US 20190175120A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2019/0175120 A1**

Huang (43) **Pub. Date: Jun. 13, 2019**

(54) **METHOD, MODULE AND SYSTEM FOR ANALYSIS OF PHYSIOLOGICAL SIGNAL**

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(21) Appl. No.: **16/214,176**

(22) Filed: **Dec. 10, 2018**

Related U.S. Application Data

(60) Provisional application No. 62/596,912, filed on Dec. 11, 2017.

Publication Classification

(51) **Int. Cl.**

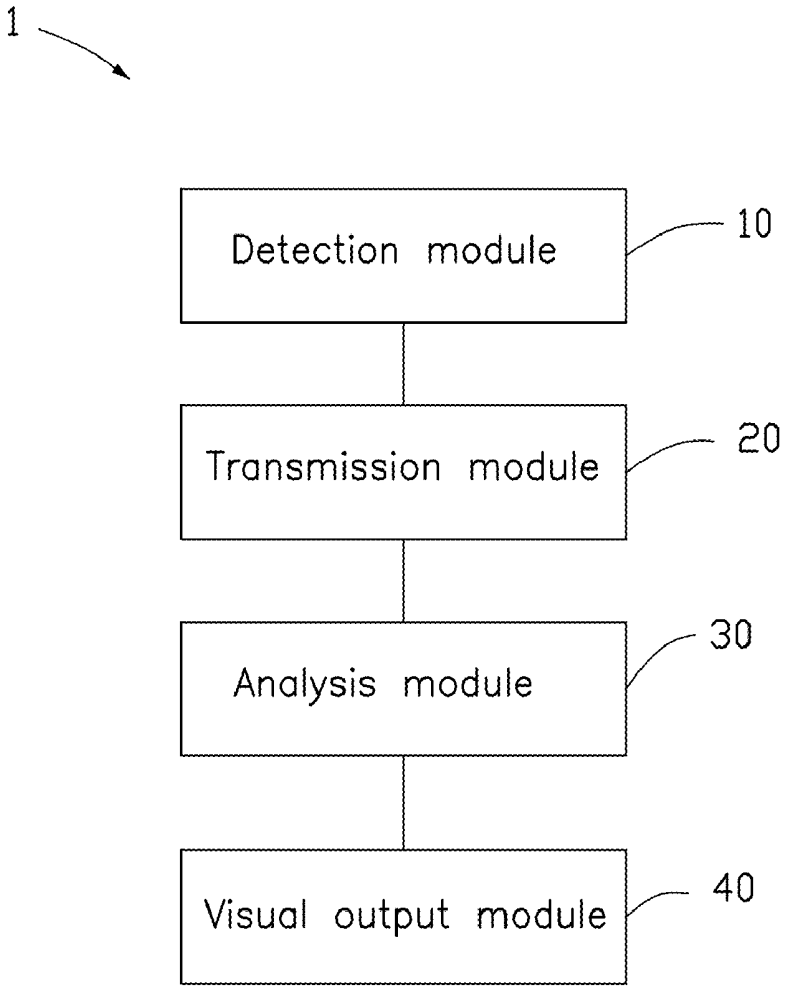
A61B 5/00	(2006.01)
A61B 5/021	(2006.01)
A61B 5/044	(2006.01)
A61B 5/0488	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 5/743*** (2013.01); ***A61B 5/021*** (2013.01); ***A61B 5/72*** (2013.01); ***A61B 5/0488*** (2013.01); ***A61B 5/044*** (2013.01)

(57) **ABSTRACT**

The present disclosure provides a non-transitory computer program product embodied in a computer-readable medium, and when executed by one or more analysis module, providing a visual output for presenting physiological signals of a cardiovascular system. The non-transitory computer program product comprises a first axis representing subsets of intrinsic mode functions (IMFs); a second axis representing a function of signal strength in a time interval; and a plurality of visual elements, each of the visual elements being defined by the first axis and the second axis, and each of the visual elements comprising a plurality of analyzed data units collected over the time interval.



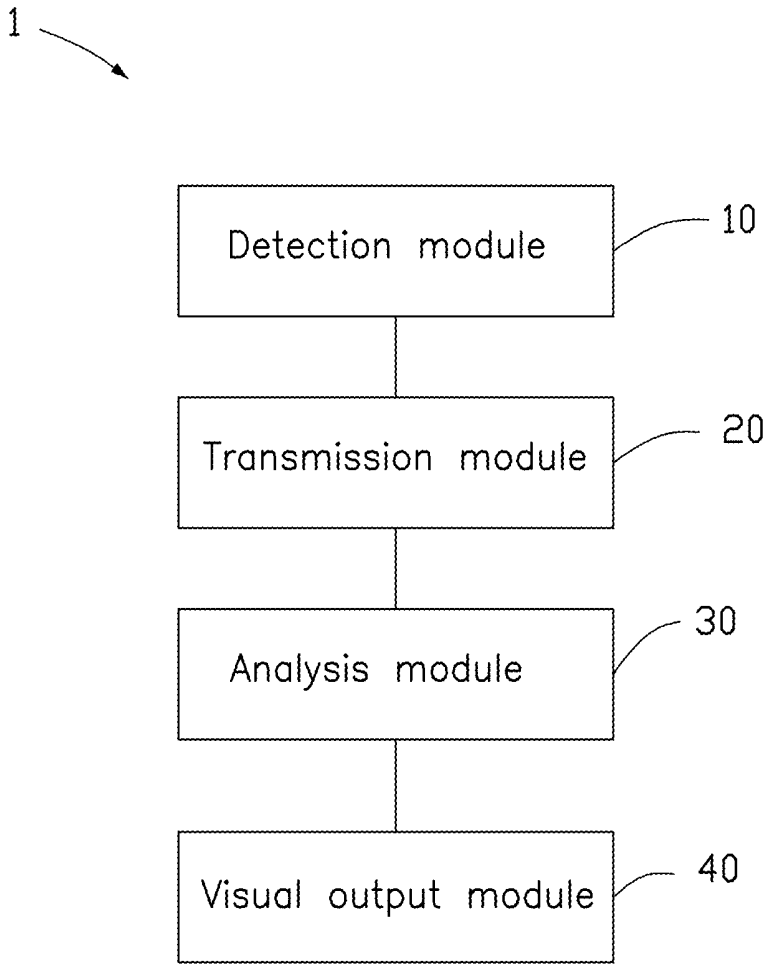

1
Detection module
10
Transmission module
20
Analysis module
30
Visual output module
40

FIG. 1

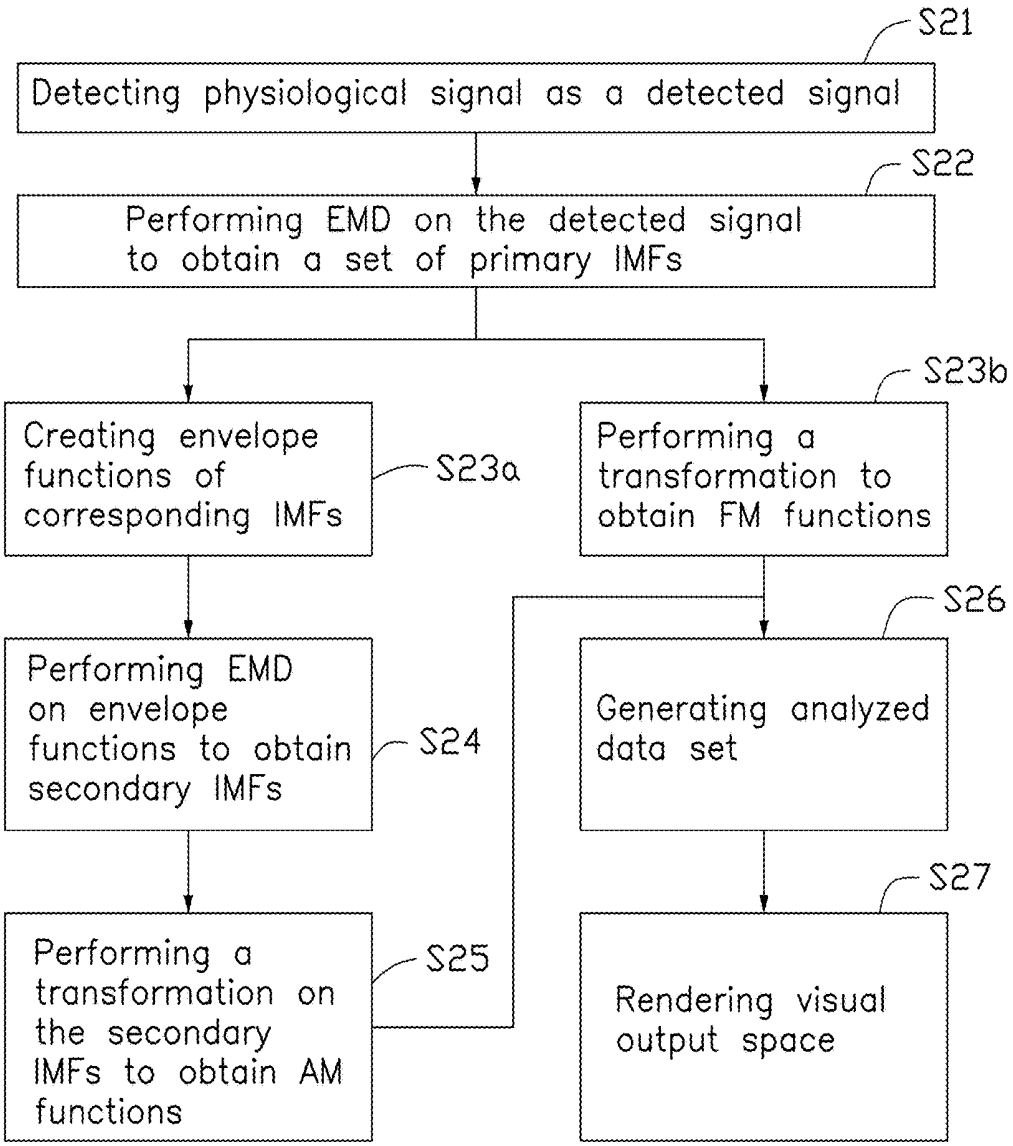

S21
Detecting physiological signal as a detected signal
S22
Performing EMD on the detected signal to obtain a set of primary IMFs
S23b
Creating envelope functions of corresponding IMFs
S23a
Performing a transformation to obtain FM functions
S26
Performing EMD on envelope functions to obtain secondary IMFs
S24
Generating analyzed data set
S27
Performing a transformation on the secondary IMFs to obtain AM functions
S25
Rendering visual output space

FIG. 2

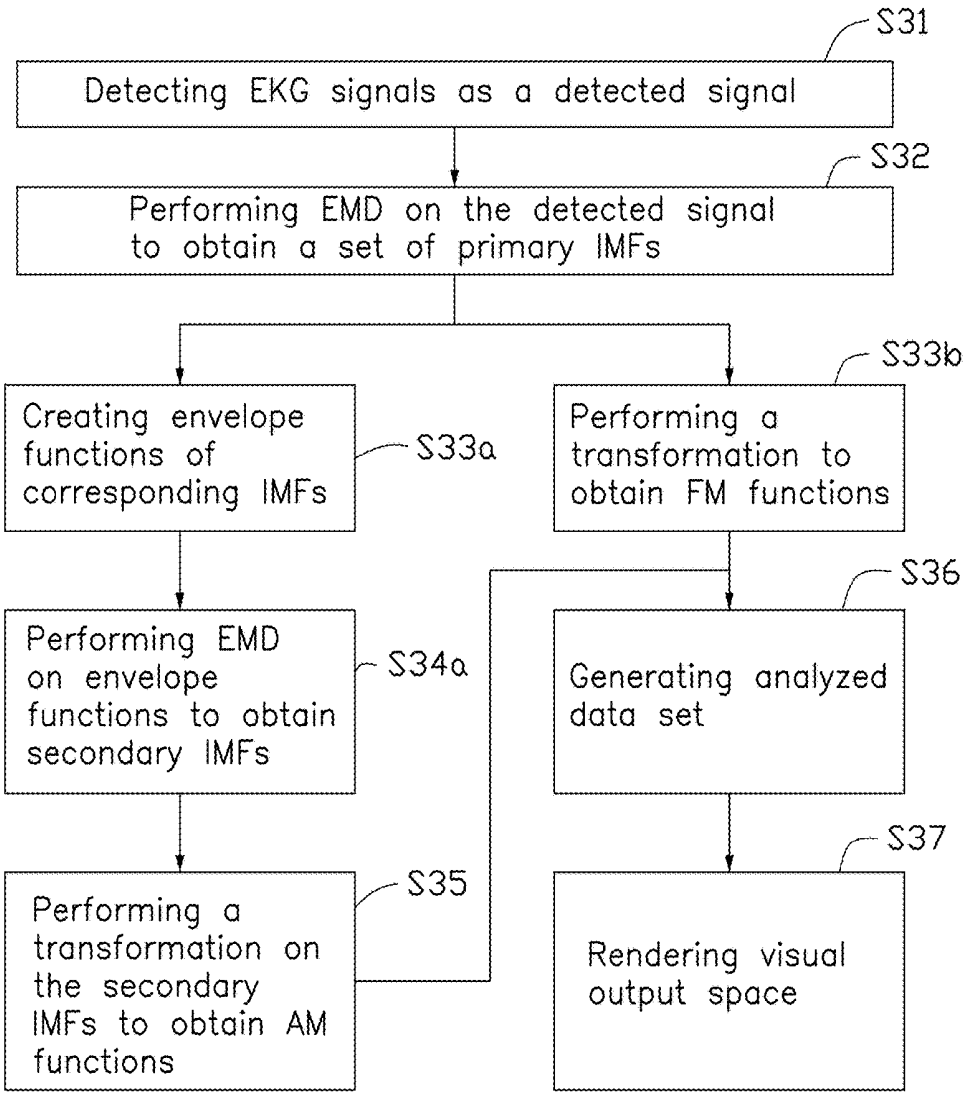

S31
Detecting EKG signals as a detected signal
S32
Performing EMD on the detected signal to obtain a set of primary IMFs
S33b
Performing a transformation to obtain FM functions
Creating envelope functions of corresponding IMFs
S33a
S36
Performing EMD on envelope functions to obtain secondary IMFs
S34a
Generating analyzed data set
S37
Performing a transformation on the secondary IMFs to obtain AM functions
S35
Rendering visual output space

FIG. 3

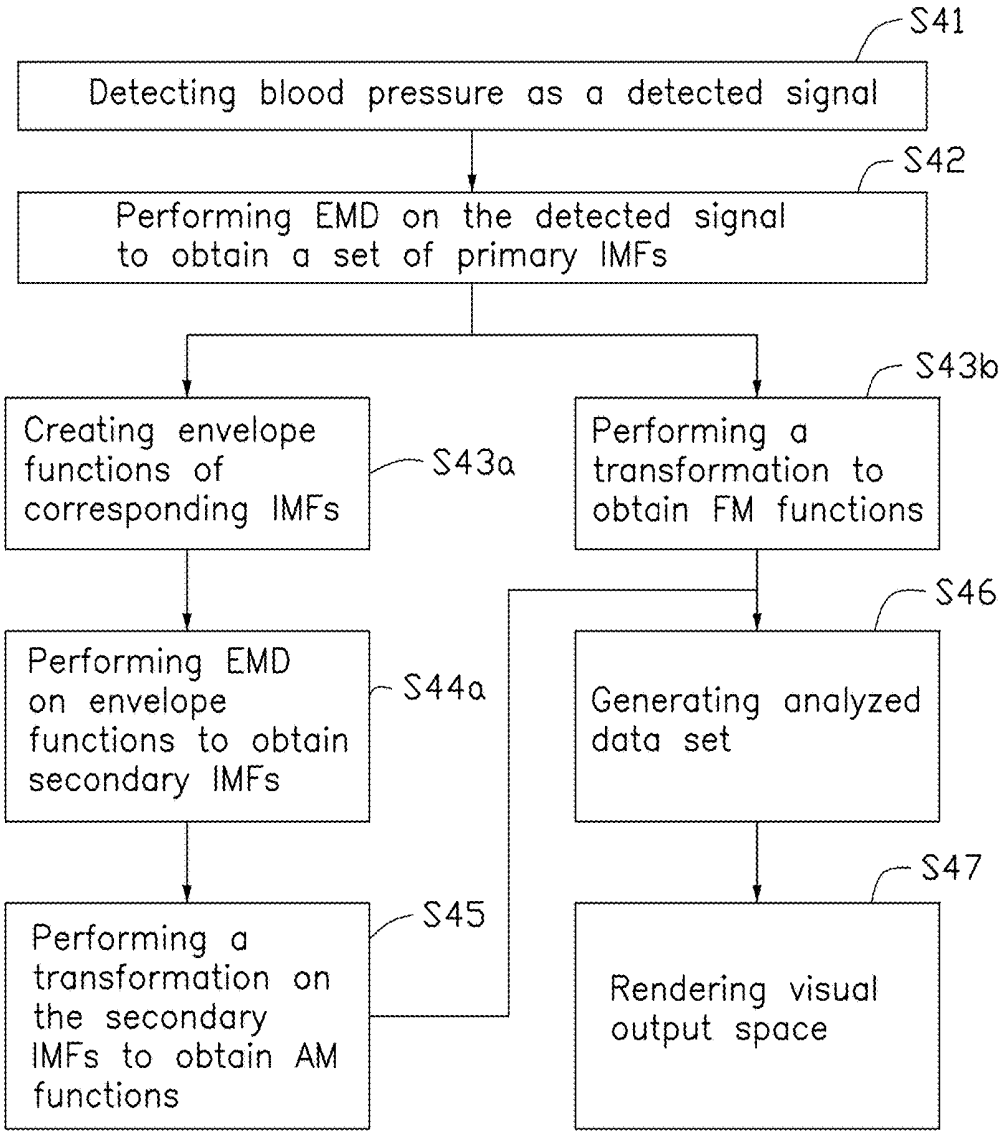

S41
Detecting blood pressure as a detected signal
S42
Performing EMD on the detected signal to obtain a set of primary IMFs
S43b
Performing a transformation to obtain FM functions
Creating envelope functions of corresponding IMFs
S43a
S46
Generating analyzed data set
Performing EMD on envelope functions to obtain secondary IMFs
S44a
S47
Rendering visual output space
Performing a transformation on the secondary IMFs to obtain AM functions
S45

