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DOI:
10.1117/12.2507223

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ABSTRACT

Photonics based imaging is a widely utilised technique for the study of biological functions within pre-clinical studies. It is a sensitive and non-invasive technique that is able to detect distributed (biologically informative) visible and near-infrared light sources providing information about biological function. Compressive Sensing (CS) is a method of signal processing that works on the basis that a signal or image can be compressed without important information being lost. This work describes the development of a CS based hyperspectral Bioluminescence imaging system that can be used to collect compressed fluence data from the external surface of an animal model, due to an internal source, providing lower acquisition times, higher spectral content and potentially better tomographic source localisation.

Keywords: Hyperspectral, Bioluminescence, Compressive Sensing, Spectrometer, Tomography

1. INTRODUCTION

Bioluminescence Imaging (BLI) is light based imaging technology which has been shown to be a sensitive and non-invasive pre-clinical methodology. The technology is based on the detection of visible and near-infrared light produced by, for example, luciferase-catalyzed reactions (bioluminescence), which allows for the non-invasive detection and 2D visualization of functional activity within intact living animals and is becoming widespread due to the prognostic insights it can provide into established model of disease. BLI has a number of advantages over fluorescence imaging, for example, in BLI there is no need for external excitation of the exogenous contrast as the signal is generated directly by the luciferase-catalysed reactions, and typically the signal is well localised (i.e. sparse)[1].

The basic idea of Compressive Sensing (CS) theory is that when the image of interest is very sparse or highly compressible in some basis (i.e., most basis coefficients are small or zero-valued, which is true for Bioluminescence due to the localisation of the sources), relatively few well-chosen observations are sufficient for the reconstruction of the image. These observations must obey certain properties: in particular, the observations should randomly sample the entirety of the image. The acquisition of a small number of such distributed measurements, followed by reconstruction (subject to a maximum sparsity constraint) is the essence of CS: the data that is acquired is a "compressed" representation of the image, and the full image data can be reconstructed exactly with high probability. This technique therefore finds the basis of a signal that is sparse or compressible, meaning that a signal of length **n** can be represented by $\boldsymbol{k \ll n}$ nonzero coefficients. A sparse signal can be represented with high accuracy by only keeping the values and locations of the largest coefficients of the signal.

In this work, the development of a CS based hyperspectral imaging system is presented. An experimental phantom study is carried out to demonstrate that an internal light source can be tomographically reconstructed using measured compressed hyperspectral data from the external surface with good accuracy.

2. THEORY

Compressive or Compressed Sensing is a signal processing technique that utilises the sparse nature of real-world signals in order for them to be compressed either in its original domain or in some transform domain. It works in a similar way

to standard image/signal compression algorithms such as JPEG-2000, where the data vector which represents the raw pixels of the image is transformed using the discrete wavelet transform (DWT). Once the image has been transformed, all of the small wavelet coefficients below a threshold are set to zero leaving behind a sequence that can be stored efficiently and when required can be inverse-transformed to provide an approximate representation of the original image or signal[2]. The basis or domain of a signal that is sparse or compressible is found when using this technique, meaning that a signal of length **n** can be represented by $\boldsymbol{k \ll n}$ nonzero coefficients, where **k** is the sparseness. It is therefore possible to represent a sparse signal with high accuracy by only using the values and locations of the largest coefficients of the signal.

By using this concept, it is possible to create a new framework for both acquiring signals and how sensors are designed. If a signal is sparse or compressible, it is possible to acquire a signal with less samples than is classically suggested within the Nyquist-Shannon sampling theorem, which states there needs to be a minimum number of measurements taken in order to perfectly capture an arbitrary signal[3]. In CS, rather than first sampling at a high rate and then compressing the collected data, it is possible to directly collect the compressed data. This enables a potentially massive reduction in the sampling and computational costs of measuring signals that are sparse[4].

