claim 1). Is the semicolon intended to introduce a new step, or to further limit a detail of a previous step?

12. **Regarding claims 1, 18, and 35,** the second recitation of "a segment" makes it unclear whether this is the same as, or different than, the segment contemplated by the first recitation of "a segment."

13. **Regarding claims 3 and 20,** the second and third recitations of "a narrow band spectrum" make it unclear whether they are the same as, or different than, the narrow band spectrum contemplated by the first recitation of "a narrow band spectrum."

14. **Regarding claim 19,** the recitation of "a noise quality index" in line 1 makes it unclear whether this is the same as, or different than, the noise quality index already introduced in claim 18.

15. **Regarding claim 35,** there is insufficient antecedent basis for the recitation of "the one or more processors" in line 3.

16. **Claims 2-17, 19-34, and 36** are rejected because they depend on rejected claims.

Claim Rejections - 35 USC § 101

17. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

18. **Claims 1-36 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a judicial exception (i.e., a law of nature, a natural phenomenon, or an abstract idea) without significantly more.**

19. Claims 1, 18, and 35 are directed to the abstract idea of an idea "of itself." The claimed method, system, and computer program product merely describe the concept of gathering and manipulating data by reciting structure and steps that mathematically process the data (e.g. obtaining a time frequency spectrum, obtaining a noise quality index, applying a statistical learning method). These steps merely employ mathematical

relationships to manipulate existing information to generate additional information comprising a determination of whether or not a segment is corrupted by motion and noise artifacts. This idea is similar to the basic concept of manipulating information from source devices using mathematical relationships (e.g. creating device profiles based on processed information, using known mathematical techniques), such as in Digitech Image Techs., LLC v Electronics for Imaging, Inc., 758 F.3d 1244, 111 U.S.P.Q.2d 1717 (Fed. Cir. 2014), which has been found by the courts to be an abstract idea. Therefore, the claims are directed to an abstract idea.

The claims do not include additional elements that are sufficient to amount to significantly more than the judicial exception because the elements are merely directed to insignificant data gathering and processing structure and steps (e.g. receiving a PPG). Furthermore, the additional elements or combination of elements in the claims, other than the abstract idea per se, amount to no more than a recitation of generic computer structure to perform generic computer functions (the processors, computer usable media, etc. - see the below art rejections), that serve to generally link the abstract idea to a particular technological environment or field of use. When considered separately and in combination, these additional claim elements do not provide meaningful limitation to transform the abstract idea into a patent eligible application of the abstract idea such that the claims amount to significantly more than the abstract idea itself.

Dependent claims 2-17, 19-34, and 36 merely further define the abstract idea and are, therefore, directed to an abstract idea for similar reasons: they merely further describe the manipulation of data (e.g. determining a dominant frequency, normalizing the time frequency spectrum, determining a residual noise power, determining a projected difference, determining a heart rate frequency difference, wherein the noise quality index is a weighted sum of different values, etc.), further define the abstract idea (e.g. wherein the statistical learning method is a Support Vector Machine, wherein the noise quality index is the residual noise power, etc.), and pre-solution activity (e.g. wherein the PPG signal is

preprocessed, wherein the time frequency spectrum is obtained using variable frequency complex demodulation, etc.). These encompass the abstract ideas of gathering and manipulating data and do not, when viewed alone or in ordered combination, add anything significantly more than the abstract ideas. Their collective functions merely provide computer/electronic implementation and processing, and no additional elements beyond those of the abstract idea of gathering and manipulating data. Looking at the limitations as an ordered combination adds nothing that is not already present when looking at the elements individually. There is no indication that the combination of elements improves the functioning of a computer, output device, improves technology other than the technical field of the claimed invention, etc. Therefore, the claims are rejected as being directed to non-statutory subject matter.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale or otherwise available to the public before the effective filing date of the claimed invention.
>
> (a)(2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was effectively filed before the effective filing date of the claimed invention.

21. **Claims 1, 2, 15, 16, 18, 19, 32, 33 and 35 are rejected under 35 U.S.C. 102(a)(1) as being anticipated by US Patent Application Publication 2011/0077484 ("Van Slyke").**

22. **Regarding claim 1,** Van Slyke discloses [a] computer implemented method for detection of motion and noise artifacts in a Photoplethysmogram (PPG) or equivalent signal (Abstract), the computer implemented method comprising: obtaining a time frequency

spectrum of a segment of the PPG or equivalent signal (¶ 0079, the scalogram); obtaining, from the time frequency spectrum, a noise quality index for the segment; the noise quality index being used to determine whether a segment is corrupted by motion and noise artifacts (¶¶s 0087-0089, converging on a stable solution and detecting regions of artifact, using scalogram magnitude values as an input); and applying a statistical learning method to determine whether the segment is corrupted by motion and noise artifacts or not corrupted by motion and noise artifacts (¶ 0089, the neural network).

23. **Regarding claim 18,** Van Slyke discloses [a] system for detection of motion and noise artifacts in a Photoplethysmogram (PPG) or equivalent signal (Abstract), the system comprising: a processor (Abstract, ¶¶s 0006, 0007, etc.) configured to: receive the PPG or equivalent signal (Abstract, ¶ 0007 - the PPG must be received before it is processed); obtain a time frequency spectrum of a segment of the PPG or equivalent signal (¶ 0079, the scalogram); obtain, from the time frequency spectrum, a noise quality index for the segment; the noise quality index being used to determine whether a segment is corrupted by motion and noise artifacts (¶¶s 0087-0089, converging on a stable solution and detecting regions of artifact, using scalogram magnitude values as an input); and apply a statistical learning method to determine whether the segment is corrupted by motion and noise artifacts or not corrupted by motion and noise artifacts (¶ 0089, the neural network).

24. **Regarding claim 35,** Van Slyke discloses [a] computer program product comprising: tangible computer usable media, having computer readable code embodied therein (¶¶s 0052, 0053, 0056), the computer readable code, when executed by the one or more processors, causes the one or more processors to: obtain a time frequency spectrum of a segment of the PPG or equivalent signal (¶ 0079, the scalogram); obtain, from the time frequency spectrum, a noise quality index for the segment; the noise quality index being used to determine whether a segment is corrupted by motion and noise artifacts (¶¶s 0087-0089, converging on a stable solution and detecting regions of artifact, using scalogram magnitude values as an input); and apply a statistical learning method to determine

whether the segment is corrupted by motion and noise artifacts or not corrupted by motion and noise artifacts (¶ 0089, the neural network).

25. **Regarding claims 2 and 19,** Van Slyke discloses all the features with respect to the corresponding claims 1 and 18, as outlined above. With respect to claim 2, Van Slyke further discloses wherein obtaining a noise quality index comprises: determining a dominant frequency in the time frequency spectrum of the segment (¶¶s 0061, 0070); and normalizing the time frequency spectrum to a total power in a narrow band centered at the dominant frequency (¶ 0118).

Claim 19 is rejected in like manner.

26. **Regarding claims 15, 16, 32, and 33,** Van Slyke discloses all the features with respect to the corresponding claims 1 and 18, as outlined above. With respect to claims 15 and 16, Van Slyke further discloses wherein the PPG or equivalent signal is preprocessed before obtaining the time frequency spectrum, wherein the PPG or equivalent signal is preprocessed by filtering with a bandpass filter of predetermined bandwidth (¶ 0075 describes band-pass filtering signal 416, which is the signal received from the input signal generator).

Claims 32 and 33 are rejected in like manner.

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

28. **Claims 3, 4, 6, 20, 21, and 23 are rejected under 35 U.S.C. 103 as being unpatentable over Van Slyke in view of US Patent 5,853,364 ("Baker") and International Application Publication WO 2013/043157 ("Brockway").**

29. **Regarding claims 3 and 20,** Van Slyke teaches all the features with respect to the corresponding claims 2 and 19, as outlined above. With respect to claim 3, Van Slyke does not appear to explicitly teach determining a first trace of amplitudes in a narrow band spectrum of the time frequency spectrum centered at the dominant frequency; determining a second trace of amplitudes in a narrow band spectrum of the time frequency spectrum centered at twice the dominant frequency; determining a third trace of amplitudes in a narrow band spectrum of the time frequency spectrum centered at three times the dominant frequency; subtracting the first, second and third traces of amplitudes from the time frequency spectrum; and obtaining, after subtracting, a total power remaining in the time frequency spectrum; the total power remaining hereinafter referred to as a residual noise power (although Van Slyke does teach determining multiple traces of amplitudes in the spectrum - Figs. 3A, 3B, and 3C).

Baker teaches determining first, second, and third traces of amplitudes in narrow band spectra of a spectrogram, the traces centered at a dominant frequency and harmonics thereof (col. 13, lines 10-28, col. 16, line 46, first four harmonics). These traces are notched out, leaving only noise (col. 13, lines 10-28).

Brockway teaches obtaining a total power of noise of a particular data subset (Fig. 4, computation of noise power).

It would have been *prima facie* obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to determine a dominant frequency band, as well as first and second harmonics thereof, and then subtract them out from the time frequency spectrum to obtain a total power of noise remaining in the spectrum, as in Baker and Brockway, for the purpose of isolating the noise to thereby ascertain its effects (in the form of e.g. a signal-to-noise ratio, as in Fig. 4 of Brockway), or for the purpose of enabling

removal of the noise to thereby improve the signal and its diagnostic efficacy (Baker: Abstract, col. 13, lines 10-28).

Claim 20 is rejected in like manner.

30. **Regarding claims 4 and 21,** Van Slyke-Baker-Brockway teaches all the features with respect to the corresponding claims 3 and 20, as outlined above. With respect to claim 4, Van Slyke does not appear to explicitly teach wherein the noise quality index is the residual noise power. However, it would have been *prima facie* obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to incorporate the residual noise power of Baker and Brockway into the noise quality index calculations of Van Slyke, for the purpose of having additional means by which to detect regions of artifact, thereby improving detection and removal of the artifact (as already contemplated by Van Slyke above).

Claim 21 is rejected in like manner.

31. **Regarding claims 6 and 23,** Van Slyke-Baker-Brockway teaches all the features with respect to the corresponding claims 3 and 20, as outlined above. With respect to claim 6, Van Slyke does not appear to explicitly teach determining a different in frequency between the first trace and the second and third traces; the difference in frequency referred to as a projected difference.

Baker teaches determining a difference in frequency between the dominant frequency and its harmonics (col. 16, lines 34-37 - also see col. 13, lines 10-28, which state that the harmonics are a matter of choice. Additionally, they are multiples of the fundamental frequency simply by their nature (see US Patent Application Publication 2008/0167564 ("Hete") Fig. 5 and ¶ 0057). Therefore, their frequency difference with the first trace is known).

It would have been *prima facie* obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to determine a frequency difference between the first trace and the second and third traces, as a natural outflow of the harmonic

selection described in Baker, for the purpose of enabling removal of the noise to thereby improve the signal and its diagnostic efficacy (Baker: Abstract, col. 13, lines 10-28).

Claim 23 is rejected in like manner.

32. **Claims 5 and 22 are rejected under 35 U.S.C. 103 as being unpatentable over Van Slyke-Baker-Brockway in view of non-patent publication Couceiro, Ricardo, et al. "Detection of motion artifacts in photoplethysmographic signals based on time and period domain analysis."** ***2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*****. IEEE, 2012 ("Couceiro").**

33. **Regarding claims 5 and 22,** Van Slyke-Baker-Brockway teaches all the features with respect to the corresponding claims 4 and 21, as outlined above. With respect to claim 5, Van Slyke-Baker-Brockway does not appear to explicitly teach wherein the statistical learning method is a Support Vector Machine (SVM).

Couceiro teaches the use of an SVM to distinguish between clean and corrupted sections of a PPG signal (Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to use an SVM in the combination, the use being a simple substitution of one known component (neural network methods) for another (support vector machine methods) with predictable results (classification of data based on statistical learning).

Claim 22 is rejected in like manner.

34. **Claims 9, 12, 26, and 29 are rejected under 35 U.S.C. 103 as being unpatentable over Van Slyke-Baker-Brockway in view of US Patent Application Publication 2016/0270733 ("Hansson").**

35. **Regarding claims 9, 12, 26, and 29,** Van Slyke-Baker-Brockway teaches all the features with respect to the corresponding claims 6, 3, 23, and 20, as outlined above. With

respect to claim 9, Van Slyke-Baker-Brockway does not appear to explicitly teach determining a difference between the dominant frequency and a heart rate obtained from peak to peak intervals from the PPG or equivalent signal in a time domain; the difference between the dominant frequency and the heart rate obtained from peak to peak intervals hereinafter referred to as a heart rate frequency difference.

Hansson teaches combining heart rate results obtained from time domain data (based on RR intervals) with those obtained from frequency domain data (a peak in a spectral diagram - the peak associated with the dominant frequency in a particular range).

It would have been *prima facie* obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to combine time domain and frequency domain measures by obtaining their difference, for the purpose of evaluating their reliability/consistency to thereby improve measurement quality.

Claims 12, 26, and 29 are rejected in like manner.

36. **Claims 17 and 34 are rejected under 35 U.S.C. 103 as being unpatentable over Van Slyke-Baker-Brockway in view of US Patent Application Publication 2008/0287815 ("Chon").**

37. **Regarding claims 17 and 34,** Van Slyke-Baker-Brockway teaches all the features with respect to the corresponding claims 1 and 18, as outlined above. With respect to claim 17, Van Slyke-Baker-Brockway does not appear to explicitly teach wherein the time frequency spectrum is obtained using variable frequency complex demodulation.

Chon teaches obtaining a time frequency spectrum using variable frequency complex demodulation (Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to use variable frequency complex demodulation to obtain the time frequency spectrum of the combination, as a simple substitution of one known component (continuous wavelet transform - see ¶¶s 0004 and

0062 of Van Slyke), for another (variable frequency complex demodulation), with predictable results (obtaining a time frequency spectrum - see ¶¶ 0018-0020 of Chon, suggesting that they are alternatives). Further, using variable frequency complex demodulation results in more accurate measurements (Chon: ¶ 0020).

Claim 34 is rejected in like manner.

38. **Claim 36 is rejected under 35 U.S.C. 103 as being unpatentable over Van Slyke in view of Couceiro.**

39. **Regarding claim 36,** Van Slyke teaches all the features with respect to claim 35, as outlined above. Van Slyke does not appear to explicitly teach wherein the statistical learning method is a Support Vector Machine (SVM).

Couceiro teaches the use of an SVM to distinguish between clean and corrupted sections of a PPG signal (Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to use an SVM in Van Slyke, the use being a simple substitution of one known component (neural network methods) for another (support vector machine methods) with predictable results (classification of data based on statistical learning).

Allowable Subject Matter

40. Claims 7, 8, 10, 11, 13, 14, 24, 25, 27, 28, 30, and 31 are allowable over the prior art. Therefore, they will be allowed if related 35 USC 112(b) and 35 USC 101 rejections are overcome. As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements (i.e., the claim, drawing, and specification objections) or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

41. The following is a statement of reasons for the indication of allowable subject matter: the prior art of record fails to teach or fairly suggest a noise quality index from a time frequency spectrum, the noise quality index being based on a weighted sum of residual noise power, as specified, and a projected difference or a heart rate frequency difference, as specified, in combination with all other recited limitations.

Conclusion

42. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANDREY SHOSTAK whose telephone number is (408)918-7617. The examiner can normally be reached Monday - Friday 9 am - 5 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Charles Marmor II can be reached on (571) 272-4730. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NAVIN NATNITHITHADHA/
Primary Examiner, Art Unit 3735

/ANDREY SHOSTAK/
Examiner, Art Unit 3735

Notice of References Cited	Application/Control No. 15/010,345	Applicant(s)/Patent Under Reexamination Chon et al.	
	Examiner ANDREY SHOSTAK	Art Unit 3735	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20080287815-A1	11-2008	Chon; Ki H.	A61B5/0806	600/507
*	B	US-20110077484-A1	03-2011	Van Slyke; Braddon M.	A61B5/02416	600/324
*	C	US-5853364-A	12-1998	Baker, Jr.; Clark R.	A61B5/02416	600/300
*	D	US-20080167564-A1	07-2008	Hete; Benard F.	A61B5/02405	600/508
*	E	US-20160270733-A1	09-2016	Hansson; Per	A61B5/0215	1/1
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N	WO-2013043157-A2	03-2013	WO	BROCKWAY MARINA	A61B5/7203
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Couceiro, Ricardo, et al. "Detection of motion artifacts in photoplethysmographic signals based on time and period domain analysis." 2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE, 2012. (Year: 2012)
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/010,345	Chon et al.
	Examiner	Art Unit
	ANDREY SHOSTAK	3735

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

CLAIMS

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	09/07/2018								
	1	✓								
	2	✓								
	3	✓								
	4	✓								
	5	✓								
	6	✓								
	7	✓								
	8	✓								
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	31	✓								
	32	✓								
	33	✓								
	34	✓								
	35	✓								
	36	✓								

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/010,345	Chon et al.
	Examiner	Art Unit
	ANDREY SHOSTAK	3735

CPC - Searched*		
Symbol	Date	Examiner
A61B5/7207,1455,7267,725,7257,02416	09/05/2018	AS

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor search in PALM and EAST	09/05/2018	AS
Text search in EAST	09/05/2018	AS
Classification search in EAST, limited by text and/or date	09/05/2018	AS

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L13	576	heart adj rate with spectr$2 same2 heart adj rate with interval	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/07 07:03
L14	86	heart adj rate with spectr$2 same heart adj rate with interval same (difference or compar$4)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/07 07:12
L15	4	heart adj rate with spectr$2 same heart adj rate with interval same (difference or compar$4) same noise	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/07 07:17
L16	179	noise same heart adj rate same (frequency with differen$3 or projected adj differen$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/07 09:26
L17	97	noise same heart adj rate with (frequency with differen$3 or projected adj differen$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/07 09:27
L18	1	noise same (heart or pulse) adj rate with differen$3 with (time adj domain or peak adj3 peak or interval) with (frequency adj domain or (dominant or fundamental) with frequency)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/07 10:12
S1	1	("20080287815").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2018/09/05 13:45
S2	9	("6862558" | "20050070774" | "20060200035" | "20060211930").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 13:46
S3	1	("20130172760").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2018/09/05 13:48
S4	1	("20130191035").PN.	US-PGPUB; USPAT;	OR	OFF	2018/09/05 13:51

			USOCR			
S5	12	("20060122476" | "20090326349" | "20100016693" | "20080287815" | "20100298656").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 13:52
S6	1	("20130190638").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2018/09/05 13:56
S7	0	(("20110158259").PN.").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2018/09/05 13:57
S8	2	("20110158259").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 13:57
S9	1	("20160367198").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2018/09/05 13:59
S10	1	("20160361021").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2018/09/05 14:03
S11	16	("9713428" | "20140309943" | "9872652" | "8945017").PN.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 14:04
S12	13	(chon with ki or chong with jowoon or dao with duy or salehizadeh with hamed).as,aanm,in. and (time adj frequency adj spectrum)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 14:10
S13	2	("20080287815" | "20110077484").PN.	US-PGPUB; USPAT	OR	ON	2018/09/05 14:31
S14	42757	(A61B5/7207 or A61B5/1455 or A61B5/7267 or A61B5/725 or A61B5/7257 or A61B5/02416).cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 15:08
S15	2	S14 and time adj frequency adj spectrum and ($5plethysmogra$4 or pleth or ppg) and motion with noise with artifact and support with vector with machine	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 15:12
S16	12	S14 and time adj frequency adj spectrum and ($5plethysmogra$4 or pleth or ppg) and motion with noise with artifact	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 15:12
S17	4	(("20120190947") or ("20130144180") or ("20130191035") or	US-PGPUB; USPAT;	OR	OFF	2018/09/05 15:18

		("8755876")).PN.	USOCR			
S18	16	S14 and time adj frequency adj spectr$2 and ($5plethysmogra$4 or pleth or ppg) and motion with noise with artifact	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 15:19
S19	4	S18 not S16	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 15:19
S20	16	(vfcdm or variable with frequency with complex with demodulation) with (tfs or time adj frequency adj spectr$2)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 15:22
S21	17	(vfcdm or variable with frequency with complex with demodulation) and ($5plethysmogra$4 or pleth or ppg)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/05 15:24
S22	42768	(A61B5/7207 or A61B5/1455 or A61B5/7267 or A61B5/725 or A61B5/7257 or A61B5/02416).cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 08:06
S23	737	($5plethysmogra$4 or pleth or ppg) and (svm or support adj vector adj machine)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 08:18
S24	263	($5plethysmogra$4 or pleth or ppg) and (svm or support adj vector adj machine) and (motion with noise)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 08:18
S25	3	S24 and (time adj frequency adj spectr$2)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 08:19
S26	148	S24 and harmonic	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 08:19
S27	2	S22 and noise adj quality adj index	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT;	OR	ON	2018/09/06 08:20

			IBM_TDB			
S28	30	S26 and total adj power	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 08:22
S29	4	S22 and projected adj difference	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 08:28
S30	4	S22 and residual adj noise adj power	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 08:31
S31	128	extract with trace with power	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 09:38
S32	340	extract$3 with trace with power	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 09:38
S33	16	extract$3 with trace with power with noise	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 09:39
S34	362	extract$3 with (band or scale) with power with noise	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 09:40
S35	623	(extract$3 or subtract$3) with (band or scale) with power with noise	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 09:41
S36	403	(extract$3 or subtract$3) with (band or scale) with (fundamental or dominant) adj frequency	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 09:41
S37	5	(extract$3 or subtract$3) with (band or scale) with (fundamental or dominant) adj frequency same noise same power	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT;	OR	ON	2018/09/06 09:42

			IBM_TDB			
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S39	1	("20160022164").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2018/09/06 10:06
S40	16	"2013043157"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 10:28
S41	24	heart adj rate with frequency adj difference	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 10:57
S42	356	heart adj rate with frequency with difference	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 10:59
S43	14	heart adj rate with time adj domain with (dominant or fundamental) adj frequency	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 11:00
S44	44	heart adj rate with harmonic same (spectrogram or scalogram)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 13:29
S45	0	(fundamental or dominant) with frequency same peak adj to adj peak with interval	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 15:18
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S47	1674	(fundamental or dominant) with frequency same peak adj3 peak	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 15:18
S48	63	(fundamental or dominant) with frequency same peak adj3 peak with	US-PGPUB; USPAT;	OR	ON	2018/09/06 15:18

		interval	USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB			
S49	39	(fundamental or dominant) with frequency same peak adj3 peak with interval with frequency	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 15:19
S50	57	noise adj3 quality adj3 index	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2018/09/06 15:24

EAST Search History (Interference)

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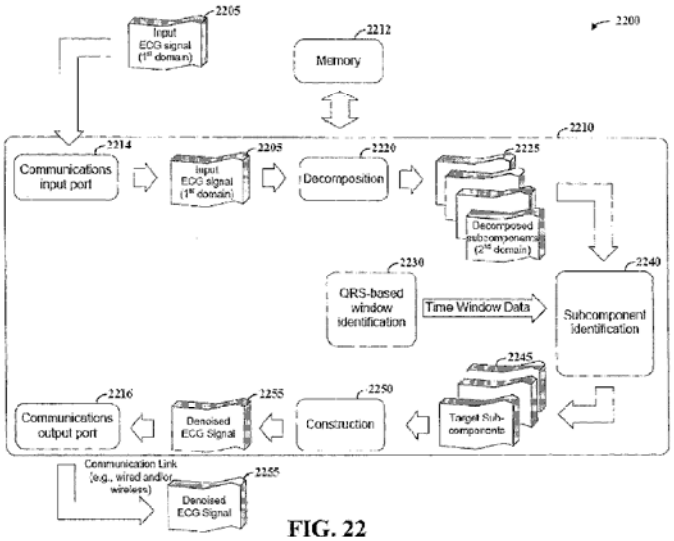


FIG. 22

(57) **Abstract**: Physiological signals are denoised. In accordance with an example embodiment, a denoised physiological signal is generated from an input signal including a desired physiological signal and noise. The input signal is decomposed from a first domain into subcomponents in a second domain. Target subcomponents of the input signal that are associated with the desired physiological signal are identified, based upon the spatial distribution of the subcomponents. A denoised physiological signal is constructed in the first domain from at least one of the identified target subcomponents.