FIG. 4

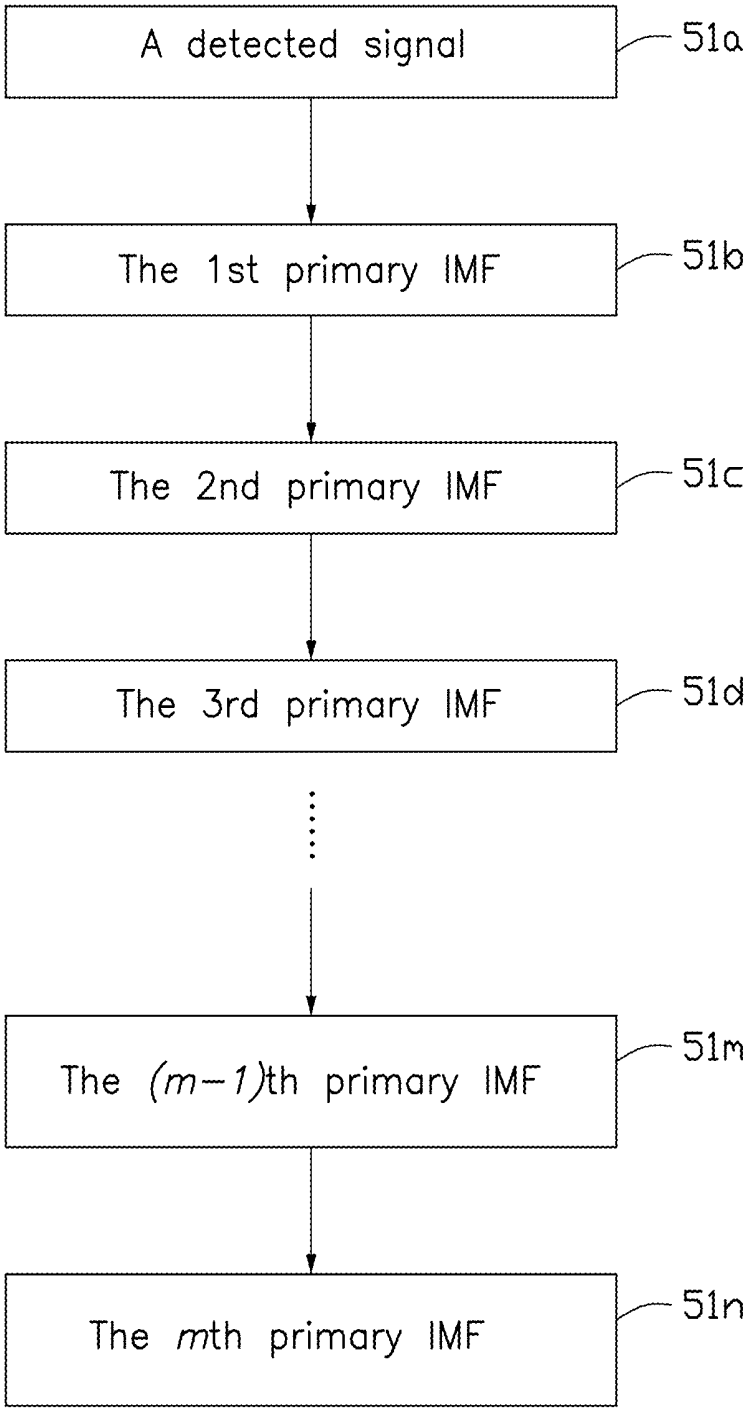

A detected signal
51a
The 1st primary IMF
51b
The 2nd primary IMF
51c
The 3rd primary IMF
51d
The (m−1)th primary IMF
51m
The mth primary IMF
51n

FIG. 5A

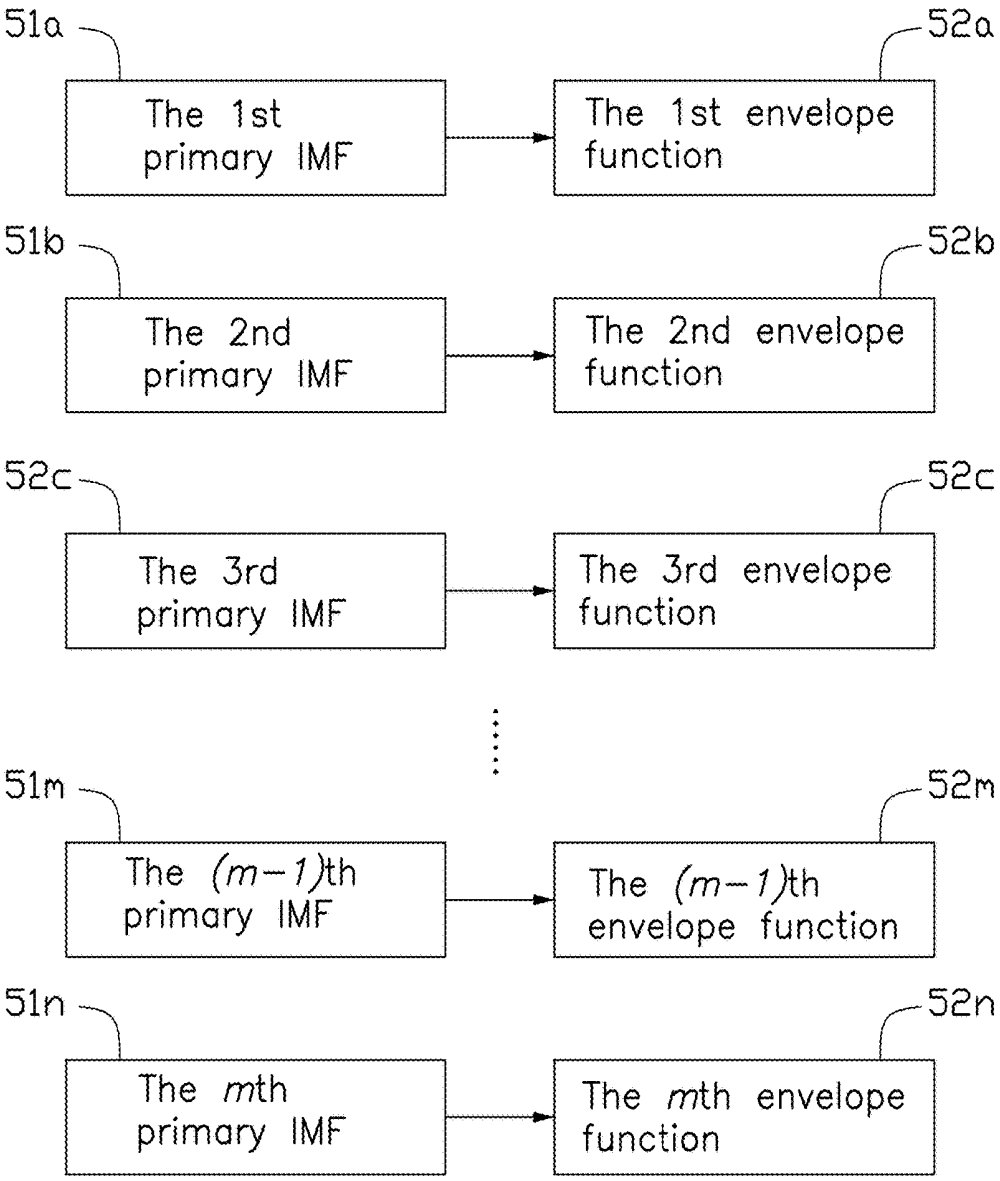

51a
The 1st primary IMF
52a
The 1st envelope function
51b
The 2nd primary IMF
52b
The 2nd envelope function
52c
The 3rd primary IMF
52c
The 3rd envelope function
51m
The (m−1)th primary IMF
52m
The (m−1)th envelope function
51n
The mth primary IMF
52n
The mth envelope function

FIG. 5B

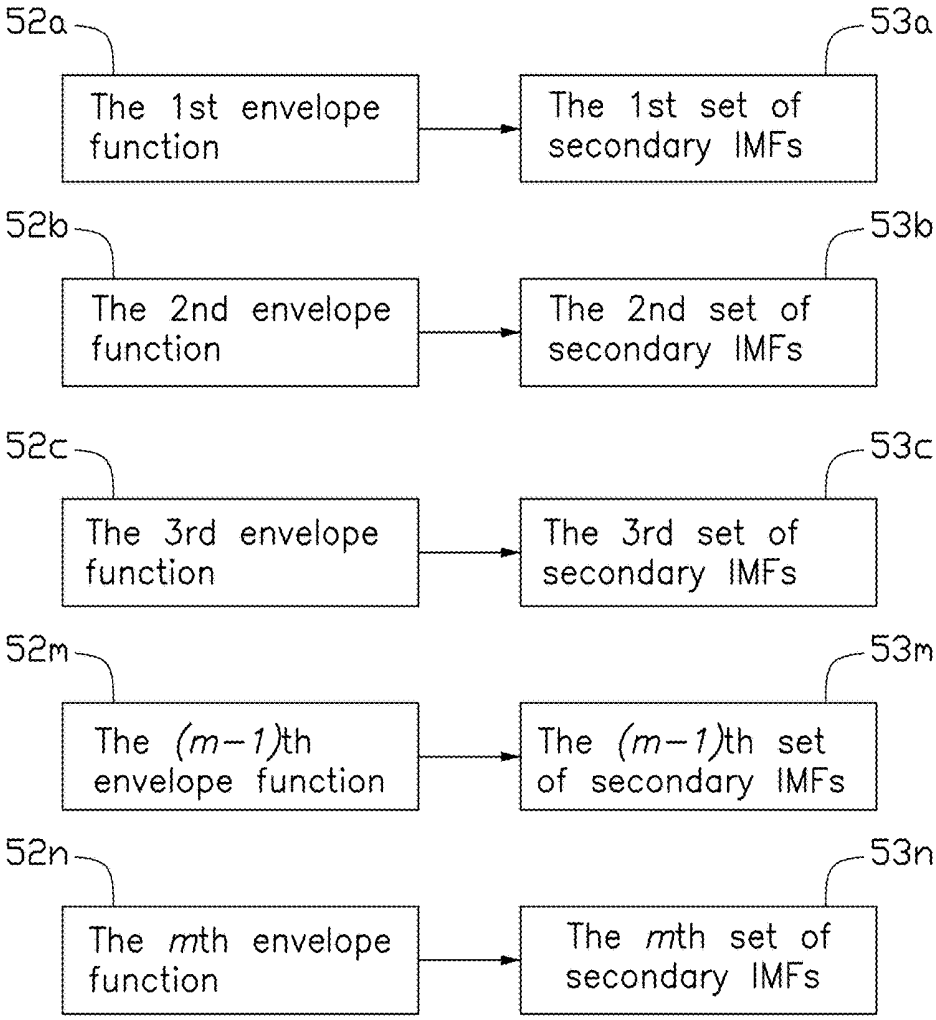

52a
The 1st envelope function
53a
The 1st set of secondary IMFs
52b
The 2nd envelope function
53b
The 2nd set of secondary IMFs
52c
The 3rd envelope function
53c
The 3rd set of secondary IMFs
52m
The (m−1)th envelope function
53m
The (m−1)th set of secondary IMFs
52n
The mth envelope function
53n
The mth set of secondary IMFs

FIG. 5C

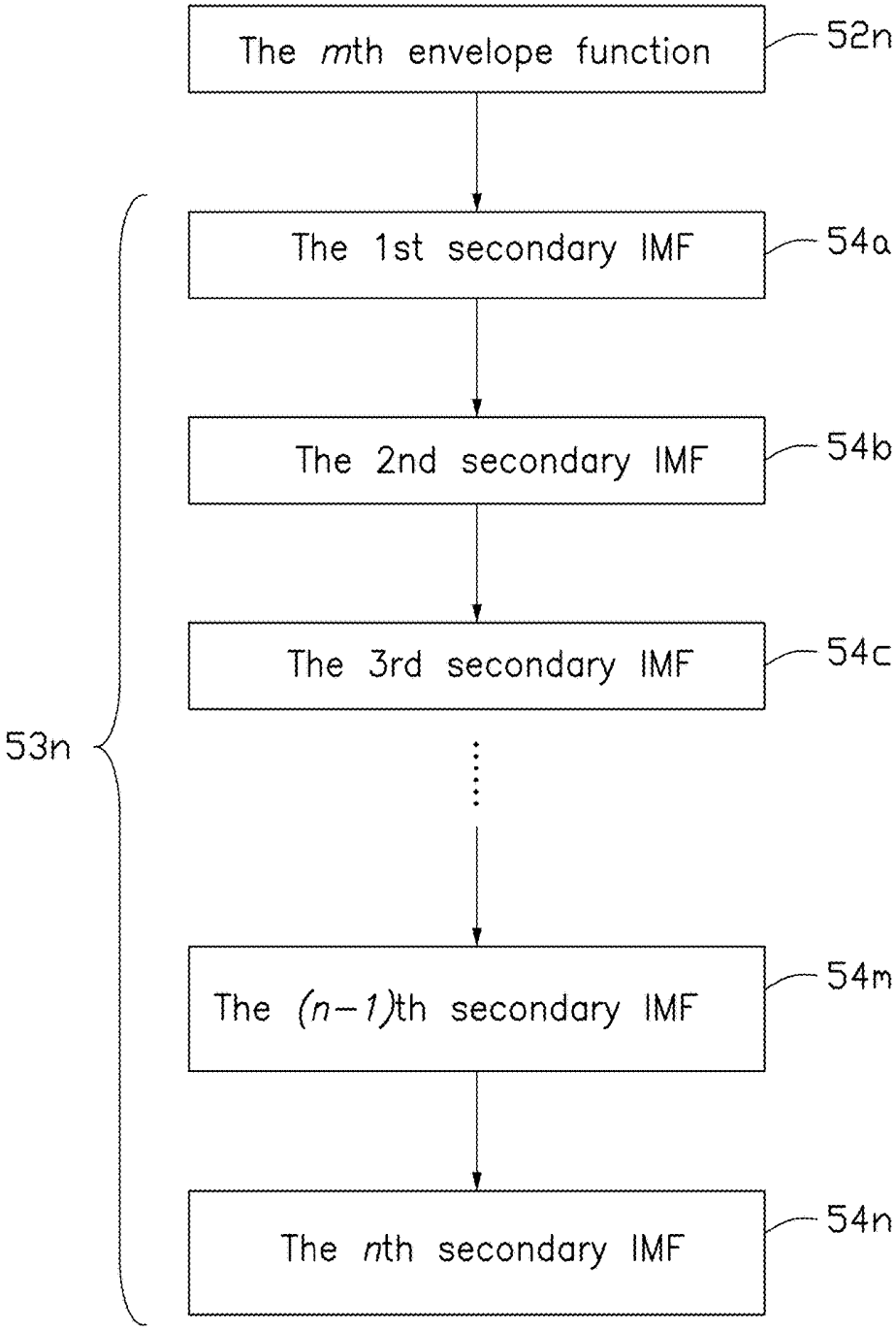

The mth envelope function
52n
The 1st secondary IMF
54a
The 2nd secondary IMF
54b
The 3rd secondary IMF
54c
53n
The (n−1)th secondary IMF
54m
The nth secondary IMF
54n

FIG. 5D

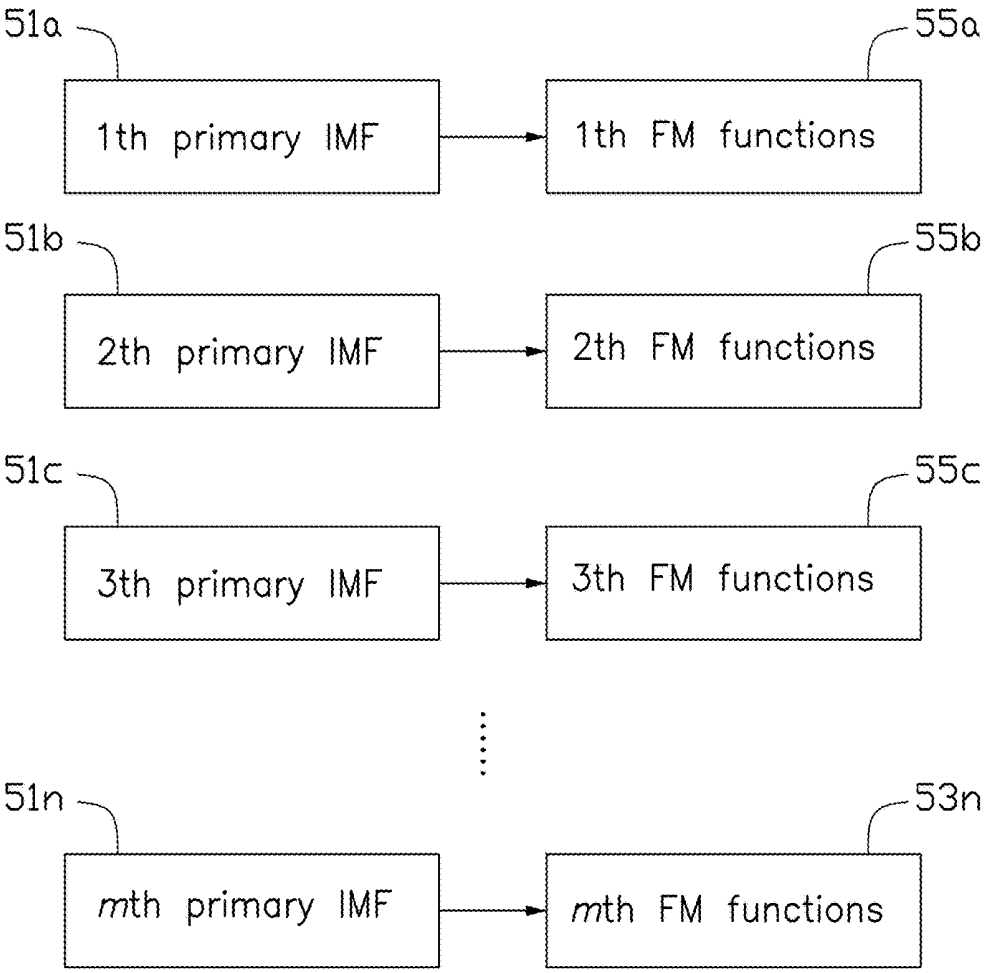

51a
1th primary IMF
55a
1th FM functions
51b
2th primary IMF
55b
2th FM functions
51c
3th primary IMF
55c
3th FM functions
51n
mth primary IMF
53n
mth FM functions

