Precision Medicine

VOICE-BASED DETECTION OF PARKINSON DISEASE

Benchmark vs. Logistic Regression, Random Forest, Boosted Tree & Neural Network

UC#17 — 2024/03 (v2.0)

xtractis.ai

PROBLEM DEFINITION

GOAL

Design an AI-based decision system that accurately and instantly diagnoses Parkinson disease from simple voice recordings to obtain a rational diagnosis of the patient's condition.

PROS & BENEFITS

- Identify the parameters involved in the Parkinson disease and enhance medical knowledge by helping neurologists understand the causal relationships between these parameters, their combination, and the disease.
- Help the medical profession to make earlier and more personalized decisions through rapid, systematic, and explainable diagnoses.
- Use a model with simple recordings to limit medical protocols that can be costly.

REFERENCE DATA

Source:
Sakar, C.O., Dept of Computer Engineering, Bahcesehir University, Istanbul, Serbes, G., Dept of Biomedical Engineering, Yildiz Technical University, Istanbul, Gunduz, A., Dept of Neurology, Cerrahpaşa Faculty of Medicine, Istanbul University-Cerrahpaşa, Nizam, H., Dept of Computer Engineering, Istanbul University-Cerrahpaşa, Sakar, B.E., Dept of Software Engineering, Bahcesehir University, Istanbul, Türkiye.

Dataset:
Dua, D. and Graff, C. (2019). UCI Machine Learning Repository [http://archive.ics.uci.edu/ml]. Irvine, CA: University of California, School of Information and Computer Science

Variable to Predict: The model diagnoses the patient's condition from the voice recordings as **PARKINSON | NO PARKINSON**

Potential Predictors: 753 potential predictors, clinically useful information from various speech signal processing applied on each recording [Time Frequency Features, Mel Frequency Cepstral Coefficients (MFCCs), Wavelet Transform based Features, Vocal Fold Features and tunable Q-factor Wavelet transform (TQWT) features …].

Observations: 756 reference voice recordings (for a total of 252 patients who sustained phonation of the vowel '***a***' with 3 repetitions).

642 recordings compose a Learning Dataset for model induction using Training and Validation Datasets.

114 recordings compose an External Test Dataset to check the top-model's performance on real unknown data and for benchmarking.

Learning Dataset: 642 patients | 84.92% 80% for Training, 20% for Validation	
NO PARKINSON	PARKINSON
163 | 25.4%	479 | 74.6%

External Test Dataset: 114 patients | 15.08%	
NO PARKINSON	PARKINSON
29 | 25.4%	85 | 74.6%

MODEL TYPE

Regression | Multinomial Classification | **Binomial Classification** | Scoring

XTRACTIS-INDUCED DECISION SYSTEM

☑ **Intelligible Model, Explainable Decisions**

- The top-model is a decision system composed of 26 gradual rules without chaining aggregated into 2 disjunctive rules.
- Each rule uses from 1 to 24 predictors among the 92 variables that XTRACTIS automatically identified as significant (out of the 753 features describing each recording).
- Only a few rules are triggered at a time to compute the decision.

☑ **High Predictive Capacity** It has a pretty good Real Performance (on unknown data).

☑ **Ready to Deploy** It computes real-time predictions up to 70,000 decisions/second, offline or online (API).

XTRACTIS PROCESS

STEPS	Reference Data	**INDUCTION**	XTRACTIS Top-Model	New Cases	**DEDUCTION**	**NO PARKINSON** / **PARKINSON** Automated Decision (detect Parkinson Disease)
SOFTWARE ROBOTS	XTRACTIS® **REVEAL** Delivers the decision system + its Structure & Performance Reports			XTRACTIS® **PREDICT** Delivers the decision + the Prediction Report explaining its reasoning		

TOP-MODEL INDUCTION

INDUCTION PARAMETERS

Powered by:
XTRACTIS® REVEAL
v13.0.45667

1. We launch 1,000 inductive reasoning strategies; each strategy is applied to 20 different 5-fold-partitions of the Learning Dataset to get a reliable assessment of the descriptive and predictive performances, respectively from Training and Validation Datasets.
2. Each strategy thus generates 100 unitary models called **Individual Virtual Expert** (IVE), whose decisions are aggregated with 3 possible operators into a **College of Virtual Experts** (CVE).
3. Among the 3,000 induced CVEs, the top-CVE with the best predictive performance remains complex: 2,014 rules share 464 predictors.

