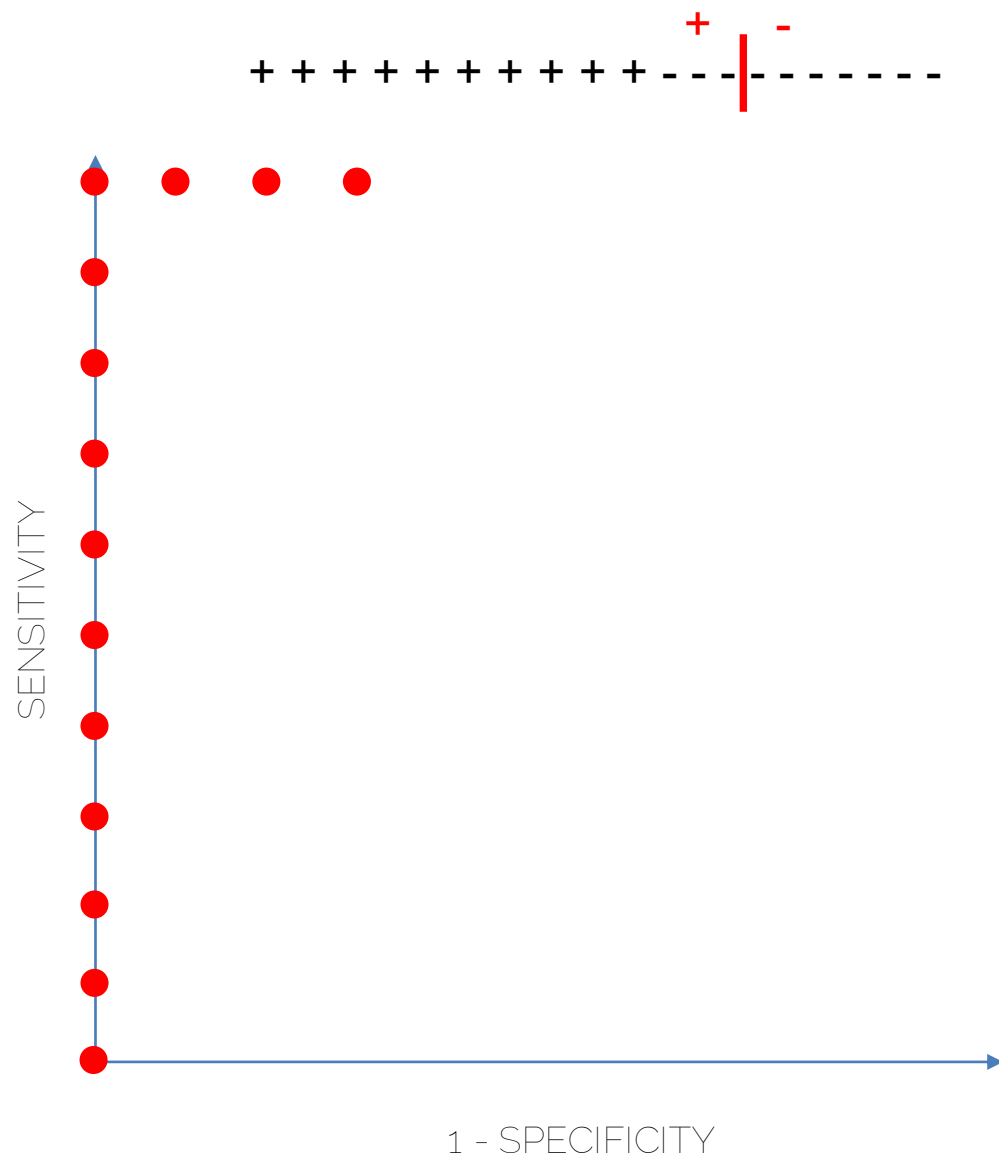
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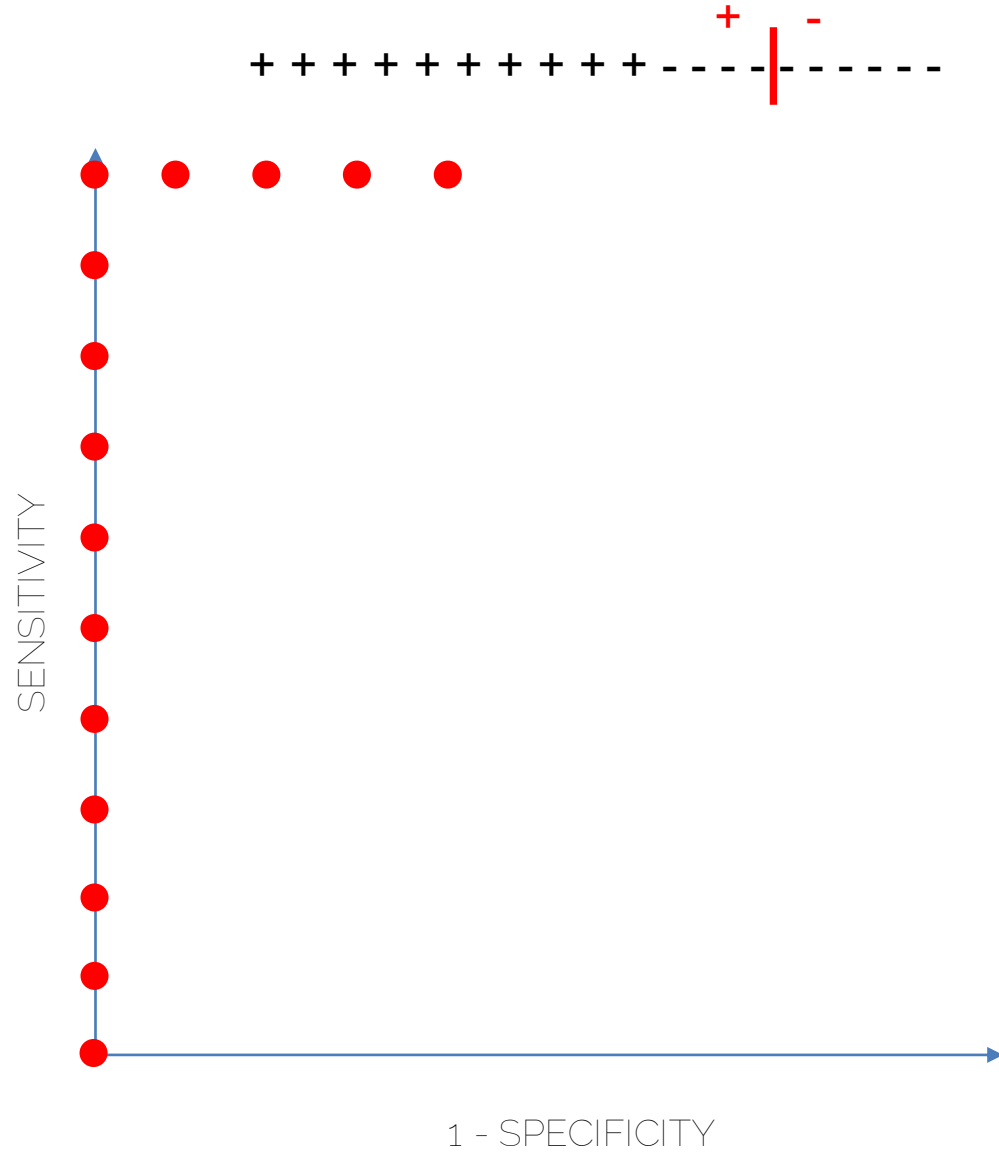
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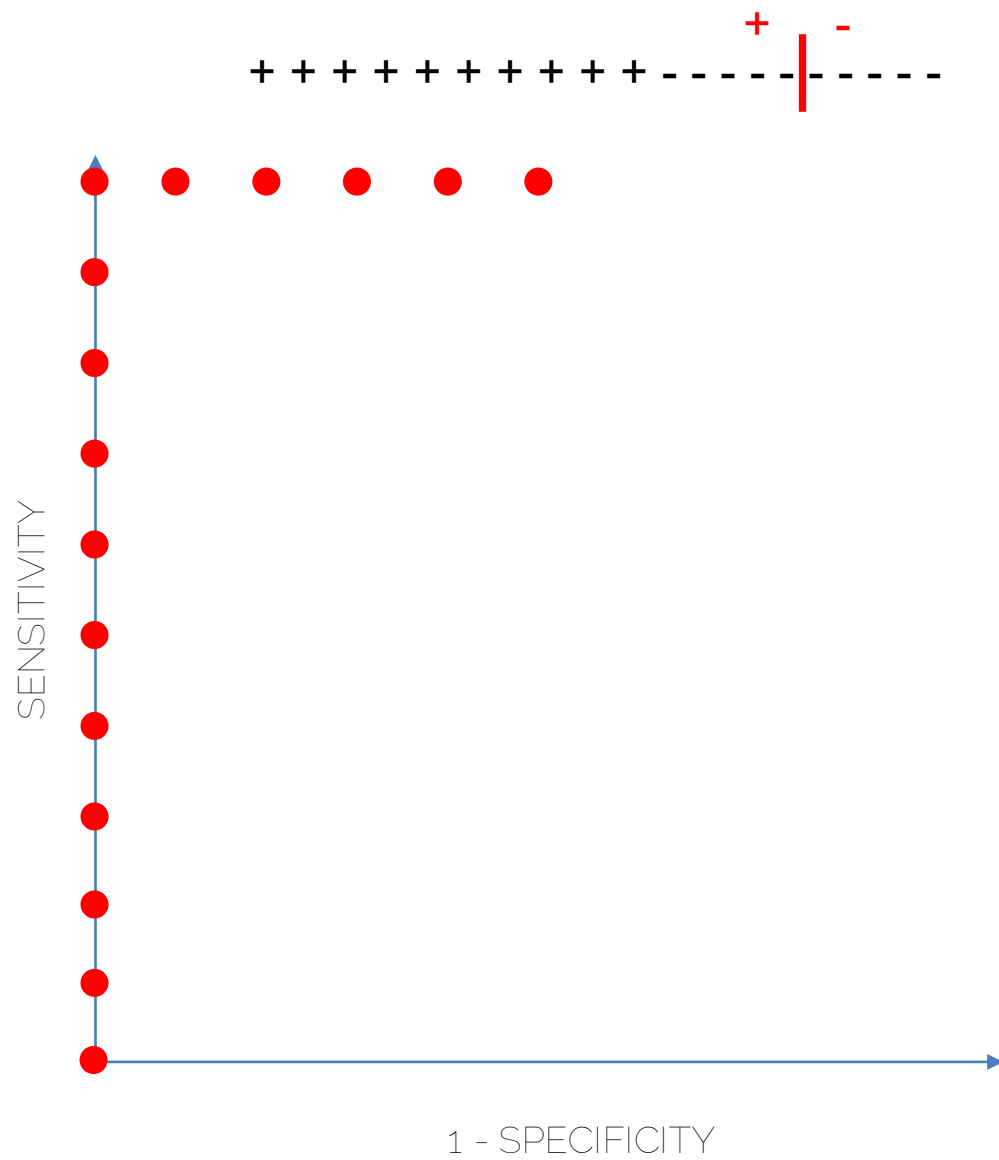
