

Review Article

RECEIVER OPERATING CHARACTERISTIC CURVE: TYPES, CALCULATION AND APPLICATIONS IN IMMUNOLOGICAL FIELD

Nisreen Waleed Mustafa^{*1}, Ola Abdul Shaheed Naser² and Zaid Nabeel Elia³

¹Basra University, Pharmacy College, Basra, Iraq

²Basra University, Science College, Biology Department, Basra, Iraq

³Erbil Polytechnic University, Erbil Technical Health College, Medical Laboratory Technology Department, Erbil, Iraq

Abstract

A Receiver Operating Characteristic Curve (ROC curve) study was a very well method for determining how well an indicator may distinguish between those who develop disease and those that don't. The ROC curve is a valuable tool for organizing and displaying effectiveness of the classifier. ROC curves were extensively employed in medical decision-making and have become increasingly popular within machine learning and statistical research in recent times. Despite ROC graphs appear to be straightforward, they are subject to a number of typical misunderstandings and problems when used in practice. The purpose of this review is to provide an overview of ROC curve as well as guideline for use them in medical research. Also includes a summary of some recent breakthroughs in the calculation of the ROC curve, as well as some of its applications in field of Immunology.

Article History

Received : 25.06.2021

Accepted : 25.07.2021

Published: 20.08.2021

Key words: Sensitivity, Specificity, ROC curve, AUC and Diagnostic accuracy.

1. Introduction

A Receiver Operating Characteristic (ROC) graph is the visible, organizational, and chosen tool for classifiers effectiveness of the training (Swets *et al.*, 2000). Engineers created the ROC curve throughout World War II to recognize enemy things on battlefields (Collinson, 1998). Its application in other fields was quick, and then used to explore perceptual recognition of alarms in psychology (Swets, 1986a). It's been widely used in a variety of fields over the decades, such as atmospheric sciences, life sciences, developmental

psychology, finance, geology, and sociology (Krzanowski and Hand, 2009).

ROC analysis is now widely utilized in machine learning and deep learning, and additional applications in economic have indeed arisen (Lasko *et al.*, 2005). Morrison *et al.* (2003) established the ROC curve as just a simple and effective tool for comparing the precision of reference variables of microbiological beach quality of water in another context. Because of ROC curve assessment was raised independently by vary fields, several strategies and tools are detected by vary names in several groups (Gonçalves *et al.*, 2014).

**Corresponding author:* Nisreen Waleed Mustafa

The ROC curve is a graphical depiction of a quantitative method model's performance, displaying its sensitivity (Se) (percentage of true positives) versus the fraction of false positives (1-specificity) (Sp) for various test quantities (Hoo *et al.*, 2017). The likelihood of a truly ill person having a positive test result is Se, while the likelihood of a truly non-diseased person having a negative diagnosis is Sp. We work with probability distribution of belong to a certain test set given the real classification employing true/false positive/negative rates or specificity and sensitivity (Krzanowski and Hand, 2009), in a two-class classification (e.g., unhealthy and non-diseased people, spamming or not phishing, fraudulently or not credit card fraud activities) (Gonçalves *et al.*, 2014).

Even though the ROC curve only became famous in the 1970s, one of early uses of ROC analysis in healthcare was reported in the 1960s (Lusted, 1960). Medical technology now provides a wide range of options for diagnosing and predicting disease development, and fresh medical tests and indicators are being researched all the time (Zhou *et al.*, 2011). ROC analysis is a method for evaluating the discriminate performance of a continuous variable that represents a diagnostic test, a marker, or a classifier (Gonçalves *et al.*, 2014).

Screening tools are essential in modern healthcare, not just for verifying the existence of disease, but mostly for ruling out disease in specific patients. Dichotomous tests have two occupational divisions, including such positive and negative, while polytomous tests get more than two types, such as positive, undetermined, and negative. When a test produces quantitative numbers, like bilirubin levels, it is considered continuous; when it produces groups, including the Mantoux test, it is termed nominal. In both circumstances, sensitivity and specificity can really be computed, but the ROC curve is only applicable to continuous or ordinal tests (Kumar and Indrayan, 2011).

Clinical decision-making and research operationalization are both reliant on accurate and objective explanations of phenomena or results (e.g. sick vs. healthy, severe vs. mild, operable vs. inoperable). Unfortunately, such categorizations are often not clear or unambiguous, and secondary factors might well be required. Furthermore, numerous conditions, like diabetes (fasting hyperglycaemia versus oral glucose tolerance test), crucialis chemia (medical variables versus proportion arterial restriction), and depression (DSM V criteria vs. Beck inventory), have varydiagnostic systems, each with varying sensitivity and specificity (Forkmann *et al.*, 2009). In reality, the parameters used it to categorize outcomes are rarely perfectly predicted, resulting in the wrong classification of a fraction of illness (false negatives) or healthy people (false positives), hence it's critical to compare the efficacy of diverse classification methods. The ROC curve is among the most extensively used statistical estimators for evaluating the behavior of classificatory methods (Hoo *et al.*, 2017). A most prevalent uses for ROC curves include classification systems based on medical symptoms, diagnostics scales, radiological findings, screenings of various substances, and, most importantly, the selection of suitable points of confinement to improve the efficiency of screening procedures (Forkmann *et al.*, 2009).