Given the small number of reference cases in the reference dataset, the XTRACTIS **CVE→IVE** Reverse-Engineering process is necessary to get a more intelligible model:

4. We build a synthetic dataset composed of 32,100 new cases simulated by deduction from the top-CVE, around the 642 original learning cases but distinct from them.
5. We apply 500 induction strategies to the same single 34% Training | 33% Validation | 33% Test partition of this new dataset: XTRACTIS induces 500 IVEs.
6. The top-IVE selected is the one that is the most intelligible while being as efficient as the top-CVE.

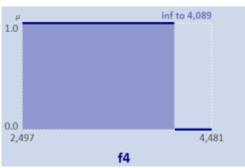
Total number of induced unitary models	Criterion for the induction optimization	Validation criterion for the top-model selection	Duration of the process (Induction Power FP64)
100,500 IVEs	F_1-Score	F_1-Score	75.8 days (1 Tflops)

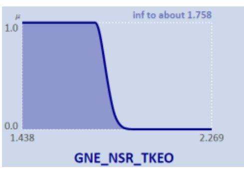
TOP-MODEL STRUCTURE

The top-IVE model has a rather poor intelligibility as it combines 92 predictors into 26 rules with 9.3 predictors per rule on average. But it remains acceptable given the high level of complexity of the phenomenon having initially 753 potential predictors. This model's Structure Report reveals all the internal logic of the decision system and ensures that the model is understandable by the human expert. It is a transparent model that can be audited and certified before deployment to end-users.

PREDICTORS

- 92 features identified out of 753
- Ranked by individual contribution (1 strong, 20 medium & 70 weak signals): #1 tqwt_maxValue_dec_19 / #2 tqwt_stdValue_dec_5 /…
- Labeled by nominal, binary, and fuzzy classes
  Examples: **binary nominal** "{Male}"
  binary interval "inferior to 4,089"
  fuzzy interval "inferior to about 1.758





RULES

- 26 connective fuzzy rules without chaining (aggregated into 2 disjunctive fuzzy rules)
- 1 to 24 predictors per rule (on average, 9.3 predictors per rule)
- Example: fuzzy rule **R8** uses 6 predictors and concludes PARKINSON. 25 other rules complete this model.

IF	gender	IS {Male}
AND	f4	IS inferior to 4,089
AND	GNE_NSR_TKEO	IS inferior to ~1.758
AND	tqwt_energy_dec_18	IS inferior to ~0.206
AND	tqwt_minValue_dec_9	IS superior to ~0.142
AND	tqwt_maxValue_dec_26	IS inferior to ~1.12
THEN	Diagnosis	IS PARKINSON

TOP-MODEL PERFORMANCE

The top-IVE performances, measured in Training/Validation/Test on synthetic data, then in External Test on reference data, guarantee the model's predictive and real performances.

	Synthetic Data			Reference Data
Performance	DESCRIPTIVE	PREDICTIVE	REAL	REAL
Dataset	34% Training	33% Validation	33% Test	External Test
F_1-Score	97.73%	97.84%	97.18%	88.46%
Classification Error	1.14%	1.08%	1.42%	5.45%

EXPLAINED PREDICTIONS FOR 3 UNKNOWN CASES

Powered by: XTRACTIS® PREDICT v13.0.45667

CASE
(from the External Dataset,
i.e., not included in the Learning Dataset)

DEDUCTIVE INFERENCE OF RULES

AUTOMATED DECISION

RECORDING #217

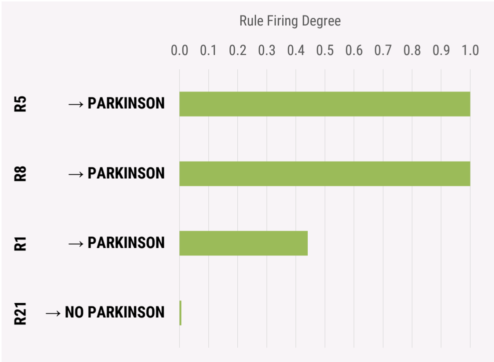
actual value = PARKINSON	
PPE	0.757
DFA*	0.853
…	…
gender	Male

Real Time

For this patient, 4 rules are triggered:

R5 and **R8** are fired at 1.000, and **R1** at 0.441 to conclude PARKINSON,
R21 at 0.006 to conclude NO PARKINSON.