A number of methods can be employed to recover the raw signal from the compressed data that is measured. The classical approach to solving this problem is to minimise the l_2 norm (energy) of signal **x** such that:

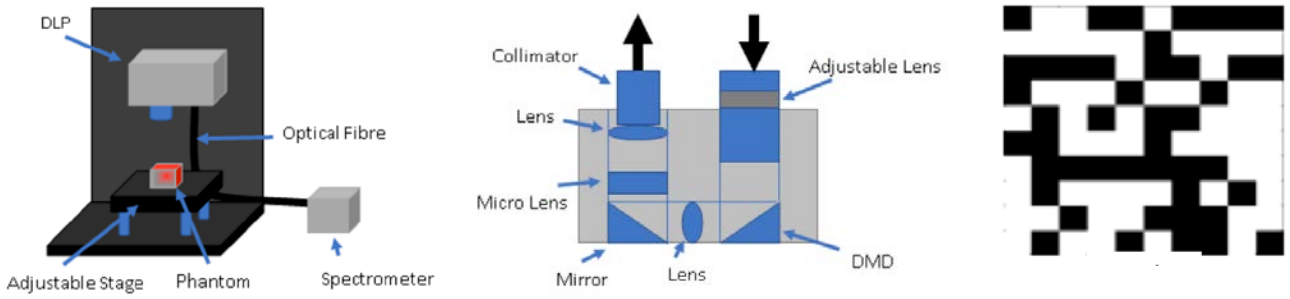
$$Ax = b \tag{1}$$

Where, **A** is a random **m**x**n** matrix made up of 1's and –1's and **b** is the measured data of length **m**. This method also referred to as least squares and has a simple closed form solution, however this method almost never finds a sparse solution and often returns a nonsparse solution with many nonzero values. The correct approach is to minimise the l_0 norm of the signal which finds the sum of the zeroth power of the components that make up the signal so will in-turn find the sparsest solution[5]. However, solving this is both numerically unstable and NP-complete, meaning that is it near impossible to find the correct solution without exhaustive enumeration of all of the nonzero values in the signal. A method that can be employed is to minimise the l_1 norm of signal, which assuming the signal is sparse, can recover the exact sparse solution. If it is assumed that instead of the signal being sparse, the gradient of the underlying signal or image is sparse, it is possible to recover the signal by minimising the total variation (TV) of the signal instead of the l_1-norm[6].

3. MATERIALS AND METHODS

3.1 Imaging System

Figure **1** presents a schematic of the imaging system that has been developed, showing the different components that allow making measurement from a sparse source distribution map. A Texas Instruments DLP Lightcrafter 4500 has been modified so that the digital micro-mirror device (DMD) within it can be used to direct random projections of the imaging scene into a spectrometer. The DLP is modified by removing the three LEDs that are part of the system and then attaching one end of an optical fibre in its place for detection. The DMD within the DLP is an array of 912 by 1140 micro mirrors that can be individually controlled to be in either an 'off' or 'on' position. This allows for random binary patterns to be created as shown in Figure 1(c). The spectrometer used in the system is an Ocean Optics Flame S-VIS-NIR, which has an optical detection range of 350nm to 1000nm with a spectral resolution of 0.4nm, which is suitable as the wavelengths detected for a typical BLI are in the red visible wavelengths of around 600nm. It contains a 200μm slit and uses a Sony ILX511B linear silicon CCD array to detect the incident light. Both the DLP and the spectrometer are controlled using a MATLAB script that automatically collects data once the desired resolution, number of measurements and acquisition time have been selected. The system includes an adjustable stage that the object being imaged can be placed on to correct and set the imaging field of view and focus. The whole system fits within a housing to render the system dark and eliminates any background light that may cause the signal to noise ratio of the system to reduce.



(a) (b) (c)

Figure **1:** a) Schematic of the whole imaging system. b) Schematic of the lens within the DLP. c) An example of the binary patterns displayed on the DMD.

Hyperspectral data is collected from a mouse phantom containing an internal light source using a 20×20 pixel random binary projections of the imaging field into the spectrometer. The binary patterns that are used are created randomly ensuring that there is a 50% 'fullness', meaning there are equal amounts of 0's and 1's. The data is then formatted using a spectrum of the object being imaged with all of the mirrors on, so that it can be displayed as if the random patterns were formed of 1's and -1's. The reconstructions were carried out using 240 (60% of the total number of pixels) random projections at the desired wavelength.

