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Analysis And Comparison Of Ventricular Cardiac Arrhythmia Classification Using Sodium Potassium Pump Channel Parameters With ANN And KNN Classifier

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ABSTRACT

Aim: The intent of this research is to analyze and compare ventricular cardiac arrhythmia classification using sodium potassium pump (Na^+/K^+) channel parameters with Artificial Neural Network (ANN) and K-Nearest Neighbor (KNN) classifiers. **Materials and Methods:** P.J.Noble and A.V.Panfilov model (PJAV) is used for human ventricular study based on the action potential distance. PJAV uses alternative methods of computer simulations which include major ions, pumps and exchangers. Sample was calculated by keeping threshold 0.05, G Power 80%, confidence interval 95% and enrolment ratio as 1. Number of samples considered is 20. According to these data the accuracy is obtained from the classifiers by training novel ANN and KNN classifiers by alternating the Cross fold validation to obtain 20 different samples. These samples are imported to Statistical Package for the Social Science (SPSS) software for graphical representation and overall accuracy. **Result:** The concluded results shows that ANN has accuracy of 12.25% with standard deviation (4.0911) and Standard error mean (0.9148). Similarly KNN produces an accuracy value of 4.54 % with standard deviation (2.5732) and Standard error mean (0.5754). **Conclusion:** As of the results, it clearly shows that ANN has better accuracy for classification than KNN.

Keywords

Ventricular Cardiac Arrhythmia, Sodium Potassium Pump, exchangers, Novel ANN and KNN Classifiers, Action Potential, Bradycardia, Tachycardia.

Imprint

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INTRODUCTION

Ventricular Cardiac Arrhythmia is an improper electrical activity that has many types but occurs because of the main major reasons that are abnormality in the impulse initiation and abnormality in the impulse propagation which may be because of the improper action potential occurred by the major ions, pumps and exchangers (Hoffman and Rosen 1981). Sodium Potassium (Na^+/K^+) was first discovered by Skou in 1957 and was awarded nobel prize in 1997 in chemistry. The activity of the sodium potassium siphon is managed by a phosphoprotein phospholemman, whose unphosphorylation prompts restraint of the pump and whose phosphorylation prompts an increment in pump action. It has 3 phosphorylation destinations, 2 palmitoylation locales and 1 glutathionylation site, which clarifies the large number of signs equipped for animating and restraining the pump. Sodium Potassium Pump is also an enzyme which involves α and β subunits is essential for its function (Youssef'] n.d.). Na^+/K^+ Pump is seen as a principle reason for active cell transport through the membranes. It is involved in major diseases like heart failure and ischemia. In our review we will concentrate on how important Sodium Potassium Pump is in regulating proper repolarisation function and action potential (Bueno-Orovio et al. 2014). Na^+/K^+ Pump functions to balance the intracellular Na^+ concentration, its work is to activate three Na^+ in exchange to two K^+. Arrhythmias like Chronic Atrial Fibrillation (CAF) reduces the length of Action Potential (AP). The Na^+/K^+ Pump Current (I_p) is studied from various cardiac tissues and (Bueno-Orovio et al. 2014) myocytes of pig, sheep, rabbits and dog, but not directly into any cells or tissues from the human heart. So,because of this reason computation methods are used to study the human heart (Workman, Kane, and Rankin 2003).

Many studies related to Ventricular Cardiac Arrhythmia and Na^+/K^+ Pump have done during the year 2016 – 2021 (≅ 35,200 as per google scholar data) in which Science Direct have published 15 articles and Pubmed have published 20 articles till the current year

