

## **Research Paper**

# **Complexity Analysis of Pulse Oximeter Signals for Predicting Changes in Cardiorespiratory Control System with Aging**

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### **ARTICLE INFO**

#### **Article history:**

Received: 9 October 2022

Revised: 23 October 2022

Accepted: 26 October 2022

Available online: 02-11-2022

#### **Keywords:**

Complexity analysis

Machine learning

Oxygen saturation variability

Prediction

### **Abstract**

The complexity-based methods and machine learning have provided great potential in intelligent signal processing. In this study, we used complexity-based methods such as approximate entropy, sample entropy, permutation entropy, spectral entropy and singular value decomposition entropy to detect changes occurring in cardiorespiratory system with aging using the complex structure of pulse oximeter signals. The dataset used in this study comprises of 36 healthy subjects, out of which 20 subjects are young and 16 are elderly. We use complexity-based methods such as approximate entropy, sample entropy, permutation entropy, spectral entropy and singular value decomposition entropy as feature sets and machine learning techniques including artificial neural networks, k-nearest neighbor, logistic Regression and random forest algorithms for developing prediction model. We used evaluation metrics true positive rate (TPR), false positive rate (FPR), precision, recall, F-Measure, and area under receiver operator characteristic curve (AUC) and total accuracy. The developed prediction model detects malfunction of cardiorespiratory control system in elderly subjects with an accuracy average of around 80%. The outcomes of the study can be helpful for clinicians for developing therapeutic interventions, and government for devising management strategies for those suffering from chronic obstructive pulmonary diseases and heart failure in elderly subjects.

## **Introduction**

Cardiovascular disease (CVD) and Chronic obstructive pulmonary disease (COPD) frequently coexist in elderly population and their cohabitation is linked with adverse clinical outcomes (Okada et al., 2021). Patients suffering from CVD and COPD experience high rates of morbidity, higher hospitalization, poor quality of life and years last to disability (Mannino et al., 2008; Miller et al., 2013). The incidence of CVD and COPD reflects the malfunctioning of cardiorespiratory control system (CRCS), which maintains adequate oxygen in the body. During hypoxia (insufficient oxygen) the cardiorespiratory control system tries to restore or adapt to it by increasing blood flow and ventilation (Okada et al., 2021).

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Pulse oximetry is a non-invasive technique used by to detect hypoxia in various clinical settings such as surgery, critical care, or outpatient clinics (Jubran, 2015). The use of pulse oximetry allows the avoidance of invasive arterial blood gas analysis and aids in detecting hypoxia, which is defined as a SpO<sub>2</sub> value of less than 95% (Amoian, 2013). The oxygen saturation variability (OSV) has the potential to assess the functions of CRCS in healthy subjects and changes occurring due aging/disease. The use of OSV is well known in preterm infants, and a steady increase in the value is observed during the postnatal period with a change in mean oxygen saturation (Dipietro et al., 1994). A recent study in Bangladesh found that using measures that can quantify OSV can improve the instrument's sensitivity and specificity to identify critically ill infants in hospitals (*Garde et al., 2016*). The main problem with characterizing variability using OSV is the failure to define normal variability in healthy individuals and linear OSV measures to quantify variability, which may not capture the pattern of SpO<sub>2</sub> fluctuation (Bhogal and Mani, 2017). Healthy biological systems exhibit remarkably complex patterns and have the capability to function and adapt in a dynamical environment (Peng et al., 2009). Aging and disease perturb the complexity (dynamical capability) of a system, making it less adaptable to internal and external stimuli due to decoupling between its sub-systems (Peng et al., 2009).