3.2 Tissue Mimicking Phantom

The phantom used in this work is an XFM-2 Fluorescent Phantom (Caliper Life Sciences Inc.) which is a mouse shaped phantom made of polyurethane material with incorporated scattering particles and dyes to mimic the optical properties of live tissue. Optical properties of the phantom are spectrally varying and is stated by the manufacturer as having an absorption of 0.01 mm^{-1} and an isotropic scattering of 1 mm^{-1} at a wavelength of 600nm. The phantom is designed to be used with rods that contain a fluorescent probe at the tip which can be inserted into the phantom at two different depths. This was modified by inserting an optical fibre connected to an Ocean Optics halogen light source into the phantom in order to simulate an internal bioluminescent light source. Figure **2** show the phantom and the fibre that can be inserted at two different depths.

3.3 Compressive Sensing Algorithm

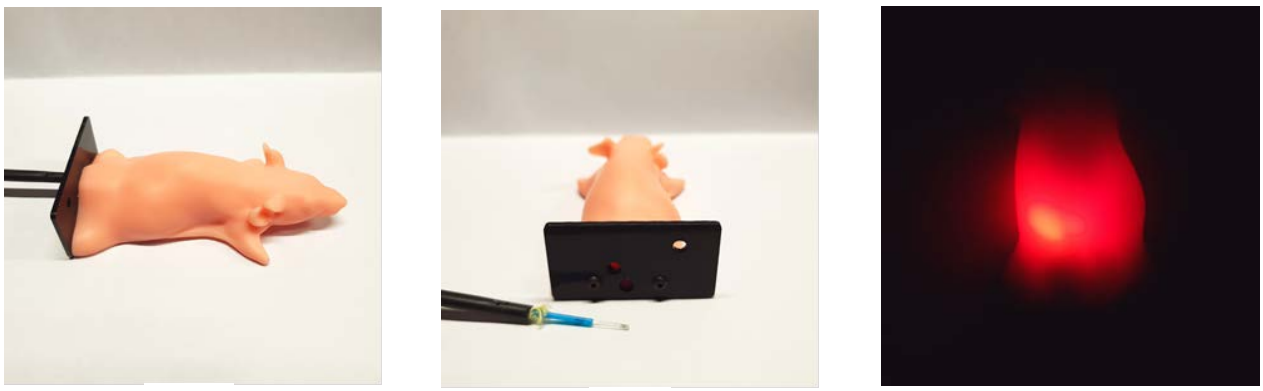
Surface fluence images are reconstructed from compressed data using the total variation minimisation by augmented Lagrangian and alternating direction algorithm (TVAL3) developed by Chengbo Li at the Department of CAAM, Rice University in Houston[7]. This is a total variation (TV) minimization algorithm and works by combining a classic augmented Lagrangian method with an appropriate variable splitting and nonmonotone alternating direction method. This is done by reformulating the minimisation problem as an alternative problem known as augmented Lagrangian function. An iterative method is then used to implement this function by finding minimising parameters by means of an alternating direction algorithm. It is shown that this algorithm outperforms other available TV and l_1 norm optimisation algorithms in both speed and reconstruction quality[6].

3.4 Tomographic Reconstruction

Tomographic reconstruction is carried out using the established software package NIRFAST[8]. Within this package a compressive sensing based optimisation algorithm has been developed that uses a forward model of light propagation through the phantom based on the diffusion approximation of the radiative transport equation[9].

Images are reconstructed from the compressed hyperspectral data and are corrected for the relative spectral response of the system. The images are then registered to the model of the phantom using affine registration and the surface fluence data is taken at each detector point. This data is then normalised and fed into the NIRFAST software for tomographic

reconstruction. Four different wavelengths (610nm, 620nm, 630nm and 640nm) are used for tomographic reconstruction as it has been shown that use of multi/hyper-spectral data improve the accuracy and quality of the reconstructions[10].



(a) (b) (c)

Figure **2: a)** XFM-2 Fluorescent phantom. b) Back of the mouse phantom showing the channels and the optical fibre used. c) An image of the phantom using a CMOS camera with the light source on inside the phantom, showing surface fluence distributions.

4. RESULTS AND DISCUSSION

Figure **3(a)** shows the mesh that was created within NIRFAST and Figures **3(b)**-**(c)** show the raw reconstructed surface fluence and the registered and normalised surface fluence respectively. The light source was placed within the top channel on the phantom which is located 20mm along the y axis from the bottom, -5mm from the centre on the x axis and at a depth of 10 mm.