The ROC analysis can be used to: assess a continuous marker's exclusionary ability to accurately assign into a two-group classification; (ii) find an optimal cut-off point to least misidentify the two topics; (iii) compare the effectiveness of two or more screening procedures or indicators; and (iv) investigate inter-observer variations when two or more researchers assess the same thing. Numerous parametric, semiparametric, and nonparametric approaches use ROC curve estimation (Gonçalves *et al.*, 2014). Sensitivity and specificity can be calculated among all potential threshold levels whenever the responses of a diagnostic test are continuous or on an ordinal scale (minimum five sections). Sensitivity and specificity are inversely connected, with sensitivity increasing as specificity decreasing through various thresholds. The

Receiver Operating Characteristic (ROC) curve is a graph that shows the entire picture of the exchange between sensitivity and (1- specificity) over a set of points of confinement. The area under the ROC curve is a useful indicator of a diagnostic test's intrinsic validity (Kumar and Indrayan, 2011).

2. Background and Rationale of ROC Analysis

Electronic signal detection theory gave rise to ROC analysis inside the early 1950s (Swets, 1986b). One of early applications was already in radar, where it was used to distinguish observer variation from of the signal's inherent detectability. In the early 1950s, psychologists applied ROC approach to identify the relationship between the qualities of sensory cues as well as the characteristics of psychological state (Green and Swets, 1966). ROC approach has been used in radiography and radionuclide scanning since the early 1960s. Lusted (1960) computed first ROC curve in interventional imaging by re-analyzing originally collected reports on the identification of pulmonary tuberculosis and demonstrating the reciprocal relationship here between percentage of false positive and false negative evidence from multiple chest film explanation experiments (Lusted, 1960). ROC method has been introduced to diagnostic testing methods by several authors. Dorfman and Alf's work in 1968 was a game-changer in terms of objective curve fitting and the use of computers software in ROC analysis (Dorfman and Alf, 1968). In 1968, an automatic program using the maximum - likelihood technique under the binormal hypothesis was created. Since then, various significant methodologic improvements have been applied in ROCFIT, CORROC, ROCPWR, and LABROC, Metz's ROC data analysis tools project at the University of Chicago. They are freely available on the internet (Hajian Tilaki, 2013). ROC analysis has become a prominent tool for measuring the results of diagnostic imaging systems throughout the last 4 decades. The precision indices made from ROC analysis aren't affected by oscillations produced by arbitrarily defined detection criteria or cut-offs, that is most diverse aspect of this method. In other terms, the

choice strategy (the propensity of a readers or spectator to choose a given threshold on the separators variable) and the previous likelihood of the signal have no effect upon on accuracy indexes (Swets, 1986b). The intrinsic ability of the assay to recognize between sick and healthy individuals is detected by the produced summary measure of precision, such as AUC (Metz, 1978). Can one evaluate proctored exams or determine whether various combinations of tests (e.g., imaging modalities or readers) can increase diagnostic accuracy to use this as a metric of diagnostic performance (Hajian Tilaki, 2013).

3. How to make ROC curve

True positive, true negative, false positive, and false negative are all elements that must be understood before creating a ROC curve. When compared the findings of a test to the clinical truth, which is detected by use of diagnostic processes rather than the test in issue, multiples principles are being used (Ekelund, 2012). The idea of a partition (decision) variable underpins the theory of a ROC curve. If the threshold value for positively on the decision axis is changed, the frequency of positive and negative diagnostic test findings will fluctuate. The selection scale is really only implicit when the outcomes of a medical diagnosis are evaluated based on individual judgment. A hidden or unmeasured parameter is a decision variable like this (Hajian-Tilaki, 2013).

A ROC curve is generated by plotting true positive TPF (sensitivity) versus false positive FPF (1-specificity) through multiples cutoffs. The ROC curves that relate to increasing diagnostic test discriminating capability are gradually nearer to the top left hand corner of the ROC curve (Figure - 1). The efficacy of a diagnostic test that is not better than a placebo, i.e. a test that produce positive or negative results un-connected to the true clinical state, is reflected by a ROC curve which lies on the vertical line. The probability value is really the ratio of a 2 functionals defining (the dispersion of the separators variables throughout the afflicted and non-diseased individuals) at a certain point on a ROC curve (Greiner *et al.*, 2000). A concave ROC curve

correlates to a monotonically growing likelihood ratio (Swets, 1986b). Rather of relying on a single operating point, the AUC describes the full region of the ROC curve (Hanley and McNeil, 1982).

The AUC is a useful and integrated assessment of sensitivity and specificity that shows the intrinsic reliability of diagnostic tests (Kumar and Indrayan, 2011).