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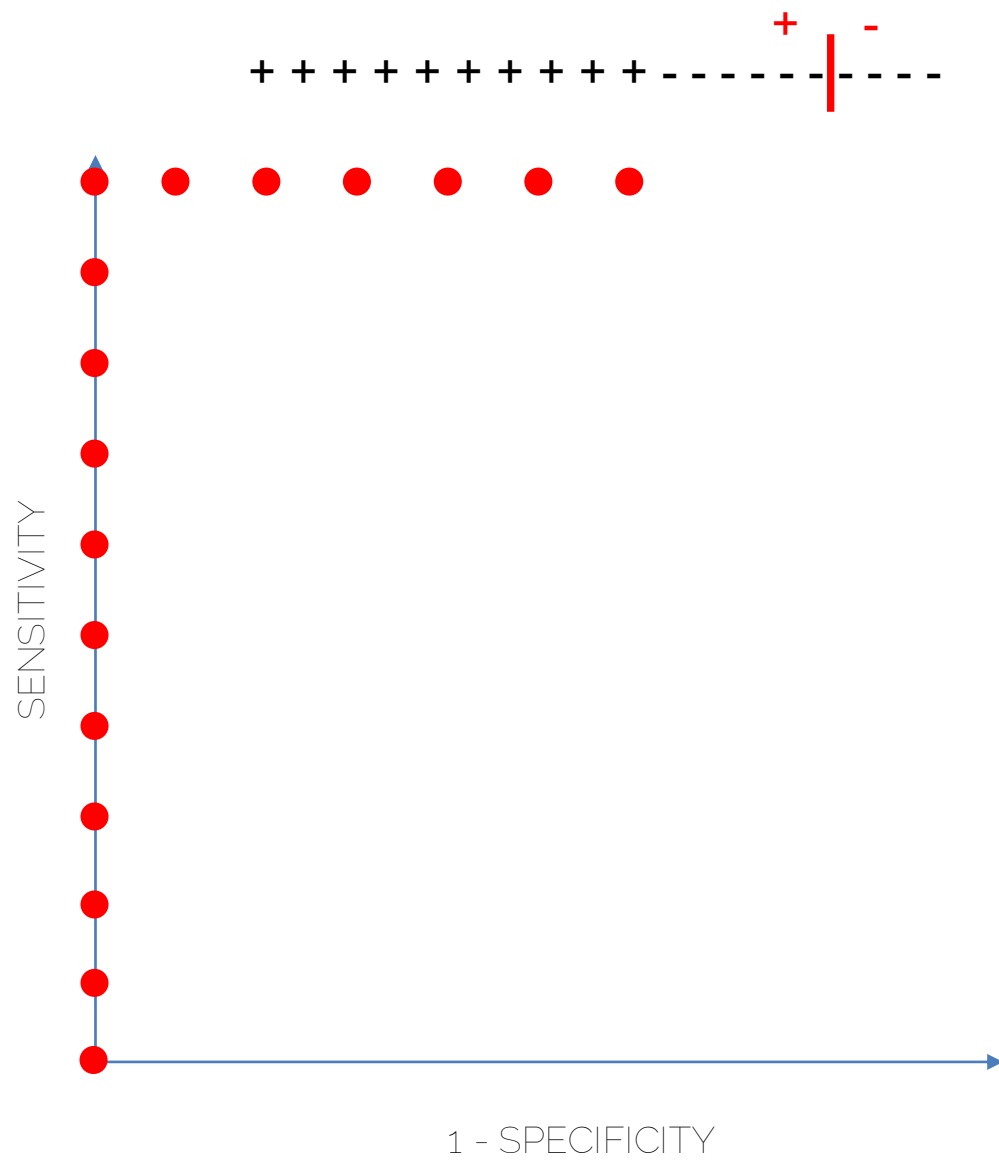
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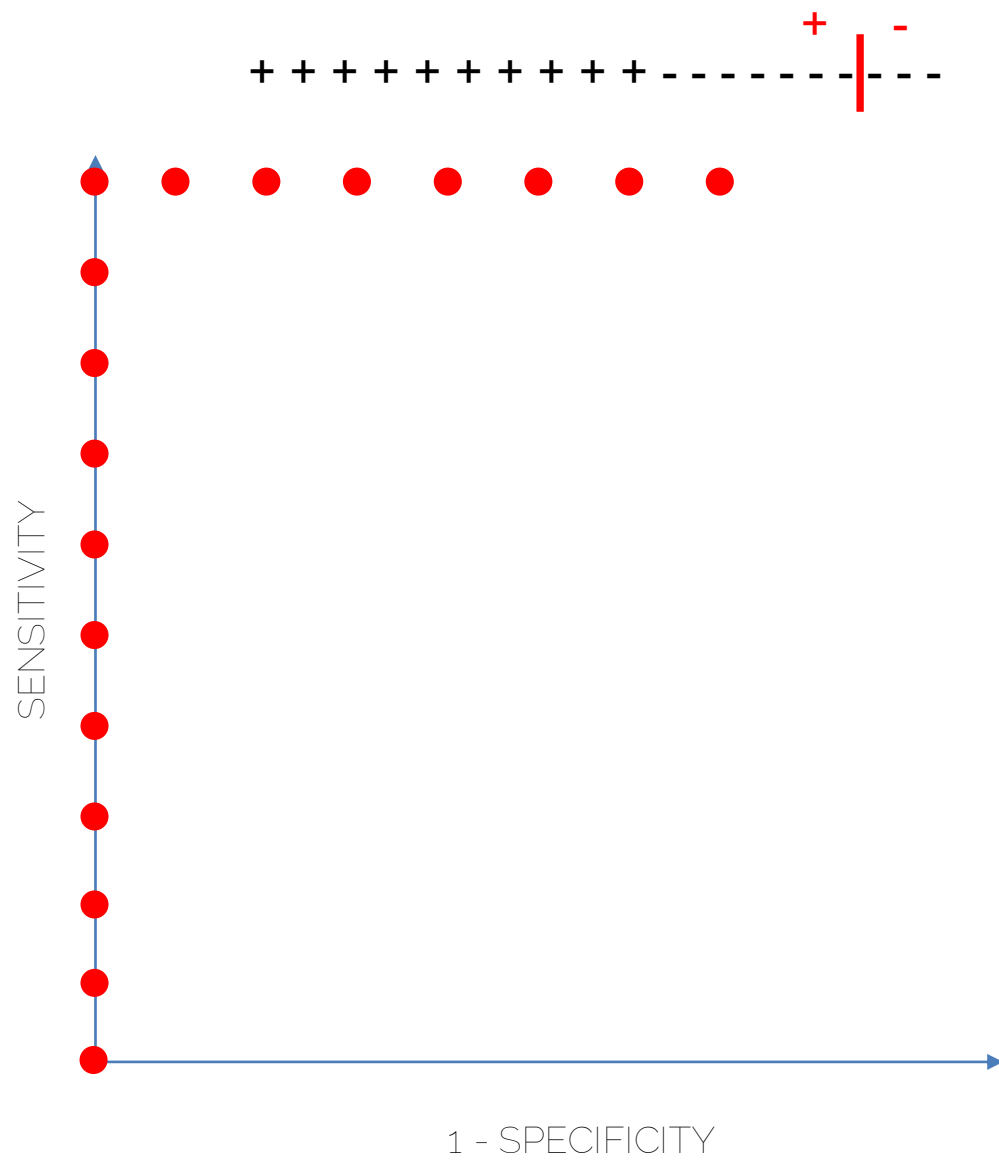
