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Focusing and scanning through scattering media in microseconds

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Recent advances in computational wavefront shaping have made optical focusing through scattering media a reality. However, most current techniques are too slow to focus, much less image through dynamically changing living biological tissue, such as blood-perfused neural networks, which can decorrelate in milliseconds. We introduce a phase control technique using programmable acoustic optic deflectors (AODs) that is orders of magnitude faster than existing wavefront shaping methods. It is based on sending an array of RF-encoded beams through the medium and measuring the phases of all scattered beams simultaneously with a fast single-pixel detector in just 10 μs. Using the AODs, we then phase conjugate the beams to form a spatio-temporal focus. We also demonstrate two-dimensional scanning of the focus on a sub-millisecond time scale.

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Recent developments in the field of wavefront shaping (WFS) have demonstrated control and optical focusing through scattering media [1]. Scattering of coherent illumination in complex media such as biological tissue generates random interference patterns, known as speckle [2]. However, speckle can be manipulated to form a spatial, and in some cases temporal [3], focus by controlling the complex incident wavefront. Some recent methods for focusing light through scattering media include adaptive feedback to correct the incident wavefront [4], optical or digital phase conjugation and time reversal [5,6], or measuring and transpose-conjugating the transmission matrix [7].

Changes in the fine structure of a random medium affect scattering of light and the resulting speckle fields. The speckle decorrelation time determines the duration over which wavefront optimization or phase conjugation is valid. Living biological tissues are extremely challenging for focusing since blood flow can decorrelate speckle and suppress any focus enhancement within a few milliseconds [8]. It is even more challenging to scan a focus through a dynamic scattering medium in order to form an image within the speckle decorrelation time.

Iterative WFS using spatial light modulators (SLMs), including sequential and genetic algorithms [4], requires thousands of measurements to form a focus. Liquid-crystal SLMs typically used for WFS phase modulation have millisecond (ms)-regime refresh rates and are thus not suitable for fast dynamic focusing. The use of deformable mirror devices (DMDs) [9] or other micro-electro-mechanical systems (MEMS) [10] to modulate phase can speed up WFS by 1–2 orders of magnitude, but is still too slow for millisecond-scale dynamics. Recently, real-time continuous focusing within 2 ms has been demonstrated with WFS at 350 KHz using a 1D grating light valve (GLV), which to our knowledge is currently the fastest iterative focus optimization method [11].

Compared to iterative WFS, focusing by phase conjugation requires only a single measurement of the propagating scattered light field to generate a phase-conjugated focus. However, photorefractive (analog) time-reversal phase conjugation can take seconds to record a volume hologram [5]. Digital phase conjugation allows much faster focusing using DMDs [6] and binary ferroelectric SLMs [12]. However, even the fastest method takes milliseconds to form a focus.

Acousto-optics (AO) can provide a much faster method than SLMs or DMDs for controlling wavefront amplitude and phase, frequency modulation, as well as steering beams [13]. AO devices have been used for applications such as optical computing, laser displays, spectral filtering, and optical tweezers [14] and FBASIS microscopy [15,16]. Wavefront modulation for fast scanning microcopy [17] as well as wavefront shaping and aberration correction [18] have also been demonstrated using AO.

In this work, we use AO in a different way, by generating and frequency encoding multiple optical beams in parallel to focus and scan light through scattering media. Doppler Encoded Episodic Phase Conjugation (DEEPC) results in momentary constructive coherent summation of speckle in space and time, much like a linear rogue oceanic wave [19]. DEEPC is inspired by SLM-based parallel frequency-multiplexed phase conjugation in scattering media [20], while enabling over 6 orders of magnitude faster focusing and sub-millisecond image scanning.

Like the SLM-based method [20], DEEPC relies on simultaneously modulating the phases of N spatial modes illuminating the sample with N distinct frequencies Ω_n and recording the interference of the scattered temporally modulated light with a reference wavefront at the desired focus location behind or inside a scattering medium. We Fourier-transform the detected signal to recover the local phases of each mode, then conjugate them so that the modes interfere constructively to form a focus.

Yet, our method is not limited by the slow phase-only modulation of SLM pixels or camera frame rate, instead relying on the inherent Doppler encoding and RF-electronic control of AO-diffracted beams, as well as wide-bandwidth single-pixel detection of local intensity modulation at the desired focus.

