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Coherent Laser Source for High Frame-Rate Optical Time-Stretch Microscopy at 1.0 μm

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***Abstract*—We demonstrate a coherent picosecond pulsed fiber laser for the high frame-rate optical time-stretch microscopy at 1.0 μm. The spectrum of a picosecond pulsed laser is commonly broadened before the time-stretch imaging, which however will degrade its stability and coherence. As a result, it is required to enhance the degraded signal-to-noise ratio by averaging, which would compromise the frame rate on the other hand. Instead of pursuing such kind of spectrum-broadened picosecond pulsed laser sources, we propose a pulse train extracted directly from an all-normal dispersion mode-locked fiber laser with a rectangle-shaped optical spectrum. It delivers stable and coherent performance for the serial time-encoded amplified microscopy at 1.0 μm. With this robust picosecond pulsed laser, real-time stain-free flow imaging with a frame rate of 26.25 MHz and a spatial resolution of < 2 μm is demonstrated. Featured with the compact configuration and good coherence property, it is a promising picosecond pulsed fiber laser source for the ultrafast interferometric time-stretch microscopy at 1.0 μm.**

***Index Terms*—Medical and biological imaging, supercontinuum generation, ultrafast technology, ytterbium mode-locked laser.**

I. Introduction

In GREAT demand for the studies of high-speed dynamical phenomena and high–throughput cellular/molecular diagnostics, the imaging system with high temporal resolution has attracted great attention in recent years [1], [2]. Nowadays, the world-fastest charge-coupled devices (CCD) and complementary metal–oxide–semiconductor (CMOS) imagers can operate at a frame rate of 1 and 10 MHz [3], respectively. However, this kind of imagers is featured with relatively long shutter or exposure times, a time-consuming readout process, and a fundamental tradeoff between sensitivity and speed [4]–[6]. Thus, it does not facilitate the real-time high-speed imaging with high spatial resolution and sensitivity. In addition, it requires high-power illumination focusing on the biological samples, which is harmful for the specimens. While the CCD/CMOS imagers are still the mainstream in optical microscopy applications, the serial time-encoded amplified microscopy (STEAM) recently has been proposed and demonstrated to support real-time ultrahigh frame-rate imaging without sacrificing the sensitivity [7], [8]. Based on the space-frequency-time mapping and single-pixel detection, it eliminates the requirement of CCD/CMOS imagers. With the commonly available components and techniques at the telecommunication window, i.e., 1.5 μm, prior works on the STEAM were mostly demonstrated at this wavelength [7]–[15]. For optical diagnostics and biophotonic applications, however, the 1.0-μm spectral window is more favorable [16].

In theory, a broad optical spectrum is required to conduct the unique space-frequency-time encoding process in the STEAM system [7]. As a potential candidate, supercontinuum (SC) generated by pump pulses along a piece of highly-nonlinear fiber (HNLF) has been used to implement the STEAM systems at both 1.0 μm [16] and 1.5 μm [7], [10]–[15]. The numerical simulation results have revealed that the nonlinear effects, including four-wave mixing, modulation instability (MI) and stimulated Raman scattering, play a key role in the SC generation with long pulses [17]. Unfortunately, MI is initiated from the noise, featuring this kind of SC picosecond pulse train with a large shot-to-shot fluctuation and bad temporal coherence outside the pumped area. Thus, the averaging operation is usually conducted to enhance the signal-to-noise ratio (SNR) of the STEAM signal with such kind of picosecond SC source, which however limits the frame rate and hinders the real-time flow imaging. Consequently, the frame rate of a STEAM system with picosecond SC at 1.0 μm is limited to 10 MHz for the static imaging [16]. Those shortcomings do not facilitate most of the applications in the scope of observing transient processes and rapid dynamics. In this regard, a stable pulse train directly extracted from a resonator with a broad and flat optical spectrum is an ideal candidate for the real-time high frame-rate optical time-stretch microscopy.