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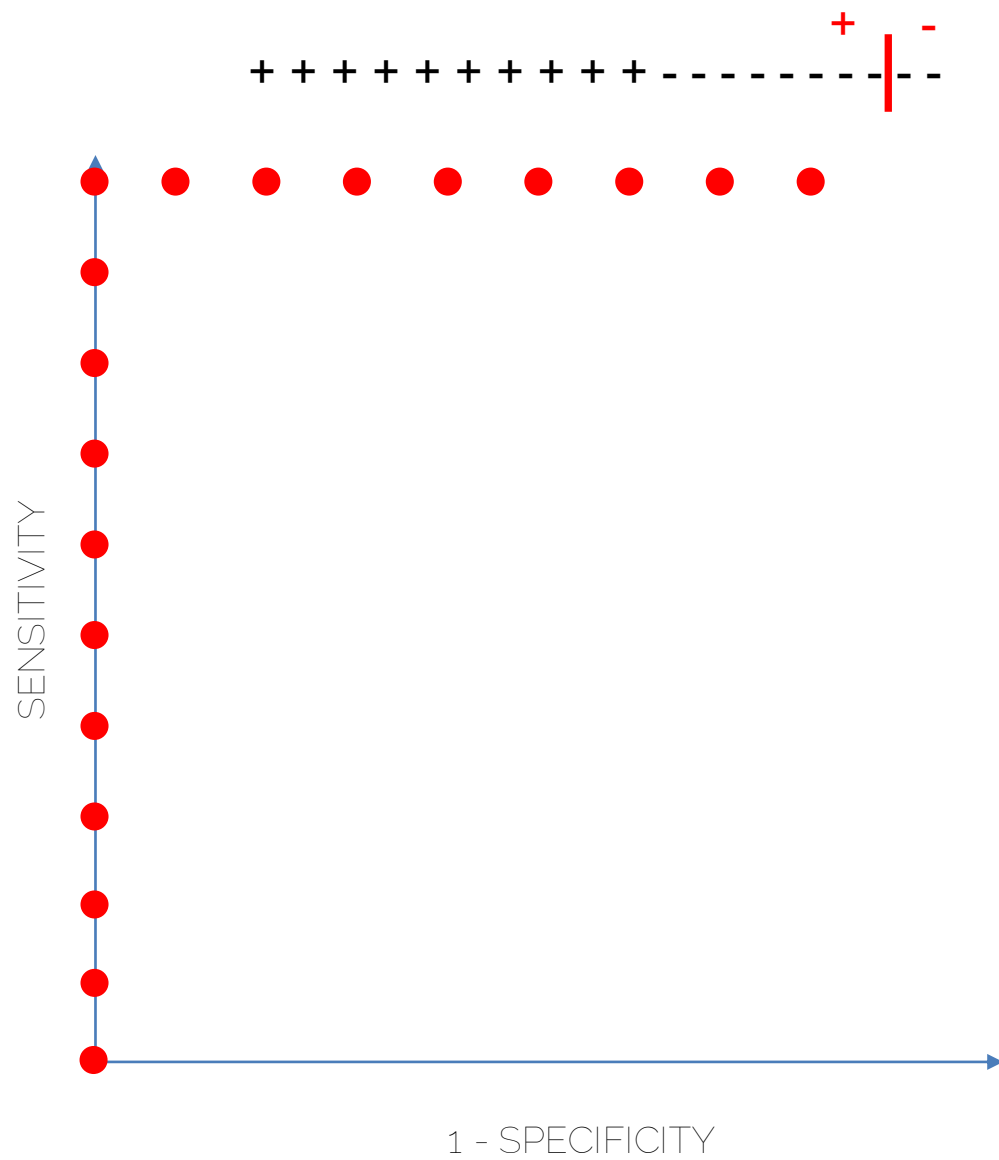
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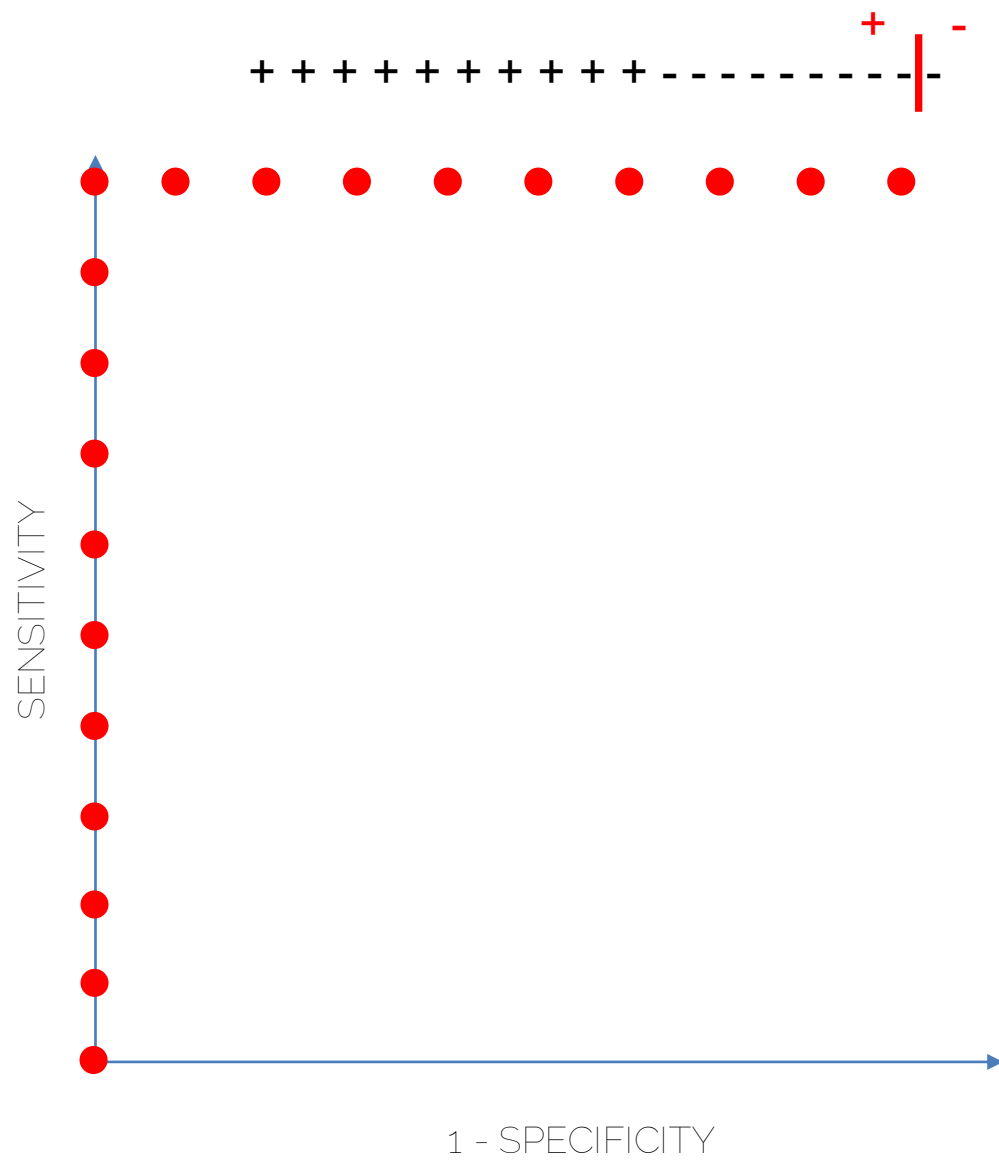