Researcher developed numerous complexity-based methods for analyzing biomedical signals to illustrate value of complexity in physiological or clinical settings and used the different complexity measures as features for machine learning techniques for prediction adverse clinical outcomes (Aziz et al., 2014; Altan et al., 2016; Awan et al., 2019; Choudhary et al, 2019; Aziz et al., 2021; Al-Jedaani et al, 2022). In a recent study (Bhogal and Mani, 2017) researchers used complexity-based methods such as detrended fluctuation analysis (Peng et al., 1994), sample entropy (Richman and Moorman, 2000), and multiscale entropy Costa et al., 2002) to characterize patterns of OSV and determine changes that occur with aging. The complexity-based methods and ML techniques used for analyzing biomedical signals such heart rate variability and stride rate variability can have the potential to use these methods in OSV analysis. Thus, using complexity based methods and ML techniques can be developed to help physicians gain greater insights and to make better decisions in clinical assessments and diagnosis. The present study is aimed to use complexity-based such as approximate entropy (Pincus, 1991), sample entropy (Richman and Moorman, 2000), permutation entropy (Bandt and Pompe, 2002), spectral entropy (Devi et al., 2021) and singular value decomposition entropy (Rodriguez et al., 2022) for quantifying the complexity of OSV data of young and elderly subjects. The prediction model is developed using machine learning (ML) techniques, including Artificial Neural Networks (ANNs), K-Nearest Neighbor (KNN), Logistic Regression, Random Forest (RF), stochastic gradient descent (SGD), Sequential Minimal Optimization (SMO), and Decision Tree (DT). These ML are techniques used because of their wide use in biomedical decision making and predictive analytics (Aziz et al., 2014; Altan et al., 2016; Awan et al., 2019; Choudhary et al, 2019; Aziz et al., 2021; Al-Jedaani et al, 2022).

The rest of this article is organized into 4 sections. Section 2 details the materials and methods, section 3 present the results, section 4 provides the discussion of presented results and section 5 presents the conclusion.

### Material and Methods

In Figure1 schematic diagram of the prediction model developed using complexity-based entropy measures, population characteristics, and ML techniques for prediction of malfunctioning of CRCS in elderly subject is shown.

### Dataset

The data used in this study is taken from the research resource for complex physiological signals (Goldberger et al., 2000; Bhogal and Mani, 2017). The database comprises of 36 individuals

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(17 male and 19 female). Descriptive statistics of the young and elderly subject are detailed in Table 1.

The dataset is split into young subjects (age < 35 years) and elderly subjects (subjects aged  $\geq$  35 years). The young subjects comprised of 20 individuals (9 male and 11 female) and elderly subjects comprising of 16 individuals (8 male and 8 female). The mean and standard deviation (SD) of ages of the young subjects is 21.05, 1.36 years and that of elderly subject is 49.94, 10.39

