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Fast 3D in vivo swept-source optical coherence tomography using a two-axis MEMS scanning micromirror

Karthik Kumar¹, Jonathan C Condit², Austin McElroy³, Nate J Kemp³, Kazunori Hoshino², Thomas E Milner² and Xiaojing Zhang²

¹ Department of Electrical and Computer Engineering, University of Texas, Austin, TX 78712, USA
² Department of Biomedical Engineering, University of Texas, Austin, TX 78712, USA
³ CardioSpectra, Incorporated, San Antonio, TX 78229, USA

E-mail: john.zhang@engr.utexas.edu

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Abstract

We report on a fibre-based forward-imaging swept-source optical coherence tomography system using a high-reflectivity two-axis microelectromechanical scanning mirror for high-speed 3D in vivo visualization of cellular-scale architecture of biological specimens. The scanning micromirrors, based on electrostatic staggered vertical comb drive actuators, can provide ±9° of optical deflection on both rotation axes and uniform reflectivity of greater than 90% over the range of imaging wavelengths (1260–1360 nm), allowing for imaging turbid samples with good signal-to-noise ratio. The wavelength-swept laser, scanning over 100 nm spectrum at 20 kHz rate, enables fast image acquisition at 10.2 million voxels s⁻¹ (for 3D imaging) or 40 frames s⁻¹ (for 2D imaging with 500 transverse pixels per image) with 8.6 μm axial resolution. Lateral resolution of 12.5 μm over 3 mm field of view in each lateral direction is obtained using ZEMAX optical simulations for the lateral beam scanning system across the scanning angle range of the 500 μm × 700 μm micromirror. We successfully acquired en face and tomographic images of rigid structures (scanning micromirror), in vitro biological samples (onion peels and pickle slices) and in vivo images of human epidermis over 2 × 1 × 4 mm³ imaging volume in real time at faster-than-video 2D frame rates. The results indicate that our system framework may be suitable for image-guided minimally invasive examination of various diseased tissues.

Keywords: optical coherence tomography (OCT), swept-source, MEMS, scanning micromirror, high-speed 3D imaging

(Some figures in this article are in colour only in the electronic version)

1. Introduction

Optical coherence tomography (OCT) has emerged as a high-resolution biomedical diagnostic imaging technique of choice in situations where biopsy is difficult, for image-guided microsurgery, and for three-dimensional reconstruction of pathology [1]. OCT has been shown to discriminate architectural layers and identify morphological changes in highly scattering tissue. High-resolution 3D imaging can enhance a physician’s understanding of pathology by providing tomographic, microscopic and en face views simultaneously [2]. Miniaturization of optical diagnostic equipment for clinical implementation necessitates alternative beam-deflection mechanisms to galvano-metric scanning. Proximal scanning mechanisms have been extensively investigated [3–7] wherein a single-mode fibre fused to a focusing microlens and prism is either translated along the length of the probe [3], or rotated about the probe axis [4, 6], or operated in a helical scan mode that is a superposition of
these two scans [5]. Proximal scanning systems, besides suffering from slow scan rates, poor precision and repeatability, are only useful in sideways-imaging probes for visualization in tubular structures such as the gastrointestinal tract and oesophagus. 3D OCT probes require miniaturized distal scanning mechanisms and advancements in catheter design to image in narrow, sensitive and non-tubular human organs. Forward-imaging configurations are well suited to this task, but are significantly harder to assemble in compact form factor as compared with the sideways-imaging probes [7]. Distal scanning can be performed by scanning the fibre, objective lens, and by beam steering using paired angle-polished rotating GRIN lenses or scanning micromirrors. Fibre and objective scanning can be performed using piezoelectric actuators [8] and tuning forks [9]. However, these suffer from limited field of view and slow scan rates, respectively. Microelectromechanical system (MEMS) technologies offer the unique capability to package micro-optical elements with actuators on a chip scale for imaging in \textit{in vivo} environments. Previous studies have utilized one-dimensional [6, 10–13] and two-dimensional [14, 15] distal-end MEMS scanning systems to perform time- and spectral-domain OCT. MEMS elements have also been used for dynamic beam focus control in several OCT modalities [16–18] and can enable compact frequency-tuneable lasers [19, 20] for swept-source OCT. Angular [21] and staggered [22–24] vertical comb-driven micromirrors, a subset of MEMS scanning systems, are useful for building forward-imaging probes, providing large actuation torque and scanning angles with smooth optical surfaces and low dynamic mirror deformation due to high mirror layer thickness. Such mirrors have previously been used in confocal microscopy [25], two-photon microscopy [26] and time-domain optical coherence tomography systems [14].