22 other rules are not activated.



NUMBER OF TRIGGERED RULES
4 / 26

FUZZY PREDICTION
{ PARKINSON | 1.000,
NO PARKINSON | 0.006 }

FINAL PREDICTION
{ PARKINSON }

The system delivers a correct detection compared to the observed case:

PARKINSON

RECORDING #34

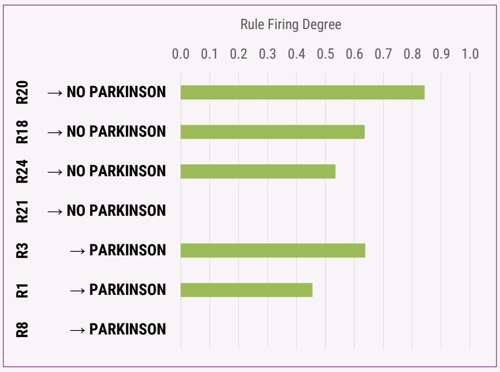
actual value = NO PARKINSON	
PPE	0.821
DFA	0.668
…	…
gender	Male

Real Time

For this patient, 7 rules are triggered:

R20 is fired at 0.843, **R18** at 0.636, **R24** at 0.535 and **R21** at 2.16e-04 to conclude NO PARKINSON,
R3 at 0.445, **R1** at 0.455 and **R8** at 6.32e-08 to conclude PARKINSON.

19 other rules are not activated.



NUMBER OF TRIGGERED RULES
7 / 26

FUZZY PREDICTION
{ NO PARKINSON | 0.843,
PARKINSON | 0.638 }

FINAL PREDICTION
{ NO PARKINSON }

The system delivers a correct detection compared to the observed case:

NO PARKINSON

RECORDING #53

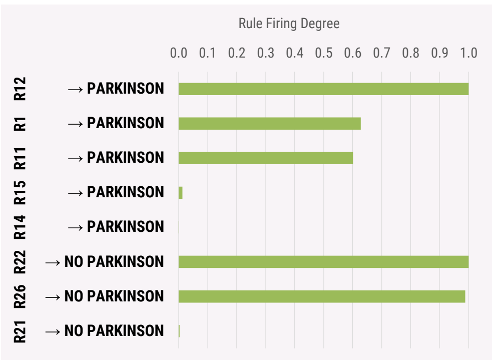
actual value = PARKINSON	
PPE	0.834
DFA	0.579
…	…
gender	Female

Real Time

For this patient, 8 rules are triggered:

R12 is fired at 1.000, **R1** at 0.628, **R11** at 0.601, **R15** at 0.013 and **R14** at 0.001 to conclude PARKINSON,
R22 at 1.000, **R26** at 0.988 and **R21** at 0.003 to conclude NO PARKINSON.

16 other rules are not activated.



NUMBER OF TRIGGERED RULES
8 / 26

FUZZY PREDICTION
{ PARKINSON | 1.000,
NO PARKINSON | 1.000 }

FINAL PREDICTION
REFUSAL

The system cannot decide between the 2 classes, so it refuses to decide.

More reference data near this recording profile should eliminate the undecidability of the updated model in this decision space area.

**Predictor value outside the variation range of the model but inside the allowed extrapolation range. XTRACTIS will refuse to give a result for an extrapolation far from the allowed extrapolation range. It is one situation of the" Refusal" prediction.*

TOP-MODELS BENCHMARK: DECISION STRUCTURE & INTELLIGIBILITY × PERFORMANCE SCORES

MODELING PARAMETERS

	XTRACTIS	LOGISTIC REGRESSION	RANDOM FOREST	BOOSTED TREE	NEURAL NETWORK
MODELS RELEASE	2023/05	2023/05	2023/05	2023/05	2023/05
ALGORITHM VERSION	XTRACTIS **REVEAL** 13.0.45667	Python 3.9.10 | Scikit-Learn 1.1.2	Python 3.9.10 | LightGBM 3.3.2	Python 3.9.10 | LightGBM 3.3.2	Python 3.9.10 | TensorFlow 2.10.0 | Keras 2.10.0
CROSS-VALIDATION TECHNIQUE	20×5 folds for each CVE model. Then 1-Split Validation for each IVE model: 34% Training | 33% Validation | 33% Test	20×5 folds for each CVE model	20×5 folds for each CVE model	20×5 folds for each CVE model	20×5 folds for each CVE model
NUMBER OF EXPLORED STRATEGIES(1)	1,000 induction strategies for the CVE on Training / Validation data. 500 induction strategies for the IVE on synthetic data	1,000 data analysis strategies on Training / Validation data	1,000 ML strategies on Training / Validation data	1,000 ML strategies on Training / Validation data	1,000 ML strategies on Training / Validation data
TOP-MODEL SELECTION(2)	Top-CVE among 3,000 CVEs. Then Top-IVE among 500 IVEs	Top-CVE selected among 1,000 CVEs, then single model obtained by applying best CVE strategy on 100% of the Learning Dataset			