At 1.5 μm, a femtosecond nonlinear polarization rotation (NPR) mode-locked fiber laser is characterized with a broad optical spectrum, which benefits from the flexibility in the dispersion management of the optical fiber at this wavelength [18], [19]. When it is used directly to conduct STEAM, however, the non-flat optical spectrum does not facilitate the space-frequency-time mapping process of a signal. It is because that the amplitude of the serial time-encoded waveform of a spatial signal will become non-uniform and finally the weak part of it will be buried in the noise. Thus, the femtosecond pulsed laser

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at this wavelength is often required to nonlinearly broaden and slightly flatten its optical spectrum, which however would make the system more complex and costly [10]–[13]. On the contrary, induced by the balance between the spectral broadening and gain-narrowing in an all-normal dispersion cavity [20], the NPR mode-locked ytterbium fiber laser at 1.0 μm can directly deliver a pulse train with a broad rectangle-shaped optical spectrum. Thus, it eliminates the requirements of spectral broadening and flattening, which makes the system more compact and reduces the cost of the imaging system. In addition, the all-normal dispersion mode-locked laser at 1.0 μm delivers picosecond pulse, which is easier to amplify, compared with the femtosecond pulse provided by the NPR mode-locked fiber laser at 1.5 μm. Such a novel fiber laser has been widely studied recently, but its practical applications have been rarely presented yet [21]–[24]. Here, we present an all-normal dispersion mode-locked ytterbium fiber laser with a wide tuning range (1025–1085 nm) and a rectangle-shaped optical spectrum for the STEAM application. By comparing with the commonly-used SC laser source, we demonstrate that it is a promising candidate for the real-time high frame-rate optical time-stretch microscopy at 1.0 μm.

II. Coherent Laser Source

The experimental setup of the mode-locked ytterbium fiber laser by a NPR technique is shown in the dotted box in Fig. 1(a). A piece of the double-cladding highly-doped ytterbium fiber (DC Yb fiber) was served as the gain medium, whose length is around 1 m. This active fiber was pumped by a 980-nm laser diode (LD) through a 980/1060 nm wavelength-division multiplexing (WDM) coupler. A polarization insensitive isolator (ISO) was employed to ensure the unidirectional operation. The pulse compression inside the cavity was realized by two polarization controllers (PCs) and a polarization beam splitter (PBS): the PCs were used to adjust the state of polarization of the lightwave inside the cavity, while the PBS provided polarization-dependent loss. By adjusting the orientation of the PCs, we can filter out the peak of the pulse after the PBS and block the edge of the pulse, and then the initial noise-like pulse was compressed to a stable ultrashort optical pulse after enough round trips. A free-space bandpass filter was utilized to induce spectral filtering effect and realize wavelength-tunable operation simultaneously. All the collimators were used to extract the lightwave out or couple it back into the fiber. The round-trip time of the cavity was about 38.1 ns, corresponding to a repetition rate of 26.25 MHz. By rotating the incident angle of the filter, the central wavelength of a mode-locked spectrum can be tuned from ~1025 to ~1085 nm continuously, as shown in Fig. 1(b). The output power measured at the PBS varied in the range of 9.65 and 10.48 mW when the central wavelength was tuned over this range, owing to the different cavity loss at different central wavelength.

To quantify the stability and coherence of the mode-locked pulse train, we fixed the central wavelength of the mode- locked laser at ~1064 nm [the green curve in Fig. 1(c)]. As can be observed, the pulse train delivers an almost rectangle-shaped optical spectrum benefiting from the balance between the spectral broadening and gain-narrowing in the all-normal dispersion regime [20]. The pulsed duration is 4.2 ps with 1.1-ps jitter as shown in the inset of Fig. 1(c). In order to investigate the temporal coherence of the mode-locked pulse, the pulse train was launched into a homemade Mach–Zehnder interferometer (MZI) with a path difference almost equal to the separation of the adjacent pump pulses, i.e., ~7.47 m, corresponding to a

