Towards high speed needle microscopy through a multimode fiber by single pixel imaging

Chaitanya K. Mididoddi, Michael R. Hughes

Chaitanya K. Mididoddi, Michael R. Hughes, "Towards high speed needle microscopy through a multimode fiber by single pixel imaging," Proc. SPIE 10854, Endoscopic Microscopy XIV, 1085417 (26 February 2019); doi: 10.1117/12.2509869

SPIE.

Event: SPIE BiOS, 2019, San Francisco, California, United States

Towards High Speed Needle Microscopy Through a Multimode Fiber by Single Pixel Imaging

Chaitanya K. Mididoddi[a] and Michael R. Hughes[a]

[a]Applied Optics Group, School of Physical Sciences, University of Kent, Canterbury, United Kingdom CT2 7NH

ABSTRACT

We present a proof of concept for microscopy through a multimode fiber using single pixel imaging. We present two implementations, one using galvo scanners and a diffuser plate and one using a digital micromirror device (DMD). Using these setups we can generate thousands of distinct speckle patterns at the distal end of a 50 micron core fiber as illumination patterns for single pixel imaging. We show that the correlation between speckle patterns can be made as low as 30% and the repeatability as high as 98% for a sample of 3200 patterns, and show example single pixel images using a distal detector.

Keywords: Single-Pixel Imaging, Multimode fibre, DMD, Fluorescence, Endomicroscopy

1. INTRODUCTION

Fluorescence endomicroscopy enables real time imaging of tissue *in situ* in contrast to the long processing times and invasiveness associated with biopsy.[2] Conventional confocal endomicroscopy systems are broadly classified into distal scanning and proximal scanning[2] based on the approach used for scanning the tissue. In distal scanning mechanisms, single mode fibres are used for transmission and collection of light. This achieves good lateral resolution, but the distal tip is larger in size due to the need for a fibre scanning mechanism, restricting the range of clinical applications. Proximal scanning approaches use a fibre bundle made up of a few thousand step index fibre cores[2] with an external laser scanning unit coupled to the proximal end of the bundle. The size of the distal tip can therefore be reduced and high speed image acquisition achieved. However, as each fibre acts as an image pixel, resolution is limited to around 6 microns. A distal lens can improve resolution, but at the cost of reduced field-of-view and a larger probe diameter.

For applications such as needle microscopes, unconventional techniques have been suggested to obtain a high resolution image through an ultra-thin probe. Wavefront shaping at the proximal end of a fibre bundle using a spatial light modulator allows a scanning focused spot to be created at the distal end following a calibration.[4] This improves resolution, but with a limited field-of-view. A similar approach has been applied to imaging through multimode fibres, this time relying on interference between fibre modes.[5–7,9,10] Again, such approaches require a prior calibration, and so are only suitable for rigid probe imaging, since any bending of the fibre changes the relative phase between the fibre modes and so destroys the calibration. The need to generate a complex wavefront for each point on the image also leads to low imaging speeds.

An alternative and less explored approach to image transmission through multimode fibres is single pixel imaging.[11] In single pixel imaging a set of calibrated illumination masks are projected onto the sample and the response of the sample to each pattern is spatially integrated onto a high speed detector such as photodiode. The image can then be reconstructed using numerical inversion methods. The masks can be either a set of harmonic patterns on a particular basis such as the wavelet domain[12] or the Fourier domain[13,14] or a set of random patterns.[17] One potential advantage of single pixel imaging is that it allows for compressive sensing, where the number of illumination masks is lower than the number of pixels in the reconstructed image.