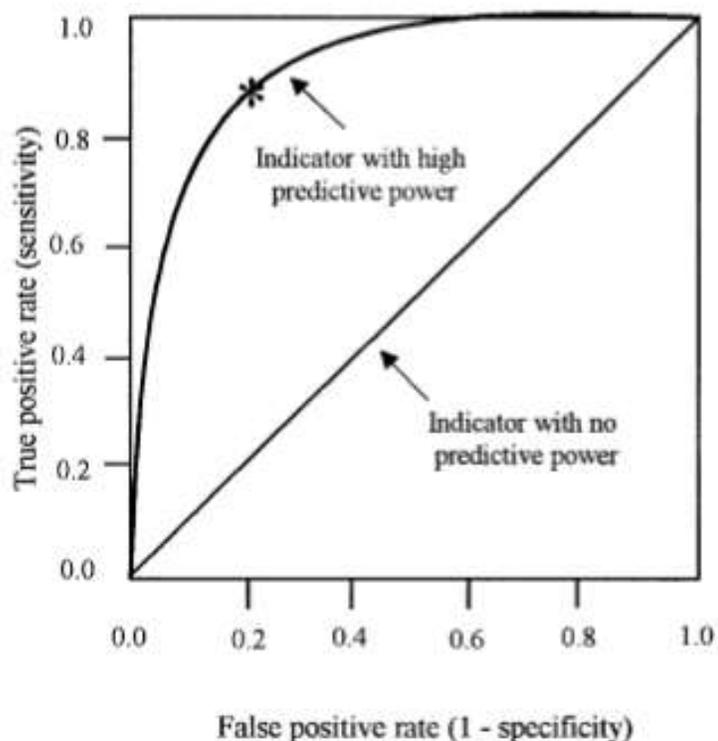


Figure - 1: ROC curve

Diagnostic accuracy

Diagnostic accuracy refers to a test's capacity to distinguish between both the potential associated and normal health. Diagnostic tests can be used to quantify its discriminative capacity. Just some few diagnostic accuracy measures (DAM) are employed for assessing diagnostic accuracy within medical research, despite the huge number of DAM (Imundi, 2009) (Table - 1).

- a) Sensitivity (Se), Specificity (Sp), Diagnostic odds ratio (DOR), and likelihood ratios for positive and negative results (LR + and LR -, correspondingly) that really are critically dependent on the true illness condition and are prevalent invariant.

- b) Overall diagnostic accuracy (ODA) is a prevalence-dependent metric that is determined conditioned upon on true clinical condition.
- c) Positive and negative predictive values (PPV and NPV) are predominance values that also are determined depending upon on test outcome (Shiu and Gatsonis, 2008).

Diagnostic accuracy metrics were not set markers of a test's effectiveness; some may be highly sensitive to sickness incidence, while some are extremely sensitive to the disease's range and description. The Diagnostic accuracy depends on

- a) A screening or detecting test's risk is detection by its diagnostic accuracy and is appeared as the potential return. As a outcome, it is due to the following (Table - 2).

- b) The predicted losses for the testing technique, measured on same scale for a true negative test, a false negative outcome, a true positive outcome, and a false positive outcome.
- c) The chances of a true negative, a false negative, a true positive, and a false positive outcome. (Chatzimichail and Hatjimihail, 2020).

Table - 1: Diagnostic accuracy measurements with free vibration and likelihood Assumptions

Measure	Natural Frequency Definition	Probability Definition
Sensitivity (<i>Se</i>)	$\frac{TP}{FN+TP}$	$Pr(T D)$
Specificity (<i>Sp</i>)	$\frac{TN}{TN+FP}$	$Pr(\bar{T} \bar{D})$
Positive Predictive Value (<i>PPV</i>)	$\frac{TP}{FP+TP}$	$Pr(D T)$
Negative Predictive Value (<i>NPV</i>)	$\frac{TN}{TN+FN}$	$Pr(\bar{D} \bar{T})$
Overall Diagnostic Accuracy (<i>ODA</i>)	$\frac{TN+TP}{TN+FN+TP+FP}$	$Pr(D) Pr(T D) + Pr(\bar{D}) Pr(\bar{T} \bar{D})$
Diagnostic Odds Ratio (<i>DOR</i>)	$\frac{TN}{FN} \frac{TP}{FP}$	$\frac{Pr(T D)}{Pr(\bar{T} \bar{D})} \frac{Pr(\bar{T} \bar{D})}{Pr(T D)}$
Likelihood Ratio for a Positive Result (<i>LR+</i>)	$\frac{TP(FP+TN)}{FP(FN+TP)}$	$\frac{Pr(T D)}{Pr(\bar{T} \bar{D})}$
Likelihood Ratio for a Positive Result (<i>LR-</i>)	$\frac{FN(FP+TN)}{TN(FN+TP)}$	$\frac{Pr(\bar{T} \bar{D})}{Pr(T D)}$
Youden's Index (<i>J</i>)	$\frac{TN}{TN+FP} - \frac{FN}{FN+TP}$	$Pr(T D) + Pr(\bar{T} \bar{D}) - 1$
Euclidean Distance (<i>ED</i>)	$\sqrt{\left(\frac{FN}{FN+TP}\right)^2 + \left(\frac{FP}{TN+FP}\right)^2}$	$\sqrt{Pr(\bar{T} \bar{D})^2 + Pr(T D)^2}$
Concordance Probability (<i>CZ</i>)	$\frac{TN}{TN+FP} \frac{TP}{FN+TP}$	$Pr(T D) Pr(\bar{T} \bar{D})$
Risk (<i>R</i>)	$l_0 + \frac{l_{TN}TN + l_{FN}FN + l_{TP}TP + l_{FP}FP}{TN+FN+TP+FP}$	$l_0 + l_{TN}Pr(\bar{D})Pr(\bar{T} \bar{D}) + l_{FN}Pr(D)Pr(\bar{T} \bar{D}) + l_{TP}Pr(D)Pr(T D) + l_{FP}Pr(\bar{D})Pr(T \bar{D})$

