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(54) Title: IMPROVED ULTRASOUND IMAGING OF VASCULATURE

(57) Abstract: The current invention concerns a method, a computer system, and a computer program product for blood vessel image extraction from ultrasound signals, and a method and apparatus for ultrasound imaging. A set of ultrasound signals at successive times in a plurality of spatial points is obtained. The ultrasound signals are decomposed as a sum of terms. Each term consists of a time-independent spatial component image factor and a space-independent temporal component signal. The spatial component images are mutually orthonormal. The temporal component signals are mutually orthogonal. A sharpened spatial image for each of multiple spatial component images is determined. A processed image being a bilinear combination of multiple sharpened spatial images is generated.



IMPROVED ULTRASOUND IMAGING OF VASCULATURE

Technical field

- 5 The invention pertains to ultrasound Doppler imaging of vasculature.

Background

10 Ultrasound Doppler imaging is an important imaging technique for blood vasculature. Traditionally, ultrasound imaging is realized via focused beams, wherein multiple lines are scanned sequentially in time. Measurements for different lines are thereby not coherent in time. Moreover, scanning a two- or three-dimensional area requires a considerable amount of time.

15 E. Mace et al., *Nature Methods* 8(8), 662-664 (2011), doi: 10.1038/nmeth.1641 and E. Mace et al., *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control* 60(3), 492-506 (2013), doi: 10.1109/tuffc.2013.2592 disclose ultrasound power Doppler imaging via plane waves, which allows ultrafast and time-coherent imaging of a two- or three-dimensional area. Backscattered echoes of a set of plane
20 wave emissions tilted at different angles are coherently compounded to improve quality. Each compound image provides a time sample (denoted t_j) of the complex IQ signal, alternatively called spatiotemporal cineloop, $s(r_i, t_j)$ for each pixel r_i . Via a high-pass filter, temporal discrimination of slower tissue movement and faster red blood cell movement is performed per pixel. The technique is used for functional
25 ultrasound imaging of brain vasculature.

C. Demene et al., *IEEE Transactions on Medical Imaging* 34(11), 2271-2285 (2015), doi: 10.1109/tmi.2015.2428634 and A. Urban et al., *Jacobs Journal of Molecular and Translational Medicine* 1(1), 007 (2015) disclose an improved discrimination of
30 tissue and red blood cell movement. When (relative) tissue motion is important (e.g. free hand imaging, vibrations or cardiac movement) or when blood flow velocities become slow (e.g. in small vessels), tissue and red blood cell movement are not separable based on a frequency cut-off. Instead, a spatiotemporal singular value decomposition of the complex IQ signal $s(r_i, t_j) = \sum_{k=1}^N \lambda_k p_k(r_i) a_k(t_j)$ allows to isolate
35 tissue movement from blood flow movement. Tissue movement is spatially coherent and more energetic, resulting in the largest singular value contributions of the decomposition, which may be eliminated to obtain the blood signal.

The scattering of waves from a small vessel may result in an image with a broadened representation of the small vessel. In case from a certain point of view small vessels cross or are proximate, it may no longer be possible to discern the separate vessels.

5

The present invention aims to provide an improved representation of small vessels in an ultrasound Doppler image.

10 The present invention aims to resolve at least some of the problems mentioned above.

Summary of the invention

15 In a first aspect, the present invention provides a method for blood vessel image extraction from ultrasound signals, according to claim 1.

In a second aspect, the present invention provides a method for ultrasound imaging, according to claim 11.

20 In a third aspect, the present invention provides a computer system for blood vessel image extraction from ultrasound signals, according to claim 12.

In a fourth aspect, the present invention provides a computer program product for blood vessel image extraction from ultrasound signals, according to claim 13.

25

In a fifth aspect, the present invention provides an apparatus for ultrasound imaging of vasculature, according to claim 14.

30 The present invention enables resolving small vessels in ultrasound imaging. The present invention in particular solves undesirable blurring when ultrasound waves are scattered off small vessels.

Description of figures

35 **Figures 1, 2 and 3** show schematic representations of embodiments of a method according to the present invention.

Figure 4 shows a set of exemplary images to illustrate several steps of an embodiment of a method according to the present invention.

Figures 5a and 5b shows two exemplary ultrasound Doppler images, the former
5 obtained with a prior art method, the latter obtained with an embodiment of a method according to the present invention.

Detailed description of the invention

10 The present invention concerns a method, a computer system, and a computer program product for blood vessel image extraction from ultrasound signals. The present invention furthermore concerns a method and an apparatus for ultrasound imaging. The invention has been summarized in the corresponding section above. In what follows, the invention is described in detail, preferred embodiments are
15 discussed, and the present invention is illustrated by means of examples.

Unless otherwise defined, all terms used in disclosing the invention, including technical and scientific terms, have the meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. By means of further
20 guidance, term definitions are included to better appreciate the teaching of the present invention.

"A", "an", and "the" as used herein refers to both singular and plural referents unless the context clearly dictates otherwise. By way of example, "a compartment" refers
25 to one or more than one compartment.

"Comprise", "comprising", and "comprises" as used herein are synonymous with "include", "including", "includes" or "contain", "containing", "contains" and are inclusive or open-ended terms that specify the presence of what follows (e.g.
30 component) and do not exclude or preclude the presence of additional, non-recited components, features, elements, members, steps, known in the art or disclosed therein.

"Based on" as used herein is synonymous with "based at least in part on" and is an
35 inclusive or open-ended term that specifies the presence of what follows and does not exclude or preclude the presence of additional, non-recited components, features, elements, members, steps, known in the art or disclosed therein.

In a first aspect, the present invention provides a method for blood vessel image extraction from ultrasound signals. The method comprises several steps. A set of ultrasound signals of biological tissue of a living subject comprising blood vessels is obtained. The set comprises ultrasound signals at successive times in a plurality of spatial points. The set of ultrasound signals is decomposed as a sum of multiple terms. Each term consists of a time-independent spatial component image factor and a space-independent temporal component signal factor. One of ordinary skill in the art will appreciate that hereby a factor may be composite, i.e. may comprise or may be split up into multiple factors. The spatial component images are mutually orthonormal. The temporal component signals are mutually orthogonal. A sharpened spatial image is determined for each spatial component image of multiple spatial component images. A processed image is generated. The processed image is a bilinear combination of determined sharpened spatial images.

In a preferred embodiment, the plurality of spatial points is a multidimensional grid of spatial points. Preferably, the grid is a rectangular grid. Preferably, the set of ultrasound signals comprises ultrasound signals at successive times in each point of a multidimensional rectangular grid of spatial points. Preferably, the multidimensional grid is a two-dimensional or three-dimensional grid of spatial points. Preferably, each spatial point of the multidimensional rectangular grid corresponds to a pixel of the multidimensional rectangular processed image.