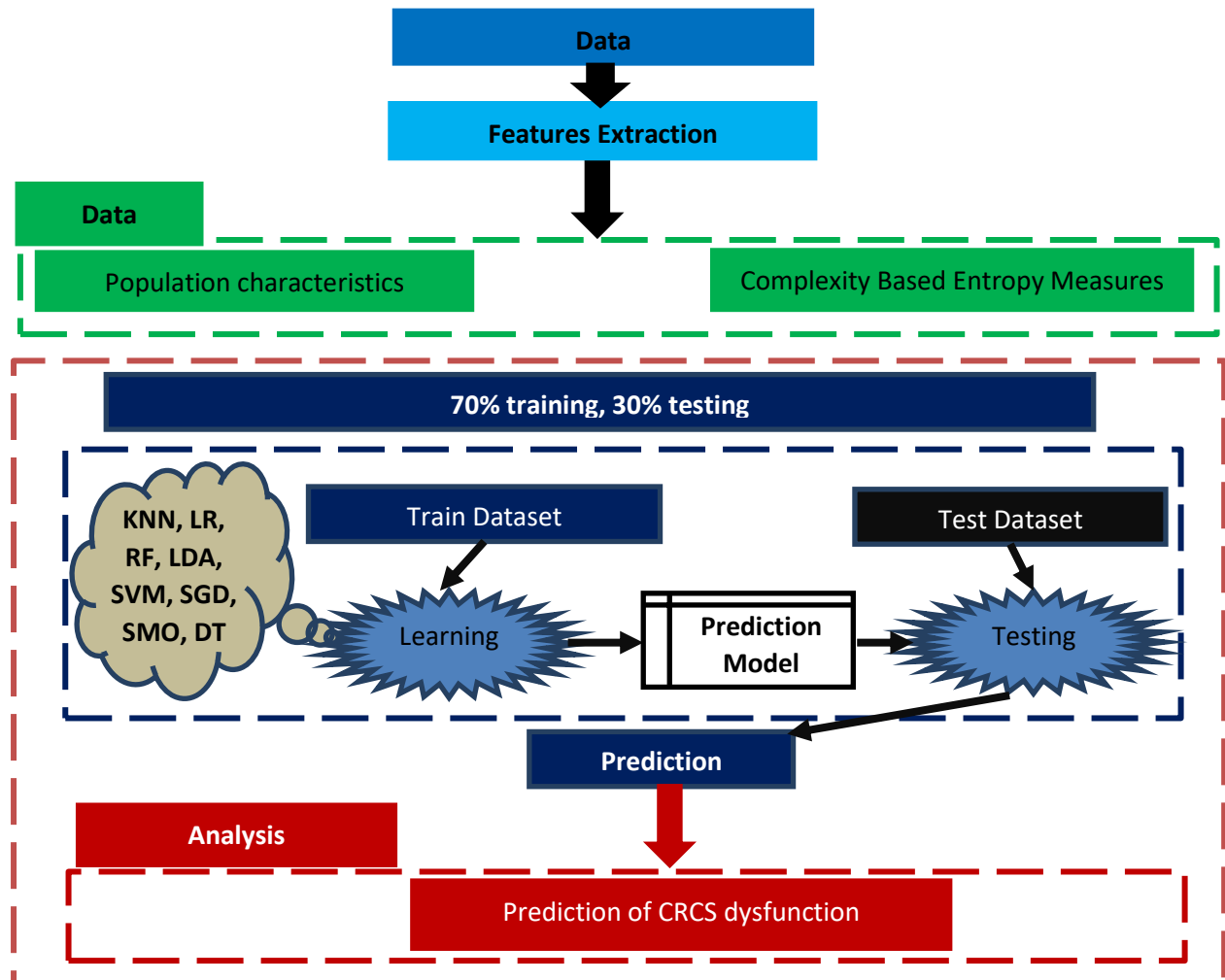


Figure 1: Schematic illustration prediction model for detection of CRCS dysfunction

Table 1: Populations of the young and elderly subjects

	Young	Old
Subjects	20	16
Age groups	< 35 years	$\geq$ 35
Age (mean, SD) years	21.05, 1.36	49.94, 10.39
Gender	9 M, 11F	8 M, 8F
BMI (mean , SD) kg/m <sup>2</sup>	22.42, 2.44	24.03, 2.95

\*Male (M) and Female (F)

years. The mean and SD of BMI of the young subjects is 22.42, 2.44 and elderly subject is 24.03, 2.95 kg/m<sup>2</sup>. The oxygen saturation data is acquired using a pulse oximeter connected to an AD convertor (ADInstrument Ltd, Australia). In original study (Bhogal and Mani, 2017), the subjects suffering from sickle cell anemia, chronic obstructive pulmonary disease, asthma, and pulmonary fibrosis were excluded. The data acquisition details and data cleaning detailed in the study conducted by Bhogal

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and Mani, 2017. The pulse oximeter signals were initially for over a one-hour period at a sampling frequency 1kHz and then resolution was reduced to 1Hz using standard de-sampling protocol.

