(54) Title: APPARATUS AND METHOD FOR PERFORMING PHOTOACOUSTIC TOMOGRAPHY

(57) Abstract: A method and apparatus are provided for performing photoacoustic tomography with respect to a sample that receives a pulse of excitation electromagnetic radiation and generates an acoustic field in response to said pulse. One embodiment provides an apparatus comprising an acoustically sensitive surface, wherein the acoustic field generated in response to said pulse is incident upon said acoustically sensitive surface to form a signal. The apparatus further comprises a source for directing an interrogation beam of electromagnetic radiation onto said acoustically sensitive surface so as to be modulated by the signal; means for applying a sensitivity pattern to the interrogation beam; and a read-out system for receiving the interrogation beam from the acoustically sensitive surface and for determining a value representing a spatial integral of the signal across the acoustically sensitive surface, wherein said spatial integral is weighted by the applied sensitivity pattern. The apparatus is configured to apply a sequence of sensitivity patterns to the interrogation beam and to determine a respective sequence of values for said weighted spatial integral for generating a photoacoustic image.
APPARATUS AND METHOD FOR PERFORMING PHOTOACOUSTIC TOMOGRAPHY

Field of the Invention

The present application relates to a method and apparatus for performing photoacoustic tomography, and in particular to providing such a method and apparatus having a reduced image acquisition time.

Background of the Invention

Photoacoustic tomography (PAT) is an emerging biomedical imaging modality with both pre-clinical and clinical applications, and can provide complementary information to established imaging techniques [2, 30]. In the majority of such established imaging techniques, either the useful contrast mechanism is of low resolution, or high resolution images that are of limited contrast. PAT is an example of “imaging from coupled physics”, a new class of techniques, in which contrast induced by one physical mechanism is read by a different physical mechanism, so that both high resolution and high contrast can be obtained at the same time.

In PAT, ultrasound waves are excited by irradiating tissue with modulated electromagnetic radiation from a laser, usually pulsed on a nanosecond timescale. The wavelength of the electromagnetic radiation is typically in the optical or near infrared band. In general, the longer wavelengths allow greater penetration of the radiation into the tissue, of the order of several centimetres. The radiation is then absorbed within the tissue and leads to a slight rise in temperature, typically about 0.1K, which is sufficiently small to avoid any physical damage or physiological change to the tissue. The rise in temperature causes the emission of ultrasound (acoustic) waves, which are broadband (approximately tens of MHz) and relatively low amplitude (less than 10 kPa). These ultrasound waves propagate to the surface of the tissue, where they can be detected by a suitable mechanism, for example, a single mechanically scanned ultrasound receiver or an array of receivers. A PAT image is then (re)constructed from the received ultrasound signals based on the determined travel time and an assumed speed of sound propagation through the tissue.

From a theoretical perspective, the forward problem in PAT describes the acoustic propagation of the initial pressure:

\[ p_0(r) \rightarrow y(m,t) = \Lambda(c,\mu)p_0(r), \]  

Equation (1)

where \( r \) is a position vector, \( p_0(r) \) is the pressure at location \( r \) at time \( t=0 \), \( \Lambda \) is the Green’s operator of the wave equation, which in general depends on the sound speed \( c(r) \) and
attenuation $\mu(r)$, both of which are potentially dependent on location $r$, and $y(m,t) = \rho(r,t)|_{r=m}$ is the time series data recorded at a detector. The inverse problem is to recover the initial pressure $\rho_0$ from the time series data, thereby effectively reconstructing an image which reflects the distribution of absorption of the excitation radiation.

Many approaches are available for performing this image reconstruction, including analytical methods based on the Spherical Mean Radon Transform (SMRT), which require the assumption of uniform sound speed, and time reversal methods, which are able to accommodate tissue-realistic acoustic attenuation and heterogeneous sound speed. Following reconstruction, the photoacoustic image can be used as an input to a second inversion step known as Quantitative Photoacoustic Tomography (QPAT), which outputs spatial maps of concentrations of chromophores corresponding to physiological components.

An important difference between PAT and conventional ultrasound (US) is that in the latter, the image contrast is determined by differences in acoustic impedance – which are frequently not that great between different tissue types. In contrast, in PAT the differences in optical absorption between different tissue types can be much greater, thereby providing very good image contrast. As an example, haemoglobin exhibits strong preferential optical absorption, hence PAT can provide very detailed images of microvasculature (which are difficult to obtain using conventional ultrasound, due to weak echogenicity). In addition, the exciting laser radiation may be tuned to a specific wavelength, for example, to correspond to an absorption peak of a particular substance. By acquiring images at multiple different wavelengths, PAT is able to map the distribution of various biochemicals in great detail.

The growth of interest in PAT in the last decade has been rapid, and it has been used to visualise, inter alia, small animal anatomy, pathology and physiology, murine cerebral vasculature [31], capillary beds in vivo [33], implanted subcutaneous tumours [16], [33], murine embryos [15], and in vivo atherosclerosis [1]. As noted above, PAT can be used spectroscopically for molecular and genomic imaging, differentiating endogenous chromophores or contrast agents according to their absorption spectra, and also for functional imaging, such as measuring changes in blood oxygenation and flow. High frame rate (>10Hz) photoacoustic imaging systems have been demonstrated using curved and linear piezoelectric arrays, but they are usually limited to 2D (planar) imaging, rather than 3D (volume) imaging. Further information about PAT can be found in [34].

At UCL, an ultrasound detection array has been developed based on a Fabry-Perot interferometer for use in PAT – see “Backward-mode multi-wavelength photoacoustic scanner using a planar Fabry-Perot polymer film ultrasound sensor for high-resolution three-dimensional imaging of biological tissues” by Zhang et al, Applied Optics, 47, 4, 561-577, 1 February 2008. This Fabry-Perot interferometer detector can record acoustic pressure with very small element sizes while retaining high sensitivity, thereby generating high quality, high
resolution three-dimensional photoacoustic images (something that is difficult, if not impossible, with conventional arrays of piezo-electric sensors for detecting ultrasound).

However, a significant bottleneck in state of the art high resolution PAT systems is the data acquisition time. For example, in the Fabry-Perot interferometer detector mentioned above, the acquisition time for a static image is at least several minutes. At present therefore, such high resolution PAT systems are too slow for effective real-time or dynamic imaging of physiological processes.

Summary of the Invention

The invention is defined in the appended claims.

The approach described herein provides compressed measurement acquisition in PAT, whereby encoding with patterns incoherent to the pressure at all time steps is used to form a compressed measurement. A considerably lower number of compressed measurements than regular measurements is needed for exact reconstruction under a hypothesis of compressibility of the data/PAT image in an a priori chosen basis. Such an approach helps to support a PAT system which allows fast dynamic imaging of time-varying physiological processes, for example, functional studies of blood flow and oxygen saturation changes, investigations of trauma response and microcirculation, and pharmacokinetics, such as drug uptake and perfusion.