TP: True positive
 FP: False positive
 TN: True negative
 FN: False negative
 NPV: Negative predictive value
 PPV: Positive predictive value
 PLR: Positive likelihood ratio
 NLR: Negative likelihood ratio

Table - 2: The possible test outcomes

		populations	
		nondiseased	diseased
test results	negative	true negative (<i>TN</i>)	false negative (<i>FN</i>)
	positive	false positive (<i>FP</i>)	true positive (<i>TP</i>)

The following assumptions are made for calculating diagnostic accuracy:

- A standard (“gold standard”) diagnostic procedure for reliably categorizing a person as unwell or non-diseased exists (Bloch, 1997).
- The variables of the measure's distributions are known.
- In both the afflicted and non-diseased individuals, the estimated values or their transformations are distributed normally (Gillard, 2012).
- Inside the diagnostic threshold range, measurement uncertainty is regularly distributed and homoscedastic.
- The patients were classed as test-positive if the reading exceeds the cut-off value; alternatively, the patients are labeled as test-negative (Chatzimichail and Hatjimihail, 2020).

ROC curve and area under curve (AUC)

The (0, 0) point with in ROC space is formed when a distinguishing cut-off values for predictor factor is determined to be less than lowest value recorded. As even the recognizing cut-off value is raised to accommodate ever high data sets, a sequence of points within the ROC space are produced that could be related by a curve. The (1, 1) point is produced by a recognized cut-off higher value than the high value seen (Figure - 3). The diagonal line connecting (0, 0) and (1, 1) suggests that test results are no more accurate than statistical inferences. The greatest area between point within ROC space and diagonal line, the greater test's predictive value. Lower is positive (lower

sensitivity). Likewise, if a greater cut-off value is applied, the classifier's specificity and sensitivity would be reduced. The AUC (also known as the c-statistic) is a diagnostic metric which can be used to assess a test's capacity to separate a patient's genuine disease condition. The AUC is a one-dimensional measure that describes the ROC curve's "overall" location. It's fascinating because it can be interpreted in a meaningful way. The AUC can be defined as the likelihood that a randomly selected unhealthy subject will be evaluated or scored as being more probable to be unhealthy than a random selection non-diseased participant. This analysis was based on nonparametric Mann-Whitney U statistics, which are used to calculate AUC (Hanley and McNeil, 1982). The average value of sensitivity for all conceivable values of specificity is the alternate meaning. An index like this is extremely beneficial when comparing two diagnostic tests (or systems). When comparing two tests, it is preferable to examine the complete ROC curve instead of a single point (Hajian-Tilaki, 2013).

AUC values, in generally, reflect exclusionary type as follows:

- $AUC=0.5$ no favoritism.
- $0.6 \geq AUC > 0.5$ Poor favoritism
- $0.7 \geq AUC > 0.6$ Acceptable favoritism
- $0.8 \geq AUC > 0.7$ Excellent favoritism
- $AUC > 0.9$ Outstanding favoritism

AUC could also be used to discover the best cut-off value for a particular test, and to also analyse the outcomes of two or more different tests (Figure - 4) (Yang and Berdine, 2017, Hajian-Tilaki, 2013).