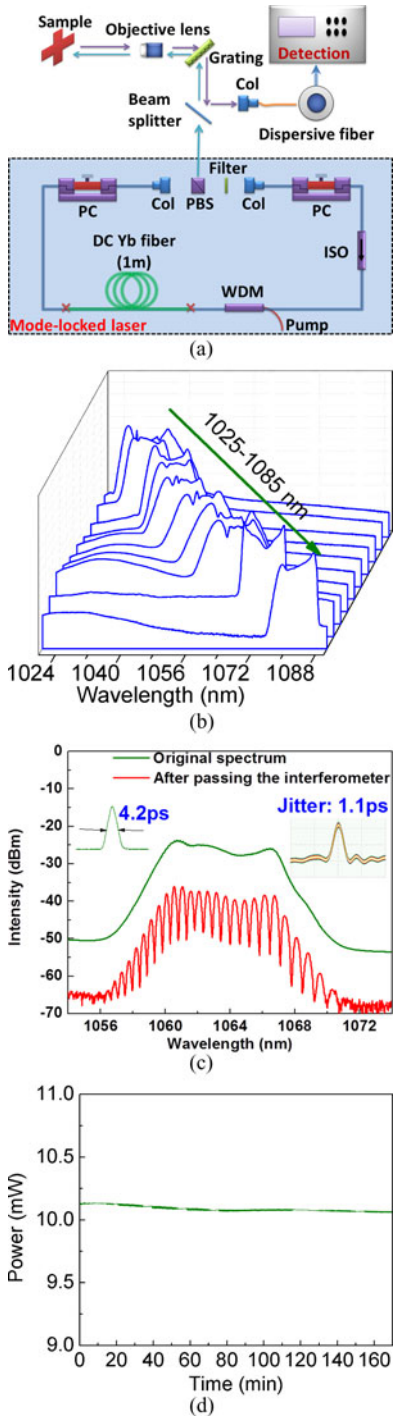

Fig. 1. (a) The experimental setup of the mode-locked ytterbium fiber laser and the STEAM schematic. (b) The optical spectra of the mode-locked pulse with different central wavelength. (c) The optical spectra of the mode-locked pulse centered at 1064 nm. Inset: the autocorrelation trace (left) and the eye diagram of the mode-locked pulse (right). (d) The optical output power over 170 min at 1064 nm.

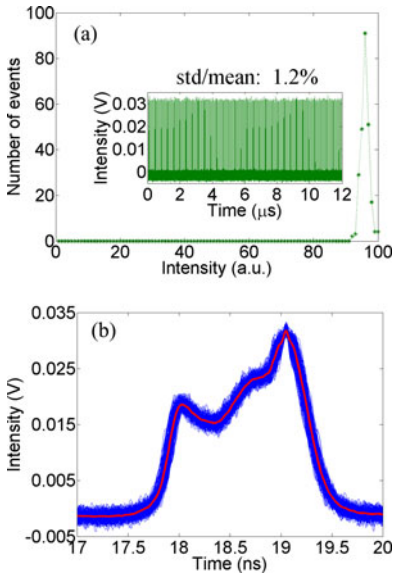

Fig. 2. (a) The histogram of the pulse train. Inset: the pulse train recorded by the real-time oscilloscope. (b) 250 stretched pulses overlapped together, where the red curve is the calculated average from those pulses.

round-trip time of 38.1 ns. As can be observed from the red curve of Fig. 1(c), the interference spectrum reveals a stable modulation structure, produced by the temporal overlapping of the neighboring mode-locked pulses. The contrast ratio of the interference fringe is around 15 dB. The coherence characteristic of other central wavelength was also examined by the same method, and similar results were obtained for the wavelength from 1025 to 1068 nm. For the wavelength longer than 1068 nm, however, the contrast ratio of the interference fringe was reduced to around 10 dB, which can be attributed to the increasing ASE noise at around 1030 nm associated with the mode-locked pulse [as shown in Fig. 1(b)]. To examine the long-term stability of the mode-locked pulse, the optical power at 1064 nm was recorded over 170 min by a power meter (Thorlabs, PM100D), and it showed a ~0.03-dB fluctuation, as shown in Fig. 1(d). With the excellent temporal coherence and broad rectangle-shaped spectrum, it is a promising broadband laser source for the real-time interferometric time-stretch microscopy at 1.0 μm.