WO 2013/043157 A2

PHYSIOLOGICAL SIGNAL DENOISING

FIELD

Various aspects of the present disclosure relate to the processing of physiological signals, and more particular aspects relate to removing noise and extracting and compressing information.

BACKGROUND

Implantable and external devices are used to monitor physiologic signals of human and animal subjects. These devices may incorporate various types of sensors and can measure and record signals from those sensors for processing by a system or monitoring center located remote from the subject, or in other cases, the device may perform some or all of the desired signal processing and forward the resulting information to a remote system for display, recording, or further processing.

The signal processing is performed to extract information from the signal in order to assess the physiological condition of the monitored subject and often to evaluate the response of the subject to a therapy or experimental protocol. For example, devices that measure ECG and blood pressure are routinely used to assess cardiovascular function. Clinicians can use this information to make therapy decisions and researchers can use this information to assess the safety and utility of experimental therapies. This information is also used for closed loop control of therapy delivery. In other examples, measurements of peripheral nerve activity (PNA), respiration, blood oxygen, blood glucose, EEG, EMG, heart sounds and blood flow signals are processed to extract information for clinical or research purposes.

There is an increasing reliance on automatic processing to extract information in order to reduce labor and costs and to more consistently and accurately evaluate the condition of the subject. In therapeutic devices automatic extraction of this information is often essential for feedback control. However, accurate automatic extraction of information is often challenging or is compromised by the presence of in-band noise. By and large, previous approaches to processing physiological signals containing significant levels of in-band noise (*e.g.,* ambulatory ECG recordings) have been generally incapable of providing sufficiently accurate indications of signal characteristics to enable highly automated processing thereof (*i.e.*, with little or no human intervention). Processing techniques have been developed that significantly reduce in-band noise, but these techniques distort signal

morphology and hence result in either loss of information or inaccurate information. Reducing in-band noise without introducing significant distortion has proven challenging.

In some physiologic signal processing applications, automated analysis is complicated by the fact that measured signals are the result of activity of multiple sources, referred to as multi-source signals. An example of a multi-source signal is ECG measured on the surface of the body where electrical activity is sensed from the atria and ventricles as well as skeletal muscles. It is useful, for example, to observe atrial activity independent of ventricular activity in order to improve the detection of atrial arrhythmias. Current techniques for providing signal source extraction of multi-source signals, such as independent component analysis (ICA), assume independence of sources and performance is compromised when this assumption in invalid, such as is the case when separating atrial and ventricular activity in an ECG. In addition, ECGs are often recorded from ambulatory subjects using a small number of sensing leads, further complicating signal source extraction due to the mixing of sources inherent in a small number of leads.

Other signals, such as peripheral nerve activity (PNA) and brainstem auditory response, have proven difficult to analyze because of very low signal-to-noise ratio (SNR). Visual analysis of these signals is often inadequate to detect important features and obtain a quantitative evaluation.

Many physiological signal processing techniques have been difficult to successfully implement under certain conditions, particularly when processing signals from ambulatory subjects where the signals are often quite noisy. For example, measurements of ECG parameters such as heart rate, QT interval, PR interval, as well as systolic and diastolic blood pressure may contain errors as a result of the presence of noise. Detection of ventricular and atrial arrhythmias in ECG may have excessive incidence of false positives due to the inability of a signal processing algorithm to provide accurate detection, particularly in the presence of noise. Likewise, the presence of noise may result in inaccurate and inconsistent evaluation of cardiac pathologies that are reflected in ECG morphology. Because of lack of confidence in the accuracy of results, human review has often been used to confirm results or correct errors made by automated analysis algorithms.

Inaccuracies in performance can also result in excess telecom costs when monitoring ambulatory subjects. For example, some types of ambulatory ECG monitoring devices employ on-board signal processing to detect arrhythmias and forward the detected arrhythmias to a monitoring center where they are further processed and reviewed by a human being using a data review system. Because of limitations in existing algorithms, there

is a high rate of false positive arrhythmia detections in the ambulatory device that results in a high volume of data transmitted from the patient to a monitoring center. These aspects can result in excessive telecommunications expense, the need for additional memory in the ambulatory monitoring device, and additional expense to manually review the data received at the monitoring center.

Various methods of data compression are also limited in their ability to provide high levels of compression with minimal signal distortion in part due to the presence of noise. More efficient data compression can reduce the volume of data that must be stored in memory on an ambulatory monitoring device as well as reduce the volume of data transmitted from the monitored subject. In certain applications, this can result in a reduction in telecom expense and a reduction in power consumption in the ambulatory monitoring device, leading to a reduction in the device size and extension of battery life.

The presence of noise in physiological signals can be a limiting factor in providing accurate and consistent computerized evaluations and extraction of information, but the removal of noise has been complicated by the fact that the noise often has spectral content that falls within the bandwidth of the signals of interest (referred to as in-band noise). For example atrial signals can be contaminated by electrical activity of the ventricle, and ECG signals can be contaminated by EMG from the skeletal muscles. The plethora of signal sources contained within a limited number of channels measured in a surface ECG, with each channel containing mixed interdependent signals, renders the independent observation of the sources of these multisource signals a very difficult problem. This problem is further complicated when signals are acquired from closely spaced electrodes and are contaminated by noise, as is usually the case when monitoring patients outside a clinic or hospital. This characterization is not only common to electrocardiogram (ECG) signals acquired with surface or subcutaneous leads but is also common to electrograms (EGM) measured with intracardiac leads, blood pressure signals, pulse oximetry signals, peripheral nerve activity (PNA) recordings, signals representing non-invasive measurements of intracranial pressure, and other physiologic signals collected from ambulatory subjects. Current filtering techniques such as bandpass filtering are effective in removing noise without distorting the signal when the spectral content of the noise and signal are separated in the frequency domain. Many filtering techniques capable of removing in-band noise such as independent component analysis require that noise and signal content are uncorrelated and independent, an inaccurate assumption for most physiological signals.

Certain efforts have been made for removing at least some in-band noise or denoising of physiological signals, but the success such efforts has been limited. Techniques that have proven effective at removing in-band noise have done so at the expense of signal fidelity. Various techniques have also been limited in their ability to report characteristics of information derived by an algorithm relative to noise, artifact, or signal morphology changes. These and other matters have presented challenges to the design and implementation of devices, systems and methods for processing physiological signals.

SUMMARY

Various aspects of the present disclosure are directed to devices, methods and systems involving physiological signal processing, in a manner that addresses challenges and limitations including those discussed above.

Various aspects of the present invention are directed to adequately denoising signals to facilitate the processing of such signals for the automatic detection of certain characteristics therein (*e.g.*, without human intervention), such as for identifying cardiac events in an ECG signal. Such an approach involves using a processing circuit with respective programming modules that can be accessed and used to carry out denoising functions to overcome technical limitations of previous systems, which had rendered such systems incapable of achieving denoising that is adequate to enable further (accurate) processing and identification of events represented by the signals.

By way of example, previous techniques have been incapable of denoising signals without significantly distorting the underlying signal of interest. Suppression of in-band noise combined with signal morphology preservation has here-to-fore not been achieved. Illustratively, multiple copies of a substantially noise-free single-channel 30-minute digitized human ECG recording sampled at 250 Hz, with average heart rate of about 83 BPM, are each contaminated with a different level of additive band-limited (0.5 to 100 Hz) white noise. In accordance with various embodiments, a denoising system is used to denoise such a contaminated signal having an input signal-to-noise ratio (*e.g.*, computed as SNR_A as discussed herein) ranging from 0 to 40 dB and therein provide a resulting signal exhibiting characteristics relative to noise suppression and signal morphology preservation that enable systems to automatically evaluate signal events and identify feature points with a level of accuracy otherwise unachievable. When processing such a contaminated signal with input signal-to-noise ratios ranging from 0 to 40 dB (*e.g.*, using a signal-to-noise ratio SNR_A as discussed herein) a signal-to-noise ratio improvement ranging from about 26 to about 14 dB,

respectively, is achieved. This improvement in SNR_A is achieved with negligible distortion of the ECG waveform, with the quality of signal reconstruction (QSR) obtained ranging from about 97.5 to 99.8% for input SNR_A ranging from 0 to 40 dB, respectively. The resulting signal thus enables the implementations and operations of systems for automatically characterizing signal events. Using these approaches, events characterized in signals can be readily and automatically detected with a high degree of confidence, relative to the ability to do so with previous approaches incapable of generating signals exhibiting such denoised characteristics. Such a system can be implemented, for example, as part of signal sensing circuit involving signal acquisition leads and corresponding controller circuitry (*e.g.*, an ECG system), enhancing the performance of the circuit and related system.

According to an example embodiment, a denoised physiological signal is computed from an input signal including a desired physiological signal and noise as follows. The input signal is decomposed from a first domain into subcomponents of the input signal in a second domain. Target subcomponents of the input signal that are associated with the desired physiological signal are identified, based upon a spatial distribution of the subcomponents. A denoised physiological signal is constructed in the first domain from at least one of the identified target subcomponents.

Another example embodiment is directed to a system for computing a denoised physiological signal from an input signal including a desired physiological signal and noise. The system includes means for decomposing the input signal from a first domain into subcomponents of the input signal in a second domain, and means for identifying target subcomponents of the input signal that are associated with the desired physiological signal based upon a spatial distribution of the subcomponents. The system further includes means for computing a denoised physiological signal in the first domain from at least one of the identified target subcomponents. The various means may, for example, be carried out using a computer processor or other logic circuit, such as programmed computer or special-purpose processor.

In accordance with various example embodiments, a physiological signal is denoised. In various implementations, denoising is carried out using techniques including those referred to herein as Multi-Domain Signal Processing (MDSP), for which exemplary embodiments are described. The captured signal is received in a first domain and is decomposed into subcomponents in a second domain. The resulting subcomponents in the second domain are processed based upon the spatial distribution of the subcomponents using, for example, spatially selective filtering or principal component analysis to identify

those subcomponents that are primarily associated with noise in a time segment. Subcomponents identified as primarily associated with noise are removed and the remaining subcomponents are combined to reconstruct a denoised signal in the first domain.

Another example embodiment is directed to a method for computing a denoised physiological signal from an input signal including a desired physiological signal and noise. The input signal is decomposed from a first domain into subcomponents of the input signal in a second domain. From the decomposed subcomponents, target subcomponents of the input signal that are associated with the desired physiological signal are identified based upon the spatial distribution of the subcomponents. A denoised physiological signal is constructed in the first domain from at least one of the identified target subcomponents.

Another example embodiment is directed to a method for reducing the power of an undesired signal in a recording of a quasi-periodic mammalian physiological signal containing desired components and undesired components. A transform is used to decompose the physiological signal into subcomponents representing the signal in a time-frequency domain. At least two time windows are identified in a cycle of the signal, each time window having a different band of frequencies associated with desired components of the signal. In the at least two time windows, ones of the subcomponents associated with the desired signal components are identified as subcomponents having spectral content overlapping a band of frequencies associated with desired signal components within said at least two time windows. A denoised physiological signal is constructed using at least one of the identified subcomponents within each of the at least two time windows.

In another aspect of the present disclosure, a dynamic signal-to-noise ratio is computed as the ratio of power contained in the subcomponents primarily associated with signal and subcomponents primarily associated with noise.

In another aspect of the present disclosure, the subcomponents associated with a signal wave of a physiological signal are denoised and are combined to form a denoised emphasis signal of the signal wave. The emphasis signal is subsequently evaluated to identify feature points of the signal wave.

In another aspect of the present disclosure, feature points of signal waves are evaluated to detect clinically significant events and signal morphology characteristics.

In another aspect of the present disclosure, a validity metric, computed as a function of a dynamic signal-to-noise ratio and signal morphology characteristics, is used to assess the accuracy, consistency, and validity of feature points, morphology characteristics, and detected events.

In yet another aspect of the present disclosure, the denoised signal or its subcomponents and detected features are used to facilitate signal compression to reduce stored and communicated data volume.

In yet another aspect of the present disclosure, signal compression and feature and event detection improvements are used to implement a device of reduced size and enhanced performance.

The above summary is not intended to describe each embodiment or every implementation of the present disclosure. The figures and detailed description that follow more particularly exemplify various embodiments.

BRIEF DESCRIPTION OF THE DRAWINGS

The disclosure may be more completely understood in consideration of the following detailed description of various embodiments of the disclosure in connection with the accompanying drawings, in which:

FIG. 1 shows a data flow diagram of Multi-Domain Signal Processing applied to denoising a captured signal, consistent with an example embodiment of the present disclosure;

FIG. 2 shows a data flow diagram of Multi-Domain Signal Processing applied to extraction of a signal from a captured physiological signal, consistent with an example embodiment of the present disclosure;

FIG. 3 shows scatter plots, in which FIG. 3a shows a scatter plot of subcomponents of a noisy signal before application of PCA and ICA, and FIG. 3b shows a scatter plot of subcomponents of the same noisy signal of FIG. 3a after application of PCA and ICA, in accordance with one or more example embodiments of the present disclosure;

FIG. 4 illustrates a data flow diagram for computing a dynamic signal-to-noise ratio, according to an example embodiment of the present disclosure;

FIG. 5 shows an example of denoising and QRS detection in a rabbit ECG with non-sustained ventricular tachycardia, and illustrates a confidence signal computed using dynamic signal-to-noise ratio updated for every cardiac cycle, according to an example embodiment of the present disclosure;

FIG. 6 shows an example of denoising on a 3-lead ECG signals using PCA, ICA, and MDSP, according to another example embodiment of the present disclosure;

FIG. 7 shows results representing denoising of MDSP, PCA, and bandpass filtering, in connection with another example embodiment of the present disclosure;

FIG. 8 shows denoising for a single channel noisy ECG signal, in connection with an example embodiment of the present disclosure;

FIG. 9 shows an example of atrial activity extraction from a surface ECG signal containing atrial flutter, in connection with another example embodiment of the present disclosure;

FIG. 10 shows an example of atrial activity extraction from a surface ECG signal containing atrial fibrillation, in connection with another example embodiment of the present disclosure;

FIG. 11 shows an example of denoising on single channel peripheral nerve activity (PNA) recording corrupted with noise, in connection with another example embodiment of the present disclosure;

FIG. 12 shows a data flow diagram for computing an emphasis signal and finding a feature point in a signal waveform, and example signal waveforms and corresponding emphasis signals and feature point markers, according to another example embodiment of the present disclosure;

FIG. 13 shows an example of QRS detection for a challenging ECG recording, according to another example embodiment of the present disclosure;

FIG. 14 shows a data flow diagram for computing an emphasis signal corresponding to a respiration pattern, according to an example embodiment of the present disclosure;

FIG. 15 shows an example of respiration signal extraction in an ECG recording, according to another example embodiment of the present disclosure;

FIG. 16 illustrates an apparatus for efficient wireless communication of an ECG along with data flow diagrams for ECG signal compression, according to an example embodiment of the present disclosure;

FIG. 17 shows an example of 3D ECG cycle plot as an intermediate step in ECG compression, in connection with another example embodiment of the present disclosure;

FIG. 18 shows a system for evaluating ECG strips captured by an ambulatory monitoring device along with data flow diagrams for determining if a strip contains an arrhythmia and assessing the validity of the result, according to an example embodiment of the present disclosure;

FIG. 19 illustrates an apparatus for improving the signal-to-noise ratio of an ECG signal and related flow chart for processing an ECG signal, in accordance with one or more example embodiments of the present disclosure;

FIG. 20 illustrates an approach for spatially selective filtering, and partitioning of a cardiac cycle of an ECG signal, according to another example embodiment of the present disclosure;

FIG. 21 illustrates a signal flow diagram for an embodiment of denosing applied to an ECG signal, according to another example embodiment of the present disclosure;

FIG. 22 illustrates a system for denoising an ECG signal, in accordance with one or more example embodiments of the present disclosure;

FIG. 23a shows plots representing SNR_A improvement and QSR for MDSP denoising of ECG recordings with controlled levels of imputed band-limited white noise, in accordance with a particular embodiment;

FIG. 23b shows example ECG recording according to a controlled application with 0 dB SNR_A imputed band-limited white noise (top) and post-MDSP denoising (bottom), in accordance with another example embodiment; and

FIG. 24 shows modules/flow functions for denoising a signal, in accordance with another example embodiment of the present invention.

While the disclosure is amenable to various modifications and alternative forms, specifics thereof have been shown by way of example in the drawings and will be described in detail. It should be understood, however, that the intention is not to limit the disclosure to the particular embodiments described. On the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the scope of the disclosure including aspects defined in the claims.

DETAILED DESCRIPTION

Various example embodiments of the present disclosure relate to circuits, devices and systems that process physiological signals, and in many implementations, that process such signals to reduce noise, extract information, characterize signals, and/or compress the volume of data. While the present disclosure is not necessarily limited to such applications, various aspects of the disclosure may be appreciated through a discussion of examples using this context.

As discussed hereinabove, various circuits, devices and systems that process noisy physiological signals (*e.g.,* ambulatory ECG recordings) are incapable of accurately identifying signal characteristics, such as those relating to an event represented by signals (*e.g.*, a cardiac event) or a feature point of the signal (*e.g.,* T-wave offset), in a manner that is sufficiently reliable to permit accurate computer-based identification of the signal

characteristics. This presents a significant challenge to the implementation of such circuits, devices and systems for carrying out signal evaluation. Accordingly, various aspects of the present invention are directed to addressing these challenges, with various implementations directed to denoising signals and providing the denoised signals for evaluation in identifying signal characteristics such as events. Other aspects are further directed to using the denoised signals to automatically identify such characteristics or events with a degree of reliability facilitated via the denoising.

Many embodiments described here are referred to as including an approach involving "Multi-Domain Signal Processing" (MDSP), for which many different embodiments are described by way of example (*e.g.*, as involving signal processing in two or more domains). In connection with various embodiments, the term Multi-Domain Filtering (MDF) is used herein to refer to embodiments that use one or more MDSP-based embodiments to denoise physiologic signals. Various embodiments are also directed to circuits, devices and systems for processing a broad range of physiological signals including but not limited to signals corresponding to ECG, blood pressure, respiratory, heart sounds, EEG, peripheral nerve activity, activity, temperature, photoplethysmography, tissue impedance, blood glucose, and EMG. Certain embodiments are further directed to one or more of: improving the accuracy and consistency of information provided under a broad range of use scenarios, extending battery life of monitoring devices, providing a desirably-sized monitoring device (*e.g.*, a reduced, or small size), and improving and/or reducing the need for human review of analysis results and the associated expense of doing so.