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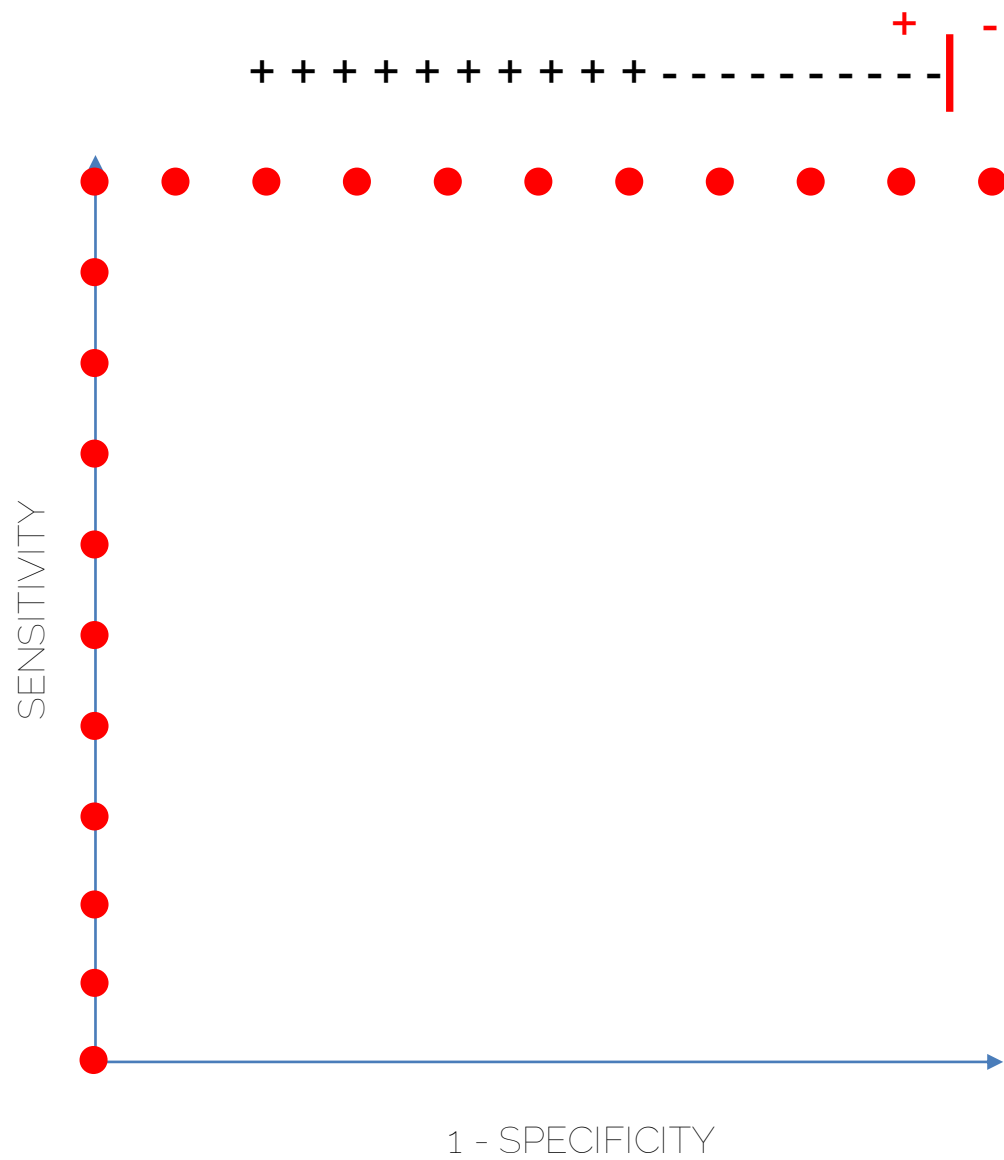