FIG. 5E

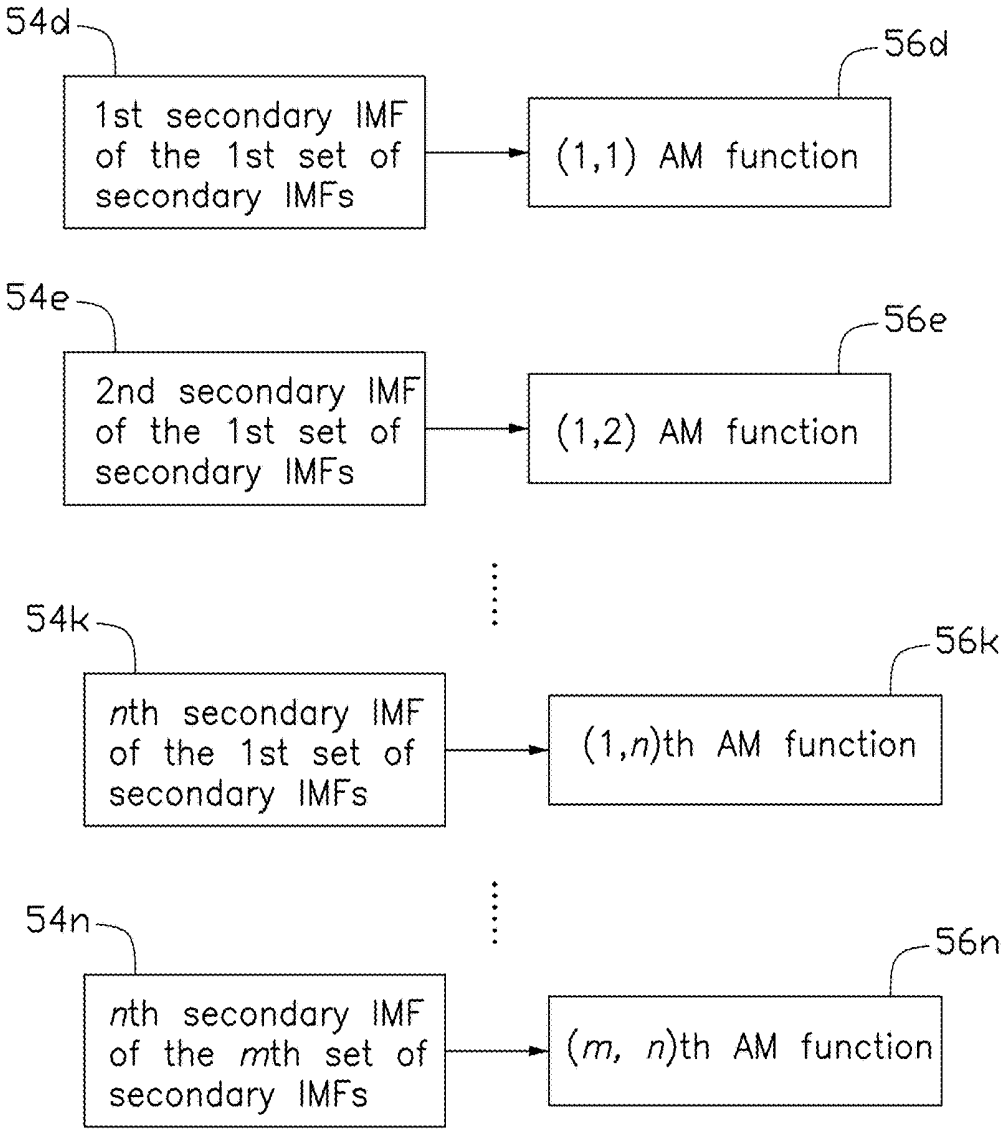

54d
1st secondary IMF of the 1st set of secondary IMFs
56d
(1,1) AM function
54e
2nd secondary IMF of the 1st set of secondary IMFs
56e
(1,2) AM function
54k
nth secondary IMF of the 1st set of secondary IMFs
56k
(1,n)th AM function
54n
nth secondary IMF of the mth set of secondary IMFs
56n
(m, n)th AM function

FIG. 5F

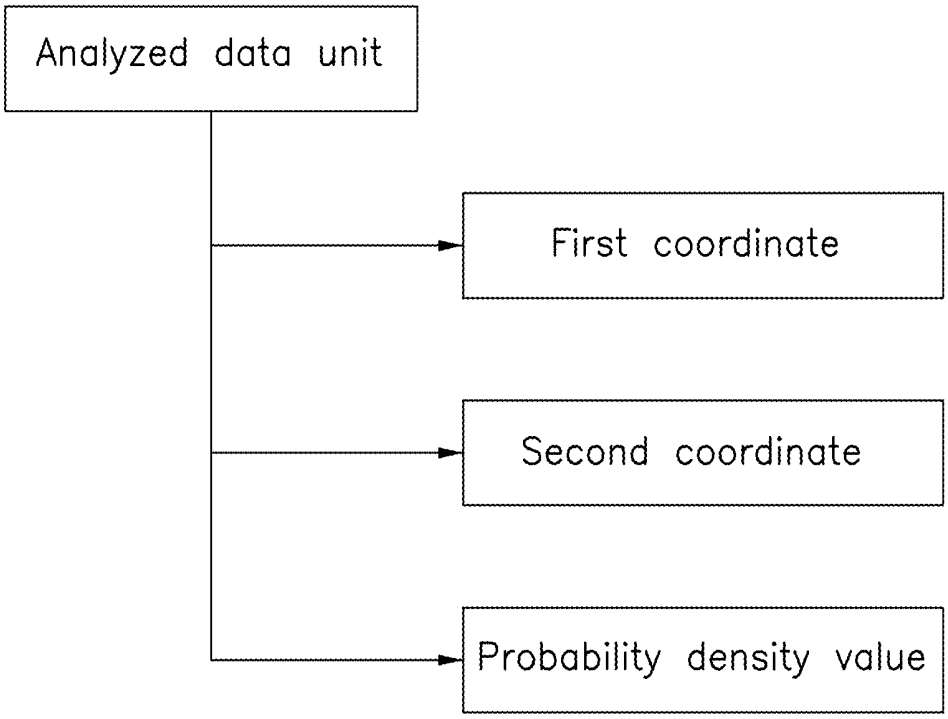

Analyzed data unit
First coordinate
Second coordinate
Probability density value

FIG. 6

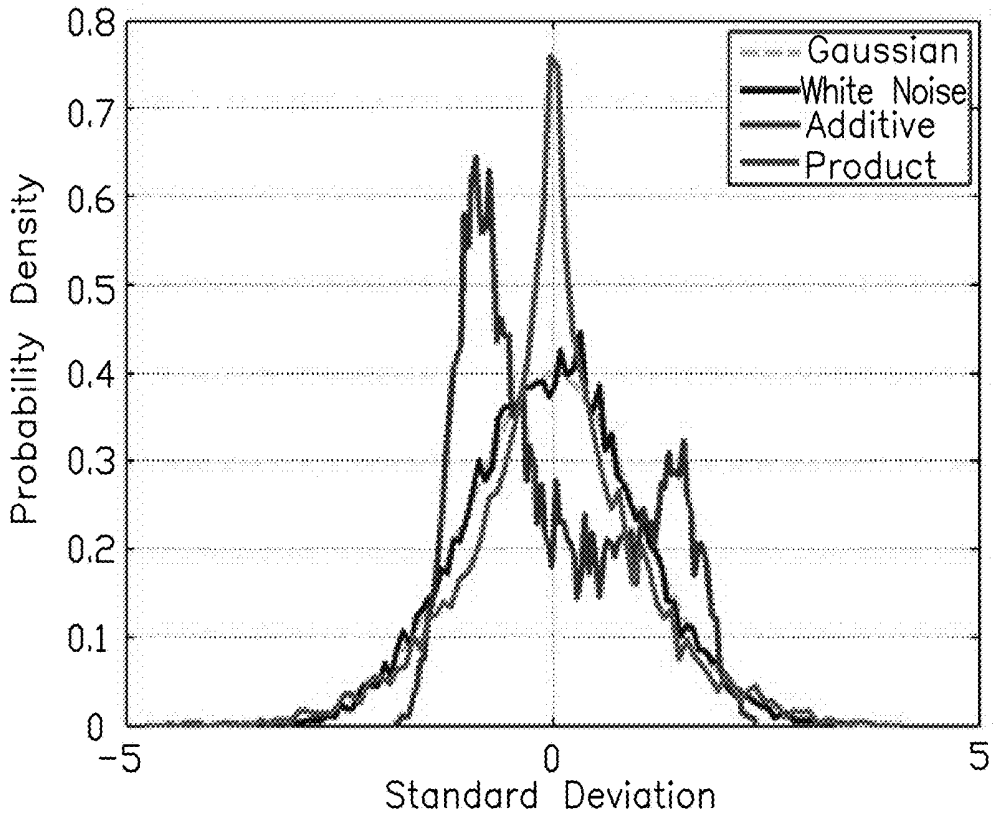

0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Probability Density
-5
0
5
Standard Deviation
Gaussian
White Noise
Additive
Product

FIG. 7

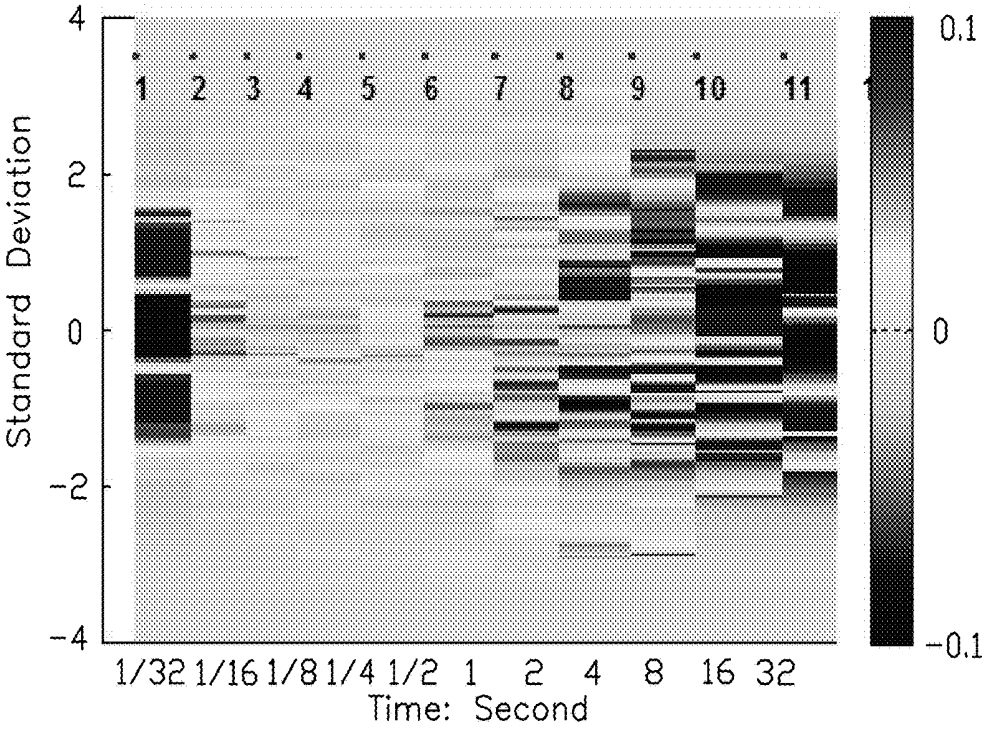

4
2
0
−2
−4
Standard Deviation
1 2 3 4 5 6 7 8 9 10 11
0.1
0
−0.1
1/32 1/16 1/8 1/4 1/2 1 2 4 8 16 32
Time: Second

FIG. 8A

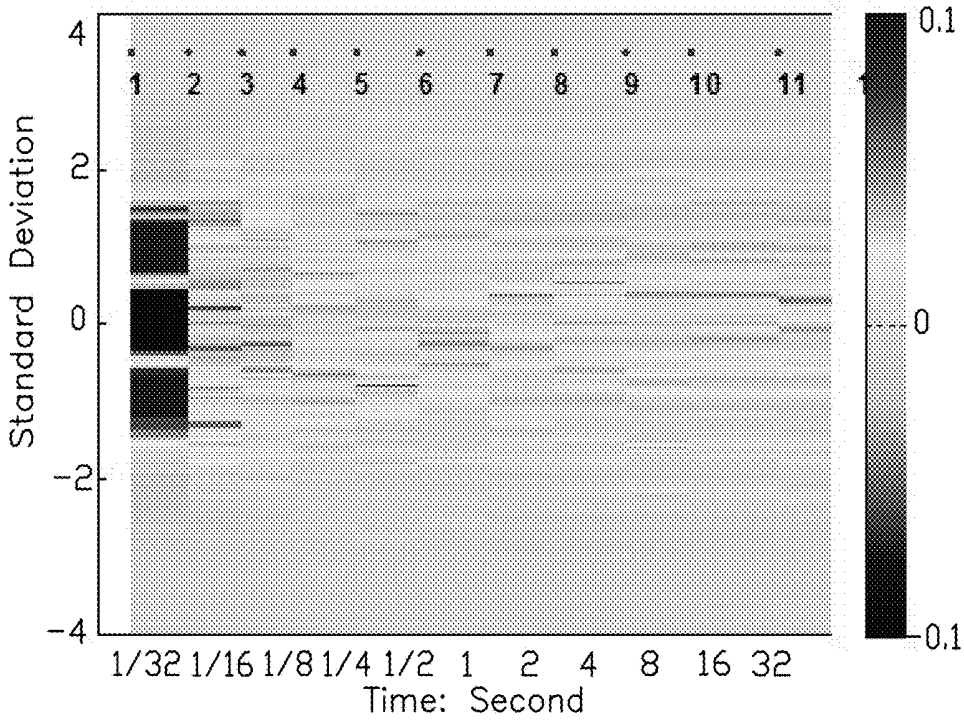

4
2
0
−2
−4
Standard Deviation
1 2 3 4 5 6 7 8 9 10 11
0.1
0
−0.1
1/32 1/16 1/8 1/4 1/2 1 2 4 8 16 32
Time: Second

FIG. 8B

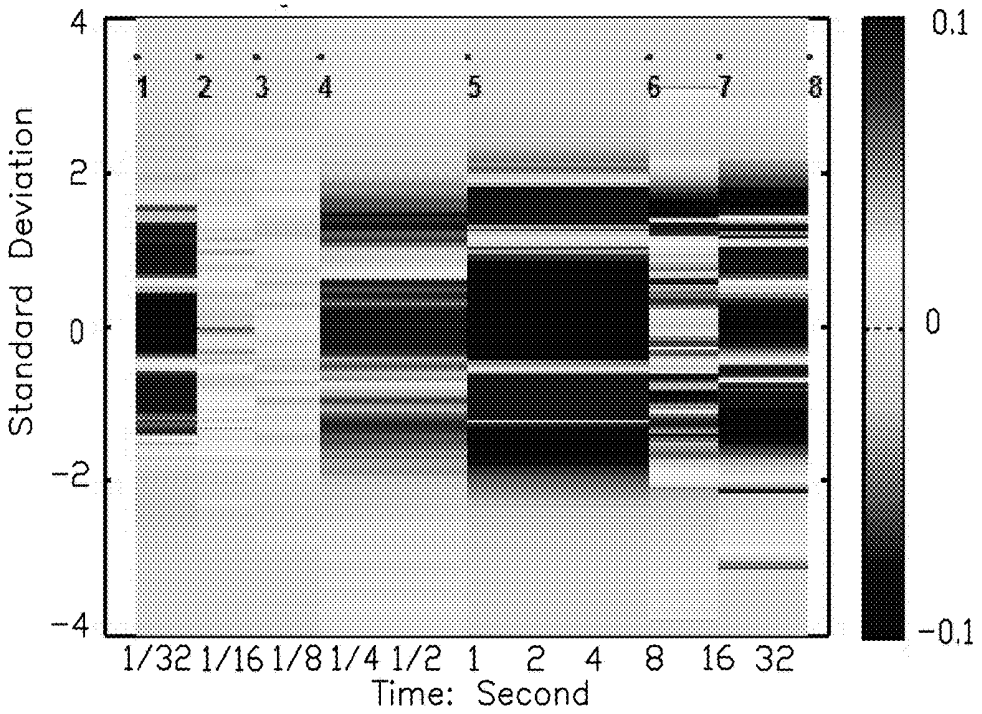

4
2
0
-2
-4
Standard Deviation
1 2 3 4 5 6 7 8
1/32 1/16 1/8 1/4 1/2 1 2 4 8 16 32
Time: Second
0.1
0
-0.1

FIG. 8C

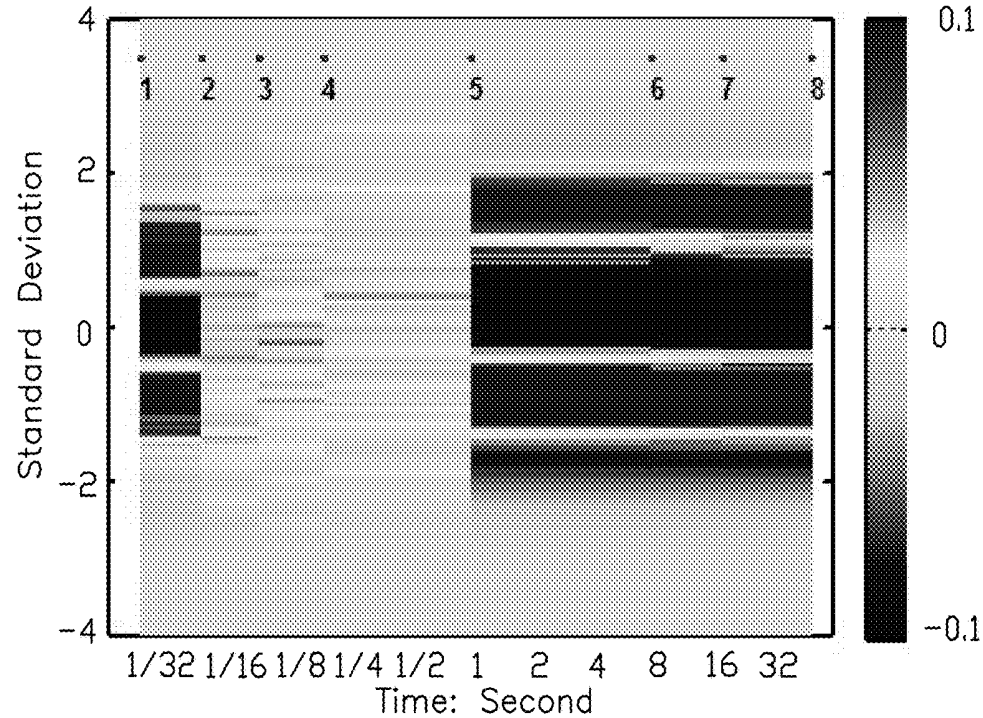

4
2
0
-2
-4
Standard Deviation
1 2 3 4 5 6 7 8
1/32 1/16 1/8 1/4 1/2 1 2 4 8 16 32
Time: Second
0.1
0
-0.1