In a second aspect, the present invention provides a method for ultrasound imaging, comprising a method according to the first aspect, wherein the step of obtaining the set of ultrasound signals comprises several steps. Ultrasound waves are emitted to said biological tissue of a living subject comprising blood vessels. Ultrasound waves are received at least in part from the biological tissue. Said set of ultrasound signals is obtained based on the received ultrasound waves. Preferably, the emitted ultrasound waves are plane or diverging ultrasound waves. More preferably, the emitted ultrasound waves are a set of plane or diverging ultrasound waves tilted at different angles. Preferably, the received ultrasound waves are backscattered waves off the biological tissue of the set of plane or diverging ultrasound waves. Preferably, the received backscattered waves are coherently compounded.

Some of the method steps may be computer-implemented. The step of decomposing the set of ultrasound signals as a sum of multiple terms is preferably computer-

implemented. The step of determining a sharpened spatial image for each of multiple spatial component images is preferably computer-implemented. The step of generating a processed image is preferably computer-implemented. The methods according to the first and second aspects may therefore be computer-implemented methods. In a computer-implemented method according to the first aspect, obtaining the set of ultrasound signals may be receiving the set of ultrasound signals via a communication module. In a computer-implemented method according to the first aspect, obtaining the set of ultrasound signals may be obtaining the set of ultrasound signals via a data acquisition card. In a computer-implemented method according to the first aspect, obtaining the set of ultrasound signals may be reading the set of ultrasound signals from a non-transitory computer-readable storage medium. In a method according to the second aspect, obtaining the set of ultrasound signals comprises emission of ultrasound waves, reception of ultrasound waves, and obtaining the ultrasound signals based on the received ultrasound waves, for example via a data acquisition card. Preferably, the ultrasound signals are computer-readable, more preferably digital, ultrasound signals.

In a third aspect, the present invention provides a computer system for blood vessel image extraction from ultrasound signals. The computer system comprises one or more processors. The computer system is configured for performing a method according the first aspect of the present invention.

In a fourth aspect, the present invention provides a computer program product for blood vessel image extraction from ultrasound signals. The computer program product comprises instructions which, when the computer program product is executed by a computer, such as a computer system according to the second aspect of the present invention, cause the computer to carry out a method according to the first aspect of the present invention. In the fourth aspect, the present invention may furthermore provide a tangible non-transitory computer-readable data carrier comprising the computer program product.

In a fifth aspect, the present invention provides an apparatus for ultrasound imaging of vasculature. The apparatus comprises an ultrasonic wave emitter, an ultrasonic wave receiver, and a computer system according to the third aspect of the present invention. The apparatus is configured for performing the method according to the second aspect of the present invention. Preferably, the apparatus is configured for emitting plane or diverging ultrasound waves via the ultrasonic wave emitter. More

preferably, the apparatus is configured for emitting a set of plane or diverging ultrasound waves tilted at different angles via the ultrasonic wave emitter. Preferably, the apparatus is configured receiving ultrasound waves backscattered off biological tissue. Preferably, the apparatus is configured for coherently
 5 compounding the received backscattered ultrasound waves.

One of ordinary skill in the art will appreciate that the aspects of the present invention are interrelated. Therefore, every feature disclosed above or below may relate to each aspect of the present invention, even if it has been disclosed in
 10 conjunction with a particular aspect of the present invention. One of ordinary skill in the art will furthermore appreciate that several features of the present invention may be disclosed in terms of exemplary mathematical formulae.

The present invention enables resolving small vessels in ultrasound imaging. The
 15 present invention in particular solves undesirable blurring when ultrasound waves are scattered off small vessels. The present invention furthermore allows for real-time image acquisition on available computing systems.

Figure 1 shows a schematic representation of several features of an embodiment
 20 of a method according to the present invention. A set of ultrasound signals $s(\mathbf{r}_i, t_j)$ of biological tissue of a living subject comprising blood vessels is obtained (101). The set comprises ultrasound signals at successive times (time samples) t_j in a plurality of spatial points $\mathbf{r}_i$. The set of ultrasound signals is decomposed as a sum of multiple terms (102):

$$25 \quad s(\mathbf{r}_i, t_j) = \sum_{k=1}^N \lambda_k p_k(\mathbf{r}_i) a_k(t_j).$$

Each term consists of a time-independent spatial component image factor p_k and a space-independent temporal component signal factor $\lambda_k a_k$. The spatial component images p_k are mutually orthonormal, i.e. p_k with $1 \leq k \leq N$ is a set of orthonormal time-independent spatial component images. Mutual orthonormality of the spatial
 30 component images over the plurality of spatial points may be expressed as:

$$\sum_{i=1}^{N_r} p_k(\mathbf{r}_i) p_l^*(\mathbf{r}_i) = \delta_{k,l},$$

with N_r the number of spatial points $\mathbf{r}_i$ in the plurality of spatial points, * denoting complex conjugate, and $\delta_{k,l}$ Kronecker delta: $\delta_{k,l} = 1$ if k equals l , and $\delta_{k,l} = 0$ otherwise. The temporal component signals $\lambda_k a_k$ are mutually orthogonal. Mutual

orthogonality of the temporal component signals over the successive times may be expressed as:

$$\sum_{j=1}^{N_t} \lambda_k a_k(t_j) \lambda_l a_l^*(t_j) = \delta_{k,l} \lambda_k^2 \sum_{j=1}^{N_t} a_k(t_j) a_k^*(t_j),$$

with N_t the number of successive times t_j . A sharpened spatial image q_k is determined for each spatial component image p_k of multiple spatial component images (103). A processed image I is generated (104), being a bilinear combination of multiple sharpened spatial images q_k with weight coefficients $\beta_{k,l}$:

$$I(\mathbf{r}_i) = \sum_{k,l=n_f \geq 1}^N \beta_{k,l} q_k(\mathbf{r}_i) q_l^*(\mathbf{r}_i).$$

One of ordinary skill in the art will appreciate that in case $n_f > 1$, a sharpened spatial image q_k may be, but does not have to be, determined for each spatial component image p_k with $1 \leq k < n_f$.