First, hyperspectral data was collected using random binary projections of the imaging field after which surface fluence images were reconstructed at wavelengths of 610nm, 620nm, 630nm and 640nm with a bandwidth 5nm. Tomographic reconstruction of the source was then carried out in NIRFAST.

Figures **4(a-c)** show the actual target position of the light source within the mouse phantom and figures **4(d-f)** show the tomographically reconstructed source. The image of the tomographically reconstructed source has been thresholded to values above full-width-half-maximum. As the true location of the source is known, it is possible to calculate the percentage error in the localisation of the reconstructed source which was found to be 2.21%.

In previous work involving bioluminescence tomographic, surface fluence data is collected using a CCD along with filters for which data is collected individually for each wavelength[11], making the collection of hyperspectral data unfeasible. Using this new method of data collection, it is possible to collect hyperspectral data whilst using fewer measurements than previously done, which opens the door for high speed data collection as well as having the ability to use and differentiate between multiple light sources of different wavelengths. The effect of filter bandwidth on the quantitative accuracy of bioluminescence tomography has also ben investigated and found to have dramatic effects on the reconstruction accuracy[12]. In this proposed method, as no filters are used and the spectral resolution of the measurements can be better controlled, the effect of filter bandwidth is minimized, however this should further be investigated.

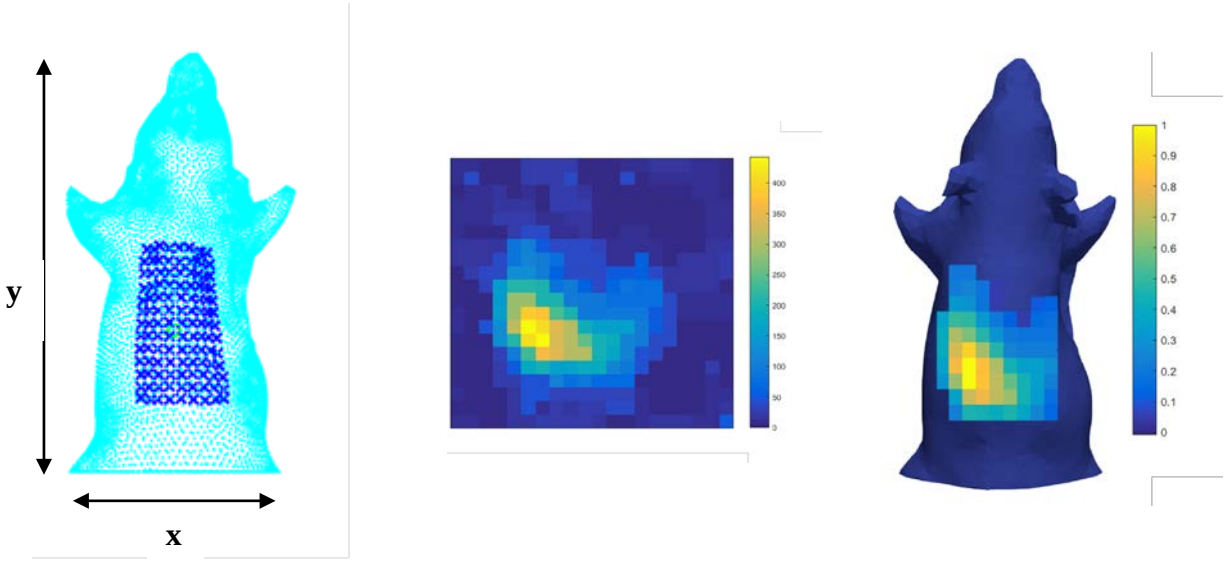


Figure **3:** a) Mesh of the XFM-2 phantom showing the detector points that are used. b) Raw reconstruction of the surface fluence at 640nm. c) Registered and normalised surface fluence of the internal light source.

5. CONCLUSION

Practical experiments have shown that tomographic reconstruction of a light source within a mouse-like phantom can be carried out using a compressive sensing based hyperspectral imaging technique with good accuracy. Using this method has the potential to bring a number of advantages to the field of bioluminescence tomography such as the ability to collect hyperspectral data at high speeds with much less measured data than currently collected. In a filter based CCD setup, each wavelength measurement typically relies on ~50s of measurements, providing data at spectral bandwidth of ~20nm. Using the method, it is possible to dramatically improve on this data collection time while providing much better spectrally resolved data.