FIG. 8D

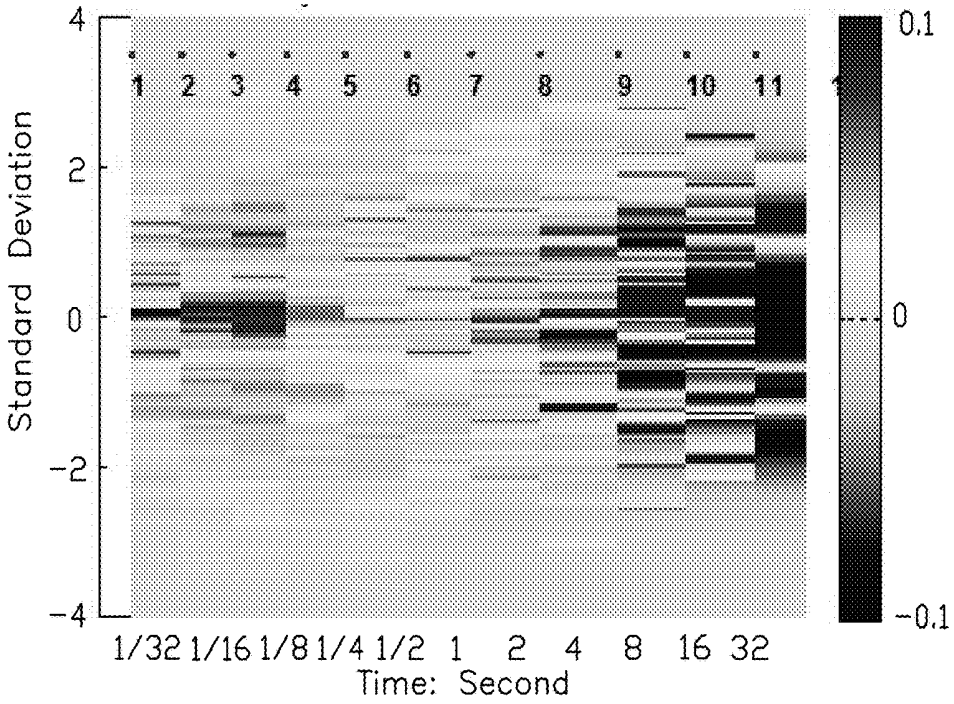

4
2
0
-2
-4
Standard Deviation
1 2 3 4 5 6 7 8 9 10 11
0.1
0
-0.1
1/32 1/16 1/8 1/4 1/2 1 2 4 8 16 32
Time: Second

FIG. 8E

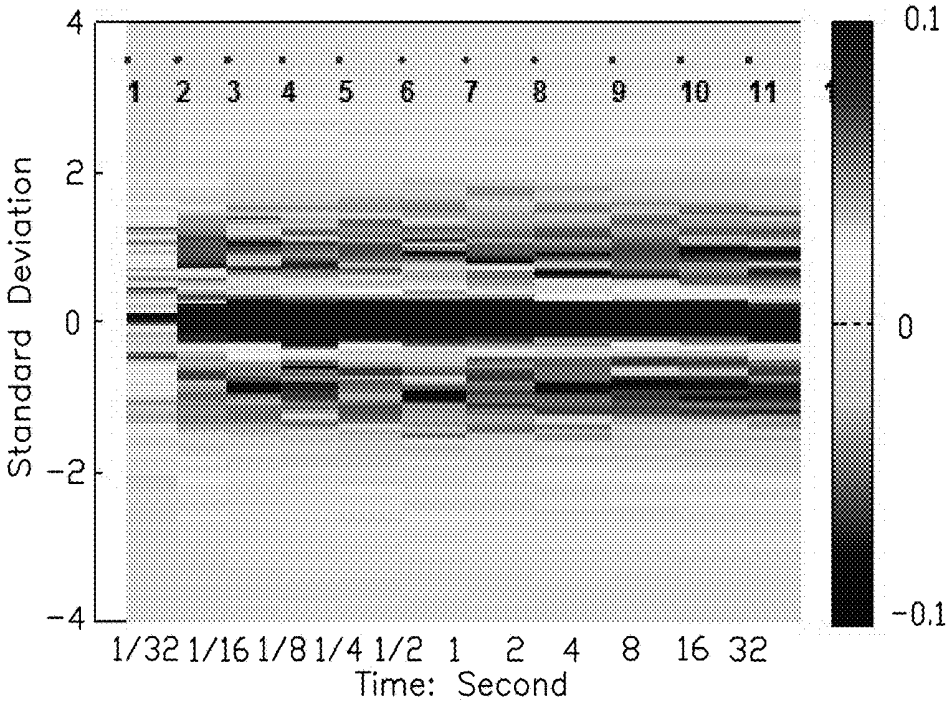

4
2
0
-2
-4
Standard Deviation
1 2 3 4 5 6 7 8 9 10 11
0.1
0
-0.1
1/32 1/16 1/8 1/4 1/2 1 2 4 8 16 32
Time: Second

FIG. 8F

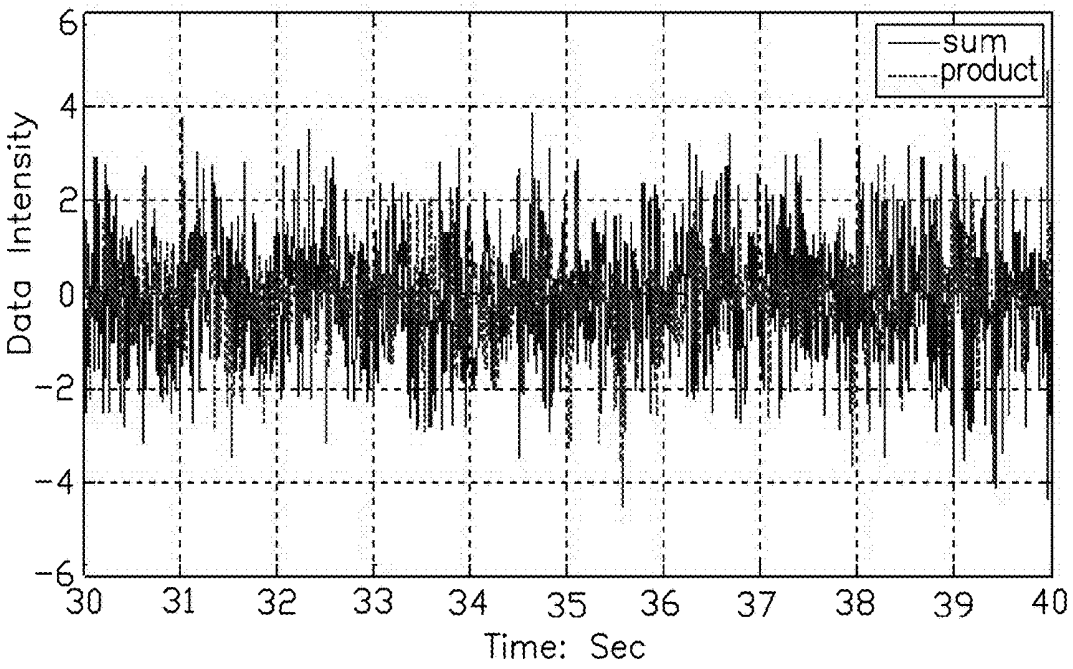

sum
product
Data Intensity
6
4
2
0
−2
−4
−6
30
31
32
33
34
35
36
37
38
39
40
Time: Sec

FIG. 9A

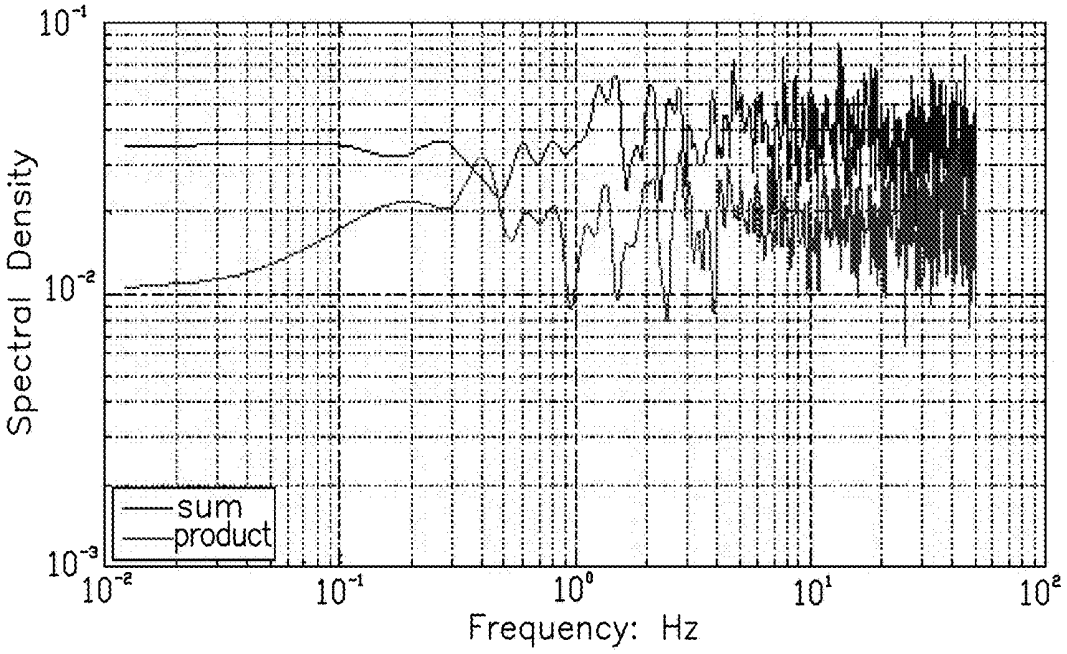

Spectral Density
10^{-1}
10^{-2}
10^{-3}
sum
product
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
Frequency: Hz

FIG. 9B

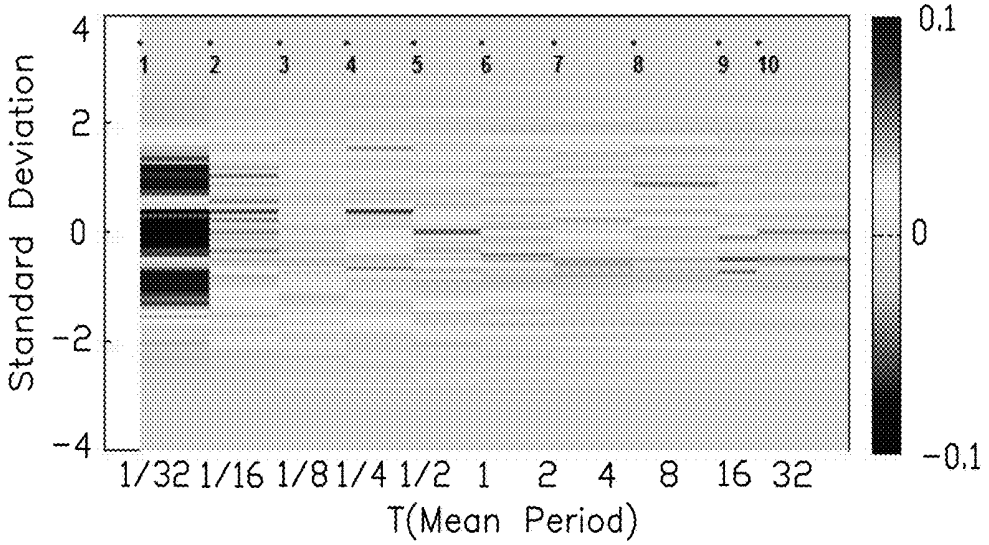


FIG. 10A

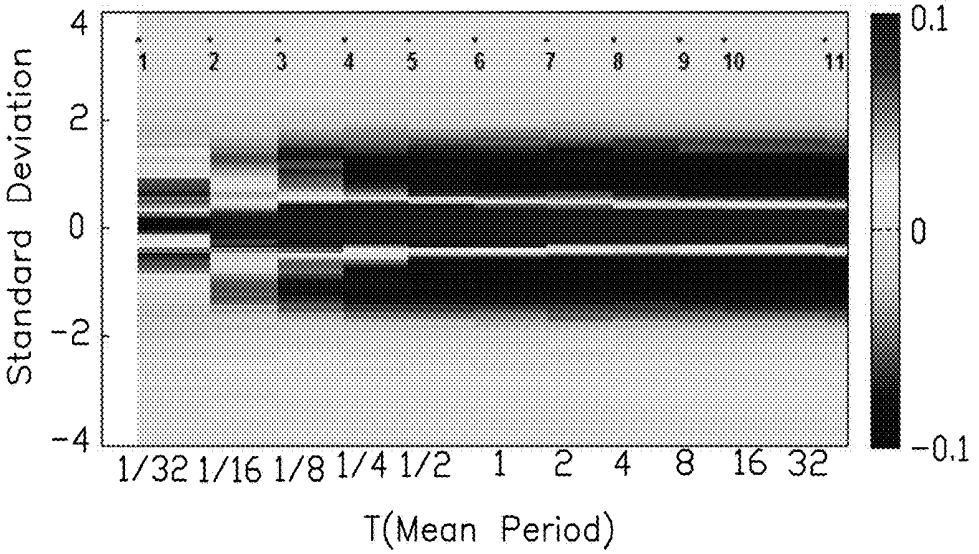


FIG. 10B

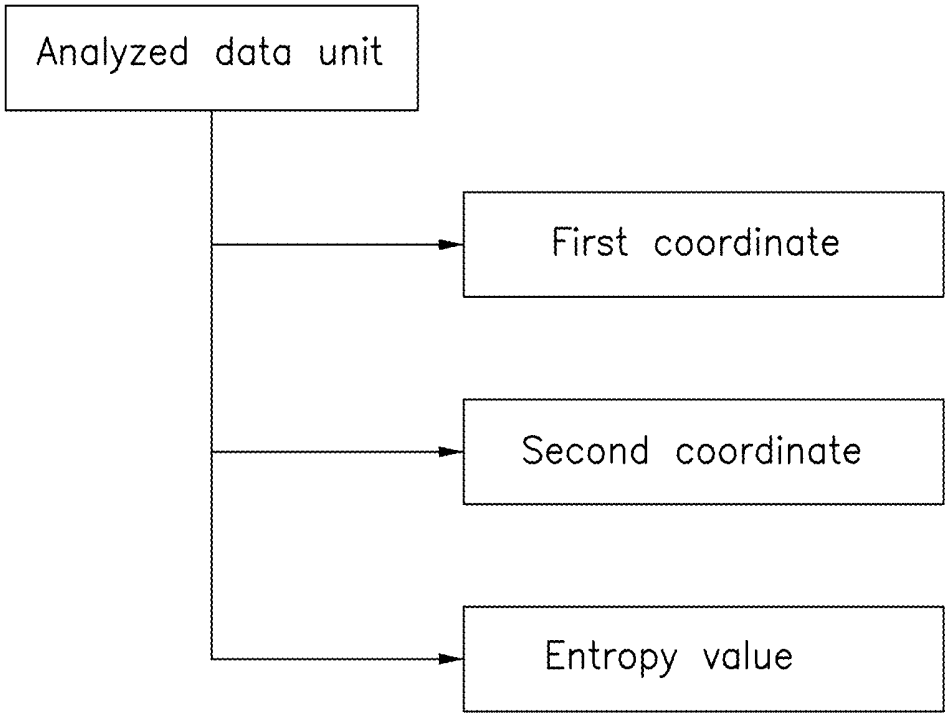

Analyzed data unit
First coordinate
Second coordinate
Entropy value

FIG. 11

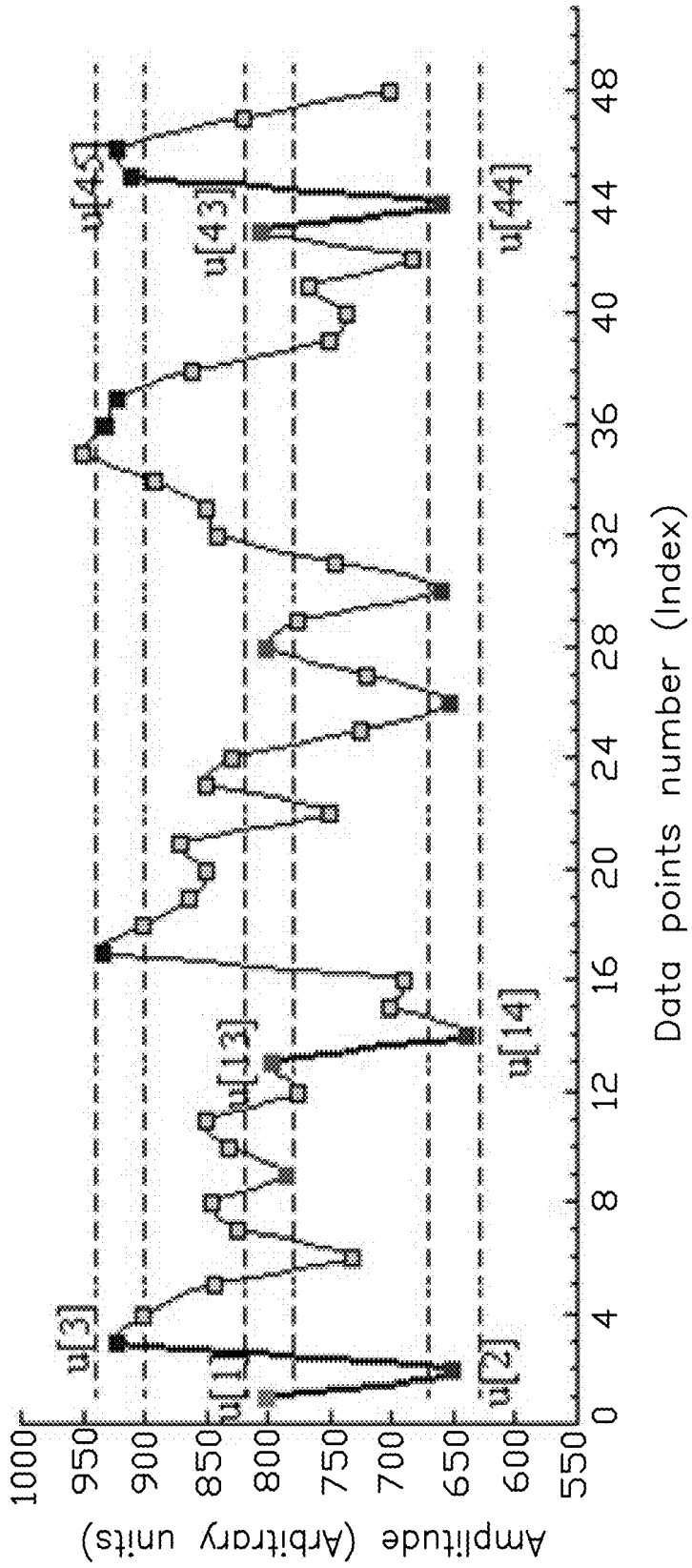

u[3]
u[1]
u[13]
u[2]
u[14]
u[43]
u[42]
u[44]
Amplitude (Arbitrary units)
Data points number (Index)
1000
950
900
850
800
750
700
650
600
550
0
4
8
12
16
20
24
28
32
36
40
44
48

