Components for Highly Advanced time-Resolved fluorescence Microscopy based on Nonlinear Glass fibres

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Publishable summary

Lead contractor for this deliverable

Name: *MULTITEL asbl*
Contact Person: *Yves Hernandez*
Address: *2, rue Pierre et Marie Curie, 7000 Mons Belgium*
Phone: *+32 65 34 28 30*
Fax: *+32 65 34 28 30*
E-mail: *hernandez@multitel.be*

Supervisor for this deliverable

Name: *PMC*
Contact Person: *Yves Hernandez (MULTITEL)*
Date of approval: *09.04.2013*

Authors: Yves Hernandez
Participants: *All partners*

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Any work or result described in this report is in principle genuinely a result of this project. When some results from other work or projects are used, related sources are properly referenced in the text.

http://www.charming-project.eu

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1 Publishable summary

1.1 Description of project context and objectives

The project CHARMING aims at developing compact and fully fibred visible lasers for fluorescence spectroscopy and high resolution confocal microscopy systems. Various visible lasers are required for these applications, with the following characteristics:

- Picosecond pulses at repetition rates adjustable from 1MHz to 80MHz;
- Average output power from 5mW to 500mW (at 40MHz or 80MHz);
- Polarization maintaining single-mode output, with very stable pointing.

Today semiconductor laser diodes are available from 350 to 500 nm. To cover the spectra between 515 nm and 630 nm frequency conversion technologies are employed. In order to guarantee a perfect Gaussian beam overlap between all wavelengths, free space frequency doubling and subsequent fibre coupling is used. This solution suffers from important drawbacks in terms of stability, compactness and cost. To avoid these issues, new functions, fully integrated into fibre, need to be developed like in particular wavelength conversion. Fibre devices for Second Harmonic Generation (SHG) have been proven at laboratory scale but breakthrough approaches are required for this technology to be integrated in future systems. Various innovative approaches, in particular the use of Micro-structured Optical Fibres (MOF), will be investigated to convert this promising technology into potential products. SHG and other fibred functions will be developed to demonstrate efficient devices to cover the whole visible wavelength range and their integration into new imaging systems.

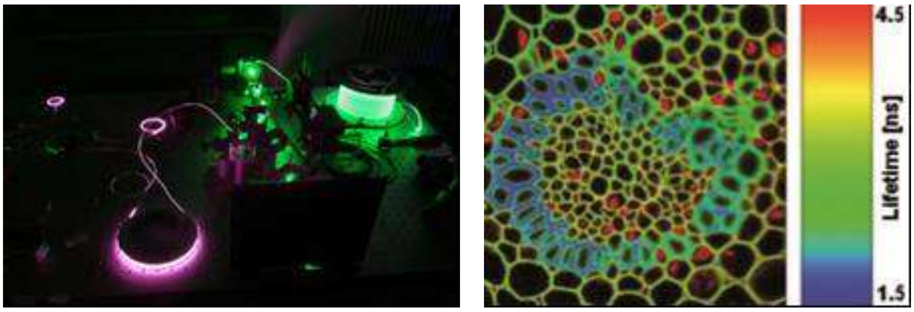


Figure 1: Multi-wavelength fibre laser system (left) and auto-fluorescence imaging of the lily-of-the-valley fragrance receptor– with potential use in cancer prostate detection-(right).

Finally, the performances of the devices will be pushed beyond these specifications (in the Watt level) for targeting a broader potential impact.

1.2 Work performed since the beginning of the project and the main results achieved so far

The project is at middle course. Important work has been carried on the individual elements:

- Micro-structured fibres for SHG,
- PPSF devices,
- Electro-optical fibre modulators,
- Laser diodes and amplifiers.

New micro-structured fibres have been developed by FORC. The complexity of fabrication induced some delay in delivery.