We diffract an array of uniquely frequency-shifted laser probe beams as well as a common reference beam by driving an AOD, located in a conjugate image plane of a microscope, with a multitone RF signal $s(t) = \sum_{n=0}^{N} c_n \cos(\Omega_n t - \psi_n)$, where c_n and Ω_n are the amplitudes and frequencies of each tone, with $n = 0$ corresponding to the stronger well-separated reference beam, and the RF phases ψ_n are randomized to avoid generating an acoustic pulse. This results in a linear array of illumination beams overlapping on the scattering sample, each arriving at a slightly different angle, taking a random path in the medium, and accumulating a specific optical phase, thereby probing a distinct spatial mode. At the desired focal plane, each scattered probe beam interferes with the scattered reference beam to form a speckle pattern component with a unique RF temporal modulation. Unlike phase-only SLMs, which allow amplitude modulation at the cost of resolution or efficiency, with the AOD the amplitudes of the beams can be set independently along with their phases to optimize focus and coherent gain. The number and angles of the beams are also programmable.

A fast single-pixel detector [e.g., avalanche photodiode (APD)] behind a pinhole at the desired focus location in the speckle field measures an intensity signal $i_d(t)$ due to the coherent sum of N probe beams and a single reference beam given by

$$i_d(t) \propto |\mathcal{E}_p(t)|^2 = \left| \sum_{n=0}^{N} |a_n| e^{j(\omega_0 t - \Omega_n t - \phi_n)} \right|^2, \quad (1)$$

where $\mathcal{E}_p(t)$ is the time-varying net speckle field at the pinhole location, $|a_n|$ and ϕ_n are the local amplitude and phase of the nth beam with an RF Doppler shift Ω_n, and ω_0 is the optical frequency. The pinhole size is chosen to approximately match the smallest speckle to maximize modulation and photon flux.

We then Fourier-transform the detector signal to estimate the probe beam phases relative to the reference beam. To reject interference between the probe beams, we set the reference beam RF Doppler shift Ω_0 such that all frequency differences $\Omega_{n,0} > \Omega_{n,k}$ for $n, k \in [1..N]$ fall within the passband of a filter $H(\Omega)$. The resulting filtered Fourier transform can be written as

$$\mathcal{F}\{i_d(t)\}H(\Omega) = \sum_{n=1}^{N} |\alpha_n| e^{j\varphi_{n,0}} \delta(\Omega - \Omega_{n,0}) * \text{sinc}(\Omega T_M), \quad (2)$$

where each impulse δ corresponds to a distinct interferometric beat, $\Omega_{n,0}$ is the frequency difference between the nth probe beam and the reference beam, while $|\alpha_n|$ and $\varphi_{n,0}$ are the measured amplitude and phase of the corresponding Fourier peak, respectively. The spectrum is convolved with a sinc function due to the finite measurement time T_M, which must be longer than the inverse frequency spacing of the beams to resolve the Fourier coefficients.

To form a focus, we then turn off the reference beam and program the AOD with $s'(t) = \sum_{n=1}^{N} c_n \cos(\Omega_n t - \psi_n - \varphi_{n,0})$ to negate the measured probe beam phases and produce constructive interference at the detector. Due to translation of the acoustic waves within the AOD crystal (and the resulting Doppler shifts of the probe beams), the conjugated speckle patterns combine constructively at the focus only during a short window of time [typically a few nanoseconds (ns)]. Thus, to produce a high-contrast focus, we pulse the laser illumination periodically and in synchrony with the RF waveforms driving the AOD, such that the instantaneous intensity at the focus can be written as

$$|\mathcal{E}_p(t = 0)|^2 = \left| \sum_{n=1}^{N} |\alpha_n| e^{-j(\phi_{n,0} - \varphi_{n,0})} \right|^2 \approx \sum_{n=1}^{N} |a_n|^2. \quad (3)$$

As depicted in Fig. 1, this process can be viewed as an engineered instantaneous spatiotemporal alignment of the phasors in a Rayleigh-distributed random walk [2]. At the instant of focus, the field distribution can be considered as a snapshot of a phase-conjugated time-reversed wavefront, even though we do not physically reverse any wavefronts originating from the focus.

Once the focus has been formed behind a thin scattering sample, correlation of speckle fields known as the memory effect allows scanning of the focused beam within a limited area by tilting the illumination [21]. Scanning in 2D can be accomplished by using a second AOD and shifting the frequencies of the AOD drive signals, making the system well suited for fast and configurable post-focusing scanning without additional components.