In the following discussion, reference is made to cited references listed in a numbered order near the end of this document, which are fully incorporated herein by reference. These references may assist in providing general information regarding a variety of fields that may relate to one or more embodiments of the present disclosure, and further may provide specific information regarding the application of one or more such embodiments.

According to an example embodiment, physiological signals of a subject are captured by an implantable or external device. This device can be implemented as a part of a system that measures, processes, and evaluates physiological data from animal or human subjects for research, therapy titration, diagnosis, or delivery of medical care. The device may temporarily store the processed signals for later transmission to a system remote from the subject for further processing, display, and reporting to a medical care provider or researcher. The processed signals may be transmitted in real time or they may be used

within a therapy delivery device as part of a system to control or advise administration of a therapy. In yet another embodiment, unprocessed or partially processed signals may be transmitted to a device or system located outside the body of the subject for processing, display, review, reporting, or retransmission to another system.

In many applications, physiological signals processed in accordance with the embodiments discussed herein are multisource signals, meaning that the signal observed by electrodes or leads includes components that are the result of many physiological processes and sources that are often interdependent. For example, an ECG signal measured at the surface of the body may include signals emanating from sources such as the atria, ventricles, electrical noise (*e.g.*, from sources outside the body), noise from muscular electrical activity, signals resulting from pathologies such as conduction defects, scars in tissue from myocardial infarction, ischemia resulting from reduced blood flow to a region of the heart, and other representative examples. In these and other contexts, various embodiments of the present disclosure are directed to addressing challenges relative to the analysis of ECG signals, such as those that benefit from independent analysis for denoising and evaluation of cardiac function.

The terms "quasi-periodic", "signal wave", "feature point", "parameter", and "event" are used in connection with the discussion of various embodiments as follows. The term quasi-periodic refers to a periodic signal with a period with a cycle length that varies with time, and a signal wave is a particular portion or aspect of a period of a physiological signal. For example, an ECG signal may include signal waves referred to as P, Q, R, S, T and U waves. Another example signal wave is the QRS complex portion of an ECG (*e.g.*, the portion of an ECG signal corresponding to the depolarization of the left and right ventricles). In an arterial pressure signal, the dicrotic notch is a signal wave.

Regarding the term "feature point," many physiological signals can be characterized as having features and parameters. A feature point is an identified point within a physiological signal, which may be useful for characterizing the signal and related characteristics of the signal's source. For instance, in heart-related signals, such as ECG, arterial pressure, and blood flow, most cardiac cycles have a feature point or points of interest. Examples include a point corresponding to the onset of the Q-wave (*e.g.*, Q-wave onset) or offset of the T-wave (*e.g.*, T-wave offset) in an ECG or systole in an arterial blood pressure signal. Each of these feature points can be described by time of occurrence and amplitude, and consecutive feature points can be combined to form a feature signal.

With further respect to the term "feature point," it is sometimes useful to combine feature points over a predetermined period of time, referred to as a feature signal, to compute a parameter. For example, systole feature points can be combined to compute a mean systolic pressure. Computing a parameter can have the effect of reducing or eliminating short-term physiological fluctuations (*e.g.*, changes with respiration) in the feature signal that are not of interest to the user.

Regarding the term "event," physiological signals may include information that can be used for identifying the onset and offset of an event, or simply the fact that an event occurred. For example, when monitoring the ECG of a subject it may be useful to know that an arrhythmic event such as ventricular tachycardia or atrial fibrillation has occurred. In additional embodiments, information is combined from multiple signals to compute features and parameters. For example, the QA interval (the time difference between Q-wave onset and the upstroke of an arterial pressure wave) can be used as a surrogate for cardiac contractility, and employs both a pressure and an ECG signal from a subject. QA interval feature points are computed for a cardiac cycle, can be used to create a feature signal, and averaged over a predetermined period of time to create a QA parameter.

Regarding the terms referring to a "desired physiological signal," such a signal refers to a signal that is to be extracted. This signal may correspond, for example, to a physiological signal within an input signals that include the physiological signal and noise. In this context, the noise may also include a physiological signal that is not the desired physiological signal. For instance, where a desired physiological signal is an ECG signal from a subject's heart, other physiological signals included with an input signal, such as a respiratory signal, are not desirably extracted.

A "captured signal" is a signal that is sensed and recorded (*e.g.*, digitized), and may also be conditioned. Conditioning of the signal may involve amplification and the application of a filter to remove much of the noise that is outside the bandwidth of the signal. Following digitization, additional filtering may be applied to further remove noise from outside the signal bandwidth, typically using linear filtering techniques such as a finite impulse response filter.

A "denoised" signal is a captured signal that has been processed to remove noise, such as by removing undesirable signal components or subcomponents having spectral content within a bandwidth of a selected (*e.g.*, target, or desired signal), or in-band noise. Denoising can be useful for rendering clarity to the desired signal as a result of suppression

of undesired signal components (*e.g.*, noise), hence making the desired signal more suitable for analysis.

In accordance with other example embodiments of the present disclosure, in-band noise of a physiological signal is reduced using a technique involving a multi-domain filtering-type of approach, referred to in connection with various embodiments as MDF, as may be implemented with one or more circuits, devices or systems. Resulting (output) signals are thus denoised, in the context that at least some noise components in the physiological signal have been removed, relative to the resulting signal (*e.g.*, as re-generated from components of the physiological signal, in a different domain). These denoised signals facilitate the use of computer-type circuits to automatically evaluate the signals for identifying characteristics therein with a high degree of reliability.

In one embodiment, signals captured in a first domain are decomposed into subcomponents in a second domain. To remove in-band noise from the captured physiological signal, the subcomponents in the second domain are processed based on their spatial distribution using, for example, spatially selective filtering or principal component analysis to identify those subcomponents that are primarily associated with noise. Those subcomponents that are identified as primarily associated with noise are removed and the residual subcomponents (those not having been removed) are combined to reconstruct a denoised signal in the first domain. A subcomponent occurring in a time window within a cycle of the pseudo-periodic signal is said to be associated with a signal if it contains frequencies within a band that has previously been characterized as being present in the signal. A subcomponent within a time segment is considered to be primarily associated with noise if the energy associated with the signal is attributed primarily (*e.g.*, more than half) to noise. In some embodiments, a larger tolerance for noise is set, to permit signals with larger noise content to be processed without distorting the signal (*e.g.*, where a desired signal is expected to include a substantial portion of noise). Under such conditions, processing of the detected signal can be carried out with the understanding that noise forms a majority of the power in the subcomponent. In some implementations, a signal is treated as primarily associated with noise when at least about 60% of the signal's energy at that time segment is noise energy. Likewise, a subcomponent within a time segment is considered to be primarily associated with signal if at least half or more (*e.g.*, 60%) of its energy is within the band of frequencies characterized as being present in the signal.

In the context of various embodiments, references to the removal of subcomponents may not involve any removal or modification of the subcomponents, but rather involve a

selective combination of those subcomponents that have been determined to be desirable. For example, for a physiological signal having various subcomponents, certain components can be identified as likely representing components of a signal corresponding to a particular physiological characteristic that is to be analyzed. These identified (desirable) components can be selectively combined, leaving behind other subcomponents. In this context, undesirable subcomponents are not necessarily removed, but rather, have not been used when forming a recombined signal corresponding to a received physiological signal.

The subcomponents that result from decomposition in Multi-Domain Signal Processing (MDSP) embodiments are also used in other aspects of physiologic signal processing, for various embodiments. A characteristic of MDSP is that a signal wave in a multisource physiological signal can be represented using a small number of subcomponents that contain most of the energy of the signal wave. For example, in an ECG decomposed into 4 levels using a discrete wavelet transform, a group of 3 subcomponents may contain most of the energy found in the P-wave of an ECG while most of the energy of a QRS complex may be contained in 4 subcomponents. A subcomponent or its time segment containing a significant amount of energy of a signal at that time segment is said to be associated with the signal at that time segment. As applicable here, a significant amount of energy of a subcomponent is an amount of energy, corresponding to the time segment, that is at least half of the total energy of the signal during the time segment. In various implementations, a subcomponent may be associated with more than one signal wave.

Subcomponents or their time segments associated with a signal wave can be identified, isolated, and used to construct a signal wave independent of other signal waves in a multisource signal. For example, subcomponents associated with a P-wave of an ECG can be identified within the second domain independent of ventricular electrical activity, and used to reconstruct a denoised signal representative of atrial activity. Another group of subcomponents is associated with the T-wave of an ECG, and are used in the extraction of repolarization activity. Signal source extraction of the signal subcomponents in a multisource signal can lead to more accurate analysis and evaluation of certain physiological functions. Another embodiment involving signal source extraction is directed to the extraction of fetal ECGs from ECG signals captured from a pregnant female. Yet another example embodiment is directed to extracting an oxygen saturation signal from a photoplethysmography signal.

Subcomponents can also be used to compute a denoised emphasis signal that exaggerates the features of particular signal waves to facilitate the identification and

detection of feature points. For example, subcomponents associated with the T-wave of an ECG can be identified and used to compute a denoised emphasis signal that exaggerates the T-wave relative to other ECG signal waves to facilitate accurate and consistent detection of T-wave offset.

In some embodiments, physiological signal subcomponents are used to compute a dynamic signal-to-noise ratio (dSNR) that represents the ratio of signal energy relative to noise energy on a sample-by-sample basis, or longer period of time such as for one or more cardiac cycles of an ECG. The dSNR can be used for computing a validity signal for assessing the accuracy and reliability of information derived from the captured physiological signal. In some embodiments, the dSNR is used to directly assess the accuracy and reliability of derived information. If dSNR for a cardiac cycle or a portion of a cardiac cycle is low, for example, certain information derived from the ECG for that cardiac cycle may not be accurate and, if it is very low, a cardiac cycle may be uninterpretable.

MDF denoising and other aspects of one or more MDSP-based embodiments are directed to facilitating the efficient compression of physiological signals, which can be used to reduce the volume of data corresponding to sensed signals. Reducing the amount of data (e.g., by eliminating or omitting noise) serves to help the efficient storage of data, and also to reduce the amount of data needed in communications which can be helpful, for example, to simplify wireless transmission protocol. For example, various MDSP-based embodiments involve compressing ECG signals at compression rates of 15:1 to 20:1 (*e.g.*, relative to an original physiological signal prior to denoising) with minimal signal distortion. An MDSP approach is used to achieve accurate identification of cardiac cycles of a denoised ECG, and significantly reduce in-band noise. These identification and denoising approaches are used in connection with one or more of a variety of compression algorithms, in accordance with various embodiments, together with identified redundancies in adjacent cardiac cycles to achieve efficient compression.

In some embodiments, an MDF-based approach is used to remove noise from peripheral nerve activity (PNA) signals and facilitate the accurate quantification of PNA. In these and/or other embodiments, an MDSP-based approach is used across a broad range of physiological signal processing applications with related processing without necessarily relying upon assumptions regarding the independence of signal and noise sources, and/or based upon an assumption (for processing) that physiological signals being processed are quasi-periodic signals.

In the following discussion, reference is made to various documents or other references listed near the end of this patent document, by numerals within square brackets. The information in the documents/references to which these numerals refer may be implemented in connection with one or more example embodiments, and are fully incorporated herein by reference.

Various embodiments are directed to processing signals from ambulatory subjects under conditions in which noise is common and measurements are often obtained using a limited number of closely-spaced electrodes, or a single cannulation of a vessel, such as in the case of blood pressure measurements. Such signals often include aspects of signals emanating from multiple sources that are generally interdependent. For example, heart activity in an atrial chamber usually initiates activity in a ventricular chamber. Statistically, this situation is characterized by mutual dependency of signal sources contaminated by noise. This violates a central assumption of independence of sources that is fundamental to successful application of many current techniques used to separate signal source and noise in multisource signals, such as independent component analysis (ICA) [1]. Various embodiments are directed to processing related signals, without necessarily assuming such independence, to obtain a denoised signal for a desired signal (*i.e.*, a signal corresponding to a characteristic to be detected).

The problem of extracting source signals from the multisource physiological signals contaminated with noise can be expressed mathematically as:

$$x(t) = As(t) + n(t) \qquad (1)$$

where $s(t) = (s_1(t),...,s_P(t))$ is a vector of source signals that are mixed together by an unknown mixing matrix A of size M x P, where M is a number of observed signals and P is a number of source signals and additive noise $n(t) = (n_1(t),...,n_P(t))$. The extraction of source signals is achieved by estimating the inverse of a mixing matrix A and computing the denoised and separated signals $s(t) = (s_1(t),...,s_P(t))$ from the observed signals $x(t) = (x_1(t),...,x_M(t))$ according to the formula $s(t) = A^{-1}x(t) - A^{-1}n(t)$. When the number of leads M is less than the number of sources P, which is most often the case in physiologic monitoring, the mixing matrix A_{MxP} is underdetermined. In addition, the sources that make up multisource physiological signals are often not independent. In this situation the matrix A_{MxP} is not invertible, rendering it difficult to estimate an inverse of the M x P mixing matrix

and recover unmixed sources from mixed observations, as is the case when using ICA techniques.

Turning now to the figures, Figure 16 shows an example system implementation involving a specific aspect of the implementation of various embodiments, as applicable to circuitry, related programming and corresponding data that relates to electrodes, signal lines and processing circuitry for controlling and evaluating ECG signals obtained via the electrodes. While various aspects of Figure 16 are discussed in greater detail later in this document, reference to this figure may be made in connection with the following (and above) discussion in considering functionality of such a system (*e.g.*, via modules implemented in code and used by such a system to process data signals and both generate and evaluate denoised signals).

Figures 1 and 2 show signal denoising and signal source extraction, respectively, as carried out in a three-step process in accordance with another example embodiment of the present disclosure. The first step, 102 and 202 in Figures 1 and 2 respectively, involves decomposing an input signal 101 and 201 into subcomponents in a second domain. Decomposition steps 102 and 202 are performed using one of a variety of transforms that is used for accurate signal reconstruction. Such transforms may involve using, for example, a discrete cosine transform, a wavelet related transform, a synchrosqueezed wavelet transform, a Karhunen-Loeve transform, a Fourier transform, a Gabor transform, or a filter bank, as may be implemented by signal-processing circuitry. In Figures 1 and 2, the set of subcomponents resulting from the decomposition steps 102 and 202, respectively is referred to as D2sub. The dimension of the first domain is defined by the number of observed, or captured, signal channels. The dimension of the second domain is defined by the number of channels multiplied by the number of subcomponents in each channel. The second step involves the identification of signal and noise subcomponents in the second domain followed by removal of unwanted subcomponents, including noise.

Various embodiments herein refer to identifying subcomponents based upon the spatial distribution of the subcomponents. Such identification may involve, for example, identifying subcomponents based upon their relationship with one another as a function of time. For example, a time-based separation of the subcomponents in a particular signal can be used to identify a characteristic to which the subcomponents pertain, as relative to an expected distribution for the particular signal. In the context of a cardiac signal, a time-based position can be used to identify portions of a cardiac cycle.

Referring to Figure 1, subcomponents of the set D2sub that are primarily associated with noise are identified and removed to create a subset D2s of residual denoised subcomponents, to denoise a desired signal. Referring to Figure 2, if signal source extraction is performed, such as when an atrial activity signal is extracted from a surface ECG, the subcomponents associated with the signal sources to be extracted are identified and the other subcomponents are removed to create a subset D2soi containing energy associated with the desired signal. In certain embodiments involving both denoising and signal source extraction, subcomponents to be removed are identified based upon their spatial distribution using, for example, Spatially Selective Filtering (SSF) or Periodic Component Analysis (πCA). At decision steps 103 and 203 in Figures 1 and 2, the signal is processed at block 104/204 if the dimension of the first domain is greater than 1, or at block 105/205 if the dimension of the first domain is not greater than one.

If the dimension of the first domain is greater than 1, then SSF, πCA, Principal Component Analysis (PCA), and Independent Component Analysis (ICA) can be used in combination (*e.g.*, as in blocks 104 and 204). If the dimension of the first domain is equal to 1, then SSF or πCA can be used to evaluate the spatial distribution of the subcomponents, as in 105 and 205. Once the subcomponents associated with noise are identified they are effectively removed by setting them to zero. Following removal of the subcomponents associated with noise, the subcomponents are said to be denoised. In the case of signal source extraction, those subcomponents associated with noise and those not associated with a signal source to be extracted are identified and effectively removed by setting them to zero.

In step 106, the denoised signal subcomponents, referred to as subset D2s, are reconstructed in the first domain to provide denoised output signal 107 by performing the inverse of the transform used to decompose the signal. If signal source extraction is performed only those subcomponents not removed and identified as associated with the desired signal sources, referred to as subcomponent subset D2soi, are reconstructed into the extracted desired signal 207 in Figure 2.

Various embodiments directed to MDSP approaches use a mathematical representation of physiological signals as a linear combination of basis functions. Each of these basis functions is chosen to fit a prominent feature, or signal wave, of a signal source. For example, a basis function might represent a type of QRS complex contained in an ECG signal. In one embodiment, decomposition is achieved by representing the observed signals as a linear combination of basis functions,

$$s_i(t) = \sum_{k=1}^{K} \varphi_k(t) d_{ik}, i = 1:P, \quad x_i(t) = \sum_{k=1}^{K} \varphi_k(t) c_{ik}, i = 1:M \tag{2}$$

where d_{ik} and c_{ik} are decomposition coefficients or subcomponents. In some embodiments, the elements φ_k may be mutually dependent and form an overcomplete set referred to as a "dictionary" D. The elements are selected to provide a sparse representation of the signal sources, meaning that most of the decomposition coefficients d_{ik} and c_{ik} in equation (2) are close to or equal to zero. A combination of basis functions or elements of the dictionary forms the second domain.

Higher sparsity provides for greater statistical independence of signal source and noise subcomponents. This property of sparse decomposition is used to facilitate effective identification and extraction of signal source subcomponents and removal of noise. Sparse decomposition, for example, can result in a concentration of signal energy in a relatively small number of large decomposition coefficients while noise is spread out across many basis functions and represented by small decomposition coefficients as described in equation (2).

The sparsity criteria can be used to choose a dictionary that provides for sparse decomposition of the signal sources and hence improved signal source extraction and denoising. In certain embodiments it may be advantageous to choose an over-complete dictionary D in order to increase the degree of sparsity of the decomposition. The examples of dictionaries that are relevant to this embodiment include eigenfunctions [2], wavelet related transforms, including wavelet packets, shift-invariant or stationary wavelets [3] and a synchrosqueezed wavelet transform [29], cosine transform [4], Fourier basis [5] or Gabor basis and their combinations [6]. A custom dictionary that achieves a higher degree of sparsity can also be designed by a number of methods for finding basis functions that represent building blocks of the signal [7]. The examples of these methods are matching pursuit [5], orthogonal matching pursuit [8], basis pursuit [9], K-SVD [10], bounded error subset selection [11] or orthogonal subspace pursuit. In general, the dictionary design methods use a representative set of training signals, to find a dictionary that leads to the best representation for each signal wave in this set, under strict sparsity constraints:

$$\min_{D,c} \{\| x - Dc \|_F^2\} \quad \text{subject to } \| c \|_0 \leq T$$

where $\| . \|_0$ is a l^0 norm, counting the nonzero entries of a vector, T is a constraint on the maximum number of non-zero elements allowed, and $\| . \|_F^2$ is a Frobenius norm. For

example, a representative set of training signals can be a set of ECG recordings with a broad range of morphologies that include normal sinus rhythm, conduction abnormalities, pathologies, arrhythmias for a particular species. The set should include a sample of each morphology that the algorithm may experience during analysis of an ECG recording of the species.

In one embodiment the custom dictionary is build using the following iterative procedure. A vector is selected from the training set and is represented as a sparse linear combination of initial dictionary elements. This can be accomplished, for example, by finding elements that are maximally correlated with the vector. This subset of elements form a subspace that is decorrelated from the rest of the training set (*e.g.*, by using singular value decomposition (SVD)). The decorrelated subset is added to the dictionary and the elements of the training set that lie in this subspace are removed from the training set. The process is repeated until an error threshold is reached or an allowed number of iterations is exhausted.

In another embodiment decomposition into the second domain is achieved by applying an adaptive filter that automatically selects the frequency bands, or subbands of wavelet filters or a filter bank, in which subcomponents of the signal sources are most independent. Then each subcomponent $x_i(t), i = 1:M,$ can be represented as a sum of subband signals

$$x_i(t) = x_{i,1}(t) + \ldots + x_{i,K}(t) \tag{3}$$

where K is the number of chosen subbands. The filter coefficients can be adaptively tuned to reduce and/or minimize the mutual information and increase independence between the filter outputs as described by Zhang, *et al.* [12]

In an embodiment involving a wavelet-related transform decomposition, the first decomposition step for an observed signal with M channels into a wavelet-related dictionary D can be formally described as iterative multiplication of the observed signal by an operator matrix W^j with each iteration step j making up a decomposition level. In this embodiment, the operator matrix W^j is a Toeplitz matrix with the entries formed by a wavelet impulse response. The size of the matrix operator W^j is NxN where N is the number of samples of the observed signal. N is greater than both the number of sources P and the number of observed signals M. Wavelets may be used to generate subcomponents having characteristics of both sparse and subband decomposition. In some implementations, a wavelet decomposition is computed via iterative convolution with wavelet filters or filter banks as described by Vaidyanathan [13].

