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Fiber Lasers for medical diagnostics and treatments:
State of the art, challenges and future perspectives
(Keynote Paper)

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ABSTRACT

Fiber laser is a fast growing yet quite young type of laser with huge potential in healthcare due to versatility and reliability. The talk discusses present and future for fiber lasers for medical applications and address future challenges and competitions with other sources.

Keywords: Fiber Lasers, Mid-Infrared, Medical Diagnostic, Biomedical Imaging

1. INTRODUCTION

Fiber lasers since their invention, over fifty years ago by E. Snitizer [1-3], have progressed at a different pace then solid-state lasers due to the constrain of drawing quality fibers. No much of a progress for nearly twenty years until the telecom boom, who boosted high-quality silica fiber for transmission, cheap and powerful fiber coupled 980-nm semiconductor lasers and Er-doped active fibers for amplifiers [4,5]. We can therefore state that among the various type of lasers, fiber lasers are, both as research and commercial tools, the youngest, yet the fastest growing due to several factors: reliability, efficiency, lower power consumption and overall cost, high power, high beam quality and flexibility (fiber non-linearity is easily exploited) [6-8]. As example, commercially available laser with 10 kW output power in single mode fibers were developed less than ten years ago [9]. Nowadays fiber laser are the tools boosting almost any type of industry and research activity from advanced manufacturing to sensing of pollutants, to life science and of course, to medical investigation and treatments. In this paper the author first discusses the state of the art in term of available output wavelength from fiber lasers and how they can satisfy requirements to operate in the first four optical biological windows [10]; second is briefly addressed, from a general point of view, where fiber lasers may offer a key advantage compared to most sophisticated solid-state laser systems or the cheaper compound semiconductor lasers; third indications on the extension of the available wavelength interval are given, focusing on Visible/UV and mid-infrared lasers (MIR) continuum generation and on the new class of mid-infrared fiber laser [11-15]. The paper does not aim to be exhaustive, nor to provide a summary of all contributions so far in the field, but to provide indications on the role fiber lasers may play in the future in the medical field and which new tools an end user may expect to find available in the next future.

2. DIRECT EMISSION AND OPTICAL BIOLOGICAL WINDOWS

Fiber light sources are now widely used, yet are mostly based on few main components, originated by telecom research, the (Al-)silicate fiber and the 980-nm diode pump diodes. Is therefore not surprising that almost all applications for manufacturing and most of the others rely mainly on Yb or Er fiber lasers, both pumped at 980 nm, and only recently on Tm fiber lasers pumped at 780 nm. This may not be evident from Figure 1, showing the main direct emission from fiber lasers. The vertical dashed areas represent the optical windows for biological investigation [10,16] we will discuss it later in this section. To appreciate Figure 1 we should also remember that that main efficient transitions, able to generate high power are around 1 micron (Yb), 1.5 micron (Er), 2 micron (Tm and Ho) and around 3 micron (Er),the latter using flurozirconate fibers [17]. The other demonstrated transitions are quite at an early development stage missing further

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development and often high-power pump diode at the desired required wavelength. We also note the four micron operation of Ho lasers was achieved at cryogenic temperature [18]. The conclusions we can draw from Figure 1 is that even considering all possible wavelength transitions is not possible to fully cover the optical spectrum, nor, for example, the 3rd and 4th biological windows were interesting applications are awaiting a reliable and cheap tool.

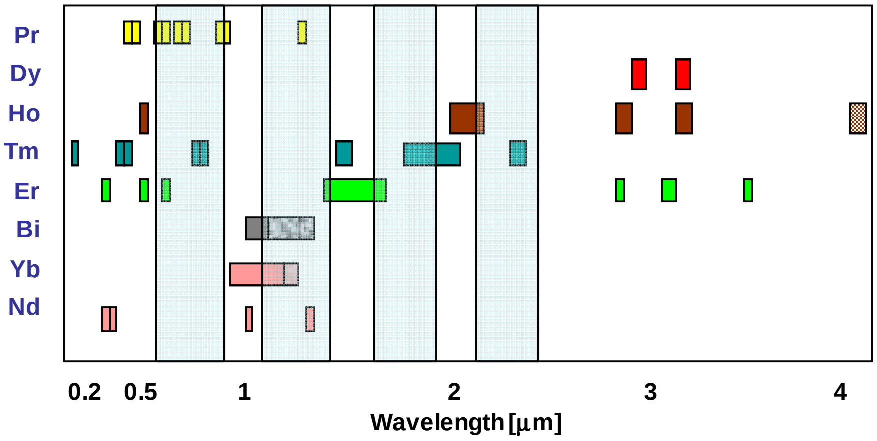

Figure 1: Table of main results of direct emission from fiber lasers with four biological optical windows (gray areas, first on the left).

