Data Science 1 (2021) 1-6 **IOS Press**

Electrocardiogram arrhythmia detection with novel signal processing and persistent homology-derived predictors

Hunter Dlugas*

Department of Mathematics, Wayne State University, MI, USA E-mail: fy7392@wayne.edu

Abstract. Many approaches to computer-aided electrocardiogram (ECG) arrhythmia detection have been performed, several of which combine persistent homology and machine learning. We present a novel ECG signal processing pipeline and method of constructing predictor variables for use in statistical models. Specifically, we introduce an isoelectric baseline to yield non-trivial topological features corresponding to the P, Q, S, and T-waves (if they exist) and utilize the N-most persistent 1-dimensional homological features and their corresponding area-minimal cycle representatives to construct predictor variables derived from the persistent homology of the ECG signal for some choice of N. The binary classification of (1) Atrial Fibrillation vs. Non-Atrial Fibrillation, (2) Arrhythmia vs. Normal Sinus Rhythm, and (3) Arrhythmias with Morphological Changes vs. Sinus Rhythm with Bradycardia and Tachycardia Treated as Non-Arrhythmia was performed using Logistic Regression, Linear Discriminant Analysis, Quadratic Discriminant Analysis, Naive Bayes, Random Forest, Gradient Boosted Decision Tree, K-Nearest Neigh-2.2 bors, and Support Vector Machine with a linear, radial, and polynomial kernel Models with stratified 5-fold cross validation. The Gradient Boosted Decision Tree Model attained the best results with a mean F1-score and mean Accuracy of (0.9677, 0.946), (0.839, 0.946), and (0.943, 0.921) across the five folds for binary classifications of (1), (2), and (3), respectively.

Keywords: arrhythmia classification, electrocardiogram, persistent homology, topological data analysis, signal analysis

*Corresponding author. E-mail: fy7392@wayne.edu.

^{2451-8484 © 2021 -} IOS Press. All rights reserved.

2 H.D. Dlugas / ECG arrhythmia detection with novel signal processing and persistent homology-derived predictors

1. Introduction

Cardiovascular diseases are among the leading causes of death per the World Health Organization and the Centers for Disease Control and Prevention [1, 2]. Arrhythmias are heart rhythms other than normal sinus rhythm with a heart rate between 60 beats/minute and 100 beats/minute; that is, arrhythmias are heart rhythms that are either too fast, too slow, abnormal, and/or irregular. Most arrhythmias must be treated since they can either lead to 1) more chaotic electrical activity of cardiac muscle resulting in loss of cardiac output and/or 2) the formation of thromboemboli (e.g. as in atrial fibrillation) possibly resulting in stroke [3].

The contraction and relaxation of cardiac muscle cells is driven by ion movement across cell membranes and must be coordinated in order for the heart to pump blood effectively. This ion movement is governed by an electrochemical potential comprised of 1) ion concentration gradients and 2) electric potentials. The depolarization and subsequent repolarization of cardiac muscle cells causes changes in electric potential on the body surface which can be measured non-invasively using an electrocardiogram (ECG). Therefore, ECG analysis is important for accurate diagnosis, treatment, and prevention of cardiovascular diseases.

Topological data analysis (TDA) refers to a collection of methods concerned with quantifying 'shapes' of data which are invariant under continuous deformations such as stretching and twisting. The main tool of TDA is persistent homology which quantifies the homology of structures within the data which persist over a range of scales. Persistent homology has been applied to many tasks across various fields such 2.2 as electroencephalogram analysis [28], genomics [34, 35, 37–40, 42, 43], classifying skin lesions based on images [36], and tumor segmentation on histology slides [41]. Cycle representatives - which will be described in Section 1.1 - of topological features have shown utility in various fields outside of ECG analysis such as analyzing structures on the atomic scale [14] and in structural engineering [15].

Several approaches to computer-aided ECG rhythm classification have been performed, including neu-ral networks [6, 7, 18, 19, 21, 23–27, 29–33], wavelet transformation and independent component anal-ysis [8, 20], using higher-order statistics of wavelet-packet decomposition coefficients as features [9], and support vector machines using projected and dynamic ECG features [22]. In the field of computer-aided ECG analysis, TDA has been used to construct metrics of heart rate variability [4, 5]. Computer-aided ECG rhythm classification methods which utilize TDA include modular neural networks with topological-based features [10], fractal dimension in tandem with neural networks [11], mapping ECGs to a high-dimensional space prior to computing topological features and using a random forest model [12], and utilizing a sliding window and Fast Fourier Transform to process the ECG signal prior to computing topological features and using support vector machines [13]. These approaches construct topological predictor variables utilizing

- only birth and death radii statistics [12].
- birth and death radii statistics along with fractal dimension statistics [11].
- birth and death radii statistics along with persistent entropy [10, 13].

To the author's knowledge, constructing predictor variables for use in machine learning models to classify ECG rhythms based off of information derived from cycle representatives has not yet been performed. Additionally, to our knowledge, there has been no computer-aided ECG analysis which utilizes

only the *N*-most persistent topological features for use in rhythm classification, nor has there been an approach which introduces an isoelectric baseline into ECG signals to yield non-trivial topological features
 corresponding to P, Q, S, and T-waves (if they are present to begin with). Introducing an isoelectric baseline prior to computing persistent homology and utilizing the *N*-most persistent topological features and
 properties of their area-minimal cycle representatives for use in constructing predictor variables makes
 the approach taken here distinct from other combinations of TDA and machine learning described in the
 literature.

- In Section 1.1, we give a brief overview of the aspects of persistent homology utilized in this study. The Appendix formalizes the intuition underlying persistent homology described in Section 1.1. The Methods portion is split into three parts: Section 2.1 describes the novel ECG processing pipeline, Sec-tion 2.2 describes the construction of predictor variables primarily based off of the topological features of the processed ECG signal, and Section 2.3 describes the specific classification tasks along with the statistical models and evaluation metrics used. The Results/Discussion section presents the evaluation metrics and ROC curves for each statistical model used. The Conclusion section contains a brief com-parison between the method proposed here and other methods which use TDA and machine learning for rhythm classification in addition to describing some future directions.

1.1. Intuition Behind Persistent Homology

The background on persistent homology presented both here and in the Appendix is restricted to twodimensional data and one-dimensional homology features. The methods discussed generalize to higher dimensions, but we restrict our focus to the relevant dimensions used in the ECG analysis presented here. A toy example dataset *X* and its persistent homology are used to build some intuition for persistent homology. The informal treatment of persistent homology described in this section is made rigorous in the Appendix.