Referring again to Figures 1 and 2, another example embodiment is implemented at step 2, for an MDSP-based approach. The statistical independence of at least some subcomponents related to signal sources and noise is leveraged to identify those subcomponents associated with signal sources and those associated with noise. For example, in case of wavelet decomposition, the equation (1) becomes

$$W_x^j = A_j W_s^j + W_n^j, j = 1 : NL + 1 \quad (4)$$

where NL is the number of decomposition levels or subbands. The mixing matrix A is indexed by j, denoting that the sources are mixed differently in each subband according to their spectral distribution.

The subcomponents associated with signal sources can be identified based on spatial distribution of subcomponents in time using one of several techniques, many of which involve finding the mixing matrices A_j and then inverting them to calculate the signal source subcomponents. Examples of techniques that are applicable to identification of subcomponents associated with noise and subcomponents associated with signal sources (i.e. the desired signal) include principal component analysis (PCA), independent component analysis (ICA), periodic component analysis (πCA) techniques and spatially selective filtering as shown in blocks 104 and 105 of Figure 1 and blocks 204 and 205 of Figure 2. These techniques can be used separately or in combination to achieve acceptable performance.

In one embodiment, spatially selective filtering (SSF) is employed to identify subcomponents associated with the desired signal and is used in combination with PCA or ICA in blocks 104 and 204 if the input signal consists of two or more channels. In one embodiment, if the input signal is a single channel signal (dimension of the first domain =1), then only SSF is employed in blocks 105 and 205 to identify subcomponents associated with noise.

In another embodiment, periodic component analysis (πCA) is employed to identify subcomponents associated with the desired signal and is used in combination with PCA or ICA in blocks 104 and 204 if the input signal consists of two or more channels. In one embodiment, if the input signal is a single channel signal (dimension of the first domain =1), then only πCA is employed in blocks 105 and 205 to discriminate between subcomponents associated with a desired signal and subcomponents associated with noise.

When using the PCA technique to identify subcomponents associated with signal sources, an inverse of the mixing matrix A_j is estimated using singular value decomposition

or eigenvalue decomposition of the covariance matrix of signal subcomponents. This PCA approach involves rotating and scaling the data in order to orthogonalize independent subcomponents. The orthogonalized subcomponents with low signal power are often associated with noise and can be removed to achieve denoising. PCA can be used as a preliminary step prior to applying ICA technique.

In various embodiments involving the use of an ICA technique to identify subcomponents associated with signal sources, an inverse of the mixing matrix A_j is estimated [1,14] as a solution of an optimization problem that maximizes independence between the signal sources. For example, ICA techniques can use either higher-order statistics of signal components or information-theoretic criteria to maximize independence. Information theoretic criteria that can be applied include maximization of negentropy or its approximation, minimization of mutual information, maximum likelihood estimation , maximum a posteriori probability , or expectation–maximization of Gaussian mixture models of sources. These solutions can be approximated via efficient numerical methods [1], such as FastICA and JADE algorithms. The Figure 3a provides a scatter plot image of subcomponents in the second domain prior to the application of PCA and ICA in the denoising process. Figure 3b demonstrates an example result of denoising and subcomponent separation achieved by applying a combination of PCA and ICA techniques. Note that application of PCA and ICA has achieved a decorrelation of the subcomponents and alignment along the coordinate axis 302 of the scatter plot, indicating a large degree of independence has been achieved between the subcomponents (*e.g.*, relative to alignment in with coordinate axis 301 Figure 3a). This high degree of independence between subcomponents that occurs as a result of the denoising process facilitates efficient removal of noise and signal source extraction.

In embodiments involving the use of πCA technique to identify signal sources, an inverse of the mixing matrix A_j is estimated as a solution of an optimization problem that separates subcomponents based on their periodicity or quasi-periodicity [15]. Instead of diagonalizing and inverting the covariance matrix as is done with PCA, the πCA technique jointly diagonalizes the covariance matrix and an autocorrelation matrix. The autocorrelation matrix is calculated as an average of autocorrelation matrices computed over time lags corresponding to period lengths.

In one embodiment, a quasi-periodic signal can be phase-wrapped by mapping the period length to a linear phase $\varphi(t)$ ranging from $-\pi$ to $+\pi$ assigned to each sample. The autocorrelation matrix can then be calculated in the polar coordinates in which cardiac cycles

are phase aligned. The technique involves extracting most pseudo-periodic subcomponents corresponding to a desired physiologic signal. The technique is efficient at identifying signal source and noise subcomponents but relies on accurate detection of cycles such as cardiac or respiratory cycles. It can be used in combination with spatially selective filtering (SSF), a technique that facilitates better cycle detection.

In another embodiment, referring to Figure 2, signal sources are identified and separated in the second step, blocks 204 and 205 as discussed above, using spatially selective filtering. Spatially selective filtering [16,17] techniques detect signal-related features and pass them across the subcomponents while blocking features inherent to noise. The technique relies on the differences of noise and signal distributions between subcomponents.

In one embodiment, a signal decomposition is carried out in which signal energy is concentrated in a small number of large subcomponent coefficients while noise is spread out across many decomposition levels and is represented by small coefficients. Techniques similar to wavelet thresholding [18] can be used to remove this noise, but their use may result in a degradation of signal morphology.

In another embodiment, spatially selective filtering (SSF) is used. When the physiological signal is pseudoperiodic and the frequency content of the signal varies predictably over the course of a cycle, spatially selective filtering may be used. For example, when the physiological signal is an ECG, SSF can exploit the fact that many noise subcomponents throughout all but the QRS complex of the cardiac cycle are confined to decomposition levels that represent high frequencies, while the QRS complex often has high amplitude across multiple subcomponents. In an embodiment that employs SSF, a fiducial point in a cycle of a pseudoperiodic signal is identified by computing a time function that measures spatial distribution of subcomponents and comparing the time function to a threshold. In one embodiment the time function is a point-wise product of subcomponents corresponding to lower frequencies. In another embodiment, the point-wise product is normalized to match the energy of a subcomponent. In another embodiment the time function is a cross-correlation between subcomponents that correspond to lower frequencies.

To identify a fiducial point in a cycle, the computed time function is compared to a threshold to identify locations of peaks and valleys that occur simultaneously across multiple subcomponents. For example, when the physiological signal is an ECG, large peaks and valleys of the time function may correspond to a QRS wave. In each cardiac cycle, the subcomponents within a window corresponding to the QRS complex are preserved and the

subcomponents outside of the QRS window that correspond to higher frequencies are zeroed out or filtered.

Referring to Figure 20, a cardiac cycle of an ECG is partitioned into time windows 2002 and 2003: 2002 containing the QRS complex and 2003 spanning the remainder of the cardiac cycle. The subcomponents associated with both low and high frequencies, represented by region 2004, are preserved within the time window 2002 containing the identified QRS complex. The low-frequency subcomponents associated with the desired signal, present in window 2003 and represented by region 2005, are preserved and subcomponents associated with high frequencies are removed. In another embodiment, subcomponents associated with low-frequencies, represented by region 2007, are preserved throughout the cardiac cycle and subcomponents associated with high frequencies are preserved in a time window represented by region 2006. In one embodiment time window 2002 is a rectangular-shaped window that transitions at the window boundaries as a step function, as in Figure 20(c). In another embodiment, the leading and/or trailing edges of time window 2002 transition to zero gradually to reduce the potential for signal distortion near the beginning and end of window 2002. In one embodiment, window 2002 transitions in time as a linear function and the shape is trapezoidal, as in Figure 20(d). In Figure 20(d), time span 2008 designates the base of the trapezoidal window and corresponds to window 2002. In another embodiment, window 2002 transitions as a monotonic region of a cosine or other function that provides a gradual transition from low to high and high to low at the leading and trailing edge, respectively, of the window. Region 2009 corresponds to windows 2003 and 2005, the portion of the cardiac cycle outside QRS window 2002, where low frequency content (*e.g.*, subcomponents associated P and T-waves) is preserved and high frequency content is rejected.

Use of SSF is not limited to pseudoperiodic signals. For example, in another embodiment, SSF is used to remove EMG artifact from non-quasiperiodic PNA signals. SSF is used to detect high amplitude EMG artifact as large peaks present in multiple subcomponents simultaneously. A time window containing artifact can be identified by comparing a point-wise product of subcomponents or a cross-correlation of subcomponents to a threshold. The EMG noise can then be removed by zeroing most or all subcomponents in the time window.

In some embodiments the spatially selective filtering is combined with one or more of PCA, ICA, or πCA. For example, the subcomponents that were identified as noise at the PCA stage can be further filtered to remove only some segments that have spatial and

temporal characteristics of noise. In another example, the subcomponents that were identified as signals at the PCA stage can be further filtered to remove additional time segments from subcomponents that have spatial and temporal characteristics of noise.

The choice of a technique for identification of subcomponents for denoising or signal source extraction depends upon signal and noise characteristics of the physiologic signal, spatial distribution of its subcomponents and the signal acquisition and processing environment. For example, it may be useful to process multi-channel signals with PCA and ICA techniques and their combinations with spatially selective filtering. When processing ECG signals obtained from an implanted single lead device, spatially selective filtering or *πCA* may be applied, as in blocks 105 and 205 in Figures 1 and 2, respectively.

In some embodiments, step three as shown in blocks 106 and 206 of Figures 1 and 2, respectively, involves reconstructing the subcomponents remaining following denoising and signal source extraction, $s(t) = (s_1(t),...,s_P(t))$, in the first domain. This is accomplished by an inverse transform of extracted signal sources or denoised signal sources. If wavelet-based decomposition is employed, the reconstruction step can be formally described as iterative multiplication by an inverse of the operator matrix W^j with each iteration step j corresponding to a reconstruction level.

Referring to Figure 4, other example embodiments involve a circuit and approach for computing a dynamic signal-to-noise ratio (dSNR) in a manner that can be updated on a sample-by-sample basis. dSNR can be used to assess the accuracy and reliability of information derived from the physiological signal and, in some embodiments, can be combined with other signal information such as ECG arrhythmic event information to compute a validity metric to assess the validity of information extracted from a signal. If dSNR for a cardiac cycle is low, for example, information derived from the ECG for that cardiac cycle may not be accurate.

A dynamic signal-to-noise ratio (dSNR) can be computed as the ratio of the energies in signal and noise subcomponents. In one embodiment, referring to Figure 4, an input signal 401 in a first domain is decomposed in process 402 into subcomponents, referred to as set D2sub, in a second domain. At decision point 403, the signal processing flow proceeds according to the dimension of the first domain. If the dimension of the first domain equals 1, then subcomponents primarily associated with noise, referred to as set D2n, are identified in process 405 using SSF. In another embodiment, the subcomponents primarily associated with noise are identified in process 405 using . Subcomponents of set D2n are combined to compute an estimate of noise energy and residual subcomponents, referred to as set D2s, are

combined to compute an estimate of signal energy in process 407. The SNR is then computed in process 409 to create output dSNR value 410 according to formula:

$$SNR_{dB} = 10\log_{10}(\frac{P_{signal}}{P_{noise}}) = 20\log_{10}(\frac{A_{signal}}{A_{noise}})$$

Where P_{signal} and P_{noise} are respective signal and noise energy and A_{signal} and A_{noise} are respective signal and noise amplitude.

If the dimension of the first domain is larger than one, a PCA or ICA technique can be used in process 404 for initial subcomponent denoising. The noise subcomponents extracted at this initial denoising step can be discarded and the residual noise and signal subcomponents can be identified using SSF or πCA in process 406. In process 408, the noise subcomponents identified at this stage, D2n, are used to calculate an estimate of noise energy and the residual subcomponents, D2s, are used to compute an estimate of signal energy. The SNR is then computed in process 409 (*e.g.*, as described above). In alternate embodiments measurement of signal energy Ps and noise energy Pn can be used to compute other metrics indicative of signal quality such as a difference between Ps and Pn and a ratio of Ps/Pn.

In other embodiments, a signal-to-noise ratio is estimated using conventional approaches following denoising of the signal using an MDSP embodiment. In one embodiment, the noise is measured between signal waves by computing the peak amplitude and density of zero crossings or variability of signal in a segment between signal waves. In other embodiments, a signal-to-noise ratio is estimated by computing a spectral distribution of the denoised signal. For example, in an ECG signal, peaks in the spectral distribution are evaluated to determine the relative power in the spectrum that occurs within and outside of the normal range of the QRS complex, T-wave, and P-wave.

In one embodiment dSNR is updated for each cardiac cycle. Alternative implementations may update dSNR more or less often. For example, it may be useful in some embodiments to compute a value of dSNR for a window of two to ten cardiac cycles and use this value in calculation of the validity metric for all cardiac cycles within the window. Figure 5 provides an example of a dynamic confidence signal (dCS), also referred to as a validity metric in some embodiments, derived from dSNR computed for a rabbit ECG signal 501, with dCS shown in the dashed line 505 in the top plot, and the bottom plot showing automatic marking of QRS complexes (squares as 504) and detected VT (circles as 503), in accordance with another example embodiment. The dynamic confidence signal 505 (dashed) is updated for each cardiac cycle. The dCS is updated every cardiac cycle and the

value of dCS reflects changes in signal amplitude relative to the level of noise in the recording. Despite the low signal-to-noise ratio, all QRS complexes (as indicated by the squares 504 marking bottom ECG trace) and non-sustained episodes of ventricular tachycardia (marked by circles 503 marking bottom ECG trace) are detected. These signals can be output and used to provide an indication upon which a degree of confidence in automated signal event detection can be based.

In various embodiments, MDSP-based approaches as discussed herein are used to denoise and extract information from a physiologic signal acquired in a low SNR environment. For example, a collar or spring-loaded clip placed on the neck of an animal with embedded ECG electrodes can be used to collect ECG signals in animals non-invasively. While such an approach may result in a low SNR, denoising approaches such as discussed herein can be used to glean meaningful data from the ECG signals. Another embodiment is directed to placing a collar or spring-loaded clip on the neck of an animal, or a collar placed around the tail or limb, which can house light emitting diode transmitters and light receiving sensors to collect photoplesythmography signals. In one embodiment, the collar or clip includes two pairs of light transmitters and receivers placed at different locations on the neck of the animal in order to achieve redundancy and improved noise suppression. In another embodiment a cage floor having ECG sensors is used to collect ECG signals from the animal feet. These applications are exemplary of many applications characterized by low SNR, for which denoising approaches as discussed can be used to render the applications viable for analysis.

In the following examples, performance aspects are discussed as may be relevant to various embodiments is illustrated and analyzed, many of which involve the analysis of ECG and PNA signals that can be challenging to carry out using other approaches. In many of the examples discussed here, the signal sources are contaminated with noise and the number of sources is larger than the number of observed signals. Although embodiments of the present disclosure can be used with a broad range of physiological signals, exemplary performance is illustrated with ECG and PNA signals that are problematic for traditional signal processing approaches because of contamination with in-band noise that could not be substantially reduced without distorting signal morphology. Such embodiments are applicable to the use of MDSP-based approaches as discussed herein, to achieve certain performance-related conditions or characteristics, which can be measured or relatively characterized in manners as discussed herein. Accordingly, various embodiments are directed to approaches to achieving such things as levels or degrees of noise reduction,

signal quality, cardiac (or other signal) event detection accuracy and more, as facilitated using aspects of the disclosure as described herein.

Various MDSP-based embodiments are directed to denoising a physiological signal while preserving the morphology of a desired signal within the physiological signal (*e.g.*, as recorded). Quality of signal reconstruction (QSR) is a metric commonly employed to assess the ability of a noise removal technique to preserve morphology of the desired signal in signals with moderate to high signal to noise ratio. QSR is defined as the mean squared error between the original signal x_{cl} and denoised signal x_{den} calculated sample-by-sample as a percentage of the original signal variance.

$$QSR = 100\% * (1 - \frac{\sum_i (x_{cl}^i - x_{den}^i)^2}{\sum_i (x_{cl}^i)^2})$$

QSR of a denoised signal would be close to 100% if the original recording is contaminated with minimal noise and if distortion introduced into the desired signal by denoising was very small.

Figure 6 shows plots characterizing an example MDF-based embodiment directed to removing noise from input 3-lead ECG signals 601,602, and 603, as may be implemented (by way of example) from a PhysioNet [19] database. Results of ICA and PCA applied directly to the signal are also shown for comparison. The ECG recordings of Figure 6 represent signals with portions that are relatively noise free (601) and portions that are noisy (602 and 603), demonstrating the removal of noise with an MDF-type approach as discussed herein while also preserving morphology. In such a short recording, the character of the denoising technique, whether MDF, ICA, or PCA, is relatively consistent throughout the duration. Evaluating QSR for the portion which is relatively noise free, therefore, provides an indication of a technique's ability to preserve morphology while a visual inspection of the noisy portion provides for a qualitative assessment of the ability of a particular technique to suppress noise. For the relatively noise free portion, the MDF-based approach shows QSR values of 98%, 99%, and 92% for the top 610, middle 611, and bottom 612 traces, respectively, indicating that distortion was negligible. The PCA approach shows QSR values of 83%, 68%, and 71%, for the top 604, middle 605, and bottom 606 traces, respectively, indicating significant distortion of signal content. The ICA approach shows QSR values of 2%, 1%, and 4%, for the top 607, middle 608, and bottom 609 traces, respectively, indicating very significant distortion of signal content. Accordingly, various MDSP-based

embodiments are directed to processing signals to address challenges relating to such QSR values that may be insufficient, if processed otherwise.

Figure 7 shows characteristic results of denoising using an MDF-type approach (in accordance with an example/experimental-type embodiment), Butterworth bandpass filtering (BPF) with a pass-band of 1 to 60 Hz, and PCA. A relatively noise-free ECG from the PhysioNet Long-Term ST database (record s30661) is corrupted with increasing levels of band-limited (.05 to 70Hz) white noise, and processed in accordance with an example embodiment. The denoising results are quantified measuring QSR and input and output signal SNR according to the formula:

$$SNR_{dB} = 20\log_{10}(\frac{\sigma_{signal}}{\sigma_{noise}})$$

where σ_{signal} and σ_{noise} are respective clean-signal and noise standard deviations.

Referring to the plots 710 and 711 of Figure 7, SNR and QSR versus input signal SNR achieved by MDF, PCA, and BPF are illustrated. Plot 710 illustrates the SNR improvement by comparing input SNR (on x-axis) to denoised signal SNR (on y-axis). Plot 711 illustrates the corresponding QSR for the same range of input SNR. For example, as illustrated in plot 710, an input signal with 4 dB SNR is denoised with an MDF-based approach, a 9 dB SNR improvement is achieved. Referring to the plot 711, 95% of the original clean signal content is preserved following MDF denoising of an input signal with 4 dB SNR. With increasing input SNR, QSR performance for the MDF-based embodiment quickly approaches 100% with an approximately linear denoising characteristic as measured by SNR on a logarithmic scale. Similar processing with a two-lead ECG generates similar results observed for an MDF-based embodiment. As shown in the Figure 7 the PCA and BPF results can be improved upon using various embodiments as discussed herein.

Referring to the ECG tracings 707, 708, and 709 of Figure 7, these three tracings illustrate an input noise-free signal 707; signal 708 corrupted with band-limited white noise to reduce SNR to 4 dB, and signal 709 denoised with an MDF-based approach. Adding band-limited white noise to achieve a 4 dB SNR renders the T and P waves indiscernible, as indicated in the middle tracing, while application of MDF restores the P and T waves.

Figure 8 shows another example embodiment, involving the use of MDF to suppress noise while preserving morphology for a single-channel ECG signal as implemented, for example, with an ECG processing circuit and evaluation system. Plot 801 is an input ECG recording corrupted with noise, and plot 802 shows the result of applying MDF filtering. The noise present in the input signal has similar characteristics (frequency content and

amplitude) as QRS complexes which would result in QRS detection errors without denoising. The application of MDF is used to avoid potential QRS detection errors, and can remove most of the noise while preserving morphology of QRS, P, and T waves, allowing for high accuracy detection of all ECG features, including QRS complex, P, and T-waves.

The embodiments shown in Figures 6, 7, and 8 characterize an example use of MDF to suppress in-band noise while substantially preserving signal morphology, in accordance with various embodiments. This combination of attributes is useful for a multitude of applications, including clinical diagnosis and research involving the measurement and analysis of physiological signals. Waveform morphology is preserved for a variety of applications, such as for detecting abnormalities in cardiac function from an ECG, evaluating respiratory function from a respiratory signal, evaluating a signal from a photoplethysmography sensor for measuring oxygen saturation, evaluating sleep stages from an EEG, and other applications. For example, preserved QRS morphology is used in diagnosing bundle brunch block or ventricular hypertrophy, T-wave morphology is used in measuring repolarization abnormalities in clinical care and drug toxicity studies, and ST segment changes are used when diagnosing ischemia, electrolyte imbalance, and Brugada syndrome. In another example, the ability to preserve P wave and QRS complex morphology facilitates the analysis of time correspondence of P wave and QRS complex to diagnose AV block.