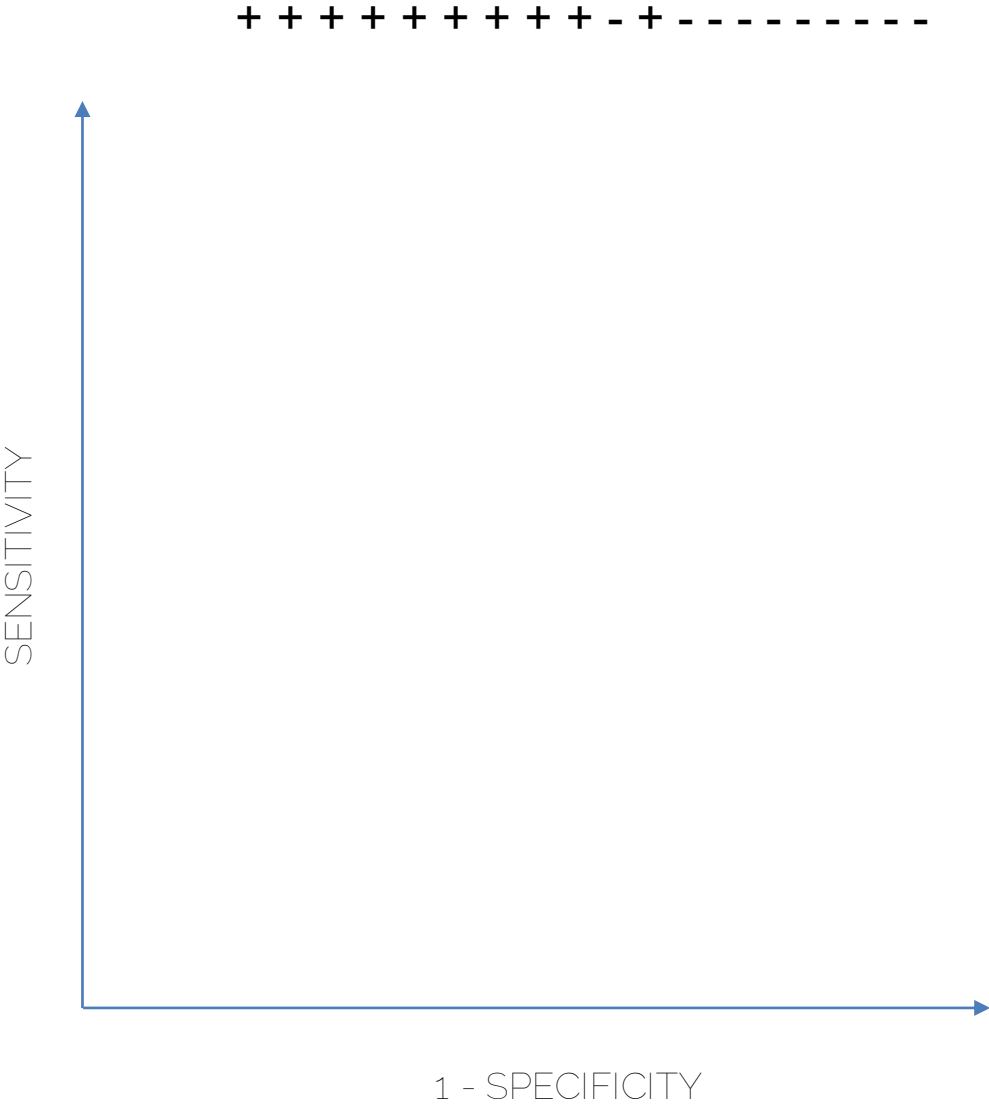
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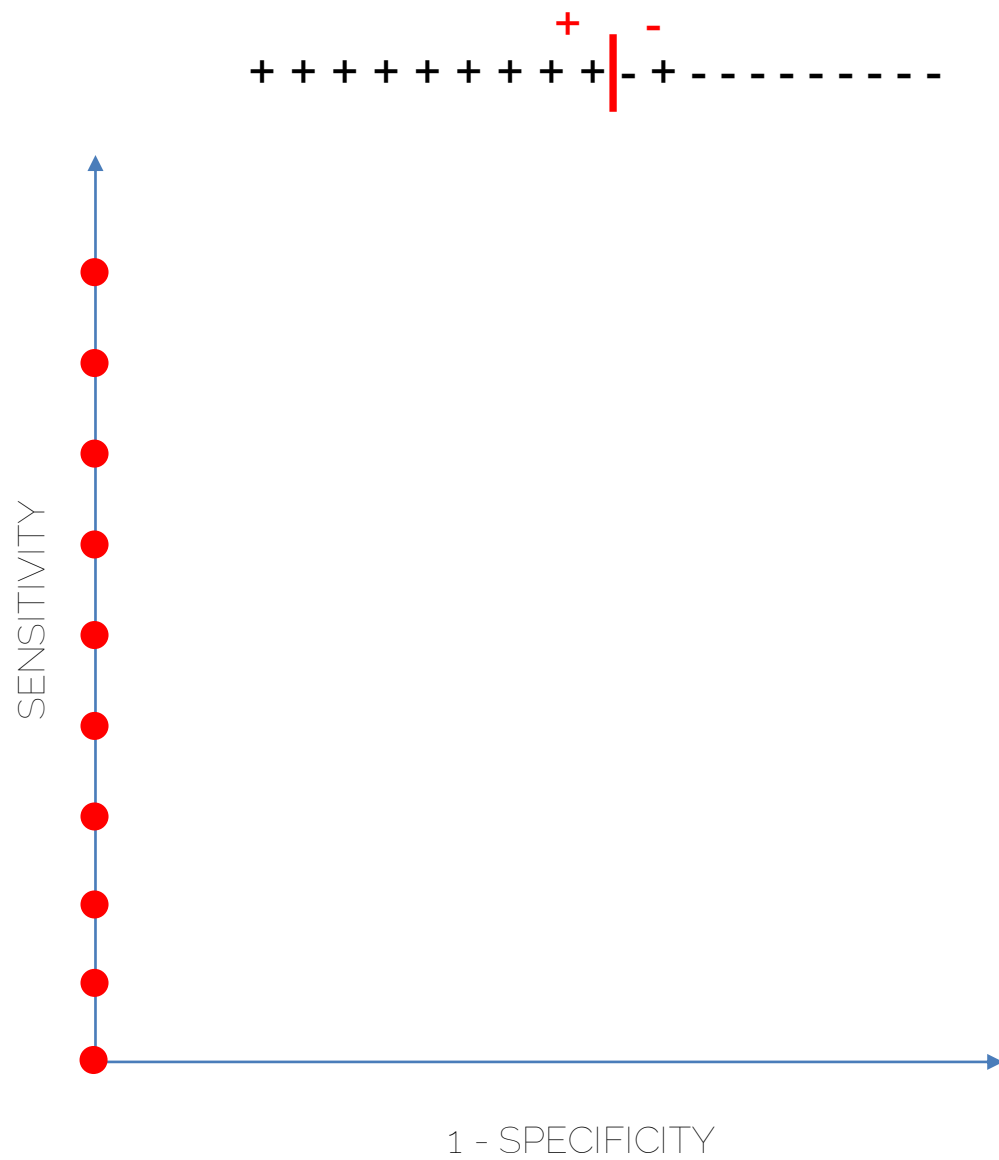
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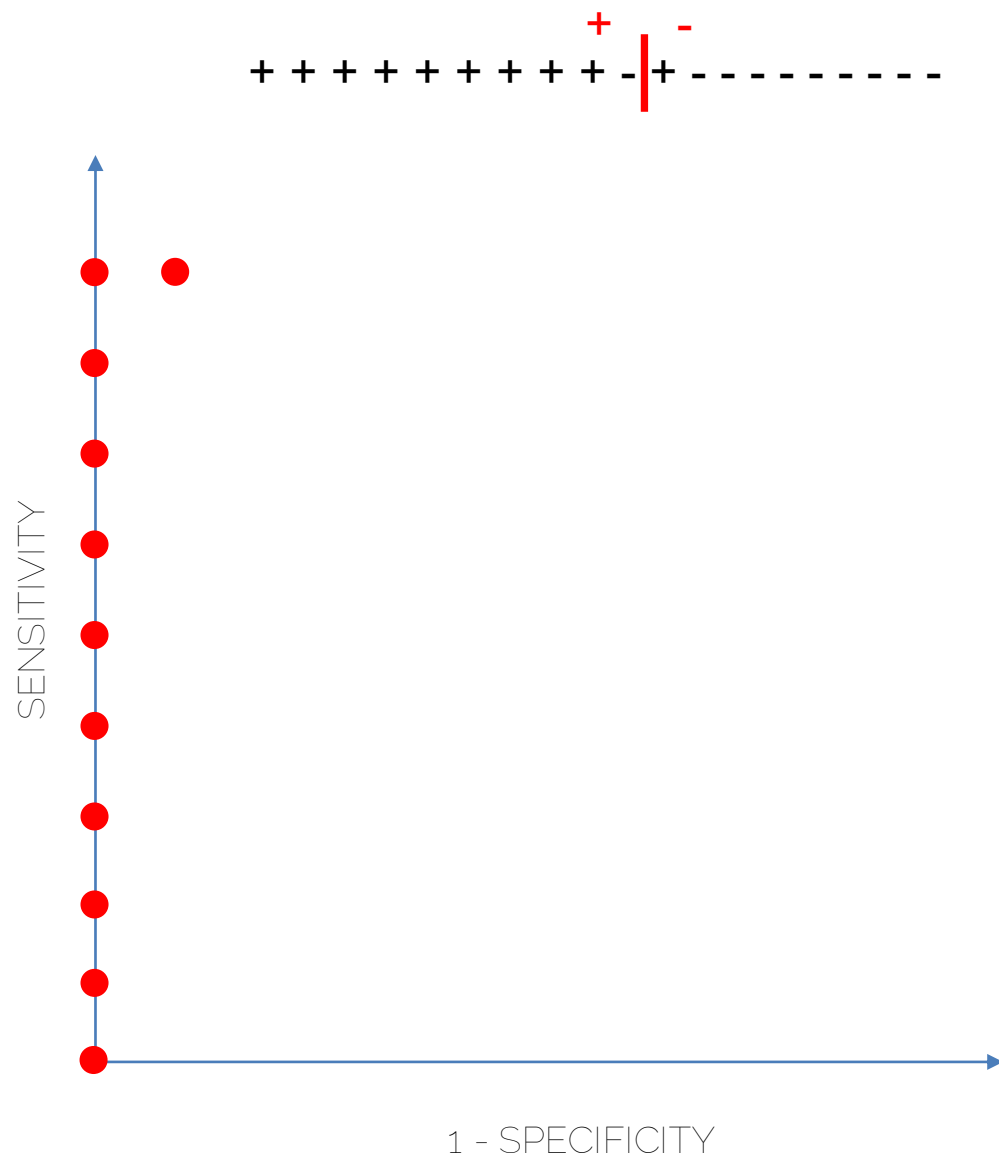
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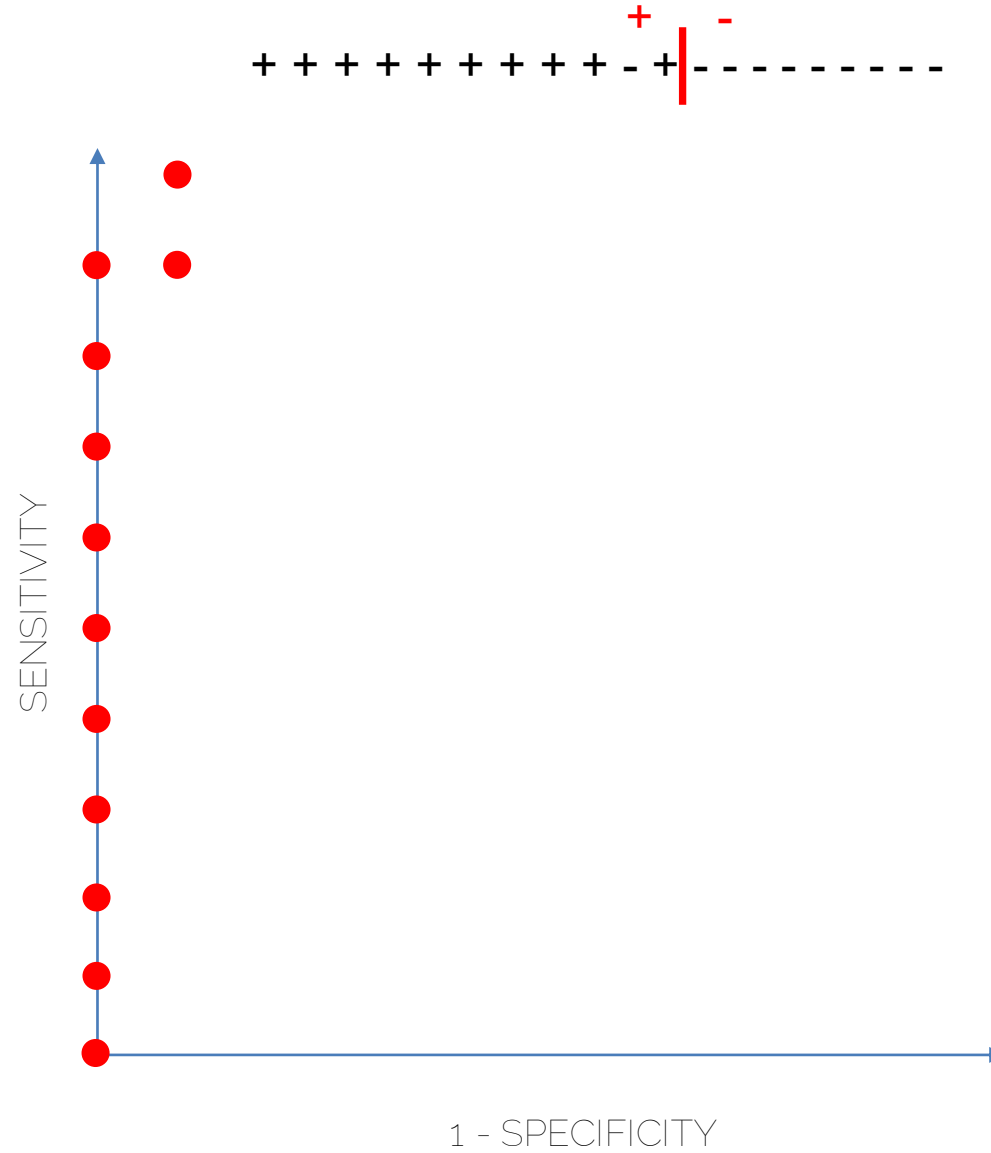