Consider the set of points in the plane \mathbb{R}^2 shown in Fig. 1. Consider drawing a circle around each point, each with the same radius r. We will refer to the union of these circles as the Geometric Čech Complex of radius r, denoted $\check{C}_r(X)$, not to be confused with the Čech complex of radius r, which commonly refers to an abstract simplicial complex. Observe that for r < 0.57, none of the circles comprising $\tilde{C}_r(X)$ overlap around a "void" of non-overlapping space. Furthermore, observe that for $r \in [0.57, 0.81)$, the circles comprising the smaller loop of points nearby the point (1,1) overlap such that there is a "void" of non-overlapping space enclosed by their region of overlap. Hence for $r \in [0.57, 0.81)$, there exists a non-contractible loop within $\check{C}_r(X)$. "Non-contractible" here means that the loop drawn around the void of non-overlapping space cannot be continuously deformed down to a single point without leaving $\check{C}_r(X)$; that is, the loop gets "stuck" on the void encircled by $\check{C}_r(X)$. This non-contractible loop can be continuously deformed to construct another non-contractible loop "stuck" around the same void. These two non-contractible loops are *homotopic* to one another. For example, the green and red loops in Fig. 1 are homotopic. The set of all possible non-contractible loops "stuck" around some void encircled by $\tilde{C}_r(X)$ forms an equivalence class of non-contractible loops, i.e. a set of non-contractible loops where any two non-contractible loops in the set are homotopic. In practice, rather than homotopy, we use a weaker but more technically-involved equivalence relation on loops called homology to utilize efficient





Fig. 2. Relationship between Geometric Čech Complex of Radius *r* and Geometric Realization of Radius *r* Vietoris Rips Complex. A-C: Geometric Čech Complex of Radius 0.2, 0.5, 0.71 depicted in black, respectively; D-F: Geometric Realization of Radius 0.2, 0.5, 0.71 Vietoris Rips Complex, respectively.

algorithms such as Ripser [44] and GUDHI [45] in computing topological features. For a rigorous treat ment of homotopy and homology, see [17].

For a given two-dimensional dataset *X* such that there exists a non-contractible loop ℓ within $\check{C}_r(X)$, we define the *birth radius* of the equivalence class of non-contractible loops containing ℓ as the smallest real number *b* such that some loop in $\check{C}_r(X)$ which is equivalent to ℓ and which is contained in the subset $\check{C}_b(X)$ of $\check{C}_r(X)$ exists. Similarly, we define the *death radius* of the equivalence class of non-contractible loops containing ℓ as the smallest real number *d* such that $r \leq d$ and such that ℓ becomes contractible

when regarded as a loop in $\tilde{C}_d(X)$. That is, the birth radius of an equivalence class of non-contractible loops is the smallest radius at which the equivalence class of that non-contractible loop forms, and the death radius is the smallest radius at which it vanishes (i.e., becomes contractible). For $r \in [b, d]$, the equivalence class of non-contractible loops 'persists,' and this motivates the definition of the persistence of an equivalence class of non-contractible loops as the difference between the death radius and the birth radius. The two non-trivial equivalence classes of non-contractible loops in Fig. 1 have coordinates (0.57, 0.81) and (1.55, 3.01) in the persistence diagram and correspond to the subset of data clustered near (1, 1) and the subset of data clustered near (8, 8), respectively. Note that the larger loop-like struc-ture of data in the upper-right corner of each subplot has a larger persistence than the smaller loop-like structure of data in the lower-left corner of each subplot (i.e. 3.01 - 1.55 = 1.46 > 0.81 - 0.57 = 0.24).

The cycle representatives of a given equivalence class of non-contractible loops $\{\ell_{\alpha}\}_{\alpha \in I}$ (note that I is an uncountable indexing set) with birth radius b and death radius d are the subsets of the data which give rise to non-contractible loops in $\check{C}_r(X)$ with birth radius b and death radius d. For example, the cycle representatives of the equivalence class of non-contractible loops with birth radius 0.5 and death radius $\frac{\sqrt{2}}{2} \approx 0.71$ in Fig. 2 are given by $\{\{a, b, c, d\}, \{a, b, c, d, e\}\}$. The Python package Homeloud can be used to identify cycle representatives which are optimal in some sense such as having the minimum number of points or spanning the minimum area among all cycle representatives [48]. Associating a single optimal cycle representative to each equivalence class of non-contractible loops is important 1) for reproducibility and 2) to select cycle representatives which more closely resemble the P, Q, S, and T-waves for the relevant H1 features. 2.2

2. Methods

The free and publicly available Shaoxing Hospital Zhejiang University School of Medicine electrocardiogram (ECG) database was used in this study [47]. This database consists of 10646 12-lead ECG signals, each spanning 10 seconds with a sampling frequency (i.e. the number of electric potential differences recorded per second) of 500Hz, of which 10605 have non-empty Lead 2 signals. This study strictly utilizes Lead 2, i.e. the 'rhythm lead', so the term "ECG signal" is used to refer to Lead 2 ECG signals. Each ECG signal is labeled with one of 11 rhythms by professional experts. The distribution of these 11 rhythms across the 10605 signals is shown in Table 1.

ECG signals are typically characterized as 1-dimensional lists of real numbers of length $F \cdot t_{max}$ where F is the sampling frequency of the ECG machine (i.e. the number of electric potential differ-ences recorded per second), t_{max} is the total amount of time (in seconds) over which the signal was gathered, and each real number in the list represents the signal amplitude at the given time index. In order to compute 1-dimensional topological features of an ECG signal, the ECG signal must be con-sidered as a subset of \mathbb{R}^2 . Therefore, rather than treat a given ECG signal S as a one-dimensional list with a sampling frequency F over a length of time t_{max} , we use the equivalent formulation of S given by $S = \{(t, f(t)) \mid t \in D\} \subset \mathbb{R}^2$ where $D = \{\frac{i}{F} \mid i \in \{1, ..., F \cdot t_{max}\}\}$ represents the set of time indices and $f: D \to \mathbb{R}$ defines the signal amplitude at each time index.