TOP-MODEL STRUCTURE

	XTRACTIS	LOGISTIC REGRESSION	RANDOM FOREST	BOOSTED TREE	NEURAL NETWORK
NUMBER OF PREDICTORS (out of 12,600 Potential Predictors)	**92**	**610**	**366**	**431**	**753**
AVERAGE NUMBER OF PREDICTORS PER RULE OR EQUATION	**9.3** per rule	**610.0** per equation	**7.5** per rule	**4.7** per rule	**254.6** per equation
STRUCTURE OF THE DECISION SYSTEM	**26** fuzzy rules without chaining (aggregated into 2 disjunctive fuzzy rules) Only a few rules are triggered at a time to compute a prediction	**1** linear equation	**56** trees without chaining **2,416** binary rules	**1** chain of **110** trees **1,467** binary rules Tree #N corrects the error of the N-1 previous trees	**3** hidden layers | **42** hidden nodes **43** equations 42 unintelligible synthetic variables

TOP-MODEL SCORES

	Random(3)	XTRACTIS	LoR	RFo	BT	NN
INTELLIGIBILITY Score(4)		1.22	0.00	0.00	0.00	0.00
CVE Real Performance (F_1-Score) in External Test		86.79	74.07	86.21	87.27	81.63
Gap to CVE Leader in External Test		**-0.48**	**-13.20**	**-1.06**	**0.00**	**-5.64**
IVE Real Performance (F_1-Score) in External Test	*51.72*	88.46	73.47	83.02	91.23	73.08
Gap to IVE Leader in External Test		**-2.77**	**-17.76**	**-8.21**	**0.00**	**-18.15**
Average Real Performance in External Test	*51.72*	87.63	73.77	84.62	89.25	77.36
PERFORMANCE Score(4)		**-1.63**	**-15.48**	**-4.64**	**0.00**	**-11.90**

(1) For all algos: on the same Learning Dataset. All Models are optimized according to their Validation F_1-Score.
(2) All top-models are selected according to their Validation F_1-Score while checking that it remains close to their Training F_1-Score.
(3) Baseline performances that models must exceed to perform better than chance (P-value = 0.001; 100,000 models generated by random permutation of the output values). The value of each performance criterion is generally achieved by a different random model.
(4) See Appendices for explanations and detailed results. Performance Scores are calculated on all available unknown data.

More Use Cases:
xtractis.ai/use-cases/

APPENDIX 1 — Calculation of the Intelligibility × Performance Scores

AI Technique #i	T_i	$i \in [1 ; n]$ n = number of AI Techniques benchmarked in terms of data-driven modeling = 5
Benchmark #k	B_k	$k \in [1 ; p]$ p = number of Benchmarks for the Use Case ∈ {1, 2, 3}

Remarks:

- In case of a small number of reference data, a CVE model (College of Virtual Experts) is generated by each explored strategy of T_i, generally via an N×K-fold cross validation. In this case, a Benchmark is led with the top-CVE on the External Test Dataset (ETD, composed of unknown reference cases). Then, a top-IVE model (Individual Virtual Expert) is generated from the top-CVE, through the XTRACTIS® reverse-engineering process, or for the other T_i, by applying the top-strategy, which has generated the top-CVE, on the Training and Validation Datasets. And a second Benchmark is led with this top-IVE on the same ETD.
- In case of a huge number of reference data, an IVE is generated by each explored strategy of T_i, via a 1-split validation. In this case, Benchmarks are led with the top-IVE on the Test Dataset (TD, composed of unknown reference cases) and on the available ETDs.
- Each Benchmark uses the latest versions of the following algorithms available at the date of the benchmark. XTRACTIS®: REVEAL; Logistic Regression: Python, Scikit-Learn; Random Forest & Boosted Tree: Python, LightGBM; Neural Network: Python, TensorFlow, Keras.
- Each B_k uses exactly the same TD and ETD for each T_i model.
- No Regression models can be obtained by Logistic Regression. So, this Data Analysis technique is benchmarked only for Classification or Scoring problems.
- The Holy Grail for critical AI-based decision systems is to obtain a model with the highest Performance <u>and</u> the highest Intelligibility scores (top-right corner of the graph).