In another embodiment, an MDSP-based approach is used for denoising and signal source extraction for monitoring a fetal ECG. In this embodiment, an ECG is recorded by placing sensing leads on the surface of the skin of the mother, typically in the lower abdomen. In one embodiment, individual sources that make up a fetal ECG are separated from the remaining subcomponents in the second domain by applying ICA signal source extraction techniques in step 2 of the MDSP embodiment. In another embodiment the fetal ECG is extracted from the other subcomponents by spatially selective filtering, periodic component analysis, or their combination (*e.g.*, in step 2 as shows in Figures 1 and 2 above). In this embodiment, the undesired sources, such as maternal ECG, are treated as noise and removed, leaving the denoised fetal ECG.

In another embodiment, an MDSP-based technique is used for measuring a degree of synchronization of uterine contractions of a pregnant female for predicting and detecting labor. In this embodiment, an electrohysterogram (EHG) is collected from the female abdomen. In one embodiment, an MDF-based approach as discussed herein is used to remove ECG artifacts from the EHG signal. In one embodiment, the degree of

synchronization of contractions in denoised EHG signal is measured by amplitude correlation via linear or nonlinear regression and the frequency relationship measured as coherence, or the amplitude and phase synchronization in the time-frequency domain. In another embodiment, a cross wavelet coherence function is used to measure amplitude correlation between two contraction bursts. In another embodiment, an envelope of a multi-channel EHG signal is calculated using a Hilbert transform or low-pass filtering of a rectified EHG signal to measure amplitude of a contraction wave and its spatial synchronization.

In other embodiments, a MDSP approach as discussed herein is used for detecting atrial arrhythmias in an ECG. In these embodiments, atrial activity can be extracted by applying ICA, SSF, PCA, πCA , or their combination, as part of step 2 (process 204 and 205) as shown in Figure 2. When used for detecting atrial arrhythmias, step 2 involves removing subcomponents associated with ventricular activity and noise.

In one embodiment, when processing a single channel ECG to evaluate atrial activity, process 205 employs SSF to remove ventricular activity and noise. In another embodiment, when processing a single channel ECG, process 205 employs πCA to remove ventricular activity and noise. In some embodiment SSF or πCA can be used to identify the boundaries of a window containing the QRS complex and T-wave of a cardiac cycle so that the contents of the window containing the QRS complex and T-wave can be removed. In some embodiments, identification of the window further involves the use of emphasis signals in a manner similar to that described in Figure 12 and associated text.

In one embodiment, when evaluating atrial activity in an ECG signal containing more than a single channel either SSF or πCA can be used in combination with PCA or ICA to identify ventricular activity and noise and to identify a window containing the QRS complex and T-wave of a cardiac cycle. As for single channel ECG, some embodiments of multichannel ECG may employ the use of emphasis signals in a manner similar to that described in Figure 12 and associated text to indentify the boundaries of a window containing the QRS complex and T-wave. Once the boundaries of the window containing the QRS complex and T-wave are identified, they can be removed to facilitate evaluation of atrial activity.

In Figure 9, the results of atrial activity extraction are illustrated on an atrial flutter recording from the PhysioNet database. Plots 901, 902, and 903 show ECG recorded from surface leads. Plot 904 is a recording from an intracardiac catheter located near an atrial free wall. The intracardiac recording is shown as an exemplary benchmark of atrial activity. Plot

905 shows the atrial activity separated from the surface ECG recordings using an MDSP-based embodiment. Note that the locations of P-waves on the plot 905 of extracted atrial activity matches locations of atrial depolarizations recorded from intracardiac lead shown in 904. The gaps in atrial activity coincide with ventricular depolarizations (*i.e.*, QRS complexes) and repolarizations (T-waves). Analysis of the separated atrial activity can significantly improve the accuracy of atrial flutter detection.

In Figure 10, the results of atrial activity extraction are illustrated on an atrial fibrillation recording from the PhysioNet database. During atrial fibrillation the P-waves often degenerate into more fractionated and variable f-waves which are barely visible in surface recording traces 1001, 1002, and 1003 shown in Figure 10. Despite that, the atrial activity signal 1005 extracted using an MDSP embodiment clearly shows the f-waves that coincide with the atrial depolarization trace 1004 recorded using an intracardiac lead. The only gaps are when atrial activity coincides with ventricular depolarizations (*i.e.*, QRS complexes) and repolarizations (T-waves).

Figures 9 and 10 demonstrate that various MDSP-based embodiments are capable of extracting atrial activity from ECG recordings. There are a number of ways that extracted atrial activity can be used to improve the accuracy of atrial flutter and fibrillation detection and discrimination. For example, spectral analysis of the extracted atrial activity signal can be used to quantify P-wave regularity and frequency and discriminate between atrial fibrillation and flutter. In one embodiment, atrial rate can be estimated by spectral analysis. In another embodiment, extracted subcomponents corresponding to atrial activity can be analyzed in the second domain to estimate the atrial rate. In another embodiment, a P-wave similarity measure is used to detect and discriminate between atrial fibrillation and flutter. In another embodiment, zero crossings can be used to estimate atrial rate in the segments where atrial activity is present. The analysis of atrial activity can be combined with analysis of cardiac cycle variability and regularity as well as PR interval variability to further improve the accuracy of atrial fibrillation and flutter detection. In one embodiment, the validity of a detected atrial arrhythmia event is determined by comparing the dynamic confidence signal (dCS) to a threshold. In one embodiment, dCS is computed using dSNR. In another embodiment, dCS is computed using a combination of dSNR and one or more of a rhythm characteristic such as presence of bigeminy, presence of trigeminy, and presence of PVCs. False positive detections of an atrial arrhythmia event during noisy ECG segments can thereby be reduced.

In other embodiments an MDSP-based approach is used for separating ventricular depolarization and repolarization activity. This may be useful for assessing repolarization activity for the risk stratification of sudden cardiac death. Once repolarization activity is extracted, it can be used to assess T-wave alternans and morphology, ST elevation in ischemia, and other cardiac abnormalities that can be useful for assessing cardiovascular risk.

Another embodiment is directed to using MDF for removing high amplitude noise from PNA signals. In particular, this is useful when removing high amplitude noise from PNA recordings such as those from the vagal nerve, sympathetic nerves, or motor nerves. In this embodiment, the high amplitude noise or artifact is detected by identifying undesired peaks in subcomponents that do not overlap the band of frequencies associated with desired signal. In Figure 11 exemplary performance of an MDF embodiment is illustrated on a single channel PNA input signal 1101 with high amplitude EMG noise. Plot 1101 is a PNA recording from a rat renal nerve while plot 1102 is the denoised signal following application of MDF. The MDF embodiment extracts the signal source from a very low SNR acquired signal while preserving PNA information. It removes nearly all noise and artifacts from the recording including myoelectric artifacts (EMG), electrical, and other noises while preserving information regarding the underlying PNA. An MDF embodiment could be used to extend the life of preparations where PNA is recorded by improving the ability to extract accurate information from PNA signals with low SNR. In PNA recording preparations for research in animal models, it is also common to dose the subject with a drug that shuts down PNA so that baseline noise can be measured and subsequently subtracted from the neural signal. This procedure can be dangerous for the subject and is labor intensive and cumbersome for the researcher. The MDF embodiment removes background noise automatically and eliminates the need for such an intervention.

In connection with another example, embodiment, PNA is quantified from recordings such as discussed above, via the computation of integrated sympathetic nerve activity. In one embodiment for computing a PNA envelope, an orthogonal component of the denoised PNA signal is computed using a transform such as a Hilbert transform, or similar transform. An envelope is computed as the square root of the sum of the squared denoised PNA signal and its orthogonal denoised component. This provides an accurate representation of neural activity without the phase delays inherent in conventional approaches. The neural activity represented by the signal envelope has a much lower frequency content compared to the raw

PNA signal and thus substantially reduces the bandwidth and sampling rate requirement of a system for measuring PNA activity.

Monitoring devices that transmit raw PNA signals as may be used in accordance with this or other embodiments, such as that available from Telemetry Research, Auckland, NZ, employs a sampling rate of about 8,000 Hz. By employing this embodiment to calculate an accurate PNA envelope, the sampling rate can be reduced to 100Hz or less, resulting in a reduction of transmitted bandwidth of a factor of 80 and a reduction in current drain of a wireless transmitter used to transmit data from an ambulatory subject.

In another embodiment, an MDSP-based approach is used for removing noise and extracting signal sources from signals acquired as a result of programmed periodic stimulation, such as auditory brainstem response and in peripheral nerve stimulation therapies where evoked response is analyzed to titrate therapy or peripheral nerve recruitment. These signals are often characterized by low SNR and a limited number of observed channels. These signals are also characterized by a consistent response following a consistent stimulation regimen. These signals can be segmented in the time domain based upon knowledge of timing of stimulation. Segmentation in the time domain allows for the creation of the equivalent of multiple channels from the observed signal, hence increasing the number of dimensions in the first domain. Following decomposition into the second domain, one or more MDSP-based embodiments previously described can be applied for denoising and signal source extraction. In one embodiment, segmentation of the signal according to timing of stimulation facilitates the use of principal component analysis (PCA) following decomposition to remove noise. Further application of SSF following PCA can further suppress noise. For auditory brainstem response, an MDSP-based embodiment can be used to improve the accuracy of intracranial pressure estimation, such as with a system similar to that described in US Patent Publication No. 2008/0200832, and U.S. Patent No. 6,589,189, which are fully incorporated herein by reference.

In the case of a peripheral nerve stimulation therapy, evoked responses can be analyzed to titrate therapy targeted at specific nerve fibers or monitor neuropathy progression. For example, in vagal nerve stimulation applied for cardiovascular therapy, the stimulation protocols are optimized to selectively recruit efferent smaller fibers that control heart function and block stimulation of efferent larger fibers and afferent fibers that could invoke pain or coughing reflex. Such approaches may be implemented in accordance with that described in U.S. Patent Publication No. 2008/0065158, which is incorporated herein by reference. A device employed for neural stimulation may incorporate a feedback control of

stimulation by observing parameters of an evoked response. In this type of neural stimulation device, an MDSP-based embodiment could be applied to assess evoked response resulting from nerve stimulation targeted at a specific nerve fiber type. In some implementations, an MDF-based embodiment is used to achieve an accurate assessment of the response of particular nerve fibers to changes in programmed stimulation parameters such as timing, frequency, pulse width, pulse repetition, duty cycle and amplitude of stimulation in order to appropriately affect therapy.

In another embodiment, an MDSP-based embodiment is used to monitor neuropathy progression by measuring changes in nerve conduction velocity of small diameter axons. The changes in these axons can serve as an earlier marker of neuropathy development. An MDSP-based embodiment that involves segmenting the evoked response signal and denoising as described above is used to remove background noise and for measurement of evoked response amplitude and time. In many embodiments, this approach is used to facilitate the detection of changes in axons that can otherwise be challenging to detect due to low amplitude and phase cancellation of evoked response potentials.

In another embodiment, MDSP is used for detecting feature points of a physiological signal such as a QRS onset, P-wave onset, or T-wave offset in an ECG signal or systole and diastole in an arterial blood pressure signal. Referring to Figure 12, a feature point detection embodiment involves a processing circuit and related modules that use one or more selected denoised signal subcomponents to compute an emphasis signal that emphasizes a signal wave or feature point of interest, computed as a linear or non-linear combination of selected subcomponents that are associated with the signal wave of interest. In another embodiment, the emphasis signal is computed by performing the inverse of the transform used for decomposing the physiological signal on the selected subcomponents. In some embodiments it may be useful to differentiate the signal following the inverse transform.

Referring to Figure 12, subcomponents used to compute the emphasis signal are generated as a result of the decomposition process 1205 of input signal 1200 using an MDSP embodiment, as described herein. The subcomponents that contain the majority of the energy of the signal waves are selected for the emphasis signal and are denoised in process 1206 using an MDSP embodiment. The emphasis signal computed in process 1207 may include frequency subbands matching the spectral energy of particular signal waves of interest or a subset of basis functions tuned to the signal wave or feature point of interest and its variations across a range of normal, perturbed, and pathological conditions. In another embodiment wavelet related subcomponents can be used to compute the emphasis signal in

process 1207. The specific subcomponents used depend upon the decomposition technique used, sampling rate, and the species from which the physiologic signal was recorded. Example emphasis signals of an ECG are shown in 1202. 1204, 1211, and 1213 of Figure 12, along with corresponding ECG waveforms 1201, 1203, 1210, and 1212. The vertical dashed lines in Figure 12 show the point of feature point detection in each ECG waveform and corresponding emphasis signal.

The transition points of the emphasis signal are evaluated in process 1208 to detect feature points, shown by example in 1214 and 1215, of the physiologic signal to create output 1209 representing the time of the feature point. In one embodiment, the pattern of significant peaks, valleys, and zero crossings within the emphasis signal are used to detect feature points. In another embodiment, the feature points are detected by applying a threshold to the emphasis signal. In yet another embodiment, the feature points are detected by applying pattern or template matching.

The following illustrative example demonstrates exemplary performance of an embodiment involving the detection QRS complexes in an ECG. For QRS detection, an MDSP-based approach is used to compute an emphasis signal from a combination of denoised subcomponents that are algorithmically selected to include, for example, complexes that are wide, narrow, premature, fractionated, biphasic, monophasic, fibrillatory, tachycardic, or complexes that have been distorted as a result of a pharmacological agent.

Figure 13 provides an illustration of an ECG signal 1301 that is processed in accordance with such an approach, to address problems that may relate to the presence of bigemeny, tall T-waves, and low QRS amplitude, in addition to rapid changes in QRS amplitude. An emphasis signal computed as described in this MDSP embodiment facilitates the detection of all QRS complexes, as shown by the circles as in 1302 of Figure 13, with no false detection on T-waves. When tested on the MIT BIH Arrhythmia database, a QRS detection accuracy of 99.8% sensitivity and 99.8% positive predictive value can be achieved on single lead ECGs. Feature detection can be enhanced by using and analyzing multiple lead recordings, using an MDSP-based approach to leverage redundancies between the leads in a manner that is more efficient at removing noise.

In another example embodiment, an MDSP approach is used for extracting a respiration signal from an ECG, blood flow, photoplethysmosgraphy, thoracic impedance, or an arterial blood pressure signal. Figure 14 shows one such implementation, in which a respiration signal is extracted using one or more selected denoised signal subcomponents to compute an emphasis signal that is associated with a respiratory pattern. In some

embodiments, the subcomponents are filtered with a low-pass filter to extract the low-frequency respiration signal.

In other embodiments, the emphasis signal is combined with a heart rate signal to improve the accuracy of computed respiratory parameters. For example, canines have pronounced respiratory sinus arrhythmia which is characterized by heart rate changes that correlate to respiration; these characteristics can be used in connection with these embodiments, for extracting, processing or otherwise using canine respiration signals.

Referring again to Figure 14, subcomponents resulting from decomposition in process 1402 of input signal 1401 are used to compute an emphasis signal, using an MDSP approach such as described in connection with one or more example embodiments herein. Subcomponents are denoised in process 1403 using an MDSP embodiment as described herein. Subcomponents that contain a majority of the energy of the respiration pattern are selected and combined to create an respiratory emphasis signal in process 1404, also using an MDSP embodiment as discussed herein. The emphasis signal may include frequency subbands matching the spectral energy of particular signal waves of interest or a subset of basis functions tuned to the signal wave or feature point of interest and its variations across a range of normal, perturbed, and pathological conditions. The emphasis signal is processed in 1405 using zero crossings or spectral analysis to compute respiratory parameters.

In another embodiment (*e.g.*, relative to Figure 14), wavelet related subcomponents are used to compute an emphasis signal. The specific subcomponents that are used are selected relative to one or more of the decomposition technique used, sampling rate, and the species from which the physiologic signal was recorded.

In some embodiments, the noise level of an ECG is measured using an embodiment described above, and zero crossings that occur too frequently during noisy segments are discarded (or simply not used). In another embodiment, the emphasis signal can be low-pass filtered prior to measurement of respiration rate and tidal volume. The tidal volume can be extracted by measuring peak and valley amplitude between valid zero crossings. In another embodiment, the tidal volume is computed as a function of area under the curve between valid zero crossings.

Figure 15 illustrates another example embodiment as directed to the processing of a primate ECG. Plot 1501is a noisy input ECG, plot 1502 is an ECG denoised with a MDF-based approach as described herein, and plot 1503 is an extracted respiration emphasis signal. The residual noise level is measured and is shown on the bottom plot as a dotted line. This approach is used to assess the validity of the respiration signal. Zero crossings can be

discarded or otherwise not used if the noise exceeds a predetermined threshold (*e.g.*, as with the sample 23,500 in Figure 15).

An additional MDSP embodiment is directed to detecting events in a physiological signal by combining aspects of feature point detection and signal source extraction as discussed herein, to detect cardiac abnormalities and arrhythmias of ventricular and atrial origin, such as ventricular fibrillation, tachycardia, bradycardia, atrial fibrillation and flutter, AV block and others. In one embodiment, the intervals between QRS complexes are computed to detect rate abnormalities indicative of tachycardia or bradycardia. In another embodiment, a transition to tachycardia and QRS complex morphology are evaluated to discriminate between sinus-, supra-ventricular or life-threatening ventricular tachycardia. In another embodiment, the ventricular rhythm statistics and separated atrial activity rate are evaluated to detect atrial fibrillation and flutter.

Another embodiment of involving an MDSP-based approach is used to achieve efficient compression of quasi-periodic signals such as ECG signals, such as by suppressing noise while preserving signal morphology and providing accurate feature point detection. In one embodiment, arrhythmic events are detected and ECG traces corresponding to these events are compressed to reduce the data storage and transmission bandwidth required to communicate the signal to a location remote from the monitored subject. Referring to Figure 16, an ECG signal sensed by electrodes 1601is conditioned by signal conditioning circuits 1602. The digitized signal 1609 is decomposed in process 1610 and denoised in process 1611 using MDSP techniques described herein. An emphasis signal is computed and QRS complexes detected in process 1612 using an MDSP embodiment described herein. Cardiac events are detected in process 1613 using predefined thresholds for heart rate and morphology. The denoised ECG traces of detected arrhythmic events are reconstructed in process 1614. The ECG traces are segmented into cardiac cycles and are aligned using a feature point of the QRS complex in time to form an image in process 1615.

The two-dimensional (2D) image plot thus formed includes consecutive cardiac cycles in one dimension and the ECG signal of each cardiac cycle in the other dimension. An illustration of the 2D image is shown as a 3D plot by way of example in Figure 17. Plot 1701 shows a 3D plot of sequential cardiac cycles with cardiac cycle length equalization (*e.g.*, sequential RR intervals are padded by a constant value at the end of the cycle to ensure that all cardiac cycle lengths are equal). The redundancy between adjacent beats results in more efficient compression. However, due to physiologic factors such as respiration or rhythm disturbances the adjacent beat redundancy might be low. In the 3D ECG plot 1702, cardiac

cycles are sorted by length (*e.g.*, RR interval), resulting in smoother beat transitions that lead to more efficient compression. Accordingly, the image can be efficiently compressed by leveraging redundancies between adjacent cardiac cycles. In addition, redundancies across adjacent subbands or wavelet scales can be utilized by wavelet or cosine transforms of the image. Examples of techniques used in process 1616 that could be utilized to achieve efficient compression of the 2D image include transform, subband or wavelet based encoding techniques such as embedded zerotree wavelet (EZW) [20], set partitioning in hierarchical trees (SPIHT) [21], modified SPIHT [22] and embedded block coding with optimal truncation (EBCOT) encoding algorithms [23]. Compression ratios on the order of 15:1 to 20:1 with less than 5% distortion can be achieved using this technique on denoised ECG signals.

In another embodiment, a quasi-periodic signal is compressed by phase wrapping cardiac cycles and converting the source signals into a polar or cylindrical system of coordinates (38). Then the signal can be efficiently represented by a 3 dimensional plot of phase-aligned cardiac cycles and compressed.

In another embodiment a denoised ECG is compressed by computing a template QRS complex and subtracting it from detected normal QRS complexes. The residual signal has lower frequency content and can be compressed by a lossy compression technique that can include subsampling and quantization. The decompression technique makes use of lossless coding of the QRS template and QRS complex locations as well as lossy coding of the residual signal to reconstruct the ECG signal with small amount of distortion.

Other MDSP-based embodiments are used to compress blood pressure, pulse oximetry signals, respiration, heart sounds, and other pseudoperiodic signals. In order to achieve high levels of compression with any of these embodiments without introducing significant signal distortion, accurate QRS or cardiac cycle detection and effective noise suppression (denoising) are used. In some implementations, creating the intermediate representation of the signal that leverages redundancy between the cycles by sorting cycles by length, as in plot 1702 of Figure 17, is used to achieve a high compression rate. Accurate cycle detection is used to mitigate the introduction of noise and artifacts into the reconstructed signal following compression and decompression.

Another embodiment is directed to an MDSP-based approach used to compress PNA signals and other non-quasi periodic signals, where the denoising provided by MDSP leads to a sparse signal as demonstrated in plot 1102 of Figure 11. Note that the denoised signal is almost always near zero in the absence of a neural spike. The sparse signal is compressed

using one or more compression schemes, such as direct time-domain coding or transform based coding. In general, a compression scheme for a particular physiological signal is selected based upon the ability of a given scheme to leverage redundancies in the signal.