In a preferred embodiment, each temporal component signal consists of a real-valued positive decomposition coefficient factor and a normalized temporal component signal factor. The normalized temporal component signals are mutually orthonormal. Preferably, the decomposition of the set of ultrasound signals as a sum of multiple terms is performed via a singular value decomposition. A decomposition coefficient is then a singular value. With non-limiting reference to the exemplary mathematical formulae above, a_k with $1 \leq k \leq N$ is then a set of orthonormal space-independent temporal component signals, and λ_k are then the real-valued positive singular values. Preferably, the singular values are arranged in order of decreasing magnitude with increasing decomposition index k : $\lambda_k \geq \lambda_{k+1} > 0$. Mutual orthonormality of the normalized temporal component signals over the successive times may be expressed as:

$$\sum_{j=1}^{N_t} a_k(t_j) a_l^*(t_j) = \delta_{k,l}.$$

In a preferred embodiment, a filtering step is performed. The filtering step may comprise application of a high-pass filter to the set of ultrasound signals, preferably prior to the decomposition of the set of ultrasound signals as a sum of terms. This allows for discrimination of slower tissue movement and faster red blood cell movement per spatial point. The filtering step may additionally or alternatively comprise the generation of a processed image without the contribution of one or

more of the terms corresponding to the largest decomposition coefficients. With non-limiting reference to the exemplary mathematical formulae above, n_f is then larger than one: $n_f > 1$. This allows for improved discrimination of slower tissue movement and faster red blood cell movement, as disclosed in the background section above.

In a preferred embodiment, determination of a sharpened spatial image for a spatial component image comprises several steps. Positions of local maxima are determined. A sharpened spatial image is generated, wherein the sharpened spatial image is a linear combination of peak functions. Hereby, each peak function of the linear combination is maximal at the position of one of the local maxima. Preferably, positions of local maxima of the spatial component image are determined.

Preferably, the linear combination of peak functions is a linear combination, over the positions of the local maxima, of a reference peak function shifted to a position of a local maximum and weighted with the value of the spatial component image at the position of the local maximum. Preferably, the reference peak function is proportional to one of a Dirac function or a Gaussian function.

Figure 2 shows a schematic representation of several features of an embodiment of a method according to the present invention. A set of ultrasound signals $s(r_i, t_j)$ of biological tissue of a living subject comprising blood vessels is obtained (201). The set comprises ultrasound signals at successive times t_j in a plurality of spatial points r_i . The set of ultrasound signals is decomposed via a spatiotemporal singular value decomposition as a sum of multiple terms (202):

$$s(r_i, t_j) = \sum_{k=1}^N \lambda_k p_k(r_i) a_k(t_j).$$

Herein, p_k with $1 \leq k \leq N$ is a set of orthonormal time-independent spatial component images; a_k with $1 \leq k \leq N$ is a set of orthonormal space-independent temporal component signals; and λ_k are time- and space-independent real-valued positive singular values sorted in order of decreasing magnitude: $\lambda_k \geq \lambda_{k+1} > 0$. For each spatial component image p_k of multiple spatial component images (p_k with $1 < n_f \leq k < N$), a sharpened spatial image q_k is generated (203) as follows. Positions $r_{m,k}$ of local maxima of the spatial component image p_k are determined. A sharpened spatial image q_k is generated. The sharpened spatial image is a linear combination, over the positions of the local maxima of the spatial component image, of a

reference peak function $g(r)$ which is maximal at $r = \mathbf{0}$ shifted to a position $r_{m,k}$ of a local maximum and weighted with the value $p_k(r_{m,k})$ of the spatial component image at the position of the local maximum:

$$q_k(r_i) = \sum_{m=1}^{N_k} g(r_i - r_{m,k}) p_k(r_{m,k}).$$

- 5 Herein, N_k is the number of local maxima of the spatial component image p_k . A processed image I is generated (204), being a bilinear combination of multiple sharpened spatial images q_k with weight coefficients $\beta_{k,l}$:

$$I(r_i) = \sum_{k,l=n_f}^N \beta_{k,l} q_k(r_i) q_l^*(r_i).$$

- 10 Herein, $n_f > 1$. A filtering step is hence performed by generating a processed image without the contribution of one or more of the terms corresponding to the largest singular values of the spatiotemporal singular value decomposition of the set of ultrasound images.

- 15 **Figure 3** shows a schematic representation of several features of an alternative embodiment of a method according to the present invention. A set of ultrasound signals $s(r_i, t_j)$ of biological tissue of a living subject comprising blood vessels is obtained (301a). The set comprises ultrasound signals at successive times t_j in a plurality of spatial points r_i . A high-pass filter is applied to the set of ultrasound signals (301b), yielding a filtered set of ultrasound signals. The filtered set of
20 ultrasound signals is decomposed via a spatiotemporal singular value decomposition as a sum of multiple terms (302):

$$s(r_i, t_j) = \sum_{k=1}^N \lambda_k p_k(r_i) a_k(t_j).$$

- 25 Herein, p_k with $1 \leq k \leq N$ is a set of orthonormal time-independent spatial component images; a_k with $1 \leq k \leq N$ is a set of orthonormal space-independent temporal component signals; and λ_k are time- and space-independent real-valued positive singular values sorted in order of decreasing magnitude: $\lambda_k \geq \lambda_{k+1} > 0$. For each spatial component image p_k ($1 \leq k < N$), a sharpened spatial image q_k is generated (303) as follows. Positions $r_{m,k}$ of local maxima of the spatial component image p_k are determined. A sharpened spatial image q_k is generated. The sharpened
30 spatial image is a linear combination, over the positions of the local maxima of the spatial component image, of a reference peak function $g(r)$ which is maximal at $r =$

$\mathbf{0}$ shifted to a position $\mathbf{r}_{m,k}$ of a local maximum and weighted with the value $p_k(\mathbf{r}_{m,k})$ of the spatial component image at the position of the local maximum:

$$q_k(\mathbf{r}_i) = \sum_{m=1}^{N_k} g(\mathbf{r}_i - \mathbf{r}_{m,k}) p_k(\mathbf{r}_{m,k}).$$

Herein, N_k is the number of local maxima of the spatial component image p_k . A
 5 processed image I is generated (304), being a bilinear combination of multiple
 sharpened spatial images q_k with weight coefficients $\beta_{k,l}$:

$$I(\mathbf{r}_i) = \sum_{k,l=1}^N \beta_{k,l} q_k(\mathbf{r}_i) q_l^*(\mathbf{r}_i).$$

A filtering step is hence performed by applying a high-pass filter prior to the
 spatiotemporal singular value decomposition.

10

Most preferably, the peak function is configured to increase the resolution of the
 vessels. Most preferably, the peak function is configured to obtain an image of the
 vessels at an image distance scale which is smaller than the ultrasound resolution
 distance scale. Most preferably, the peak function comprises a decay distance which
 15 is smaller than the ultrasound resolution distance.