(2021). Large amounts of concentration gradients of Na^+ and K^+ are taken care by the Na^+/K^+ Pump, this pump doesn't work on equilibrium state like other secondary or primary active transports. In which the ratio of Na^+ and K^+ out and in of the cell is 3:2. The concentration ratio of Na^+ and K^+ inside and outside of the cell is about 0.3027 and 0.9788 and the sum of the Na^+ and K^+ equilibrium potential is -30mV. These results suggest that the ratio of Na^+/K^+ and ion concentration plays an important role (Xu 2013). Sodium potassium pump is most widely recognized as an important part in active ion transport in the cellular membrane of the cardiac tissue. They maintain the Na^+ and K^+ gradients which is very crucial for cardiac electrophysiology. Na^+/K^+ Pump is responsible for major diseased conditions including heart failure and ischemia. Stimulation studies have confirmed that Na^+/K^+ Pump is responsible for cardiac repolarization such as APD restoration. (Bueno-Orovio et al. 2014). The Na^+/K^+ Pump is considered to be a protein machine with more moving parts. The ATP is important in the pump; it shifts the shape for creating a space outside of the cell. Through which the Na^+ is released and K^+ is picked up. And finally the cleavage is shifted where K^+ released inside the cell which will be surrounded by oxygen from the protein ("Sodium-Potassium Pump" n.d.). The Na^+/K^+ Pump is an electromagnetic transmembrane ATPase which is present in the outer plasma membrane of the cellon the cytosolic side.The Na^+/K^+ Pump helps in balancing the membrane potential in cells and osmotic equilibrium. The Na^+ and K^+ strike across the concentration gradients. It maintains the concentration of Na^+ extracellularly and K^+ intracellularly, this concentration has an important role in stabilizing the resting potential, regulating cell volume and cell signal transduction. In the case where Na^+ is excessive intracellularly and K^+ extracellularly, Na^+/K^+ ATPase can no longer pump them out of the cell. Which drives in the Na^+/Ca^{2+} exchanger whose function is to pump Na^+ into the cell and Ca^{2+} out of the cell, since Na^+ cannot be pumped out there occurs cardiac contractility causing a decrease in heart rate. This paper is best in my opinion with all necessary information in detail. (Pirahanchi, Jessu, and Aeddula 2021).

Our team has extensive knowledge and research experience that has translate into high quality publications (Chellapa et al. 2020; Lavanya, Kannan, and Arivalagan 2021; Raj R, D, and S 2020; Shilpa-Jain et al. 2021; S, R, and P 2021; Ramadoss, Padmanaban, and Subramanian 2022; Wu et al. 2020; Kalidoss, Umapathy, and Rani Thirunavukkarasu 2021; Kaja et al. 2020; Antink et al. 2020; Paul et al. 2020; Malaikolundhan et al. 2020)

Since it is difficult to research the human cardiac system in real time to get human experimental data and research prediction (CA). But in animal studies, CA analysis is possible. We cannot prefer animal data because there are many variations in the AP characteristics when compared to humans AP. The alternative way to analyze such CA is through a computational approach. The intent of this research is to analyze and compare ventricular cardiac arrhythmia classification using sodium potassium pump (Na^+/K^+) channel parameters with Artificial Neural Network (ANN) and K-Nearest Neighbor (KNN) classifiers.

MATERIALS AND METHODS

This research is worked out in the Digital Signal Processing laboratory in the department of Biomedical Engineering, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences. The research analysis is carried out in a single group with different sodium potassium pump parameter conditions. Sample size was calculated by keeping threshold 0.05, G Power 80%, confidence interval 95% and enrolment ratio as 1. Number of samples considered is 20 for each analysis. Dataset is obtained by using computer simulations (Matlab). It contains about 20 samples each which is labeled as Normal, Bradycardia and Tachycardia. The parameters to identify the accuracy are Voltage,Current and Activation Gate of the channels ((Izeboudjen, Larbes, and Farah 2014)).

The values for the sodium potassium pump channels are obtained by alternating the values from normal (0.03mM). Initially the Normal value is obtained, later the values for 50% decrease (0.015mM) and 100% increase (0.06mM) is obtained. This is done for the Extracellular Sodium Potassium Pump Channel. It is observed that there is a slight decrease in AP distance (APD) when the value is decreased to 50% which means the number of heart beats per minute increases which leads to tachycardia. When the value is increased 100% it is observed that there is a slight increase in the APD, the number of heart beats decreases per minute which leads to Bradycardia (Sachse 2005). Based on this the dataset is tabulated in Microsoft Excel sheet and imported to the Classification learner. Model Type is selected as KNN and ANN

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

dv/dt is Membrane Potential (MP) (mV), C_m is the Membrane Capacitance (MC) (μF), I_{ion} is total ionic current (pA), I_{stim} is stimulation current (pA) as given in Equation (1).