Brief Description of the Drawings

Various embodiments of the invention will now be described in detail by way of example only with reference to the following drawings:

Figure 1 is a schematic diagram of a known apparatus for PAT;
Figure 2 is a schematic diagram of an apparatus for performing PAT in accordance with an embodiment of the invention;
Figure 3 shows two examples of mask patterns for use with the apparatus of Figure 2 (for simplicity, the number of pixels per mask pattern is reduced in Figure 3).
Figure 4 is a simplified flowchart of a method for obtaining a PAT image from data acquired using the apparatus of Figure 2 in accordance with an embodiment of the invention.
Figure 5 is an example of image reconstruction from compressed measurements.
Figures 6 and 7 provide schematic illustrations of the dynamic reconstruction of an image acquired by compressed sensing in accordance with one embodiment of the invention.
Figure 8 is an example of variation in sensitivity for a given wavelength across the surface of an FP interferometer detector such as included in the apparatus of Figures 1 and 2.

**Detailed Description**

In PAT a short (ns) pulse of near-infrared or visible light is sent into tissue, whereupon absorption of photons generates a small local increase in pressure which propagates to the surface as a broadband ultrasound pulse. The amplitude of this signal is recorded at the tissue surface, such as by an array of sensors, and an image reconstruction algorithm is employed to estimate the original 3D pressure increase due to optical absorption – this is the photoacoustic image.

Figure 1 is a schematic diagram of a PAT system including a Fabry-Perot interferometer detector 20 as described in the above-referenced paper by Zhang et al.. A sample of tissue 12 being imaged is subjected to an excitation beam 11 comprising a pulse of electromagnetic radiation (optical, near infrared, or microwave) from excitation laser 10, which may be a multiple wavelength laser or a single wavelength laser. The output from excitation laser 10 typically falls within the wavelength range 400-2000 nm (although microwaves might also be used). The electromagnetic radiation 11 is absorbed within the tissue 12, resulting in the generation of ultrasound waves 14 which propagate from the absorption locations to the surface of tissue sample 12.

The tissue sample 12 rests on (is in acoustic contact with) a sensor head 100 comprising a substrate 115 on which is formed a Fabry-Perot (FP) interferometer detector 20. As the ultrasound waves 14 reach the surface of the tissue sample 12, they cause corresponding changes in the optical thickness of the Fabry-Perot interferometer detector 20 at the locations where the ultrasound waves exit the tissue sample, thereby allowing the Fabry-Perot interferometer detector 20 to detect these ultrasound waves. Conceptually, we can regard the acoustic wave pressure as forming an image which is detected using the sensor head 100. More particularly, the sensor head 100 produces, for each monitored location of the FP detector 20, a time series representing the arrival of ultrasound waves arising from the excitation pulse at that particular location.

The Fabry-Perot interferometer detector 20 and its operation are described in detail in the above-referenced paper by Zhang et al. – we present here a high-level and somewhat simplified description (for full details, please see the cited paper). The Fabry-Perot interferometer detector 20 utilises an interrogation laser 121 which generates an interrogation optical beam 131, for example at a wavelength of 1550 nm, which is used in conjunction with sensor head 100 for ‘reading’ the image formed on the FP detector. The
optical beam 131 is directed to a beam-splitter 122, from where it passes through a quarter wavelength ($\lambda/4$) plate 124 onto a scanning mirror 126 (described in more detail below). The scanning mirror 126 directs the interrogation beam through an objective (convex) lens 128 to form an incident interrogation beam 132 which is focussed onto the underside of the sensor head 100. The sensor head 100 functions, in effect, as a thin film Fabry-Perot cavity, whereby a first portion of the incident beam is reflected from a first (lower) surface of the FP detector 20, while a second portion of the incident beam passes further into the FP detector 20 and is reflected from a second (upper and opposing) surface of the FP detector 20. The first and second reflected portions re-combine, and interfere with one another, to form a reflected interrogation beam 135 (more accurately, the interference occurs between multiple reflections within the sensor head). The reflected beam 135 returns along the path of the incident beam 132, travelling back from the sensor head 100 through the objective lens 128, the scanning mirror 126 and the quarter wavelength ($\lambda/4$) plate 124 to the beam splitter 122. The two passages through plate 124 rotate the polarisation state by 90 degrees, relative to the original beam 131, hence the reflected interrogation beam 135 is directed by the beam splitter 122, as indicated by arrow 136, onto photodetector (photodiode) 150, which is connected to a digitizing oscilloscope (DSO) 155 (and from there to a computer, not shown in Figure 1).

The scanning mirror 126 is used to build up an image of the sensor head 100 by sequentially directing the incident interrogation beam 132 to different locations on the sensor head 100, as indicated by arrow 140. In particular, by suitable displacements and/or rotations of the scanning mirror 126, the incident interrogation beam 132 steps across the two-dimensional underside of the sensor 100 in order to ‘read’ an ultrasound image produced by acoustic waves 14 on the FP interferometer detector 20.

In the absence of an excitation beam 11, the resulting image acquired by scanning the interrogation beam 132 across the sensor head generally includes sets of fringes, which arise from slow variations in the thickness across the sensor head, and hence in the amount of interference between the first and second reflected portions (as noted above, more accurately, the interference occurs between multiple reflections within the sensor head). In the presence of the excitation beam 11, the ultrasound waves 14 induce an acoustic modulation of the optical thickness of the sensor head 100, which produces a small additional phase shift between the first and second reflected portions. When the interrogation wavelength is set to the peak derivative of the interferometer transfer function, which represents the reflected intensity versus wavelength, this additional phase shift is linearly converted, in accordance with the transfer function of the interferometer 20, into a corresponding modulation of the reflected optical power, which can be picked up by the
photodiode 150 and DSO 155. Accordingly, for each scanning position, a time series representing the acoustic ultrasound signal at that location is obtained.

The acquired data set is therefore three-dimensional (two spatial, one temporal) and provides $y(m,t)$ from Equation (1) above, where $m$ represents an $x,y$ location in the plane corresponding to the FP interferometer detector 20. As part of the image reconstruction process, the value of the initial pressure distribution is first recovered, $p_0(r)$, (by inverting Equation (1)), to form a three-dimensional PAT image. This recovered image may be used as the initial step of a second reconstruction problem, Quantitative Photoacoustic Tomography (QPAT), whose aim is to quantitatively represent the three-dimensional (spatial) distribution of chromophores within tissue 12. The final output of this image reconstruction is therefore a single three-dimensional image at time $t=0$, i.e. when $p = p_0$. In other words, timing information in the acquired data $y(m,t)$ does not reflect changes in the sample with time (it is not a dynamic image), but rather the travel time of the acoustic signal since $t=0$, which in turn reflects the distance that the signal has travelled (and also the speed of sound along that path). If we consider a simplified model in which the acoustic signal just propagates in a $z$ direction, perpendicular to the FP interferometer 20 and sensor head 100, which have a substantially two-dimensional ($x,y$) geometry, then the spatial information in $y(m,t)$ would represent a projection of the three-dimensional sample onto the planar geometry of the sensor head 100, and the timing information would then encode travel time data for the acoustic signal to provide information directly in respect of the third spatial dimension ($z$). However, since the acoustic signal travels spherically outwards (rather than just along the $z$-axis), this in effect mixes the coordinates, so that the signal $y(m,t)$ originates from a surface in the sample 12 defined by the radial distance $ct$ where $t$ is the travel time from $m$ and $c$ is the propagation speed.