The experimental setup is depicted in Fig. 2. We used a 150 mW 532 nm Coherent Compass 315M-150 laser to illuminate a pair of cascaded orthogonally coupled AODs (Crystal

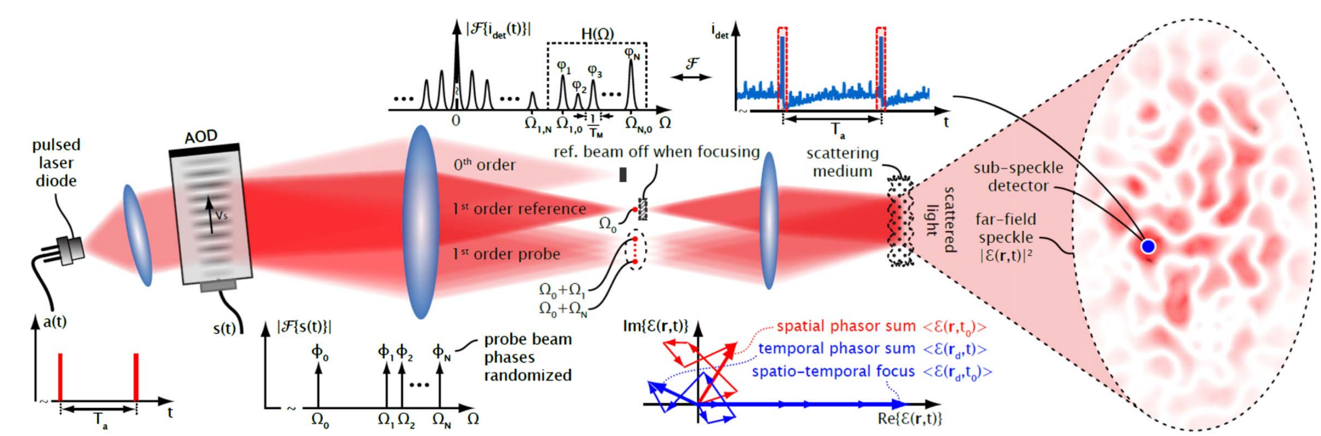

Fig. 1. DEEPC concept. A laser-illuminated AOD driven with a multi-frequency signal diffracts a frequency-mapped array of probe beams and a reference beam, which recombine in a conjugate plane to illuminate a scattering object from varying angles. The temporal signal from a pinhole detector in the far-field speckle pattern is Fourier-transformed to decode the local probe beam phases. A focus is formed by turning off the reference beam, acousto-optically conjugating the phases, and pulsing the laser during the spatio-temporal alignment of the local component speckle phasors.

Technology 4109-3) with a 5 mm diameter beam, giving a time-bandwidth product TB > 400 for each axis. We used a Tektronix AWG5014 arbitrary waveform generator (AWG) to program one of the AODs to diffract a linear array of 100 probe beams spaced by 200 KHz around an 80 MHz center frequency, as well as a 10-times-stronger co-propagating reference beam at 60 MHz. The second AOD was used only for 2D scanning of the phase-conjugated focus and was driven with a single RF tone during measurements. We coupled the resulting beam array into an epi-illumination port of a Nikon Optiphot 2 microscope to illuminate a ground glass diffuser (Thorlabs DG05-1500) via a Nikon MPLAN 20 × 0.4 NA objective. On the transmission side, we placed a 0.5 mm diameter 1 GHz Hamamatsu C5658 APD detector in the speckle field at a ~35 cm distance from the diffuser to record the frequency-multiplexed signal. The detector signal was amplified, acquired for 10 μs (without averaging) using a Tektronix MDO4034 oscilloscope, and processed using FFT algorithms in Matlab to recover the probe beam phases. The AWG was then re-programmed with the conjugated signal and the reference beam removed to generate an instantaneous focal spot at the detector location. To "freeze" the temporary focus enhancement, we used an acousto-optic modulator (AOM) (NEOS N23080) to modulate the laser, generating 50 ns pulses with a 10 μs repetition period (a pulsed laser diode could be used instead). The pulse width was chosen to match the 20 MHz bandwidth of the frequency comb, maximizing both enhancement and photon flux. Finally, we used a beam splitter to direct 20% of the light toward a lensless Ximea xiQ CMOS camera to image the enhanced focus and scanned spots obtained by frequency-shifting the phase-conjugated AOD drive signals.