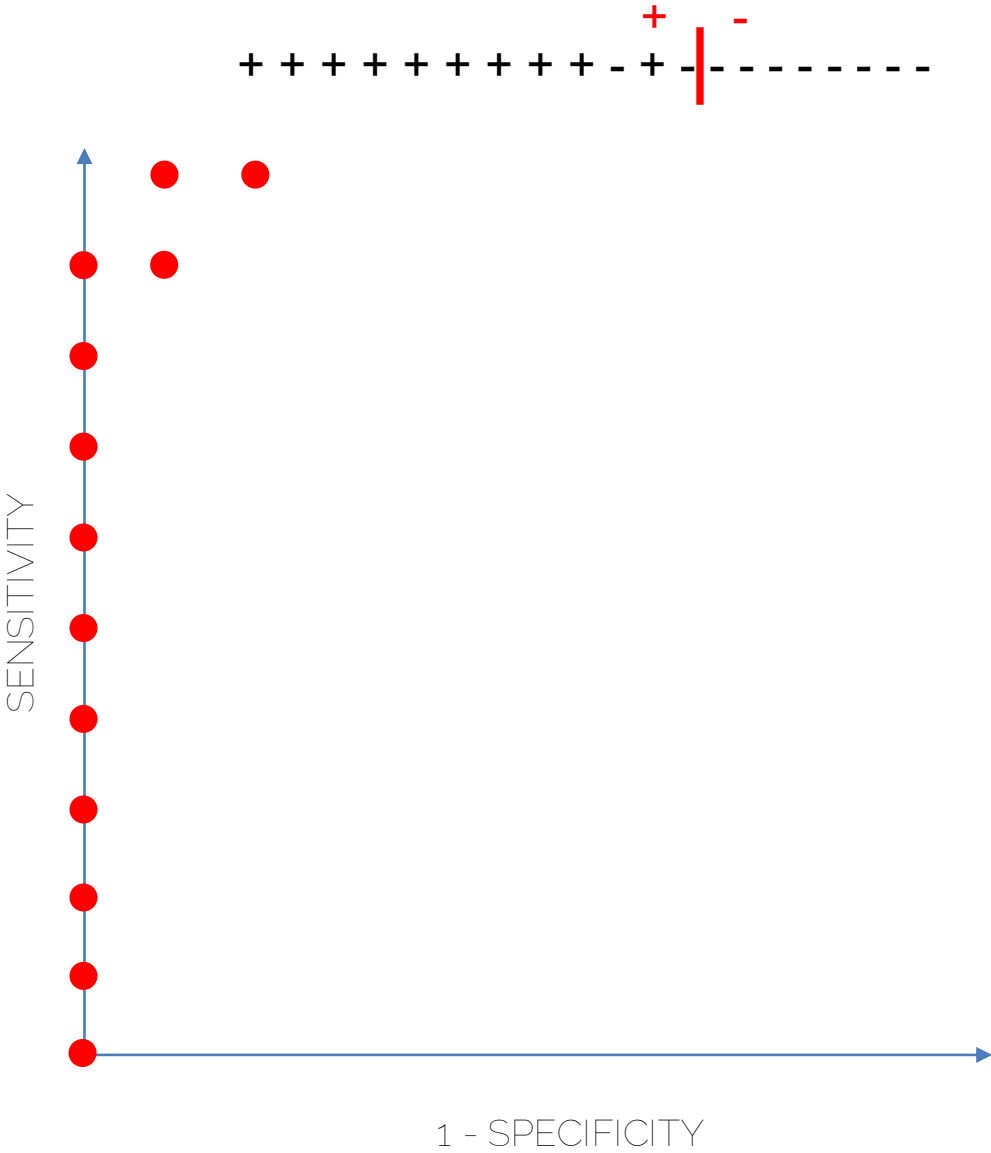
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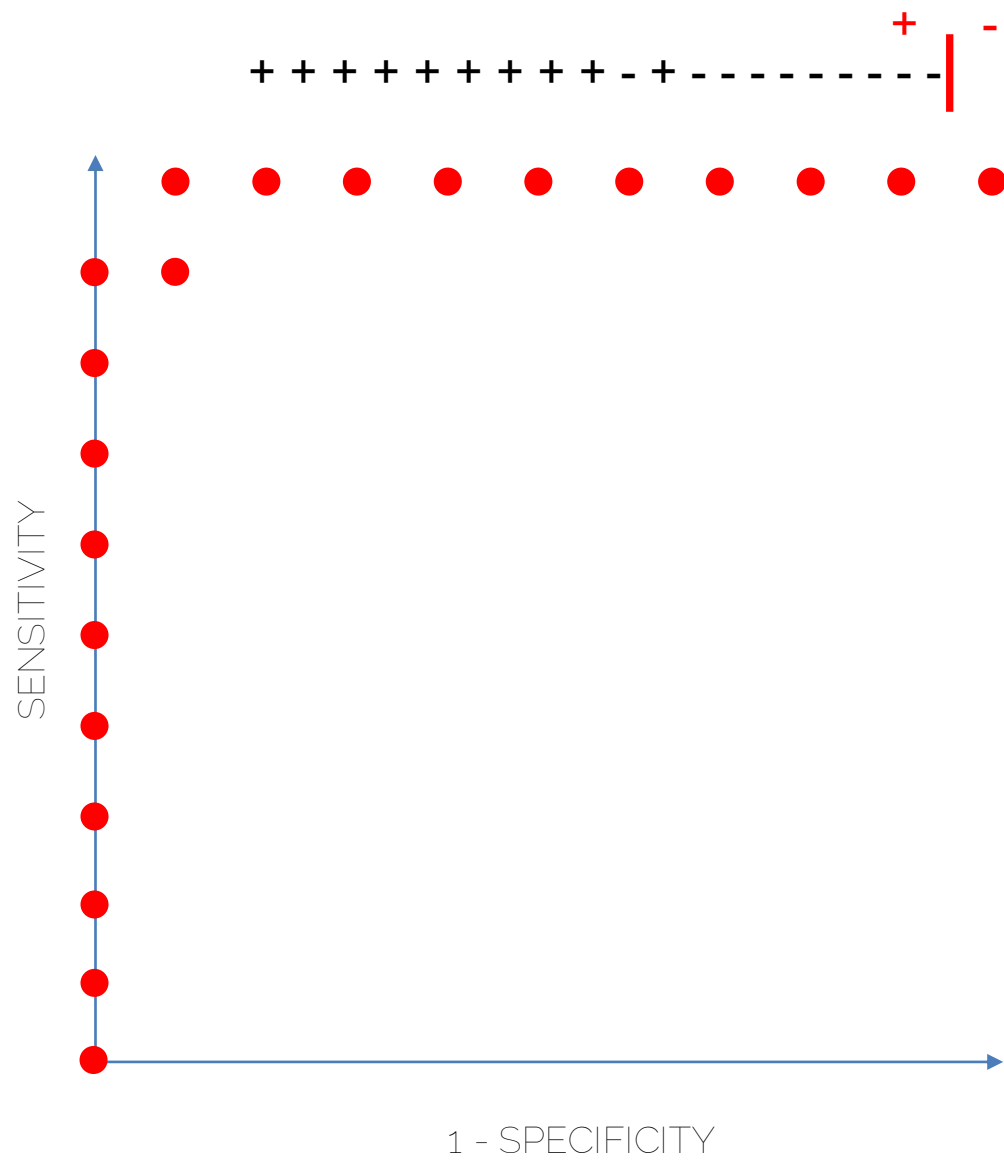
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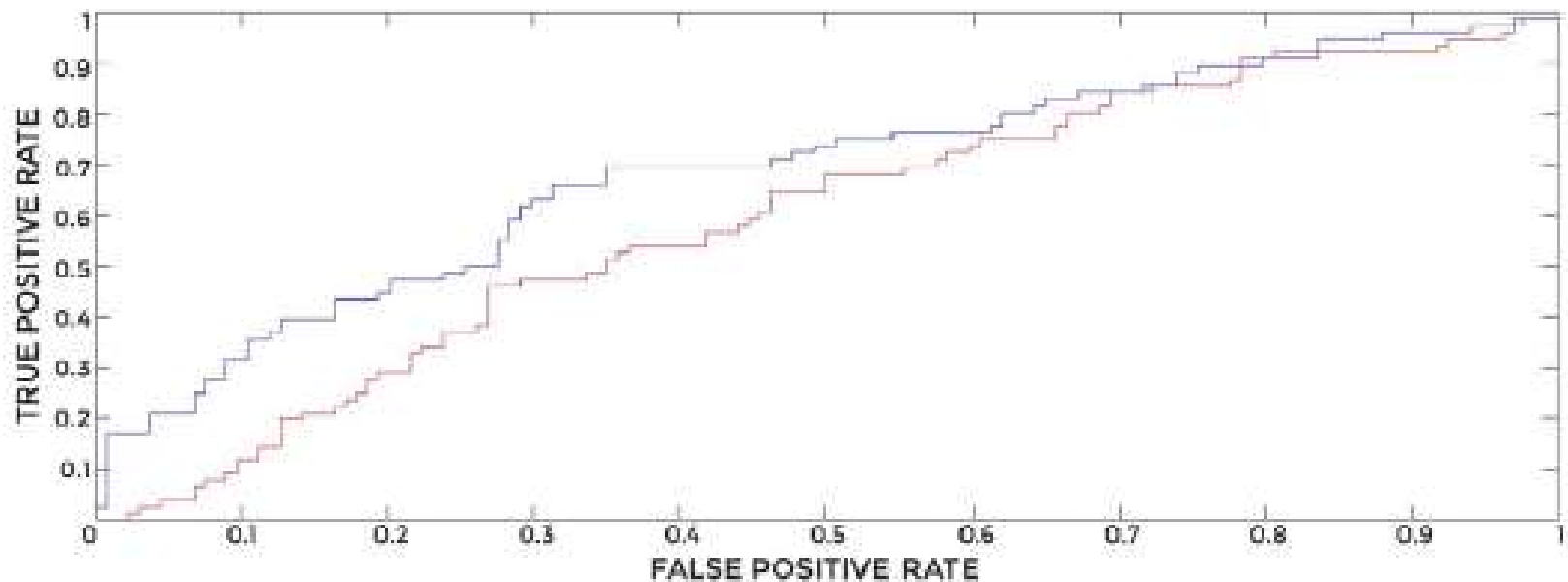
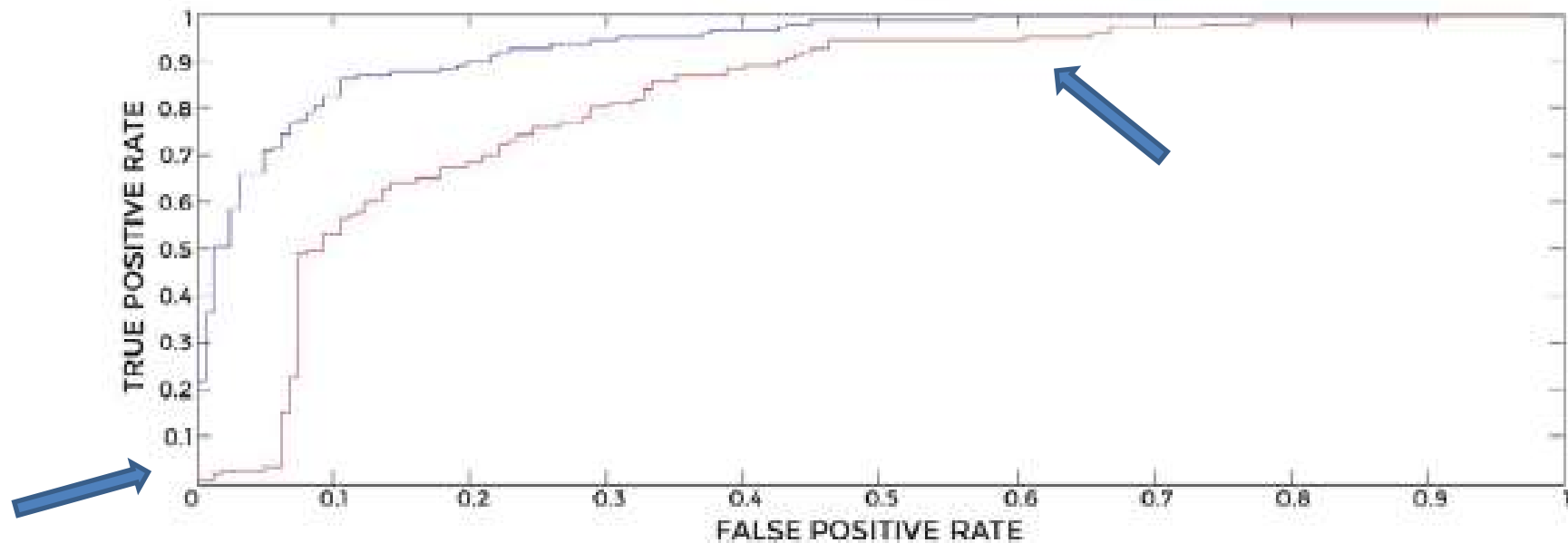


