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A novel intelligent system based on adjustable classifier models for diagnosing heart sounds

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A novel intelligent diagnostic system is proposed to diagnose heart sounds (HSs). The innovations of this system are primarily reflected in the automatic segmentation and extraction of the first complex sound (CS_1) and second complex sound (CS_2); the automatic extraction of the secondary envelope-based diagnostic features γ_1, γ_2, and γ_3 from CS_1 and CS_2; and the adjustable classifier models that correspond to the confidence bounds of the Chi-square (χ^2) distribution and are adjusted by the given confidence levels (denoted as β). The three stages of the proposed system are summarized as follows. In stage 1, the short time modified Hilbert transform (STMHT)-based curve is used to segment and extract CS_1 and CS_2. In stage 2, the envelopes CS_{1F_E} and CS_{2F_E} for periods CS_1 and CS_2 are obtained via a novel method, and the frequency features are automatically extracted from CS_{1F_E} and CS_{2F_E} by setting different threshold value (Thv) lines. Finally, the first three principal components determined based on principal component analysis (PCA) are used as the diagnostic features. In stage 3, a Gaussian mixture model (GMM)-based component objective function $f_{et}(\mathrm{x})$ is generated. Then, the χ^2 distribution for component k is determined by calculating the Mahalanobis distance from x to the class mean μ_k for component k, and the confidence region of component k is determined by adjusting the optimal confidence level β_k and used as the criterion to diagnose HSs. The performance evaluation was validated by sounds from online HS databases and clinical heart databases. The accuracy of the proposed method was compared to the accuracies of other state-of-the-art methods, and the highest classification accuracies of 99.43%, 98.93%, 99.13%, 99.85%, 98.62%, 99.67% and 99.91% in the detection of MR, MS, ASD, NM, AS, AR and VSD sounds were achieved by setting $\beta_k (k = 1, 2, \ldots, 7)$ to 0.87, 0.65, 0.67, 0.65, 0.67, 0.79 and 0.87, respectively.

Background. As an efficient method, using heart sound (**HS**) analysis is often used to evaluate heart function; this approach has been widely used to diagnose heart disease and evaluate heart functions, such as congenital heart disease classification[1], ventricular septal defect detection[2], blood pressure estimation[3] and congenital heart disease screening[4], for children and adults. A normal **HS** is primarily composed of two basic sounds: the first sound (S_1) which is generated by the closing of aortic valves and the vibrations associated with tensing of the chordate trendiness and the ventricular walls, the second sound (S_2) is produced by the closure of the aortic and pulmonic valves at the beginning of is volumetric ventricular relaxation. However, **HS**s with unitary murmurs generally occur between S_1 and S_2 with different noise patterns[5]. Therefore, analyses of S_1, S_2, and the period between S_1 and S_2 play important roles in characterizing **HS** features with different types of information. Detailed information for S_1, S_2, and the sounds between S_1 and S_2 can be used to accurately classify **HS**. Additionally, to avoid analyzing the sounds between S_1 and S_2, which are generally segmented from **HS**s with low accuracy, S_1 and part of the period between S_1 and S_2 are integrated to obtain CS_1, and S_2 and the part of the period between S_1 and S_2 are integrated to form CS_2. Then, the features are efficiently extracted from CS_1 and CS_2. Finally, a classification method is established to diagnose heart diseases.

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Need for research.

- CS_1 **and** CS_2 **extraction** The studies regarding **HS** segmentation can be summarized into two branches: one branch includes studies that segment each cardiac cycle into a sequence of four heart stages: $S_1 \longrightarrow Systole\ period \longrightarrow S_2 \longrightarrow Diastole\ period$[6,7]. As a result, the four fundamental stages to be segmented are different due to the nonstationary nature of an abnormal **HS**s signal and the effect of background noise. The other branch includes studies that segment a periodic **HS**s into a sequence of two heart stages, which are expressed as

$$\underbrace{CS_1}_{One\,part\,of\,Diastole \to S_1 \to One\,part\,of\,Systole} \rightarrow \underbrace{CS_2}_{The\,other\,of\,Diastole \to S_2 \to The\,other\,of\,Systole} \text{based on}$$

the **STMHT** algorithm; this approach was reported to be successfully applied in diagnosing heart diseases, such as in ventricular septal defect (**VSD**) diagnosis[8] and several kinds of heart disease diagnosis[9]. Moreover, study[9] noted that the use of frequency features was more efficient in distinguishing normal from abnormal sounds than was the use of time features. Therefore, an efficient frequency feature extraction method should be developed.

- **Feature extraction** As an important component of efficient feature extraction, the frequency width of the envelope over a given threshold value (Thv) has been verified to be useful for detecting heart diseases[8–11]. However, for many types of **HS**s, it is difficult to extract frequency widths with an unsuitable Thv due to the existence of a non smooth envelope. To extract the frequency widths for a smooth envelope without setting different Thv values, the smooth envelope can be treated as a secondary envelope, as proposed in[9], and used to automatically extract the frequency feature matrix based on the **STMHT** technique; this method was successfully applied to detect different types of heart diseases. However, for mitral stenosis and mitral regurgitation noises, the feature matrix was not easily extracted because the second frequency component was missing. Therefore, to improve the classification accuracy for diagnosing different types of heart disease and simplify the complexity of the diagnostic method, the smooth envelopes for CS_1 and CS_2 extraction in the frequency domain must be considered; additionally, more frequency widths corresponding to different Thv values should be used, and dimensionality reduction should be employed to reduce the number of features considered . Such a classification method could be applied in the efficient extraction of features for diagnosing heart diseases.

- **Classifier model** Gaussian mixture models (**GMM**s) have been used in a wide variety of clustering applications[12–18] due to their powerful mathematical characteristics. Confidence regions are used to diagnose the detection data **x** in **GMM**s, and the optimal confidence regions is determined based on Mahalanobis distance following the Chi-square (χ^2) distribution. Thus, classifier models with adjustable sizes corresponding to the confidence bounds of the Chi-square (χ^2) distribution, which can be adjusted by changing the desired confidence level (denoted as β), are proposed. The χ^2 confidence bounds used as the classification criteria are employed to diagnose heart diseases.

Major contributions and organization.

In summary, this study proposes an innovative and intelligent system. The major contributions in this study are (1) the **STMHT**-based CS_1 and CS_2 are automatically located and extracted; (2) a novel method for obtaining the secondary curves of CS_1 and CS_2 are extracted in the frequency domain; (3) frequency features are automatically extracted over the given threshold value; (4) the diagnostic features γ_1, γ_2 and γ_3 are determined based on **PCA**; and (5) the confidence region of the χ^2 distribution, which are adjusted based on the desired β, is determined and used as the classification criterion for diagnosing a given **HS**. The remainder of this paper is organized as follows. Section "Methodology" presents the approach for determining the diagnostic features $[\gamma_1, \gamma_2, \gamma_3]$, and a definition of the confidence region-based diagnostic method for diagnosing heart diseases. In "Performance evaluation" section, the performance of the proposed method is compared with that of other efficient methods for diagnosing heart diseases. In "Conclusion" section, the conclusions are provided. Finally, the future study is pointed out in "Future study".

Methodology

This study was approved by the ethics committee of Nanyang Institute of Technology (Approval Number:2016-06) and the informed consent was waived by the ethics committee of Nanyang Institute of Technology. The present study was also conducted in accordance with the tenets of the 1975 Declaration of Helsinki, as revised in 2008[19].