Figure 3 shows our first results demonstrating enhanced focusing behind a diffuser obtained by measuring the phases of 100 beams in just 10 μs and conjugating them. By pulsing the laser only at the time of temporal focusing, as indicated by the red rectangles in Fig. 3(c), a spatially focused spot was clearly observed. The camera image of Fig. 3(e) shows focusing with an enhancement of ~58 ×, calculated as the peak intensity to average background ratio. As shown in Figs. 3(d) and 3(f), placing the pinhole within a dark (but not fully nulled) reference speckle instead of a bright one results in comparable focus enhancement,

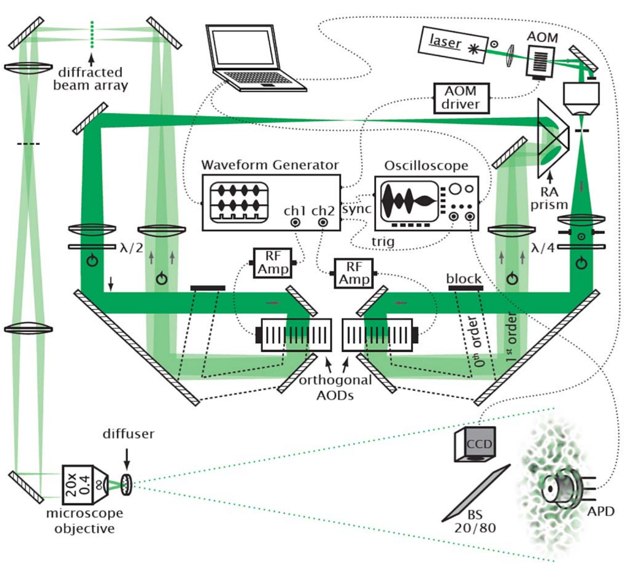

Fig. 2. DEEPC experiment (only two array beams shown for clarity).

demonstrating the method's wide dynamic range (due to coherent gain) allowing focusing at almost any pinhole position.

Due to the memory effect, it is also possible to form an image through a thin scattering medium by scanning the phase-conjugated spot over a limited area. To accomplish this, both AOD signals are sequentially frequency-shifted, thereby tuning the diffraction angles of the phase-conjugated beams in 2D. Each speckle-sized resolvable spot produced in this way corresponds to a ~100 kHz frequency shift and can be addressed in ~10 μs. Figure 3(g) shows an example of scanning a focal spot though 8 different locations on a 300 kHz frequency grid in just 80 μs.

Visualization 1 shows another scanning example where 100 angles (or spots) are sequentially addressed using a 200 KHz frequency spacing. Such wide-field scanning is possible since it is not limited by the memory effect due to single-surface scattering by the ground glass sample. In this case we slowed down the scan to match the video rate. However, with a fast single-pixel detector, the full addressable field of 200 × 400 speckle-sized resolvable spots, limited by the AOD time-bandwidth products, could be scanned in ~1 s, or potentially even in a few milliseconds by instead placing the sample in a Fourier plane, where the illumination angle is scanned by the traveling acoustic wave.

While the results in Fig. 3 demonstrate measurement of 100 different complex modes propagating within the scattering medium in just 10 μs and scanning of the spot in under 1 ms, it currently takes much longer to process the data, conjugate the phases, and reprogram the AWG to form a focus. However, these bottlenecks can be overcome to allow high-speed continuous focusing. For example, a modern FPGA takes under 1 μs to perform a 1,024-point FFT [22], which is sufficient to resolve hundreds of frequency-encoded probe beams. The same FPGA could then be used to adaptively generate the AOD signal to produce a focus on the same 10 μs time scale.

While our experiments were not limited by SNR, in other scenarios, such as imaging in biological tissues where the speckle fields are sampled by embedded fluorescent beads (or other guide stars), weak signals could require additional averaging and reduce acquisition speed. Nevertheless, we are encouraged by our previous experiments with F-BASIS microscopy, where we were able to form 3D images of fluorescent beads in a few milliseconds using a comparable number of RF-encoded beams and a fast PMT detector with biocompatible irradiance levels [16]. Recording fluorescence guide-star signals in an epi-microscopy configuration could allow non-invasive focusing and imaging inside scattering media.

While the intensity enhancement in our experiments did not scale with N as predicted by theory, and is ~2 × lower than the number of beams, this can be attributed in part to photon and laser intensity noise, unmodulated light, as well as AO diffraction and RF-electronic nonlinearities. Rejecting weak RF beats visible in Fig. 3(a), which may be incorrectly conjugated, could reduce distortion of the temporal foci and improve enhancement.