Further author information: (Send correspondence to M.R.H.)
M.R.H.: E-mail: M.R.Hughes@kent.ac.uk, Telephone: +44 1227 816782
C.K.M.: E-mail: ckm22@kent.ac.uk, Telephone: +44 1227 83772

Endoscopic Microscopy XIV, edited by Guillermo J. Tearney, Thomas D. Wang, Melissa J. Suter, Proc. of SPIE Vol. 10854, 1085417 · © 2019 SPIE
CCC code: 1605-7422/19/$18 · doi: 10.1117/12.2509869

The single pixel imaging method can be implemented through a multimode fibre by using speckle patterns generated at the distal end of the fibre as the illumination masks.[8] This was originally demonstrated in principle using a relatively slow and inefficient setup, using an SLM to change the input fields at the proximal end of the fibre and hence generate a series of different speckle patterns at the distal end. The imaging speed therefore depends on the rate at which the speckle patterns can be generated, since a number of patterns on the order of the number of pixels (resolution elements) in the image is required. Very recently, a fluorescence based multimode fibre endomicroscopy system based on single pixel imaging was demonstrated.[19] This system uses a digital micromirror device (DMD) to generate input patterns at high speed and compressive sensing to reduce the number of patterns and hence the acquisition time. However, the long reconstruction time for compressive sensing means that the approach is still not real-time.

With the aim of ultimately performing single pixel imaging through fibres at high frame rates, in this paper we demonstrate two ways of generating input patterns and hence distal speckle patterns: a galvo scanning system, and a digital micromirror device (DMD) system. We evaluate the correlation and stability of the speckle patterns generated by both systems. We then demonstrate that the patterns are suitable for single pixel imaging by using a camera to simulate a point detector at the distal end of the fibre.

2. METHODS

Schematics for the two systems are shown in Fig. 1. Figure 1.a shows the experimental setup with a DMD, and Fig. 1.b shows the experimental setup with galvo mirrors and a diffuser. In Fig. 1.a, a He-Ne laser (Melles Griot 05-LHP-111, 5mW) with a wavelength of 633 nm is expanded with a 4f beam expanding setup and directed to the DMD, a Texas Instruments Lightcrafter 6500. The DMD is programmed with a series of binary patterns, which are demagnified via a 10X microscope objective onto a multimode fibre (Thorlabs FG050UGA) of 50 μm core diameter, 0.22 NA and length 7 cm. Interference between fibre modes results in a speckle pattern at the distal end of the fibre, and changing the binary pattern on the DMD changes the speckle pattern. The patterns are imaged via a 10X microscope objective onto a CCD camera (Guppy pro f-033B, 9.9μm pixel size, 656 x 492 resolution). .

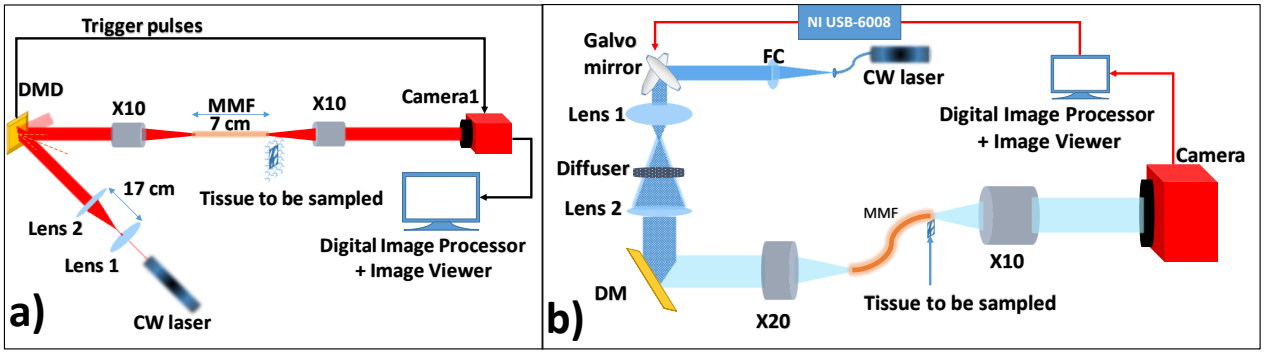

Figure 1. (a) Single pixel endomicroscopy system with DMD. CW: continuous wave, Lens 1: f=20 mm, Lens 2: f=150mm, DMD: Digital Micromirror Device, TI Lightcrafter 6500, Camera: CCD camera Guppy pro f-033B, MMF: Multimode Fibre. (b) Single pixel endomicroscopy system with galvo mirrors and diffuser. FC: Fibre collimator f=19 mm, Lens 1: f=20mm, Lens 2: f=75mm, DM: Dichroic Mirror, MMF: Multimode Fibre with 1 m length