The flow chart of the proposed intelligent system, shown in Fig. 1, consists of three stages: the automatic location and extraction of CS_1 and CS_2; the automatic determination of frequency features γ_1, γ_2 and γ_3; and the establishment of the Mahalanobis distance criterion-based diagnostic method. In stage 1, the **STMHT**-based curve (denoted as HS_{STMHT}), which is extracted for the HS_E envelope generated by the **HS**, is used to segment and extract CS_1 and CS_2 from the **HS** (Fig. 1A). In stage 2, the envelopes $CS1_{FE}$ and $CS2_{FE}$ for every period $CS1$ and $CS2$ are obtained via a novel method, and the frequency features are automatically extracted from $CS1_{FE}$ and $CS2_{FE}$ by setting different Thv lines. Finally, the first three principal components, γ_1, γ_2 and γ_3, which express 86.7% of the FF information, are determined and used as diagnostic features (Fig. 1B, C). In stage 3, the **GMM**-based mixed classification objective function $f_{et}(\mathbf{x})$ which combines component k with respect to the parameters π_k, μ_k, and Σ_k and the features $\mathbf{x} = [\gamma_1, \gamma_2, \gamma_3]$, is generated. Then, the χ^2 distribution for component k is determined by calculating the Mahalanobis distance from **x** to the class mean μ_k of component k, and the adjustable confidence bound (denoted as MDC_k shown in Fig. 1E) is determined to diagnose heart diseases.
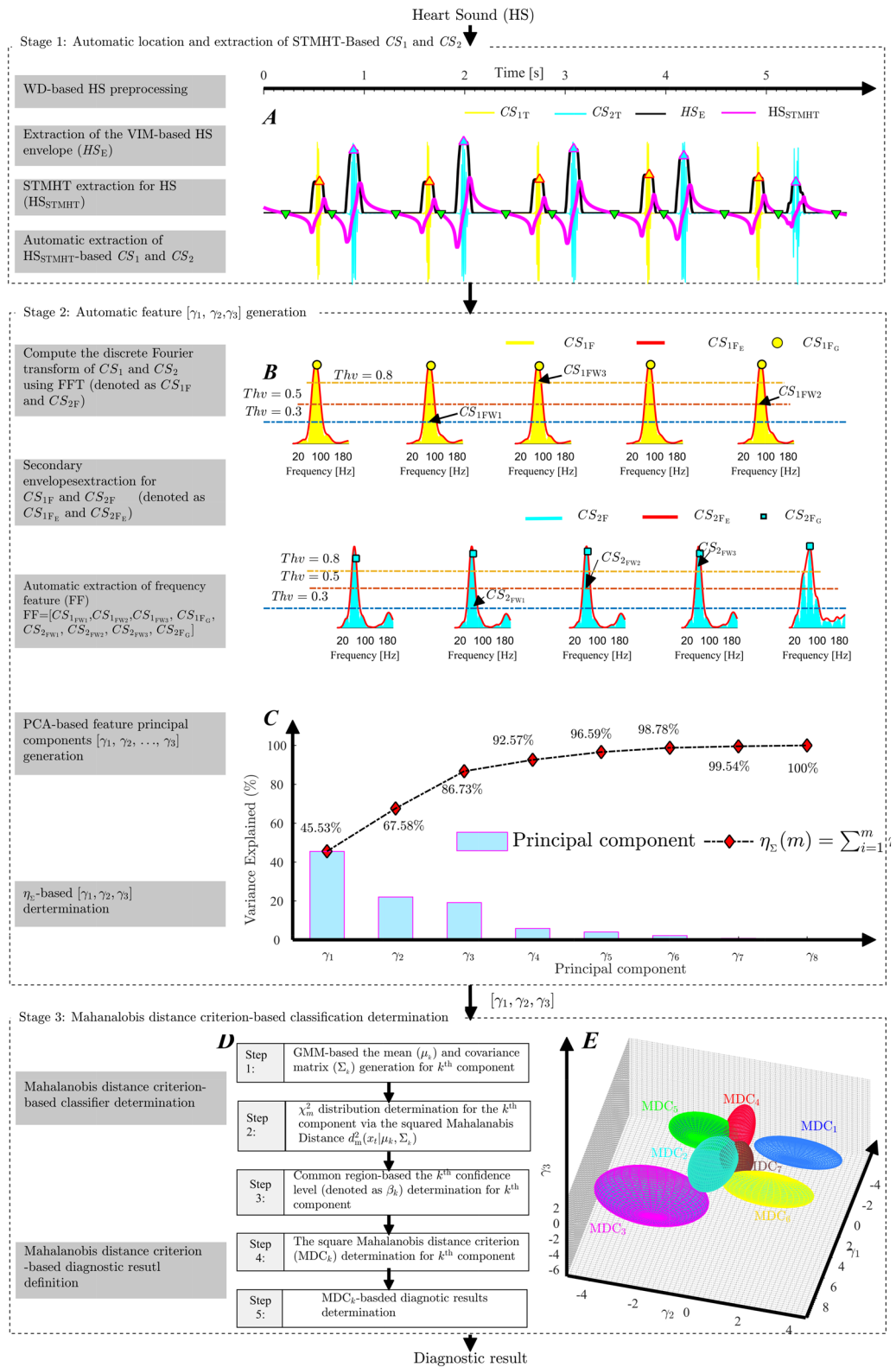
Figure 1. Flow chart of the proposed methodology.
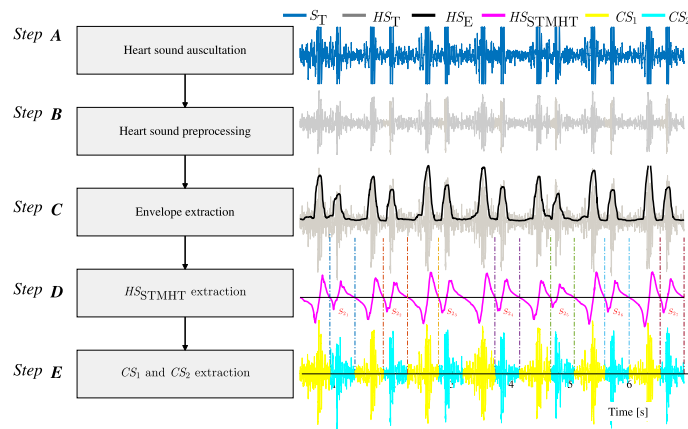
Figure 2. Flow chart of the CS_1 and CS_2 extraction.

Stage 1: Automatic extraction of CS_1 and CS_2.   As shown in Fig. 2, five steps consisting of heart sound auscultation, heart sound preprocessing, heart sound envelope extraction, STMHT extraction, and CS_1 and CS_2 extraction, which is used to construct the procedure of the CS_1 and CS_2 extraction and is detailed in the following steps.

Step A: Heart sound auscultation.   Auscultation is performed for the purposes of examination cardiovascular. As described in previous study[8], the original heart sound, denoted as S_T (colored in blue line as shown in Fig. 2), are collected by 3M-3200 electronic stethoscope with a $F_s = 44.1 kHz$ sample rate which is widely used by many doctors and produced by American 3M company[20], and the tricuspid area is selected as the auscultation area due to the tricuspid area reported to supply more important information[21]. Meanwhile, you can hear the sounds when auscultating heart sounds, ensuring that we avoid as much environmental noise as possible during the auscultation procedure. Even so, the collected heart sounds still need to be preprocessing for canceling the invalid components.

Step B: WD-based heart sound preprocessing.   **HS**s are reported to be primarily dispersed in the frequency range of 20∼700 Hz[2,8,9]. Therefore, according to the sampling frequency (Fs = 44.1 kHz), WD-based **HS**s are filtered to obtain the efficient frequency components (21.5 ∼ 689 Hz). The Daubechies wavelet 10 (*d*B10) has been used to give the maximum signal-to-noise ratio and minimum root-mean-square error for **HS**s[22]. Therefore, *d*B10 is selected for use as the mother wavelet for preprocessing **HS**s. A filtered and normalized sound, colored by gray and denoted as HS_T, is shown in Fig. 2.

Step C: heart sound envelope (HS_E) extraction.   The Viola integral-based envelope, denoted as HS_E, is extracted from the heart sound HS_T, as reported in studies[8,9]; this envelope can effective overcome amplitude variations and complex backgrounds and noise. This concept is described as follows. Consider a filtered sound $HS_T[m]$ for $m = 0, 1, \ldots, M-1$, where M denotes the number of **HS**s. In a W_m neighborhood of time m, called the width W_m time scale, the M-point envelope $HS_E[m]$ is obtained by Eq. (1):

$$HS_E[m] = \frac{1}{2W_m + 1} \sum_{k=m-W_m}^{m+W_m} \left(HS_T[k] - \overline{HS}_T[m]\right)^2, m = W_m, W_m + 1, \ldots M - 1 - W_m, \tag{1}$$
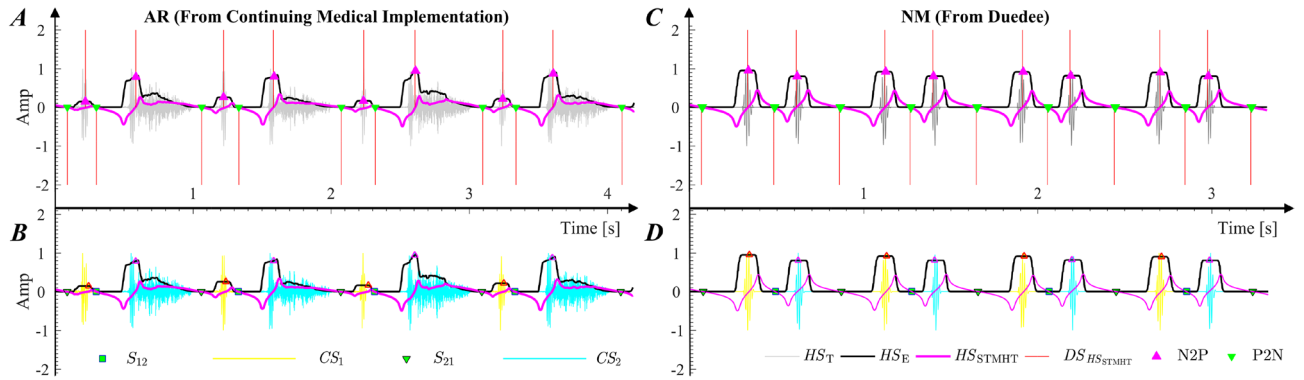
where

$$\overline{HS}_T[m] = \frac{1}{2W_m + 1} \sum_{k=m-W_m}^{m+W_m} HS_T[k], \tag{2}$$

$W_m = 2205$ if the duration of CS_1 or CS_2 greater than 0.13 s. Finally, normalization is performed by setting the maximum amplitude of HS_E to 1 (Fig. 2).

Step D: STMHT extraction for HS.   Given an M-point **HS**, the **STMHT** for the **HS**s , HS_{STMHT}, is computed from Eq. (3)

$$\text{HS}_{STMHT}[n] = \sum_{m=n-\frac{N-1}{2}}^{n+\frac{N-1}{2}} HS_E[m] W_N[m-n] W_E\left[m - (n - \frac{N-1}{2})\right], \tag{3}$$

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Figure 3. The automatic extraction procedures for CS_1 and CS_2. **A-B** show the procedure for an example of a typical **AR** from the database in[26]. **C-D** show the procedure for an example of a typical normal sound database[27].

$$W_E[i] = \begin{cases} \dfrac{cos(\frac{N-1-2i}{2N}\pi) - cos(\frac{N-1-2i}{2}\pi)}{Nsin(\frac{N-1-2i}{2N}\pi)} & \text{for} \quad i = 0, 1, \ldots, N-1 \\ 0 & \text{for} \quad i = \frac{N-1}{2} \end{cases}. \tag{4}$$

where $n = (N-1)/2, \ldots, M-1-(N-1)/2$, and $W_N[l](l = -(N-1)/2, \ldots, (N-1)/2)$ is a moving window of odd length N. According to studies[2,8], the length N is set to 44101.

