Original Article

Analysis And Comparison Of Fuzzy Based Purkinje Fibre Cell Synchronization And Coordination Classification using Potassium Channel Parameters With ANN And KNN Classifier

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Abstract

Aim: The goal of this study is to compare fuzzy based purkinje fiber cell(PFC) synchronization and coordination categorization using potassium(K^+) channel parameters with K Nearest Neighbor (KNN) and Artificial Neural Network (ANN).
Materials and Methods: The PFC Aslanidi model(AM) is used to classify cardiac arrhythmias of K^+ channel at different malfunction conditions. In AM, the K^+ channel dynamics are well described based on the PFC dataset. ANN and KNN classifiers are used to classify the different PFC classification. Sample size was calculated by keeping threshold 0.05, G Power 80%, confidence interval 95% and enrolment ratio as 1. 20 samples are taken for each analysis to predict the accuracy of the Novel ANN and KNN classifier. Finally, using the Statistical Package for the Social Science (SPSS) programme, the collected dataset(resultant accuracy) can be calculated.
Result: PFC normal Action Potential (AP) having AP Duration (APD) is 290ms and Total Cycle Length (TCL) is 1000ms at K^+ extracellular levels as 5.4mM. Whereas in abnormal AP indicates APD is 280ms and TCL is 900ms at K^+ extracellular levels as 10.4mM. A 10% decrease in APD with normal PFC AP and 10% drop in TCL is responsible for Tachycardia (fast heartbeat), Then PFC data(Normal, Tachycardia, Bradycardia) are sent into the Novel ANN and KNN classifier algorithms. Using SPSS software, the results reveal that ANN accuracy is higher than KNN. Group 1 KNN has a mean of 63.410, a standard deviation of 4.3533, and a standard error mean of .9734, whereas group 2 ANN has a mean of 66.055, a standard deviation of 1.0329, and a standard error mean of .2310. Conclusion: Therefore the changes in PFC K^+ channel leads to Hypokalemia which results in cardiac arrhythmia of resting membrane potential and the duration of both the action potential, to a higher extent than the normal. The paper concludes that the ANN classifier predicts better classification in identifying the accuracy of potassium channel parameters when compared to the KNN classifier of PFC synchronization and coordination.
Keywords: Purkinje Fibre Cell, Cardiac Arrhythmia, Potassium Ion Concentration, Potassium Channel, Novel ANN and KNN Classifier, Action Potential, Computational Biology.

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INTRODUCTION

Cardiac K+ channels are membrane-spanning proteins that allow K+ ions to pass across the cell membrane while following an electrochemical gradient. They control the form and duration of the cardiac action potential (CAP), as well as the resting membrane potential and the frequency of pacemaker cells (Tamargo 2004). Every year, roughly three million people die of sudden cardiac death around the world. A complicated combination of substrates and triggers frequently results in these deaths. One such trigger is a disruption in potassium balance in cardiac cells. Hypokalemia, as well as more transitory decreases in plasma potassium content, are therefore important to be noted which causes cardiac arrhythmia. Surprisingly, discovering drugs would give a significant favorable effect on mortality and morbidity rates in heart failure patients which raise plasma potassium levels. As a result, paying extra attention to hypokalemia and maintaining plasma potassium levels in the upper normal range may be

advantageous(Kjeldsen 2010). The research is about the mechanism of potassium ion concentration which gives resting values by returning the membrane potential of an excitable cell. Research shows that depolarisation occurred after the sodium influx then the potassium initiated to the exterior side. Later found that potassium ion concentration represents repolarization in the heart possessing depolarizing current(Ik) which responds to adrenergic activation. The study suggests that an iks function in human heart is to protect against disease phenotypes from lesion and pathological action potential in repolarization reserve. The 2 inward potassium currents (iks,ikr) requires physiological nature, single molecules and the current hypothesis must have an constructed computational biology models to function as a blockers(Roden and Yang 2005).The contraction of heart conductive systems are responsible for changes in membrane potential called action potential (AP). The five phases of cardiac action potential are; firstly phase0 lasts only a few milliseconds (rapid depolarisation). Phase1 occurs with small repolarisation and phase 2 occurs (about 100 to 400 ms) plateau at depolarised level.Phase 3 occurs at a plateau potential (repolarization). Next rapid depolarization occurs at Phase 4. The outward component potassium ions are carried by permeable transmembrane proteins (Chmelova et al. 2019). So lastly, suggest that by analyzing purkinje fibre cell synchronization and coordination using K^+ parameters with ANN Classifier to diagnose the potassium channel dysfunction. The main function of purkinje fibre or pacemaker cells is to initiate electric signals which are responsible for contraction of the heart to pump the blood (Gomes and Anthony Gomes 2021). Drugs identified during the past years related to heart diseases such as myocardial infarction, hypertrophy and atherosclerosis are causing side effects to the patients. So in this research we are going to analyze the physiological behavior of the purkinje cell based on the function of the K^+ to research how it causes cardiac arrhythmia (CA) and address the exact cure for the heart patients to survive (Yang et al. 2021)