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \quad (2)$$

Equation (2) is used to find the accuracy using the confusion matrix obtained from the classifiers individually. Using SPSS software finally we are calculating the group statistics containing the standard deviation, mean and standard error mean.

Artificial Neural Network

ANN is a system on the basis of mathematical algorithms obtained from the neuroscience field and characterized by arithmetic operations. This network works well on parallelism, classification, optimization and generalization. ANN is an architecture of the neuron. It is a computing system that characterizes the highly computing interconnected neurons or processing elements (Izeboudjen, Larbes, and Farah 2014). In our research ANN classifier is used to classify the input 20 samples as normal, tachycardia and bradycardia.

K – Nearest Neighbor

KNN is a non-parametric method; a type of nearest neighbor classifier is simple and often shows good performance. Its function is to store training patterns and search for the "K" nearest pattern to find the test pattern data. Many new improvements are made in KNN like Weighted K- Nearest Neighbor Classifier (WK-NNC) and K- Nearest Mean Classifier (KNMC). All KNN classifiers use the same procedure of fixing the K value and identifying its nearest neighbor. In our research we are identifying the neighbors for normal, tachycardia and bradycardia (Viswanath and Hitendra Sarma 2011).

Statistical Analysis

For the computational simulation, the tool used is IBM SPSS Statistics 28.0.0.0. To test the samples independent sample t test to test the accuracy, standard deviation and mean and to compare the groups KNN and ANN labeled as group 1 and 2 respectively. The output of SPSS software is represented in tables and graphs through which the results conclude ANN produces better accuracy compared to KNN. ANN has accuracy of 12.25% with standard deviation (4.0911) and Standard error mean (0.9148). Similarly KNN produces an accuracy value of 4.54 % with standard deviation (2.5732) and Standard error mean (0.5754) ((Izeboudjen, Larbes, and Farah 2014)).

RESULTS

Figure 1 (a) represents the normal AP and APD pattern of a good cardiac health person in which the Na^+/K^+ Pump value is fixed to the normal (0.03mM).

Figure 1 (b) represents the abnormal AP and APD pattern when Na^+/K^+ Pump value is increased by 100%