In this work, we present high-speed 3D swept-source optical coherence tomography employing a high-reflectivity two-axis vertical comb-drive scanning micromirror that can be configured into a compact forward-imaging probe. The scanning micromirror offers the advantages of silver-coated reflecting surface, two-axis rotation about a single in-plane pivot point, and high-speed arbitrary scan patterns for \textit{en face} imaging. Spectral domain (i.e. Fourier-domain/swept-source) techniques have been shown to provide significant signal-to-noise ratio and imaging speed advantages over time-domain OCT [27, 28]. Swept-source OCT (SS-OCT), in particular, enables real-time micron-resolution diagnostic imaging over millimetre depth range due to improvements in spectral range, linewidth and scan speed of swept wavelength lasers. High-speed 3D imaging over $2 \times 1 \times 4 \text{ mm}^3$ volume at $\sim 12.5 \mu\text{m}$ lateral and $\sim 8.6 \mu\text{m}$ axial resolutions is demonstrated using the system. Tomographic, \textit{en face} and cross-sectional slices through 3D volumetric images of both \textit{in vitro} and \textit{in vivo} samples acquired at over 10 million voxels per second are presented.

2. Experimental methods

2.1. Two-axis MEMS scanning micromirror

We employed a staggered vertical comb-driven two-axis scanning micromirror for distal beam scanning. Staggered vertical comb drives combine the advantages of large scanning angles, high electrostatic actuating torque, favourable voltage pull-in characteristics, low mirror dynamic deformation under resonant operation and optically smooth mirror surfaces. The mirror is fabricated by a five-mask process employing double-bonded SOI wafers and self-aligned deep reactive ion etching (DRIE) steps. Figure 1(a) outlines the silicon micromachining process used to fabricate the scanning mirrors. Coarse features of stationary electrostatic actuating comb drives are etched by deep reactive ion etching (DRIE) into the 30 $\mu\text{m}$ conductive

![Figure 1. High-reflectivity two-axis vertical comb-drive scanning micromirrors. (a) Process flow for device fabrication. (b) Scanning electron micrographs (SEM) of scanning micromirrors depicting mirror and frame design, torsion springs, stator and rotor combs, bond pads and backside DRIE release window.](image)
affords a critical mask alignment tolerance of half the comb thickness, and polished to give a smooth (less than 50 nm RMS surface roughness) optical surface. The mirror and rotor comb features are fabricated in this layer. A layer of 1.5 μm thick silicon dioxide, serving as a silicon etch hard mask, is deposited by low pressure chemical vapor deposition (LPCVD). After dry etching through the top device layer to expose alignment marks in the lower silicon layer, electrical bond pad features are etched partially (1.2 μm) and the exact features of the scanning micromirrors are etched through the oxide layer by reactive ion etching (RIE). The oxide layer is used as an etch mask to perform a DRIE–oxide RIE–DRIE sequence to create rotor comb features, bond pad vias to the lower silicon layer, and trim the underlying stator combs to match the lateral position of the stator comb features. This self-aligning technique [22, 23] affords a critical mask alignment tolerance of half the comb width (3.0 or 3.5 μm in our case) for stable and reliable scanner operation. A backside window is DRIE-etched beneath the device to release the micromirror, while simultaneously dicing the wafer into device chips. The remaining exposed oxide is removed from the front and backside by RIE. A (100) silicon wafer is anisotropically wet etched in potassium hydroxide using a silicon nitride masking layer at 70 °C to create a hard mask for sputtering. Using this hard mask, the micromirrors are selectively coated with metal by electron beam evaporation. The micromirror has design dimensions of 500 μm × 700 μm for compact oblique (up to 45°) illumination with a 500 μm diameter laser spot, and is coated with 125 nm of silver, resulting in greater than 90% uniform reflectance over the source spectrum. The silver films showed high reflectivity range during our experimentation period of approximately two weeks. However, we observed blackening of the films at an extended period of time after the experiments, and reflectivity dropped to <30% at 1310 nm. In future experiments, we plan to incorporate gold instead of silver coatings that are inert and more suitable for long-term use. An important advantage of this scanner design is that, in a single plane, the mirror is suspended within a frame by the inner torsion springs and the frame is suspended by the outer torsion springs aligned in the orthogonal direction. This enables two-dimensional rotation about a single pivot point, reducing optical field distortions. Scanning electron micrographs of the device are shown in figure 1(b).