The real-time pulse train recorded by a 16-GHz real-time oscilloscope is shown in the inset of Fig. 2(a), where the observation time was 12 μs and the pulse repetition rate was 26.25 MHz. 250 pulses from the recorded pulse train were used to calculate the histogram of the pulse intensity, as illustrated in Fig. 2(a). As can be observed there, the intensity of the mode-locked pulse has a very small fluctuation, giving a ratio of standard deviation to the mean (std/mean) of the pulse intensity at 1.2%. To examine the performance of the frequency-time mapping, the pulse train was stretched by a 5-km single-mode fiber (SMF) with total group-velocity dispersion around 0.15 ns/nm. 250 stretched pulses were recorded by the same real-time oscilloscope, and then overlapped together, as shown in Fig. 2(b). Ignoring the noise from the detection system (random noise with an amplitude of ~2 mV),it reveals that the stretched pulses deliver stable frequency-time mapping. The average of those stretched pulses, illustrated as the red curve in Fig. 2(b), is consistent with its optical spectrum [Fig. 1(c)], indicating a linear frequency-time mapping process.

III. Commonly-Used Laser Source for STEAM

Generally speaking, a commercially available picosecond laser source at 1.0 μm has a spectral bandwidth less than 1 nm. In order to utilize it in the space-frequency-time mapping inside the STEAM system, we have to broaden its spectrum to over 10 nm, with a flat top at the same time, as shown in [16](the first demonstrated 1.0-μm STEAM). Unfortunately, both the stability and coherence property of the generated SC pulse are poor due to the nonlinear effects in the SC generation process. To elaborate it further, we conducted experimental analyses to examine the degraded performance of the SC with a picosecond pump pulsed laser here.

A picosecond pulsed laser, time-bandwidth LYNX, was utilized as the pump source for the SC generation. Its pulsed duration was measured to be 9 ps, and the optical spectrum is shown as the green curve in Fig. 3(a), which reveals a narrow bandwidth (<0.5 nm). Fig. 3(b) shows the histogram of the pump pulse intensity, which was calculated from 250 pulses recorded by the real-time oscilloscope. The std/mean of the pump pulse intensity was 1.7%, comparable with that of the homemade all-normal dispersion mode-locked ytterbium fiber laser presented above. After passing the pump pulse through a 20-m photonic crystal fiber, the generated SC pulse spectrum is shown in Fig. 3(a). Noted that the generated SC pulse has been amplified by a commercial ytterbium-doped fiber amplifier to boost up its power density (~3 mW/nm), which is essential for the STEAM process, otherwise the signal would be deeply buried in the noise after the space-frequency-time mapping. Then, the generated SC was launched into a MZI to examine the temporal coherence. The optical path difference of the MZI is about 9.8 m, consistent with the 50-ns temporal separation of the pump pulse (i.e., a repetition rate of 20 MHz). The interference spectrum is depicted as the blue curve in Fig. 3(a). It reveals interference fringes around the pump region, as shown in the inset of Fig. 3(a). Outside the pump region, however, no such interference fringe can be observed, suggesting poor coherence in these regions. To investigate the pulse-to-pulse fluctuation of the generated SC pulse, a longpass filter (beyond 1075 nm) was used to extract the redshift part of the SC. The histogram of the redshift SC is shown in Fig. 3(c), together with the real-time pulse train in the inset. It is clear that the distribution of the SC pulse intensity has a wider distribution range compared with that of the original pump pulse, and the std/mean has increased from 1.7% to 14.9%. The timing jitter of the SC pulse was measured to be 4.1 ps, which was also worse than that of the all-normal dispersion mode-locked pulse. The overlapped pulses of the redshift part after stretching by the same SMF, as shown in Fig. 3(d), however are very noisy due to the noise-initiated MI effect with random phase distribution.