PERFORMANCE Score

For each B_k, we calculate the values of the Performance Criterion (PC) on the same ETD for all the T_i top-CVEs; and on the same TD and ETDs for all the T_i top-IVEs. The PC is: RMSE in percentage for a Regression; F_1-Score for a Binomial Classification; Average F_1-Score or Average F_2-Score for a Multinomial Classification; Gini index for a Scoring.
Then, we compare the value of the PC of each T_i top-CVE (resp. top-IVE) to the best value of this PC reached by the best T_i top-CVE (resp. top-IVE) on ETD (resp. on TD and ETDs).

For Regression, we calculate for each T_i top-model (CVE and IVE): $PS(T_i, B_k) = Best\_PC(B_k) - PC(T_i, B_k)$.

For Classification and Scoring, we calculate for each T_i top-model: $PS(T_i, B_k) = PC(T_i, B_k) - Best\_PC(B_k)$.

Performance Score of T_i

$$\boxed{PS(T_i) = \text{Mean}\left(PS(T_i, B_k)\right)_{k \in [1 ; p]}}$$

<u>Remark:</u>

- Each PS varies theoretically from -100 (Lowest Score) to 0 (Highest Score), but practically between -50 and 0.

INTELLIGIBILITY Score

We consider the T_i top-IVE. Its Intelligibility Score IS(T_i) is valued from 0.00 to 5.00 regarding the structure of the model: number of predictors, classes, rules, equations, trees, synthetic variables, modalities to predict for classifications (or numeric variables to predict for regressions or scoring). The more compact the model, the higher its IS.

The IS of each T_i is obtained by accumulating the following five penalty values to the ideal IS value of 5.00 (each penalty has a null or a negative value):

- Penalty 1 (logarithmic penalty regarding the number of predictors):

$$\text{Pen1}(T_i) = \min(0\,, 1 - \log_{10} number\ of\ predictors)$$

Examples: *Pen1 = 0.00 for up to 10 predictors*
Pen1 = −3.00 for 10.000 predictors

- Penalty 2 (linear penalty regarding the average number of rules or equations per modality to predict):

$$\text{Pen2}(T_i) = \min\left(0\,, 0.01 - \frac{average\ number\ of\ rules\ or\ equations\ per\ modality\ to\ predict}{100}\right)$$

Examples: *Pen2 = 0.00 for 1 rule or equation per modality to predict on average*
Pen2 = −3.00 for 301 rules or equations per modality to predict on average

- Penalty 3 (linear penalty regarding the average number of predictors per rule or equation):

$$\text{Pen3}(T_i) = \min\left(0\,, \frac{9 - 3 \times average\ number\ of\ predictors\ per\ rule\ or\ equation}{7}\right)$$

Examples: *Pen3 = 0.00 for up to 3.0 predictors per rule or equation on average*
Pen3 = −3.00 for 10.0 predictors per rule or equation on average

- Penalty 4 (linear penalty regarding the number of chained trees, here for BT only):

$$\text{Pen4}(T_i) = \min(0\,, 1 - number\ of\ chained\ trees)$$

Examples: *Pen4 = 0.00 for 1 tree*
Pen4 = −3.00 for 4 chained trees

- Penalty 5 (maximum penalty due to unintelligibility of synthetic variables, here for NN only):

$$\text{Pen5}(T_i) = -5$$

Intelligibility Score of T_i

$$\boxed{IS(T_i) = \max(0.00\,, 5.00 + (Pen1+Pen2+Pen3+Pen4+Pen5))}$$

<u>Remarks:</u>

- For the difference between the Intelligibility and the Explainability of a model, please see the XTRACTIS® Brochure, page 7.
- The real complexity of the process/phenomenon under study is intrinsic, i.e., it could not be reduced or simplified, but only discovered; thus, the top-model will be complex if the process/phenomenon turns out to be complex [Zalila 2017]. Consequently, for some complex process/phenomenon, IS can be equal to 3.00 or less, even if Ti natively produces intelligible models (XTRACTIS, Random Forest).
- For similar structures, the Boosted Tree model is always less intelligible than the Random Forest one, as it is composed of chains of trees, instead of a college of trees (see Penalty 4).
- Neural Network model has always the lowest IS of 0.00, because it uses synthetic unintelligible variables (hidden nodes) in addition to all the potential predictors (see Penalty 5).