The DMD has 1920 x 1080 mirrors of size 7.56 μm, with an overall chip size of 14.5 mm x 8.1 mm, but only an area of 264x264 pixels was used, determined by the size of the fibre as imaged onto the DMD. There are two possible approaches for generating binary random patterns on the DMD. In video pattern mode a composite RGB image, sent to the DMD via HDMI, is split into 24 binary patterns (one pattern per bit plane) and a specific binary pattern can be programmed to be displayed on DMD at any time. The advantage of this method is that it doesn't require storage of patterns on the DMD, and so the number of patterns is unlimited, but the update rate is limited 1440 Hz. We also noted that it is crucial to set the video card capability to full dynamic

range so that all bit planes are transmitted with high stability. Alternatively, in pre-stored pattern mode the patterns are stored in memory on the DMD. This allows for the fastest pattern display (up to 9325 Hz), but storage is limited to 400 patterns. However, by flipping and inverting the patterns, the maximum number of usable random patterns can be increased to 3200. This was the mode used for the results reported below.

In the galvo system, the output from a fibred laser diode (488 nm) is collimated and directed to a 2-axis galvo mirror system (Thorlabs GVS002) which is controlled by an NI multifunctional I/O device (NI USB-6008) via a LabVIEW program. A diffuser is placed in the path at a point close to a plane conjugate to the fibre input face. By changing the positions of the two galvo mirrors, the input field is therefore varied. The exact position of the diffuser is optimised to minimise correlation between speckle patterns while maximising light throughput. For this system the fibre used was Thorlabs M42L01, 0.22 NA, 50 μm core diameter, 1 m in length. At the distal end, the speckle patterns are magnified with a 10x objective onto a CMOS camera (FL3-U3-13S2M-CS, 1328 x 1048 resolution, 3.63 μm pixel size).

For calibration of either system, a set of speckle patterns is generated sequentially, either by changing the pattern on the DMD or changing the positions of the galvo mirrors, and each is recorded by the camera at the distal end. After calibration, a sample is placed in direct contact with the distal end of the fibre and the same set of patterns is re-generated. In order to simulate single pixel imaging (which in a clinical system would involve collecting light using the same fibre) the images on the distal camera, which are the responses of the sample to each pattern, are spatially integrated, giving a single value measurement for each pattern. This forms a system of linear equations which can be solved by matrix inversion to reconstruct the image.

3. RESULTS

The correlation between different speckle illumination patterns should be as low as possible for single pixel imaging, as spurious correlations will introduce noise. This was assessed by calculating the correlation coefficient between the different speckle patterns obtained from a complete calibration set. Figure 2 shows the calculated correlation between all possible pairings of 3200 patterns generated using the DMD system and the galvo system. It can be seen that correlation is as low as 30% in both cases. Note that, in the DMD system, due to use of the pattern inversion procedure to extend the number of patterns, the correlation of the 1st and 1600th patterns is high. The mean intensity values for each of the patterns are also shown. For the galvo system there is some variation in the mean power, while for the DMD system the power is more uniform.

It is clearly important that the speckle patterns do not change between calibration and imaging. This requires stability both of the system and the fibre. Environmental disturbances such as changes in temperature are therefore a potential issue. The self-correlation of a single speckle pattern over time is shown for both systems in Fig. 3. In both setups, good correlation is maintained for several minutes.

In order to confirm that the speckle patterns are suitable for single pixel imaging, proof of concept imaging was carried out using tissue paper placed in direct contact with the fibre. Measurements were made by spatially averaging over each image of the distal end of the fibre, simulating a single pixel detector. Example results are shown for the DMD system in Fig. 4 and the galvo system in Fig. 5. The ground truth was obtained simply by averaging the raw images acquired by the camera during the imaging phase.