FIG. 12

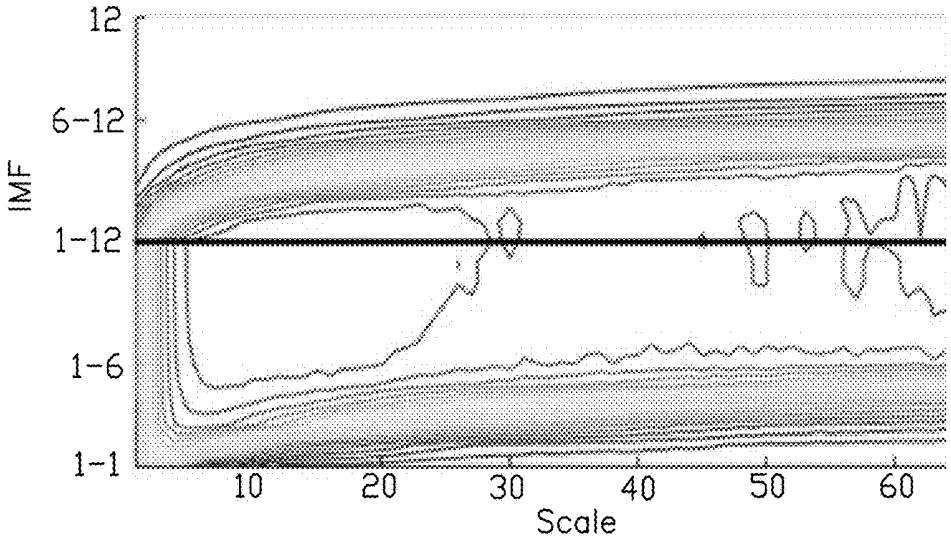


FIG. 13A

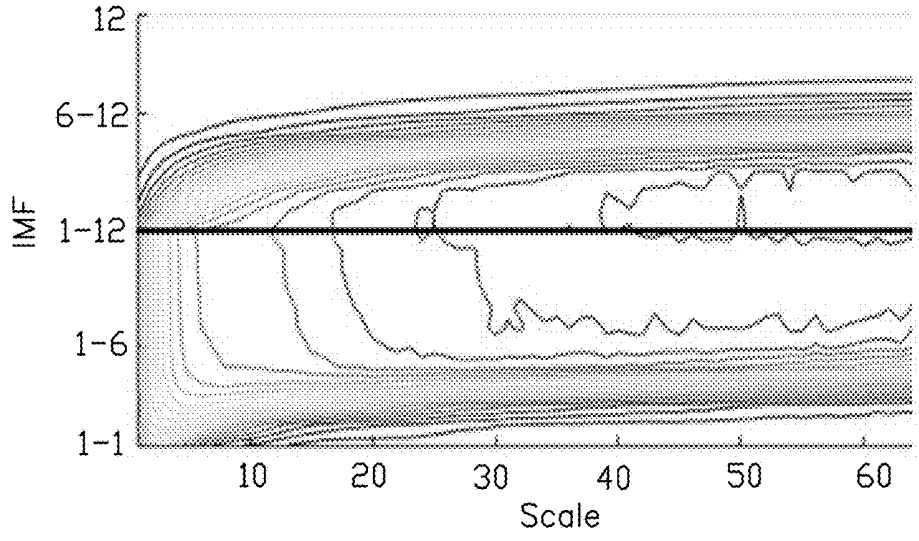


FIG. 13B

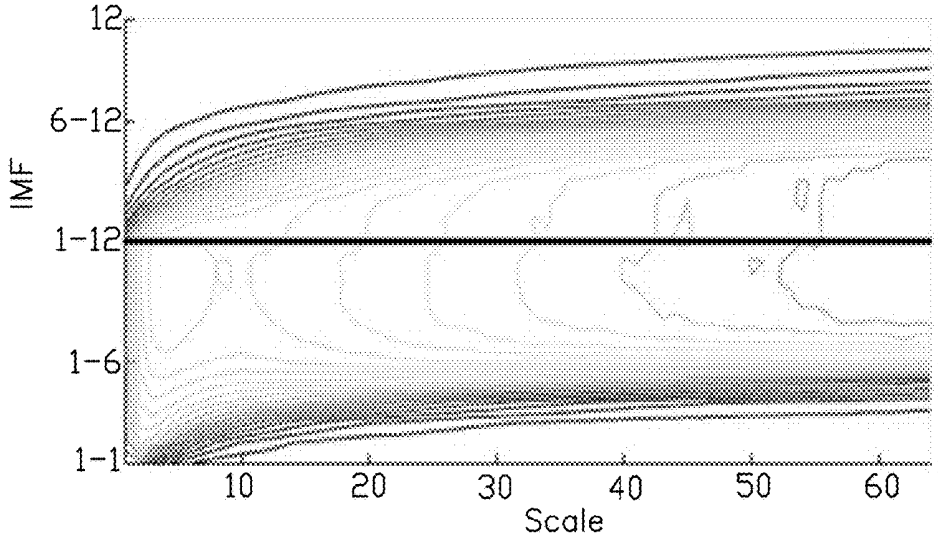


FIG. 13C

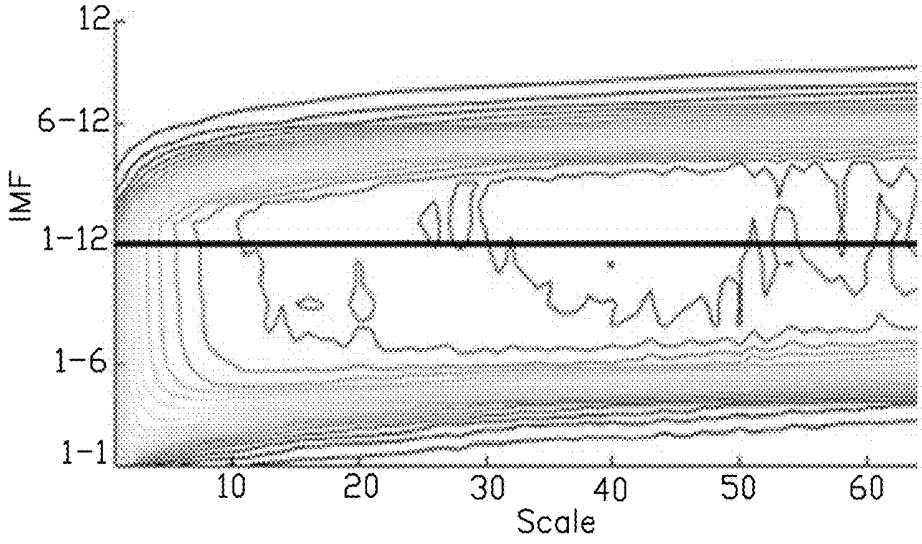


FIG. 13D

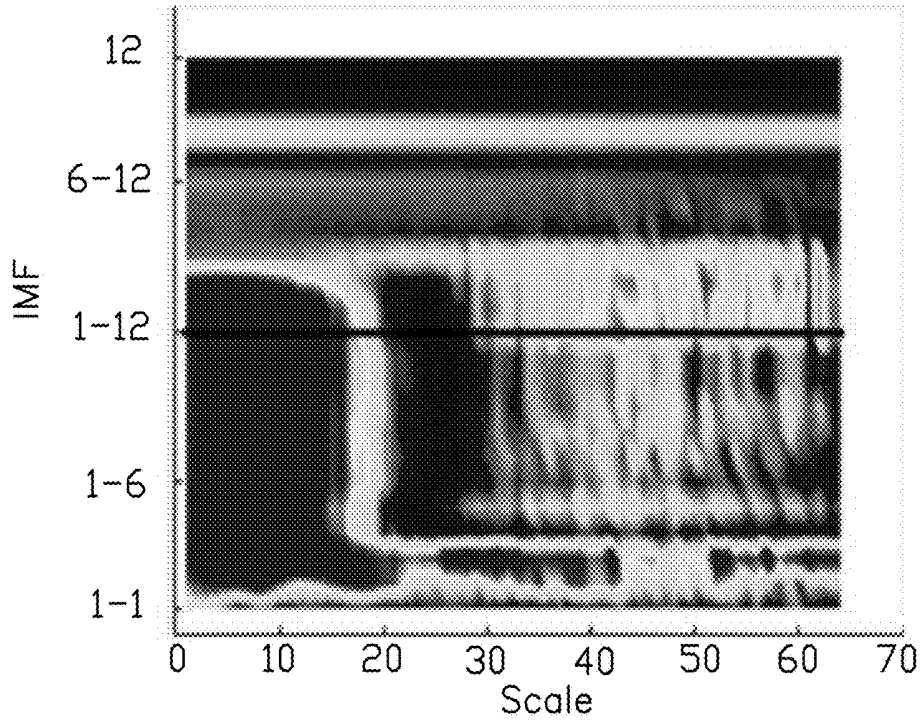


FIG. 14A

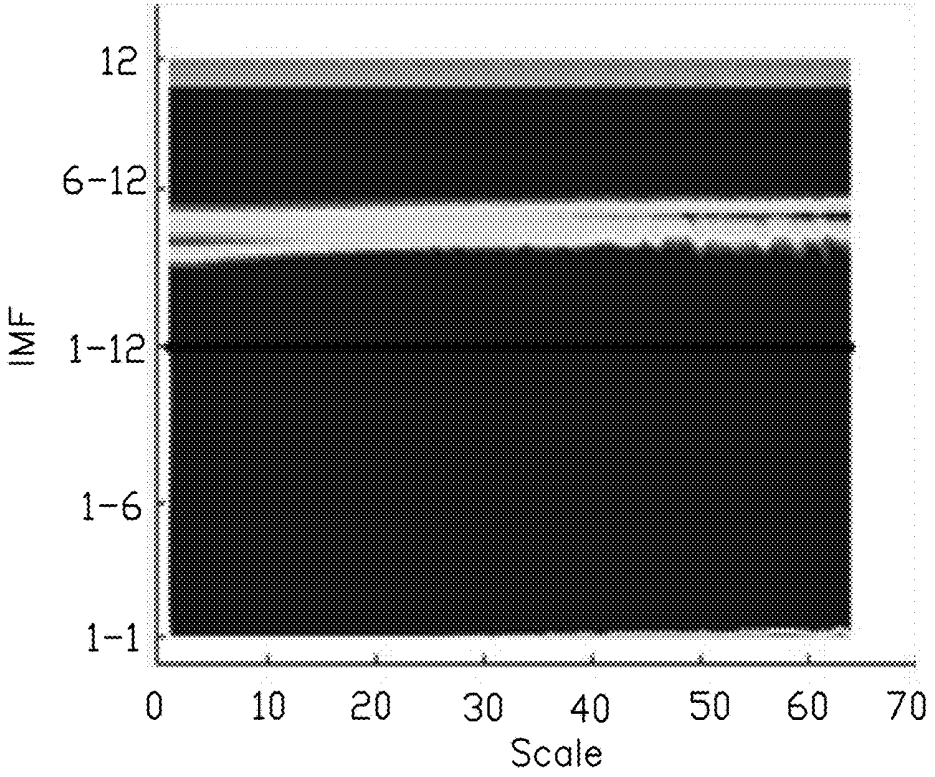


FIG. 14B

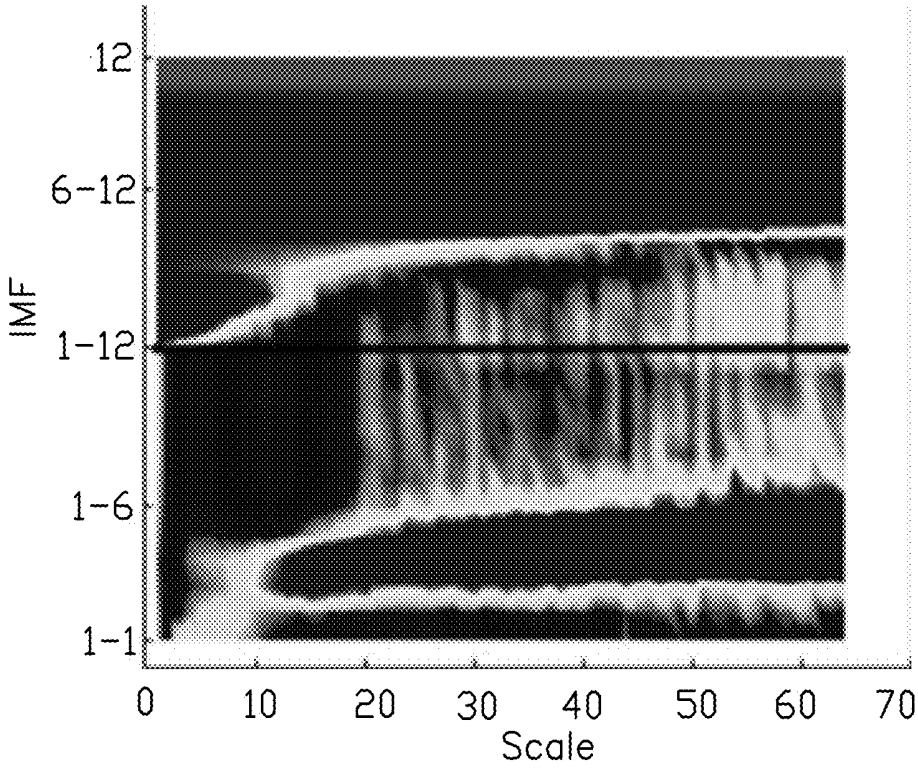


FIG. 14C

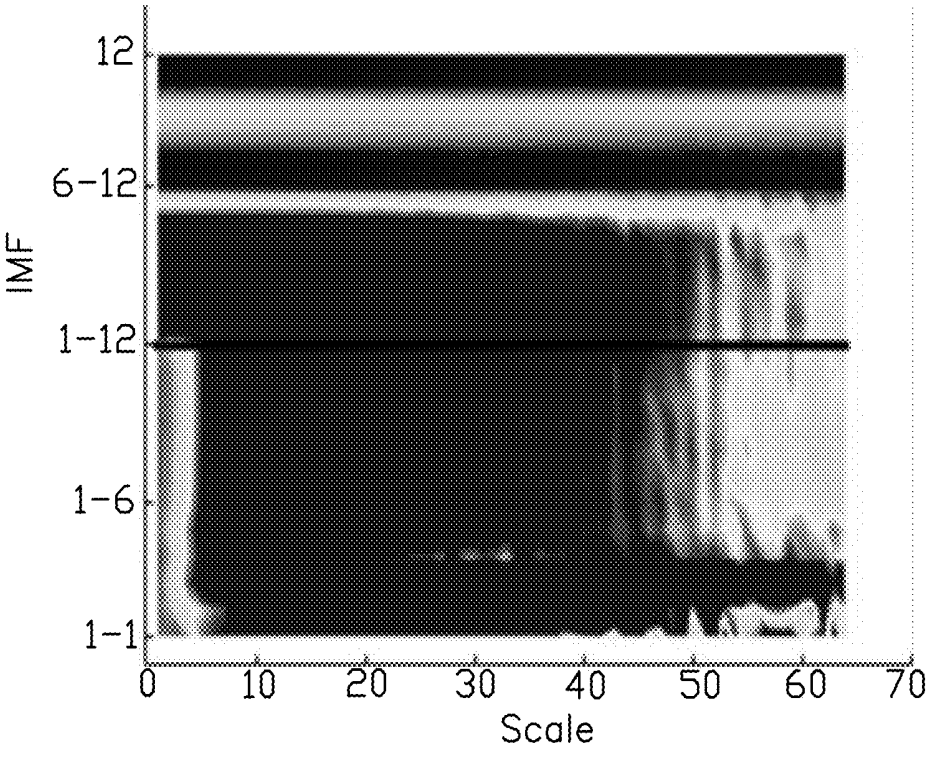


FIG. 14D

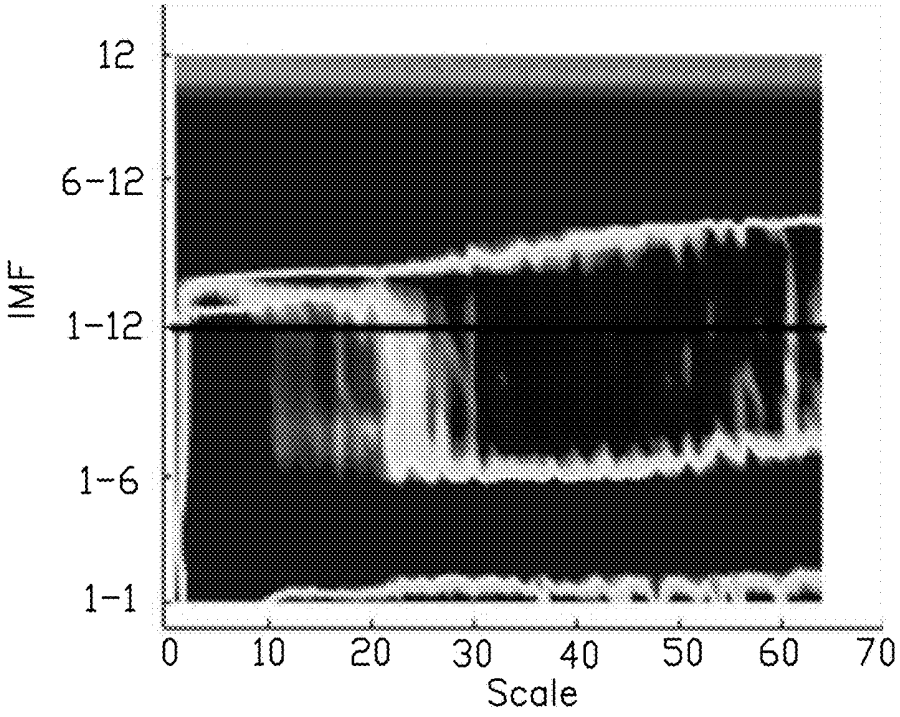


FIG. 14E

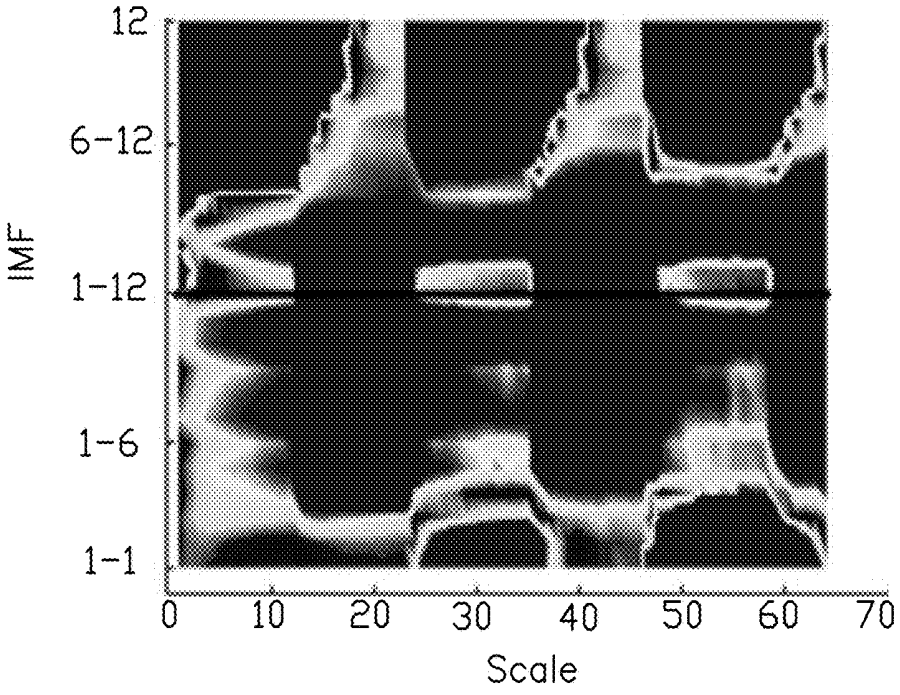


FIG. 14F

METHOD, MODULE AND SYSTEM FOR ANALYSIS OF PHYSIOLOGICAL SIGNAL

CROSS-REFERENCE TO RELATED APPLICATION

[0001] The present disclosure claims the benefit of U.S. provisional patent application No. 62/596,912, filed on Dec. 11, 2017, the entirety of which is incorporated herein by reference.