The micromirror exhibits resonance on the inner and outer axes at 2.28 kHz and 385 Hz, respectively, and ±9° optical deflection on both axes for applied voltages of 110 V at low frequencies (figure 2). Secondary peaks are also observed at half and twice the actual resonant frequency of the vibration modeshape, as expected [30]. Due to the highly capacitive nature of the electrostatic actuators, the micromirror actuation requires very low current (usually of the order of 1–10 nA) for operation in non-resonant mode and around 2.4 μA in resonant mode on either axis.

2.2. Swept-source OCT instrument

We incorporated our system on a 12” × 12” miniature optical breadboard in a forward-imaging configuration for our distal beam-scanning mechanism that can be further miniaturized into an OCT endoscope suitable for imaging in non-tubular organs of the human body. Figure 3 illustrates the principle of operation of swept-source OCT with MEMS scanning micromirrors. Fibre-based instrument layout and swept-source configuration similar to that used in [31] is adopted due to the high sensitivity demonstrated by the approach, ease of alignment, portability and manoeuvrability after incorporation of the scanning micromirror and optical elements into a miniaturized distal probe. The sample and reference arms are designed to have optical path lengths matched to within a few tens of micrometres. Illumination from the swept-wavelength laser is split equally into the sample and reference arms by the 2 × 2 fibre coupler. The phase difference between sample and reference arm reflections as a function of optical frequency is measured over the 100 nm spectral range by sampling the interference signal between the reflections from the two arms through the infrared photodetector as the illumination wavelength is varied. The Fourier transform of this spectral interference signal provides a map of the reflectivity profile of the sample as a function of depth [32]. The two-axis MEMS scanning micromirror moves the beam spot laterally in two dimensions (in raster fashion) and the axial reflectivity profiling is performed at each point to develop a 3D image of the sample volume. Optical design simulations in ZEMAX software indicate that the Steinheil triplet lenses (JML Optical, TRP14340/100, 0.6 NA, 7.9 mm
Figure 3. MEMS scanning micromirror based fast 3D in vivo swept-source optical coherence tomography. (a) Principle of 3D SS-OCT incorporating a high-reflectivity two-axis MEMS scanning micromirror in forward-imaging configuration. (b) Optical characteristics of the lateral beam-scanning system—ZEMAX simulation. A 3 mm linear scan of $\sim$12.5 $\mu$m focused spot is obtained when the micromirror provides $\pm$10$^\circ$ of optical deflection to the 500 $\mu$m diameter laser spot.

EFL) provide aberration-free focus of the 500 $\mu$m diameter collimated broad-spectrum illumination, resulting in a beam spot size of approximately 12.5 $\mu$m on the sample, and a lateral scan range of approximately 3 mm when the micromirror, positioned at the back focal plane of the lens, produces an optical deflection of $\pm$10$^\circ$. The laser performs 20 000 sweeps per second over 100 nm spectral range centred at 1310 nm, theoretically providing $\lambda^2/2\Delta\lambda = 8.6$ $\mu$m axial resolution and 4 mm imaging depth. In practice, the imaging depth of optical coherence tomography is limited to 1.5–2 mm due to degradation of the signal-to-noise ratio by light scattering in turbid samples.