To address the problem of wavelength gaps so far frequency manipulation is the only solution if we want (almost) all fiber systems. New wavelengths in the visible, for example, are infact often commercially generated not by direct emission but by playing with frequency(-ies) (doubling, tripling, summing) of Er- and Yb-fiber lasers often using non-linear external crystals. A good example of this approach is reported in Ref.19. This allows to cover the left side of the most efficient transitions. Gaps in the output wavelengths on the red side of the most efficient transitions may instead be covered by one or more Raman shifts or, for pulsed operation, by soliton self-frequency shift. A few example are now given. The advantage of long wavelength optical windows relies on the specific photon/tissue interaction: the 3rd window (1600 nm – 1870 nm) offer a good balance between absorption and scattering and therefore can be exploited for deep imaging, while the 4th window (2100 nm – 2300 nm) may be used to study high collagen content tissues like bones and malignant tissues [10]. Figure 1 shows a clear gap between the longest achievable wavelength with erbium and the shortest achievable with thulium (roughly 1630 nm to 1800 nm). For continuous wave lasers two Raman shifts may bring from the most efficient Er transition around 1550 nm wavelength to around 1700 nm. In Ref.20 a 1542 nm Er/Yb based source is frequency shifted by a two-stage cascaded Raman resonator with intermediate wavelength of 1630 nm and output wavelength of 1708 nm, a specific wavelength also useful for treatment of sebaceous glands in human skin. In case of short pulse sources output red-shift can be achieved by self-frequency shift (intrapulse Raman scattering) [21,22]. In both case the extra stage after the seed laser, cascaded Raman resonators in first case or a nonlinear fiber in the second case, are simply spliced to the output fiber of the seed lasers and the increased footprint is a fraction of the volume of the seed lasers and do not decrease the device reliability.

3. REPLACING EXPENSIVE TOOLS

Fiber lasers are somehow in the middle of two strong competitors, large benchtop solid-state lasers and cheap compound semiconductor lasers. If we look at UK numbers we notice that the number of Hospitals and Universities are in the order of 10^2, Genaral Practices (GPs) are in the order of 10^4 [23,24], Hospital beds 10^5 [24] and population 6 10^7. If no high power or specific pulse shape is required for an handheld devices, possibly to be used at GP levels, the only financially solutions is likely to use compound semiconductor lasers to reduce costs. They offer cheap compact solutions for devices to be produced in large number. Eventually compact fiber lasers with a specific applications may found their way into GP practices. However fiber laser offer quality, lower cost, and reliability required for hospital applications and are able both to win the competition of compound semiconductor lasers (in term of performance and sometime reliability) and to replace more expensive system based on solid state lasers (thanks to lower cost, better reliability) such Ti:Sapphire lasers and optical parametric oscillator systems. The same way they can replace tools in R&D laboratories. Fiber lasers also offer a small footprint, for example the footprint of a 4W 1060-nm 80 MHz fs lasers able to replace a fixed wavelength Ti:Sapphire is only about 0.3x0.3x0.06 m^3. A good example of all-fiber systems developed to substitute larger solid-state system based on Ti:Sapphires is reported for CARS microscopy in Ref.26 and for coherent anti-Stokes Raman scattering microscopy in Ref.27.

4. FIBER FOR CONTINUUM GENERATION UV TO MIR

Several biomedical applications may require the use of a source able to generate short pulses in the UV and entire visible spectral region. This ability is a key issue for several applications and in particular for material investigation, the possibility of investigating proteins and their interactions in living cells, and biomedical applications [28,29]. Confocal laser scanning microscopy and fluorescence lifetime imaging microscopy also require coherent laser sources in this range. Standard solutions is to use a Ti:Sapphire laser and exploiting supercontinuum (SC) generation in highly-nonlinear microstructured fiber [30] followed by spectral filtering to select the desired wavelength. However the SC spanning is limited at a green/blue edge due to the large dispersion of silica in the blue and UV spectral region. One possibility to overcame this limitations is to propagate into high order modes were waveguide dispersion shift the zero dispersion wavelength towards shorter wavelength. In Ref.31 and Ref.32 authors report on a source able to provide probe pulses in the UV visible range (300 nm to 700 nm) and on the demonstration of its application to neural rat cell and hyperspectral (fluorescence lifetime) imaging measurements.

Mid-infrared continuum sources are also fundamental to address the mid-infrared spectral region that is of great technical and scientific interest because most molecules display fundamental vibrational absorptions in this region, leaving distinctive spectral fingerprints. It is therefore of key importance for several applications ranging from early cancer diagnostics [33] to food quality control [34]. Wide spectra spanning above 15 microns have been achieved [35]. However one of the first and most significant result that showing the future possibilities of all fiber sources is the results reported Nottingham University, UK and DTU, Denmark. A supercontinuum spectrum spanning 1.5 micron to 11.7 micron was achieved using a fs pump at 4.5 micron (the potential emission wavelength of a Pr-doped fiber lasers), and up to 13.3 micron was achieved with pumping at 6.3 micron [36]. The work was within the Minerva FP7 project and more information can be found in Ref.37.