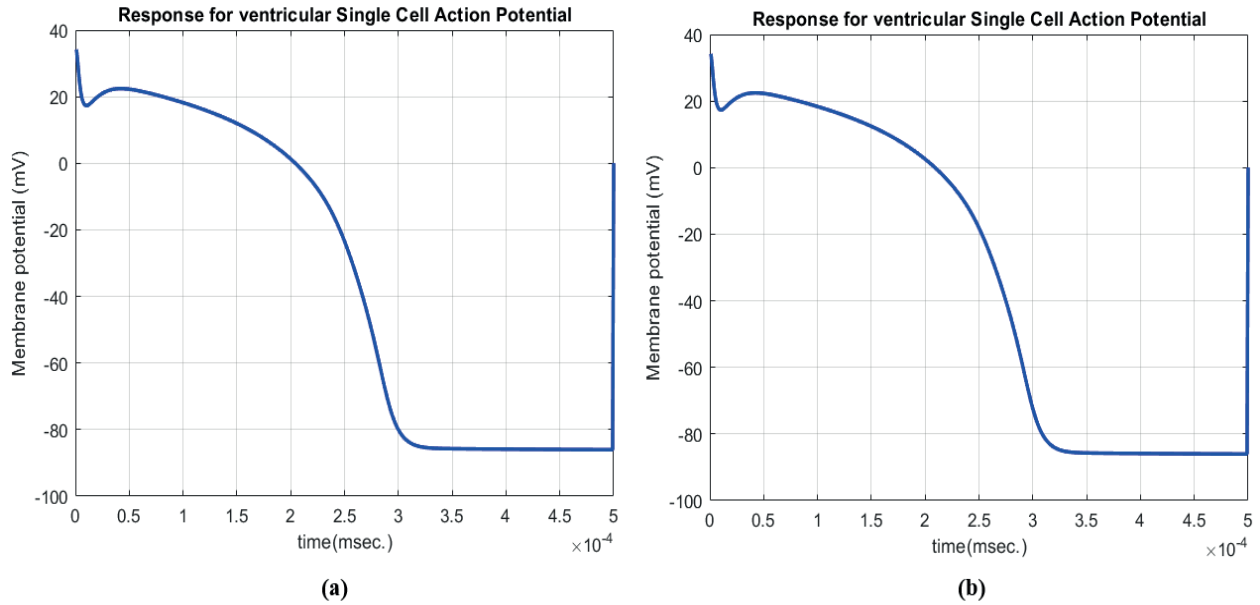


Fig. 1: (a) Normal ECG pattern when the sodium potassium pump (Na+/K+) channel is at normal condition (0.03mM). (b) Abnormal ECG pattern when the sodium potassium pump (Na+/K+) channel value is increased by 100% (0.06mM)

(0.06mM) a minute increase in the APD is noticed considerably which might lead to bradycardia.

Figure 2 represents a confusion matrix of ANN Sample sets which simplify the data into matrix format. This matrix represents the True Negative, True Positive, False Positive and False Negative.

Figure 3 represents a confusion matrix of ANN Sample sets which simplify the data into matrix format. This matrix represents the True Negative, True Positive, False Positive and False Negative.

Figure 4 Displays graphical representation of accuracy of two groups obtained from SPSS software. Where X-axis is group (KNN and ANN) and Y-axis is accuracy (%)

Table 1 represents the accuracy obtained through ANN and KNN classifiers for sodium potassium pumps. It contains 20 sample data that were loaded to the SPSS software..

Table 2 represents the group statistics of the accuracy rate of the two Novel ANN and KNN classifiers, their standard deviation, mean and standard error mean. KNN shows accuracy of 4.54 % and ANN is 12.25%.

Table 3 represents the independent t test data obtained from the SPSS software which compares the mean between two unrelated groups and checks if the data is different.

DISCUSSION

Figure 1 (a) represents the normal ECG pattern with regular AP and APD obtained by setting Na^+/K^+ Pump value as 0.03mM.The APD will be at 3 x 10^{-4} m/

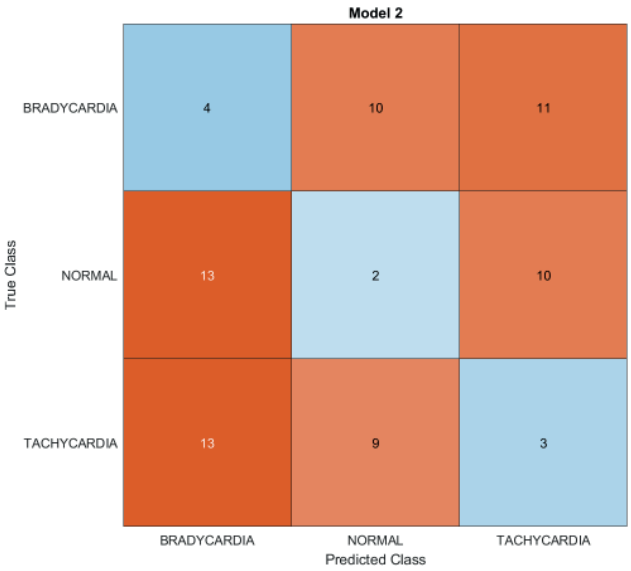


Fig. 2: Confusion Matrix of Artificial Neural Network (ANN)