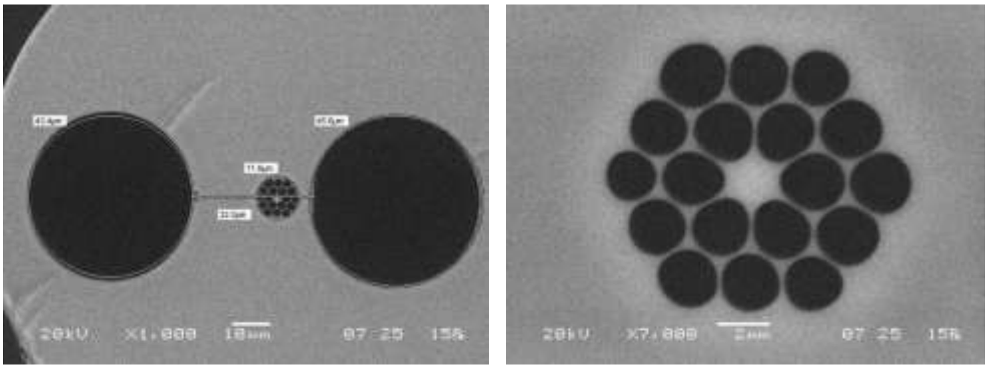


Figure 2: Pictures of a micro-structured fibre fabricated for 1064 nm operation: (left) large view with the two large air holes that will be used for electrodes insertion and poling and (right) zoom on the microstructure.

These fibres were ready end of December 2012 and are at the moment being tested at ORC. Poling of such fibre has been done and first tentative of periodic erasure has been done as well but not tested yet.

PPSF devices have been fabricated very recently on fibres from the project, with Aluminium core doping. This activity suffered important delay due to the installation of the periodic erasure system at ORC. The periodic erasure system at ORC is now running since February 2013. Three devices matching the wavelength of a nanosecond laser available at MULTITEL were fabricated. Two of them are under test. The length of the devices was limited to 20 cm. Nevertheless we obtained about 5% efficiency with 180 W peak power. These figures should be corrected (efficiency increased) by taking into account the laser spectral linewidth that was slightly larger than the acceptance bandwidth of the device. More than 60 mW of green light were obtained during this experiment.

Figure 3: Pictures of the SHG experiment carried on with device C17 from ORC.

Electro-optical modulation has been achieved with frequencies in the MHz level. Limitations for increasing frequency of operation come from the electrical consumption of the driver. A new electrode material has been introduced in the fabrication of these devices. This is the first time such electrode is used for fabricating this type of devices. This new electrode material presents the advantage of having a low fusion temperature. Then it makes possible to use these liquid electrodes for poling of fibres with the possibility of removing the electrodes after poling. This is of great importance in view of second harmonic generation devices fabrication.

New laser diodes have been developed by Nanoplus and evaluated by Picoquant. The diodes at 1.12 and 1.18 µm prove to be good candidates for gain-switching. A new cavity design is being prepared by Nanoplus and to be tested at 1.12 µm.

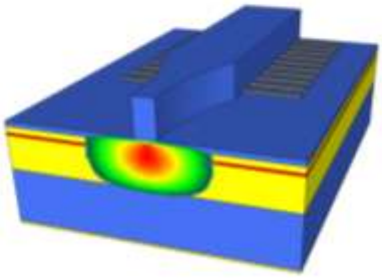


Figure 4: Drawing of the asymmetric laser cavity currently developed by Nanoplus.

For the moment diodes at improved diodes at 1.12 µm are being integrated by PICOQUANT. The output power has already been increased by 70% and longer cavities are being mounted to correct the last remaining issue which is the wavelength drift during direct modulation. The new asymmetric diode design will permit to gain in output power as well. If the design performs correctly it will be transferred to 1.18 µm. PICOQUANT also demonstrated gain-switching at high frequencies (160 MHz) which was not originally planned in the DOW but was a demand arising from market follow-up. Successful amplification at 1.12 µm was demonstrated both by MULTITEL and PICOQUANT on mode-lock and gain-switched lasers respectively, using alumina-silicate ytterbium doped fibre from IXFIBER. As a back-up side experiment we demonstrated 560 nm light generation with a commercially available fibre coupled device. At 1180 nm, pulsed operation could be achieved or by gain-switching or by Raman conversion from 1120 nm to 1180 nm but amplification is not yet solved. Important improvements on Bismuth fibres were made at FORC with an interesting gain coefficient at -20°C operation.