In the implementation of Zhang et al., the acquisition time is approximately 1 second per scan step. This acquisition time is dominated by the time taken to rearm the DSO 155 between acquisitions, and also the download time from the DSO 155 to the computer (although it is suggested that the latter could be reduced by providing the DSO with an on-board memory to buffer results across different scan locations). Having an acquisition time of 1 second per scanning step results in an overall acquisition time of 1 hour for a 60x60 pixel image – which is a rather small image size. The overall acquisition time for a 600x600 pixel image would be 100 hours or four days, so this is a lengthy procedure and is clearly much too slow to investigate in vivo dynamic processes.

In general terms, the ultimate limit to the data acquisition rate in PAT is set by the propagation time for the (ultra)sound to cross the specimen. As an example, if a sample has a depth of 15mm, the propagation time is approximately 10 $\mu$s, giving a maximum data acquisition rate of 100 kHz. One practical limitation is the rate at which the laser 10 can be
pulsed. As an example of this limitation, currently available laser systems that produce a single wavelength pulse of sufficient power for PAT typically have a maximum pulse repetition rate of 1000 Hz. If the system of Figure 1 could operate at this rate, then a 600x600 image could be produced in approximately 6 minutes (360 seconds). However, this is still significantly too slow to image dynamic physiological changes, for which a frame rate of at least 1 Hz (i.e. a frame acquisition time of < 1 second) is generally required.

Figure 2 is a schematic diagram of a PAT system in accordance with an embodiment of the invention which is a modification of the system shown in Figure 1. In general, components in the embodiment of Figure 2 which are (at least substantially) the same as the corresponding components in the embodiment of Figure 1 are denoted by matching reference numerals. Please refer to the description of Figure 1 above for further information about these corresponding components.

In Figure 2 (as in Figure 1), a sample of tissue 12 being imaged is subjected to an excitation beam 11 comprising a pulse of electromagnetic radiation (optical or near infrared or microwave) from excitation laser 10, which may be a multiple wavelength laser or a single wavelength laser. The electromagnetic radiation 11 is absorbed within the tissue 12, resulting in the generation of ultrasound waves 14 which propagate from the absorption locations to the surface of tissue sample 12.

The tissue sample 12 rests on (is in acoustic contact with) a sensor head 200 comprising a substrate 115 on which is formed a Fabry-Perot interferometer detector 20. As the ultrasound waves 14 reach the surface of the tissue sample 12, they cause corresponding changes in the optical thickness of the Fabry-Perot interferometer detector 20 at the locations where the ultrasound waves exit the tissue sample, thereby allowing the Fabry-Perot interferometer detector 20 to detect these changes. Although the sensor head 200 in Figure 2 is the same as or similar to the sensor head 100 in Figure 1, there are significant differences between Figure 1 and Figure 2 in terms of how the apparatus reads (interrogates) the sensor head 200.

The apparatus of Figure 2 includes an interrogation laser 121 which generates an interrogation optical beam 131 for use in conjunction with the sensor head 100 for reading the image produced by the FP interferometer detector 20. In contrast to the system of Figure 1, the interrogation optical beam is formed to have a relatively broad cross-section in the plane perpendicular to the direction of propagation of the beam. The broader cross-section is formed using convex lens 161 (or any other suitable set of optical components).

The interrogation optical beam 131 is then reflected by a micromirror array 170, which is described in more detail below. Note that the interrogation optical beam 131 may have a cross-section to match the whole active surface of micromirror array 170. The optical beam 131 is reflected by micromirror array 170 to a beam-splitter 122, from where it passes
through a quarter wavelength ($\lambda/4$) plate 124 as for the configuration of Figure 1. A pair of objective lenses 128A and 128B is located between the quarter wavelength plate 124 and the sensor head 200. This pair of objective lenses 128A and 128B (or any other suitable set of optical components) increases the cross-section of the incident interrogation optical beam 132 from the size as determined by the micromirror array 170 to a size corresponding to the desired (physical) size of the image to be obtained. Accordingly, the same micromirror array 170 can be used with different sizes of sample 12 and/or different sizes of sensor head 100.

As described above, the sensor head 200 functions as a thin film Fabry-Perot cavity, whereby a first portion of the incident beam 132 is reflected from the first (lower) surface of the FP interferometer detector 20, while a second portion of the incident beam 132 passes into the FP interferometer detector 20 and is reflected from the second (upper) surface of the FP interferometer detector 20. The first and second (and subsequent) reflected portions then re-combine and interfere with one another, to form a reflected interrogation beam 135. The reflected beam 135 returns along the path of the incident beam 132, travelling back from the sensor head 20 through the objective lenses 128B, 128A and the quarter wavelength ($\lambda/4$) plate 124 to the beam splitter 122. The two passages through plate 124 rotate the polarisation state by 90 degrees relative to the original beam 131, hence the reflected interrogation beam 135 is directed by the beam splitter 122 to a convex lens 162 which focusses the (relatively broad) reflected interrogation beam, as indicated by arrow 136, onto photodetector (photodiode) 150. This photodiode is connected to a digitizing oscilloscope (DSO) 155 and from there to a computer (not shown), as per the configuration of Figure 1.

As for the system of Figure 1, in the presence of the excitation beam 11, the ultrasound waves 14 induce an acoustic modulation of the optical thickness of the FP interferometer detector 20, which produces a small additional phase shift between the first and subsequent reflected portions. This additional phase shift is linearly converted, in accordance with the transfer function of the interferometer 20, into a corresponding modulation of the reflected optical power, which can be picked up by the photodiode 150 and DSO 155. However, in contrast to the system of Figure 1, which builds up an overall image of the photoacoustic waves by sequentially scanning the incident interrogation beam 132 across different locations on the sensor head 200, the system of Figure 2 effectively interrogates the complete image provided by the sensor head 200.

Figure 3 illustrates two example mask patterns, which for ease of representation are 6x6 patterns comprising a set of binary pixel values. The actual mask patterns used in conjunction with the embodiment of Figure 2 have many more pixels (as described below) to give better image resolution, and comprise random patterns drawn from, for example, Bernoulli/Gaussian distribution [7]. In addition, the mask patterns shown in Figure 3 are binary masks, with pixel values of 0 or 1, as are the mask patterns used in conjunction with
the embodiment of Figure 2, but greyscale masks having intermediate values can also be used.