The Number of articles published over the last 5 years in Google scholar is 358 and Research gate is 224. The K^+ main function is to maintain electrical activity in the excitable cell. It is also responsible for resting potential and duration of action potential.This mechanism regulates the modulation of electrical and mechanical activity of the heart through normal physiological conditions. If any difficulties occur in heart functioning, the several types of potassium ion concentration give great potential to the heart as a therapeutic agent (Shorofsky and Balke 2001).In this article paper, action potential plateaus occurs by the membrane current region of purkinje fibre. Under a voltage clamp conditions have been investigated in a range of potentials.Changes of slow outward current occur in the plateau region which are different from potassium activated current in the pacemaker region was discovered (Noble and Tsien 1969). In this research,the early phase of repolarization and setting the plateau regions in AP is the main function of transient k+ ions. Transmural gradient(Ito) in ventricular repolarization having higher density in epicardial myocytes than in endocardial. Greater reduction of Io in epicardial myocytes can result in heart failure. Use potential therapeutic strategy for heart failure which restores K^+ current by summarizing physiological and pathological role cardiac Io (He, Feng, and Wang 2015). In this review paper they examine the role of three repolarizing potassium currentsSuch as Transient outward current (Ito), Inward rectifying current (Ik1), Late outward rectifying current(Ik). These types come under normal physiological conditions regulated by the action potential duration of cardiac purkinje and ventricular muscle fibers (Surawicz 1992).The best study paper in my knowledge is the three phases of repolarizing potassium currents which regulates duration of AP in purkinje and ventricle fibre muscle cells. Ito creates the early plateau region and limits durations at long cycles.Ik1 controls the repolarization phase and maintains the plateau region. Finally in purkinje and ventricular muscle fibre, Ik controls action potential duration (APD) within a cycle length. If we know the path of duration and plateau region by analyzing it we can create a diagnosis method to treat heart patients (Surawicz 1992).
Every research paper has its own research ideas and studies of different things like animal based models give somewhat average results in diagnosis. We cannot use humans for testing so a suitable diagnostic for this specific answer, the K^+channel which causes Cardiac Arrhythmia(CA) has yet to be established. So, in this research paper, we'll discuss the specific cause of the problem by observing changes in the Action potential pattern and doing a simulation research to anticipate the outcome in a short period of time, which could be valuable in early diagnosis approaches that could help heart patients to live longer lives.

MATERIALS AND METHODS

The computational biology study is carried out in the Digital Signal Processing laboratory of the Saveetha School of Engineering.The investigation is conducted in a single group under various potassium parameter settings. Using prior study data (Pedraza et al. 2020) on Clinicalc.com, sample size was estimated with a threshold of 0.05, G Power of 80%, confidence interval of 95%, and enrollment ratio of 1. For each analysis, 100 samples are taken into account and splited into 20 samples, Preparation of the sample group consists of the following steps: Normal AP is defined as a k^+=5.4 value then, dysfunction dataset such as k^+= 50% decreasing(2.7), and 100% increasing(10.8) are

considered (Henriquez et al. 2001). Each ventricular dynamics of a single cell is treated as a single potential node in this model. The aslanidi model of human purkinje fibre cell is used for simulation analysis in this study of computational biology (Stewart et al. 2009)

$$C_m\,(dV/dt) = -\,(I_{ion}) \quad \ldots\ldots\ldots\ldots(1)$$

The following differential equation(1) of AM can be used to describe the electrophysiological examination of a purkinje fibre single cell. The gap junctions were consistently dispersed along the fiber's length, and the gap junction was modelled as a 2.5nS linear, constant conductance(m) (Malathi and Reddy 2006). The Accuracy of 20 samples are validated by using this Equation(2),,

$$\text{Accuracy} = \frac{\square\square+\square\square}{\square\square+\square\square+\square\square+\square\square} \quad \ldots\ldots\ldots\ldots(2)$$