In both cases the imaging speed was limited by the camera acquisition frame rate. For the DMD system, acquisition took 144 s for 3200 patterns, while for the galvo system acquisition time was 137 s for 7852 patterns (due to a higher frame rate camera). In a practical imaging system the camera would be replaced by a point detector at the proximal end of the fibre, and so the pattern update rate would become the limiting factor. The galvo system therefore represents the most promising avenue for high speed imaging, providing that the pattern reproducibility is sufficiently high when driven at high speed.

4. CONCLUSION

We have presented galvo and DMD based setups for generating speckle patterns at the distal end of a multimode fibre, and shown both to be potential means of performing single pixel imaging. To convert this to a practical fluorescence endomicroscopy system, returning fluorescence would be spatially intergrated by the fibre, and this would be collected at the proximal end by a photodetector.

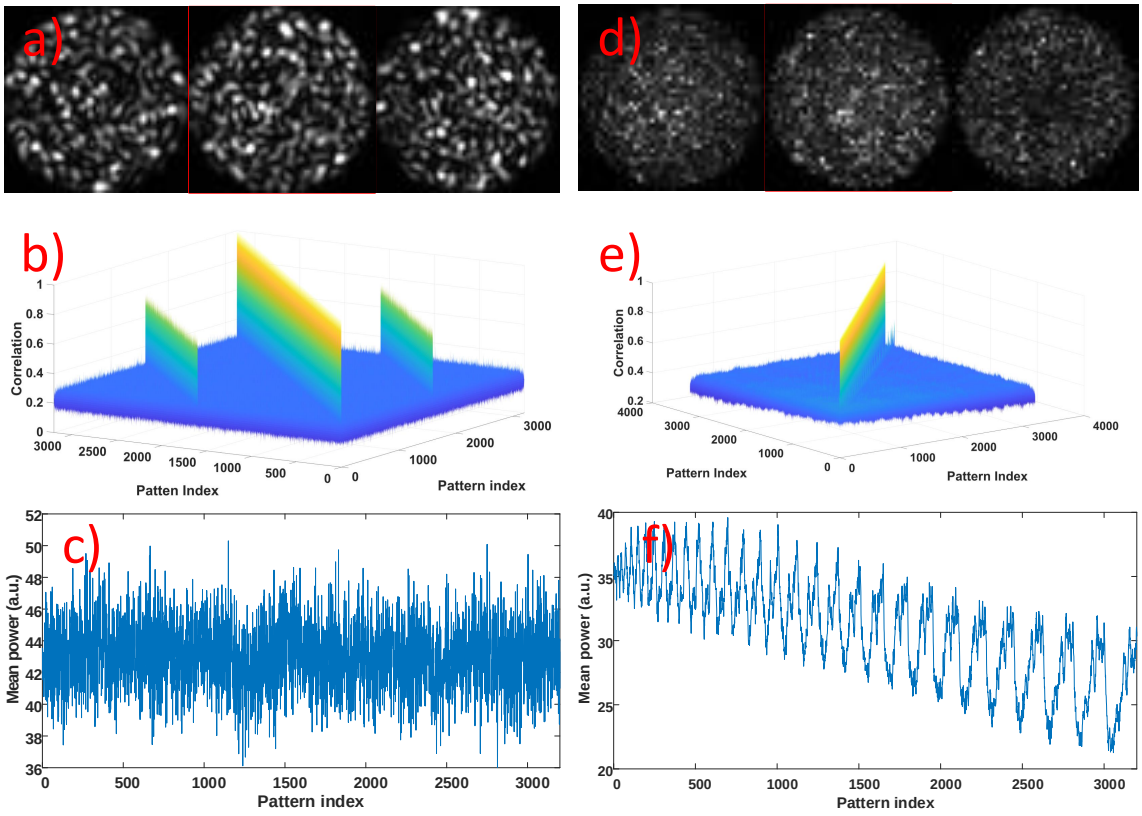

Figure 2. Correlation of speckle patterns generated with DMD system and galvo system. a) Example of three patterns recorded from DMD system; b) Correlation matrix among all combinations of the DMD patterns; c) Mean value of the DMD patterns against pattern index; d) Examples of three patterns recorded from galvo system; e) Correlation matrix among all combinations of the galvo patterns; f) Mean value of the galvo patterns against pattern index.