Step E: Automatic extraction of CS_1 *and* CS_2. The characteristics of HS_{STMHT} considered in studies[2,8], as shown in Fig. 3A, C, are summarized as follows: ① The negative-to-positive (**N2P**) points of HS_{STMHT}, denoted by ▲, correspond to the geometry center peaks of S_1 and S_2; ② The geometry center between S_1 and S_2, denoted by ▼ is determined by the positive-to-negative **P2N** points of HS_{STMHT}. Moreover, the interval from S_2 to S_1 is generally greater than that from S_1 to S_2 in one period of an **HS**[23–25]. Therefore, the **N2P** and **P2N**-based CS_1 and CS_2 features can be automatically segmented from one period of an **HS** and extracted by two procedures, as described as follows.

(1) N2P **and** P2N **location**

The algorithm for detecting N2P and P2N is detailed as follows.

① First, the signum function of HS_{STMHT}, denoted as $S_{HS_{STMHT}}$, is calculated by

$$S_{HS_{STMHT}} = \begin{cases} -1 & \text{if} \quad HS_{STMHT} < 0, \\ 0 & \text{if} \quad HS_{STMHT} = 0, \\ +1 & \text{if} \quad HS_{STMHT} > 0. \end{cases} \tag{5}$$

② Then, the variation in $S_{HS_{STMHT}}$ ($DS_{HS_{STMHT}}$) is determined from Eq. (6)

$$DS_{HS_{STMHT}}[i] = S_{HS_{STMHT}}[i+1] - S_{HS_{STMHT}}[i], i = 1, 2, \ldots, n. \tag{6}$$

③ Finally, **N2P** and **P2N** are determined by

$$\begin{cases} \text{N2P} = i/F_S & \text{if} \quad DS_{HS_{STMHT}}[i] = +2 \\ \text{P2N} = i/F_S & \text{if} \quad DS_{HS_{STMHT}}[i] = -2 \end{cases} \tag{7}$$
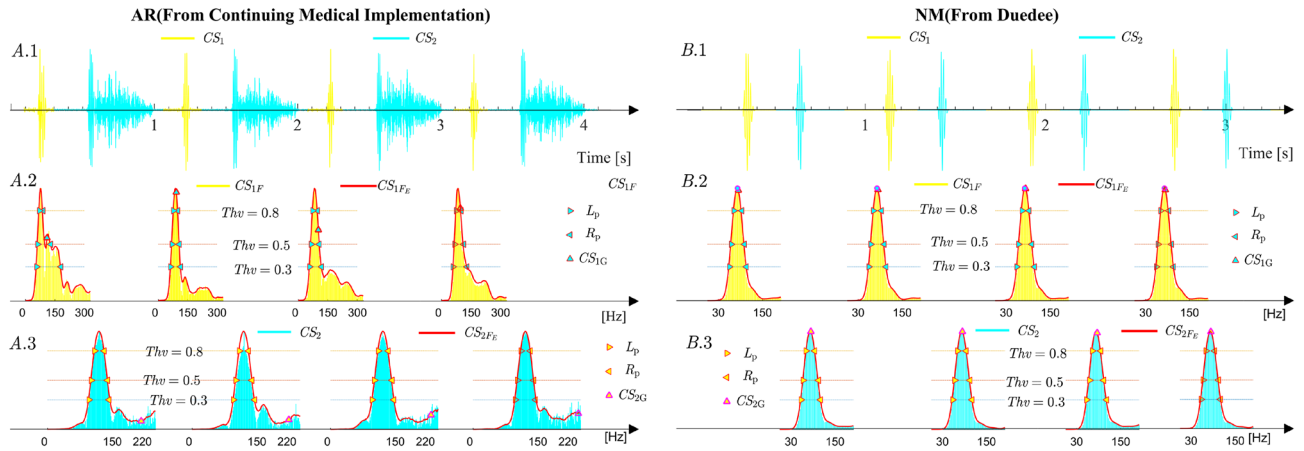
(2) **Automatic extraction of** CS_1 **and** CS_2

① Calculate the difference between two adjacent **N2P**s, denoted as D_{N2P}, with Eq. (8)

$$D_{N2P}[i] = \text{N2P}[i+1] - \text{N2P}[i], i = 1, 2, \ldots, n. \tag{8}$$

② Determine the points CS_{12} and CS_{21} that are used for segmentation from CS_1 to CS_2 and from CS_2 to CS_1, respectively, by using Eq. (9).

$$\begin{cases} CS_{21}[i] = \text{P2N}[i], CS_{12}[i] = \text{P2N}[i+1], & \text{if} \quad D_{N2P}[i] < D_{N2P}[i+1] \\ CS_{21}[i] = \text{P2N}[i+1], CS_{12}[i] = \text{P2N}[i+2], & \text{Otherwise} \end{cases}. \tag{9}$$

③ Extract CS_1 (denoted as CS_{1i}) and CS_2 (denoted as CS_{2i}) for the ith period of an **HS** as follows

Figure 4. Example of feature definition and automatic extraction.

$$\begin{cases} CS_{1i} = HS_{\mathrm{T}}[CS_{21_i} : CS_{12_i}] \\ CS_{2i} = HS_{\mathrm{T}}[CS_{12_i} : CS_{21_{i+1}}] \end{cases} \tag{10}$$

The automatic extraction procedures for CS_1 and CS_2 are illustrated in Fig. 3. Figure 3(A, B) show a typical **AR** sound, and the typical **NM** sound is shown in Fig. 3(C, D).

Stage 2: Automatic feature generation.

Feature definition. To extract the efficient frequency widths, as shown in Fig. 4, the smooth envelopes for CS_1 and CS_2 in the frequency domain are firstly generated, and then the frequency widths corresponding to different Thv values are extracted.

(**1**) **Secondary envelopes CS_{1F_E} and CS_{2F_E} generation:** Given an M-point **HS**, the secondary envelope in the frequency-domain, denoted as HS_{F}, can be calculated from Eq. (11):

$$HS_{F_E}[k] = \frac{\sum_{l_1}(L_1 + L_2 + 1 - |l_1|)HS_{\mathrm{F}}[k + l_1] - \sum_{l_2} HS_{\mathrm{F}}[k + l_2]}{(2L_1 + 1)(2L_2 + 1)}, \tag{11}$$

where l_1, l_2 and $HS_{\mathrm{F}}[k]$ are defined by Eq. (12):

$$\begin{cases} l_1 = -(L_1 + L_2), -(L_1 + L_2) + 1, \ldots, (L_1 + L_2) \\ l_2 = -(L_1 - L_2 - 1), -(L_1 - L_2 - 1) + 1, \ldots, (L_1 - L_2 - 1) \\ HS_{\mathrm{F}}[k] = \left| \sum_{m=0}^{M-1} HS_T[m + 1] e^{(-j\frac{2\pi kl}{\mathrm{M}})} \right|, \quad k = 0, 1, 2, \ldots, M - 1 \end{cases}, \tag{12}$$

$|\cdot|$ is the absolute value sign, $2L_1 + 1$ is the first window width, and $2L_2 + 1$ is the second window width. According to studies[9,28], L_1 and L_2 are set to 9 and 17, respectively. Moreover, HS_{F_E} is also normalized by setting the maximum amplitude of HS_{F_E} to 1. The secondary envelopes for CS_1 and CS_2, denoted as CS_{1F_E} and CS_{2F_E} respectively, are illustrated by using the examples described in Fig. 3 which are first automatically generated based on Eq. (11), are shown in Fig. 4, where the plots in Fig. 4A.2 describe the results of CS_{1F_E} corresponding to CS_1 in Fig. 4A.1, the plots in Fig. 4B.2 describe the results of CS_{1F_E} which corresponds to CS_1 in Fig. 4B.1, the plots in Fig. 4A.3 describe the results of CS_{2F_E} corresponding to CS_2 in Fig. 4A.1, and the plots in Fig. 4B.3 describe the results of CS_{1F_E} which corresponds to CS_2 in Fig. 4B.1.

(**2**) **Definition and automatic extraction of frequency features:** The frequency features are illustrated in Fig. 4(B, C), and their gravities are calculated by

$$\begin{cases} CS_{1\mathrm{G}} = \frac{\sum_{k=0}^{M-1} k \times CS_{1F_E}[k]}{\sum_{k=0}^{M-1} CS_{1F_E}[k]} \\ CS_{2\mathrm{G}} = \frac{\sum_{k=0}^{M-1} k \times CS_{2F_E}[k]}{\sum_{k=0}^{M-1} CS_{2F_E}[k]} \end{cases}, \tag{13}$$

The frequency widths over a given threshold value are defined and calculated by

$$\begin{cases} CS_{1\mathrm{FWi}} = R_{p_i} - L_{p_i} \\ CS_{2\mathrm{FWi}} = R_{p_i} - L_{p_i} \end{cases}, i = 1, 2, 3. \tag{14}$$

where L_{p_i} and R_{p_i} are the ith left and right intersections, respectively, of CS_{1F_E} and CS_{2F_E} over the *Thv* lines (*Thv* =0.3, 0.5 and 0.8). Moreover, the frequency features are expressed based on Eq. (15) and described in Table 1.

$$\mathrm{FF} = [CS_{1\mathrm{FW1}}, CS_{1\mathrm{FW2}}, CS_{1\mathrm{FW3}}, CS_{1\mathrm{G}}, CS_{2\mathrm{FW1}}, CS_{2\mathrm{FW2}}, CS_{2\mathrm{FW3}}, CS_{2\mathrm{G}}] \tag{15}$$

Feature index	Feature's symbol	Feature description	Unit
1	CS_{1FW1}	The frequency width of CS_1 corresponding to $Thv = 0.3$	Hz
2	CS_{1FW2}	The frequency width of CS_1 corresponding to $Thv = 0.5$	Hz
3	CS_{1FW3}	The frequency width of CS_1 corresponding to $Thv = 0.8$	Hz
4	CS_{1G}	The Center of gravity of CS_1 in frequency-domain	Hz
5	CS_{2FW1}	The frequency width of CS_2 corresponding to $Thv = 0.3$	Hz
6	CS_{2FW2}	The frequency width of CS_2 corresponding to $Thv = 0.5$	Hz
7	CS_{2FW3}	The frequency width of CS_2 corresponding to $Thv = 0.8$	Hz
8	CS_{2G}	The Center of gravity of CS_2 in frequency-domain	Hz