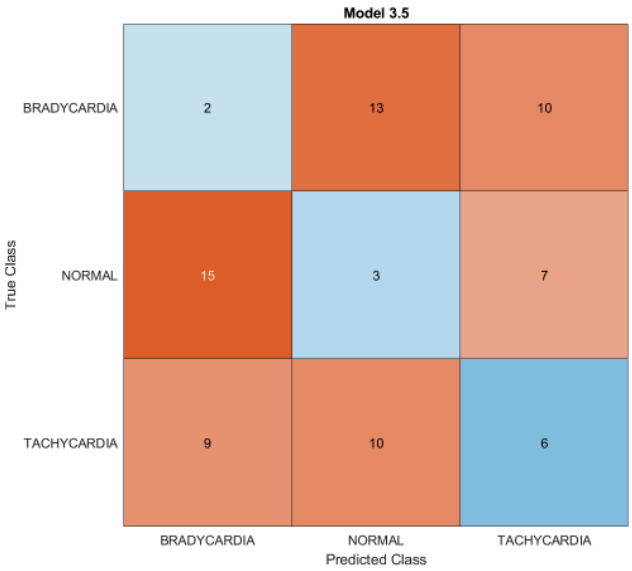


Fig. 3: Confusion Matrix of K-Nearest Neighbor (KNN)

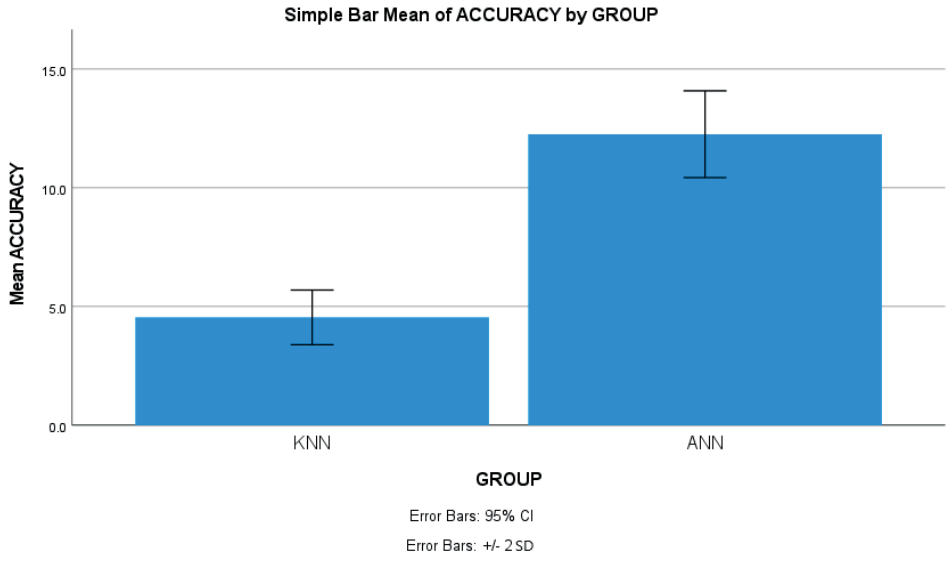


Fig. 4: Mean accuracy rate of accuracy rate of the two groups K-Nearest Neighbor (KNN) and Artificial Neural Network (ANN). X axis: K-Nearest Neighbor (KNN) and Artificial Neural Network (ANN); Y axis: Mean accuracy rate SD+-2.

Table 1

Accuracy obtained for Sodium Potassium Pump 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 SODIUM POTASSIUM PUMP	ACCURACY OBTAINED THROUGH KNN FOR SODIUM POTASSIUM PUMP
1	1.3	13.3
2	1.3	4
3	1.3	5.3
4	5.3	13.3
5	6.7	14.3
6	7.7	15.3
7	8.3	13.3
8	6.3	11.3
9	7.3	14.3
10	1.3	13.3
11	6.7	5.3
12	5.3	5.3
13	1.3	13.3
14	5.3	13.3
15	3.3	14.3
16	8.1	14.3
17	3.1	14.3
18	4.3	5.3
19	5.3	11.3
20	1.3	16.3

Table 2

The Group statistics of the accuracy rate of the 2 ANN and KNN, their standard deviation, mean and standard error mean. The Accuracy Rate of ANN is 12.25% and KNN classifier has an accuracy rate of 4.54%.