5. MIR QUEST: EXPERIMENTS AND SIMULATION

Finally we have the missing laser, the mid-infrared one and by mid-infrared the author means lasers operating at above 3 micron where the MIR interval starts. A region merging with the fingerprint region and therefore able to detected 3D structures and discriminate among isomer species [11]. A lot of work was done in 3 micron Er-doped fluorozirconate fibers [17] and recent progresses shows possibility of extending the output wavelength of non MIR fiber lasers towards 3.5 micron. The group of Vallée at Laval, Quebec, Canada explored a set of possibilities: a single Raman shift was first used to achieve 3.3 micron emission with a 3-micron Er-doped fiber laser as seed [38], 3.4 micron continuous wave watt level emission was demonstrated using a Tm-doped pumped Er lasers [39] and by exploiting soliton self frequency shift of a 2.8 micron fs Er-doped lasers the full wavelength interval up to 3.6 micron was covered reporting a fully pulsed source with output tunable from 2.8 micron to 3.6 micron [40]. However despite seminal papers published years ago by the group at US Naval Research Labs [41,42] direct lasing action above 3.5 micron using new rare-earth such as Dy, Pr, Tb and soft glass fibers was not yet achieved in fiber [43]. Several reasons are involved, including the difficulty to exactly calculate fiber losses. Only recently more accurate simulations based on new spectroscopic data were carried out for Pr-doped chalcogenaide fiber lasers [44]. However in the last ten years the world of MIR compound semiconductor lasers made significant advances. The group of Prudenzano in Bari, Italy, very recently proposed a synergy with the world of MIR quantum cascade lasers (QCL) by proposing the possibility of in-band pumping Dy 4.5 micron transition [45,46]. Figure 2 shows the Dysprosium energy level scheme.

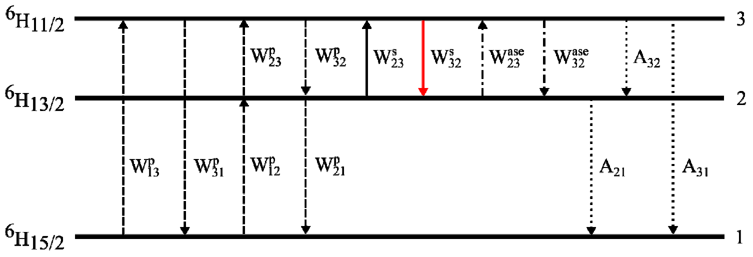

Figure 2. Diagram of Dy^{3+} energy levels and transitions [from Ref.45]. The 4.5 micron transition, in red, is between $H_{11/2}$ and $H_{13/2}$ levels

In this paper two QCL lasers are used, the first at 2850 nm to promote ions from ground level to lower laser lever $H_{13/2}$, the second laser at 4092 nm to generate inversion [46], see the set-up in Fig.3. In the second paper [47] the scheme proposed by Quimby [42], to pump directly into $H_{11./2}$ upper lasers levels and deplete the lower laser level by recirculating 3 micron radiation, was simplified proposing direct pumping at 1.7 micron into the upper laser level and the low efficiency of this scheme be compensated by using a MOPA configuration that exploited the unabsorbed pump to pump the amplification stage. Both schemes are reported in Figure 3 and we can appreciate the simplicity of a standard configuration we may hopefully see soon available for use. An alternative method to extend wavelength up to 5 microns was investigated at Tucson, Arizona, US. In Ref.48 is suggested that using tellurite fibers and one or two Raman shifts in a Raman cascaded resonator configurations the full 3 micron to 5 micron wavelength interval can be covered. This work would extend results of Ref. 38.

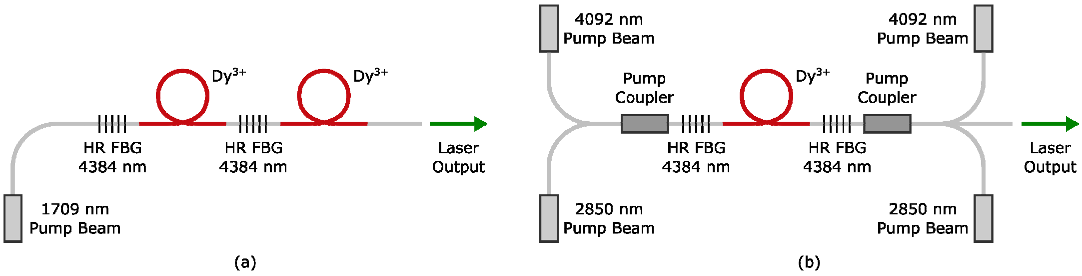

Figure 3. Schematics of the proposed pumping configurations: (a) MOPA [47] and (b) Double Pump [46]. [From Ref.45]

6. CONCLUSION

An excursus on what fiber laser may offer in the near future for medical applications is presented. The paper highlights the main challenge in the field and the author is confident that breakthrough of a new family of efficient fiber lasers in the Mid-infrared will be soon available. In parallel replacement of Ti:Sapphire based system for specific applications will progress. The overall outcome will be availability of cheaper and reliable laser tools that will benefit medical field and will enlarge the number of research group involved in the biomedical field.

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