Table 1. Description of the frequency domain feature matrix FF.
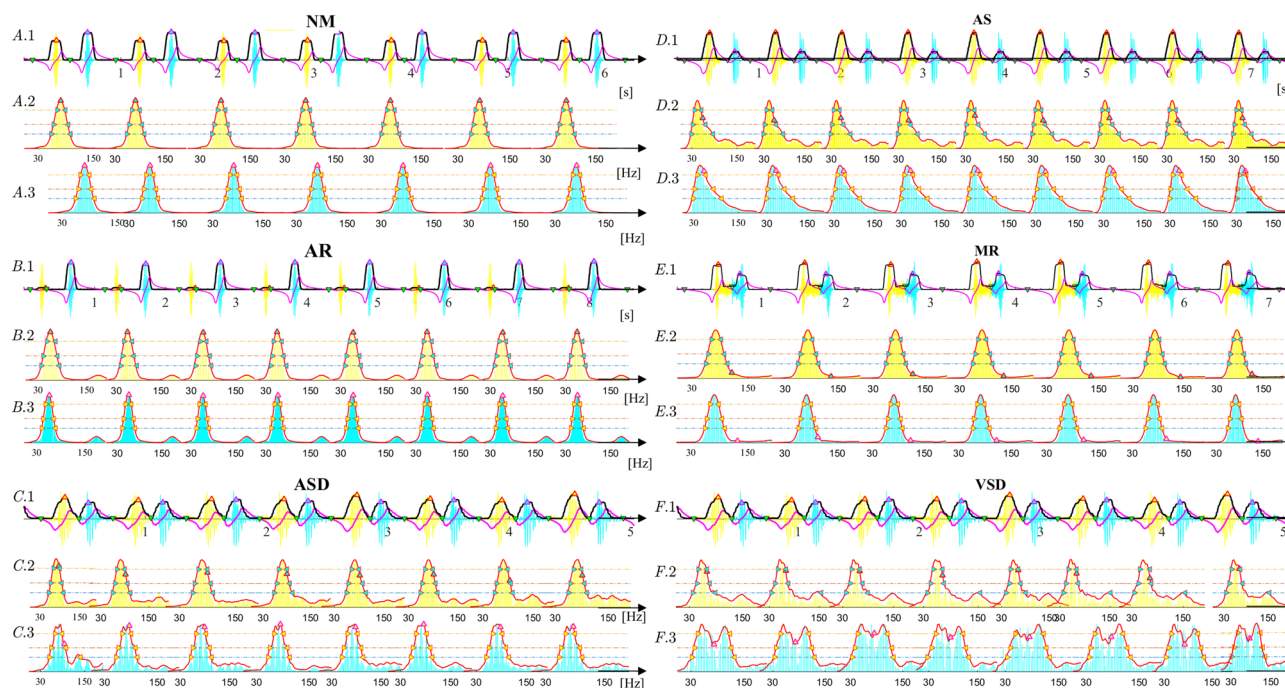
Figure 5. Examples of a typical normal sound and six types of typical heart disease sounds.

Experimental results for several typical types of heart disease. The features FF of six typical and normal sounds are illustrated in Fig. 5. From Fig. 5, CS_1 and CS_2 are first automatically located and extracted, then, the envelopes for every CS_1 and CS_2 are extracted by Eq. (11). Finally, the features defined by Eq. (15) for CS_1 and CS_2 in the frequency domain are automatically extracted with Eqs. (13-14). The experimental sounds are 665-period **AR** sounds (3M database[29], medical sound library[30], heart auscultation sounds[31], auscultation sound[32], continuing medical implementation[26], sounds Database of the University of Dundee[27], and patients only with **AR** disease from the Nanyang First People's Hospital), 381-period **AS** sounds (continuing medical implementation[26], sounds database of the University of Dundee[27], 3M database[29], medical sound library[30], auscultation sound[32], and patients only with **AS** disease from the Nanyang first People's Hospital, and heart auscultation sounds[31]), 315-period **ASD** sounds (Medical sound library[30], heart auscultation sounds[31], 3M database[29], patients only with **ASD** disease from the Nanyang First People's Hospital, and medical sound library[30]), 769-period **MR** sounds (3M database[29], sounds database of the University of Dundee[27], heart auscultation sounds[31], medical sound library[30], and auscultation sound[32]), 439-period **MS** sounds(3M database[29], auscultation sound[32], medical sound library[30], and continuing medical implementation[26]), and 1056-period **NM** sounds(3M database[29], Michigan database[33], medical sound library[30], ThinkLabs database[34], and healthy undergraduates from Nanyang Institute of Technology, China)(whom I thank for the data used in this study)). Moreover, the boxplots for the features are plotted in Fig. 6, where Fig. 6A shows the features extracted from CS_1 and Fig. 6B shows the features from CS_2 for each type of heart disease. The scatter plots of features in Fig. 6 illustrate the discrimination ability of the model in distinguishing among different heart diseases and highlighting the following findings: ① The **MS** and **VSD** sounds are easy to distinguish from the other sounds by using CS_{1FW1} (Fig. 6A), and by using the CS_{2FW1} (Fig. 6B), the **VSD** sound is easy to distinguish from the other sounds; ② The **MS** sound is easy to distinguish from the other sounds based on CS_{1FW2} (Fig. 6A), and by using the CS_{2FW2} (Fig. 6B), the **AR** and **VSD** sounds
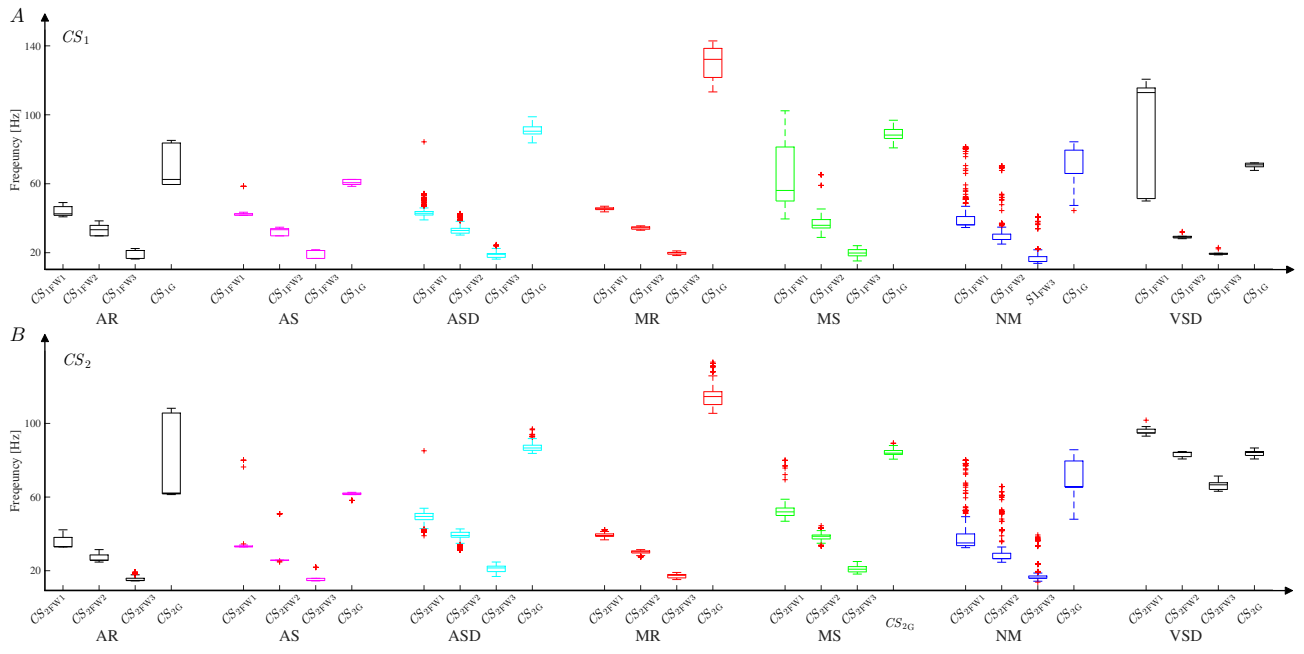
Figure 6. Box plot representation of FF for each type of heart disease. *A* shows the box plots for features from CS_1. In addition, *B* represents the features from CS_2.

are distinguished from other sounds; ③ The **NM** sound is easy to distinguish from other sounds using CS_{1FW3} (Fig. 6A). ④ The **AR** and **VSD** sounds are easy to distinguish from the other sounds using CS_{2FW3}, as shown in Fig. 6B; ⑤ Fig. 6A indicates that CS_{1G} can be used to easily distinguish **MR** from other sounds and the **AS** and **ASD** sounds from other sounds; ⑥ Fig. 6B shows that the distribution of CS_{2G} from **AS** sounds is different from that for other sounds, except **NM** sounds. The analysis results discussed above indicate that different combinations of several features defined by Eq. (15) can be used to distinguish among various types of heart disease. Therefore, to simplify features and develop a diagnostic method that is simple and effective, dimension reduction is used to determine new features; this process is described in detail as follows.

Algorithm 1: principal components analysis on the data set **FF**

1. Calculate the standardized features Z

$$Z = (\mathrm{FF} - \mu_{\mathrm{FF}})/\sigma_{\mathrm{FF}},$$

   where μ_{FF} and σ_{FF} are the mean and standard deviation along each column of FF, respectively.

2. Calculate the covariance matrix $\Sigma = Z'Z$

3. Compute the eigenvalues λ_i and eigenvectors ξ_i

$$\Sigma \xi_i = \lambda_i \xi_i (i = 1, 2, \ldots, p),$$

   where p is the number of features.