The output, as detected by photodiode 150 of Figure 2, represents a spatial integral of the image signal produced by the sensor head 20 weighted according to the given mask pattern applied to the micromirror array 170. In other words, in the case of a binary mask, the output effectively adds together the values of the regions of the image signal produced by the sensor head 200 in which the mask is reflective (a value of one) and ignores the other regions of the image signal for which the mask is non-reflective (a value of zero). Therefore each mask pattern results in a corresponding output detected at the photodiode. By utilizing a sequence of different mask patterns, and obtaining a corresponding sequence of output values from the photodiode 150, a data set is acquired, from which the overall image produced by the Fabry-Perot interferometer detector 20 can be reconstructed, as well as the initial pressure distribution \(p_0\).

More particularly, the output data signal from the system of Figure 2 is a set of time series \(s_i(t)\), where \(i = 1 \ldots N\) is an index to identify the mask pattern \(M_i\), used for that time series. We can relate \(s_i(t)\) to the signal \(y(m,t)\) received at the FP interferometer detector 20 (and which is measured directly with the apparatus of Figure 1), as follows:

\[
s_i(t) = \sum_{x,y} y(m(x,y), t) \times M_i(x,y), \quad \text{Equation (2)}
\]

where \(x,y\) represent (i) coordinates on the acoustic sensing plane of defined by the FP interferometer detector 20, and (ii) corresponding coordinates in the plane of a mask pattern such as shown in Figure 3 (as projected onto the sensing plane), and the summation is across the whole area of the sensing plane (upon which the interrogation beam 132 is incident), and wherein \(M_i(x,y) = 0 \text{ or } 1\) for a binary mask such as shown in Figure 3, or more generally \(0 \leq M_i(x,y) \leq 1\) for a greyscale mask.

The system of Figure 2 therefore operates in accordance with a technique referred to as compressed sensing. Thus in most image acquisition systems, a spatial distribution of data signals is acquired, for example, using a rectangular array of pixels, where the image is defined by the luminosity (or some other parameter) detected in each pixel in the array. In a typical image, there are significant correlations (redundancy) between the luminosity values of different pixels, which can be exploited by compression algorithms such as JPEG2000. In compressed sensing however, rather than first acquiring a complete image which is later subjected to compression processing, the amount of data acquired in the first place is restricted. It has been found that the number of compressed measurements when performing compressed sensing is generally (significantly) smaller than the number of measurements made in a more conventional system (which does not use compressed sensing/measurements). One example of such an approach is the Rice 'single-pixel'
camera [12] which records an image through a small number of random sums of pixels rather than as individual spatial points. More precisely, a signal $y$ in an $N$ dimensional space can be adequately represented in an \textit{a priori} chosen basis $\Psi$ with only a small number of non-zero coefficients, $y = \Psi z$. In compressed sensing, the information of an image is directly measured by sensing a signal $y$ with a properly constructed matrix $A$ with number of rows $M < N$ to give a much shorter data vector $s = Ay$. The original signal is then recovered through a solution of the optimisation problem:

$$\text{OP}_q: \min_z J_q(z), \text{ such that } \|s-A\Psi z\|_2 \leq \delta,$$

where $J_q(z) = \|z\|_q$ (length of vector $z$ in the $q$-norm) and $\delta$ allows for measurement noise. Whilst $q=0$ is the ‘ideal’ measure of sparsity (the number of non-zero elements), the corresponding optimisation problem is classically computationally intractable (NP-hard), and so is commonly replaced by a better behaved approximation such as the convex relaxation ($q=1$). Compressed sensing theory then specifies conditions under which the sparsest solution can be robustly recovered by solving (\text{OP}_1). A variety of specific algorithms are available for solving this problem, including Orthogonal Matching Pursuit [27], message passing [11], iteratively reweighted norm [8], and Bregman-type [32] methods. In medical imaging, compressed sensing has been effective, for example, in dynamic MRI [21] and dynamic CT [25]. Compressed sensing for PAT has also been reported, but for quite a different approach from that described herein. In particular, some such existing approaches have used compressed sensing in conjunction with patterned \textit{excitation} light [24], rather than patterned \textit{interrogation} light as described herein. Other existing approaches have recognised PAT images can be represented sparsely in some basis, and then used this understanding to regularise image reconstructions from spatially undersampled data [13, 23]. However, the approach described herein is not directly motivated by such spatial undersampling, but rather provides a way of acquiring compressed measurements (in contrast, compressed sensing may be used to refer to L1 reconstruction, i.e. to the reconstruction of sparse signals, even without taking compressed measurements, as per [13 and 23]).

Returning to Figure 2, in one implementation, the excitation laser 10 is a diode-pumped Q-switched Nd:YAG laser (Ekspla NL 220S, 1 kHz pulse repetition rate) (see www.ekspla.com). The trigger from the excitation laser is used to control switching of the mask patterns, i.e. from one mask pattern to the next mask pattern, by the micromirror array 170. The interrogation laser 121 is a 1490-1640nm high power fibre-coupled tunable laser (Yenista Tunics T100S-CL-WB) (see www.yenista.com) which is used to produce interrogation beam 131 which illuminates the micromirror array 170. A beam shaper (not shown in Figure 2), such as available from Topag Lasertechnik (see www.topag.de),
converts the Gaussian beam profile from the interrogation laser 121 into a square top hat profile to provide uniform illumination of the micromirror array 170.

In one implementation, the micromirror array 170 comprises a Digital Micromirror Device 0.7" XGA 2xLVDS DMD from Texas Instruments (see www.ti.com and TI DN 2509929, Rev A, September 2008). This device comprises 1024x768 pixels and is therefore used to apply mask patterns accordingly (as opposed to the simple 6x6 mask patterns shown in Figure 3). The frame rate is up to 22 kHz for binary patterns. The pitch of the micromirrors is 13.7μm, corresponding to a device size of 14x10.5mm. However, as shown in Figure 2, the interrogation beam 132 reflected from the micromirror array 170 can be scaled by a suitable optical system, such as lens combination 128A, 128B, to provide a desired image scale size on the Fabry-Perot interferometer detector 20. For example, a 2:1 scaling for the interrogation beam 132 gives a pixel scale of 27.4μm and an overall image size of 28x21mm on sensor device 200. If a larger or denser array is required, two or more micromirror arrays could be used in combination with one another, placed side by side. The micromirror array 170 is controlled by a development platform, Discovery 4100 (see http://www.ti.com/tool/dlpd4x00kit), which presents a USB 2.0 interface to a control computer (not shown in Figure 2) to allow the micromirror array 170 to be programmed with the desired patterns.

In one implementation, the photodetector 150 comprises a balanced photodetector built from matched photodiodes. This allows higher intensities for the interrogation light beam 131, which in turn helps to improve the signal-to-noise ratio of the resulting PAT images. The DSO 155, for example as available from Tektronix (see www.tek.com), samples the output from the photodetector 150 at 250MHz, thereby allowing the full bandwidth of the photoacoustic signal to be detected. The DSO is provided with on-board memory to avoid the need for mid-measurement data downloads (which would interrupt, and hence slow down, the data acquisition process). Note that since each mask pattern only produces a single output sample (representing a compressed measurement), these on-board memory requirements are relatively modest.