The model is created with MATLAB software and a novel Euler integration approach. Finally, we use group Samples(KNN and ANN) to validate our results of normal and dysfunctional channel potentials and mean values, as well as the standard deviation of dependent variables and std error mean, using the Statistical Package for the Social Sciences (SPSS) software.

KNN ALGORITHM

It's a Supervised machine learning algorithm. This method can be used to address both classification and regression problems. The number of nearest neighbours to a new unknown variable that must be forecasted or categorised is represented by the symbol 'K.' The innovative KNN method is a simple but effective classification algorithm. The main drawbacks of KNN are (1) its low efficiency (being a lazy learning approach, it cannot be employed in many applications like dynamic web mining for an outsized repository) and (2) its reliance on selecting a "good value" for k. (Guo et al. 2004).

ANN ALGORITHM

An Artificial neural network is an example of supervised learning. An artificial neural network in the form of connected network units was used to get the knowledge of training. Humans have a difficult time retrieving this information, the rule was extracted for data mining classification as a result of this factor. The dataset is the starting point for the classification technique, the data set consists of two parts: a training sample and a test sample. The training sample is used to train the network, while the test sample is used to assess the accuracy of the network classifier. A variety of approaches, such as cross validation, random sampling, and the hold-out method, can be used to partition a data collection(AnwarFahmy and Al Raddady 2013). According to the simulation results, the KNN classifier has the lowest accuracy value, while the ANN classifier has the most precise value.

Statistical analysis

The computational biology study model is created with MATLAB software and a novel Euler integration approach. Finally, we use group Samples (KNN and ANN) to validate our results of normal and dysfunctional channel potentials and mean values, as well as the standard deviation of dependent variables and std error mean, using the Statistical Package for the Social Sciences (SPSS) software. Action potential is the dependent variable and ion concentration is the independent variable (Stewart et al. 2009**).**

RESULT

Figure 1 shows the potassium channel parameter of a single purkinje fibre cell includes a peak amplitude(PA) of 27.6mv, a plateau potential(PP) of 0.2ms, an action potential duration(APD) of 290ms, and a maximum diastolic potential(MDP) of -75mv in the Normal Action Potential.

Figure 2 displays a single PFC abnormal Action potential (Bradycardia) having PA of 24mv, PP of 0.8ms, APD of 280ms and MDP of -61mv of the K^+ parameter.

Figure 3 & 4 the Novel ANN and KNN classifier confusion matrix depicts the accuracy rate by revealing negative as non disease and positive as diseased. True Negative(TN) which represents there is no disease observed, True Positive(TP) gives out diseased observation such as both tachycardia or bradycardia , False Negative (FN) describe one normal non diseased and abnormal(Tachycardia or Bradycardia), False Positive(FP) includes normal or abnormal(Tachycardia) and abnormal(Bradycardia) sample value.

Figure 5 plots a graph comparing KNN and ANN to display the bar mean of accuracy by group using SPSS.

Table 1 denotesaccuracy obtained for the Potassium Ion channel by the Artificial Neural Network (ANN) and K-Nearest Neighbor (KNN). 20 sample data were loaded in SPSS for analysis.

Table 2 represents the statistical analysis of Group 1 KNN has a mean of 63.410, a standard deviation of 4.3533, and a standard error mean of .9734, whereas group 2 ANN has a mean of 66.055, a standard deviation of 1.0329, and a standard error mean of .2310.
Table 3 shows Independent samples tested by analysis of accuracy using Levene's test and t-test for equality of variances and means keeping equal variances and assumed and not assumed.