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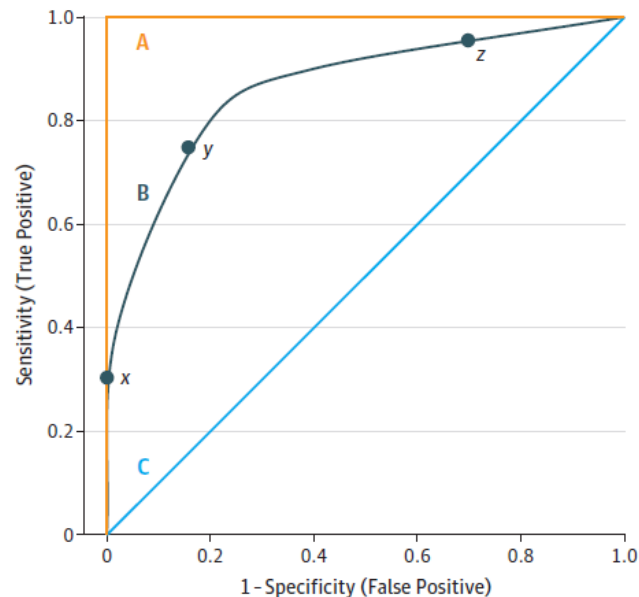


# Discrimination and Calibration of Clinical Prediction Models

**Discrimination refers to how well the model differentiates those at higher risk of having an event from those at lower risk.**

Discrimination depends on the distribution of patient characteristics in the population in which the model is being used. A model could well discriminate patients with events from those without events in a heterogeneous population with widely different values of predictors included in the model (e.g., age, sex, laboratory values); however, the same model could fail to discriminate patients in a more homogeneous population.