1	Table 1							
2	Rhythm Distrib	Rhythm Distribution						
3	Rhythm	Count (Total=10605)	Proportion					
4	Atrial Flutter	445	0.042%					
5	Atrial Fibrillation	1780	0.168%					
	Atrial Tachycardia	121	0.011%					
	Atrioventricular Node Reentrant Tachycardia	16	0.002%					
	Atrioventricular Reentrant Tachycardia	8	0.001%					
	Sinoatrial Block	399	0.038%					
	Sinus Atrium to Atrial Wandering	7	0.001%					
	Sinus Bradycardia	3888	0.367%					
	Sinus Rhythm	1826	0.172%					
	Sinus Rachycardia	1568	0.148%					
3	Supraventricular Tachycardia	547	0.052%					
1	•							

In the remainder of this section, we describe 1) ECG signal processing prior to extraction of topological features, 2) the construction of predictor variables derived from persistent homology, and 3) the statistical modeling approaches and evaluation metrics used. A flowchart providing an overview of our approach to arrhythmia detection is shown in Fig. 3.

2.1. Electrocardiogram Signal Processing

Given a raw ECG signal $S = \{(t, f(t)) \mid t \in D\} \subset \mathbb{R}^2$ with time domain $D = \{\frac{h}{F} \mid h \in \{1, ..., F * t_{max}\}\}$ and signal amplitude given by $f: D \to \mathbb{R}$, the signal is first normalized by applying the transformation $g: f(D) \rightarrow [0,1]$ given by:

$$g(f(t)) = \frac{f(t) - \min\{f(D)\}}{\max\{f(D)\} - \min\{f(D)\}}.$$
(1)

The resulting signal $S_{normalized} = \{(t, g(f(t))) \mid t \in D\} \subset \mathbb{R}^2$ has maximum amplitude $\max\{g(f(D))\} = 1$ and minimum amplitude $\min\{g(f(D))\} = 0$. Since equivalence classes of non-contractible loops are not scale-invariant, this normalization is necessary for the magnitude of persistent homology statistics to be comparable across ECG signals.

Next, an isoelectric baseline is included in Snormalized in order to form 'loop-like' structures with non-trivial topological properties in the ECG signal corresponding to the P, Q, S, and T-waves (if they are present). This is done by inserting the 'baseline' value computed as the median of g(f(D)) at the be-ginning of the signal and between every pair of consecutive time indices, doubling the number of points of the signal while still spanning the same amount of time. More explicitly, after the inclusion of the isoelectric baseline to $S_{normalized}$, we obtain the signal $S_{processed} = \{(t, h(g(f(t)))) \mid t \in E\}$ where $E = \{\frac{i}{2F} \mid i \in \{1, ..., 2 \cdot F \cdot t_{max}\}\}$ and $h : [0, 1] \to [0, 1] : g(f(\frac{i}{F})) \mapsto \begin{cases} \text{median}\{g(f(D))\} & \text{if i is odd} \\ g(f(\frac{i}{F})) & \text{if i is even} \end{cases}$

2.2



nates of the area-minimal cycle representative (T, A), we compute the effective centroid coordinates as

• $y = \frac{A - baseline}{1 - baseline}$ where baseline represents the amplitude value of the isoelectric baseline

• $x = t_R - T$ where t_R is the time-coordinate of the onset of the subsequent QRS-complex.

(x, y) where

median $\{g(f(D))\}$.

8 H.D. Dlugas / ECG arrhythmia detection with novel signal processing and persistent homology-derived predictors

All equivalence classes with centroid time coordinate T larger than the largest onset of the QRS-complex are discarded to ensure that the effective centroid time coordinates can always be computed. This effec-tively trims S_{processed} to end with a point representing the onset of a QRS-complex. Furthermore, all equivalence classes of non-contractible loops with area-minimal cycle representative centroid amplitude coordinate A larger than $\frac{1-baseline}{2}$ where $baseline = median\{g(f(D))\}\$ are discarded to obtain a larger proportion of highly-persistent equivalence classes of non-contractible loops corresponding to clinically-relevant subsets of ECG signals such as P, Q, S, and T-waves. The computation of the effective centroid time coordinate is designed to be a proxy of the clinically-relevant PR-interval for equivalence classes of non-contractible loops that represent P-waves. The computation of the effective centroid amplitude co-ordinate normalizes the amplitude coordinates of centroids of area-minimal cycle representatives across signals with differing isoelectric baselines.

The onset of each QRS-complex in the processed ECG signal S processed is identified using Zong, Moody, and Jiangs' approach of "passing S processed through a low-pass filter, applying a transformation with a non-linear scaling factor to enhance the QRS-complexes and suppress unwanted noise, and apply-ing adaptive thresholds to the signal to determine the onset of each QRS-complex" [49]. The persistent homology of the processed signal S processed is then computed, and the N-th most persistent H1 fea-tures are used to construct predictor variables for use in rhythm classification for $N \in \{5, 6, ..., 29, 30\}$. Specifically, for each of the N-th most persistent H1 features, the persistence, birth radius, effective time-coordinate of the centroid of the area-minimal cycle representative relative to the subsequent QRScomplex, effective amplitude-coordinate of the centroid of the area-minimal cycle representative relative to the isoelectric baseline, and Shannon entropy of the vector $\frac{(a,b,c,d,e)}{\text{sum}((a,b,c,d,e))}$ where a = persistence, b =birth radius, c = death radius, d = centroid time-coordinate, and e = centroid amplitude-coordinate are used as predictor variables. Additional predictor variables include the mean and standard devia-tion of the persistences, birth radii, area-minimal cycle representative centroid time coordinates, and area-minimal cycle representative centroid amplitude coordinates of the N-most persistent equivalence classes of non-contractible loops along with the mean and standard deviation of the RR-intervals. Lastly, the total number of R-waves, the total number of H1 features, and the Shannon entropy of the normalized distribution of all H1 persistences are also used as predictor variables.

2.3. Statistical Modeling and Evaluation

Three different binary classifications are carried out:

- Atrial Fibrillation vs. Non-Atrial Fibrillation
 - Arrhythmia vs. Normal Sinus Rhythm
- Arrhythmias with Morphological Changes vs. Sinus Rhythm with Bradycardia and Tachycardia Treated as Non-Arrhythmia
- Note that the motivation behind performing the binary classification of Arrhythmias with Morphologi cal Changes vs. Sinus Rhythm with Bradycardia and Tachycardia Treated as Non-Arrhythmia is that the
 topological predictor variables constructed are a better proxy of the shape of the ECG signal than of the
 periodicity of the signal. For each of the three binary classifications, Logistic Regression, Linear Dis criminant Analysis, Quadratic Discriminant Analysis, Naive Bayes, Random Forest, Gradient Boosted
 Decision Tree, K-Nearest Neighbors, and Support Vector Machine with Linear, Radial, and Polynomial