4. Estimating high-valued Eigenvectors

   (1). Arrange all the Eigenvalues (λ_i) in descending order

   (2). Choose a threshold value, θ

   (3). Number of high-valued λ_i can be chosen so as to satisfy the relationship $\left(\sum_{i=1}^{m} \lambda_i\right)\left(\sum_{i}^{p} \lambda_i\right) \geq \theta$, where m is the number of high valuated λ_i chosen.

   (4). Select eigenvectors corresponding to selected high valued $\lambda_i (i = 1, 2, \ldots, m)$.

5. Extract low dimensional feature vectors (principal components) from raw feature matrix.

$$\gamma_i = (\mathrm{FF} - \mu_{\mathrm{FF}})/\sigma_{\mathrm{FF}} \xi_i$$

Diagnostic feature determination. To simplify the computation when using features to diagnose heart diseases, **PCA**, a linear dimensionality reduction technique for finding principal components and replacing high-dimension data in many studies, such as studies on heart arrhythmias classification[35], heart disease classification[2,36], emotion recognition[37], respiratory rate extraction[38] and electrocardiogram heart disease diagnosis[39], is employed to generate a few efficient principal components to characterize **HS** features and diagnose heart diseases. The algorithm corresponding to the generation of new features via **PCA** for a given data set **FF** is described as **Algorithm 1**. The eigenvector ξ_i in **Algorithm 1**, which corresponds to the eigenvalue λ_i and is calculated for the matrix Z in step 2, as shown in Table 3, is the actual weighted coefficient for the ith principal component γ_i. Table 3 shows that the largest absolute coefficients in the first principal component γ_1 are CS_{1FW1}, CS_{2FW2} and CS_{1FW2}; the second principal component γ_2 is mainly weighted based on CS_{1G}, CS_{2FW2}, CS_{1FW1} and CS_{2FW3}; and the third component γ_3 is mainly weighted based on CS_{1FW2}, CS_{1FW3} and CS_{2FW3} (Table 3). To determine the smallest number of principal components m should be considered, the Pareto chart is used; this chart provides a tool for visualizing the Pareto principle, which states that observing a small set of variables that influence a common outcome is more common than detecting many variables that influence the same outcome. This approach has been used to determine the percent variability explained by each principal component (Fig. 7A). Therefore, according to the smallest m value such that $\eta_\Sigma(m) > 80\%$[40], combined with the scatter plot for the first m principal components, the smallest m is determined. The Pareto chart of the **PCA** results in Fig. 7A shows the explained variance and accumulated variance for each principal component γ_i, where $i = 1, 2, \ldots, 8$. According to Fig. 7A, 67.58% of the total variance is captured by the first two components, γ_1 and γ_2, and 86.73% of the total variance is captured by the first three components γ_1, γ_2 and γ_3. Therefore, the following conclusions can be obtained.

- γ_1 and γ_2 lead to a dimensionality reduction of 75% (from 8 to 2 variables) and only 32.42% information loss. The scatter diagram of γ_1 and γ_2 given in Fig. 7B indicates that although the distribution region corresponding to each type of heart disease is obviously different and the overlaps between **MR** and other diseases, **AR** and other diseases, and **VSD** and other diseases are small, the overlaps among **MS**, **ASD**, **NM**, and **AS** are relatively large; therefore, it is difficult to accurately distinguish among these four types of heart diseases.
- However, the scatter diagram of γ_1, γ_2 and γ_3, plotted in Fig. 7C, shows that there are different distribution regions for these types of heart diseases. In addition, $\eta_\Sigma(3) = 86.73\%$, as shown in Fig. 7A, based on feature number determination[40]. Thus, γ_1, γ_2 and γ_3 lead to a dimensionality reduction of 62.5% (from 8 to 3 variables) with only 13.27% information loss. The scatter diagram of γ_1, γ_2 and γ_3 in Fig. 7C is used to verify the different distribution regions corresponding to these types of heart diseases.

Therefore, m is set to 3, and the new 3-dimensional feature matrices consisting of γ_1, γ_2 and γ_3 (see Fig. 7C) are used to diagnose heart diseases.

Stage 3: classification based on the squared Mahalanobis distance criterion. *Classifier determination.* The squared Mahalanobis distance classification criterion-based diagnostic methodology, consisting of the five sequential steps as shown in the flow chart (Fig. 8A), is proposed to diagnose **HS**s and is described in the following 5 steps.

Step 1: GMM-based μ_k and Σ_k generation. In the design step of **GMM**, the estimated target function, $f_{et}(\mathbf{x})$, is a mixture of d-dimensional normal Gaussian distributions $p(\mathbf{x}|\mu_k, \Sigma_k)$ that reflect the training pattern of each component; it is assumed that components can be modeled by mixtures of normal Gaussian distributions by

$$f_{et}(\mathbf{x}) = \sum_{k=1}^{K} \pi_k p(\mathbf{x}|\mu_k, \Sigma_k), \tag{19}$$

where

$$p(\mathbf{x}) = \frac{1}{\sqrt{(2\pi)^d \mid \Sigma_k \mid}} \exp^{\left(-\frac{1}{2}(\mathbf{x}-\mu_k)^{\mathrm{T}}\Sigma_k^{-1}(\mathbf{x}-\mu_k)\right)} \tag{20}$$

expresses the posterior probabilities corresponding to each component; K is the number of components; π_k corresponds to the mixed weights, such that $\sum_{k=1}^{K} \pi_k = 1$; and μ_k and Σ_k are the mean value and covariance matrix of the kth component, respectively. Because the goal is to maximize the function $f_{et}(\mathbf{x})$, the parameters (π_k, μ_k, and Σ_k) are determined based on the **EM** algorithm[41] for a set of sample records. Based on the types of heart disease described in Sect. 2.2 and the scatter diagram plotted in Fig. 7C, the number of Gaussian mixture components is set to $K = 7$, and the *fitgmdist* function in MATLAB 2018b is used to return a **GMM** with $K = 7$ components fitted to the features $[\gamma_1, \gamma_2, \gamma_3]$ established in Sect. 2.2 using the **EM** algorithm by assigning a posterior probability to each component density with respect to each observation. Furthermore, the regularization value is set as 0.01 to avoid ill-conditioned covariance estimates, and the number of optimization iterations is set to 1000 based on experience. The Gaussian mixture parameter estimates for π_k, μ_k and Σ_k are obtained and shown in Table 4. To characterize the 3-dimensional interspace corresponding to each 3-dimensional Gaussian component for diagnosing heart diseases, the 3-dimensional interspaces can be used as 3-dimensional classifiers to diagnose heart diseases with high classification accuracy; the overlapping interspace between two random

Statistics	Frequency features ($\mu_{FF} + \sigma_{FF}$)							
	Features from CS_1				Features from CS_2			
	CS_{1FW1}	CS_{1FW2}	CS_{1FW3}	CS_{1G}	CS_{2FW1}	CS_{2FW2}	CS_{2FW3}	CS_{2G}
$\mu_{FF} \pm \sigma_{FF}$	45.3± 11.8	33.1± 5.8	18.8± 3.6	80.6± 21.7	44.1± 23.1	32.2± 9.1	18.4 ± 6.5	79.8±18.9