The following non-limiting list provides several examples of functions to which the
 reference peak function $g(\mathbf{r})$ may be proportional:

- a Dirac function $\delta(\mathbf{r})$, which equals 1 in $\mathbf{r} = \mathbf{0}$ and equals 0 elsewhere;
- 20 • a Gaussian function $\exp(-\alpha|\mathbf{r}|^2)$ with α a real-valued positive scalar,
 preferably whereby α is larger than the inverse of the square of the
 ultrasound resolution distance;
- a power function $h(\mathbf{r} \neq \mathbf{0}) = \rho|\mathbf{r}|^{-\gamma}$ and $h(\mathbf{r} = \mathbf{0}) = \sigma$ with γ, ρ, σ real-valued
 positive scalars;
- 25 • an exponential function $\exp(-\varphi|\mathbf{r}|)$ with φ a real-valued positive scalar,
 preferably whereby φ is larger than the inverse of the ultrasound resolution
 distance.

In a preferred embodiment, the weight coefficients of the bilinear combination are
 30 calculated based on the mutually orthogonal temporal component signals.

In a first further preferred embodiment, the weight coefficients of the bilinear
 combination are diagonal in the decomposition index and comprise a magnitude
 proportional to the square of the 2-norm of the corresponding temporal component

signal. In case decomposition coefficients have been obtained, the magnitude of the weight coefficients of the bilinear combination is then proportional to the square of the corresponding decomposition coefficients. This first preferred embodiment corresponds to a blood volume image or power Doppler image obtained based on the sharpened spatial images.

In a second further preferred embodiment, the weight coefficients are proportional to a moment of a product of Fourier transforms of the corresponding temporal component signals. Preferably, the order of the moment equals one. This second preferred embodiment corresponds to an axial blood velocity image or color Doppler image obtained based on the sharpened spatial images.

With non-limiting reference to the exemplary mathematical formulae above, in the first further preferred embodiment the weight coefficients $\beta_{k,l}$ of the bilinear combination are diagonal in the decomposition index k,l and comprise a magnitude proportional to the square of the 2-norm of the corresponding temporal component signal $\lambda_k a_k$:

$$\beta_{k,l} = \sum_{j=1}^{N_t} \lambda_k a_k(t_j) \lambda_l a_l^*(t_j) = \delta_{k,l} \lambda_k^2.$$

With non-limiting reference to the exemplary mathematical formulae above, in the second further preferred embodiment the weight coefficients $\beta_{k,l}$ of the bilinear combination are proportional to a moment of order z of a product of Fourier transforms $\lambda_k A_k(\omega)$, $\lambda_l A_l(\omega)$ of the corresponding temporal component signals $\lambda_k a_k(t)$, $\lambda_l a_l(t)$:

$$\beta_{k,l} \propto \lambda_k \lambda_l \sum_{\omega=\omega_{min}}^{\omega_{max}} A_k(\omega) A_l^*(\omega) \omega^z.$$

Herein, $A_k(\omega)$ is a Fourier transform of the normalized temporal component signal $a_k(t)$, and ω_{min} and ω_{max} are bounds for the interval for the frequency ω . For example: $t_j = (j-1)\Delta t$ (with $1 \leq j \leq N_t$); $\omega_x = (x-1)\Delta\omega$ (with $1 \leq x \leq N_t$);

$$\Delta\omega = \frac{2\pi}{N_t \Delta t};$$

$$A_k(\omega_x) = \frac{1}{\sqrt{N_t}} \sum_{j=1}^{N_t} a_k(t_j) e^{-i \frac{2\pi}{N_t} (x-1)(j-1)};$$

and

$$\beta_{k,l} = \lambda_k \lambda_l (\Delta\omega)^z \sum_{x=1}^{N_t} A_k(\omega_x) A_l^*(\omega_x) (x-1)^z.$$

One of ordinary skill in the art will appreciate that the case $z = 0$ corresponds to the first further preferred embodiment above. Preferably, $z = 1$.

- 5 In a preferred embodiment, the apparatus comprises a portable or implantable ultrasound device. The device comprises the emitter and the receiver. The device further either comprises the computer system, or is configured for data communication with the computer system. Preferably, the device is a portable head-mountable ultrasound device, more preferably a portable head-mountable
- 10 ultrasound helmet. The apparatus may be configured for repetitive generation of a processed image for studying blood flow evolution. The apparatus may be used for functional brain imaging. The apparatus may further comprise one or more physiological sensors, in addition to the ultrasonic receiver, in order to correlate blood flow evolution with physiological data obtained via the physiological sensors.
- 15 The one or more physiological sensors may comprise one or more physiological sensors from the list comprising a blood oxygen level sensor such as an optical oximeter, a electrophysiological sensor such as an electrocardiograph sensor or electroencephalograph sensor, a respiration sensor, and a temperature sensor such as an infrared temperature sensor. Most preferably, the apparatus comprises an
- 20 electrophysiological sensor. Preferably, the electrophysiological sensor is configured for electroencephalography.

In a preferred embodiment, the method is performed repetitively for generating multiple processed images for studying blood flow evolution. The method may be

25 used for functional brain imaging. The method may comprise the step of comparing and/or correlating blood flow evolution with electrophysiological recordings. Preferably, the electrophysiological recordings are electroencephalographical recordings.

- 30 Any aspect of the present invention may be used for studying blood flow evolution via repetitive generation of a processed image, such as for determining functional responses in a brain. Functional brain imaging may be used to indirectly study brain activation by hemodynamic changes in response to a certain function or stimulus.

Any aspect of the present invention may be used for imaging blood vasculature in a brain, an eye, a heart, a kidney, a liver, a lung, a muscle, a thyroid, or a tumor.

Any aspect of the present invention may be used for computer-implemented
5 anomaly detection, such as via heuristic rules or via classification based on a machine learning algorithm trained with pre-classified data.

Reference is made to E. Mace et al., *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control* 60(3), 492-506 (2013), doi: 10.1109/tuffc.2013.2592 for an
10 exemplary disclosure of prior art ultrasound signal acquisition, which may also be used in conjunction with the present invention. The present invention relates in particular to the processing of a set of ultrasound signals, i.e. once a set of ultrasound signals has been obtained. For details of ultrasound signal acquisition used in conjunction with **Figures 4 and 5** below, reference is made to this prior art
15 document.