FIELD

[0002] The present disclosure is generally related to the method, module and system for analysis of physiological signal. More particularly, the present disclosure is directed to a method, module and system for analysis of electrical activities of the cardiovascular system.

BACKGROUND

[0003] Physiological signals provide valuable information for evaluation, diagnosis, or even prediction of physical conditions of a living organism. Each type of physiological signals obtained from a living organism represents the status of a particular system of the living organism.

[0004] Various physiological signals can be obtained from a living organism, including but not limited to: electrocardiography (EKG) signals, electromyography (EMG) signals, electroretinography (ERG) signals, blood pressure, pulse oximetry (SpO_2) signals, body temperature, and spirometry signals. A plurality of metrics can be obtained from measurement of one or more physiological signals, including but not limited to: electric current, electric impedance, pressure, flow rate, temperature, vibration, breath rate, weight, pulse amplitude, pulse wave velocity, or frequency of physiological events. Also, the metrics can be recorded in a time varying fashion. Metrics can be measured by one or more devices and then stored as the physiological signals. The physiological signals can be further processed into quantitative or qualitative information that are important in clinical evaluation, diagnosis, staging or prognosis.

[0005] Physiological signals may be presented by a graph with signal strength or power over time, such as EKG or EMG. However, in frequencies or wave characteristics shown in the graph, noise or disturbances are considered as irrelevant information when conducting analysis of acquired metrics. Moreover, wave patterns hidden in the acquired metrics could be a reference for clinical evaluation, diagnosis, staging or prognosis. Thus, signal processing is a vital part for visualizing and extracting useful information from physiological measurements.

[0006] The non-stationary and non-linear nature of many physiological wave signals pose significant obstacles for signal processing. Conventional approaches for signal processing of physiological wave signals have failed to provide an effective solution to the obstacles. For instance, Fourier transformation are often used to interpret linear and stationary wave signals, such as spectrum analysis; however, due to its mathematical nature and probability distribution, Fourier transformation is unable to provide meaningful visualization results from non-stationary and non-linear wave signals.

[0007] Another conventional approach for signal analysis is the probability distribution function. The probability distribution function is another tool for study non-deterministic phenomena. Nevertheless, the signals described by conventional probability distribution function need to be stationary and with large amplitude variations. Conventional probability distribution function is unable to provide insights from non-stationary and non-linear wave signals.

[0008] The Holo-Hilbert spectral analysis (HOSA) is a tool for visualizing non-stationary and non-linear waves. The mathematics behind HOSA has been summarized in Huang et al (Huang, N. E., Hu, K., Yang, A. C., Chang, H. C., Jia, D., Liang, W. K., Yeh, J. R. Kao, C. L., Juan, C. H., Peng, C. K. and Meijer. J. H. (2016). On Holo-Hilbert spectral analysis: a full informational spectral representation for nonlinear and non-stationary data. *Phil. Trans. R. Soc. A,* 374(2065)). HOSA adopts some of the mathematical methodologies of Hilbert-Huang transformation when analyzing non-stationary and non-linear waves. However, the application of HOSA on analysis of EKG signals has never been explored and exploited.

[0009] Due to the lack of adequate signal processing tools, data associated with acquired physiological signals often need to be analyzed by trained professionals, in addition to available algorithms or software embedded instruments. Physiological measurement data could be massive in terms of their quantity and complexity. For instance, a Holter monitor can generate EKG data of an individual continuously for 24 hours. The complexity and amount of the acquired 24-hour EKG data are overwhelming even for well-trained professionals, therefore increasing the chances of missed detection or misinterpretation of EKG deviation or abnormal EKG signals.

[0010] Given the non-linear and non-stationary nature, and the inherent complexity and quantity of physiological signals of the cardiovascular system, there is a need for an efficient and intuitive mean for analysis and visualization of EKG. Specifically, a novel probability distribution function and a multiscale entropy generated by HOSA are proposed in the present disclosure to reveal the subtlety and nuance of the variations in physiological signals.

SUMMARY OF THE INVENTION

[0011] It is an object of the present disclosure to provide HOSA-based methods and systems for analysis of physiological signals of the cardiovascular system.

[0012] It is an object of the present disclosure to provide one or more visual outputs of electrocardiography (EKG) signals, electromyography (EMG) signals, or blood pressure signals.

[0013] It is also an object of the present disclosure to provide one or more visual outputs of abnormal EKG, EMG, or blood pressure.

[0014] It is also an object of the present disclosure to provide one or more visual outputs to compare physiological signals of the cardiovascular system in different groups of subjects, different subjects, or different time intervals of the same subjects.

[0015] It is also an object of the present disclosure to provide applications of HOSA in diagnosis of cardiovascular system diseases.

[0016] An embodiment of the present disclosure provides a non-transitory computer program product embodied in a computer-readable medium, and when executed by one or more analysis module, providing a visual output for presenting physiological signals of a cardiovascular system. The non-transitory computer program product comprises a

first axis representing subsets of intrinsic mode functions (IMFs); a second axis representing a function of signal strength in a time interval; and a plurality of visual elements, each of the visual elements being defined by the first axis and the second axis, and each of the visual elements comprising a plurality of analyzed data units collected over the time interval. Wherein each of the analyzed data units comprises a first coordinate, a second coordinate, and a probability density value generated from an intrinsic probability density function of one of the subsets of IMFs, the first coordinate is one of the subsets of IMFs, and the second coordinate is an argument of the function of signal strength.

[0017] In a preferred embodiment, the second axis is a standard deviation or a z-value of the signal strength in the time interval.

[0018] In a preferred embodiment, the probability density value is generated from a subset of primary IMFs of secondary IMFs, each of the primary IMFs is generated from an empirical mode decomposition (EMD) of a plurality of the physiological signals, and each of the secondary IMFs is generated from an EMD of the primary IMF.

[0019] In a preferred embodiment, the physiological signals are EKG signals, EMG signals, or blood pressure signals.

[0020] In a preferred embodiment, the probability density value is indicated by different colors, grayscales, dot densities, contour lines, or screentones.

[0021] Another embodiment of the present disclosure provides a system for analyzing the physiological signals of the cardiovascular system. The system comprises a detection module for detecting the physiological signals of the cardiovascular system; a transmission module for receiving the physiological signals from the detection module and transmitting the physiological signals to the analysis module; and analysis module for generating a plurality of analyzed data sets from the physiological signals, each of the analyzed data sets comprising a plurality of analyzed data units; and a visual output module for rendering a visual output space according to the analyzed data sets generated by the analysis module, and displaying a visual output. Wherein the visual output comprises a first axis representing subsets of intrinsic mode functions (IMFs), a second axis representing a function of signals strength in a time interval, and a plurality of visual elements defined by the first axis and the second axis, and each of the visual elements comprises a first coordinate, a second coordinate, and a probability density value generated by an intrinsic probability density function of one of the subsets of IMFs, the first coordinate is one of the subsets of IMFs, and the second coordinate is an argument of the function of signal strength.

[0022] Another embodiment of the present disclosure provides a non-transitory computer program product embodied in a computer-readable medium, and when executed by one or more analysis modules, providing a visual output for presenting physiological signals of a cardiovascular system. The non-transitory computer program product comprises a first axis representing a scale of intrinsic multiscale entropy (iMSE); a second axis representing cumulative IMFs; and a plurality of visual elements, each of the visual elements being defined by the first axis and the second axis, and each of the visual elements comprising an analyzed data unit collected over a time interval. Wherein each of the analyzed data units comprises a first coordinate of the first axis, a second coordinate of the second axis, and an iMSE value generated from the IMFs.

[0023] In a preferred embodiment, the IMFs are a set of primary IMFs or a set of secondary IMFs, each of the primary IMFs is generated from an EMD of a plurality of the physiological signals, and each of the secondary IMFs is generated from an EMD of the primary IMF.

[0024] In a preferred embodiment, the iMSE value is indicated by different colors. grayscales, dot densities, contour lines, or screentones.

[0025] Another embodiment of the present disclosure provides a system for analyzing the physiological signals of the cardiovascular system. The system comprises a detection module for detecting the physiological signals of the cardiovascular system; a transmission module for receiving the physiological signals from the detection module and transmitting the physiological signals to the analysis module; an analysis module for generating a plurality of analyzed data sets from the physiological signals, each of the analyzed data sets comprising a plurality of analyzed data units; and a visual output module for rendering a visual output space according to the analyzed data sets generated by the analysis module, and displaying a visual output. Wherein the visual output comprises a first axis representing a scale of iMSE. a second axis representing cumulative IMFs, and a plurality of visual elements defined by the first axis and the second axis, and each of the visual elements comprising an analyzed data unit collected over a time interval and each of the analyzed data units comprises a first coordinate of the first axis, a second coordinate of the second axis, and an iMSE value generated from the IMFs.

BRIEF DESCRIPTION OF THE DRAWINGS

[0026] Implementations of the present technology will now be described, by way of examples only, with reference to the attached figures.

[0027] FIG. **1** is a schematic diagram of a system for analyzing physiological signals in accordance with an embodiment of the present disclosure.

[0028] FIG. **2** is a flow diagram of a method for analyzing physiological signals in accordance with an embodiment of the present disclosure.

[0029] FIG. **3** is a flow diagram of a method for analyzing EKG signals in accordance with an embodiment of the present disclosure.

[0030] FIG. **4** is a flow diagram of a method for analyzing blood pressure in accordance with an embodiment of the present disclosure.

[0031] FIG. **5**A is a flow diagram of transforming electrical activity signals into a set of primary intrinsic mode functions (IMFs); FIG. **5**B is a flow diagram of an interpolation process; FIG. **5**C is a flow diagram of empirical mode decomposition (EMD); FIG. **5**D is a flow diagram of secondary IMFs generated from envelope functions; FIG. **5**E is a flow diagram of transforming primary IMFs into frequency modulation (FM) functions; and FIG. **5**F is a flow diagram of transforming secondary IMFs into amplitude modulation (AM) functions, in accordance with embodiments of the present disclosure.

[0032] FIG. **6** is a schematic diagram of an analyzed data unit in accordance with an embodiment of the present disclosure.

[0033] FIG. **7** is a conventional probability density function of white noise. Gaussian noise. the sum of the white noise and Gaussian noise, and the product of the white noise and Gaussian noise.

[0034] FIG. **8**A-**8**F are visual outputs of intrinsic probability density functions (iPDF) of the white noise, Gaussian noise, the sum of the white noise and Gaussian noise, and the product of the white noise and Gaussian noise, in accordance with embodiments of the present disclosure.

[0035] FIG. **9**A is a conventional time-intensity chart of additive and multiplicative effects of the product and sum of the white noise; FIG. **9**B is a conventional Fourier spectra of additive and multiplicative effects of the product and sum of the white noise.

[0036] FIG. **10**A-**10**B are visual outputs of iPDF of the product and sum of the white noise, in accordance with an embodiment of the present disclosure.

[0037] FIG. **11** is a schematic diagram of another analyzed data unit in accordance with an embodiment of the present disclosure.

[0038] FIG. **12** is a graph of data points numbers and amplitude.

[0039] FIG. **13**A-**13**D are iMSE representations of different groups with different disease states or different ages, in accordance with an embodiment of the present disclosure.

[0040] FIG. **14**A-**14**F are iMSE representations of contrasts between different groups shown in FIG. **13**A-**13**D, in accordance with an embodiment of the present disclosure.

DETAILED DESCRIPTION

[0041] It will be noted at the beginning that for simplicity and clarity of illustration, where appropriate, reference numerals have been repeated among the different figures to indicate corresponding or analogous elements. In addition, numerous specific details are set forth in order to provide a thorough understanding of the embodiments described herein. However, it will be understood by those of ordinary skill in the art that the embodiments described herein can be practiced without these specific details. In other instances, methods, procedures and components have not been described in detail so as not to obscure the related relevant feature being described. The drawings are not necessarily to scale and the proportions of certain parts may be exaggerated to better illustrate details and features. The description is not to be considered as limiting the scope of the embodiments described herein.

[0042] Several definitions that apply throughout this disclosure will now be presented.

[0043] The term "coupled" is defined as connected, whether directly or indirectly through intervening components, and is not necessarily limited to physical connections. The connection can be such that the objects are permanently connected or releasably connected. The term "comprising," when utilized, means "including, but not necessarily limited to"; it specifically indicates open-ended inclusion or membership in the so-described combination, group, series and the like.

[0044] Referring to FIG. **1**, a system for analyzing the physiological signals in accordance with an embodiment of the present disclosure is provided. The system **1** comprises a detection module **10**, a transmission module **20**, an analysis module **30** and a visual output module **40**. The system **1** is configured to detect physiological signals, to analyze physiological signals and to display graphical information of the analyzed results. The physiological signal may include but not limited to: EKG signals, EMG signals, ERG signals, blood pressure, pulse oximetry signals, body temperature, and spirometry signals. It is contemplated that the system **1** may further comprise other electrical components or modules for better performance or user experience. For example, the system **1** may comprise an amplifier module or filter module to enhance signal to noise ratio by gaining signal strength within certain bandwidth and minimizing noise from environmental interference or baseline wandering. For example, the system **1** may comprise an analog-to-digital converter (ADC) for signal digitization. For example, the system **1** may further comprise a storage module for storing the digital signals or storing the analyzed data. In one example, the detection module **10** may further comprise a data acquisition module. The data acquisition module is capable of executing the functions of the amplifier module, ADC and the storage module. Furthermore, the system **1** may comprise a user input module for use to control the system **1**, such as a keyboard, a mouse, a touch screen, or a voice control device.

[0045] The detection module **10** is configured to receive the physiological signals and to convert the physiological signals into electrical signal. The detection module **10** may convert cardiovascular activities, skeletal muscle activities, or blood pressure into electrical signals. The detection module **10** may comprise one or more sensing components, and the sensing component can be a transducer or a blood pressure meter. The transducer may be a biopotential electrode to detect the electrical potentials or a magnetoelectric transducer to detect the magnetic fields. The blood pressure meter may be an oscillometric monitoring equipment. It is contemplated that a ground electrode may be paired with the biopotential electrodes for measuring electrical potential differences and additionally a reference electrode may be presented for noise reduction. The detection module **10** may be applied on the surface of one or more specified regions of the living organism for the detection of specific physiological signals. The specified regions may include but not limited to: the chest for EKG, the skin above the skeletal muscle for EMG, or the skin above the vein for blood pressure. In one example, the detection module **10** comprises at least 10 biopotential electrodes being positioned on the limbs and the chest of the human body. The biopotential electrodes could be wet (with saline water or conducting gels) or dry electrodes.

[0046] The transmission module **20** is configured to receive the electrical signals from the detection module **10** and deliver the signals to the analysis module **30**. The transmission module **20** may be wired or wireless. The wired transmission module **20** may include an electrical conductive material delivering the detected signal directly to the analysis module **30** or to the storage module for processing by the analysis module **30** thereafter. The detected signal may be stored in a mobile device, a wearable device or transmitted wirelessly to a data processing station through RF transmitters, Bluetooth, Wi-Fi or the internet. The mobile device can be a smartphone, a tablet computer. or a laptop. The wearable device can be a processor-embedded wristband, a processor-embedded headband, a processor-embedded cloth, or a smartwatch. It is contemplated that the modules of the system **1** may be electrically coupled within a compact device or may be located discretely and coupled together by wired or wireless communication network.

[0047] The analysis module **30** is configured to process the signal by a series of steps. The analysis module **30** may be a single microprocessor, such as a general purpose central processing unit, an application specific instruction set processor, a graphic processing unit. a field-programmable gate array, a complex programmable logic device or a digital signal processor. The analysis module **30** comprises a non-transitory computer program product embodied in a computer-readable medium. The non-transitory computer program product can be a computer program, an algorithm, or codes that can be embodied in the computer-readable medium. The analysis module **30** may comprise multiple microprocessors or processing units to execute the non-transitory computer program product embodied in the computer-readable medium, in order to perform different functional blocks of the entire analysis process.

[0048] The visual output module **40** is configured to display the graphical results of the information generated by the analysis module **30**. The visual output module **40** may be a projector, a monitor, or a printer for projecting the analysis results. In the examples, the analysis result is a visual output with graphic representations, and can be displayed by the visual output module **40** on a color monitor, be printed out on a paper or an electronic file, or be displayed on a grayscale monitor.

[0049] Referring to FIG. **2**, a method for analyzing the physiological signals in accordance with an embodiment of the present disclosure is provided. The method for analyzing the physiological signals may include the steps as mentioned below. The method comprises: detecting the physiological signals as a detected signal S**21**, performing empirical mode decomposition (EMD) on the detected signal to obtain a set of primary intrinsic mode functions (IMFs) S**22**. creating envelope functions of the corresponding of IMF **523***a*, performing EMD on the envelope functions to obtain sets of secondary IMF **524**, performing a transformation on the plurality of primary IMFs to obtain the frequency modulation (FM) functions S**23***b*, performing a transformation on the plurality of secondary IMFs to generate the AM function S**25**, generating data set according to the FM function and the AM function S**26**, generating a visual output space S**27**. The EMD in S**22** can be complete ensemble empirical mode decomposition (CEEMD), ensemble empirical mode decomposition (EEMD), masking EMD, enhanced EMD, multivariate empirical mode decomposition (MEMD), noise-assisted multivariate empirical mode decomposition (NA-MEMD). The transformation in S**23***b* and S**25** can be Hilbert transform, Direct quadrature, inverse trigonometric function, or generalized zero-crossing.