### Complexity- Based Entropy Methods

The biological signals such heart rate, respiratory rate, brain signals and oxygen saturation variability data encode information about underlying physiological or pathological events. This information can be quantitatively extracted from biological signals to provide insights regarding the status of the underlying physiology. Complexity-based entropy measures are helpful to detect changes in the underlying dynamics associated with physiological or pathological events (Pincus, 1991; Richman and Moorman, 2000, Bandt and Pompe, 2002, Aziz et al., 2014; Altan et al., 2016; Awan et al., 2019; Choudhary et al, 2019; Aziz et al., 2021; Al-Jedaani et al, 2022). We used complexity-based entropy measures approximate entropy (Pincus, 1991), sample entropy (Richman and Moorman, 2000), permutation entropy (Bandt and Pompe, 2002), spectral entropy (Devi et al., 2021) and singular value decomposition (SVD) entropy (Rodriguez et al., 2022) for quantifying the complexity of OSV data of young and elderly subjects for characterizing CRCS.

### Developing Prediction Model

The population characteristics along with complexity-based entropy measures are used as feature sets. The ML techniques used for developing prediction model include ANN, KNN, DT, RF, LR, SMO and DT. The experiment used the splitting technique for training/testing data formulation and parameter optimization. Due to the small sample size, and to cover all probabilities we used splitting as 75%, 25% to evaluate the performance of classifiers for different feature extracting strategies.

### Evaluation Metrics

The true positive rate (TPR), false positive rate (FPR), Precision, Recall, F-Measure, MCC, Area under ROC and total accuracy were among the evaluation measures employed in the study. Total accuracy is an evaluation metric that is defined as a classifier's rate of correct classifications. When the classifier reaches to 100 percent or close to 100, it signifies the classifier's classification performance is excellent, and vice versa, as the accuracy percentage lowers, the classification performance decreases.

## Results and Discussion

In this study result of predictive modelling are presented to analyze data patterns for determining future events using complexity entropy measures as features and ML techniques. Table 2, shows the results of complexity analysis measures used in the study for quantifying nonlinear dynamics of the oxygen saturation data. It is evident from the Table 2, all the entropy estimates are smaller for elderly subjects compared to young subjects revealing that complexity decreases with aging. Thus, decrease in complexity can be associated negative CRCS in elderly subjects.

The population characteristics (Table 1) and entropy based complexity measures (Table 2) are used as features. We used 10-fold cross-validation for evaluating the prediction our model. Table 3 shows the results of the prediction model developed using ML techniques. The findings elucidate that DT algorithms outperform other prediction models, when comparing different performance parameters.

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**Table 2: Features extracted using complexity analysis measures**

Complexity Based Features	Young (<35) - Mean	Elderly (>=35) - Mean
Sample Entropy	0.14±0.07	0.11±0.08
Approximate Entropy	0.29±0.08	0.25±0.09
Permutation Entropy	0.28±0.07	0.23±0.08
Spectral Entropy	0.66±0.06	0.60±0.06
SVD Entropy	0.02±0.00	0.01±0.00

**Table 3: Detailed accuracy of the prediction model developed by splitting the dataset (75% for training and 25% for testing).**

ML Technique	TP Rate	FP Rate	Precision	Recall	F-Measure	MCC	AUC	Class
ANN	0.833	0.200	0.833	0.833	0.833	0.633	0.833	Young
	0.800	0.185	0.800	0.800	0.800	0.633	0.833	Elderly
KNN	0.833	0.333	0.833	0.833	0.833	0.5	0.75	Young
	0.667	0.167	0.667	0.667	0.667	0.5	0.75	Elderly
LR	0.833	0.2	0.833	0.833	0.833	0.633	0.9	Young
	0.8	0.167	0.8	0.8	0.8	0.633	0.9	Elderly
RF	0.833	0.667	0.714	0.833	0.769	0.189	0.861	Young
	0.333	0.167	0.5	0.333	0.4	0.189	0.861	Elderly
SGD	0.833	0.333	0.833	0.833	0.833	0.5	0.75	Young
	0.667	0.167	0.667	0.667	0.667	0.5	0.75	Elderly
SMO	0.667	0	1	0.667	0.8	0.632	0.833	Young
	1	0.333	0.6	1	0.75	0.632	0.833	Elderly
DT	0.833	0	1	0.833	0.909	0.791	0.972	Young
	1	0.167	0.75	1	0.857	0.791	0.972	Elderly

The Figure 2 shows the results of prediction model for different ML techniques using a bar chart. Highest prediction accuracy is provided by DT algorithms followed by the ANN and logistic regression algorithms.