2.0

2.2

ai models, see [46].					
			True	Label	
	Predicted I abel	Positive	TP	<i>FP</i>	
	Treatered Laber	Negative	FN	TN	
	I	Fig. 4. Confusio	on Matrix		
Stratified 5-fold cross ositives (FP), false no nat shown in Fig. 4 for nd (7) were computed cross the five folds w	ss-validation was pe egatives (FN), and t or each statistical mo d for each statistical ere recorded.	erformed. In rue negative odel used. T model acro	each of th es (TN) we he evaluati ss the five	e 5 folds, the re recorded ir on metrics in folds, and the	true positives (TP), false a confusion matrix like Eqs (2), (3), (4), (5), (6), mean evaluation metrics
Evaluation metrics:					
$F1\text{-}Score = \frac{1}{2 \cdot T}$	$\frac{2 \cdot TP}{P + FP + FN}$				(2)
$Accuracy = \frac{1}{TP}$	$\frac{TP + TN}{FP + FN + TN}$				(3)
Sensitivity = $\frac{1}{TP}$	$\frac{TP}{+FN}$				(4)
Specificity = $\frac{1}{TN}$	$\frac{TN}{T+FP}$				(5)
Positive Predictiv	ve Value (PPV) = $\frac{1}{T}$	$\frac{TP}{P+FP}$			(6)
Negative Predicti	ive Value $(NPV) = -$	$\frac{TN}{TN + TN}$			(7)

Random Forest:
 number of trees ∈ {500, 1250, 2000, 3000} number of variables randomly sampled ∈ {int(0.25 · T), int(0.5 · T), int(0.75 · T), T} where T is the total number of predictor variables.
Gradient Boosted Decision Tree:
* number of trees $\in \{500, 1250, 2000, 3000\}$ * interaction depth $\in \{5, 10, 15, 20\}$
 K-Nearest Neighbors: K ∈ {1, 2, 3, 4, 5, 6, 7, 8, 9, 10}. Support Vector Machine with Radial Kernel:
* $\cos t = 1.$ * $\gamma \in \{0.5, 1, 2, 3, 4, 5\}.$
• Support Vector Machine with Polynomial Kernel:
* $cost = 1.$ * degree $\in \{2, 3, 4, 5\}.$
3. Results/Discussion

The binary classification outcomes for Atrial Fibrillation vs. Non-Atrial Fibrillation, Arrhythmia vs. 2.2 2.2 Normal Sinus Rhythm, and Arrhythmia with Morphological Changes vs. Sinus Rhythm with Bradycar-dia and Tachycardia Treated as Non-Arrhythmia for the hyperparameters yielding the largest F1-Score are shown in Tables 2, 3, and 4, respectively. Observe that the Gradient Boosted Decision Tree Model outperforms all other models with respect to F1-Score and Accuracy across each of the three binary classification tasks, closely followed by the Random Forest Model. The maximum mean F1-Score at-tained by the Gradient Boosted Decision Tree Model across the five folds was 0.967, 0.839, and 0.943 for binary classification of Atrial Fibrillation vs. Non-Atrial Fibrillation, Arrhythmia vs. Normal Sinus Rhythm, and Arrhythmia with Morphological Changes vs. Sinus Rhythm with Bradycardia and Tachy-cardia Treated as Non-Arrhythmia, respectively. The corresponding mean Accuracy attained by the Gra-dient Boosted Decision Tree Model across the five folds was 0.946, 0.946, and 0.921 for binary clas-sification of Atrial Fibrillation vs. Non-Atrial Fibrillation, Arrhythmia vs. Normal Sinus Rhythm, and Arrhythmia with Morphological Changes vs. Sinus Rhythm with Bradycardia and Tachycardia Treated as Non-Arrhythmia, respectively.

Model	F1-Score	Accuracy	Sensitivity	Specificity	PPV	NPV	Opti
Logistic Regression	0.938	0.896	0.947	0.646	0.930	0.712	,
Linear Discriminant Analysis	0.934	0.890	0.941	0.637	0.928	0.686	
Quadratic Discriminant Analysis	0.917	0.864	0.908	0.642	0.927	0.585	
Naive Bayes	0.890	0.818	0.880	0.511	0.899	0.463	
Random Forest	0.955	0.925	0.964	0.734	0.947	0.803	
Gradient Boosted Model	0.967	0.946	0.959	0.880	0.975	0.813	
K-Nearest Neighbors	0.942	0.894	0.925	0.712	0.952	0.660	
Support Vector Machine: Linear Kernel	0.941	0.898	0.935	0.706	0.942	0.705	
Support Vector Machine: Radial Kernel	0.927	0.868	0.869	0.856	0.991	0.272	
Support Vector Machine: Polynomial Kernel	0.937	0.890	0.908	0.749	0.964	0.539	
	r	Table 3					
Binary Classification	Outcomes:	Arrhythmia	vs. Normal Si	nus Rhythm.			
Model	F1-Score	Accuracy	Sensitivity	Specificity	PPV	NPV	Opt
Logistic Regression	0.634	0.876	0.622	0.929	0.647	0.922	
Linear Discriminant Analysis	0.629	0.867	0.652	0.912	0.607	0.927	
Quadratic Discriminant Analysis	0.481	0.709	0.783	0.694	0.347	0.939	
Naive Bayes	0.460	0.673	0.809	0.644	0.322	0.942	
Random Forest	0.829	0.942	0.812	0.969	0.847	0.961	
Gradient Boosted Model	0.839	0.946	0.815	0.974	0.866	0.962	
K-Nearest Neighbors	0.722	0.899	0.747	0.924	0.664	0.964	
Support Vector Machine: Linear Kernel	0.638	0.889	0.743	0.910	0.563	0.958	
Support Vector Machine: Radial Kernel	0.720	0.912	0.869	0.918	0.612	0.982	
Support Vector Machine: Polynomial Kernel	0.631	0.891	0.797	0.902	0.516	0.975	

Table 4

Model	F1-Score	Accuracy	Sensitivity	Specificity	PPV	NPV	Optimal N
Logistic Regression	0.904	0.865	0.932	0.717	0.878	0.828	30
Linear Discriminant Analysis	0.905	0.866	0.927	0.734	0.884	0.821	30
Quadratic Discriminant Analysis	0.857	0.797	0.884	0.607	0.831	0.706	25
Naive Bayes	0.859	0.794	0.912	0.536	0.812	0.735	27
Random Forest	0.933	0.906	0.952	0.805	0.915	0.885	10
Gradient Boosted Model	0.943	0.921	0.955	0.847	0.932	0.896	10
K-Nearest Neighbors	0.905	0.861	0.883	0.807	0.923	0.741	19
Support Vector Machine: Linear Kernel	0.905	0.866	0.886	0.815	0.923	0.745	29
Support Vector Machine: Radial Kernel	0.883	0.828	0.813	0.896	0.968	0.507	5
Support Vector Machine: Polynomial Kernel	0.897	0.845	0.848	0.833	0.949	0.637	16