APPENDIX 2 — Use Case Results (all Performance criteria of all Top-Models)

Performance Criterion	Classification Error	Min. Sensitivity Specificity	Sensitivity	Specificity	PPV	NPV	**F_1-Score**	Refusal
RANDOM MODEL								
Nb of Random Permutations (P-value) = 100,000 (0.001%)								
Performance against chance (External Test)	*24.56%*	*51.72%*					*51.72%*	
XTRACTIS TOP-MODEL								
CVE - Descriptive Performance (Training)	1.09%	98.75%	99.39%	98.75%	96.43%	99.79%	97.89%	0 (0.00%)
CVE - Predictive Performance (Validation)	1.25%	96.32%	96.32%	99.58%	98.74%	98.75%	97.52%	2 (0.31%)
CVE - Real Performance (External Test)	6.14%	79.31%	79.31%	98.82%	95.83%	93.33%	86.79%	0 (0.00%)
IVE - Descriptive Performance (Training)	1.14%	97.66%	97.66%	99.27%	97.81%	99.22%	97.73%	7 (0.06%)
IVE - Predictive Performance (Validation)	1.08%	97.37%	97.37%	99.45%	98.33%	99.12%	97.84%	5 (0.05%)
IVE - Real Performance (Test)	1.42%	97.18%	97.18%	99.05%	97.18%	99.05%	97.18%	12 (0.11%)
IVE - Real Performance (642 original points)	2.49%	95.09%	95.09%	98.33%	95.09%	98.33%	95.09%	0 (0.00%)
IVE - Real Performance (External Test)	5.45%	82.14%	82.14%	98.78%	95.83%	94.19%	88.46%	4 (3.51%)
LOGISTIC REGRESSION TOP-MODEL								
CVE - Descriptive Performance (Training)	6.39%	87.73%	87.73%	95.62%	87.20%	95.82%	87.46%	
CVE - Predictive Performance (Validation)	12.31%	73.62%	73.62%	92.48%	76.92%	91.15%	75.24%	
CVE - Real Performance (External Test)	12.28%	68.97%	68.97%	94.12%	80.00%	89.89%	74.07%	
IVE - Descriptive Performance (Training)	6.39%	84.66%	84.66%	96.66%	89.61%	94.88%	87.07%	
IVE - Real Performance (External Test)	11.40%	62.07%	62.07%	97.65%	90.00%	88.30%	73.47%	
RANDOM FOREST TOP-MODEL								
CVE - Descriptive Performance (Training)	0.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	
CVE - Predictive Performance (Validation)	5.45%	86.50%	86.50%	97.29%	91.56%	95.49%	88.96%	
CVE - Real Performance (External Test)	7.02%	86.21%	86.21%	95.29%	86.21%	95.29%	86.21%	
IVE - Descriptive Performance (Training)	0.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	
IVE - Real Performance (External Test)	7.89%	75.86%	75.86%	97.65%	91.67%	92.22%	83.02%	
BOOSTED TREE TOP-MODEL								
CVE - Descriptive Performance (Training)	0.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	
CVE - Predictive Performance (Validation)	4.67%	88.34%	88.34%	97.70%	92.90%	96.10%	90.57%	
CVE - Real Performance (External Test)	6.14%	82.76%	82.76%	97.65%	92.31%	94.32%	87.27%	
IVE - Descriptive Performance (Training)	0.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	
IVE - Real Performance (External Test)	4.39%	89.66%	89.66%	97.65%	92.86%	96.51%	91.23%	
NEURAL NETWORK TOP-MODEL								
CVE - Descriptive Performance (Training)	0.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	
CVE - Predictive Performance (Validation)	4.67%	87.73%	87.73%	97.91%	93.46%	95.91%	90.51%	
CVE - Real Performance (External Test)	7.89%	68.97%	68.97%	100.00%	100.00%	90.43%	81.63%	
IVE - Descriptive Performance (Training)	0.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	
IVE - Real Performance (External Test)	12.28%	65.52%	65.52%	95.29%	82.61%	89.01%	73.08%	