DISCUSSION

Figure 1 shows the normal AP of the single PFC which has Peak Amplitude (PA) of 27.6mV, Plateau Potential is 0.2ms, APD is 290ms and Maximum Diastolic Potential (MDP) is 75mV at the condition of extracellular level of K^+ concentration at 5.4mM. By comparing AP of normal and abnormal(bradycardia), Figure 2 shows the abnormal AP of the single purkinje fibre cell which has PA is 24mV, PP is 0.8ms results in elongation of plateau potential, APD is 280ms and MDP is -61mV leads to a long relaxation phase resulting in low conduction at the condition of extracellular level of K^+ concentration at 10.4mM.

The APD displays 290ms in normal AP and in abnormal it is shortened by 280ms which also causes tachycardia(fast heartbeat), thereby shortened APD results in early repolarization phase this process produces Delayed afterdepolarization (DAD) after long resting membrane potential (Wit 2018). The MDP value of normal AP is -75mv and abnormal MDP is of -61mv. In general Normal PFC of Total Cycle Length (TCL) is 1000ms when K^+ increases to 10.8mM, the TCL of potassium PFC is 900ms so a 10% decrease can lead to tachycardia (Moskalenko 2014). Hypokalemia raises resting membrane potential and duration of both the action potential and the refractory period, to a higher extent than the normal. The occurrence of U waves higher than 1 mm and U waves larger than the T wave in the same lead are electrocardiographic criteria for hypokalemia (with associated ST-segment depression), Hypokalemia is a well-recognized risk factor for ventricular tachyarrhythmias(VTs) (Helfant 1986). The resting membrane potential (that is, from 90 mV to 80 mV) decreases as the extracellular K^+ concentration rises. As a result, the threshold potential decreases (from 75 to 70 mV); however, this 5-mV decrease is less than the resting potential decrease. As a result, the computational biology study of difference between the resting and threshold potentials drops to about 10 millivolts (as opposed to 15 mV in a physiologic milieu). As potassium levels rise, the resting membrane potential becomes less negative, lowering Vmax over time. Slowing of cardiac conduction is caused by a decrease in Vmax values, which is reflected by gradual prolonging of the P wave, PR interval, and QRS complex. In summary, modest hyperkalemia increases myocyte excitability by moving the resting membrane potential to a less negative value, bringing it closer to threshold potential; however, as potassium levels rise, myocyte depression happens, and Vmax falls (Parham et al. 2006).

Limitation includes that KNN and ANN classifiers mostly cannot be used to get a superior outcome to quickly detect and classify normal and abnormal cardiac circumstances. Studies comparing supervised learning algorithms for predicting heart disease in its early stages will be conducted in the future. Several algorithms are used to classify whether the people tested have heart disease or are healthy, including an Ensemble algorithm(boosting and bagging), decision tree (DT), Naive Bayes (NB), and random forest (RF). Then came the discovery of drugs that activate K^+ channels at an early stage of the disease.

CONCLUSION

Therefore the changes in K^+ channel leads to Hypokalemia which results in resting membrane potential and the duration of both the action potential, to a higher extent than the normal. The paper concludes that the ANN classifier predicts better classification in identifying the accuracy of potassium channel parameters when compared to the KNN classifier of PFC synchronization and coordination.

DECLARATIONS

Conflict of Interests

No conflict of interest in this manuscript.

Authors Contributions

Author SM was involved in literature survey in mathematical models, Euler integration matlab code development, Arrhythmia analysis and manuscript writing. Author SN involved in conceptualization, data validation and critical review of manuscript.