Table 2. Mean (μ_{FF}) and standard deviation (σ_{FF}) of the features.
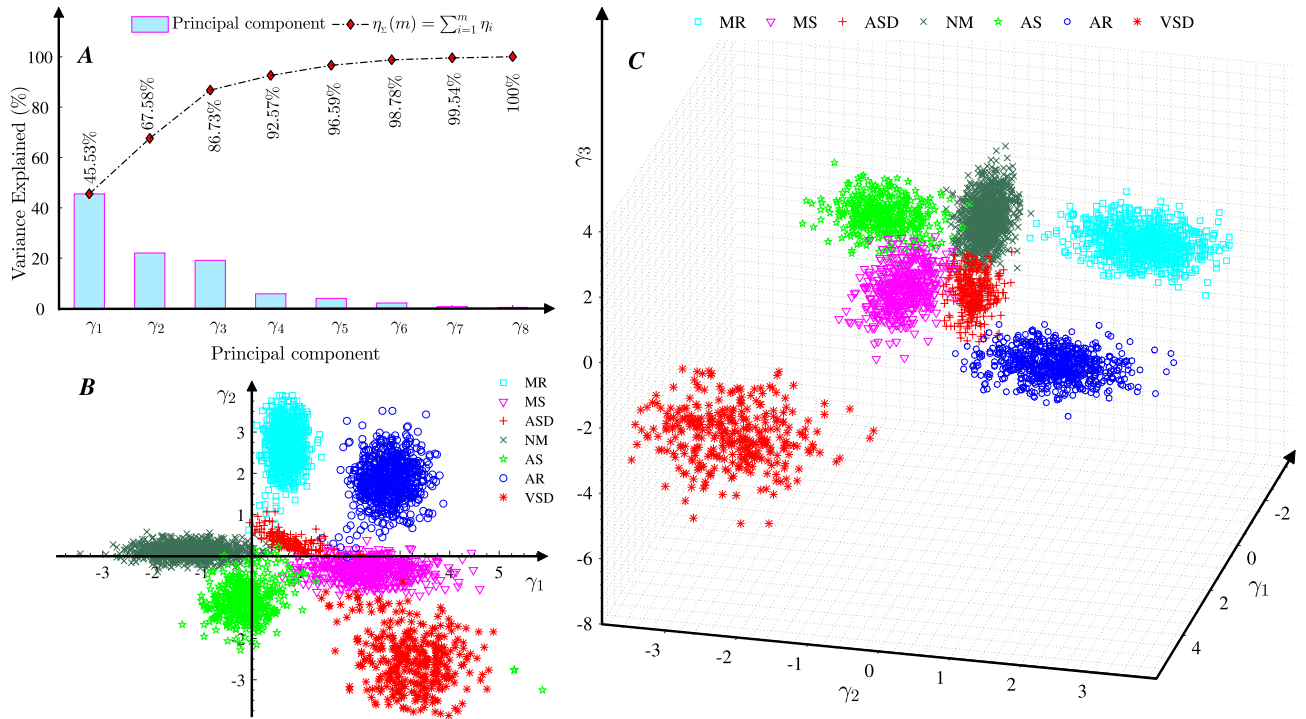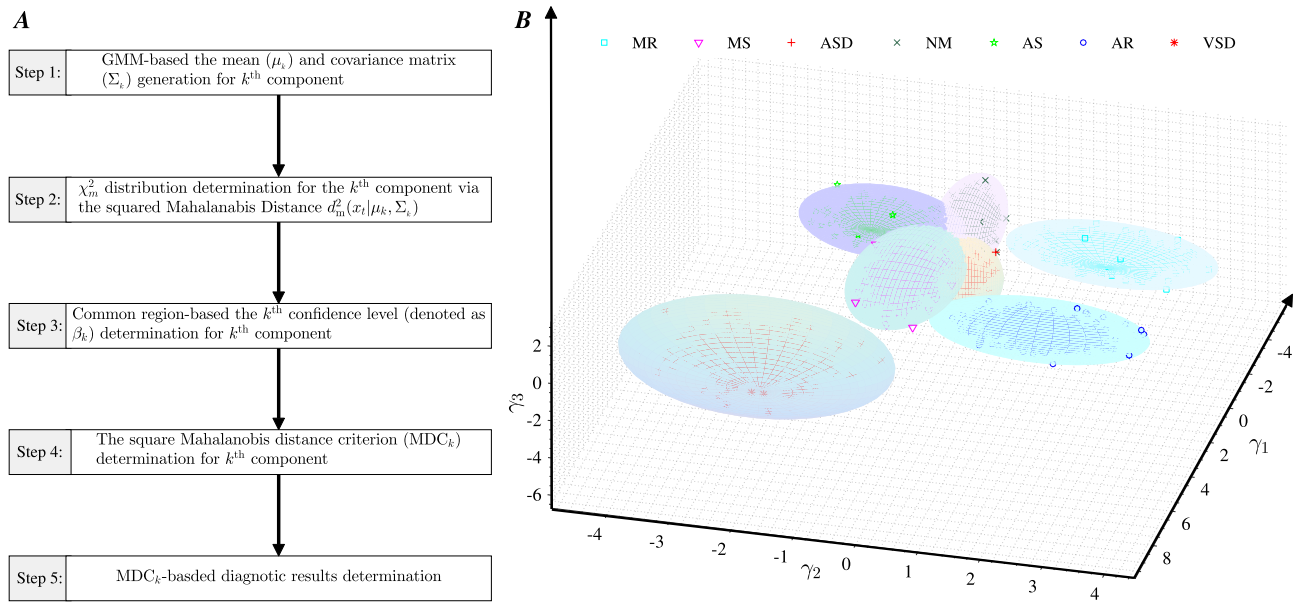

Figure 7. PCA results. **A** shows the Pareto chart of the variance by contribution of each principal component, **B** plots the scatter diagram of the first two components γ_1 and γ_2, and **C** shows the first three components γ_1, γ_2 and γ_3.

Features	Eigenvector (eigenvalue) in descending order of eigenvalues							
	$\xi_1(\lambda_1 = 3.6423)$	$\xi_2(\lambda_2 = 1.7643)$	$\xi_3(\lambda_3 = 1.5316)$	$\xi_4(\lambda_4 = 0.4671)$	$\xi_5(\lambda_5 = 0.3226)$	$\xi_6(\lambda_6 = 0.1748)$	$\xi_7(\lambda_7 = 0.0606)$	$\xi_8(\lambda_8 = 0.0368)$
$S1_{FW1}$	0.4309	-0.2169	0.0818	-0.2179	0.8062	-0.2394	-0.0499	0.0616
$S1_{FW2}$	0.3716	-0.0757	0.5303	0.0431	-0.0306	0.6778	0.2873	-0.1735
$S1_{FW3}$	0.3411	-0.0983	0.5431	0.0444	-0.4364	-0.6126	-0.1001	-0.0375
$S1_G$	0.2385	0.6501	-0.0157	-0.2122	0.0212	0.0986	-0.5500	-0.4031
$S2_{FW1}$	0.3313	0.0487	-0.2471	0.8958	0.0977	-0.0299	-0.0699	-0.0944
$S2_{FW2}$	0.4475	-0.2390	-0.2924	-0.1628	-0.3044	0.2633	-0.3928	0.5607
$S2_{FW3}$	0.3517	-0.2191	-0.5142	-0.2650	-0.2357	-0.1047	0.3750	-0.5353
$S2_G$	0.2632	0.1026	-0.0768	-0.0662	-0.0207	-0.1308	0.5506	0.4386

Table 3. Eigenvector ξ_i and eigenvalue $\lambda_i(i = 1, \ldots, 8)$ for Σ in descending order of eigenvalues.

components is made as small as possible, and the independent 3-dimensional interspace corresponding to each component is considered.

Step 2: χ_3^2 determination for the kth component in 3-dimensional interspace. Since the squared Mahalanobis distances for each Gaussian component follow the Chi-square distribution (χ_3^2) in 3-dimensional interspace, to determine the decision region for classifying the test data **x** via the components estimated in the above step, the squared Mahalanobis distance in 3-dimensional interspace for the kth component with mean μ_k and full covariance matrix Σ_k, $d_3^2(\mathbf{x}|\mu_k, \Sigma_k)$, is computed as follows:

A

Step 1:	GMM-based the mean (μ_k) and covariance matrix (Σ_c) generation for k^{th} component

Step 2:	χ_m^2 distribution determination for the kth component via the squared Mahalanabis Distance $d_m^2(x_t\|\mu_k,\Sigma_c)$

Step 3:	Common region-based the kth confidence level (denoted as β_k) determination for k^{th} component

Step 4:	The square Mahalanobis distance criterion (MDC_k) determination for k^{th} component

Step 5:	MDC_k-basded diagnostic results determination

B

Figure 8. Flow chart of the diagnostic determination and 3-dimensional surface classifier results.

| Components	Component number	Gaussian mixture parameter estimates							
		π_k		μ_k			Σ_k		
MR Classifier	$k=1$	0.1947	0.7056	2.7126	1.4950	0.0425	-0.0007	0.0013	
						-0.0007	0.2343	-0.0126	
						0.0013	-0.0126	0.2122	
MS Classifier	$k=2$	0.0827	3.2981	-2.6064	-3.7382	0.3310	-0.0094	-0.0122	
						-0.0094	0.3906	-0.0210	
						-0.0122	-0.0210	0.5386	
ASD Classifier	$k=3$	0.1130	2.3453	-0.3484	0.5773	0.5373	-0.0172	-0.0039	
						-0.0172	0.0608	-0.0053	
						-0.0039	-0.0053	0.1883	
NM Classifier	$k=4$	0.1683	2.7874	1.8620	-0.9829	0.1403	0.0107	0.0063	
						0.0107	0.2549	0.0016	
						0.0063	0.0016	0.1301	
AS Classifier	$k=5$	0.0783	0.7511	0.3199	-0.5341	0.0972	0.0077	-0.0161	
						0.0077	0.0344	-0.0050	
						-0.0161	-0.0050	0.2634	
AR Classifier	$k=6$	0.2676	-1.2294	0.1198	0.3222	0.3301	-0.0011	0.0025	
						-0.0011	0.0230	0.0005	
						0.0025	0.0005	0.3255	
VSD Classifier	$k=7$	0.0954	-0.1631	-1.1167	0.9454	0.1338	0.0048	-0.0155	
						0.0048	0.1449	-0.0095	
						-0.0155	-0.0095	0.1573	

Table 4. The Gaussian mixture parameter estimates are achieved for the new features $[\gamma_1,\gamma_2,\gamma_3]$ by setting the number of Gaussian mixture components as 7.

$$d_3^2(\mathbf{x}|\mu_k,\Sigma_k)=(\mathbf{x}-\mu_k)^{\text{T}}\Sigma_k^{-1}(\mathbf{x}-\mu_k). \tag{21}$$

Therefore, χ_3^2, which is constructed based on component k and denoted as $\chi_3^2(\mu_k,\Sigma_k)$, is determined by