The study outcomes are in line with other studies conducted to develop prediction models by extracting information encoded in the time series of biological systems and ML technique (Aziz et al., 2014; Altan et al., 2016; Awan et al., 2019; Choudhary et al, 2019; Aziz et al., 2021; Al-Jedaani et al, 2022). In this study we used Conventional ML algorithms, which require enormous amount of power to predict a scenario. In future, we can use embedded ML – TinyML paradigm aiming to shift from conventional high-end systems to low-end clients (Ray, 2022). The shifting from high end system to low end clients in biomedical field needed to take in account the accuracy of learning models, optimization processing capacity and improving reliability.

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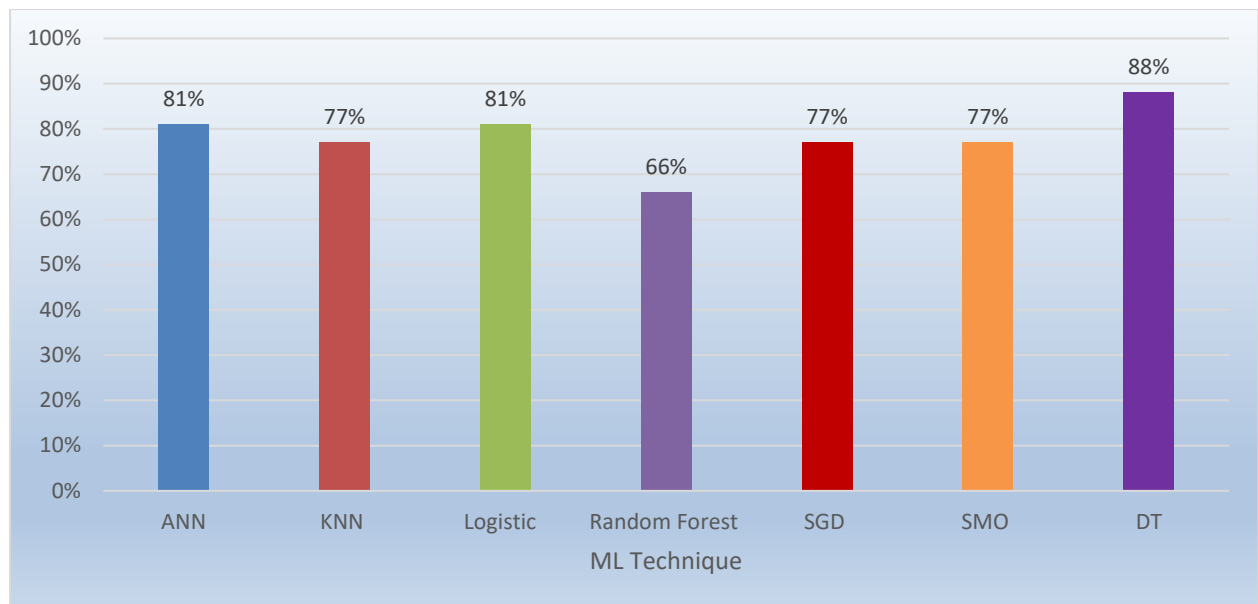


Figure 2: Accuracy of the prediction model for different ML Techniques

### Conclusion

Information encoded in complex biological signals can be extracted to develop intelligent systems for predicting changes in underlying mechanism of these systems with aging and disease. In this study, we used entropy based complexity measures, population characteristics and ML techniques to predict changes in CRCS with aging. Our study clearly elucidates that complexity of CRCS decreases with aging and can be an important biomarker of the degradation of CRCS in elderly subjects that may lead to respiratory and cardiovascular problems in them. The data used in the study is modest, further studies with large number of datasets can be helpful to provide more insight. Furthermore, TinyML paradigm can be used to prescribe the future road map for mitigating research issues in biomedical signal processing especially for the assessing CRCS.

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