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FIGURES AND TABLES

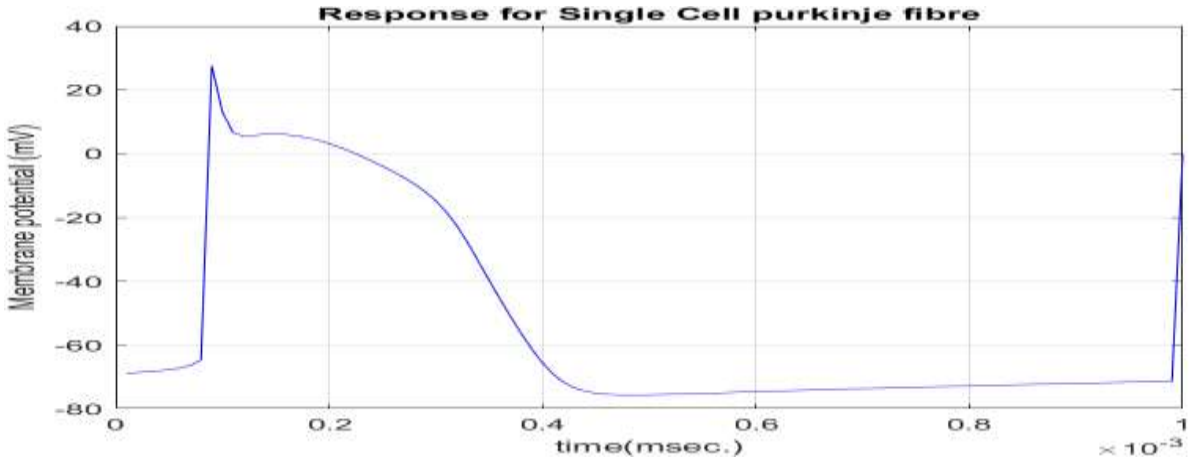

Fig. 1. Normal AP of single PFC at extracellular K^+ concentration of 5.4mM.

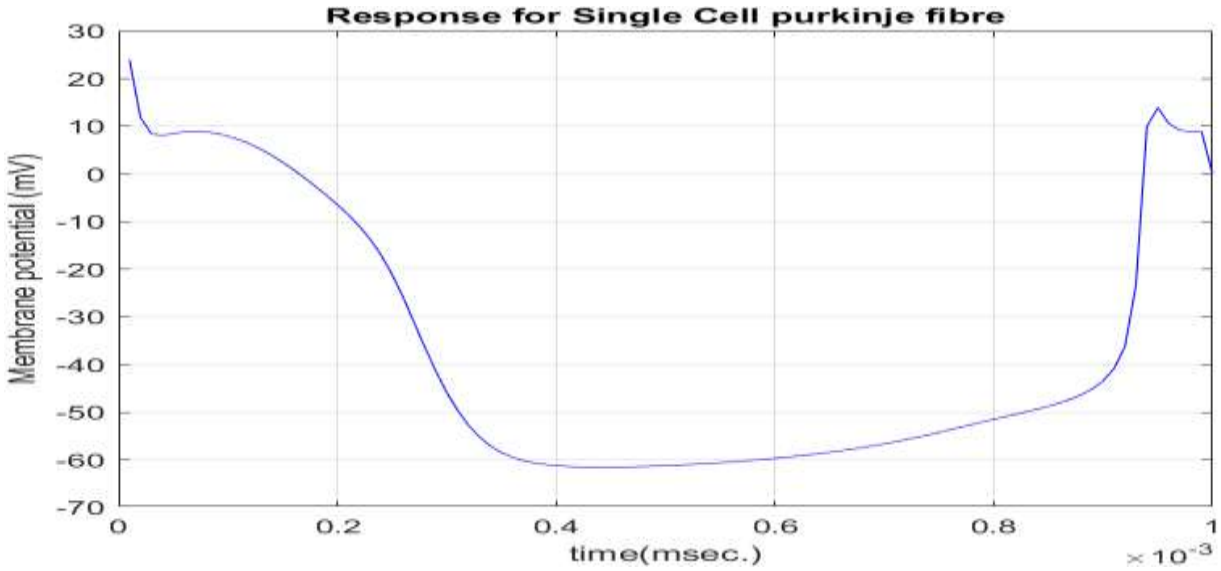

Fig. 2. Abnormal AP of single PFC at extracellular K^+ concentration of 10.8mM.