Figure 4 shows a set of exemplary images to illustrate several steps of an embodiment of a method according to the present invention. An original set of images (40a, 40b, 40c, ..., 40d) is obtained by emission and reception of ultrasound
20 waves. Each image of the set corresponds to a time sample t_j . Preferably, at least 100 images, such as 1000 images, have been obtained. Preferably, each image is oversampled at a multiple, preferably at least 4 times, such as 8 times, of the required resolution. The images of the original set appear similar, because most of the signal arises from static tissue. The blood signal is comparatively much weaker
25 (about -40 dB). After a high-pass filter or a spatiotemporal filter, the blood signal is extracted yielding the filtered set of images (41a, 41b, 41c, ..., 41d). The filtered set of images appears to contain a higher degree of dissimilarity due to the random positions of the red blood cells which scatter the ultrasound waves. After the filtering step and the spatiotemporal singular value decomposition (not necessarily in this
30 order as the filtering step may comprise discarding large singular values), a set of orthonormal time-independent spatial component images (42a, 42b, 42c, 42d) is obtained. In each spatial component image, the local maxima are detected, and a sharpened spatial image is obtained comprising just the local maxima (43a, 43b, 43c, 43d). In this case, the reference peak function is a Dirac function. A bilinear
35 combination of the sharpened spatial images is generated (44), with weight coefficients diagonal in the decomposition index and equal to the square of the corresponding singular values.

Figures 5a and 5b shows two exemplary ultrasound Doppler images. Five times 200 cross-sectional ultrasound images of the rat brain in coronal orientation have been obtained. **Figure 5a** shows a typical image of the brain vasculature after computation using a prior art power Doppler method. **Figure 5b** presents results on the same dataset of ultrasound signals, obtained with the algorithm disclosed in conjunction with **Figures 2 and 4**. The present invention allows for identification of individual small vessels that cannot be discerned according to the prior art method.

CLAIMS

1. Method for blood vessel image extraction from ultrasound signals, comprising the steps of:

- 5 – obtaining a set of ultrasound signals $s(\mathbf{r}_i, t_j)$ of biological tissue of a living subject comprising blood vessels, the set comprising ultrasound signals at successive times t_j in a plurality of spatial points $\mathbf{r}_i$;
- decomposing the set of ultrasound signals as a sum of multiple terms

$$s(\mathbf{r}_i, t_j) = \sum_{k=1}^N \lambda_k p_k(\mathbf{r}_i) a_k(t_j)$$

10 wherein each term consists of a time-independent spatial component image factor p_k and a space-independent temporal component signal factor $\lambda_k a_k$, wherein the spatial component images p_k are mutually orthonormal, and wherein the temporal component signals $\lambda_k a_k$ are mutually orthogonal;

- determining a sharpened spatial image q_k for each spatial component image p_k of multiple spatial component images;
- 15 – generating a processed image I being a bilinear combination of multiple sharpened spatial images q_k with weight coefficients $\beta_{k,l}$:

$$I(\mathbf{r}_i) = \sum_{k,l=n_f \geq 1}^N \beta_{k,l} q_k(\mathbf{r}_i) q_l^*(\mathbf{r}_i).$$

20 2. Method according to preceding claim 1, wherein determining a sharpened spatial image q_k for a spatial component image p_k comprises the steps of:

- determining positions $\mathbf{r}_{m,k}$ of local maxima of the spatial component image p_k ;
- generating the sharpened spatial image q_k being a linear combination of peak functions, wherein each peak function of the linear combination is
- 25 maximal at the position $\mathbf{r}_{m,k}$ of one of the local maxima of the spatial component image p_k .

3. Method according to preceding claim 2, wherein the linear combination of peak functions is a linear combination, over the positions of the local maxima of the spatial component image p_k , of a reference peak function $g(\mathbf{r})$ which is maximal at $\mathbf{r} = \mathbf{0}$ shifted to a position $\mathbf{r}_{m,k}$ of a local maximum and weighted with the value $p_k(\mathbf{r}_{m,k})$ of the spatial component image at the position of the local maximum:

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$$q_k(\mathbf{r}_i) = \sum_{m=1}^{N_k} g(\mathbf{r}_i - \mathbf{r}_{m,k}) p_k(\mathbf{r}_{m,k})$$

with N_k the number of local maxima of the spatial component image p_k .

4. Method according to preceding claim 3, wherein the reference peak function $g(\mathbf{r})$ is proportional to a Dirac function $\delta(\mathbf{r})$, which is nonzero in $\mathbf{r} = \mathbf{0}$ and zero elsewhere.
5. Method according to preceding claim 3, wherein the reference peak function $g(\mathbf{r})$ is proportional to a Gaussian function $\exp(-\alpha|\mathbf{r}|^2)$.
6. Method according to any one of the preceding claims, wherein the weight coefficients $\beta_{k,l}$ of the bilinear combination are diagonal in the decomposition index k,l and comprise a magnitude proportional to the square of the 2-norm of the corresponding temporal component signal $\lambda_k a_k$.
7. Method according to any one of preceding claims 1 to 5, wherein the weight coefficients $\beta_{k,l}$ are proportional to a moment of order z of a product of Fourier transforms $\lambda_k A_k(\omega)$, $\lambda_l A_l(\omega)$ of the corresponding temporal component signals $\lambda_k a_k(t)$, $\lambda_l a_l(t)$:

$$\beta_{k,l} \propto \lambda_k \lambda_l \sum_{\omega=\omega_{min}}^{\omega_{max}} A_k(\omega) A_l^*(\omega) \omega^z.$$

8. Method according to preceding claim 7, wherein the order of the moment $z = 1$.
9. Method according to any one of the preceding claims, wherein each temporal component signal $\lambda_k a_k$ consists of a real-valued positive decomposition coefficient factor λ_k and a normalized temporal component signal factor a_k , wherein the normalized temporal component signals a_k are mutually orthonormal, wherein the decomposition coefficients are arranged in decreasing magnitude $\lambda_k \geq \lambda_{k+1}$ with increasing decomposition index k , and wherein one or more of the terms corresponding to the largest decomposition coefficients do not contribute to the processed image: $n_f > 1$.

10. Method according to any one of the preceding claims, wherein said plurality of spatial points is a multidimensional grid of spatial points, preferably a two-dimensional or three-dimensional grid of spatial points, preferably wherein the grid is a rectangular grid.

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11. Method for ultrasound imaging, comprising a method according to any one of the preceding claims, wherein the step of obtaining the set of ultrasound signals $s(r_i, t_j)$ comprises the steps of:

- emitting ultrasound waves to said biological tissue of a living subject comprising blood vessels, preferably the emitted ultrasound waves plane or diverging ultrasound waves;
- receiving ultrasound waves at least in part from the biological tissue;
- obtaining said set of ultrasound signals $s(r_i, t_j)$ based on the received ultrasound waves.

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12. Computer system for blood vessel image extraction from ultrasound signals, the computing system comprising one or more processors, the computing system configured for performing the method according to any one of the preceding claims 1 to 10.

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13. Computer program product for blood vessel image extraction from ultrasound signals, the computer program product comprising instructions which, when the computer program product is executed by a computer, cause the computer to carry out the method according to any one of the preceding claims 1 to 10.