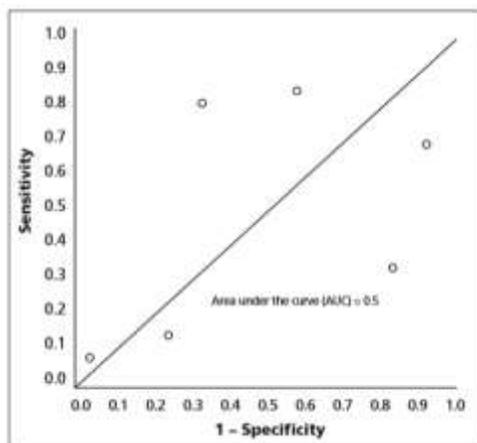


Figure - 2: ROC curve shows no favoritism power

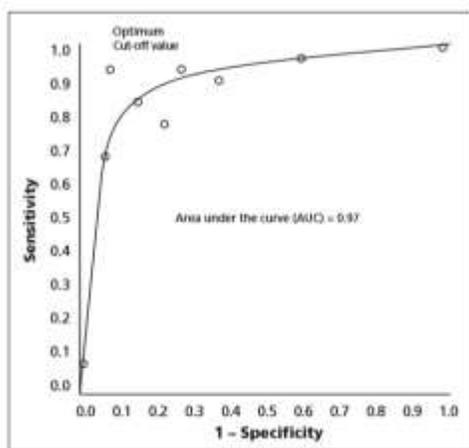


Figure - 3: ROC curve shows high favoritism power

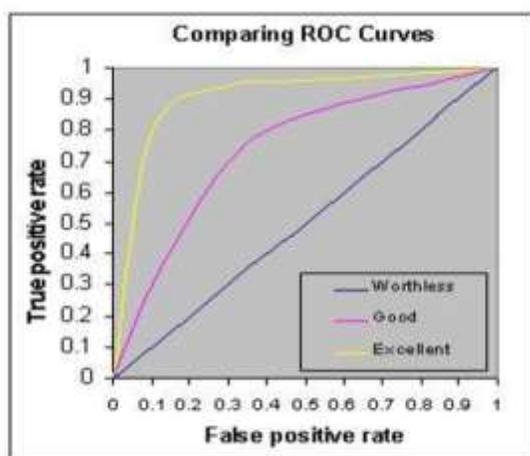


Figure - 4: ROC curve show compared between three tests

Determining the optimum cut-off value for a test

Because a ROC curve shows sensitivity and specificity determined with different cut-off values, it's vital to figure out what the appropriate cut-off value is for the greatest classification accuracy. Some cut-off value selection approaches balance sensitivity with specificity in the computation, making them simple to comprehend and perform. However, they are frequently based on erroneous assumptions (they don't taken into account of varies in illness prevalence or the ethical and financial costs related with misclassification). To address this problem, strategies for adjusting for disparities in expenses for right and wrong diagnosis are being devised. In generally, a low cut-off value could be used if an illness has a high incidence and the related costs for false positives are low; alternatively, a high cut-off value can be employed (Yang and Berdine, 2017).

Frequentist methods

For the following versions, the ROC curve can also be used:

- a) Parametric methods
 - The bi-normal estimator.
 - Durability of the bi-normal estimator.
- b) Nonparametric measurement of ROC curve
 - Empirical calculator and variants.
 - Kernel calculator (Gonçalves *et al.*, 2014).

ROC curves types

The actual ROC curve and the binormal ROC curve are also the 2 kinds of ROC curves that can be created.

- **Empirical ROC Curve**- The empirical ROC curve is perhaps the most widely used ROC curve. The true positive rate vs the false positive rate across all conceivable cut-off value is plotted on the empirical ROC curve. Every point upon on ROC curve corresponds to a distinct cutoff

value. The curve is produced by connecting the points (Gonçalves *et al.*, 2014). Cutoff levels with low false-positive rates also tend to have low true-positive rates. Even as true-positive rate rises, so does the false-positive rate. The higher the diagnostic test quality, the faster the true positive rate approaches one (or 100 %). A somewhat vertical ROC curve across (0,0) to (0,1) and afterwards horizontal to (0,1) would be a closer diagnostic test (1,1). Because it is the ROC curve of a diagnostic test which arbitrarily identifies the state (Figure - 5), so diagonal line acts as a reference line (Nakas *et al.*, 2010).

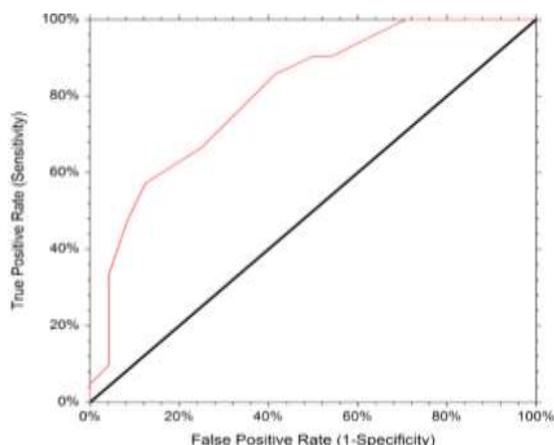


Figure - 5: Empirical ROC curve

Binormal ROC Curve

The binormal ROC curve is predicated on the idea that now the diagnostic test outcomes for the positive and negative cases can both be appeared by a normally distributed. The observed value and sample standard deviation from of the recognized positive group, as well as the known negative group, are used to calculate the binormal ROC curve. Two normal distributed are specified using these input variables and sample standard deviation. The two normal distributions are then used to create the binormal ROC curve. The binormal ROC curve is nearer to just the 45 degree diagonal line whenever the two normal distributions tightly overlay. The binormal ROC curve has a substantially bigger range from of the 45 degree diagonal line whenever the two normal

distributions intersect just in the feathers (Figure - 6) (Metz and Pan, 1999).