$$d_3^2(\mathbf{x}|\mu_k,\Sigma_k)\sim\chi_3^2(\mu_k,\Sigma_k). \tag{22}$$

Therefore, the squared Mahalanobis distance $d_3^2(\mathbf{x}|\mu_k,\Sigma_k)$ specified based on the desired confidence level, denoted as β_k, can be used as the kth classifier criterion for determining whether feature $\mathbf{x}$ belongs to the kth class.
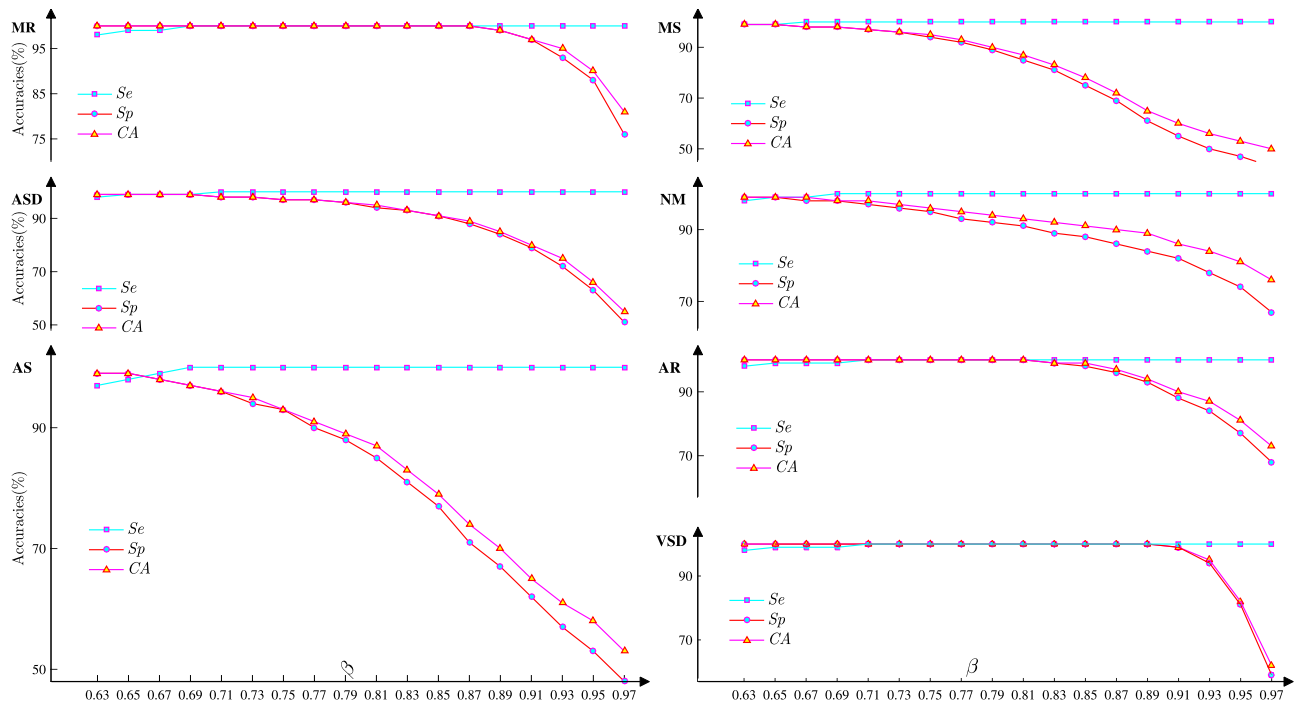
Figure 9. The achieved accuracies corresponding to classifying the heart sounds described in Sect. 2.2 by setting β form 0.63 to 0.97 with a step of 0.02.

Step 3: The kth confidence level (β_k) determination. Actually, the kth confidence region, as specified by the kth desired confidence level β_k, is surrounded by the kth ellipsoid, and this relation is expressed as

$$d_3^2(\mathbf{x}|\mu_k, \Sigma_k) \leq \text{MDC}_k = \chi^2_{3,\beta_k}, \tag{23}$$

where χ^2_{3,β_k} is the inverse of χ^2_3 for a given confidence level β_k, and MDC_k represents the classification criterion for component k and satisfies the following equation

$$\chi^2\left(d_3^2(\mathbf{x}|\mu_k, \Sigma_k) = \text{MDC}_k \big| \mu_k, \Sigma_k\right) = \beta_k \tag{24}$$

For the χ^2_3 distribution, although the confidence regions corresponding to the confidence levels of 68.3%, 95%, and 97.5% are widely used classification criteria in many studies[2,42–45], the optional β_k is identified by setting $\beta_k \in [63 : 2 : 97]\%$ combined with the following rules: 1) each ellipsoid should be as large as possible; 2) each common region should be as small as possible; and 3) the classification accuracy defined in Eq. (26) should be as high as possible. The classification accuracies for classifying sound data summarized in Sect. 2.2 are plotted in Figs. 9, and 9 shows the following results: ① For **VSD** sounds, high accuracy can be achieved by setting the desired confidence level β to each value within the interval of $(0.71 < \beta < 0.89)$, as shown in Fig. 9(**VSD**); ② For **AR** and **MR** sounds, by setting the desired confidence level β based on $\beta \in [0.69, 0.81]$, high classification accuracy could be achieved (Fig. 9(**MR** and **AR**)); ③ For **MS**, **AS** and **NM** sounds, to achieve the accurate classification of **HS**s, the interval of the desired confidence level β should be set as [0.63, 0.65] (Fig. 9); ④ For **ASD** sounds, Fig. 9(**ASD**) shows that the highest classification accuracy is achieved by setting the desired confidence level to $\beta \in [0.63, 0.69]$. Furthermore, the desired confidence level β can be adjusted to improve the classification accuracy and fit new datasets without reperforming the computations for the objective function, especially for **VSD** sounds and **MR** sounds (Fig. 9(**VSD** and **MR**)). In this study, according to the rules described above combined with the accuracy analysis results plotted in Fig. 9, the $\beta_k (k = 1, \ldots, 7)$ values are set as 0.87, 0.65, 0.67, 0.65, 0.67, 0.79 and 0.87, respectively.

Step 4: MDC_k determination corresponding to β_k. Based on the kth confidence level achieved for β_k in the above step, by using the function '*chi2inv*' in MATLAB 2018b, the inverse of χ^2_{3,β_k}, denoted as $\text{MDC}_k = \chi^2_{3,\beta_k}$, is determined. The analysis results for the kth confidence region in the 3-dimensional interspace, which is surrounded by the kth ellipsoid corresponding to the kth desired confidence level β_k, are determined and shown in Fig. 8B. Furthermore, Fig. 8B shows that the common regions between two random ellipsoids are almost zero; thus, a faulty decision process is avoided because the input will not fall into two or more categories.

Step 5: MDC_k-based diagnostic result determination. Based on the ellipsoid surfaces region shown in Fig. 8B, the diagnosis method is described as follows.

Data source	Period numbers of every type of heart disease/Patients						
	MR	MS	ASD	NM	AS	AR	VSD
Sounds in Sect. 2.2	769/10	439/5	315/7	1056/45	381/10	665/15	327/10
New sounds	156/3	132/2	82/2	183/8	126/3	153/4	70/3
Total sounds	925/13	571/7	397/9	1239/53	507/13	818/19	397/13

Table 5. Experimental sounds used to evaluate the performance.

Method	Year	Performance evaluation
♯ 1[46]	2021	The Fano-factor constrained tunable quality wavelet transform (TQWT) was the sensitivity and specificity of 86.32% and 99.44% respectively and overall score of 92.88% to detect abnormal heart sounds.
♯ 2[47]	2021	This study proposed a heart sound classification method based on improved MFCC features and convolutional recurrent neural networks, which achieved classification accuracy of 98% in the 2016 PhysioNeT/CinC Challenge database with dropout rate of 0.5.
♯ 3[48]	2020	A deep WaveNet model was proposed to classify five heart sound types and achieve high classification accuracies: 98.20% for diagnosing Normal, 95.20% for diagnosing MVP, 97.80% for diagnosing MS, 96.10% for diagnosing MR, 97.70% for diagnosing AS.
♯ 4[8]	2018	The higher CA, achieved in this study, was 95.5%, 92.1%, 96.2% and 99.0% for diagnosing small ventricular septal defect (**VSD**), moderate **VSD**, large **VSD** and normal sounds, respectively.
♯ 5[49]	2017	A rule-based classification tree method proposed by this study achieved very high CA: 95.45% for diagnosing **VSD**, 100% for diagnosing normal, 100% for diagnosing aortic stenosis and 95.45% for diagnosing aortic insufficiency.
♯ 6[50]	2016	Artificial neural networks (ANNs) was reported to achieve the second-best score compared to the other methods in classifying the phonocardiogram recordings provided by the CinC Challenge.
♯ 7[51]	2016	Random forest, a meta-learning approach that uses multiple random decision trees as base learners and aggregates them to compute the final ensemble prediction, was successfully used in sound classification such as studies.

Table 6. Efficient methods successfully used in diagnosing normal sounds from other common heart diseases.

① The 3-dimensional diagnostic features $[\gamma_1, \gamma_2, \gamma_3]$ are first transformed from the features FF (denoted as FF_s) of the testing sample and calculated with the following equation

$$\gamma_i = \frac{FF_s - \mu_{FF}}{\sigma_{FF}} \times \xi_i, i = 1, 2, 3 \tag{25}$$

where μ_{FF} and σ_{FF} are shown in Table 2.
② Then, according to the confidence region shown in Fig. 8B, the MDC_k-based diagnostic result for a test features $\mathbf{x} = [\gamma_1, \gamma_2, \gamma_3]$ is determined.
③ MDC_k-based diagnostic results for a test feature $\mathbf{x} = [\gamma_1, \gamma_2, \gamma_3]$ are determined by

$$\begin{cases} \text{Class } k, d_3^2(\mathbf{x}|\mu_k, \Sigma_k) \leq MDC_k \\ \text{Unknown class,} \qquad \text{otherwise} \end{cases}, \tag{26}$$

where class k corresponding to the type of heart disease is detailed in Table 4, and MDC_k $(1, 2, \cdots, 7)$ is 5.6489, 3.2831, 3.4297, 3.2831, 3.4297, 4.5258 and 5.6489.

Performance evaluation criteria. To evaluate the performance of these ellipsoids in 3-dimensional space, the classification accuracy (*CA*), sensitivity (*Se*) and specificity (*Sp*) values are calculated by

$$\begin{cases} CA(\%) = \frac{TP+TN}{TP+FP+FN+TN} \times 100 \\ Se(\%) = \frac{TP}{TP+FN} \times 100 \\ Sp(\%) = \frac{TN}{FP+TN} \times 100 \end{cases}, \tag{27}$$

where TP, FP, TN and FN are the numbers of true positives, false positives, true negatives and false negatives, respectively.

Performance evaluation

To evaluate the performance of the proposed methodology, the comparison between the proposed methodology and the state-of-the-art methods on the clinical sounds and online sounds data was conducted as follows.

- Total sounds: The total sounds, consisting of sounds described in Sect. 2.2 and new sounds, were summarized in Table 5 to evaluate the performance of this proposed methodology.
- State-of-the-art methods: To highlight the efficiency of the proposed methodology for diagnosing the seven typical heart diseases, the state-of-the-art methods, published in recent five years and described in Table 6, were comparatively analyzed.