Figure 4 is a simplified flowchart of a method for obtaining a PAT image from data acquired using the apparatus of Figure 2 in accordance with an embodiment of the invention. The data set output from the apparatus of Figure 2, as per operation 410 in Figure 4, comprises a set of time series of intensity values from the photodetector 150, each time series corresponding to its respective (known) mask pattern which was applied to the interrogation light beam 131 for obtaining that particular intensity time series (as per Equation 2). We can represent this output as \( s(t) = A y(m,t) \), where \( A \) is a \( n_{\text{pattern}} \times n_{\text{pix}} \) matrix, where \( n_{\text{pattern}} \) represents the total number of patterns in the sequence and \( n_{\text{pix}} \) represents the total number of pixels per mask pattern. Each row of \( A \) represents a binary or grayscale
pattern of length $n_{px}$ (Figure 3 depicts binary masks, but grayscale masks could also be utilised). Note that $s(t)$ incorporates the full set of $s_i(t)$ as defined in Equation 2 above, i.e. it includes the output for each mask $M_i$.

In operation 420, the data set is sliced by time. In other words, we collect the data values from each time series (i.e. for each mask pattern) at a specific time. At each such time step $t$, the data $y(m,t)$ is recoverable from $s(t)$ in accordance with the optimisation of Equation (3) as defined above, as per operation 430. In effect, this recovers the $y(m,t)$ time sample by time sample using the same approach as the Rice camera [12] (because each time step can be considered as representing a single image across the sensor plane which is sampled by the various mask patterns). Given the nature of wave propagation, the optimal sparsifying transformation $\psi^\mu$ may be based, for example, on 2D curvelets [5], contourlets [10] or shearlets [20].

Once $y(m,t)$ has been recovered in operation 430, then this can be transformed in operation 440 into a photoacoustic image representing the initial pressure distribution $\rho_0$, as per the inverse problem from Equation (1), and this initial pressure distribution can then be transformed in operation 450 to a three-dimensional QPAT image showing the distribution of material responsible for the absorption of the excitation radiation. Note that operations 440 and 450 are also employed with respect to the known apparatus of Figure 1, as per the paper by Zhang et al. For example, operation 440 can be performed using a reconstruction algorithm that inverts the spherical mean radon transform (SMRT), while operation 450 can be performed using quantitative photoacoustic tomography (QPAT), as discussed above.

An alternative approach to the operations 410 through to 440 is to recover the initial pressure distribution $\rho_0$ directly from the measured data from the apparatus of Figure 2, namely $s(t)$, as illustrated schematically by arrow B in Figure 4. This again can be approached through Equation (3), with $z$ now a (3D) spatially compressed representation of the initial pressure ($\rho_0$) in a basis given by the (3-D) sparsifying transform $\psi^\rho$ and the operator modified to $A\Lambda$ $\psi^\rho$. The reduction in the number of measurements (i.e. the number of mask patterns to be used), and hence the overall image acquisition time, depends on the incoherence of the resulting sampling matrix $A\Lambda$ $\psi^\rho$, which is influenced by the choice of patterns or subsampling scheme and the sparsifying transform $\psi^\rho$. 3-D extensions of curvelets and shearlets provide a suitable framework for this approach. In situations where the initial pressure distribution $\rho_0$ has a sparse representation in the (3D) curvelet frame, the result in [6] implies that both the emitted acoustic wave and the time reversed acoustic field at each time step also have a sparse representation in this basis. Accordingly, a numerical operator can be used for the forward operator $\Lambda$, taking advantage of sparse wave propagation in place of existing Fourier based pseudo-spectral methods.
Figure 5 is an example of reconstructing a compressed sensing image (for simulated data) using the method of Figure 4. The simulated data relates to a target volume of 128x128x64 voxels that contains a helical pattern, where the 128x128 voxels can be regarded as corresponding to the X-Y axes, and 64 as the Z (depth) axis. The images are displayed as maximum intensity projections onto the X-Y plane.

Figure 5A depicts the original image distribution in the target volume. Figure 5B shows the result of performing a full image reconstruction, which might be adopted, for example, by acquiring the image data using the apparatus shown in Figure 1. Figure 5C shows the result of performing an image reconstruction from data obtained using compressed sensing in accordance with an embodiment of the invention, for example, by acquiring the image data using the apparatus shown in Figure 2. The acquired data for Figure 5C is compressed to about 20% of the acquired data for Figure 5B. It can be seen that this leads to increased noise in the resulting reconstructed image, but the main features, including smaller objects, remain visible. In addition, since the noise in Figure 5 is generally random over time, it can be suppressed, for example, by averaging across a number of images. It is likely that the use of L1 reconstruction would lead to a better resulting reconstructed image. (L1 reconstruction is the solution of equation (3) above with \( q=1 \) in \( J_q(z) \)).

The approach described above can be extended to exploit spatial-temporal coherence and to provide the facility for 4D (dynamic 3D) PAT, particularly in view of the use of compressed sensing as described above to reduce image acquisition time. Such dynamic PAT represents a powerful tool for investigating physiological processes such as heart rate beating and breathing (for example). In one embodiment, this 4D PAT processes the data in its spatial Fourier representation as a function of time (k-t-space), in which the dynamic images of natural objects exhibit significant correlations – hence it is feasible to acquire only a reduced amount of data, while still obtaining improved temporal resolution. A training set is obtained from which signal correlations can be learned, thereby allowing missing data to be recovered using all available information in a consistent and integral manner [28]. In one embodiment, dictionary learning, which characterises typical images via local patches, can be combined with k-space trajectory schemes to give further improvements [14].

We can describe the dynamic PAT data in terms of two scales of time \( y(m, t, \tau) \), where \( \tau \) represents a scale of seconds representing image motion and kinetics. By taking a Fourier Transform in the detector plane coordinates \( m \rightarrow k_0 \), and in the acoustic time variable \( t \rightarrow \omega \), the k-space representation of the data is obtained, [17], and dynamic imaging is then the acquisition of data in the k-\( \tau \) space. The k-t SENSE scheme [28], or other appropriate k-space trajectory scheme, can be adapted for PAT data, having regard to the fact that only two dimensions of k-space are under the control of the experimenter (i.e.
corresponding to the two-dimensions of the pattern applied by the micromirror array 170), and also that the micromirror array 170 only supports non-negative patterns. In one embodiment, the data is processed using Markov time series methods, such as Kalman filters, which treat the spatial components of the image as coefficients of random variables which evolve over time, and therefore can be used continuously on real-time data to track changes in specific spatial-temporal components [22].

In one embodiment, an explicit kinetic model is used to derive images of rate constants for the uptake of molecules of interest, such as for kinematic studies of molecular and genomic imaging. Typically these models involve identifying two or more tissue compartments and defining a set of ordinary differential equations linking them. These models can be utilised at both the voxel level and a segmented organ level. One possibility is to apply (non-linear) estimation of the rate constant parameters to reconstructed 4D PAT images. Alternatively, it may be possible to use a direct method, in which the rate constants are recovered directly from the data without an explicit image reconstruction step (this has been shown to be more robust in other kinetic modalities [29]).