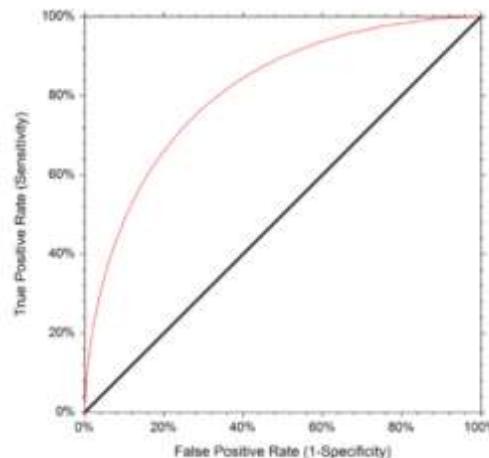


Figure - 6: Binormal ROC curve

Development methods for ROC curve

- One of major purposes of ROC curve analysis is to compare the accuracy and behavior of new evaluation techniques. Other parameters are frequently seen with diagnostic variables, however this additional information is rarely addressed when comparing these types of curves. For assessment of conditionally ROC curves, a new non-parametric test is suggested. This testing is performed on a statistics whose theoretical properties are investigated, as well as the test is calibrated using a bootstrap process. The test's actual effectiveness of level estimation and power is examined using models. A real-world application is also shown to demonstrate the technique (Fanjul-Hevia *et al.*, 2021).
- Flaih *et al.* (2021) created an Epsilon Skew bi-normal ROC curve depending on the findings of the diagnostic test, which are distributed using the ESEP distribution. They develop the BIESEP ROC variables and the AUC in further detail. The research also took into account the estimators of the BIESEP ROC curve as well as the AUC of a diagnostic test. To analyse a real dataset, we use the BIESEP ROC curve.
- The empirical ROC curve is a useful statistical tool for assessing test precision

in a variety of domains. This procedure is carried out using a variety of computational methods, one being the R ecosystem, that is an active and free to use atmosphere that facilitates the formed by different packages designed to work together more effectively in diverse approaches, resulting from different customization and capabilities but often yielding similar results. It is necessary to investigate these various packages in order to give a knowledgeable user with the easiest and most reliable execution of a required analysis. The study compiled a list of R programs that can implement ROC analysis and evaluated their effectiveness. A slick online application is given that acts as a library for all these applications, enabling for easy use (Quintas *et al.*, 2020).

- In binary classification problems, the ROC curve is a graphical tool that is often used to analyze the discriminating capacity of continuous indicators. In the field of prediction, various expansions of the ROC curve are being suggested, where even the features throughout the investigation are time-dependent happenings. The so-called cumulative/dynamic (C/D) ROC curve may be the most direct generalization. The existence of imperfect information is the key peculiarity when working with C/D ROC curve assessment. Throughout the statistical independence, several estimated strategies for tackling this filtering challenge have been proposed, with the majority of them focusing on the right-censored situation. Interval censoring is a natural result of investigations in which individuals are followed up on a regular basis. They might forget about a scheduled appointment, as well as the time constant hours are only understood to be within a particular range. This paper presents a new method for calculating the C/D ROC curve below a certain intervals censorship scheme. Numerical Simulations upon two separate scenarios are used to investigate its finite-sample nature. In terms of

absolute inaccuracy, the suggested estimation appears to be superior to the present one. The real-world data set that prompted this study exemplifies its direct use. Appendices contain the regular good scalability and an appropriate R function for its actual application (Díaz-Coto *et al.*, 2020).

- Janssens and Martens (2020) explained how well the ROC curve is a different way of presenting risk densities of unhealthy and non-diseased people, as well as how the curve of the ROC curve reveals how the risk percentages intersect. For instance, ROC curves are spherical whenever the forecasting model includes parameters with equivalent effects on disease risk and also have an angled whenever one binary potential risk has a higher influence; similarly, whenever the sample size or occurrence is minimal, ROC curves were ramped instead of smooth (when prediction model is depended on a relatively small set of categorical predictors). AUC is a metric of a forecasting model's exclusionary capability. To measure the clinical value of predictions, extra metrics should be added to the equation. (Janssens and Martens, 2020).
- Chatzimichail and Hatjimihail (2020) found that the predictive power is crucial to patient care, and calculation is essential to quality and risk monitoring in clinical practice, work established an exploration tool for the relationship between diagnostic classification accuracy and measurement error. As a result, a freely accessible immersive system for estimating, prioritizing, plotting, and comparing better statistical accuracy measures as well as the consequent risk of diagnostic or monitoring designed to assess a normally distributed metric and implemented at a specific point in time in non-diseased and unhealthy populations has been established. This is conducted to account for variations in illness prevalence,

measuring average and standard deviation, diagnostic thresholds, test standard measurement error, and predicted loss (Chatzimichail and Hatjimihail, 2020).

Recent ROC curve applications in Immunology field

Among the most recent roc curve implementations in immunology research are listed below:

- Immunogenicity findings from phase 1 vaccine trials can be hard to interpret, particularly when seropositive individuals are involved and many procedures are being used. Yu *et al.* (2018) devised three statistical approaches to define complex immunogenicity results by calculating the fraction of a sample population that attained values above threshold (Youden index [YI] threshold, receiver-operating characteristic related to baseline [ROC-B], and ROC of post dose levels [ROCP]).
 - The AUC is without a mistake the most extensively used metric of diagnostic accuracy in ROC curve evaluation for assessing the value of an indicator or comparing alternative indicators. Together with the AUC, the maximal of the Youden index, J, is frequently employed as a diagnostic accuracy metric as well as a tool for estimating an ideal cutoff point for diagnostic purposes dependent on the indicator in question. In their work, (Franco-Pereira *et al.*, 2020) The length of the binormal model-based ROC curve (LoC) was investigated as a diagnostic accuracy metric for biomarkers analysis. Normalcy constraints or same constraints following a Box–Cox transformation to normal distribution is used in LoC estimation processes. Two simulated results are taken into account. In first, the effectiveness of LoC is compared with concepts based on AUC and J, for both evaluation of a single screening tool and for the comparison of two biological markers, in a parameterized template, while being in the second, the success of
- LoC is tried to compare with approaches that rely on AUC and J, both for the evaluation of a single screening tool and for the combination of various biomarkers. They explain how the rate is influenced works and show how it can be used with variables from a colorectal cancer investigation (Franco-Pereira *et al.*, 2020).
- Single kinds of molecules have been investigated for sensitive and informative disease medical diagnostics in the realm of disease diagnosis. The Raman hyperspectroscopy technique is being used to examine rbc's in order to diagnose Celiac disease (CD). The acquired Raman spectral data was evaluated for medical testing using partial least squares discriminant analysis (PLS-DA). The effectiveness of the PLS-DA prediction algorithm was evaluated using ROC curve analysis, which resulted in 100 percent external validation of the created approach at the donor level (Ralbovsky and Lednev, 2021).
 - Six studies that looked into the validity of RTPCR were re-examined. The diagnostic performance of RT-PCR was investigated using ROC curve assessment. The AUC for RT-PCR isn't as good as it could be. To detect COVID-19 with greater sensitivity, a mixture of signs and symptoms, exposures history, and CT must be evaluated (Hasab, 2020).
 - Four chemiluminescence immunoassay methods, comprising seven IgM/IgG antibody detection Kits for Covid 19 (A IgM, A IgG, B IgM, B IgG, C IgM, C IgG, D Ab), were used to verify the threshold value. Covid 19 IgM/IgG antibody obtained test differential systems D-serum Ab's diagnosis kit is perhaps the most reliable Covid 19 antibody detection system, and it can be used as a substitute for nucleic acid testing (Wan *et al.*, 2020).

4. Conclusion

ROC graphs are an excellent way to visualize and evaluate classifiers. They can provide a more comprehensive assessment of categorization efficiency than scalar measurements like diagnostic accuracy. Statistical prediction methods can help enhance the accuracy of recurrent diagnostic judgments, and formulas for determining decision thresholds can help make such decisions more useful. The forecast rules may speed up the speed in which experts notice essential diagnostic features by standardized the characteristics that are analyzed to make a diagnosis.

5. References

- 1) Bloch, D. A. (1997). Comparing two diagnostic tests against the same "gold standard" in the same sample. *Biometrics*, 10: 73 - 85.
- 2) Chatzimichail, T and Hatjimihail, A. T. (2020). A Software Tool for Exploring the Relation between Diagnostic Accuracy and Measurement Uncertainty. *Diagnostics (Basel)*, 10.
- 3) Collinson, P. (1998). Of bombers, radiologists, and cardiologists: time to ROC. *Heart*, 80: 215-217.
- 4) Díaz-Coto, S., Martínez-Cambor, P and Perez-Fernández, S. (2020). Smooth ROC time: an R package for time-dependent ROC curve estimation. *Computational Statistics*, 1-21.
- 5) Dorfman, D. D and Alf, E. (1968). Maximum likelihood estimation of parameters of signal detection theory - a direct solution. *Psychometrika*, 33: 117-124.
- 6) Ekelund, S. (2012). ROC curves - What are they and how are they used? *Point of Care*, 11: 16-21.
- 7) Fanjul-Hevia, A., González-Manteiga, W and Pardo-FERNÁNDEZ, J. C. (2021). A non-parametric test for comparing conditional ROC curves. *Computational Statistics & Data Analysis*, 157: 107146.
- 8) Flaih, A., Akmyradov, C., Guardiola, J and Elsalloukh, H. (2021). Statistical Analysis of the Biesep ROC Curve.
- 9) Forkmann, T., Vehren, T., Boecker, M., Norra, C., Wirtz, M and Gauggel, S. (2009). Sensitivity and specificity of the Beck Depression Inventory in cardiologic inpatients: how useful is the conventional cut-off score? *Journal of Psychosomatic Research*, 67: 347-352.
- 10) Franco-Pereira, A. M., Nakas, C. T and Pardo, M. C. (2020). Biomarker assessment in ROC curve analysis using the length of the curve as an index of diagnostic accuracy: the binormal model framework. *AStA Advances in Statistical Analysis*, 1-23.
- 11) Gillard, J. (2012). A generalized Box - Cox transformation for the parametric estimation of clinical reference intervals. *Journal of Applied Statistics*, 39: 2231-2245.
- 12) Goncalves, L., Subtil, A., Oliveira, M. R and Bermudez, P. D. (2014). ROC curve estimation: An overview. *REVSTAT-Statistical Journal*, 12: 1-20.
- 13) Green, D. M and Swets, J. A. (1966). *Signal Detection Theory and Psychophysics*, Wiley New York.
- 14) Greiner, M., Pfeiffer, D and Smith, R. (2000). Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. *Preventive Veterinary Medicine*, 45: 23 - 41.
- 15) Hajian Tilaki, K. (2013). Receiver Operating Characteristic (ROC) curve analysis for medical diagnostic test evaluation. *Caspian Journal of Internal Medicine*, 4: 627 - 630.
- 16) Hanley, J. A and Mcneil, B. J. (1982). The meaning and use of the area under a Receiver Operating Characteristic (ROC) curve. *Radiology*, 143: 29-36.
- 17) Hasab, A. A. (2020). COVID-19 Screening by RT-PCR: an epidemiological modelling.