Method	MR			MS			ASD			NM			AS			AR			VSD		
	Se%	CA(%)	Sp(%)	Se%	CA(%)	Sp(%)	Se%	CA(%)	Sp(%)	Se%	CA(%)	Sp(%)	Se%	CA(%)	Sp(%)	Se%	CA(%)	Sp(%)	Se%	CA(%)	Sp(%)
♯1	92.1	86.34	87.6	88.2	86.81	87.3	91.2	84.53	85.1	86.3	82.90	81.6	90.9	98.25	**99.1**	88.2	86.05	85.4	95.2	96.31	96.8
♯2	90.6	89.93	88.3	88.8	90.32	91.3	83.9	86.12	87.21	95.9	98.3	97.7	96.3	96.1	96.02	87.1	86.31	85.9	90.6	89.3	88.1
♯3	90.1	88.6	87.5	85.1	85.69	**99.2**	81.3	80.97	80.8	93.6	91.95	90.3	87.9	85.04	83.3	92.1	88.69	85.6	88.6	86.9	85.9
♯4	90.1	87.34	86.7	83.2	86.81	87.3	90.2	83.13	82.5	85.7	81.90	80.6	91.3	90.40	90.3	87.2	84.04	83.4	96.2	97.66	97.8
♯5	88.6	85.93	85.3	86.1	89.72	90.2	79.8	82.10	82.3	96.1	98.93	**99.9**	98.3	91.95	96.2	85.1	86.97	83.6	87.5	87.19	82.1
♯6	88.1	87.6	87.8	83.1	89.36	90.2	80.3	81.67	81.8	92.6	91.63	91.3	83.9	86.04	86.3	90.1	84.69	83.6	87.6	86.03	85.9
♯7	89.7	91.64	92.1	85.2	83.52	83.3	86.3	87.49	87.6	93.7	91.61	90.9	90.1	87.05	86.7	85.2	82.21	81.6	90.8	91.63	91.7
This	100	99.43	99.3	99.2	98.93	98.9	99.6	99.13	99.1	100	99.85	99.8	98.8	98.62	98.6	100	99.67	99.6	100	99.91	99.9

Table 7. Comparative analysis of eight different methods for the diagnosis of heart diseases summarized in Table 5.

Method	Performance evaluation
♯ 1[46]	The highest classification accuracies were obtained by using the features described in Table 3 on page 28.
♯ 2[47]	The highest classification accuracies were obtained by using the 13-features extracted using MFCC algorithm.
♯ 3[48]	The highest classification accuracies were obtained by using the porposed WaveNet model consists of 6 residual blocks.
♯ 4[8]	The highest classification accuracies were obtained based on the rules described in a previous study[8].
♯ 5[49]	The highest CA results were obtained based on the following rules.
	Rule 1: If the 8th value of Lyapunov exponent (LPE$_8$) ≥ 0.79 and (LPE$_9$) ≤ 0.38 then the heart is normal.
	Rule 2: If LPE$_2$ ≤ 0.17 and (LPE$_8$) ≤ 0.79, then the heart disease is **VSD**.
	Rule 3: If LPE$_4$ ≥ 0.17, LPE$_6$ ≤ 0.39, and LPE$_3$ ≤ 0.56, then the heart disease is **MR**.
	Rule 4: If LPE$_5$ ≥ 0.17, LPE$_4$ ≥ 0.67, and LPE$_3$ ≥ 0.37, then the heart disease is **MS**.
	Rule 5: If LPE$_7$ ≥ 0.54, LPE$_3$ ≥ 0.29, and LPE$_5$ ≥ 0.49, then the heart disease is **AR**.
	Rule 6: If LPE$_8$ ≥ 0.39, LPE$_5$ ≥ 0.72, and LPE$_2$ ≤ 0.68, then the heart disease is **ASD**.
	Rule 7: If LPE$_9$ ≥ 0.64, LPE$_3$ ≥ 0.39, and LPE$_7$ ≥ 0.21, then the heart disease is **AS**.
	Rule 8: If none of these conditions are met, the **HS** is undefined.
♯ 6[50]	The most accurate results were obtained by the structure consisting of one input layer with 60 neurons, one hidden layer with 11 neurons and one output layer with five neurons.
♯ 7[51]	The most accurate results were obtained by setting the number of features at each node, the number of trees and the maximum depth of trees to 1, 108, and 36, respectively.
This method	The most accurate results were obtained for the diagnosis of **MR**, **MS**, **ASD**, **NM**, **AS**, **AR** and **VSD** at $Thv = 0.4, 0.3, 0.2, 0.2, 0.4, 0.1$ and 0.2, respectively.

**Table 8.** The highest accuracies corresponding to the parameters set in every state-of-the-art method.

● Comparsion results: The comparison results were summarized in Table 7, where the parameters corresponding to the state-of-the-art methods were described in Table 8. The results in Table 7 support the following conclusions.
● Although using the method #1 to diagnose **AS** yielded a higher Sp than that of the proposed method, the CA was lower than that of the proposed method, partially due to the high Se achieved by the proposed method.
● Although using the method #3 to diagnose **MS** yielded a higher Sp than that of the proposed method, the CA was lower than that of the proposed method, partially due to the high Se achieved by the proposed method.
● Although using the method #5 to diagnose **NM** yielded a higher Sp than that of the proposed method, the CA was lower than that of the proposed method, partially due to the high Se achieved by the proposed method.
● For other sounds, the classification accuracies achieved in the proposed method were all greater than those of the other methods listed in Table 7 .

Overall, the efficiency of the proposed method in diagnosing **MR**, **MS**, **ASD**, **NM**, **AS**, **AR** and **VSD** diseases was evaluated by comparison with the other efficient methods listed in Table 7.

Conclusion

A novel intelligent system was proposed for diagnosing heart diseases with high CA. The innovation of this approach is primarily reflected in: 1) the automatic extraction of secondary envelope-based frequency features; 2) the automatic determination of **PCA**-based diagnostic features γ_1, γ_2 and γ_3; and 3) the determination of adjustable confidence regions corresponding to the χ^2 distribution. The confidence regions are obtained by calculating the Mahalanobis distance, which is adjusted by the desired confidence level β, and the results were used as the classification criteria for diagnosing heart diseases. The procedure for the implementation of the intelligent
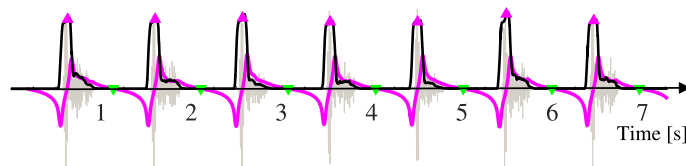
Figure 10. An example of a **AR** sound from database[26].

system involved three stages. Stage 1 described the location and extraction of **STMHT**-based CS_1 and CS_2. In stage 2, in the frequency domain, a novel method was first proposed to generate the envelopes CS_{1F_E} and CS_{2F_E}; then, based on the Thv lines, FF was automatically extracted. Finally, based on **PCA**, the first three principal components, γ_1, γ_2 and γ_3, which expressed 86.7% of the FF information, were determined and used as diagnostic features. In stage 3, the **GMM**-based objective function $f_{et}(\mathbf{x})$ with respect to the features $\mathbf{x} = [\gamma_1, \gamma_2, \gamma_3]$ and the parameters $[\pi_k, \mu_k, \Sigma_k]$, where $k = 1, 2, \ldots, K$, was generated. Then, the χ^2 distribution for component k was determined by calculating the Mahalanobis distance from $\mathbf{x}$ to the class mean μ_k of component k, and the confidence region for component k was determined by adjusting the optimal confidence level β_k and used as the criterion (denoted as MDC_k) to diagnose a given **HS**. The performance evaluation was validated by sounds from online **HS** databases and clinical heart databases. The accuracy of the proposed method was compared to the accuracies of other well-known classifiers, and the highest classification accuracies of 99.43%, 98.93%, 99.13%, 99.85%, 98.62%, 99.67% and 99.91% in the detection of **MR**, **MS**, **ASD**, **NM**, **AS**, **AR** and **VSD** sounds were achieved by setting $\beta_k(k = 1, 2, \ldots, 7)$ to 0.87, 0.65, 0.67, 0.65, 0.67, 0.79 and 0.87, respectively. Therefore, this proposed intelligent diagnosis system provided an efficient way to diagnose seven types of heart diseases.

The advantages and limitations were summarized as follows:

● **Advantages:** ① CS_1 and CS_2 were automatically extracted to reduce difficulty in segmenting each cardiac cycle into a sequence of four heart stages: $S_1 \longrightarrow Systole\ period \longrightarrow S_2 \longrightarrow Diastole\ period$; ② More features could be extended by setting even more threshold values for the unknown heart diseases, especially for the heart sound with the compound heart diseases; ③ Every classifier achieved in this study could be adjusted based on the desired β for fitting incremental new features without being retrained via huge training features.

● **Limitations:** ① This methodology was impossible to diagnose the sounds when CS_1 and CS_2 cannot be segmented and extracted via the **STMHT** method for a given heart sound such as that plotted in Fig. 10; ② The proposed classifier might not be satisfied with the compound heart diseases due to the distribution of features extracted from which can not fit a single Gaussian distribution.

Future study

Future study focused on how to handle the sounds (such as some **AR** sounds) when CS_1 and CS_2 cannot be segmented and extracted via the **STMHT** method will be explored, and on how to build the classifier model for fitting the compound heart diseases will be further studied.

Research statement

The study was conducted at Nanyang Institute of Technology and Nanyang First People's Hospital, Henan, China from December 2017 to June 2021, and was approved by the ethics committee of Nanyang Institute of Technology and First People's Hospital (Approval Number: V6.0). Informed consent was waived due to the retrospective design of the study. The study complies with the Declaration of Helsinki.

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Author contributions

Sun, Biqiang Zhang and Huang: collection, organizing, and review of the literature. Sun, Biqiang Zhang and Huang: preparing the manuscript. Sun, Huang, Biqiang Zhang, He, Yan, Fan, Jiale Zhang and Chen: manuscript revision and modification. All authors read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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