[0050] Detecting the physiological signals as one or more detected signals S**21** is performed at the detection module. Referring to FIG. **3**, the physiological signal may be EKG signals, in accordance with an embodiment of the present disclosure. Referring to FIG. **4**, the physiological signal may be blood pressure, in accordance with an embodiment of the present disclosure. In one example, the detected signal may be acquired and stored by the data acquisition module in the form of electrical potential (preferably measured by voltage) with corresponding temporal sequences. The detected signal may be stored as a detected data set comprising a plurality of detected data units and each detected data unit comprises at least a signal strength and a time interval. A sampling rate of the data acquisition module may determine a time interval of adjacent data. As illustrated in FIG. **1**, the analysis module **30** generates the analyzed data set from the detected signal and the analyzed data set may be stored in the storage module for visual output module **40** thereafter. The analyzed data set comprises a plurality of analyzed data units.

[0051] The processes S**22**, S**23***a*, S**23***b*, S**25**, S**32**. S**33***a*, S**33***b*, S**35**, S**42**, S**43***a*, S**43***b*, and S**45** are further elaborated in FIG. **5**A to FIG. **5**F, in accordance with embodiments of the present disclosure. The detected signals are consequently transformed or decomposed into primary IMFs, secondary IMFs. envelope functions, AM functions, and FM functions.

[0052] Referring to FIG. **5**A, a plurality of EMDs for detected signals are provided in accordance with an embodiment of the present disclosure. The detected signal is transformed into a set of primary IMFs by EMDs. The plurality of EMDs in FIG. **5**A correspond to S**22** of FIG. **2**, S**32** of FIG. **3**, or S**42** of FIG. **4**. The EMD is a process comprising a series of sifting process to decompose a signal into a set of IMFs. For example, a plurality of primary intrinsic functions is generated from the detected signal by EMD. A sifting process generates an intrinsic function from the detected signals. For example, a first sifting process generates a first primary IMF **51***b* from the detected signal **51***a*; a second sifting process generates a second primary IMF **51***c* from the first primary IMF **51***b*; a third sifting process generates a third primary IMF **51***d* from the second primary IMF **51***c*; a mth sifting process generates a mth primary IMF **51***n* from the (m−1)th primary IMF **51***m*. The number of sifting processes is determined by stopping criteria. The stopping criteria may depend on the signal attenuation or the variation of the mth primary IMF **51***n*.

[0053] Furthermore, EMD may comprise masking procedure or noise (even pairs of positive and negative values of the same noise) addition procedure with variable magnitude adapted for each sifting step to solve mode mixing problems. It is contemplated that EMD may be achieved by ensemble techniques.

[0054] Referring to FIG. **5**B, a plurality of interpolation processes is provided in accordance with an embodiment of the present disclosure. The interpolation processes in FIG. **5**B correspond to S**23***a* in FIG. **2**, S**33***a* in FIG. **3**, or S**43***a* in FIG. **4**. An envelope function is the interpolation function generated by an interpolation process from detected signals. The envelope function connects local extrema of the detected signals. Preferably, the envelope connects the local maxima of the absolute-valued function of the detected signals. The interpolation process may be achieved via linear interpolation, polynomial interpolation, trigonometric interpolation or spline interpolation, preferably cubic spline interpolation. The envelope functions in FIG. **5**B are generated from IMFs in FIG. **5**A by the interpolation processes. A first envelope function **52***a* may be generated from the first primary IMF **51***a*; a second envelope function **52***b* may be generated from the second primary IMF **51***b*; a third enveloped function **53***b* may be generated from the third primary IMF **53***a*; a (m−1)th envelope function **52***m* may be generated from the (m−1)th primary IMF **51***m*; a mth envelope function **52***n* may be generated from the nth primary IMF **51***n*.

[0055] Referring to FIG. **5**C, a plurality of EMDs is provided in accordance with an embodiment of the present disclosure. The plurality of sets of secondary intrinsic functions are generated from the envelope functions by EMD. The EMDs in FIG. **5**C correspond to S**24** in FIG. **2**, S**34***a* in FIG. **3**, or S**44***a* in FIG. **4**. The first set of secondary IMFs

53*a* is generated from the first envelope function **52***a*; the second set of secondary IMFs **53***b* is generated from the second envelope function **52***b*; the (m−1)th set of the plurality of secondary IMFs **53***m* is generated from the (m−1)th envelope function **52***m*; the mth set of the plurality of secondary IMFs **53***n* is generated from the mth envelope function **52***n*.

[0056] Referring to FIG. **5**D, a plurality of sets of secondary IMFs are provided in accordance with an embodiment of the present disclosure. The mth envelope function **52***n*, the mth set of secondary IMFs **53***n*, and the secondary IMFs included in the mth set of secondary IMFs **53***n* are illustrated in FIG. **5**D. The mth envelope function **52***n* in FIG. **5**B comprises a first secondary IMF **54***a* of the mth set of secondary IMFs **53***n*, a second secondary IMF **54***b* of the mth set of secondary IMFs **53***n*, a third secondary IMF **54***c* of the mth set of secondary IMFs **53***n*, a (n−1)th secondary IMF **54***m* of the mth set of secondary IMFs **53***n*, and a nth secondary IMF **54***n* of the mth set of secondary IMFs **53***n*. Therefore, there are IMFs in a number of m (number of the plurality of sets of secondary IMF) multiplying n (number of individual secondary IMFs in a set of secondary IMF in FIG. **5**D.

[0057] Referring to FIG. **5**E and FIG. **5**F, a series of transformation processes is provided in accordance with an embodiment of the present disclosure. The transformation process is to convert a function from real domain to complex domain. The transformation process comprises at least a transformation and a complex pair function formation. The transformation process may be a Hilbert transform, a direct-quadrature-zero transform, an inverse trigonometric function transform, or a generalized zero-crossing transform. The complex pair function formation is to combine the function as the real part of the complex pair function and the transformed function as the imaginary part of the complex pair function.

[0058] In FIG. **5**E, the FM functions are the complex pair functions generated from the plurality of primary IMFs by a proper transformation process. The transformation processes in FIG. **5**E correspond to S**23***b* in FIG. **2**, S**33***b* in FIG. **3**, or S**43***b* in FIG. **4**. The first primary IMF **51***a* is transformed into a first FM function **55***a* by the transformation process; the second primary IMF **51***b* is transformed into a second FM function **55***b* by the transformation process; the third primary IMF **51***c* is transformed into a third FM function **55***c* by the transformation process; and the mth primary IMF **51***n* is transformed into a mth FM function **55***n* by the transformation process.

[0059] In FIG. **5**F, the AM functions are the complex pair functions generated from the secondary IMFs by a series of transformation processes. The transformation processes in FIG. **5**F correspond to S**25** in FIG. **2**, S**35** in FIG. **3**, or S**45** in FIG. **4**. The first secondary IMF **54***d* of the first set of secondary IMFs may be transformed into a (1,1) AM function **56***d* by the transformation process; the second secondary IMF **54***e* of the first set of secondary IMFs is transformed into a (1,2) AM function **56***e* by the transformation process . . . and the nth secondary IMF **54***k* of the first set of the secondary IMFs is transformed into a (1, n) AM function **56***k* by the transformation process. Furthermore, the nth secondary IMF **54***n* of the mth set of secondary IMFs may be transformed into a (m, n)th AM function **56***n* by the transformation process.

[0060] Referring to FIG. **5**G, components of an analyzed data unit is provided in accordance with an embodiment of the present disclosure. In FIG. **5**G, the analyzed data unit **31** comprises a time interval **32**, a first coordinate **33**, a second coordinate **34** and a signal strength value **35**. In one embodiment, the time interval **32** is a period of time when the detection module detects the physiological signals, the first coordinate **33** indicates instantaneous frequency of FM measured by frequency (Hertz), and the second coordinate **34** indicates instantaneous frequency of AM measured by frequency (Hertz). The signal strength value **35** may indicate signal amplitude measured by electrical potential (voltage) or electrical current (ampere) or may indicate signal energy measured by energy strength per unit time interval (watt). For each analyzed data unit within the time interval, the first coordinate **33** can be the argument of the mth FM functions **55***n* in FIG. **5**E at corresponding time interval; the second coordinate **34** can be the argument of the (m, n)th AM function **56***n* in FIG. **5**F at corresponding time interval; the signal strength value **35** is the value of the envelope function at corresponding time interval. Preferably, the second coordinate **34** is larger than the first coordinate **33**.

[0061] Referring to FIG. **6**, elements of an analyzed data unit is provided in accordance with an embodiment of the present disclosure. In FIG. **6**, the analyzed data unit **60** comprises a probability density value **63**, a first coordinate **61** and a second coordinate **62**. The probability density function (PDF) is a probability density function of one subset of the IMFs. The probability density value is the probability at a specific signal strength value or at a specific instantaneous frequency. In one example, the first coordinate indicates the order number of one subset of the IMFs and the second coordinate indicates the signal strength value. In another example, the first coordinate indicates the z-value and the second coordinate indicates the instantaneous frequency. The subset of IMFs may comprise one IMF component or the combination of at least two different IMF components. The signal strength value may indicate signal amplitude measured by electrical potential (voltage) or electrical current (ampere) or may indicate signal energy measured by energy strength per unit time interval (watt). In some examples, the instantaneous frequency or the specific signal strength value may be centralized by mean and normalized by standard deviation.

[0062] The visual output space comprising a first axis, a second axis and a plurality of visual elements. Each visual elements may include one or more analyzed data units within a certain range formed by the subsets of IMFs and the probability density value. The visual output module renders visual output space according to the analyzed data set. It is contemplated that a smoothing process may be applied to the visual output space for those visual elements with sparse data units.

[0063] A smoothing process may be applied to the visual output space for the visual elements. The smoothing process may be Butterworth filter, exponential smoothing, Kalman filter, Kernal smoother, Laplacian smoothing, moving average or other image smoothing techniques.

[0064] Following the methods, principles and transformation processes illustrated in FIG. **2**-**4**, and FIG. **5**A-**5**F, a plurality of embodiments from physiological signals are demonstrated in FIG. **8**A-**8**D, FIG. **10**A-**10**B, FIG. **13**A-**13**D, and FIG. **14**A-**14**F.

[0065] As shown in FIG. **7**, a conventional probability density function of white noise, Gaussian noise and the sum of the white noise and Gaussian noise, and the product of white noise and Gaussian noise is provided. The white noise and Gaussian noise are generated from simulation data. The calibration used in FIG. **7** is demonstrated by using a white noise of 10,000 sample with a unity standard deviation value. A deterministic Stokes type wave is exemplified with the model: $y(t)=5*\cos[2*\pi*t/100+0.5*\sin(2*\pi*t/100)]$. FIG. **7** illustrates conventional PDFs for the white noise, the additive sum and the multiplicative products with the deterministic wave. Large amplitude of the deterministic Stoke type wave has overwhelmed the white noise to make the PDF of the sum bimodal, and the product super-Gaussian.

[0066] FIG. **8**A-**8**F and FIG. **10**A-**10**B are visual outputs of the iPDF, in accordance with one or more embodiments of the present disclosure. Each of the visual outputs in FIG. **8**A-**8**F and FIG. **10**A-**10**B comprise a first axis and a second axis. The first axis indicates the order numbers **1**-**11** of one subset of the IMFs, and each order number indicates an IMF component within a time interval. The second axis indicates signal strength values normalized by standard deviation. Each of the IMF component comprises a plurality of analyzed data units, and each of the analyzed data units comprises a probability density value, a first coordinate indicating the IMF component, and a second coordinate indicating the standard deviation. Each of the probability density values in FIG. **8**A-**8**F and FIG. **10**A-**10**B is generated from a subset of primary IMFs, and each of the primary IMFs are generated from an EMD, as illustrated in FIG. **5**A. The probability density value can also be generated from a subset of secondary IMFs, and the secondary IMFs are generated from the primary IMFs, as illustrated in FIGS. **5**B and **5**C. The grayscales of each of the analyzed data units represents the probability density value, with darker gray being probability density value of +0.1 or probability density value of −0.1, white being probability density value of 0, and intermediate grays between the above grayss being intermediate probability density values.

[0067] Additionally, the probability density value in the visual outputs of iPDF may be represented by different colors, dot density, or screentone. In one embodiment, the red color indicates probability density value of +0.1, the blue color indicates probability density value of −0.1, white color indicates probability density value of 0, and intermediate colors between the above colors indicate intermediate probability density values. In one embodiment, the dot density may be higher for a larger probability density value, and lower density for a smaller probability density value. In still another embodiment, the screentone with more grids may represent larger probability density value, and the screentone with more dots may represent smaller probability density value. Conversely, the colors, the grayscale, dot density, or screentone can have different meanings for various levels of the probability density value.

[0068] Referring to FIG. **8**A, a visual output of the iPDF of the Gaussian white noise is presented with IMF components, in accordance with an embodiment of the present disclosure. Each column is an IMF component or one of the subsets of IMFs, and each of the IMF component should have similar Fourier spectrum, but some of their iPDF could deviate drastically from the Gaussian because of the limited size of the sample, which make the last few IMFs lacks the sufficient degree of freedom. Of particular interest is the first IMF from the white noise, which represents the highest frequency waves near the Nyquist limit. Thus, each sample point is either a maximum or a minimum that makes the PDF of the first IMF decidedly bimodal.

[0069] Referring to FIG. **8**B, a visual output of the iPDF of partial sum of the white noise is presented with IMF components, in accordance with an embodiment of the present disclosure. Each subset of IMF comprises the sum of a plurality of IMFs. In FIG. **8**B, the distributions plotted as a function of the time scale is uniformly Gaussian, except the first IMF is bimodal. The minor deviation shown here is the fluctuation due to the size of the sampling. Larger sample would produce smoother results as dedicated by the probability law. In FIG. **8**B, the results indeed confirm the expectation for a white noise data, except the first IMF component.

[0070] Referring to FIG. **8**C, a visual output of the iPDF of the sum of the white noise and the deterministic Stokes type wave is presented with IMF components, in accordance with an embodiment of the present disclosure. The deterministic wave signal has a bimodal distribution. Other components in FIG. **6**C are still near Gaussian, except that EMD leakage had caused some fluctuations.

[0071] Referring to FIG. **8**D, a visual output of the iPDF of the partial sum of the white noise and the deterministic Stokes type wave is presented with IMF components, in accordance with an embodiment of the present disclosure. In FIG. **6**D, the distribution for the first IMF is still bimodal; the next three partial sums are nearly Gaussian as expected. The distribution changes abruptly at the fifth partial sum, when the deterministic Stokes type wave comes into the sum. As its magnitude is overwhelming, all the partial sums thereafter are all identically bimodal.

[0072] Referring to FIG. **8**E, a visual output of the iPDF of the product of the white noise and the deterministic Stokes type wave is presented with IMF components, in accordance with an embodiment of the present disclosure. The iPDF is similar to the iPDF of white noise as shown in FIG. **8**A except that the PDF of the first IMF is no longer bimodal. The modulation of a deterministic Stokes type wave has modified the range of the amplitude of the three point waves and render them nearly Gaussian distributed. The modulation effect on all the other IMFs is to make the next three IMFs slightly super-Gaussian.

[0073] Referring to FIG. **8**F, a visual output of the iPDF of the product of the white noise and the deterministic Stokes type wave is presented with IMF components, in accordance with an embodiment of the present disclosure. The iPDF are all highly super-Gaussian through all the time scales. The drastic difference between the additive and the multiplicative processes is clear: linear additive processes is simply superposition without any interactions between the wave and the white noise. The influence of the deterministic wave may show up when the scale reach the wave period locally. The multiplicative process may influence all the IMF components globally. Also, the multiplicative process may produce a global super-Gaussian distribution.

[0074] Referring to FIG. **9**A, the additive and multiplicative effects of two Gaussian distributed white noise signals are presented. It is difficult to distinguish between the additive and multiplicative processes by the morphology of the signals presented in time domain.

[0075] Referring to FIG. **9**B, the Fourier spectra of the additive and multiplicative effects of two Gaussian distrib-

uted white noise signals are presented. Both spectra have a white spectral form. Therefore, from the Fourier spectral form, it is difficult to tell the difference between additive and multiplicative processes.

[0076] Referring to FIG. **10**A, a visual output of the iPDF of the additive effects of two Gaussian distributed white noise signals are presented, in accordance with an embodiment of the present disclosure. The distribution is Gaussian except the first IMF.

[0077] Referring to FIG. **10**B, a visual output of the iPDF of the multiplicative effects of two Gaussian distributed white noise signals are presented, in accordance with an embodiment of the present disclosure. The distribution is decisively super-Gaussian.

[0078] The calibration in FIG. **8**A-**8**F and FIG. **9**A-**9**B show that even for stationary processes, iPDF provides more information on the constituting components and the underlying mechanisms involved in the data generation processes: linear additive or nonlinearly multiplicative.

[0079] In the present disclosure, intrinsic multi-scale sample entropy (iMSE) may be applied for measurement of signal complexity. The complexity of each IMFs in different scales is useful for distinguishing among various physiological or disease states. The signal may be a physiological signal, for example, blood pressure, electrocardiography (EKG) signals, or electromyography (EMG) signals.

[0080] Referring to FIG. **11**, elements of another analyzed data unit are provided in accordance with an embodiment of the present disclosure. In FIG. **11**, the analyzed data unit **111** comprises a first coordinate **112**, a second coordinate **113**, and an entropy value **114**. The entropy value **114** may be a sample entropy value or an approximate entropy value. The sample entropy value is calculated according to one subset of the IMFs at a designated scale parameter. In one example, the first coordinate **112** indicates the scale parameter. The second coordinate **113** indicates the order number of one subset of the IMFs. The subset of IMFs may comprise one IMF component or the combination of at least two different IMF components. In another example, the first coordinate **112** indicates the scale parameter, and the second coordinate **113** indicates cumulative IMFs.

[0081] The visual output space comprising a first axis, a second axis and a plurality of visual elements. Each visual elements may include multiple analyzed data units within a certain range formed by the subsets of IMFs and the probability density value. The visual output module renders visual output space according to the analyzed data set. A smoothing process may be applied to the visual output space for those visual elements with sparse data units. For example, the smoothing process may be Butterworth filter, exponential smoothing, Kalman filter, Kernal smoother, Laplacian smoothing, moving average or other image smoothing techniques.

[0082] In FIG. **12**, the sample entropy of a signal may be calculated as: log (patterns of length m)−log (patterns of length m+1). The scale parameters may be adjusted for calculating sample entropy values at different scale parameters.

[0083] MSE is based on approximate Entropy of a given data, $X=\{x_i$, for i=1 . . . n$\}$, defined as

$$E(X) = -\sum_{x_i \in \Theta} p(x_i) \log p(x_i), \tag{1}$$

where p(.) is the probability density function of a set of random numbers, Θ. The MSE is defined as the joint entropy for a set of indexed sequence of n random variables, $\{X_i\}=\{X_1, \ldots, X_n\}$, with a set of values $\theta_1, \ldots, \Theta_n$, respectively:

$$E_n = -\sum_{x_1 \in \Theta_1} \cdots \sum_{x_n \in \Theta_n} p(x_1, \ldots, x_n) \log p(x_1, \ldots, x_n), \tag{2}$$

where $p(x_1, \ldots, x_n)$ is the joint probability of the random variable, $X_1, \ldots . X_n$. As the MSE is defined in terms of probability density function, it requires the existence of a mean and a variance of the data. The probabilistic measure requirements limited the application of MSE to stationary data only.