- 18) Hoo, Z. H., Candlish, J and Teare, D. (2017). What is an ROC curve? BMJ Publishing Group Ltd. and the British Association for Accident.
- 19) Janssens, A. C. J and Martens, F. K. (2020). Reflection on modern methods: revisiting the area under the ROC curve. *International Journal of Epidemiology*, 52: 360 - 373.
- 20) Krzanowski, W. J and Hand, D. J. (2009). ROC curves for continuous data, CRC Press.
- 21) Kumar, R and Indrayan, A. (2011). Receiver operating characteristic (ROC) curve for medical researchers. *Indian Pediatrics*, 48: 277 - 287.
- 22) Lasko, T. A., Bhagwat, J. G., Zou, K. H and Ohno Machado, L. (2005). The use of receiver operating characteristic curves in biomedical informatics. *Journal of Biomedical Informatics*, 38: 404 - 415.
- 23) Lusted, L. B. (1960). Logical analysis in roentgen diagnosis: Memorial fund lecture. *Radiology*, 74: 178 - 193.
- 24) Metz, C. E. (1978). Basic principles of ROC analysis. Seminars in Nuclear Medicine, WB Saunders, 283-298.
- 25) Metz, C. E and Pan, X. (1999). "Proper" binormal ROC curves: theory and maximum - likelihood estimation. *Journal of Mathematical Psychology*, 43: 1 - 33.
- 26) Morrison, A. M., Coughlin, K., Shine, J. P., Coull, B. A and Rex, A. C. (2003). Receiver operating characteristic curve analysis of beach water quality indicator variables. *Applied and Environmental Microbiology*, 69: 6405 - 6411.
- 27) Nakas, C. T., Alonzo, T. A and Yiannoutsos, C. T. (2010). Accuracy and cut-off point selection in three-class classification problems using a generalization of the Youden index. *Statistics in Medicine*, 29: 2946 - 2955.
- 28) Quintas, J. P., Costa, F. M., Braga, A. C and Rosy, L. (2020). Application for Selecting R Packages that Perform ROC Analysis. International Conference on Computational Science and Its Applications. Springer, 199-213.
- 29) Ralbovsky, N. M and Lednev, I. K. (2021). Analysis of individual red blood cells for Celiac disease diagnosis. *Talanta*, 221: 121642.
- 30) Shiu, S. Y and Gatsonis, C. (2008). The predictive receiver operating characteristic curve for the joint assessment of the positive and negative predictive values. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 366, 2313-2333.
- 31) Šimundić, A.M. (2009). Measures of diagnostic accuracy: Basic definitions. *Ejifcc*, 19: 203 - 208.
- 32) Swets, J. A. (1986a). Form of empirical ROCs in discrimination and diagnostic tasks: implications for theory and measurement of performance. *Psychological bulletin*, 99: 181 - 186.
- 33) Swets, J. A. (1986b). Indices of discrimination or diagnostic accuracy: their ROCs and implied models. *Psychological Bulletin*, 99: 100 - 110.
- 34) Swets, J. A., Dawes, R. M and Monahan, J. (2000). Better decisions through science. *Scientific American*, 283: 82 - 87.
- 35) Wan, Y., Li, Z., Wang, K., Li, T and Liao, P. (2020). Performance verification of detecting COVID-19 specific antibody by using 4 chemiluminescence immunoassay systems.
- 36) Yang, S and Berdine, G. (2017). The receiver operating characteristic (ROC) curve. *The Southwest Respiratory and Critical Care Chronicles*, 5: 65 - 73.
- 37) Yu, L., Esser, M. T., Falloon, J., Villafana, T and Yang, H. (2018). Generalized ROC methods for immunogenicity data analysis of vaccine phase I studies in a seropositive population. *Hum Vaccin Immunother*, 14: 2692-2700.
- 38) Zhou, X.H., Mcclish, D. K and Obuchowski, N. A. (2011). Statistical methods in diagnostic medicine. Vol. 569. Hoboken: Wiley.

Access this Article in Online

Quick Response Code



Website

www.jpsscientificpublications.com

DOI Number

[DOI: 10.22192/lisa.2021.7.3.3](https://doi.org/10.22192/lisa.2021.7.3.3)

Thomson Reuters Researcher ID

[L – 5547 – 2016](#)

ISI Impact Factor

[4.206](#)

How to Cite this Article:

Nisreen Waleed Mustafa, Ola Abdul Shaheed Naser and Zaid Nabeel Elia. (2021). Receiver Operating Characteristic Curve: Types, Calculation and Applications in Immunological field. *Life Science Archives*, 7(3): 2150 – 2162.

[DOI: 10.22192/lisa.2021.7.3.3](https://doi.org/10.22192/lisa.2021.7.3.3)