Referring to Figure 18, another example embodiment is directed to using an MDSP-based approach to evaluate ECG strips captured by an ambulatory monitoring device 1801 with arrhythmic event detection capability. The captured ECG strips are forwarded to a data review system 1804 and evaluated using an MDSP-based algorithm 1800 implemented on a computing device in data review system 1804. Algorithm 1800 is used to evaluate the captured ECG strips 1805 and assign a classification to each strip. Each ECG strip is assigned one of four classifications using an MDSP-based approach for arrhythmia detection and validity, the classifications including: A) arrhythmia is present, B) no arrhythmia present , C) strip is uninterpretable, or D) uncertain (*e.g.*, the ECG strip cannot be placed with confidence in classification A, B, or C). If an ECG is classified as D, an automatic indicator can be triggered to suggest human review to determine if an arrhythmia is present. For ECG strips falling in classifications B and C, no further review is needed. Depending upon the nature of the arrhythmia and the clinical care process, ECG strips falling in classification A may be reviewed by a person to assign a suggested diagnosis prior to forwarding to a decision maker. Using this approach and considering a relatively low percentage of the ECG strips evaluated requiring review, labor and costs associated with providing review services can be substantially reduced. In addition, the quality of review services can be improved, since an accurate computer-based algorithm can provide better consistency due to elimination of subjectivity.

The system shown in Figure 18 includes ambulatory monitoring devices 1801, or subject devices, that are worn by patients being evaluated for a heart rhythm disorder or for research. Ambulatory monitoring device 1801 includes a computing circuit configured with an algorithm to evaluate the ECG signal from the patient and, if an arrhythmia is detected, capture an ECG strip containing the arrhythmia in memory. Such captured ECG strips may, for example, be one to five minutes in duration and stored in memory for later wireless communication to a base station 1802 (*e.g.*, located in the patient's home), and from the base station 1802 to a data review system 1804 via telecom or data network 1803. The data review system 1804 may be located at a center where the received ECG strips can be reviewed, if necessary, to verify the presence of an arrhythmia or to suggest a diagnosis. The information derived from the ECGs is then packaged into a report which is forwarded to a researcher or clinician for use in decision making.

The results contained in a report may be provided to physicians, clinics, hospitals, or to organizations engaged in drug safety research, and can be delivered via a service provider system/review center that processes the resulting signals using data review system 1804, possibly in combination with trained healthcare personnel. Such a review center may provide services to a large number of clinics and physicians, or it may be housed within a clinic or a research facility and provide service to one or a small number of clinics or research groups or businesses.

In some embodiments, subject devices forward full-disclosure ECG recordings, and in yet other embodiments ECG strips of 10 second to 5 minutes are captured at regular intervals for analysis at the review center without regard to the content or nature of the ECG signal. In some embodiments, the subject device from which results are communicated as above is implanted in a patient. One type of implantable device is the Reveal XT from Medtronic of Minneapolis, Minnesota.

Flow chart 1800 in Figure 18 shows an example embodiment directed to processing and evaluation of ECG strips received by data review system 1804. A captured ECG strip 1805 received at data review system 1804 is evaluated for the presence or absence of arrhythmias using an MDSP-based embodiment as described herein. Criteria 1806 input from a care provider or other decision maker is used by process 1807 to determine if an arrhythmia is present. Examples criteria 1806 include a heart rate above which a rhythm is considered to be a tachycardia, a heart rate below which a rhythm is considered to be a bradycardia, and a minimum duration atrial fibrillation (AF) episode required for an occurrence of AF to be reported as an arrhythmia. A dynamic signal-to-noise ratio (dSNR) is computed for the ECG strip in process 1808 as described herein. A validity metric (VM) may be additionally computed using the dSNR and signal morphology in process 1808. VM is compared to a Validity Threshold VT1 in decision point 1809. If VM exceeds VT1, the result is considered valid and captured ECG strip 1805 is classified "A" if process 1807 detected an arrhythmia and "B" if process 1807 did not detect an arrhythmia. If VM does not exceed VT1 at decision point 1809, then VM is compared to a threshold VT2 at decision point 1810 (VT2 < VT1). If VM exceeds VT 2, then the result is determined to be uncertain and the ECG strip is classified as "D" to indicate that review by a person should be carried out to determine whether an arrhythmia is present in the ECG strip. If VM does not exceed VT2, then the ECG strip is classified as uninterpretable ("C") and is considered uninterpretable because the noise level is too high to be evaluated by either human or by automated algorithm.

In some implementations, classifications A, B, and C are assigned with a degree of certainty, designated by the validity metrics VM1 and VM2, sufficiently high that any error in classification can be tolerated by the user (*e.g.*, 90% likelihood). In some embodiments, the threshold of certainty of the classification, VM1 and VM2, is determined by the user. Captured ECGs assigned classification D (uncertain) generally include segments for which a computing circuit configured with executable software to carry out an MDSP-based processing approach is unable to make a determination of the rhythm as being classified as A, B, or C with a sufficiently high degree of certainty. Segments with classification D may, for example, contain a level of noise such that the denoised signal is not interpretable by the algorithm, but may be interpretable by a technician, or it may contain an unusual morphology that the software was unable to recognize.

The embodiments described here for analyzing physiologic signals may be implemented in a variety of platforms that include a logic circuit or computer, with reference made herein to a logic circuit or computing circuit being applicable to a variety of such circuits operating in accordance with one or more embodiments discussed herein. In one embodiment, a microprocessor (such as Pentium or Core microprocessors available from Intel of Santa Clara, CA) in a personal computer running an operating system such as Windows (available from Microsoft of Seattle, WA) or the Unix standard (set by The Open Group of San Francisco, CA) is used to execute programming to carry out MDSP-based functions as discussed herein. In another embodiment, a microcontroller suitable for low-power applications, such as the MSP 430 available from Texas Instruments of Dallas, TX, is implemented to carry out MDSP-based functions as discussed herein. When a review center as described above is involved, a microprocessor may be used for simplicity of implementation and relatively low degree of concern about power consumption. Many implementations involving an MDSP-based approach in an ambulatory monitoring device employ a microcontroller (such as the MSP 430 above) to reduce/minimize power consumption. In other embodiments where power consumption and size are of high priority, implementation in a silicon-based state machine using a hardware description language such as VHDL may be useful.

In some embodiments, referring to Figures 16 and 19, aspects of the present disclosure are implemented using a battery powered or passively-powered device (*e.g.*, via radio frequency power) that is worn by or implanted within a human or animal subject. Depending upon the application and specific design requirements, referring to Figure 18, various aspects of MDSP-based embodiments discussed herein may be partitioned between

implementation within subject device 1801 and implementation within the data review system 1804.

Referring to Figure 19, an apparatus for improving the signal-to-noise ratio of a physiological signal is shown, in accordance with another example embodiment. While referencing an ECG signal, the apparatus shown in Figure 19 may be implemented with other signals such as blood pressure, respiration, photoplethysmography, blood glucose, blood flow, heart sounds, PNA, EMG, and EEG. In this example embodiment, ECG is sensed using either surface or implanted electrodes 1901. Signal conditioning circuits 1902 receives the signal from sensing electrodes 1901 and is conditioned to amplify and filter the signal to remove much of the noise outside the bandwidth of the ECG signal. Analog-to-digital conversion (ADC) is accomplished by an ADC on board a Texas Instruments MSP430 microcontroller 1903 (shown by way of example, and implementable with other processors).

Referring to the right side of Figure 19, digitized signal 1906 is processed by computer instructions executed by a 16-bit RISC MCU of the MSP430 1903. The digitized signal 1906 is decomposed into a combination of basis functions (subcomponents) in a second domain in process 1907. The dimension of the first domain is equal to the number of sensed ECG signals. Decomposition in process 1907 is performed using one of a discrete cosine transform, a wavelet related transform, a Karhunen-Loeve transform, a Fourier transform, a Gabor transform, and a filter bank. A subset of subcomponents containing primarily signal energy is identified using MDSP techniques (*e.g.,* one or more of SSF, PCA, ICA, and πCA) in process 1908. In process 1909, a denoised signal is reconstructed from the subcomponents identified as primarily containing signal energy by performing the inverse of the transform used to decompose the signal. It should be noted that the concepts described here can also be applied to other MDSP-based embodiments beyond denoising, including feature point detection, event detection, and computing a dynamic signal-to-noise ratio to evaluate the accuracy of information extracted from a physiological signal.

Referring back to Figure 16, another example embodiment involves using an MDSP-based approach for implementing a battery-powered apparatus capable of wirelessly communicating physiological signals. Referring to Figure 18, this apparatus is one embodiment of subject device 1801. The example refers specifically to ECG signals, but a similar embodiment can be used for other pseudoperiodic physiological signals such as arterial blood pressure, respiration, blood oxygen saturation derived from PPG, heart sounds, and blood flow for example. In this example embodiment, ECG is sensed using either

surface or implanted electrodes 1601. Signal conditioning circuits 1602 receive the signal from electrodes 1601 and amplify and filter the signal to remove much of the noise outside the bandwidth of the ECG signal. Analog-to-digital conversion (ADC) of the conditioned signal is accomplished by an ADC on board a Texas Instruments MSP430 microcontroller 1603.

Referring to the right side of Figure 16, digitized signal 1609 is processed by computer instructions executed by the 16-bit RISC MCU of MSP430 1603. The MCU is in communication with offboard memory 1605 which may be used to provide additional data storage and for storage of computer instructions. The MCU is additionally in communication with wireless transmitter 1604 that can send compressed data to wireless receiver 1606 located remote from subject device 1801 of Figure 18. Wireless receiver 1606 is further in communication with a logic circuit or computer that is configured to execute instructions to decompress the compressed signal in process 1607. In some embodiments the wireless transmitter 1604 and receiver 1606 may each be wireless transceivers capable of both sending and receiving data. An example of a wireless transceiver that may be used in connection with this embodiment is the CC2540 low-energy Bluetooth chip available from Texas Instruments (see above).

Referring to the data flow diagram on the right side of Figure 16, digitized signal 1609 is decomposed in process 1610 into a combination of basis functions (subcomponents) in a second domain. The dimension of the first domain is equal to the number of sensed ECG signals. Decomposition in process 1610 is performed using one of a discrete cosine transform, a wavelet related transform, a synchrosqueezed wavelet transform, a Karhunen-Loeve transform, a Fourier transform, a Gabor transform, and a filter bank. The subcomponents are denoised in process 1611 using MDSP techniques (*e.g.*, one or more of SSF, PCA, ICA, and πCA) and a QRS emphasis signal is computed in process 1612 as a linear combination of a subset of denoised subcomponents containing QRS signal wave energy. The emphasis signal is evaluated to detect each QRS complex, as described herein, and a feature signal containing a series of feature points indicating the R-R interval of consecutive cardiac cycles is constructed in process 1613. The feature signal and morphology of the denoised ECG are evaluated in process 1613, as described herein, to detect arrhythmic events, such as bradycardia and tachycardia, and the denoised ECG strips containing arrhythmic events reconstructed in process 1614. The denoised ECG strips to be transmitted are compressed using processes 1615 and 1616. In process 1615, ECG strips are segmented by cardiac cycle and adjacent strips are aligned using a feature point of the QRS

complex to form an image of a 3D plot similar to that shown in plot 1701 of Figure 17. The image is subsequently encoded in process 1616 by, for example, applying transform encoding, subband encoding, or wavelet based encoding, after which the encoded image is saved in memory for later wireless transmission or it may be sent immediately.

In an alternate embodiment, instead of forming the image by aligning adjacent strips, the strips are arranged by cardiac cycle length, as in plot 1702 of Figure 17. This results in additional redundancies in strips adjacent to each other in the image and hence results in more efficient compression.

In another embodiment a template QRS complex is computed and subtracted from detected normal QRS complexes. The residual signal is compressed by a lossy compression technique and the QRS template and QRS complex locations are compressed using lossless coding.

In order to meet power consumption requirements for implementation within a subject device for denoising and wireless communication, computer-executable instructions for carrying one an MDSP-based approach as discussed herein, stored as embedded code within the subject device, are configured to facilitate low-power implementation. In one embodiment, the computer instructions are optimized using integer or fixed point arithmetic and lifting or B-spline wavelet implementation [24] of a signal decomposition transform in order to reduce and/or minimize the number of clock cycles or machine states required. In such an embodiment, a portion of the computations required to analyze physiologic signals may be implemented within the subject device while others may be implemented in the data review system. In another embodiment, the subject device captures, denoises, and compresses the ECG of the subject and information is extracted from the ECG recording off-line in the data review system. The data review system may include a review function that facilitates human review of ECGs that were classified as uncertain by the algorithm.

Other embodiments are directed to a computer-based system or logic circuit, such as a computer operating using one or more processor circuits, which operate using executable modules. Each module (*e.g.*, dedicated circuitry, or software-based modules implemented with a processing circuit) is executable by a computer circuit to carry out one or more functions or processes as described herein. For instance, one such module may carry out MDSP computations upon input data such as ECG data, and transform the data into a denoised output. This transformation may involve, for example, the use of a software module that, when executed by a computer, carries out the steps as shown in Figures 1 and 2. Various other embodiments are directed to similar transformations, which may involve

taking and processing one or more inputs to generate a transformed output useful for one or more of a variety of purposes, such as for detecting physiological conditions. Accordingly, the embodiments discussed herein may be carried out using such a system and/or computer circuit and related executable modules.

In one embodiment, and referring again to Figure 19, a denoising function is implemented within a computerized apparatus configured to execute programming instructions. A digitized physiological signal 1906 is input to the computerized apparatus. The device computes a denoised output signal from the digitized input signal resulting in an improvement in SNR.

In one implementation, an input physiological signal sensed by ECG electrodes 1901 is a relatively noise-free single lead ECG recording from a human being or other mammal with a resting heart rate less than 150 BPM, contaminated with band-limited (0.5 to 100 Hz) white noise. Following denoising in processes 1907, 1908, and 1909 using an MDSP embodiment, the SNR is improved by at least 5 decibels and the mean QRS amplitude for any 10 second interval of the recording is preserved within +/- 10% of the mean QRS amplitude of the input signal for the same 10 second interval.

In this embodiment, the input ECG can be described as residing in a first domain having a dimension equal to the number of leads (*e.g.*, channels) in the recording. For example, a recording consisting of a lead set (*e.g.*, Leads I, II, and III), would have three dimensions. Referring to Figure 19, the digitized input ECG 1906 is decomposed in process 1907 into a second domain. Decomposition into the second domain results in generation of subcomponents that represent the information contained in the ECG signal. The dimension of the second domain is defined as the number of subcomponents representing each lead of the ECG multiplied by the number of leads. In one embodiment, decomposition performed in process 1907 is accomplished using a transform that largely achieves independence of the subcomponents. Independence of the subcomponents combined with qualification of the frequency content of each subcomponent facilitates a more precise identification of the association of a subcomponent or group of subcomponents with an aspect (*e.g.*, T-wave) of the ECG signal.

In another embodiment, the subcomponents in the second domain are examined in process 1908, as described herein, based on their spatial distribution in time, to identify noise and other aspects of the ECG. In one embodiment, the spatial distribution is examined using spatially selective filtering, whereby aspects or waves of the ECG associated with wider frequency band, such as the QRS complex, are identified and preserved across the

subcomponents. In this embodiment, subcomponents associated with high frequencies are preserved for a time window corresponding to the QRS complex, but are zeroed out in (or not used for) the time window corresponding to the remainder of the cardiac cycle. This allows the morphology of the QRS complex to be preserved, while removing the high frequency noise from the remainder of the cardiac cycle, where the primary signal content corresponds to lower frequencies. When the input signal is a multi-lead ECG, principal component analysis and independent component may be used in addition to spatially selective filtering to further enhance the independence of subcomponents.

In another example embodiment, referring to Figure 20, spatially selective filtering is used to remove noise from an ECG. Figure 20a (top) shows a cardiac cycle of an ECG waveform showing a P-wave, QRS complex 2001, and T-wave, as processed in connection with this embodiment. The QRS complex is detected and, referring to Figure 20b, the time spanning the beginning of Q to end of S defines time window 2002. The remainder of the cardiac cycle is defined as time window 2003. Time window 2002, containing the QRS complex, includes a wide range of frequencies ranging from low-frequencies to high-frequencies. For the ECG of a healthy human, this frequency range may span from 0.5 to 100 Hz. In order to preserve the morphology of the QRS complex, subcomponents in this frequency range are preserved and considered to be associated with a desired signal wave. In one embodiment, the beginning and end of time window 2002 are respectively defined by the onset of the Q-wave and the offset of the S-wave. In another embodiments, the beginning and end of time window 2002 are shifted somewhat earlier or later. Because the signal waves occurring in time window 2003 (*e.g.*, P-wave, T-wave) contain lower frequency components, the subcomponents comprising the low-frequencies, represented by region 2005, are preserved and the subcomponents comprising high-frequencies are removed since they are primarily are associated with noise. In one embodiment the time window 2002 is a rectangular window, in another embodiment the time window 2002 decays gradually to reduce signal distortion nearby the transition points. Figure 20d illustrates a three-dimensional view of the time-frequency trapezoidal window 2008 with vertical axis showing window amplitude. Window 2008 decays gradually to enable a graded attenuation of high frequencies (i.e. low subcomponent scales) near the edges of window 2008. The content of ECG signal at low frequencies of a cardiac cycle is preserved as shown by window 2009 and is independent of window 2008. Figure 20b is a two-dimensional projection of Figure 20d on the time-frequency plane.

In an alternate embodiment as shown in Figure 20c, subcomponents associated with higher frequencies are removed in time windows 2002 and 2003 while retaining low-frequency components represented by region 2007. Those containing the higher frequencies are then added back during the time spanning time window 2002, as represented by region 2006, to restore the higher frequency components of the QRS complex. In some implementations, this approach is carried out to mitigate or avoid morphology distortion.

In one embodiment, and referring to Figure 21, an input ECG signal 2101 is decomposed into subcomponents, as described herein, in process 2102. Transforms useful for decomposition in 2101 include discrete cosine transform, wavelet related transform, synchrosqueezed wavelet transform, Karhunen-Loeve transform, Fourier transform, Gabor transform, and filter bank. The ECG is segmented into cardiac cycles in process 2104. In one embodiment, this is accomplished by identifying a defining feature that provides a reliable fiducial point for identifying a cardiac cycle. In one embodiment, the defining feature is the QRS complex of a cardiac cycle. The QRS complex can be identified using one of a number of techniques including thresholding, adaptive thresholding, and spatially selective filtering. An embodiment of spatially selective filtering (SSF) for identifying the QRS complex can be used in processes 2102a and 2103. SSF can be implemented by computing a time function that measures spatial distribution of subcomponents and comparing the time function to a threshold function as each time point (*i.e.*, sample point). In one embodiment the time function $P_{pw}(t)$ is a point-wise product of selected subcomponents as described in process 2102a. In one embodiment the selected subcomponents are those corresponding to lower frequencies (i.e. higher scales). In one embodiment of 2102a, a pointwise product is computed as:

$$P_{pw}(t) = (a_1, a_2, \dots, a_N) \times (b_1, b_2, \dots, b_N) = (a_1 \times b_1, a_2 \times b_2, \dots, a_N \times b_N).$$

In another embodiment, the point-wise product is normalized to match the energy of a subcomponent. In another embodiment the time function $P_{pw}(t)$ is a cross-correlation between the selected subcomponents. The computed time function $P_{pw}(t)$ is compared to a threshold function $T_{pw}(t)$ at each time t in process 2103. A defining feature of a cardiac cycle is detected when $P_{pw}(t) > T_{pw}(t)$. In one embodiment $T_{pw}(t)$ is a predefined constant-value function that is determined by the statistics of the ECG signal during the first few cardiac cycles of the ECG recording being processed. For example, the threshold may be defined as a percentage of the maximum amplitude during the first few cardiac cycles. In another embodiment $T_{pw}(t)$ is an adaptive function that decays toward a predefined floor following a

predefined refractory interval after detecting the defining feature of the cardiac cycle (*i.e.*, QRS complex).

Following identification of the QRS complex the ECG is segmented by cardiac cycle in process 2104 using the QRS complex as a fiducial point. In one embodiment, each cardiac cycle is partitioned into two time windows in process 2104. Referring to Figure 20, first time window 2002 begins at the onset of the Q-wave of the cardiac cycle and ends at the offset of the S-wave. The second time window 2003 begins at the offset of the S-wave and ends at the onset of the next cardiac cycle. In other embodiments, the start and end times of windows 2002 and 2003 can differ somewhat from the above relative to the location of feature points of the QRS complex and some degree of overlap in the windows is also acceptable. In other embodiments, the cardiac cycle is partitioned into more than two time windows. For example, in an alternate embodiment a first time window includes the QRS complex, a second time window includes the T-wave, and a third time window includes the remainder of the cardiac cycle. The set of subcomponents present within time window 2002 are referred to as QRSsub and the set of subcomponents present in time window 2003 are referred to as PTsub.

In process 2105, subcomponents of the set PTsub are evaluated to identify subcomponent subset PTsubnn that overlaps the spectral content of (are associated with) a characteristic frequency band of window 2003, FBpt, of the representative ECG signal. The value of a subcomponent represents the energy of the input ECG signal contained in a narrow range of frequencies and the subcomponent is said to be associated with this narrow range of frequencies.

Process 2105 relies on knowledge of the characteristic frequency band, FBpt, of the desired ECG signal in window 2003. FBpt is pre-identified using a database of representative ECG recordings for a species as described in process 2108.