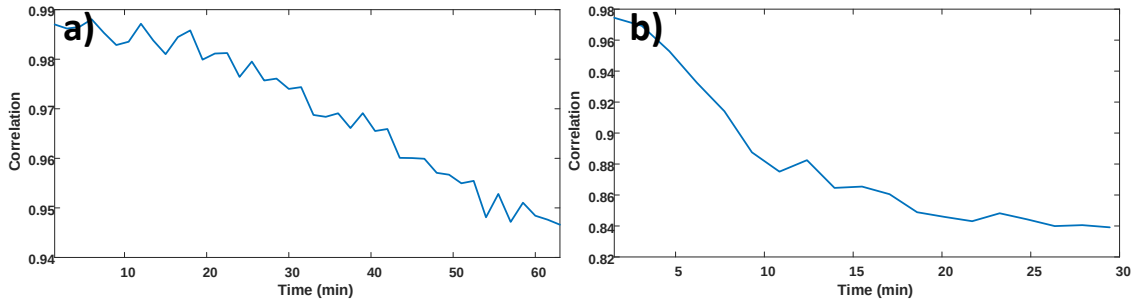

Figure 3. Change in pattern self-correlation with time for (a) DMD system and (b) galvo system.

ACKNOWLEDGMENTS

This work was supported by EPSRC Grant EP/R019274/1, Ultrathin Fluorescence Microscope in a Needle. The authors would like thank the TI community forum for technical help.

REFERENCES

[1] Vyas, K., Hughes, M., Rosa, B. G., and Yang, G.-Z., "Fiber bundle shifting endomicroscopy for high-resolution imaging," *Biomed. Opt. Express* **9**, 4649–4664 (oct 2018).

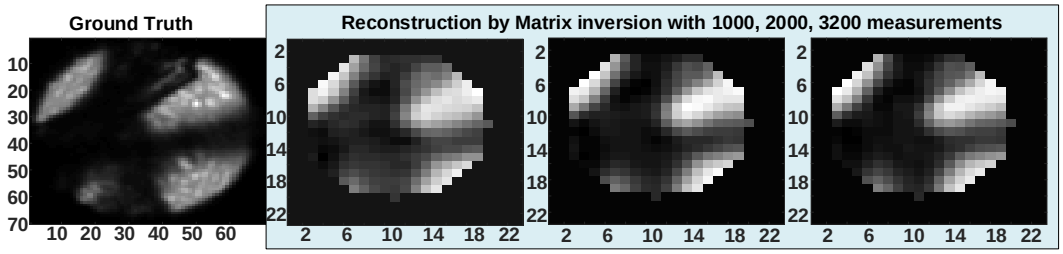

Figure 4. Transmission imaging results for the DMD system. a) Ground Truth; b) Image reconstruction using 1000, 2000 and 3200 measurements, respectively.

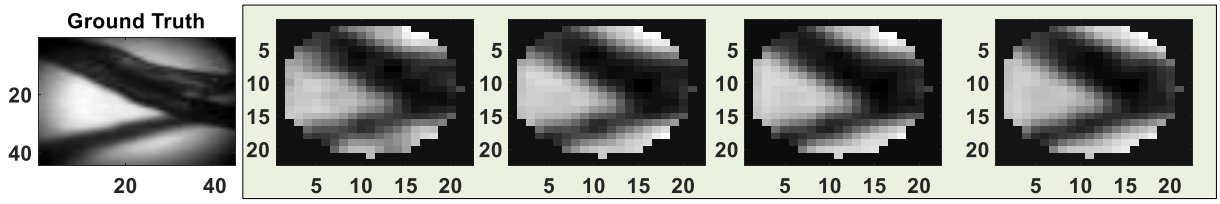

Figure 5. Transmission imaging results for the galvo system. a) Ground Truth; b) Image reconstruction using 1000, 2000 and 3000 and 7852 measurements, respectively.