GROUP STATISTICS

	Group	N	Mean	Std. Deviation	Std. Error Mean
Accuracy	KNN	20	4.540	2.5732	0.5754
	ANN	20	12.255	4.0911	0.9148

sec. Figure 1 (b) represents the abnormal ECG pattern with irregular AP and APD is obtained when Na^+/K^+ Pump value is increased by 100% (0.06mM) the APD is increased slightly to 3.18 x 10^{-4} m/sec. Na^+/K^+ Pump present in the plasma membrane is responsible for pumping three Na^+ ions out of the cell and two K^+ ions inside the cell. It is identified that Na^+/K^+ Pump abnormalities can reduce the heart rate by 43%. Leads to diseases like hypokalemia (less K^+ ions in blood). This may result in APD prolongation, reduced repolarization reserve and automaticity (Weiss, Qu, and Shivkumar 2017). Figure 2 represents the confusion matrix trained from ANN classifier in which the x-axis is the predicted class and the y-axis is the true class representing the normal, tachycardia and bradycardia. Consisting of entities as True Negative (TN), True Positive (TP), False Positive (FP), False Negative (FN). The Confusion matrix is used to measure the success rate of the classification on the basis of algorithm or human observation in comparison with the true class (Düntsch and Gediga 2019).

Figure 3 represents the confusion matrix trained from KNN classifiers represented in 3x3 matrix simplifying the dataset based on normal, tachycardia and bradycardia with entities TP,TN, FP and FN. Confusion matrix is a vastly used descriptor for accessing the classifiers accuracy. Provided in the nxn matrix where the n denotes the number of classes used to describe the classifiers performance (Düntsch and Gediga 2019). Figure 4 represents the graphical representation obtained from SPSS software in which the x-axis is groups (KNN and ANN) and y-axis is accuracy (%). This graph shows the accuracy level of the groups which clearly represents that ANN is more accurate than KNN. Statistical softwares is generally used in data analysis SPSS software seems to be the most popular among them, this is applicable in fields like medicine, social science and en-

Table 3

Independent Sample t test which compares the 2 independent groups (KNN and ANN). Datas are statistically insignificant (p=0.073)

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	5%confidence interval of the difference	
									Lower	Upper
ACCURACY	Equal variances assumed	3.399	.073	-7.139	38	<.001	-7.71150	1.0807	-9.9028	-5.5272
	Equal variances not assumed			-7.139	31.999	<.001	-7.7150	1.0807	-9.9163	-5.5137

gineering. It is used to analyze the data by a carefully identified scientific observations and process, mainly used by researchers who need not have competencies in using updated statistical tools which is owned by IBM Inc currently (Okagbue et al. 2021) Table 1 represents the data that are loaded to the SPSS software which is the accuracy of ANN and KNN classifiers for sodium potassium pump. Table 2 represents the group statistics calculating the number of samples (N), standard deviation, mean and standard error mean. All these parameters are individually compared for the two groups (KNN and ANN) and accuracy are tabulated. The SPSS package allows researchers to convert simple descriptive numbers to statistical ranges represented in graphs, tables and charts which has helped them from taking several calculations to obtain a result (Bala 2016). Table 3 represents the independent t sample test results which is used for comparing sample results with known and specified values. The task of this test is to identify which of the groups mean and standard deviation are different from the specified value. Only when the sample size is big in this condition does this sample test be used. It is widely used in medical experiments to analyze the physiological differences in diseases which in our research are normal,tachycardia and bradycardia (Skaik 2015).

The drawback of our result is though ANN makes better accuracy of 12.25% it is still less accurately diverged from various classifiers like perceptron and decision tree classifier which produces higher precision than novel ANN and KNN classifiers.

Future Works will join examining more ion channels, pumps and exchangers, its obligation to the heart normal function and accuracy rate of various classifiers will be taken a gander at and learned. Likewise, much more real life examples can be assembled and analyzed to apply it, in reality.

CONCLUSION

The conclusion exhibits that the ANN classifier has the highest accuracy. The Accuracy Rate of ANN Algorithm is 12.25% and KNN classifier has an accuracy rate of 4.54%. The Precision and Recall of ANN Algorithm is efficient in comparison with KNN.

DECLARATIONS

Conflict of Interests

No conflict of interest in this manuscript.

Authors Contributions

Author GBM 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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