In process 2106, subcomponents of the set QRSsub are evaluated to identify subcomponent subset QRSsubnn that overlaps the spectral content of (are associated with) a characteristic frequency band, FBqrs, of the representative ECG signal present in window 2002 of Figure 20. In one embodiment, the input ECG signal is preprocessed to remove out-of-band noise in a signal conditioning circuit such as 1902 in Figure 19, by a digital filter implemented in a computing or logic circuit, or a combination thereof. In one embodiment, where the energy of out-of-band noise in the input signal is negligible, the energy of the QRS subcomponents QRSsub and QRSsubnn substantially overlap.

Process 2106 relies on knowledge of the characteristic frequency band, FBqrs, of the desired ECG signal in window 2002. FBqrs is pre-identified using a database of representative ECG recordings for a species as described in process 2108.

The identification of the characteristic frequency bands for time window is performed by evaluating a database of representative ECG recordings for a species (input 2107). The database of representative ECG recordings is selected to represent a broad scope of ECG morphologies, heart rate, anomalies, noise characteristics, and pathologies. In the process 2108, the spectral content of the QRS complex is characterized and the characteristic frequency band of the QRS complex FBqrs is identified using spectral analysis techniques. The time window outside of the QRS complex in cardiac cycle is identified and the characteristic frequency band of the cardiac cycle outside of the QRS complex, FBpt, is identified using spectral analysis techniques. It should be noted that computing the characteristic frequency band is typically only performed once for the ECG sampled for a given species. Once FBpt and FBqrs are determined for a given species, they are used as parameters by the processes 2105 and 2106 and it is not necessary to recompute them.

In the process 2111 the identified target subcomponents contained in subset PTsubnn and subset QRSsubnn are combined and subjected to the inverse of the transform used in process 2102 to construct a denoised ECG signal.

Figure 22 shows a system 2200 for computing a denoised ECG signal from an input signal including a desired ECG signal and noise, according to another example embodiment. The system includes a logic circuit 2210 and a memory circuit 2212. The memory circuit 2212 stores instructions that, when executed by the logic circuit, carry out the following steps. For illustration, Figure 22 represents steps as carried out in the logic circuit 2210 with various blocks; however, various approaches for carrying out the steps may be implemented in connection with other embodiments. Moreover, the logic circuit 2210 may include two or more logic circuits, such as two or more processors that carry out different aspects of the respective steps. In addition, the various steps shown in Figure 22 and described here may be implemented using one or more embodiments as discussed above, in connection with the other figures and otherwise.

Referring again to Figure 22, an input ECG signal 2205, in a first domain, is received at a communications input port 2214, and is decomposed at block 2220 into subcomponents 2225 in a second domain. QRS window-based identification is carried out at block 2230, at which a location of the QRS complex of a cardiac cycle in the ECG signal is identified. A first time window in the cardiac cycle that includes the QRS complex is identified, along

with at least one time window in the cardiac cycle that does not include the QRS complex. The first time window and the at least one time window span the duration of the cardiac cycle.

At block 2240, and for each of the identified time windows, target subcomponents 2245 are identified as subcomponents that contain more desired ECG signal energy than noise energy. For example, when a particular subcomponent exhibits more energy associated with a desired ECG signal than energy not associated with such a signal, that subcomponent may be identified as a target subcomponent. The target subcomponents 2245 are used at block 2250 to construct a denoised physiological signal 2255.

The denoised ECG signal is then output via a communications output port 2216. This output may, for example, involve a wired or wireless communication, and may be carried out in accordance with one or more embodiments as described herein. In some implementations, some or all of the logic circuit 2210 is included as part of an implantable device, and carries out some or all of the steps in the implantable device, for generating the denoised physiological signal 2255. Using this approach, and as consistent with the above, the logic circuit 2210 can be implemented to significantly reduce the size of the denoised and compressed physiological signal 2255 (*e.g.*, as relative to approaches that do not denoise in this manner), and facilitate the communication of the denoised and compressed physiological signal using less data and, correspondingly, lower power.

Those skilled in the art will appreciate that various alternative logic circuits or computing arrangements, including one or more processors and a memory arrangement configured with program code, would be suitable for carrying out the approaches as discussed herein, including those discussed in connection with Figure 22 above, along with data structures for organizing the required data. Such computer code can be encoded in a processor executable format and may be stored on and/or provided via a variety of computer-readable storage media or delivery channels such as magnetic or optical disks or tapes, electronic storage devices, or as application services over a network. With specific reference to Figure 22, the logic circuit 2210 (and memory 2212, where appropriate) may be implemented with separate components on a circuit board or may be implemented internally within an integrated circuit. When implemented internally within an integrated circuit, the logic circuit 2210 can be implemented as a microcontroller.

The architecture of the logic circuits, processors and computer type circuits as described herein depends on implementation requirements as would be recognized by those skilled in the art. In this context, these components may be one or more general purpose

processors, or a combination of one or more general purpose processors and suitable co-processors, or one or more specialized processors (*e.g.*, RISC, CISC, and pipelined).

Referring again to Figure 22, the memory circuit 2212 may include multiple levels of cache memory and a main memory, and local and/or remote persistent storage such as provided by magnetic disks, flash, EPROM, or other non-volatile data storage. The memory circuit 2212 may be read or read/write capable. The logic circuit 2210 may store instructions (*e.g.*, software) in the memory circuit 2210, read data from and stores data to the memory circuit 2212, and communicate with external devices through the input/output ports 2214 and 2216. These functions may be synchronized by a clock signal generator that may be part of the logic circuit 2210. The resources of the logic circuit 2210 may be managed by either an operating system, or a hardware control unit.

Referring to process 1907 in Figure 19, example transforms that can be used for decomposing the signal into a second domain while enhancing, or maximizing, the independence of the subcomponents include a discrete cosine transform, a wavelet related transform, a Karhunen-Loeve transform, a Fourier transform, a Gabor transform, or a filter bank.

In another embodiment, referring to Figure 16, a denoising function and a data compression function are implemented within a computerized apparatus (*e.g.*, a logic circuit) configured to execute programming instructions. In this embodiment, denoising and compression of an ECG results in a reduction in bit rate required to retain the information in the signal. By compressing the ECG signal prior to wireless transmission, fewer bits can be used to achieve data transmission, and hence the power consumed in the transmission (*e.g.*, a telemetry link) is reduced. This approach may also be implemented when storing ECG data (or other signal data) in memory, to reduce the data storage space required.

In a more particular example embodiment, a denoising and compression involves reducing the bit rate of a signal by a factor of 15:1 to 20:1, relative to the bit rate of input signal. For instance, such a compression factor can be achieved with a 16-bit digitized single lead ECG having a bit rate of 4,000 bits per second and sampled at 250 Hz, and with band-limited (0.5 to 100 Hz) noise corresponding to a SNR of 4 dB (computed as $SNR_{dB} = 10\log_{10}(\frac{P_{signal}}{P_{noise}})$ where P_{signal} and P_{noise} are respective signal and noise energy). The compressed signal is communicated to a receiving device where the compressed ECG signal is reconstructed. The denoising approach facilitates reconstructing QRS complex, from the compressed signal, having mean amplitude for any 10-second interval therein that

differs from the mean amplitude of the input ECG by 10% or less. In one embodiment, communication is performed using a wireless link such as a Bluetooth transceiver. In some embodiments, events in the ECG, such as arrhythmias, are detected and compression and transmission of the ECG is triggered based on the presence of a detected event.

In this example embodiment, the input ECG is processed by the computerized apparatus to first denoise the signal, then detect cardiac cycles, segment the ECG by cardiac cycles and align them in time according to an identifiable fiduciary (*e.g.*, a QRS peak), and form an image consisting of aligned cardiac cycles. The image is then encoded using a lossy compression technique such as transform encoding, subband encoding, or wavelet based encoding. The encoded image contains nearly all of the information in the denoised ECG, but does so with about 15-fold fewer bits. The encoded image is reconstructed at a receiver using the inverse of the transform used to encode the image, and ECG segments are reconnected to form a denoised version of the input signal. In one embodiment, denoising prior to compression is achieved in the same manner as described herein for the apparatus used for denoising.

In another embodiment, cardiac cycles are detected by computing a QRS emphasis signal and evaluating peaks, valleys, or slopes to identify the QRS complex. In another embodiment, the QRS complex is detected and a template QRS complex that is representative of the average complex is subsequently computed. The template is then subtracted from each QRS complex, creating a time series consisting of the resulting difference. The time series of residuals is subsequently encoded using a lossy compression technique such as transform encoding, subband encoding, or wavelet based encoding. The template QRS is encoded using a lossless transform such as Huffman encoding. This approach may be useful, for example, in connection with an embodiment in which a relatively simpler and less computationally intense compression technique is appropriate (*e.g.*, where QRS morphology is not expected to change rapidly). Accordingly, the computational intensity of denoising and resulting signal quality/size can be weighed as a tradeoff, for implementation in various embodiments.

Another example embodiment is directed to a system and approach for denoising, that facilitates an improvement in signal-to-noise of between about 14 and 26 dB while preserving signal morphology for a controlled application using a signal-to-noise computation as follows. Considering a noise free single-channel 30-minute digitized human ECG recording sampled at 250 Hz with average heart rate of about 83 BPM, the signal is contaminated with controlled levels of additive band-limited (0.5 to 100 Hz) white noise.

Testing can be carried out using, for example, multiple copies of the 30-minute ECG strip, each contaminated with a known and different noise level. Each strip is processed using an MDSP-type denoising approach, and signal-to-noise ratio improvement and morphology preservation can be quantified. Signal-to-noise ratio is computed as described in the ANSI/AAMI EC57:1998 standard [27, 28], and is referred to as SNR_A.

Morphology preservation is computed as:

$$QSR = 100\%(1 - \frac{\sum_{i=1}^{N}(ECG_{clean} - ECG_{denoised})^2}{\sum_{i=1}^{N}(ECG_{clean})^2})$$

in which ECG_{clean} is the input ECG signal prior to imputing white noise and $ECG_{denoised}$ is the ECG signal after denoising/filtering. This approach quantifies preservation of signal morphology through a point-by-point comparison of the denoised signal to the clean ECG, prior to imputing noise. SNR_A improvement is calculated as SNR_A of the output signal less SNR_A of the input signal.

Figure 23a shows SNR_A improvement and QSR for MDSP denoising of ECG recordings with controlled levels of imputed band-limited white noise, in accordance with a particular embodiment. An example ECG trace is shown in Figure 23b before (top) and after (bottom) for a signal processed using an MDSP-type denoising system/approach.

Figure 23b shows an example ECG recording according to a controlled application with 0 dB SNR_A as a result of imputed band-limited white noise (top) and post-MDSP denoising (bottom), in accordance with another example embodiment. The input trace shown at the top of Figure 23b is imputed with band-limited white noise to provide SNR_A = 0 dB. In the bottom ECG trace, SNR_A has been improved by about 26 dB as a result of denoising using an MDSP-based system/approach as discussed herein. SNR_A improvements ranging from 14 to 26 dB for input SNR_A ranging from 0 to 40 dB can be realized, with a higher degree of SNR_A improvement for lower input SNR_A. QSR ranges from about 97.5 to 99.8%, indicating negligible distortion of ECG morphology. Accordingly, various circuits, systems and approaches as discussed herein may be configured for operation in accordance with Figures 23a and 23b.

In a more particular implementation, a system and/or method for denoising a signal is configured for implementation in denoising a single-channel human ECG-based signal sampled at 250 Hz and contaminated with 0.5 to 100 Hz band-limited white noise between about 0 to 40 dB SNR_A. Using approaches as discussed herein, a denoised physiological

signal is constructed by, for an input signal having a 40 dB SNR_A, constructing a denoised physiological signal having a quality of signal reconstruction (QSR) of at least 99% and a SNR_A that is at least 10 dB greater than the SNR_A of the input signal. For an input signal having a 0 dB SNR_A, a denoised physiological signal having a QSR of at least 95% and a SNR_A that is at least 22 dB greater than the SNR_A of the input signal is constructed.

Figure 24 shows a system 2400 and related flow functions for computing a denoised physiological signal from an input signal including a desired physiological signal and noise signal, in accordance with another example embodiment of the present invention. At block/module 2410, an input signal is decomposed from a first domain into subcomponents of the input signal in a second domain. These subcomponents are passed to block/module 2420, via which target subcomponents of the input signal that are associated with the desired physiological signal are identified, based upon a spatial distribution of the subcomponents. The target subcomponents are provided for block/module 2430, which constructs a denoised physiological signal in the first domain from at least one of the identified target subcomponents. The respective blocks/modules may be implemented using, for example, a processing circuit executing modules to process input signals/data and generate output signals/data as shown. In some implementations, the system 2400 includes components such as shown in Figure 16 and/or otherwise, such as ECG leads coupled to provide the input signal, and output communications devices for communicating the denoised signal and/or otherwise processing the denoised signal.

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For general information regarding a variety of fields that may relate to one or more embodiments of the present disclosure, and for specific information regarding the application of one or more such embodiments, reference may be made to the following documents, which are fully incorporated herein by reference. Various ones of these references are further cited above via corresponding numerals, and may be implemented as such.

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Based upon the above discussion and illustrations, those skilled in the art will readily recognize that various modifications and changes may be made to the present disclosure without strictly following the exemplary embodiments and applications illustrated and described herein. Such modifications and changes may include, for example, incorporating one or more aspects described in the above references and/or applying one or more embodiments thereto, or combining embodiments. These and other modifications do not depart from the true spirit and scope of the present disclosure, including that set forth in the following claims.

What is claimed is:

1. A method for computing a denoised physiological signal from an input signal including a desired physiological signal and noise, the method comprising:

decomposing the input signal from a first domain into subcomponents of the input signal in a second domain;

identifying target subcomponents of the input signal that are associated with the desired physiological signal based upon a spatial distribution of the subcomponents; and

constructing a denoised physiological signal in the first domain from at least one of the identified target subcomponents.

2. The method of claim 1, wherein the input signal is pseudoperiodic, and identifying target subcomponents based upon spatial distribution includes:

computing a point-wise product of subcomponents,

identifying a location of a defining feature of a cycle of the pseudoperdiodic signal by comparing the point-wise product to a predefined threshold,

partitioning the cycle into at least two time windows based upon said defining feature, each time window having an associated band of frequencies, and

identifying a target subcomponent in a time window as a subcomponent that contains more energy that is within the band of frequencies characteristic of the desired signal, than the energy that is outside of the band of frequencies.

3. The method of claim 2, wherein the input signal is a single-channel human ECG-based signal sampled at 250 Hz and contaminated with 0.5 to 100 Hz band-limited white noise between about 0 to 40 dB SNR_A, and constructing a denoised physiological signal includes,

for an input signal having a 40 dB SNR_A, constructing a denoised physiological signal having a quality of signal reconstruction (QSR) of at least 97% and a SNR_A that is at least 10 dB greater than the SNR_A of the input signal, and

for an input signal having a 0 dB SNR_A, constructing a denoised physiological signal having a QSR of at least 95% and a SNR_A that is at least 22 dB greater than the SNR_A of the input signal.

4. The method of claim 1, wherein identifying target subcomponents of the input signal that are associated with the desired physiological signal based upon the spatial distribution of the subcomponents includes identifying target subcomponents using spatially selective filtering to filter subcomponents.

5. The method of claim 1, wherein decomposing the input signal from a first domain to a second domain, includes using one of:

a discrete cosine transform;

a wavelet related transform;

a synchrosqueezed wavelet transform;

a Karhunen-Loeve transform;

a Fourier transform;

a Gabor transform; and

a filter bank.

6. The method of claim 1, wherein identifying target subcomponents includes filtering the target subcomponents using spatially selective filtering, and processing the subcomponents using at least one of:

principal component analysis;

independent component analysis; and

periodic component analysis.

7. The method of claim 1, wherein the input signal includes at least one of an electrocardiogram signal, a heart sound signal, a blood pressure signal, an impedance signal, a respiratory information signal, an electromyogram signal, a peripheral nerve signal, a blood flow signal, a photoplethysmography signal, and a periodic stimulation response signal.

8. The method of claim 1,

wherein the input signal includes a response to a periodic stimulation signal,

further including, before decomposing the input signal, segmenting the input signal according to the timing of the stimulation signal to assemble a plurality of signals,

wherein decomposing the input signal includes decomposing the plurality of signals into subcomponents in a second domain, and

wherein identifying target subcomponents includes applying principal component analysis to the subcomponents in the second domain.

9. The method of claim 1, wherein

decomposing the input signal includes decomposing an input signal including a desired ECG signal and noise into subcomponents, and

identifying target subcomponents includes

identifying a location of the QRS complex of a cardiac cycle in the ECG signal based upon the spatial distribution of the subcomponents;

identifying a first time window in the cardiac cycle that includes the QRS complex;

identifying at least one time window in the cardiac cycle that does not include the QRS complex; and

for each of the identified time windows, identifying target subcomponents as subcomponents that contain more energy corresponding to a desired ECG signal, than energy corresponding to noise.

10. The method of claim 9, wherein identifying target subcomponents includes identifying target subcomponents in the at least one time window that does not include the QRS complex, by identifying subcomponents having more energy associated with P and T waves than other energy.

11. The method of claim 9, wherein identifying target subcomponents includes

identifying target subcomponents in the first time window by identifying target subcomponents having more energy corresponding to the QRS complex than other energy, and

identifying target subcomponents in the at least one time window that does not include the QRS complex by identifying subcomponents having more energy corresponding to P and T waves than other energy.

12. The method of claim 9, wherein decomposing the input signal into subcomponents includes transforming the input signal from a first domain into subcomponents in a second domain using at least one of

a discrete cosine transform;

a wavelet related transform;

a synchrosqueezed wavelet transform;

a Karhunen-Loeve transform;

a Fourier transform;

a Gabor transform; and

a filter bank.

13. The method of claim 9, wherein identifying target subcomponents includes identifying target subcomponents using at least one of:

principal component analysis;

independent component analysis;

spatially selective filtering; and

periodic component analysis.

14. The method of claim 9, wherein identifying target subcomponents as subcomponents that contain more desired ECG signal energy than noise energy includes at least one of

identifying, in each of the identified time windows, target subcomponents as subcomponents that are associated with frequencies overlapping a characteristic frequency band of the desired ECG signal within said identified time window, and

deleting subcomponents that that are not associated with frequencies overlapping a characteristic frequency band of the desired ECG signal within said identified time window, the remaining subcomponents being residual subcomponents, and identifying, in each of the identified time windows, the residual subcomponents as the target subcomponents.

15. A system for computing a denoised physiological signal from an input signal including a desired physiological signal and noise, the system comprising:

means for decomposing the input signal from a first domain into subcomponents of the input signal in a second domain;

means for identifying target subcomponents of the input signal that are associated with the desired physiological signal based upon a spatial distribution of the subcomponents; and

means for computing a denoised physiological signal in the first domain from at least one of the identified target subcomponents.

16. The system of claim 15, wherein the means for decomposing, identifying and computing include a logic circuit that

decomposes input signals including an ECG signal into subcomponents,

identifies target subcomponents of the input signal by

identifying a location of the QRS complex of a cardiac cycle in the ECG signal based upon a spatial distribution of the subcomponents,

identifying a first time window in the cardiac cycle that includes the QRS complex,

identifying at least one time window in the cardiac cycle that does not include the QRS complex, and

for each of the identified time windows, identifying target subcomponents as subcomponents that contain more desired ECG signal energy than noise energy; and

computes the denoised physiological signal by using the identified target subcomponents to compute the denoised physiological signal.

17. The system of claim 15, wherein the input signal is a substantially noise-free single-channel human ECG-based signal sampled at 250 Hz and contaminated with 0.5 to 100 Hz band-limited white noise, and the means for computing a denoised physiological signal is configured and arranged to

construct, from an input signal having a 40 dB SNR_A, a denoised physiological signal having a quality of signal reconstruction (QSR) of at least 97% and a SNR_A that is at least 10 dB greater than the SNR_A, of the input signal, and

construct, from an input signal having a 0 dB SNR_A, a denoised physiological signal having a QSR of at least 95% and a SNR_A that is at least 22 dB greater than the SNR_A, of the input signal.