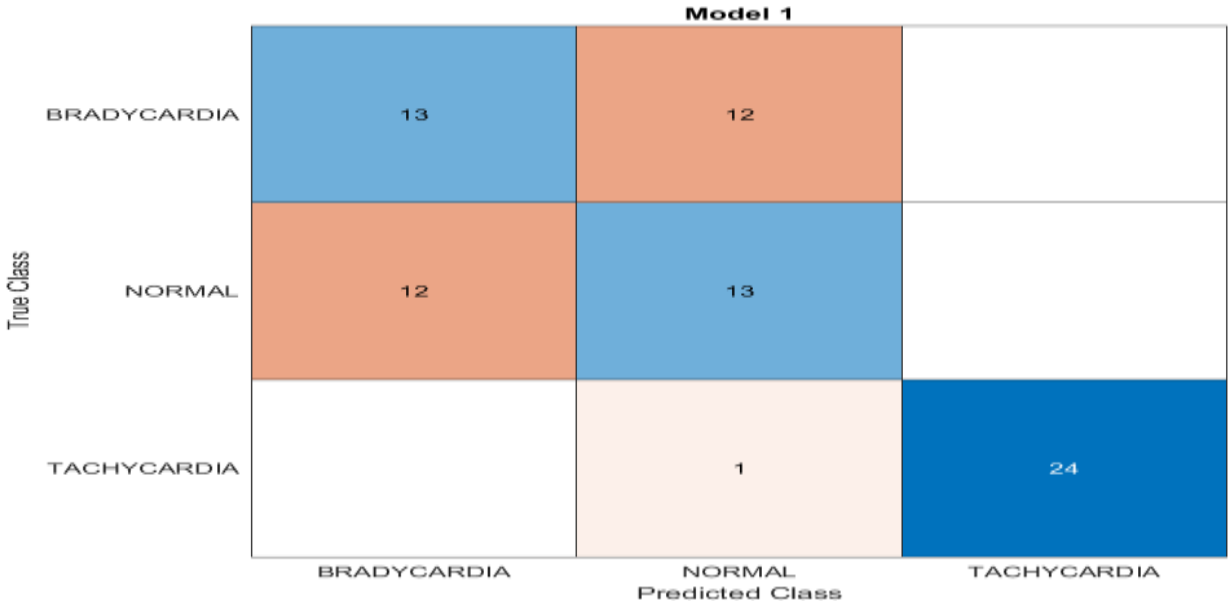

Fig. 3. Confusion matrix of KNN classifiers using K^+ channel parameters.