There are still many areas that need to be investigated in order to make this method a commercially viable option for bioluminescence tomography. Firstly, the optical properties of the phantom used are already known, whereas in practice those of a live mouse or more realistic phantoms would be unknown. Therefore, there is a need to develop a technique to measure the optical properties of the subject simultaneously with data collection so that this can be used in tomographic reconstruction. There is also a need to optimise the system that has been developed so that weak bioluminescent signals can be measured with the same accuracy as strong light signals. Tests into using multiple light signals of different wavelengths are to be carried out in order to assess the performance of the system. With the system optimised to be able to detect weak bioluminescent signals as well as have the ability to simultaneously measure the optical properties of the subject, it is suggested that this method could improve how current bioluminescent tomography is carried out.

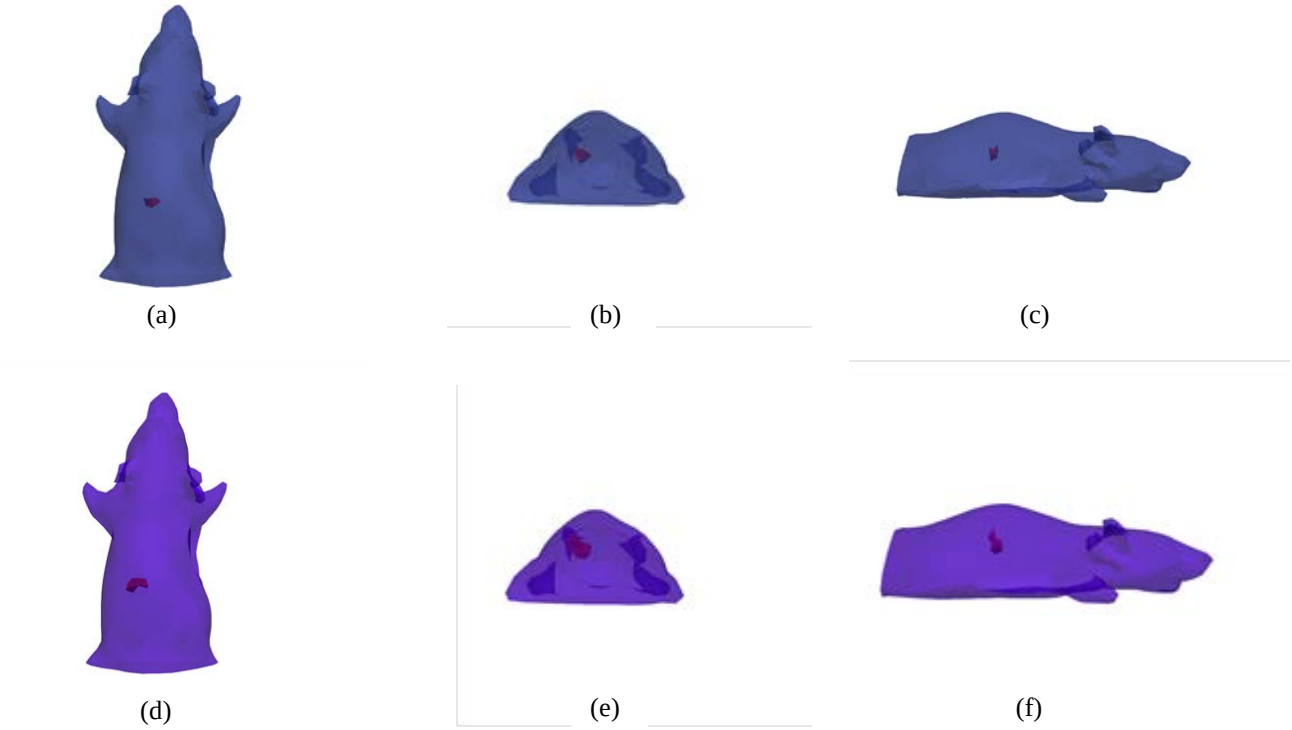


Figure **4:** a-c) The ground truth location of the light source within the phantom. d-f) Tomographic reconstruction of the optical fibre light source within the mouse phantom.

6. REFERENCES

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