Figure 1

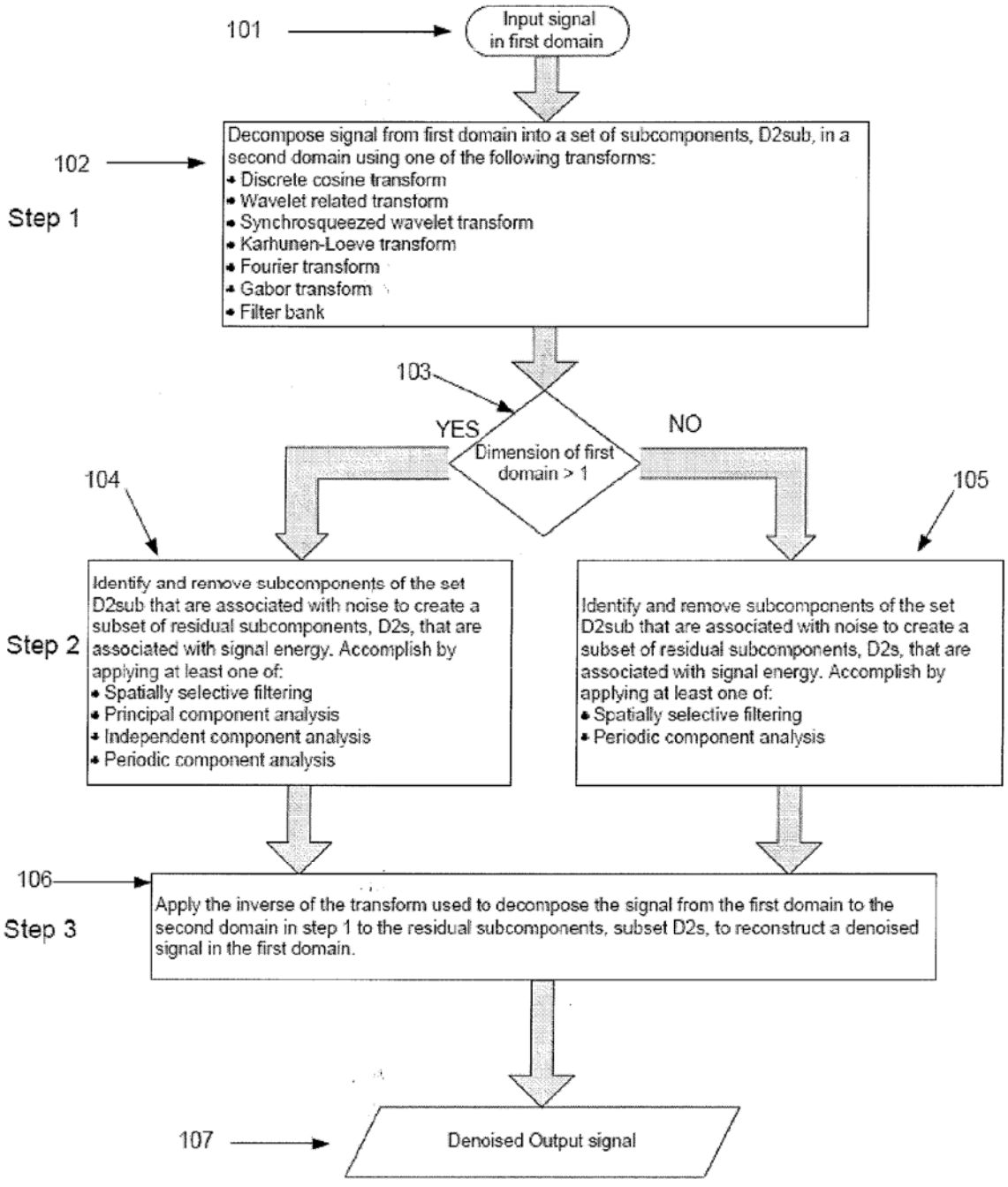

101
Input signal in first domain
102
Step 1
Decompose signal from first domain into a set of subcomponents, D2sub, in a second domain using one of the following transforms:
• Discrete cosine transform
• Wavelet related transform
• Synchrosqueezed wavelet transform
• Karhunen-Loeve transform
• Fourier transform
• Gabor transform
• Filter bank
103
YES
NO
Dimension of first domain > 1
104
105
Step 2
Identify and remove subcomponents of the set D2sub that are associated with noise to create a subset of residual subcomponents, D2s, that are associated with signal energy. Accomplish by applying at least one of:
• Spatially selective filtering
• Principal component analysis
• Independent component analysis
• Periodic component analysis
Identify and remove subcomponents of the set D2sub that are associated with noise to create a subset of residual subcomponents, D2s, that are associated with signal energy. Accomplish by applying at least one of:
• Spatially selective filtering
• Periodic component analysis
106
Step 3
Apply the inverse of the transform used to decompose the signal from the first domain to the second domain in step 1 to the residual subcomponents, subset D2s, to reconstruct a denoised signal in the first domain.
107
Denoised Output signal

Figure 2

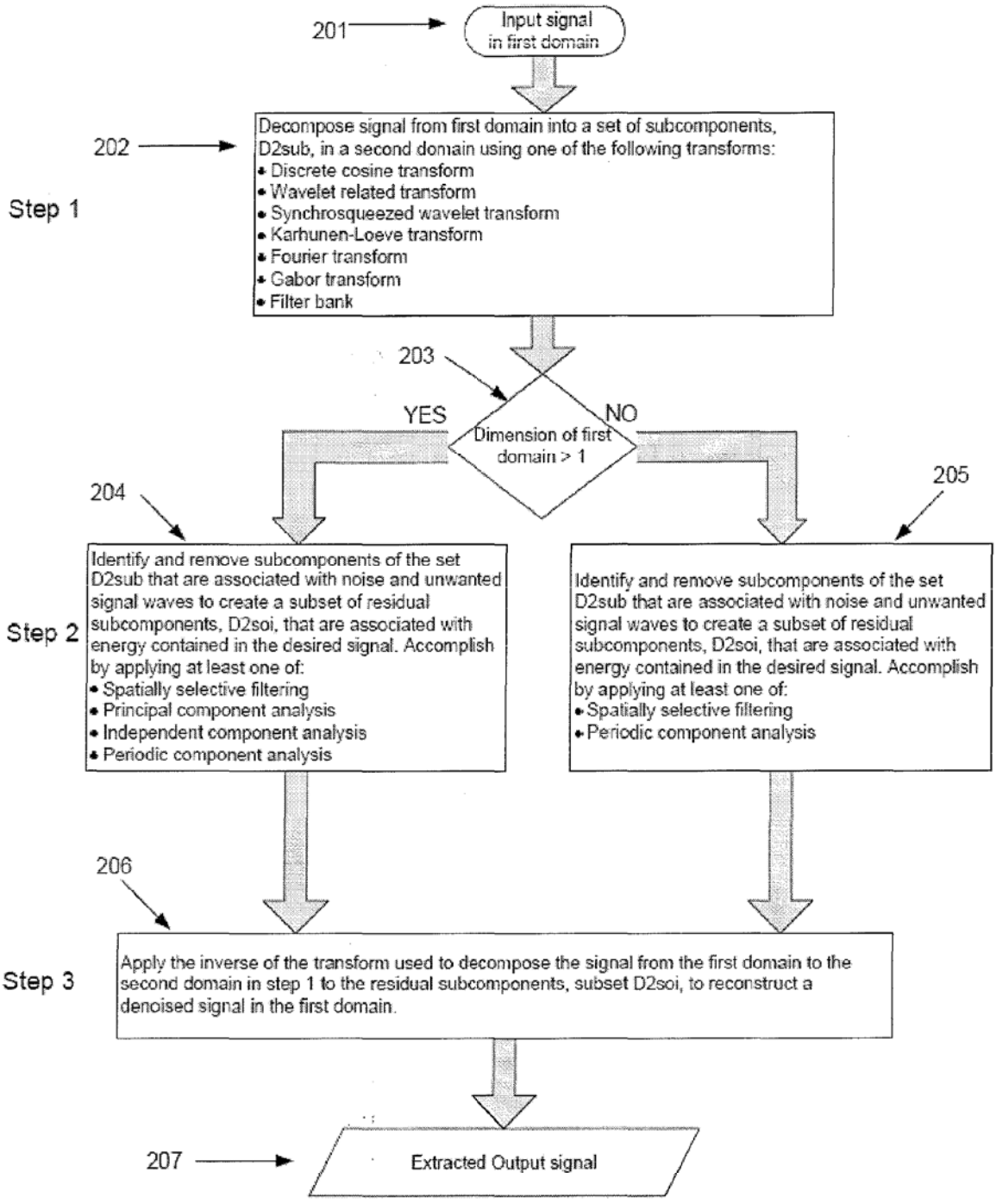

201
Input signal in first domain
202
Step 1
Decompose signal from first domain into a set of subcomponents, D2sub, in a second domain using one of the following transforms:
• Discrete cosine transform
• Wavelet related transform
• Synchrosqueezed wavelet transform
• Karhunen-Loeve transform
• Fourier transform
• Gabor transform
• Filter bank
203
YES
NO
Dimension of first domain > 1
204
205
Step 2
Identify and remove subcomponents of the set D2sub that are associated with noise and unwanted signal waves to create a subset of residual subcomponents, D2soi, that are associated with energy contained in the desired signal. Accomplish by applying at least one of:
• Spatially selective filtering
• Principal component analysis
• Independent component analysis
• Periodic component analysis
Identify and remove subcomponents of the set D2sub that are associated with noise and unwanted signal waves to create a subset of residual subcomponents, D2soi, that are associated with energy contained in the desired signal. Accomplish by applying at least one of:
• Spatially selective filtering
• Periodic component analysis
206
Step 3
Apply the inverse of the transform used to decompose the signal from the first domain to the second domain in step 1 to the residual subcomponents, subset D2soi, to reconstruct a denoised signal in the first domain.
207
Extracted Output signal

Figure 3a

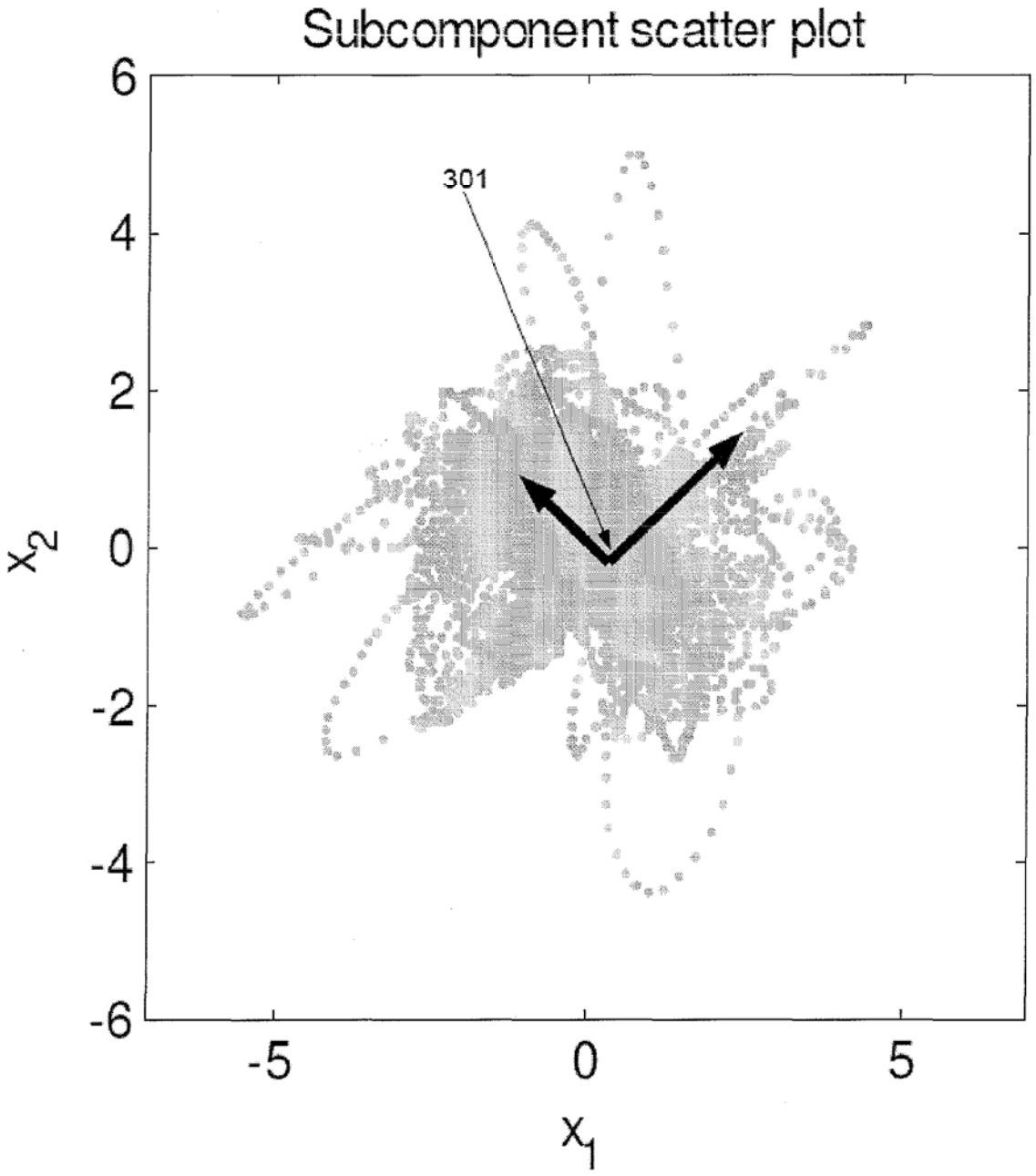


Figure 3b

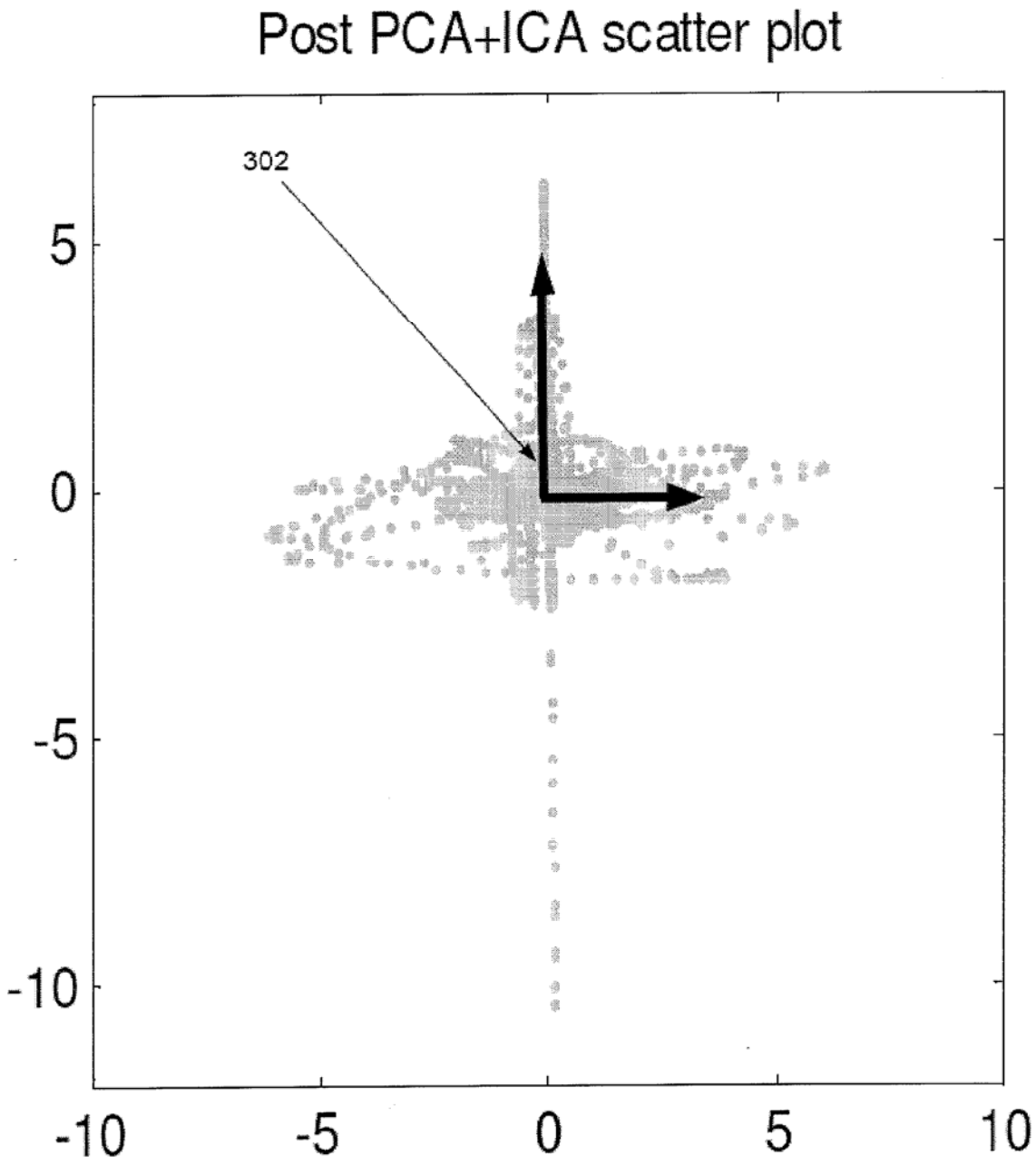
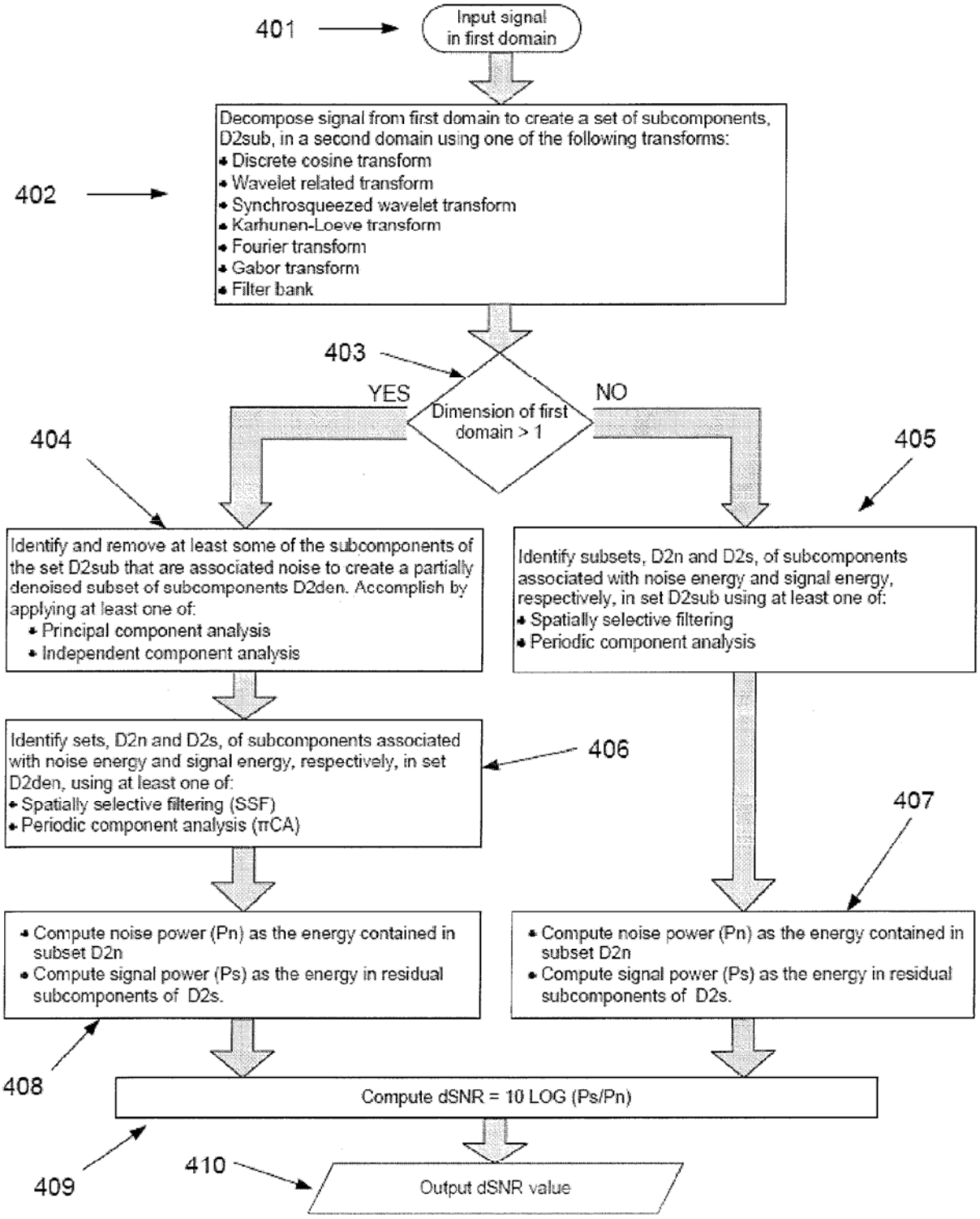


Figure 4


401
Input signal in first domain
Decompose signal from first domain to create a set of subcomponents, D2sub, in a second domain using one of the following transforms:
• Discrete cosine transform
• Wavelet related transform
• Synchrosqueezed wavelet transform
• Karhunen-Loeve transform
• Fourier transform
• Gabor transform
• Filter bank
402
403
Dimension of first domain > 1
YES
NO
404
405
Identify and remove at least some of the subcomponents of the set D2sub that are associated noise to create a partially denoised subset of subcomponents D2den. Accomplish by applying at least one of:
• Principal component analysis
• Independent component analysis
Identify subsets, D2n and D2s, of subcomponents associated with noise energy and signal energy, respectively, in set D2sub using at least one of:
• Spatially selective filtering
• Periodic component analysis
Identify sets, D2n and D2s, of subcomponents associated with noise energy and signal energy, respectively, in set D2den, using at least one of:
• Spatially selective filtering (SSF)
• Periodic component analysis (πCA)
406
407
• Compute noise power (Pn) as the energy contained in subset D2n
• Compute signal power (Ps) as the energy in residual subcomponents of D2s.
• Compute noise power (Pn) as the energy contained in subset D2n
• Compute signal power (Ps) as the energy in residual subcomponents of D2s.
408
Compute dSNR = 10 LOG (Ps/Pn)
409
410
Output dSNR value