

# Receiver operating characteristic curve generalization for non-monotone relationships

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The receiver operating characteristic curve is a popular graphical method frequently used in order to study the diagnostic capacity of continuous markers. It represents in a plot true-positive rates against the false-positive ones. Both the practical and theoretical aspects of the receiver operating characteristic curve have been extensively studied. Conventionally, it is assumed that the considered marker has a monotone relationship with the studied characteristic; i.e., the upper (lower) values of the (bio)marker are associated with a higher probability of a positive result. However, there exist real situations where both the lower and the upper values of the marker are associated with higher probability of a positive result. We propose a receiver operating characteristic curve generalization,  $g$ , useful in this context. All pairs of possible cut-off points, one for the lower and another one for the upper marker values, are taken into account and the best of them are selected. The natural empirical estimator for the  $g$  curve is considered and its uniform consistency and asymptotic distribution are derived. Finally, two real-world applications are studied. © The Author(s) 2014.

area under the curve

asymptotic distribution

receiver operating characteristic curve

resampling methods

botulinum toxin A

calcitonin gene related peptide

biological marker

botulinum toxin A

calcitonin gene related peptide

area under the curve

Article

critically ill patient

hemodialysis

hospital admission

human

leukocyte count

leukocytosis

measurement accuracy

Monte Carlo method

mortality risk

non monotone relationship

pediatric intensive care unit

phenotype

population research

probability

protein secretion

receiver operating characteristic

statistical analysis

transformed migraine

treatment response

area under the curve

blood

child

critical illness

female

migraine

mortality

sepsis

Area Under Curve

Biomarkers

Botulinum Toxins, Type A

Calcitonin Gene-Related Peptide

Child

Critical Illness

Female

Humans

Leukocyte Count

Migraine Disorders

Probability

ROC Curve

Sepsis