3. Imaging results and discussion

To demonstrate the capabilities of our scanning micromirror based swept-source OCT system, we acquired reflectivity data over a $2 \times 1 \times 4$ mm$^3$ volume of rigid structures, in vitro biological samples and in vivo human epidermis. The system acquisition rate of over 10 million volume pixels per second results in completion of one entire volume scan in approximately 15 s, representing an order-of-magnitude improvement in acquisition rate over time-domain optical coherence tomographic techniques demonstrated previously. Results of 3D imaging of rigid structures, namely one of our packaged scanning micromirrors without metal reflectivity coating, are presented in figure 4. The information present in the entire 3D volume can be represented in a 2D en face view by integrating the reflectivity along the axial direction. The micrometre-scale features, such as micromirror torsion
springs, electrical bond pads and a 20 μm diameter bonding wire connecting to the top left bond pad, are clearly visible from the en face image in figure 4(a), indicating that the system achieves the micrometre resolution predicted by our ZEMAX simulations. The subsurface stator combs for the inner rotation axis are also visible in the image, as evidenced by comparison with the scanning electron micrograph in figure 1(c). Figure 4(c) depicts tomographic cross-sectional slices across different positions of the micromirror, revealing the internal structural details of the device. The vertical comb drives typically cause large amounts of laser light scattering, leading to the grainy portions in the image, similar to speckle noise. The mirror section of the device is dark as it scatters very little of the incident light due to high transmission of silicon at infrared wavelengths.

We acquired tomographic images of in vitro biological samples at 40 frames s$^{-1}$ by operating the scanning micromirror about only one axis of rotation. Figure 5 presents tomographic images of pickle slices obtained using the scanning micromirror and a traditional galvanometric scanner from different regions of the sample, and an onion peel using the micromirror. Subsurface morphology is visible in all the images.

Finally, we obtained real-time 3D images of in vivo human finger skin using our system. Tomographic slices through the imaged volume are shown in figure 6. The micron-scale tissue architecture including skin surface, finger ridges, sweat glands, stratum corneum, epidermis and dermis are clearly visible in the slice images. In some of the images, lens flare artefacts are visible, but these can be repositioned away from the imaging region of interest by varying the path length difference between the sample surface and reference reflection.

The lateral and axial resolutions of the instrument are governed by independent factors. The axial resolution is inversely proportional to the spectral bandwidth of the swept-frequency laser. The lateral resolution is determined purely by the micromirror and scanning optics. The diameter of the scanning micromirror limits the maximum beam diameter incident on the objective lens, and therefore determines the effective numerical aperture of the focusing lens. The number of resolvable points of our system can be improved by increasing the product of the mirror diameter–scanning angle product, which is then transformed into a given lateral field of view and resolution, depending on the numerical aperture of the objective [33], which can be selected according to the requirements of the application. In our experiments, some instability in lateral scanning was observed, which can be countered by incorporation of angular position feedback sensors [34] on the scanning micromirror chip for adaptive control of scan linearity. Miniaturization of the MEMS scanning optics with the use of fibre-fused graded index (GRIN) lens collimators, stationary micro-prisms and monolithic electronics integration such as flip-chip bonding for power supply and signal conditioning will enable possible clinical application of the instrument for applications such as gastroenterology, urinary/reproductive tract and pulmonary imaging that allow catheter diameters of 5 mm [7]. Real-time in vivo volume image acquisition of subsurface morphology at micrometre resolution may enable application to minimally invasive disease diagnostics, image-guided biopsy and photodynamic therapy.

4. Conclusion

High-speed three-dimensional swept-source optical coherence tomography is demonstrated using a forward-imaging distal beam-scanning configuration incorporating a high-reflectivity two-axis scanning micromirror, which can be miniaturized into a catheter for in vivo imaging. Tomographic slice images and en face views of an imaged 2 × 1 × 4 mm$^3$ volume were acquired with estimated lateral and axial resolutions of 12.5 μm and 8.6 μm, respectively. The imaging capability of the instrument was tested on rigid structures, in vitro biological samples and in vivo imaging of human finger skin.
The imaging results indicate that the instrument is capable of micrometre-resolution imaging of subsurface morphology in turbid media. Higher-than-video-rate (40 frames s\(^{-1}\)) acquisition of 2D images and 3D imaging at over 10 million volume pixels per second in such samples was successfully demonstrated.

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