[0084] In order to make MSE useful for the physiological signals, various attempts were made to remove any possible trends from the data. But all of the attempts were ad hoc with no solid theoretical foundation or proper justifications. With the introduction of Multi-scale Intrinsic Entropy analysis from Yeh et al (Yeh, J. R., Peng, C. K., & Huang, N. E. (2016). Scale-dependent intrinsic entropies of complex time series. *Phil. Trans. R. Soc. A,* 374(2065), 20150204.) the EMD in Huang et al (Huang, N. E., Shen, Z., Long, S. R., Wu, M. C., Shih, H. H., Zheng, Q., . . . & Liu, H. H. (1998, March). The empirical mode decomposition and the Hilbert spectrum for nonlinear and non-stationary time series analysis. In *Proceedings of the Royal Society of London A: mathematical, physical and engineering sciences* (Vol. 454, No. 1971, pp. 903-995). The Royal Society.) was introduced as the tool to remove the trend of various scales systematically, for EMD endowed the resulting IMF's to have this special property. The idea is explained as follows:

[0085] When any non-stationary and nonlinear is decomposed in Intrinsic Mode Functions (IMF's) through EMD, we have

$$x(t) = \sum_{j=t}^{n} c_j(t), \tag{3}$$

where each $c_j(t)$ is an IMF except the last one, which might be a trend if there is one. By definition, each IMF should be dyadically narrow band, symmetric with respect to zero-axis, and having the same numbers of extrema as the of zero-crossings. Furthermore, by construction, the IMF component c_{j+1} is essentially derived from the trend of c_j. The Kolmogorov-Sinai (KS) type entropy for the specific intrinsic mode function is defined as

$$\Delta E_k = E_{k+1} - E_k$$

[0086] where E_k is defined as the partial sum of IMF:

$$\sum_{j=t}^{k} c_j(t). \tag{4}$$

[0087] Though the KS-type entropy is essentially the approximate the entropy of the single IMF component, the above definition is necessary to represent the influence of all other IMF's in the system, for the EMD expansion is nonlinear. Thus, this definition would include the some nonlinear summation effects, albeit incompletely. The KS-type entropy, so defined, had successfully revealed the scale dependent variations and the contribution of each IMF component to the total entropy; however, the result shows no relationship with the properties of the total data as in the original MSE as a measure of the whole system. The original MSE essentially emphasized the view of the trees rather than the whole forest. Therefore, it is impossible to make comparisons in the spirit of the original MSE. Now, we will redefine a new Intrinsic MSE with the following steps:

[0088] 1. Generating a set of IMF by empirical mode decomposition (EMD). The EMD may be any of its variations such as EEMD, CREMD, AEMD, and other decomposition methods. One example is given in Equation (3).

[0089] 2. Providing the first set of random variables as the ascending partial sums for k=1 . . . to n,

$$X_k = \sum_{j=1}^{k} c_j(t). \tag{5}$$

[0090] 3. Calculating the Approximate Entropy, E_k, for each X_k, for all k from 1 . . . to n.

[0091] 4. Providing the second set of random variables as the descending partial sums also for k=1 . . . to n.

$$Y_{n-k} = \sum_{j=k}^{n} c_j(t). \tag{6}$$

[0092] 5. Calculating the Approximate Entropy, F_k, for each Y_{n-k}, for all k from 1 . . . to n.

[0093] 6. Generating a two-dimensional plot comprising E_k and F_k in a sequential order. This final result is the new Intrinsic Multiscale Entropy (iMSE).

[0094] 7. Generating a topographic iMSE. In case data from spatially distributed multi-stations, a Topographic iMSE (TiMSE) can be constructed to represent the spatial and temporal variation of the underlying variation of the complexity condition.

[0095] In this new form, the iMSE and TiMSE would contain all the possible partial sums of the data in terms of EMD expansion, which would systematically detrend any data, stationary or non-stationary, and produce the full scale dependent MSE, temporally and spatially.

[0096] In some examples, it is important to point out that though, according to traditional physical science, the entropy is highest when the system represents a white noise. In the spirit of MSE analysis, however, only when systems with a mixture of both long and short scale correlation would we have the most complex. This special property make the MSE useful to quantify complexity in the living systems.

[0097] To illustrate the prowess of the new iMSE and TiMSE, simulated data and human physiologic data are used in the following examples.

[0098] In the present disclosure, iPDF and iMSE may be helpful for diagnosis among various cardiovascular diseases and cardiovascular disorders. The visual outputs of the iPDF and iMSE can be used to compare 2 or more states of different groups of people, different individuals, or the same individual. Specific visual output patterns of one or more neurophysiological or neuropsychiatric disorders can be identified. The specific visual output patterns may comprise a disease state, a healthy state, a good prognosis state, or other patterns relevant to diagnosis, prognosis, clinical evaluation, or staging of the disease. The comparison between the specific visual output patterns may be used to identify the difference between two groups of people with different cardiovascular disorders, two groups of people with different disease stage, two groups of people with different prognosis of disease, two individuals with different cardiovascular disorders, two individuals with different disease stage, two individuals with different prognosis of disease, or two different time intervals of the same individual. The comparison on specific patterns may lead to establish a model for the clinical evaluation, diagnosis, staging, or prognosis of the cardiovascular disorder.

[0099] A healthy state could be defined as a subject or a group of subjects without being diagnosed with particular disease(s) of interest. A disease state could be defined as a subject or a group of subject being diagnosed with particular disease(s) of interest. The healthy state and the disease state may be presented on the same subject on different time intervals or be presented on different subjects.

[0100] The present disclosure will now be described more specifically with reference to the following exemplary embodiments, which are provided for the purpose of demonstration rather than limitation.

[0101] In the following examples, iMSE may be applied to electrocardiography (ECG) to quantify the heart rate variability (HRV). It has been shown that HRV contains rich information on inter-scale interactions of the neural and physiologic mechanisms of the cardiovascular system. Furthermore, the present disclosure have also demonstrated that iMSE could separate the subtle difference between the groups of healthy elders from the young. The present disclosure uses the same data from Yeh et al (Yeh. J. R., Peng, C. K., & Huang, N. E. (2016). Scale-dependent intrinsic entropies of complex time series. *Phil. Trans. R. Soc. A,* 374(2065), 20150204.), on human heartbeat time series for subjects with different physiological and pathologic conditions. These data are available from various databases summarized by Goldberger et al (Goldberger, A. L., Amaral, L. A., Glass, L., Hausdorff, J. M., Ivanov, P. C., Mark, R. G., . . . & Stanley, H. E. (2000). PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals. Circulation, 101(23), e215-e220.). A total of 141 heartbeat time series with different physiological and pathological conditions, including healthy subjects (normal), aged subjects and disease subjects, were studied. Specifically, 72 healthy subjects were acquired from normal sinus rhythm RR interval

database and MIT-BIH normal sinus rhythm database; 44 subjects with congestive heart failure (CHF) from congestive heart failure RR interval database and BIDMC congestive heart failure database; 25 recordings of patients with atrial fibrillation (AF) from MIT-BIH atrial fibrillation database. The healthy subjects were divided into two groups by age: 44 subjects with age over 60 (66.2±3.7) years old form the group of healthy elderly and the other 28 subjects with age of 36.39±9.4 years old form the group of healthy young subjects. CHF patients were divided into two subgroups based on the severity of the disease according to the criteria of New York Heart Association functional classification: a CHF I-II group is the less severe group, and another CHF III-IV group is the most severe group.

[0102] Referring to FIG. **13**A-FIG. **13**D, iMSE representations of different groups with different disease states or different ages are provided in accordance with an embodiment of the present disclosure. The iMSE representations of the MSE means of all subjects in each group with the entropy increment matrixes are plotted in logarithmic coarse-graining iMSE scale as x-axis and cumulative IMFs as y-axis. The cumulative IMFs **1-1**, **1-6**, **1-12**, **6-12**, and **12** on the y-axis in FIG. **13**A-**13**D use bi-directional methods to represent diverse characteristics of the cumulation processes: cumulation processes from high-frequency bands and or cumulation processes from low-frequency bands. Similar to the analysis results of the simulated time series of fractional Gaussian noise, intrinsic entropies contributed by each specific IMF were evaluated with a specific coarse-graining scale. Furthermore, the specific coarse-graining scale depends on the intrinsic time scale of the corresponding IMF, indicating that the specific coarse-graining scale corresponding to the intrinsic entropy can be determined by the intrinsic time scale of the corresponding IMF. FIG. **13**A is the iMSE representation of the heartbeat time series from the 28 healthy young subjects. FIG. **13**B is the iMSE representation of the heartbeat time series from the 44 healthy old subjects. FIG. **13**C is the iMSE representation of the heartbeat time series from the 44 subjects with CHF. FIG. **13**D is the iMSE representation of the heartbeat time series from the 25 subjects with AF.

[0103] Importantly, without the troublesome detrend and filtering selections here, the iMSE representations in FIG. **13**A-**13**D reveal clear differences among different groups: When comparing iMSE representations from the healthy young subjects of FIG. **13**A and the healthy elder subjects of FIG. **13**B, as the subjects age increase, the HRV complexity decreases in the shorter scale but enhanced in the longer scale, reflecting a physiologic reality of slowing down the reactions to environmental challenges. In the CHF group of FIG. **13**C, their HRV complexity deteriorate further.

[0104] In FIG. **14**A-FIG. **14**F, iMSE representations of contrasts between different groups are provided, in accordance with an embodiment of the present disclosure. Each of the iMSEs in FIG. **14**A-**14**F is presented to identify the contrast between two different groups from FIG. **13**A, **13**B, **13**C, or **13**D. Regarding to the AF group, the original data is hard to be distinguish from white noise, and the difference between the iMSE representations in FIG. **13**B and FIG. **13**D are difficult to identify, therefore it would be hard to separate the iMSE representation of the AF group and from the healthy elder subject group. To reveal the subtlety between these groups, the iMSE is applied to examine the difference between the different groups given in FIG. **14**A-FIG. **14**F, in which all the possible pairwise differences of the groups in FIG. **13**A-**13**D are presented. In FIG. **14**A-**14**F, the differences are plotted in logarithmic coarse-graining iMSE scale as x-axis and cumulative IMFs as y-axis, wherein the cumulative IMFs uses bi-directional methods to represent diverse characteristics of the cumulation processes, as shown in FIG. **13**A-**13**D. FIG. **14**A presents the contrast between the healthy young and elder subject groups: the young show a greater entropy matrix in the fine-graining scale, and less entropy matrixes in the coarse-graining scales as expected. FIG. **14**B presents the contrast between the healthy young and the CHF group, the healthy young subject group has an overwhelming greater complexity over all scales. FIG. **14**C presents the contrast between the healthy young subject group and the AF group. First, in a descending region of scale **20-30** and cumulative IMFs of 1-6 to 1-12, the AF group exhibits a total lack of complexity in the coarse-graining scales.

[0105] FIG. **14**D presents the contrast between the healthy elder subject group and the CHF group. The patterns are qualitatively similar to the contrast between the healthy young subject group and the CHF group: an overwhelmingly greater complexity for the healthy elder subject group than the CHF group, with a few exceptional scales. Some areas on few exceptional scales in FIG. **14**D has drastically transformed from lighter gray to darker gray, this might represent drastic changes in the CHF group. FIG. **14**E presents the contrast between the healthy elder subject group and the AF group. Again, the patterns are the same as those in FIG. **14**C, except that the respiration modulation is weaker in the AF group in FIG. **14**E.

[0106] FIG. **14**F presents the contrast between the CHF group and the AF group. The differences in FIG. **14**F are in every scale. Even though the CHF group has suffered loss of complexity, they are still more complex than the AF group.

[0107] FIG. **13**A-**13**D and FIG. **14**A-**14**F illustrate the prowess and robustness of iMSE. Thus, the iMSE provided by the present disclosure is a powerful tool for the visualization, comparison, or diagnosis of cardiovascular disorders.

[0108] The embodiments shown and described above are only examples. Many details are often found in the art such as the other features of a circuit board assembly. Therefore, many such details are neither shown nor described. Even though numerous characteristics and advantages of the present technology have been set forth in the foregoing description, together with details of the structure and function of the present disclosure, the disclosure is illustrative only, and changes may be made in the detail, including in matters of shape, size and arrangement of the parts within the principles of the present disclosure up to, and including the full extent established by the broad general meaning of the terms used in the claims. It will therefore be appreciated that the embodiments described above may be modified within the scope of the claims.

What is claimed is:

1. A non-transitory computer program product embodied in a computer-readable medium and, when executed by one or more analysis modules, providing a visual output for presenting physiological signals of a cardiovascular system, comprising:

a first axis representing subsets of intrinsic mode functions (IMFs);

a second axis representing a function of signal strength in a time interval; and

a plurality of visual elements, each of the visual elements being defined by the first axis and the second axis, and each of the visual elements comprising a plurality of analyzed data units collected over the time interval,

wherein each of the analyzed data units comprises a first coordinate, a second coordinate, and a probability density value generated from an intrinsic probability density function of one of the subsets of IMFs, the first coordinate is one of the subsets of IMFs, and the second coordinate is an argument of the function of signal strength.

2. The non-transitory computer program product of claim **1**, wherein the second axis is a standard deviation or a z-value of the signal strength in the time interval.

3. The non-transitory computer program product of claim **1**, wherein the probability density value is generated from a subset of primary IMFs or secondary IMFs, each of the primary IMFs is generated from an empirical mode decomposition (EMD) of a plurality of the physiological signals, and each of the secondary IMFs is generated from an EMD of the primary IMF.

4. The non-transitory computer program product of claim **1**, wherein the physiological signals are electrocardiography (EKG) signals, electromyography (EMG) signals, or blood pressure signals.

5. The non-transitory computer program product of claim **1**, wherein the probability density value is indicated by different colors, grayscales, dot densities, contour lines, or screentones.

6. A system for analyzing physiological signals of a cardiovascular system, comprising:

a detection module for detecting the physiological signals of the cardiovascular system;

a transmission module for receiving the physiological signals from the detection module and transmitting the physiological signals to the analysis module;

an analysis module for generating a plurality of analyzed data sets from the physiological signals, each of the analyzed data sets comprising a plurality of analyzed data units; and

a visual output module for rendering a visual output space according to the analyzed data sets generated by the analysis module, and displaying a visual output,

wherein the visual output comprises a first axis representing subsets of intrinsic mode functions (IMFs), a second axis representing a function of signal strength in a time interval, and a plurality of visual elements defined by the first axis and the second axis, and each of the visual elements comprises a plurality of analyzed data units collected over the time interval, and each of the analyzed data units comprises a first coordinate, a second coordinate, and a probability density value generated by an intrinsic probability density function of one of the subsets of IMFs, the first coordinate is one of the subsets of IMFs, and the second coordinate is an argument of the function of signal strength.

7. The system of claim **6**, wherein the second axis is a standard deviation or a z-value of the signal strength in the time interval.

8. The system of claim **6**, wherein the probability density value is generated from a subset of primary IMFs or secondary IMFs, each of the primary IMFs is generated from an empirical mode decomposition (EMD) of a plurality of the physiological signals, and each of the secondary IMFs is generated from an EMD of the primary IMF.

9. The system of claim **6**, wherein the physiological signals are electrocardiography (EKG) signals, electromyography (EMG) signals, or blood pressure signals.

10. The system of claim **6**, wherein the probability density value is indicated by different colors, grayscales, dot densities, contour lines, or screentones.

11. A non-transitory computer program product embodied in a computer-readable medium, and when executed by one or more analysis modules, providing a visual output for presenting physiological signals of a cardiovascular system, comprising:

a first axis representing a scale of intrinsic multiscale entropy (iMSE);

a second axis representing cumulative intrinsic mode functions (IMFs); and

a plurality of visual elements, each of the visual elements being defined by the first axis and the second axis, and each of the visual elements comprising an analyzed data unit collected over a time interval,

wherein each of the analyzed data units comprises a first coordinate of the first axis, a second coordinate of the second axis, and an iMSE value generated from the IMFs.

12. The non-transitory computer program product of claim **11**, wherein the IMFs are a set of primary IMFs or a set of secondary IMFs, each of the primary IMFs is generated from an empirical mode decomposition (EMD) of a plurality of the physiological signals, and each of the secondary IMFs is generated from an EMD of the primary IMF.

13. The non-transitory computer program product of claim **11**, wherein the physiological signals are electrocardiography (EKG) signals, electromyography (EMG) signals, or blood pressure signals.

14. The non-transitory computer program product of claim **11**, wherein the iMSE value is indicated by different colors, grayscales, dot densities, contour lines, or screentones.

15. A system for analyzing physiological signals of a cardiovascular system, comprising:

a detection module for detecting the physiological signals of the cardiovascular system;

a transmission module for receiving the physiological signals from the detection module and transmitting the physiological signals to the analysis module;

an analysis module for generating a plurality of analyzed data sets from the physiological signals, each of the analyzed data sets comprising a plurality of analyzed data units; and

a visual output module for rendering a visual output space according to the analyzed data sets generated by the analysis module, and displaying a visual output,

wherein the visual output comprises a first axis representing a scale of intrinsic multiscale entropy (iMSE), a second axis representing cumulative intrinsic mode functions (IMFs), and a plurality of visual elements defined by the first axis and the second axis, and each of the visual elements comprising an analyzed data unit collected over a time interval, and each of the analyzed data units com-

prises a first coordinate of the first axis, a second coordinate of the second axis, and an iMSE value generated from the IMFs.

16. The system of claim **15**, wherein the IMFs are a set of primary IMFs or a set of secondary IMFs, each of the primary IMFs is generated from an empirical mode decomposition (EMD) of a plurality of electrical activity signals, and each of the secondary IMFs is generated from an EMD of the primary IMF.

17. The system of claim **15**, wherein the physiological signals are electrocardiography (EKG) signals, electromyography (EMG) signals, or blood pressure signals.

18. The system of claim **15**, wherein the iMSE value is indicated by different colors, grayscales, dot densities, contour lines, or screentones.

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专利名称(译)	用于分析生理信号的方法，模块和系统		
公开(公告)号	US20190175120A1	公开(公告)日	2019-06-13
申请号	US16/214176	申请日	2018-12-10
[标]发明人	HUANG NORDEN E		
发明人	HUANG, NORDEN E.		
IPC分类号	A61B5/00 A61B5/021 A61B5/044 A61B5/0488		
CPC分类号	A61B5/743 A61B5/021 A61B5/044 A61B5/0488 A61B5/72 A61B5/048 A61B5/0006 A61B5/04008 A61B5/4088 A61B5/7253		
优先权	62/596912 2017-12-11 US		
外部链接	Espacenet USPTO		

摘要(译)

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