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14. Apparatus for ultrasound imaging of vasculature, comprising an ultrasonic wave emitter, an ultrasonic wave receiver, and a computer system according to preceding claim 12, wherein the apparatus is configured for performing the method according to preceding claim 11, preferably wherein the apparatus is configured for emitting plane or diverging ultrasound waves via the ultrasonic wave emitter.

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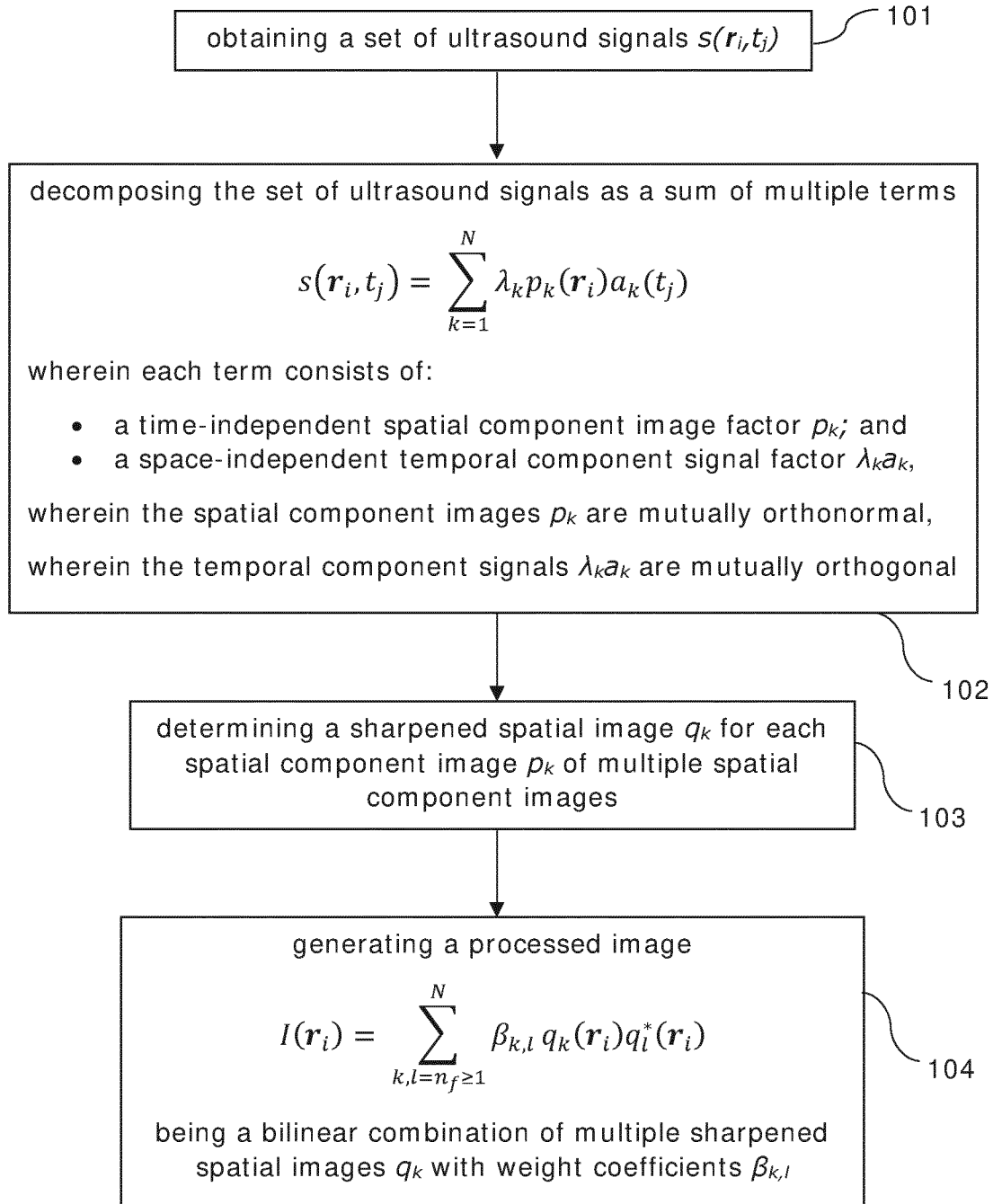
15. Apparatus according to preceding claim 14, comprising a portable or implantable ultrasound device comprising the emitter and the receiver, preferably the device being a portable head-mountable ultrasound device, more preferably the device being a portable head-mountable ultrasound helmet, the device either comprising said computer system or configured for data communication with the

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computer system, preferably the apparatus comprising an electrophysiological sensor, preferably the electrophysiological sensor configured for electroencephalography.