Figures 6 and 7 illustrate in schematic form the above approach to reconstructing dynamic (4D) PAT images in accordance with one embodiment of the invention. We assume that the total number of patterns for the sensing is PT and the time for sensing one pattern (i.e. for producing a single output value) is t1. The overall set of PT patterns is divided into N subsets, where each subset contains PT/N patterns, and hence represents a duration of t2=PT*t1/N. The duration t2 in effect represents the frame rate of the dynamic PAT data, in that data within a time period t2 is accumulated to form a single image. Therefore t2 can be regarded as corresponding to r as discussed above, which typically represents a scale of seconds for image motion and kinetics.

As shown in Figure 6, for the first timestep (at t=t2), compressed data is collected from a subset of 1/N of the total number (PT) of patterns. This data is then combined with the data in k-space from the previous N timesteps (t=-(N-1)*t2 through to t=0) (to the extent such earlier data is available) in order to generate (reconstruct) the PAT image at time t=t2. For the second timestep (at t=2*t2), compressed data is then collected from the next subset of 1/N of the total number (PT) of patterns. This data is combined with the data from the previous N timesteps (t=-(N-2)*t2 through to t=t2) in order to reconstruct the PAT image at time t=2*t2. This process then repeats continuously, whereby the PAT image at time t=n*t2 is generated by combining the received compressed data for the timestep n*t2 with the data from the previous N timesteps.

Figure 7 illustrates certain aspects of the processing of Figure 6 in more detail in accordance with one embodiment of the invention. In particular, Figure 7 depicts each subset of the patterns as a (different) set of locations in k-t space. Thus at timestep 1 (t=t2),
the acquired data corresponds to the pattern of locations in k-t space as illustrated (where each location represents a single pattern, and hence a single measurement). For Figure 7, it is assumed that no data is available prior to this first timestep, hence the image reconstruction for timestep 1 is based just on this received data (without combining with any earlier data).

At timestep 2 in Figure 7 \((t=2*t2)\), compressed data is received corresponding to the patterns representing a different subset of locations in k-t space. This data for timestep 2 is combined with the data from timestep 1 to provide a more complete (accurate) reconstruction of the PAT image. This process then repeats until at timestep \(N\), all the patterns, and hence all the locations in k-t space have been sampled. Consequently, for the next timestep, \(t=(N+1)*t\), we start again with the same subset of sampling patterns as used for timestep 1 \((t=t2)\), and the received data for this subset overwrites the data from timestep 1 at the corresponding locations in k-t space. This process repeats, such that for each new timestep, the data from \(N\) timesteps earlier is replaced in k-t space with the newly acquired data for that timestep. The output of this processing is therefore dynamic PAT data, in which the image data is updated (modified) every timestep - i.e. at a frequency of \(1/t2\).

In one embodiment, wherein the sensitivity patterns are taken from a set of linear combinations of Fourier patterns, such that over a dynamic sequence a full sampling of Fourier space (k-space) in coordinates of the acoustically sensitive surface is achieved or can be reconstructed. For example, the Fourier sampling may be reconstructed or the standard k-t-tau algorithms adapted to work with the compressed Fourier sampling.

Returning to Figure 2, the FP interferometer detector 20 may exhibit sensitivity variations across its surface due to variations in optical thickness. This means that for any given wavelength of the interrogation beam 132, only a limited portion of the detector is sensitive – for example, Figure 8 illustrates a typical pattern in which there are a few contours of uniform sensitivity, as illustrated by the bright regions in the Figure, while the dark regions between these contours are acoustically insensitive.

In order to interrogate the FP interferometer detector 20, a pre-tuning procedure is performed before acquiring the photoacoustic image. In one embodiment, this procedure involves illuminating the FP interferometer detector 20 pixel by pixel. At each pixel, the reflected light intensity is recorded as a function of wavelength, termed the wavelength interferometer transfer function (ITF). The wavelength corresponding to the maximum value of the derivative of the ITF is called the optimum bias wavelength and is the wavelength that yields the highest sensitivity for that pixel. Thus the pre-tuning procedure yields a pixel-by-pixel map of the optimum bias wavelengths.

Once the optimum bias wavelength map has been acquired, the interrogation laser 10 is set to a specific bias wavelength and then, using the micromirror array 170, only those
regions that provide high sensitivity at that wavelength are illuminated - in the context of compressed sensing, the sensitivity pattern would only be applied to this region – and the photoacoustic signal is recorded. The wavelength of the interrogation laser 10 is then adjusted to make a different part of the sensor sensitive and the photoacoustic signal is recorded again. This process is repeated for a range of wavelengths until the entire sensing region of the FP interferometer detector has been mapped – in essence varying the wavelength allows the sensitivity contours to be shifted (scanned) across the FP interferometer detector 20. The advantage of selectively illuminating the sensitive regions in this way is that it avoids detection of the high un-modulated dc optical intensity reflected from the insensitive regions which would otherwise saturate the detector and increase noise significantly.

Note that the sensitivity pattern of the FP interferometer detector 20 is generally dependent on the properties of the FP interferometer detector 20. The pre-tuning procedure may be avoided (in the sense that the optimum bias wavelength is the same across the detector) if the FP interferometer detector 20 has a very consistent thickness across all the acoustically sensitive surface, or if the finesse of the FP interferometer detector 20 is reduced (although the latter approach will lead to a photoacoustic image likewise having lower sensitivity or discrimination between different signal levels).

Although the present invention has been described in the context of particular embodiments, the skilled person will be aware of a range of other possible implementations. For example, rather than using a Fabry-Perot interferometer to perform the sensing of the acoustic field, as shown in Figure 2, various other techniques and apparatus for encoding the acoustic field on to an optical signal exist. These include the use of a multilayer optical hydrophone, such as described in [35: Klann and Koch], and the use of a glass prism covered with a water layer, such as described in [36: Köstli et al.], both of which involve the acoustic field modulating the reflected power of an incident laser beam. The device of Klann and Koch is conceptually similar to an FP interferometer detector but uses hard dielectric materials. As a result, the spatial variations in sensitivity are less than with an FP sensor, since the hard dielectric materials can be deposited with greater precision, but the device is generally not as sensitive as an FP sensor. The device of Köstli is a non-interferometric intensity-based sensor which avoids the use of an expensive narrow linewidth tunable interrogation laser. This is generally able to provide uniform spatial sensitivity, but is typically less sensitive than an FP sensor. Yakovlev [37] provides another non-interferometric intensity-based sensor in which a plasmonic metamaterial or metal is deposited onto a transparent substrate. This has the same advantages as the device of Köstli, but has higher sensitivity. A slightly different approach, in which the acoustic field impinging on a sensing surface (pellicle) is used to modulate the phase of a reflected laser
beam, is disclosed in [38: Hamilton et al.]. This is a form of interferometric sensor, but unlike an FP sensor it provides an absolute measurement of displacement.