Figure 1. Receiving Operating Characteristic Curve and Area Under the Curve (AUC)



But...

A model can have excellent discrimination (and thus a high C statistic) and still provide misleading absolute risks.

# Discrimination and Calibration of Clinical Prediction Models

**Calibration** or goodness of fit is often considered the most important property of a model, and **reflects the extent to which a model correctly estimates the absolute risk** (i.e., if the values predicted by the model agree with the observed values). Poorly calibrated models will underestimate or overestimate the outcome of interest.

Assessing calibration involves comparing predicted and observed risk at different levels in (1) the whole population (mean calibration); (2) different groups of patients based on predicted risk; or (3) different groups of patients based on combinations of predictors (covariates).

An excellent model will show strong calibration for different groups of patients with different characteristics; however, simulation exercises suggest that accurate calibration for different populations may be unrealistic.

Models that are well calibrated to predict average population risk could have poor discrimination and thus no clinical value.

A model with adequate calibration by predicted risk strata will provide useful information for clinical decision making.

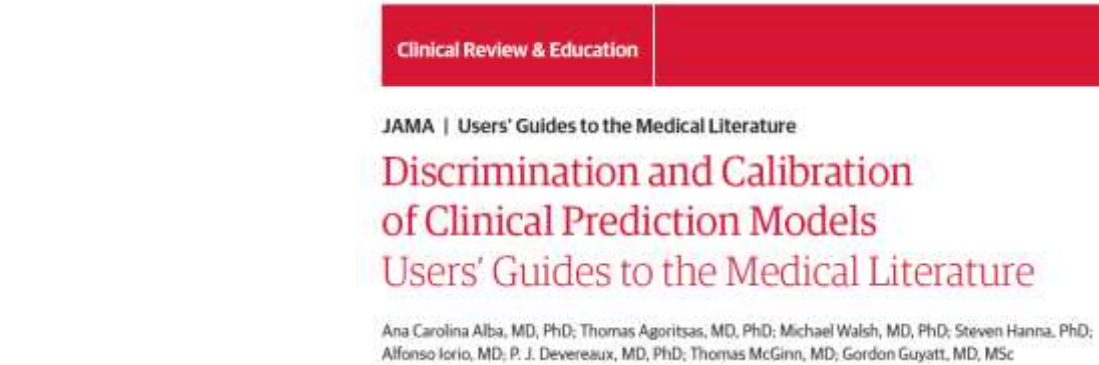
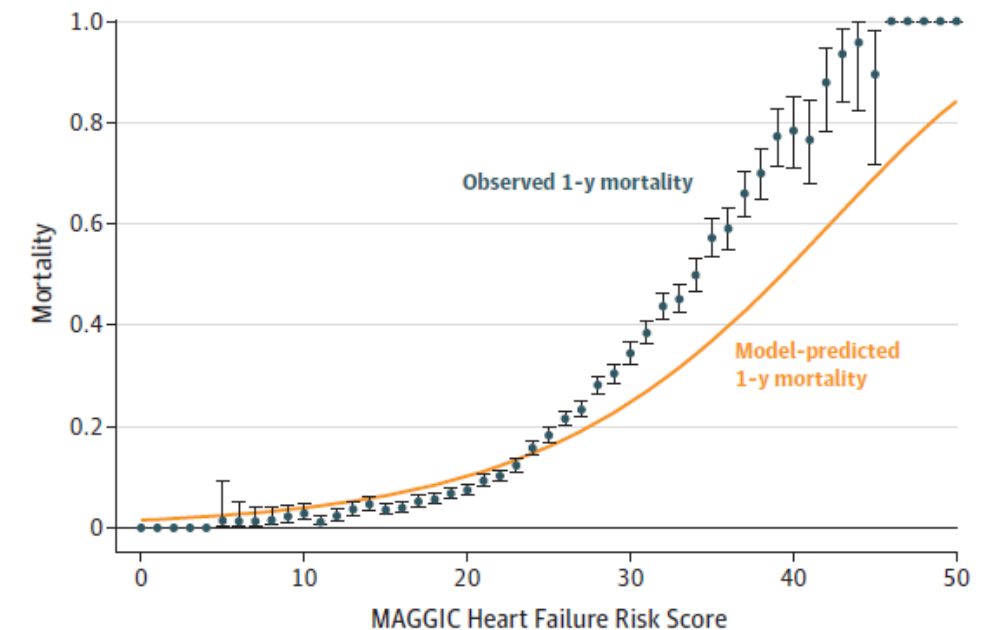


Figure 2. Observed and Predicted 1-Year Mortality



+ statistical tests, e.g. [Hosmer-Lemeshow test](#)

# Comparison of two models: net reclassification

**Net reclassification involves** classifying patients in risk categories and **determining how a new model reclassifies patients into various risk categories compared with a previous model**. Risk differences are classified based on the actual outcome patients experienced

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## Discrimination and Calibration of Clinical Prediction Models Users' Guides to the Medical Literature

Ana Carolina Alba, MD, PhD; Thomas Agoritsas, MD, PhD; Michael Walsh, MD, PhD; Steven Hanna, PhD; Alfonso Iorio, MD; P. J. Devereaux, MD, PhD; Thomas McGinn, MD; Gordon Guyatt, MD, MSc

Patients with events (n=10 000, 50% of total)

		NEW MODEL			Totals, old model
		Low risk	Moderate risk	High risk	
OLD MODEL	Low risk	2500	1200 <sup>a+</sup>	400 <sup>b+</sup>	4100
	Moderate risk	300 <sup>d+</sup>	2500	600 <sup>c+</sup>	3400
	High risk	50 <sup>e+</sup>	350 <sup>f+</sup>	2100	2500
Totals, new model		2850	4050	3100	10000

Patients without events (n=10 000, 50% of total)

		NEW MODEL			Totals, old model
		Low risk	Moderate risk	High risk	
OLD MODEL	Low risk	4000	300 <sup>a-</sup>	100 <sup>b-</sup>	4400
	Moderate risk	100 <sup>d-</sup>	4000	150 <sup>c-</sup>	4250
	High risk	50 <sup>e-</sup>	100 <sup>f-</sup>	1200	1350
Totals, new model		4150	4400	1450	10000

	Patients with events, No.		Patients without events, No.	
Correct reclassification	2200	250	Additive NRI	12
Incorrect reclassification	700	550	Absolute NRI	6%
Net reclassification	1500	-300		

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	Patients with events	Patients without events
Correct reclassification	$x^+ = a^+ + b^+ + c^+$	$x^- = d^- + e^- + f^-$
Incorrect reclassification	$y^+ = d^+ + e^+ + f^+$	$y^- = a^- + b^- + c^-$
Net reclassification	$z^+ = x^+ - y^+$	$z^- = x^- - y^-$
<input type="checkbox"/> No reclassification		
<input type="checkbox"/> Correct reclassification		
<input type="checkbox"/> Incorrect reclassification		

$$\text{Additive NRI} = \left( \frac{z^+}{\text{Total No. of patients with event}} \times 100 \right) + \left( \frac{z^-}{\text{Total No. of patients without event}} \times 100 \right)$$
$$\text{Absolute NRI} = \frac{(z^+ + z^-)}{\text{Total No. of patients}} \times 100$$