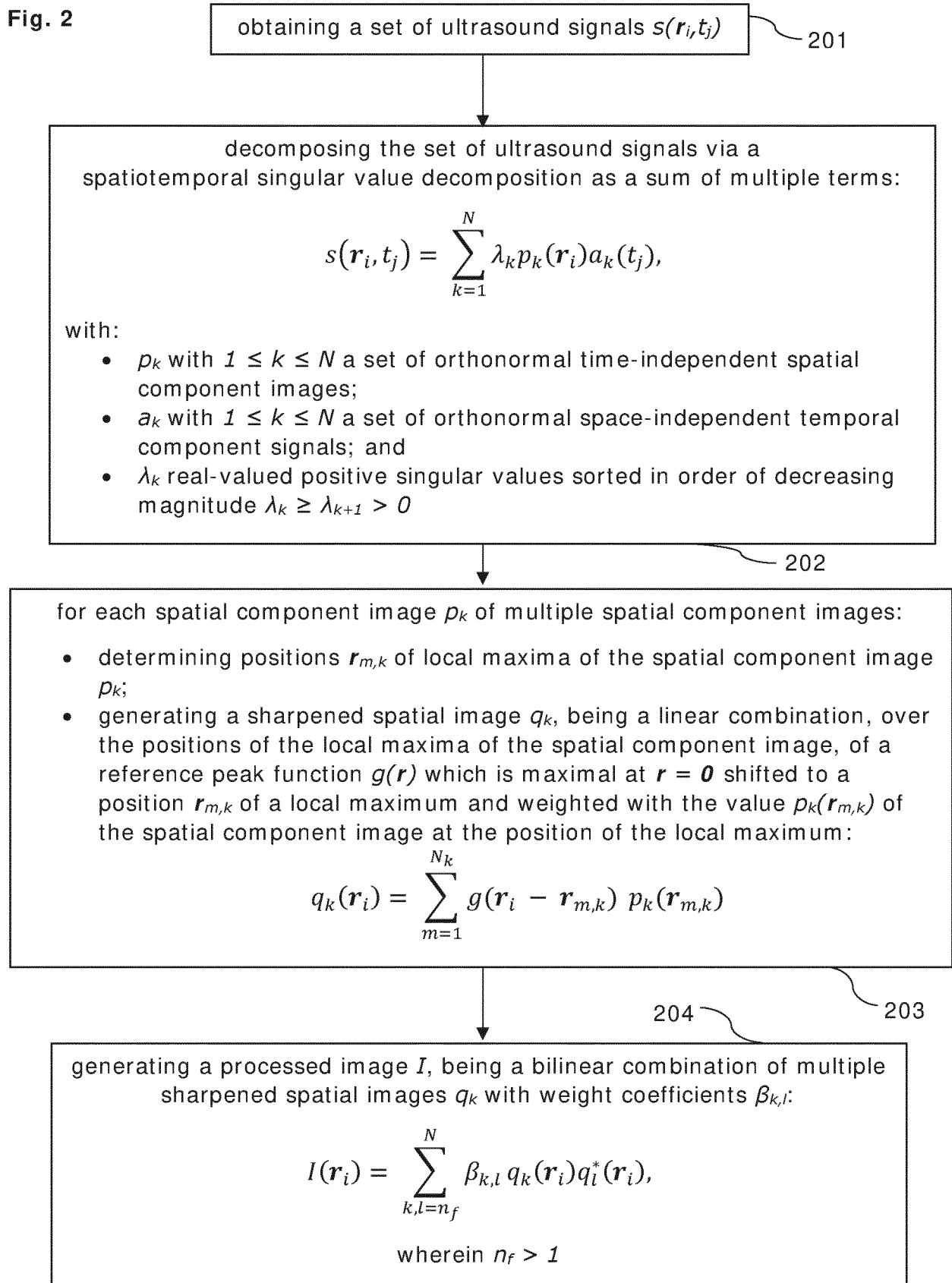
Figures

Fig. 1



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Fig. 2



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Fig. 3

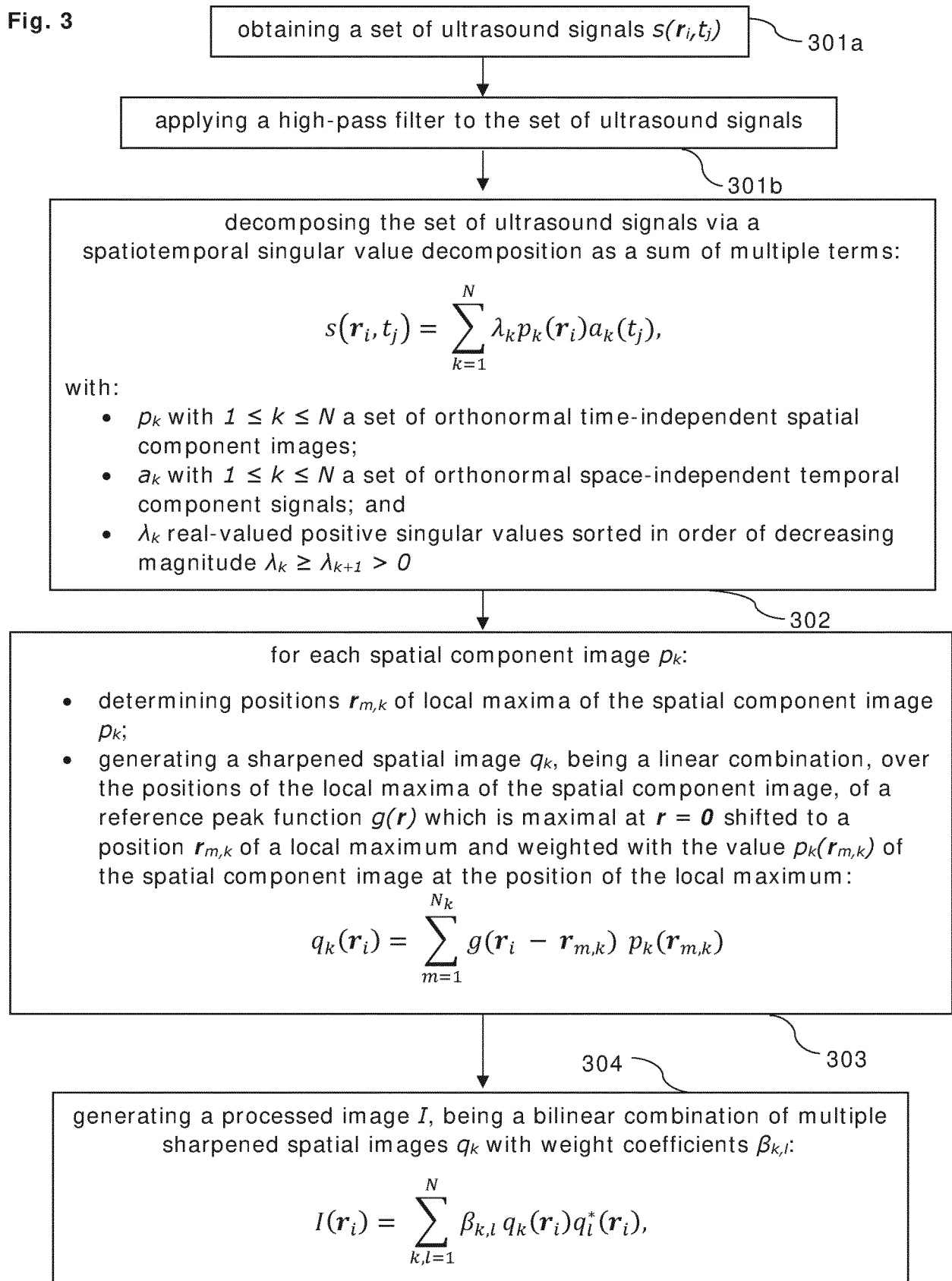


Fig. 4

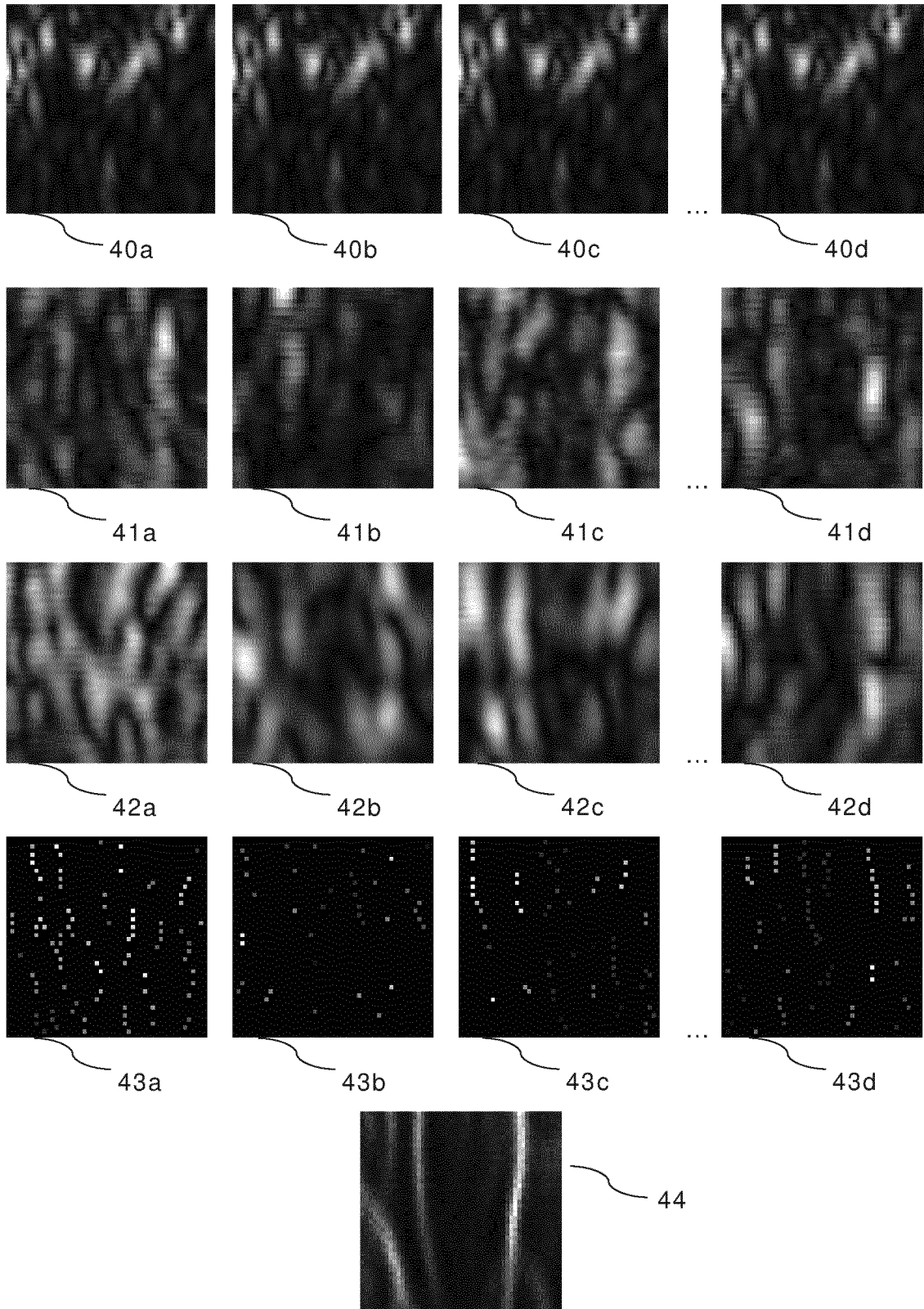
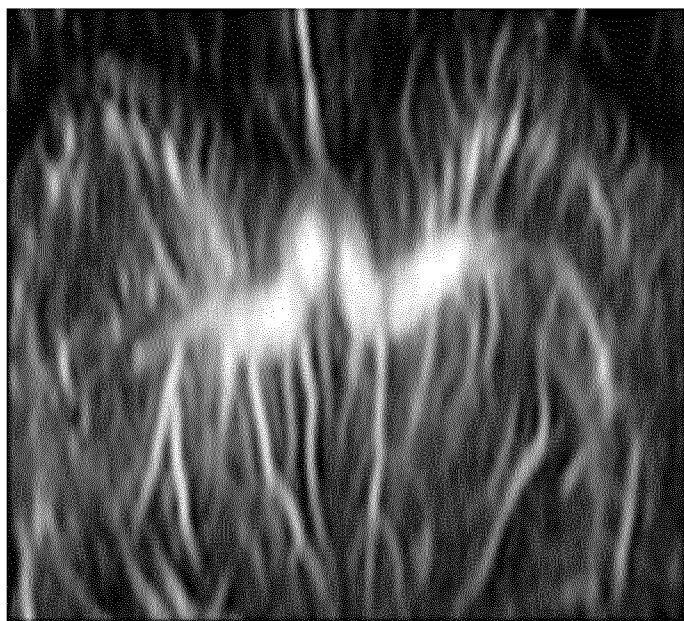


Fig. 5a



Fig. 5b



INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2020/053898

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61B8/08 G01S15/89 G06T7/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B G01S G06T

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DEMENE CHARLIE ET AL: "Spatiotemporal Clutter Filtering of Ultrafast Ultrasound Data Highly Increases Doppler and Ultrasound Sensitivity", IEEE TRANSACTIONS ON MEDICAL IMAGING, IEEE SERVICE CENTER, PISCATAWAY, NJ, US, vol. 34, no. 11, 1 November 2015 (2015-11-01), pages 2271-2285, XP011588384, ISSN: 0278-0062, DOI: 10.1109/TMI.2015.2428634 [retrieved on 2015-10-28] cited in the application the whole document ----- -/-	1-15



Further documents are listed in the continuation of Box C.



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Date of the actual completion of the international search