Devices which are less prone to sensitivity variations across the acoustically sensitive surface are beneficial, providing they can provide sufficient sensitivity, since they potentially support faster image acquisition by allowing the whole surface (or at least more of the surface) of the device to be operational simultaneously.

The compressed sensing pattern (as shown in Figure 3) is then applied to the incident laser beam (or potentially to the reflected laser beam) so as to produce a spatial weighting of the acoustic signal across the sensor surface in accordance with the applied sensing pattern. This spatially weighted version of the acoustic signal is then passed to a detector to obtain a single output value. A sequence of such (compressed) measurements can then be reconstructed into a single image, and then potentially into a sequence of images, for dynamic PAT, as described above.

A number of different devices are available to apply a sequence of sensitivity patterns to the interrogation beam instead of the micromirror array 170 – such as a spatial light modulator, a rotating wheel or polygon bearing a set of masks or mirrors across the different faces, a sliding linear strip of such masks or mirrors (or any other suitable configuration), or other types of device based on adaptive optics. A particular benefit of using a device such as a micromirror array or a spatial light modulator to apply the sensitivity patterns (rather than a rotating wheel, for example, which is provided with a fixed set and order of mask patterns) is that such a device can apply a configurable sequence of sensitivity patterns. In other words, for a rotating wheel (for example), the sequence of sensitivity patterns is, in effect, hard-coded into the sequence of mask or mirrors arranged around the wheel itself. However, for a configurable device, such as a spatial light modulator or micromirror array, the sequence of sensitivity patterns is readily programmable (i.e. customisable or configurable), which means for example that the system can be readily altered to accommodate different sets or ordering of sensitivity patterns.

In some embodiments, a single sensitivity pattern is applied for each pulse of excitation radiation. In other embodiments, a sequence of two or more sensitivity patterns is applied for each pulse of excitation radiation. In other words, a given pulse of excitation radiation results in a time series representing the acoustic signal generated by the acoustically-sensitive surface in response to the acoustic wave caused by the excitation pulse, and this time series may correspond to more than one sensitivity pattern. The sensitivity pattern which is applied to the interrogation beam may then be changed (one or more times) partway through the acoustic signal (and corresponding time series) arising from the given pulse of excitation radiation. This approach could be implemented, for
example, using an array of high speed optical modulators (to provide the rapid control and switching between the different applied sensitivity patterns).

Another potential modification of the apparatus of Figure 2 is that the micromirror array 170 (or other mechanism for applying a sensing pattern) is located downstream of the sensor head 200 in the overall optical path. For example, in some embodiments, the micromirror array may be located, for example, between the beam splitter 122 and the objective lens 162, or between the objective lens 162 and the photodiode 150 (with an appropriate change in the remaining layout to accommodate this change in configuration).

Furthermore, in relation to the dynamic imaging approach shown in Figures 6 and 7, PT (the number of patterns) does not necessarily need to fill out the k-t space, whereby the number of timesteps to be combined into a single PAT image (frame) is less than N. In other words, the dynamic imaging is used in addition to the compressed sensing, so that the recovery of each frame of the dynamic image benefits from both compressed sensing and spatially-temporal correlation exploited through k-t space schemes.

Additional implementation examples can be found in [39], the teachings of which are incorporated herein by reference.

The above embodiments involving various data processing, such as image reconstruction, which may be performed by specialised hardware, by general purpose hardware running appropriate computer code, or by some combination of the two. For example, the general purpose hardware may comprise a personal computer, a computer workstation, etc. The computer code may comprise computer program instructions that are executed by one or more processors to perform the desired operations. The one or more processors may be located in or integrated into special purpose apparatus, such as a PAT acquisition system. The one or more processors may comprise digital signal processors, graphics processing units, central processing units, or any other suitable device. The computer program code is generally stored in a non-transitory medium such as an optical disk, flash memory (ROM), or hard drive, and then loaded into random access memory (RAM) prior to access by the one or more processors for execution.

In conclusion, the skilled person will be aware of various modifications that can be made to the above embodiments to reflect the particular circumstances of any given implementation. Moreover, the skilled person will be aware that features from different embodiments can be combined as appropriate in any given implementation. Accordingly, the scope of the present invention is defined by the appended claims and their equivalents.
References

Claims

1. Apparatus for performing photoacoustic tomography with respect to a sample that receives a pulse of excitation electromagnetic radiation and generates an acoustic field in response to said pulse, said apparatus comprising:
   an acoustically sensitive surface, wherein the acoustic field generated in response to said pulse is incident upon said acoustically sensitive surface to form a signal;
   a source for directing an interrogation beam of electromagnetic radiation onto said acoustically sensitive surface so as to be modulated by the signal;
   means for applying a sensitivity pattern to the interrogation beam; and
   a read-out system for receiving the interrogation beam from the acoustically sensitive surface and for determining a value representing a spatial integral of the signal across the acoustically sensitive surface, wherein said spatial integral is weighted by the applied sensitivity pattern;
   wherein the apparatus is configured to apply a sequence of sensitivity patterns to the interrogation beam and to determine a respective sequence of values for said weighted spatial integral for generating a photoacoustic image.

2. The apparatus of claim 1, wherein the interrogation beam comprises an optical, infrared or microwave laser.

3. The apparatus of claim 1 or 2, wherein the intensity, phase, polarisation or wavelength of the interrogation electromagnetic radiation is modulated by the incident acoustic field.

4. The apparatus of any preceding claim, wherein the acoustically sensitive surface is part of a multilayer optical device such as a hydrophone, a glass prism covered with a layer of water, a pellicle, or a plasmonic metamaterial or metal deposited onto a transparent substrate.

5. The apparatus of any of claims 1 to 3, wherein the acoustically sensitive surface is part of a thin film Fabry-Perot sensor head having a thickness which is subject to acoustically induced modulation in response to the incident acoustic field.

6. The apparatus of any of claims 1 to 3, wherein the acoustically sensitivity surface has a substantially uniform sensitivity across the surface.
7. The apparatus of any preceding claim, wherein the means for applying the sensitivity pattern is able to apply a programmable sequence of sensitivity patterns.

8. The apparatus of any of claims 1 to 6, wherein the means for applying the sensitivity pattern comprises a moving film or wheel with masks, a micromirror array, or a spatial light modulator.

9. The apparatus of claim 7 or 8, wherein the means for applying a sensitivity pattern to the interrogation beam comprises a micromirror array that reflects the interrogation laser beam in accordance with said sensitivity pattern.

10. The apparatus of any preceding claim, wherein the read-out system comprises a photodetector for receiving the interrogation beam from the acoustically sensitive surface.

11. The apparatus of any preceding claim, wherein for each applied sensitivity pattern, the read-out system generates a data set comprising a time series of the value for said spatial integral.