Additionally, in our experiment, each beam illuminates the thin scattering sample at a different angle, so that the far-field speckle patterns are correlated and shifted in space. For the random walk process model to apply, the speckle shift at the pinhole due to each beam should be larger than the average speckle grain size. In practice, the shift depends on the applied RF frequency difference and may be smaller than the characteristic speckle size determined by the fine structure of the sample [2]. We observed

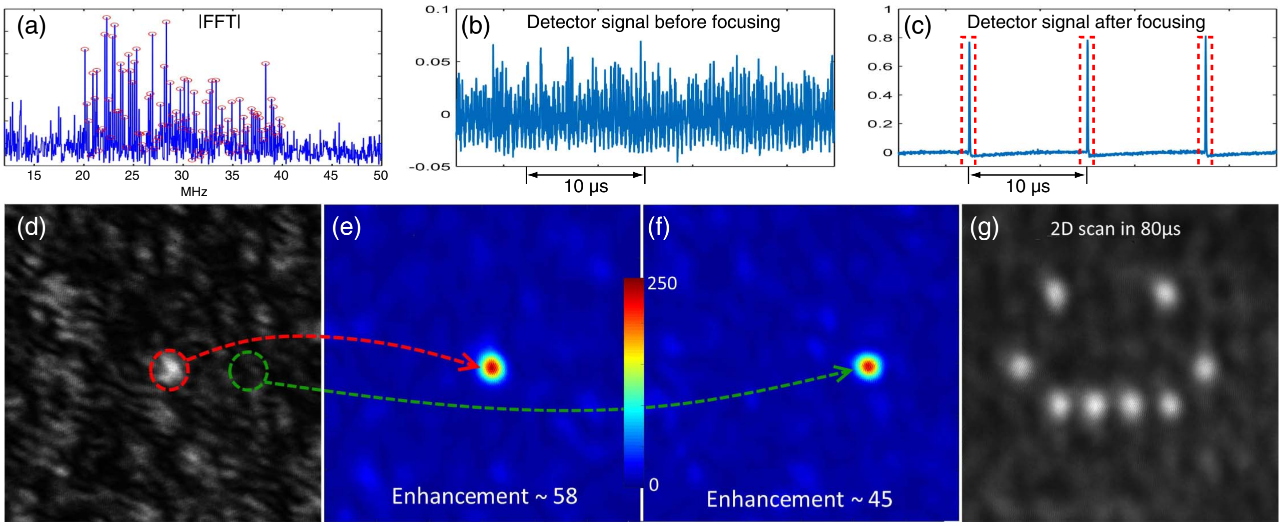

Fig. 3. Focusing and scanning results. (a) Filtered Fourier transform of detector signal showing frequency comb corresponding to probe beams. (b) Detector signal before phase conjugation. (c) Detector signal after phase conjugation showing temporal focusing (blue). The laser is pulsed for ~50 ns during focus events (red). Signal between the temporal foci is reduced w.r.t. (b) due to energy conservation. (d) Image of reference beam speckle showing pinhole locations within bright and dark speckle regions. (e-f) Corresponding foci obtained with 100 beams and a 10 μs measurement. (g) 80 μs wide-field 2D scan of the focus in (e) repeated multiple times during camera exposure, dwelling 10 μs at each of eight focal spots.

that increasing the number of beams from 100 to 400 did not improve enhancement significantly, as expected when the characteristic speckle size exceeds the speckle shift.

To maximize enhancement with this scheme, the beam spacing could be chosen to match the characteristic speckle size of the sample. To increase the number of spatial modes further, the second orthogonal AOD could be used to generate a 2D array of beams. While all of the N^2 beam phases could be measured simultaneously (using a longer T_M to resolve the tighter RF comb), the two cascaded AODs do not provide enough degrees of freedom for independent phase conjugation of N^2 beams. In this case, a separate phase modulator, such as an SLM, could be used to conjugate all of the phases in a single shot to form a focus in a few ms, which can then be rapidly scanned in 2D with AODs.

Other future DEEPC experiments may include Fourier plane illumination with spatially resolved beams and focusing through volume-scattering samples. While we did not control amplitude, adjusting drive signal coefficients c_n to compensate the measured amplitudes $|\alpha_n|$ could further improve focusing [4].

We have demonstrated high-speed phase conjugation and focusing through scattering media with a novel acousto-optic scheme employing multiple RF-encoded beams and a single-point detector. We showed a 2-orders-of-magnitude measurement speed improvement over the fastest reported phase conjugation methods, as well as sub-millisecond wide-field scanning of the focal spot faster than the typical scattering decorrelation time in living biological tissues. With agile electronics, this method could be used to attain closed-loop focusing on microsecond timescales. Furthermore, bright embedded fluorescent or scattering sources could enable focusing and imaging deep within dynamic scattering media.

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