The Receiver-Operator Characteristic curves along with the corresponding AUC values for the binary classifications of Atrial Fibrillation vs. Non-Atrial Fibrillation, Arrhythmia vs. Normal Sinus Rhythm, and Arrhythmia with Morphological Changes vs. Sinus Rhythm with Bradycardia and Tachycardia Treated as Non-Arrhythmia for the hyperparameters yielding the largest F1-Score are shown in Fig. 5, Fig. 6, and Fig. 7, respectively. Similar to the case of F1-Score and Accuracy, the Gradient Boosted De-cision Tree Model yielded the largest mean Area under Receiver Operator Characteristic Curve (AUC) across the five folds, attaining an AUC of 0.975, 0.575, and 0.887 for binary classification of Atrial Fib-2.2 rillation vs. Non-Atrial Fibrillation, Arrhythmia vs. Normal Sinus Rhythm, and Arrhythmia with Morphological Changes vs. Sinus Rhythm with Bradycardia and Tachycardia Treated as Non-Arrhythmia, respectively.





2.2



14 H.D. Dlugas / ECG arrhythmia detection with novel signal processing and persistent homology-derived predictors

[11], 100% in multiclass arrhythmia detection with small sample size (N=47) [13], and an F1-Score of 72.2% in multiclass rhythm classification [12]. The approach presented here attains similar results as

these previous studies with respect to classification outcomes while utilizing a novel ECG signal processing pipeline and topological predictor variable construction.

4. Conclusion

The method presented here differs from other methods utilizing TDA and machine learning in three main ways:

- by using information about optimal cycle representatives of equivalence classes of non-contractible loops when constructing topological predictor variables.
- by focusing only on the *N*-most persistent equivalence classes of non-contractible loops when constructing topological predictor variables.
- by introducing an isoelectric baseline to create non-trivial equivalence classes of non-contractible loops corresponding to the P, Q, S, and T-waves (if they are present to begin with).

This novel approach to ECG signal processing and construction of topological predictors yields classi-fication results on par with other methods proposed in the literature and demonstrates another example of the utility of optimal cycle representatives. Future directions include multiclass rhythm classification, other methods of defining the isoelectric baseline to account for baseline wander in longer ECG signals, including statistics derived from optimal cycle representatives in other approaches such as sliding window and Fast Fourier Transform embeddings, and including an isoelectric baseline prior to embedding ECG signals in higher dimensions. Several studies have used TDA-derived statistics as input to neural 2.2 networks [10, 11]; however, to the author's knowledge, there has been no study performed which utilizes persistence images [50] as the TDA-derived input for neural networks in arrhythmia detection, yielding another direction for future work.

There have been people working on computer-aided ECG analysis since the invention of the ECG machine. Over the past 20 years, there have been many machine learning approaches taken, yielding encouraging results. Some of these methods have involved TDA. Regardless of the type of method taken in computer-aided ECG analysis and the goodness of the evaluation metrics, we must take care to not rush to replace ECG interpretation by skilled health care professionals, however tempting the potential time and cost savings may be. In addition to the obvious danger of automated arrhythmia classification algorithms missing a harmful arrhythmia that a skilled healthcare professional would not have missed, bells and whistles from automated arrhythmia detection algorithms can lead to unnecessary medical staff fatigue and an increase in stress and adverse outcomes in hospitalized patients [51-56].

The data used in this study are free and publicly available at https://figshare.com/collections/ ChapmanECG/4560497/2 [47]. The code used in this study is free and publicly available and can be found on GitHub: https://github.com/hdlugas/ekg_tda_arrhythmia_detection.

Appendix A. Formalization of Persistent Homology Intuition

We now set out to formalize the notion of "equivalence classes of non-contractible loops that persist for a given range of radius values." Given a set of data X represented as a finite set of points in \mathbb{R}^2 , a simplicial complex is constructed as a topological space that approximates the structure of the data.

Definition A.1. A simplicial complex is a collection K of subsets of a finite set V such that:

• $\{v\} \in K$ for all $v \in V$, and

2.2

• *if* $\tau \subset \sigma$ *for* $\sigma \in K$ *, then* $\tau \in K$ *.*

An element of V is referred to as a vertex, and an element of K with cardinality n + 1 is referred to as an n-simplex.

There are several ways to construct a simplicial complex given a finite set of points in \mathbb{R}^2 , and to be consistent with the geometry of the toy examples discussed in Section 1.1, we consider the Radius rVietoris-Rips complex, a simplicial complex constructed by considering a circle of radius $\frac{r}{2}$ around each point in our dataset and then including $S \subset X$ as a simplex if the intersection of the balls of radius $\frac{r}{2}$ for each point in S is nonempty. An example of the Radius r Vietoris-Rips complex and its corresponding geometric realization for several values of r is shown in Fig 2.

Definition A.2. Given a dataset X represented as a finite subset of \mathbb{R}^2 , and given a positive real number r, the radius r Vietoris-Rips complex of X, denoted $VR_r(X)$, is the simplicial complex given by the collection of all subsets U of X with the property that if $x_1, x_2 \in U$, then $|x_1 - x_2| < r$.

Note that if $S \subset U$ for $U \in VR_r(X)$, then $|x_1 - x_2| < r$ for all $x_1, x_2 \in U$ implies $|x_1 - x_2| < r$ for all $x_1, x_2 \in S$. Thus the radius r Vietoris Rips complex of a finite subset of \mathbb{R}^2 defines a simplicial complex.

We are now in a position to be more concrete about the notion of an "equivalence class of noncontractible loops" within the geometric Čech complex, as discussed in Section 1.1. By an "equivalence class of non-contractible loops," we are referring to an element of the 1-dimensional homology group of some radius r Vietoris-Rips complex, which we now set out to define.