The experimental results show that the performance of a picosecond pulse train, especially the stability, has

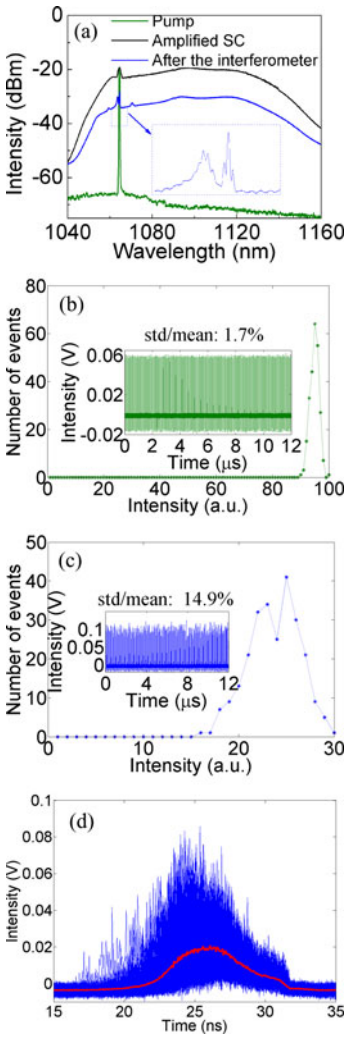

Fig. 3. (a) The optical spectra, where the green curve is the pump spectrum and blue curve is the interference spectrum after passing a MZI. Inset: the enlarged view of the pump region of the interference spectrum. (b) The histogram of the pump pulse intensity. Inset: the pump pulse train recorded by the real-time oscilloscope. (c) The histogram of the redshift part of the amplified SC pulse intensity. Inset: the pulse train recorded by the real-time oscilloscope. (d) 250 stretched pulses overlapped together, where the red curve is the calculated average from those pulses.

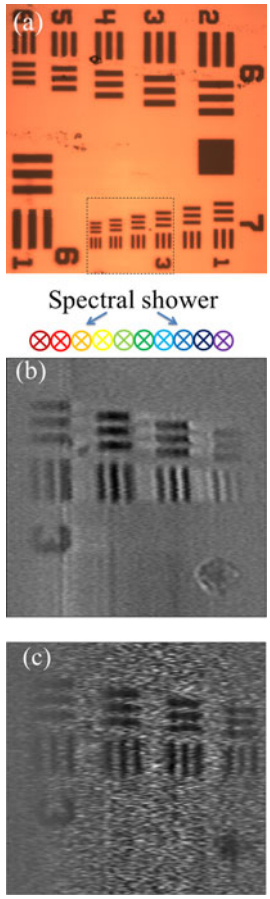

Fig. 4. (a) The light microscope image of the resolution target, where the imaged area of the STEAM has been marked with black dotted line. (b) The STEAM image by using the homemade all-normal dispersion mode-locked fiber laser. (c) The STEAM image by using the SC laser source.

been degraded significantly in the process of the spectral broadening, which actually does not facilitate the high quality imaging with the STEAM system. To stabilize the picosecond SC, stabilization techniques including triggering with a pulse-seed or CW-seed [25], [26], introducing a feedback loop [27], modulating the pump pulse train [28] and engineering the dispersion of the fiber medium [29], have been proposed. However, all these techniques inevitably raise the cost and complexity of the STEAM system. Although CW-stabilized picosecond SC has been used to demonstrate the static STEAM imaging at 1.5 μm [15], its resolution was limited to around 31.3 μm and no flow STEAM imaging of biological sample has been presented yet. Femtosecond pulse, on the other hand, has been demonstrated to support stable generation of SC pulse [17]. By using this kind of femtosecond SC source, a 6.1-MHz flow imaging of the metal microsphere flowing at a speed of 2.4 m/s was realized in [7]. However, as in the case with picosecond SC source, it requires spectral broadening and flattening. In addition, the amplification of femtosecond pulse needs complicated chirp management. Compared with those femtosecond/picosecond SC sources, the all-normal dispersion mode-locked fiber laser at 1.0 μm is superior since no spectral reshaping is required, and the pulse with picosecond duration is easier to be amplified. More importantly, the frame rate of the STEAM system with this laser is limited by the fundamental repetition rate of the mode-locked pulse, but not the noise issue. Thus, a 200-MHz frame rate can be expected by using a shorter cavity length, i.e., $\sim$1 m.