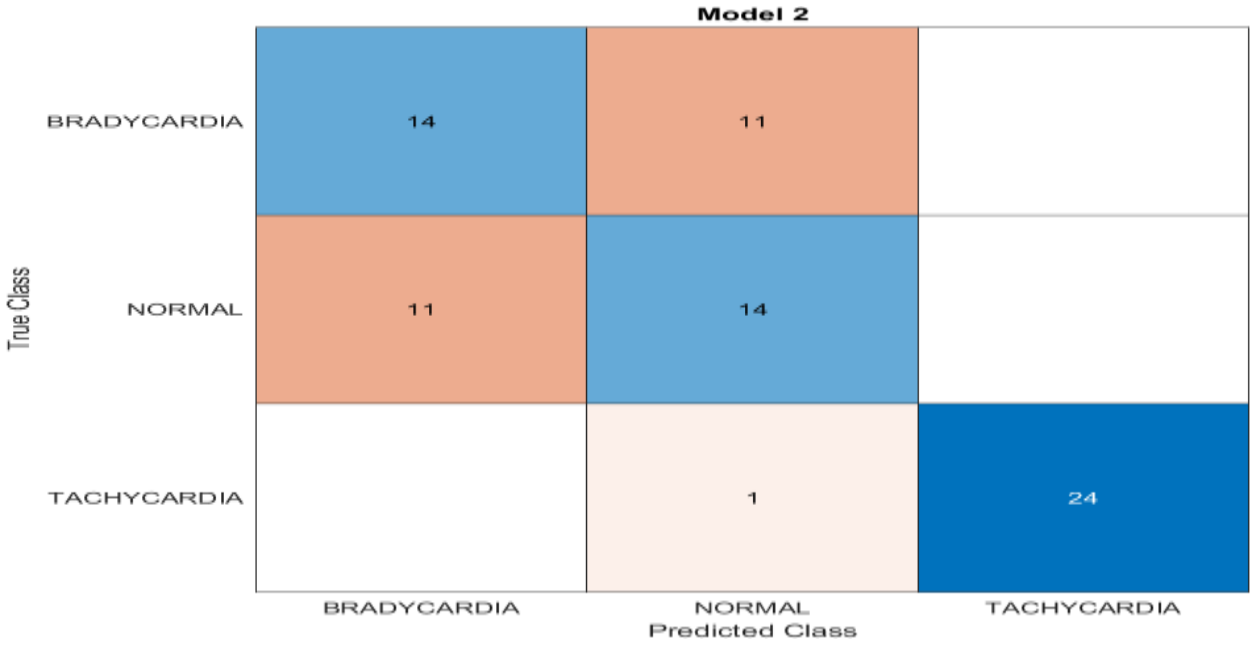

Fig. 4. Confusion matrix of ANN classifier using K^+ channel parameters.

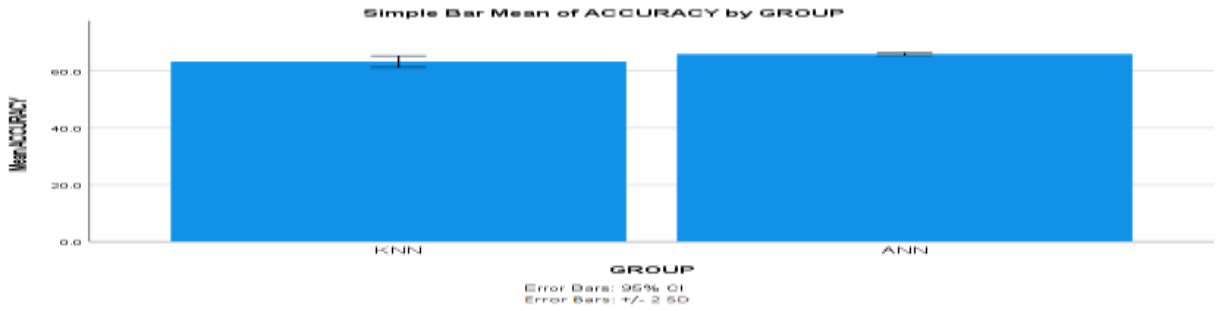

Fig. 5. By comparing PFC normal AP with abnormal AP parameters, mean and standard deviation values are plotted in the graph. X axis: difference of ANN and KNN as a group; Y axis: Mean accuracy of AP in mV. SD±2.

Table 1.Accuracy obtained for potassium channels by Artificial Neural Network (ANN) and K-Nearest Neighbor (KNN). 20 sample data were loaded in SPSS for analysis.

S.NO	ACCURACY OBTAINED THROUGH ANN FOR POTASSIUM CHANNEL	ACCURACY OBTAINED THROUGH KNN FOR POTASSIUM CHANNEL
1	66.7	69.3
2	66.7	64
3	66.7	61.3
4	65.3	61.3
5	66.7	65.3
6	66.7	66.7
7	65.3	60.3
8	65.3	62.7
9	68	74.7
10	65.3	66.7
11	68	58.7
12	65.3	61.3
13	65.3	66.7
14	65.3	61.3
15	65.3	57.3
16	65.3	61.3

17	65.3	57.3
18	68	60
19	68	69.3
20	65.3	60

Table 2. Statistical analysis of KNN and ANN accuracy by Mean, standard deviation and standard error mean for different dysfunction pairs.

ACCURACY	GROUP	N	MEAN	STANDARD DEVIATION	STD ERROR MEAN
	KNN	20	63.410	4.3533	.9734
	ANN	20	66.055	1.0329	.2310

Table3. Independent sample test analysis of Levene's Test and T-test using SPSS software for calculating KNN and ANN accuracy for potassium channels**.** The data was found to be statistically significant.

Independent Sample Test										
		Levene's Test for Equality of variances		**T-test for Equality of Means**						
		F	**Sig.**	**t**	**df**	**Sig(2.tailed)**	**Mean diff**	**Std. diff error**	**95%confidence interval of the difference**	
									Lower	**Upper**
ACCURACY	**Equal variances assumed**	23.363	<.001	-2.644	38	.012	-2.6450	1.0005	-4.6703	-.6197
	Equal variances not assumed			-2.644	21.132	.015	-2.6450	1.0005	-4.7248	-.5652