Let X be a finite subset of \mathbb{R}^2 , let r be a positive real number, and let C_n be the vector space over \mathbb{F}_2 with basis consisting of the elements of $VR_r(X)$ of cardinality n + 1 for n = 0, 1, 2. Furthermore, suppose there is an ordering on $VR_r(X)$. Consider $0 \stackrel{\delta_{-1}}{\leftarrow} C_0 \stackrel{\delta_0}{\leftarrow} C_1 \stackrel{\delta_1}{\leftarrow} C_2 \stackrel{\delta_2}{\leftarrow} 0$ where $\delta_n([x_0, ..., x_n]) =$ $\sum_{i=0}^{i} (-1)^{n} [x_0, ..., \hat{x}_i, ..., x_n]$ and \hat{x}_i indicates that x_i is omitted from the ordered simplex. The elements of C_1 are referred to as 1-chains, the elements of ker(δ_0) are referred to as 1-cycles, and elements of $im(\delta_1)$ are referred to as 1-boundaries. Since $\delta_0(\delta_1(v)) = 0$ for all $v \in C_2$, every 1-boundary is an 1-cycle. However, it is not necessarily true that every 1-cycle is an 1-boundary. Intuitively, if we think of X as a point cloud in the plane \mathbb{R}^2 , the 1-dimensional homology group of $VR_r(X)$ is defined such that its dimension over \mathbb{F}_2 counts the number of "holes" in that point cloud.

Definition A.3. Given r > 0 and $VR_r(X)$ where X is a finite subset of \mathbb{R}^2 , we follow the construction of \mathbb{F}_2 -vector spaces C_0 , C_1 , C_2 and linear transformations δ_{-1} , δ_0 , δ_1 , δ_2 as outlined above and define the first homology group of $VR_r(X)$ as the quotient vector space $H_1(VR_r(X)) = ker(\delta_0)/im(\delta_1)$. The \mathbb{F}_2 -vector space dimension $\beta_1 = \dim(H_1(VR_r(X))) = \dim(\ker(\delta_0)) - \dim(\operatorname{im}(\delta_1))$ of $H_1(VR_r(X))$ is called the first Betti number.

By increasing r, we create a sequence of Vietoris-Rips Complexes where $VR_r(X) \subset VR_{r'}(X)$ for r < r'. We then construct

$$VR_{r_0}(X) \xrightarrow{\iota_0} VR_{r_1}(X) \xrightarrow{\iota_1} \dots \xrightarrow{\iota_{m-1}} VR_{r_m}(X)$$

2.2

where $VR_{r_i}(X)$ is a proper subset of $VR_{r_i}(X)$ for i < j and i_0, i_1, \dots, i_{m-1} are inclusion homomorphisms. This induces a sequence of \mathbb{F}_2 -linear functions $i_0^*, i_1^*, \dots, i_{m-1}^*$ such that

$$H_1(VR_{r_0=0}(X)) \xrightarrow{i_0^*} H_1(VR_{r_1}(X)) \xrightarrow{i_1^*} \dots \xrightarrow{i_{m-1}^*} H_1(VR_{r_m}(X))$$

and $i_n^*([c]_V) = [i_n(c)]_W$ for $V = VR_{r_n}(X)$, $W = VR_{r_{n+1}}(X)$, and all n = 0, 1, ..., m - 1. We now give a name to the "smallest" and "largest" r > 0 such that a given 1-cycle belongs to $H_1(VR_r(X))$.

Definition A.4. Let $[c] \in H_1(VR_r(X))$ for some r > 0. The birth filtration of [c] is defined as the greatest lower bound of the set of all $\epsilon > 0$ such that [c] is in the range of the \mathbb{F}_2 -linear function $H_1(VR_{\epsilon}(X)) \rightarrow H_1(VR_r(X))$. Similarly, the death filtration of [c] is defined as the least upper bound of the set of all $\epsilon > 0$ such that [c] maps to zero under the \mathbb{F}_2 -linear function $H_1(VR_r(X)) \to H_1(VR_\epsilon(X))$. The persistence of [c] is defined as the difference between the death filtration and the birth filtration.

Up to a scaling factor in the variable r, the Geometric Čech complex of radius r is homotopy equivalent to the Radius r Vietoris-Rips complex due to the Nerve Lemma (see Corollary 4G.3 in Hatcher) [17]. Consequently, the definitions of the birth and death radius of an equivalence class of non-contractible loops presented in Section 1.1 are equivalent to the definitions of the birth and death filtration of a class $[c] \in H_1(VR_r(X))$ given in Definition A.4. For a more thorough treatment of persistent homology, see [16].

References

- [1] World Health Organization: The top 10 causes of death, https://www.who.int/news-room/fact-sheets/detail/ the-top-10-causes-of-death
- Centers for Disease Control and Prevention: Leading causes of death, https://www.cdc.gov/nchs/fastats/ leading-causes-of-death.htm
- [3] Migdady I, Russman A, Buletko AB. Atrial Fibrillation and Ischemic Stroke: A Clinical Review. Semin Neurol. 2021 Aug;41(4):348-364. doi: 10.1055/s-0041-1726332. Epub 2021 Apr 13. PMID: 33851396.
- [4] Graff Persistent homology as a new method of the assessment of heart rate variability. PLOS ONE. 16, 1-24 (2021,7), https://doi.org/10.1371/journal.pone.0253851
- [5] Chung, Y., Hu, C., Lo, Y. & Wu, H. A Persistent Homology Approach to Heart Rate Variability Analysis With an Application to Sleep-Wake Classification. Frontiers In Physiology. 12 pp. 202 (2021), https://www.frontiersin.org/article/10.3389/fphys.2021.637684
- [6] Pyakillya, B., Kazachenko, N. & Mikhailovsky, N. Deep Learning for ECG Classification. Journal Of Physics: Conference Series. 913 pp. 012004 (2017,10), https://doi.org/10.1088/1742-6596/913/1/012004
- [7] Rahhal, M., Bazi, Y., AlHichri, H., Alajlan, N., Melgani, F. & Yager, R. Deep learning approach for active classification of electrocardiogram signals. Information Sciences. 345 pp. 340-354 (2016).https://www.sciencedirect.com/science/article/pii/S0020025516300184
- [8] Ye C, C. Heartbeat classification using morphological and dynamic features of ECG signals. IEEE Trans Biomed Eng.. (2012)
- [9] Kutlu Y, K. Feature extraction for ECG heartbeats using higher order statistics of WPD coefficients. Comput Methods Programs Biomed. (2012)
- [10] Dindin, M., Umeda, Y. & Chazal, F. Topological Data Analysis for Arrhythmia Detection Through Modular Neural Networks. Advances In Artificial Intelligence. (2020)
- [11] Safarbali, B. & Hashemi Golpayegani, S. Nonlinear dynamic approaches to identify atrial fibrillation pro-gression based on topological methods. Biomedical Signal Processing And Control. 53 pp. 101563 (2019), https://www.sciencedirect.com/science/article/pii/S1746809419301375
- [12] Ignacio, P., Dunstan, C., Escobar, E., Trujillo, L. & Uminsky, D. Classification of Single-Lead Electrocardiograms: TDA Informed Machine Learning. 2019 18th IEEE International Conference On Machine Learning And Applications (ICMLA). pp. 1241-1246 (2019)