IV. Imaging Performance

To compare the performance of these two sources, they were respectively employed in the STEAM system, whose schematic diagram is shown in Fig. 1(a). The detail of the experimental setup of the STEAM system at 1.0 μm has already been covered in Ref. [6]. With the frame rates of 26.25 MHz for the all-normal dispersion mode-locked ytterbium fiber laser and 5 MHz (4 averages) for the SC pulsed laser, the STEAM images of the smallest group (Group 7 with a smallest linewidth of $\sim$2 μm) of a

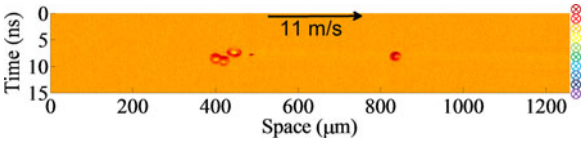

Fig. 5. Stain-free real-time image of the HeLa cells with a flow speed of ∼11 m/s. Noted that the spectral shower illuminated into the page, while it was along the horizontal direction for Fig. 4(b) and (c), and along the vertical direction here.

resolution target [Fig. 4(a)] are shown in Fig. 4(b) and (c), respectively. The images were captured by 200 line scans with a step of 0.5 μm, from top to the bottom in Fig. 4(b) and (c). It is clear that the mode-locked laser delivers a better image quality in terms of noise and image contrast compared with the SC source. It is mainly attributed to the more stable oscillation of the all-normal dispersion mode-locked fiber laser. Considering the good temporal coherence and stability of this homemade mode-locked ytterbium fiber laser, it is an ideal candidate laser source for STEAM system, especially the high frame-rate real-time interferometric optical time-stretch microscopy at 1.0 μm.

In order to further demonstrate its stable performance in the high-speed time-stretch imaging system, we utilized this mode-locked laser to conduct the ultrahigh-speed stain-free flow imaging. Different from Fig. 1(a), the STEAM setup was modified by adding another identical objective lens and a mirror behind the sample to achieve a double-pass transmission operation mode. The sample, human cervical cancer cells (HeLa), was flowing at a speed of ∼11 m/s in a polydimethylsiloxane microfluidic channel. By illuminating the spectral shower on a direction perpendicular to the flow direction, the information of the flow cells was naturally encoded into the spectral shower at a frame rate of 26.25 MHz without the scanning operation. 3000 time-stretch pulses (frames) encoded with the information of the flow cells were recorded by the real-time oscilloscope, and all of them were then digitally stacked along the flow direction as shown in Fig. 5, by which we can recover the dynamic process of the flow HeLa cells. As can be observed, the stable and clean mode-locked pulses make the cells well distinguished from the background, which again verifies that it is a promising fiber laser source for the high-speed time-stretch microscopy.

V. Conclusion

In summary, we have demonstrated a stable and coherent picosecond pulsed fiber laser for the high frame-rate real-time optical time-stretch microscopy at 1.0 μm. It has been verified experimentally that the stability of the original picosecond pulse train would be degraded significantly in the process of spectral broadening for STEAM imaging, which is mainly due to the MI effect. By mode-locking at all-normal dispersion regime, a stable broadband picosecond pulse train can be directly achieved from a compact resonator with good temporal coherence. When it is applied to the STEAM system, the image of the resolution target with higher image contrast and less noise can be obtained at a higher frame rate (26.25 MHz), compared with the picosecond pulsed SC laser. Its promising performance is also evident from the real-time stain-free flow imaging, where the cells are well distinguished from the clean background. Such a stable and coherent laser source would find applications in the ultrafast real-time interferometric time-stretch microscopy at the optimal diagnostic window (i.e., 1.0 μm). It would not only make the STEAM-based imaging system much more compact and low-cost, but also facilitate the frame-rate enhancement without degrading the stability and coherence.

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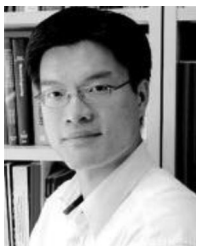

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