16 March 2020

Date of mailing of the international search report

26/03/2020

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2020/053898

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SONG PENGFEI ET AL: "Ultrasound Small Vessel Imaging With Block-Wise Adaptive Local Clutter Filtering", IEEE TRANSACTIONS ON MEDICAL IMAGING, IEEE SERVICE CENTER, PISCATAWAY, NJ, US, vol. 36, no. 1, 1 January 2017 (2017-01-01), pages 251-262, XP011638275, ISSN: 0278-0062, DOI: 10.1109/TMI.2016.2605819 [retrieved on 2016-12-30] page 2271 - page 2278 page 2283 - page 2285 -----	1-15
A	US 2018/220997 A1 (SONG PENGFEI [US] ET AL) 9 August 2018 (2018-08-09) the whole document -----	1-15
A	BAYAT MAHDI ET AL: "Multi-rate higher order singular value decomposition for enhanced non-contrast ultrasound Doppler imaging of slow flow", 2018 IEEE 15TH INTERNATIONAL SYMPOSIUM ON BIOMEDICAL IMAGING (ISBI 2018), IEEE, 4 April 2018 (2018-04-04), pages 1178-1181, XP033348406, DOI: 10.1109/ISBI.2018.8363781 the whole document -----	1-15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2020/053898

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		US 2018220997 A1	09-08-2018
		WO 2018144805 A1	09-08-2018