2.0

2.2

18 H.D. Dlugas / ECG arrhythmia detection with novel signal processing and persistent homology-derived predictors

[13] Ni, Y., Sun, F., Luo, Y., Xiang, Z. & Sun, H. A Novel Heart Disease Classification Algorithm based on Fourier Transform and Persistent Homology. (2021) 2

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

2.0

21

2.2

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

- [14] Ormrod Morley D, W. Persistent homology in two-dimensional atomic networks. J Chem Phys. (2021)
- [15] Hiraoka, Y., Nakamura, T., Hirata, A., Escolar, E., Matsue, K. & Nishiura, Y. Hierarchical structures of amorphous solids characterized by persistent homology. Proceedings Of The National Academy Of Sciences. 113, 7035-7040 (2016)
 - [16] Tamal Dey, Y. Computational Topology for Data Analysis. (Cambridge University Press, 2021)
- [17] Hatcher, A. Algebraic Topology. (Cambridge University Press, 2002)
- [18] Wang, G., Zhang, C., Liu, Y., Yang, H., Fu, D., Wang, H. & Zhang, P. A global and updatable ECG beat classification system based on recurrent neural networks and active learning. Information Sciences. 501 pp. 523-542 (2019), https://www.sciencedirect.com/science/article/pii/S0020025518305115
- [19] Wang, J. Automated detection of atrial fibrillation and atrial flutter in ECG signals based on convolutional and improved Elman neural network. Knowledge-Based Systems. 193 pp. 105446 (2020), https://www.sciencedirect.com/science/article/pii/S0950705119306653
- 11 [20] Kumar, M., Pachori, R. & Rajendra Acharya, U. Automated diagnosis of atrial fibrillation ECG signals using entropy fea-12 tures extracted from flexible analytic wavelet transform. Biocybernetics And Biomedical Engineering. 38, 564-573 (2018), 13 https://www.sciencedirect.com/science/article/pii/S0208521618300172
- [21] Guo, L., Sim, G. & Matuszewski, B. Inter-patient ECG classification with convolutional and 14 recurrent neural networks. **Biocybernetics** And Biomedical Engineering. 39. 868-879 (2019), 15 https://www.sciencedirect.com/science/article/pii/S0208521618304200 16
 - [22] Chen, S., Hua, W., Li, Z., Li, J. & Gao, X. Heartbeat classification using projected and dynamic features of ECG signal. Biomedical Signal Processing And Control. 31 pp. 165-173 (2017), https://www.sciencedirect.com/science/article/pii/S1746809416300908
- [23] Elhaj, F., Salim, N., Harris, A., Swee, T. & Ahmed, T. Arrhythmia recognition and classification using combined lin-19 ear and nonlinear features of ECG signals. Computer Methods And Programs In Biomedicine. 127 pp. 52-63 (2016), 20 https://www.sciencedirect.com/science/article/pii/S0169260715301097
- 21 [24] Asgharzadeh-Bonab, A., Amirani, M. & Mehri, A. Spectral entropy and deep convolutional neural network for ECG beat classification. Biocybernetics And Biomedical Engineering. 40, 691-700 (2020), 2.2 https://www.sciencedirect.com/science/article/pii/S0208521620300255 23
- [25] Sannino, G. & De Pietro, G. A deep learning approach for ECG-based heartbeat classifica-24 for arrhythmia detection. Future Generation Computer 86 446-455 tion Systems. (2018),pp. 25 https://www.sciencedirect.com/science/article/pii/S0167739X17324548
- [26] Yıldırım, Ö., Pławiak, P., Tan, R. & Acharya, U. Arrhythmia detection using deep convolutional neu-26 ral network with long duration ECG signals. Computers In Biology And Medicine. 102 pp. 411-420 (2018), 27 https://www.sciencedirect.com/science/article/pii/S0010482518302713
- 28 [27] Yildirim, Ö. A novel wavelet sequence based on deep bidirectional LSTM network model 29 96 for ECG signal classification. Computers In Biology And Medicine. pp. 189-202 (2018),https://www.sciencedirect.com/science/article/pii/S0010482518300738 30
- [28] Altındiş, F., Yılmaz, B., Borisenok, S. & İçöz, K. Parameter investigation of topological data 31 analysis for EEG signals. Biomedical Signal Processing And Control. 63 pp. 102196 (2021),32 https://www.sciencedirect.com/science/article/pii/S1746809420303335
- 33 [29] Midani, W., Ouarda, W. & Ayed, M. DeepArr: An investigative tool for arrhythmia detection using a contextual deep 34 neural network from electrocardiograms (ECG) signals. Biomedical Signal Processing And Control. 85 pp. 104954 (2023), https://www.sciencedirect.com/science/article/pii/S1746809423003877 35
- [30] Oh, S., Ng, E., Tan, R. & Acharya, U. Automated diagnosis of arrhythmia using combination of CNN and 36 LSTM techniques with variable length heart beats. Computers In Biology And Medicine. 102 pp. 278-287 (2018), 37 https://www.sciencedirect.com/science/article/pii/S0010482518301446
- 38 [31] Yildirim, O., Baloglu, U., Tan, R., Ciaccio, E. & Acharya, U. A new approach for arrhythmia classification using deep coded features and LSTM networks. Computer Methods And Programs In Biomedicine. 176 pp. 121-133 (2019), 39 https://www.sciencedirect.com/science/article/pii/S0169260718314329
- 40 novel time representation input based on deep [32] Huang, Y., Li, H. & Yu, X. А learn-41 Processing for ECG classification. Biomedical Signal And Control. 104628 (2023), **83** pp. ing 42 https://www.sciencedirect.com/science/article/pii/S1746809423000617
- [33] Dhyani, S., Kumar, A. & Choudhury, S. Arrhythmia disease classification utilizing ResRNN. Biomedical Signal Process-43 ing And Control. 79 pp. 104160 (2023), https://www.sciencedirect.com/science/article/pii/S1746809422006140 44
- [34] Wang T, Johnson T, Zhang J, Huang K. Topological Methods for Visualization and Analysis of High Dimensional Single-45 Cell RNA Sequencing Data. Pac Symp Biocomput. 2019;24:350-361. PMID: 30963074; PMCID: PMC6417818.
- 46