[2] Jabbour, J. M., Saldua, M. A., Bixler, J. N., and Maitland, K. C., "Confocal Endomicroscopy: Instrumentation and Medical Applications," *Annals of Biomedical Engineering* **40**, 378–397 (feb 2012).

[3] Tearney, G. J., Webb, R. H., and Bouma, B. E., "Spectrally encoded confocal microscopy," *Opt. Lett.* **23**, 1152–1154 (Aug 1998).

[4] Thompson, A. J., Paterson, C., Neil, M. A. A., Dunsby, C., and French, P. M. W., "Adaptive phase compensation for ultracompact laser scanning endomicroscopy," *Opt. Lett.* **36**, 1707–1709 (may 2011).

[5] Leonardo, R. D. and Bianchi, S., "Hologram transmission through multi-mode optical fibers," *Opt. Express* **19**, 247–254 (jan 2011).

[6] Čižmár, T. and Dholakia, K., "Exploiting multimode waveguides for pure fibre-based imaging," *Nature Communications* **3**, 1027 (aug 2012).

[7] Mahalati, R. N., Askarov, D., Wilde, J. P., and Kahn, J. M., "Adaptive control of input field to achieve desired output intensity profile in multimode fiber with random mode coupling," *Opt. Express* **20**, 14321–14337 (jun 2012).

[8] Mahalati, R. N., Gu, R. Y., and Kahn, J. M., "Resolution limits for imaging through multi-mode fiber," *Opt. Express* **21**, 1656–1668 (jan 2013).

[9] Papadopoulos, I. N., Farahi, S., Moser, C., and Psaltis, D., "High-resolution, lensless endoscope based on digital scanning through a multimode optical fiber," *Biomed. Opt. Express* **4**, 260–270 (feb 2013).

[10] Caravaca-Aguirre, A. M., Niv, E., Conkey, D. B., and Piestun, R., "Real-time resilient focusing through a bending multimode fiber," *Opt. Express* **21**, 12881–12887 (may 2013).

[11] Duarte, M. F., Davenport, M. A., Takhar, D., Laska, J. N., Sun, T., Kelly, K. F., and Baraniuk, R. G., "Single-pixel imaging via compressive sampling," **25**(2), 83–91 (2008).

[12] Alemohammad, M., Stroud, J. R., Bosworth, B. T., and Foster, M. A., "High-speed all-optical Haar wavelet transform for real-time image compression," *Opt. Express* **25**, 9802–9811 (may 2017).

[13] Zhang, Z., Ma, X., and Zhong, J., "Single-pixel imaging by means of fourier spectrum acquisition," *Nature communications* **6**, 6225 (2015).

[14] Guo, Q., Chen, H., Wang, Y., Guo, Y., Liu, P., Zhu, X., Cheng, Z., Yu, Z., Yang, S., Chen, M., et al., "High-speed compressive microscopy of flowing cells using sinusoidal illumination patterns," *IEEE Photon. J.* **9**, 3900111 (2017).

[15] Mididoddi, C. K., Feng, D., and Wang, C., "Optical phase shifting fourier transform scanning for bandwidth-efficient blind rf spectrum sensing," in [*2018 European Conference on Optical Communication (ECOC)*], 1–3 (Sep. 2018).

[16] Escobet-Montalbán, A., Spesyvtsev, R., Chen, M., Saber, W. A., Andrews, M., Simon Herrington, C., Mazilu, M., and Dholakia, K., "Wide-field multiphoton imaging through scattering media without correction," *Science Advances* **4** (oct 2018).

[17] Candes, E. J. and Wakin, M. B., "An Introduction To Compressive Sampling," (2008).

[18] Choi, Y., Yoon, C., Kim, M., Yang, T. D., Fang-Yen, C., Dasari, R. R., Lee, K. J., and Choi, W., "Scanner-Free and Wide-Field Endoscopic Imaging by Using a Single Multimode Optical Fiber," *Phys. Rev. Lett.* **109**, 203901 (nov 2012).

[19] Amitonova, L. V. and de Boer, J. F., "Compressive imaging through a multimode fiber," *Opt. Lett.* **43**, 5427–5430 (nov 2018).