12. The apparatus of claim 11, wherein a single sensitivity pattern is applied during detection of the acoustic field resulting from one pulse of excitation radiation.

13. The apparatus of claim 11, wherein a sequence of multiple sensitivity patterns is applied during detection of the acoustic field resulting from one pulse of excitation radiation.

14. The apparatus of any of claims 11 to 13, wherein the apparatus is configured to: slice the time series for each applied sensitivity pattern in said sequence, thereby producing for each time slice, a set of data values, each data value corresponding to an applied sensitivity pattern; reconstruct, for a given time slice, across all the applied sensitivity patterns in said sequence, an image of the incident acoustic field for that time slice; and reconstruct, from the reconstructed images of said time slices, a three-dimensional initial pressure distribution.

15. The apparatus of any of claims 11 to 14, wherein the apparatus is configured to perform a direct reconstruction of a photoacoustic image from said data without reconstructing the incident acoustic field at all times.
16. The apparatus of any preceding claim, wherein the apparatus is configured to apply different sensitivity patterns at successive time samples, $\tau_i$, of a dynamic sequence.

17. The apparatus of claim 16, wherein reconstruction to generate a photoacoustic image is carried out time-step by time-step using a Markov time-series approach.

18. The apparatus of claim 16 or 17, wherein dictionary learning is used to reduce the number of required sensitivity patterns, with a commensurate increase in the dynamic imaging rate.

19. The apparatus of any of claims 16 to 18, wherein the sensitivity patterns are taken from a set of linear combinations of Fourier patterns, such that over a dynamic sequence a full sampling of Fourier space ($k$-space) in coordinates of the acoustically sensitive surface is achieved or can be reconstructed.

20. The apparatus of claim 19, wherein the apparatus is further configured to reconstruct, from measurements in $k$-$t$-$\tau$ space, a 4D image in $(x,y,z,\tau)$ space.

21. The apparatus of any of claims 11 to 18 wherein the sensitivity patterns are incoherent to a curvelet or shearlet basis.

22. The apparatus of any preceding claim, wherein the apparatus is configured to: perform a pre-tuning procedure before acquiring the photoacoustic image by recording the reflected light intensity as a function of wavelength across the acoustically-sensitive surface.

23. The apparatus of claim 22, wherein the pre-tuning procedure further comprises selecting, for different locations of the acoustically-sensitive surface, the wavelength corresponding to the maximum value of the derivative of the recorded reflected light intensity as a function of wavelength, wherein the selected wavelength represents the optimum bias wavelength, thereby generating a set of optimum bias wavelengths corresponding to said different locations of the acoustically-sensitive surface.

24. The apparatus of claim 23, wherein the apparatus is configured to repeat, for each optimum bias wavelength in said set of optimum bias wavelengths, the application of a sequence of sensitivity patterns to the interrogation beam for determining a respective
sequence of values for said weighted spatial integral, wherein for each optimum bias
wavelength, a window is applied to restrict the spatial integral to the one or more locations of
the acoustically-sensitive surface corresponding to that optimum bias wavelength.

25. The apparatus of claim 24, wherein the window is applied by said means for applying
a sensitivity pattern to the interrogation beam.

26. A method for performing photoacoustic tomography with respect to a sample that
receives a pulse of excitation electromagnetic radiation and generates an acoustic field in
response to said pulse, said method comprising:

forming a signal using an acoustically sensitive surface, wherein the signal
represents the acoustic field which is generated in response to said pulse, as incident upon
said acoustically sensitive surface;

directing an interrogation beam of electromagnetic radiation onto said acoustically
sensitive surface so as to be modulated by the signal;

applying a sensitivity pattern to the interrogation beam;

receiving at a read-out system the interrogation beam from the acoustically sensitive
surface and for determining a value representing a spatial integral of the signal across the
acoustically sensitive surface, wherein said spatial integral is weighted by the applied
sensitivity pattern;

applying a sequence of sensitivity patterns to the interrogation beam to determine a
respective sequence of values for said weighted spatial integral for generating a
photoacoustic image.

27. The method of claim 26, further comprising performing an image reconstruction
process on said sequence of values for generating said photoacoustic image.

28. An apparatus as substantially as described herein with reference to the
accompanying drawings.

29. A method as substantially as described herein with reference to the accompanying
drawings.
Figure 3

Compressed Sensing Data Set \((S(t))\) 410

Data Set Sliced by time 420

Derive Image Sequence by time \((y(m,t))\) 430

Reconstruct initial pressure distribution \((p_0)\) 440

Obtain 3-D PAT image 450

Figure 4
DYNAMIC PAT (one cycle)

Timestep 1
measure

compressed data from a sub-set (1/N) of patterns
combine
combined data from N previous timesteps (eg. in k-space)
reconstruct
PAT image at time 1

Timestep 2
measure

compressed data from a sub-set (1/N) of patterns
combine
combined data from N previous timesteps (eg. in k-space)
reconstruct
PAT image at time 2

Timestep N-1
measure

compressed data from a sub-set (1/N) of patterns
combine
combined data from N previous timesteps (eg. in k-space)
reconstruct
PAT image at time N-1

Timestep N
measure

compressed data from a sub-set (1/N) of patterns
combine
combined data from N previous timesteps (eg. in k-space)
reconstruct
PAT image at time N

repeat from the top

Figure 6
DYNAMIC PAT (k-t space sampling)

**Timestep 1**
data from subset of patterns

**Timestep 2**
data from subset of patterns
combined with existing data

**Timestep N**
data from subset of patterns
full data set collected after N time steps

**Timestep N+1**
recollect data from first set of patterns
full data set consisting of previous N timesteps

*Figure 7*
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

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**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)

| G01N | A61B |

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

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

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<th>Category</th>
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<td>US 6 075 603 A (O'MEARA THOMAS R [US] ET AL) 13 June 2000 (2000-06-13) column 1, lines 8-12; column 7, lines 6-29; column 8, lines 22-26</td>
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<td>X</td>
<td>US 7 262 861 B1 (PEPPER DAVID M [US] ET AL) 28 August 2007 (2007-08-28) abstract; figures 2,5 column 1, lines 7-12; column 7, line 20 - column 8, line 14; column 9, line 54 - column 11, line 40</td>
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**Date of the actual completion of the international search**

12 September 2014

**Date of mailing of the international search report**

19/09/2014

**Name and mailing address of the ISA/Authorized officer**

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Parijsk
Tel: (+31-70) 340-2040, Fax: (+31-70) 340-3016

Filipas, Alin

Form PCT/ISA/210 (second sheet) (April 2005)
Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.☐ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2.☒ Claims Nos.: 28, 29 because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3.☐ Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 5.4(a).

Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2.☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of additional fees.

3.☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4.☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.
Continuation of Box II.2

Claims Nos.: 28, 29

Claims 28 and 29 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not defined, as they only contain references to various parts of the description and the drawings and thus leave unclear which technical features are intended to be comprised in said claims - in this respect, see also Rule 6.2(a) PCT.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.
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