1

3

4

5

6

7

8

9

10

17

2.2

[35] DeWoskin, D., Climent, J., Cruz-White, I., Vazquez, M., Park, C. & Arsuaga, J. Applications of computational homol-

2.2

ogy to the analysis of treatment response in breast cancer patients. Topology And Its Applications. 157, 157-164 (2010), https://www.sciencedirect.com/science/article/pii/S0166864109001898, Proceedings of the International Conference on Topology and its Applications 2007 at Kyoto; Jointly with 4th Japan Mexico Topology Conference [36] Chung, Y., Hu, C., Lawson, A. & Smyth, C. Topological approaches to skin disease image analysis. 2018 IEEE International Conference On Big Data (Big Data). pp. 100-105 (2018) [37] Arsuaga, J., Baas, N., Dewoskin, D., Mizuno, H., Pankov, A. & Park, C. Topological Analysis of Gene Expression Arrays Identifies High Risk Molecular Subtypes in Breast Cancer. Appl. Algebra Eng., Commun. Comput. 23, 3-15 (2012,4), https://doi.org/10.1007/s00200-012-0166-8 [38] Camara PG, Rosenbloom DI, Emmett KJ, Levine AJ, Rabadan R. Topological Data Analysis Generates High-Resolution, Genome-wide Maps of Human Recombination. Cell Syst. 2016 Jul;3(1):83-94. doi: 10.1016/j.cels.2016.05.008. Epub 2016 Jun 23. PMID: 27345159; PMCID: PMC4965322. [39] Lockwood, S. & Krishnamoorthy, B. Topological Features in Cancer Gene Expression Data. (2015,1) [40] Nicolau M, Levine AJ, Carlsson G. Topology based data analysis identifies a subgroup of breast cancers with a unique mutational profile and excellent survival. Proc Natl Acad Sci U S A. 2011 Apr 26;108(17):7265-70. doi: 10.1073/pnas.1102826108. Epub 2011 Apr 11. PMID: 21482760; PMCID: PMC3084136. [41] Qaiser, T., Sirinukunwattana, K., Nakane, K., Tsang, Y., Epstein, D. & Rajpoot, N. Persistent Homology for Fast Tumor Segmentation in Whole Slide Histology Images. Procedia Computer Science. 90 pp. 119-124 (2016), https://www.sciencedirect.com/science/article/pii/S1877050916312133, 20th Conference on Medical Image Understanding and Analysis (MIUA 2016) [42] Rabadán R, Mohamedi Y, Rubin U, Chu T, Alghalith AN, Elliott O, Arnés L, Cal S, Obaya ÁJ, Levine AJ, Cámara PG. Identification of relevant genetic alterations in cancer using topological data analysis. Nat Commun. 2020 Jul 30;11(1):3808. doi: 10.1038/s41467-020-17659-7. PMID: 32732999; PMCID: PMC7393176. [43] Seemann L, Shulman J, Gunaratne GH. A robust topology-based algorithm for gene expression profiling. ISRN Bioinform. 2012 Nov 11;2012:381023. doi: 10.5402/2012/381023. PMID: 25969748; PMCID: PMC4393071. [44] Bauer, U. Ripser: efficient computation of Vietoris-Rips persistence barcodes. Journal Of Applied And Computational *Topology*. (2021) [45] Maria, C., Boissonnat, J., Glisse, M. & Yvinec, M. The Gudhi Library: Simplicial Complexes and Persistent Homology. Mathematical Software - ICMS 2014. (2014) [46] James G, Witten D, Hastie T, Tibshirani R. An Introduction to Statistical Learning with Applications in R. (Springer New York, NY, 2021) [47] Zheng, J., Zhang, J., Danioko, S. et al. A 12-lead electrocardiogram database for arrhythmia research covering more than 10,000 patients. Sci Data 7, 48 (2020). https://doi.org/10.1038/s41597-020-0386-x [48] Obayashi, I. Volume-Optimal Cycle: Tightest Representative Cycle of a Generator in Persistent Homology. SIAM Journal On Applied Algebra And Geometry. 2, 508-534 (2018), https://doi.org/10.1137/17M1159439 [49] Zong, W., Moody, G. & Jiang, D. A robust open-source algorithm to detect onset and duration of QRS complexes. Computers In Cardiology, 2003. pp. 737-740 (2003) [50] Adams, H., Emerson, T., Kirby, M., Neville, R., Peterson, C., Shipman, P., Chepushtanova, S., Hanson, E., Motta, F. & Ziegelmeier, L. Persistence Images: A Stable Vector Representation of Persistent Homology. J. Mach. Learn. Res., 18, 218-252 (2017,1) [51] Sendelbach S, Funk M. Alarm fatigue: a patient safety concern. AACN Adv Crit Care. 2013 Oct-Dec;24(4):378-86; quiz 387-8. doi: 10.1097/NCI.0b013e3182a903f9. PMID: 24153215. [52] Ruskin KJ, Hueske-Kraus D. Alarm fatigue: impacts on patient safety. Curr Opin Anaesthesiol. 2015 Dec;28(6):685-90. doi: 10.1097/ACO.000000000000260. PMID: 26539788. [53] Johnson KR, Hagadorn JI, Sink DW. Alarm Safety and Alarm Fatigue. Clin Perinatol. 2017 Sep;44(3):713-728. doi: 10.1016/j.clp.2017.05.005. Epub 2017 Jul 14. PMID: 28802348. [54] Storm J, Chen HC. The relationships among alarm fatigue, compassion fatigue, burnout and compassion satisfaction in critical care and step-down nurses. J Clin Nurs. 2021 Feb;30(3-4):443-453. doi: 10.1111/jocn.15555. Epub 2020 Nov 28. PMID: 33174282 [55] Lewandowska K, Weisbrot M, Cieloszyk A, Mędrzycka-Dąbrowska W, Krupa S, Ozga D. Impact of Alarm Fatigue on the Work of Nurses in an Intensive Care Environment-A Systematic Review. Int J Environ Res Public Health. 2020 Nov 13;17(22):8409. doi: 10.3390/ijerph17228409. PMID: 33202907; PMCID: PMC7697990. [56] Dee SA, Tucciarone J, Plotkin G, Mallilo C. Determining the Impact of an Alarm Management Program on Alarm Fatigue among ICU and Telemetry RNs: An Evidence Based Research Project. SAGE Open Nurs. 2022 May 13;8:23779608221098713. doi: 10.1177/23779608221098713. PMID: 35592038; PMCID: PMC9112316.