1.3 The expected final results and their potential impact and use

The expected final results of the project are the demonstration of new fibre based solutions for time-resolved fluorescence microscopy, super-resolution microscopy and tryptophan imaging.
Compared to Interim report, the expected final results are unchanged although getting high power in fibre conversion at 590 nm seems the most challenging part of the project because it combines both the difficulty of amplification at 1180 nm and the fibre conversion.

Fluorescence Lifetime Imaging Systems (FLIM) are applied in many biomedical fields. In a reference from 2007 [1], researchers applied this technique for in-vivo studies to localize tumours and detect their progression with adapted fluorophores. The work was oriented towards monitoring the efficiency of drug delivery. Their set-up included fibre beam delivery and collection in order to target endoscopic applications. The most promising direction in this field is for safe in-vivo skin and tissue characterisation to identify tumours and other specific defects based on a lifetime assisted auto-fluorescence imaging. In recent years, several research consortia started to develop instruments for medical diagnosis for epidermal skin imaging, ophthalmology and endoscopic imaging inside living specimen.

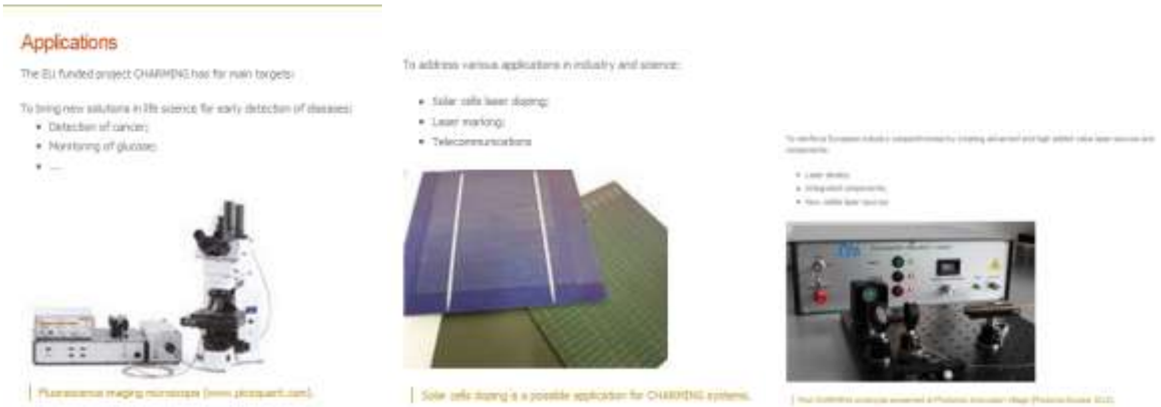
FLIM has already been applied to monitoring of nicotinamide adenine dinucleotide (NADH), an essential co-enzyme for the liver FLIM is also used in high content drug screening, to identify potential pharmaceutical ingredients in multiplexed assays and in proteomics to improve the characterisation of total protein expression maps. FLIM also applies to non-biomedical fields such as determination of impurities in metal samples for nuclear process control or semiconductor wafer analysis which are e.g. used for improving efficiency of solar cells or analyzing quality of image intensifier photo-cathodes at early production stages.

Super-resolution techniques like STED and photo-switching microscopy are just opening the doors to a truly new dimension in optical microscopy for bio-imaging. For the first time it is not only possible to really "see" the structure of cell organelles in much more detail but also to study for example the internal structure of bacteria, with a size typically far below the optical diffraction limit. The availability of laser sources as aimed at in CHARMING is bound to bring about a true positive impact for society, for biomedical research, drug discovery, cell analysis, proteomics and others.

[1] "Fluorescence Lifetime Imaging System for In Vivo Studies", M. Hassan et al, Molecular Imaging, Vol 6, No 4 (July–August 2007): pp 229–236.

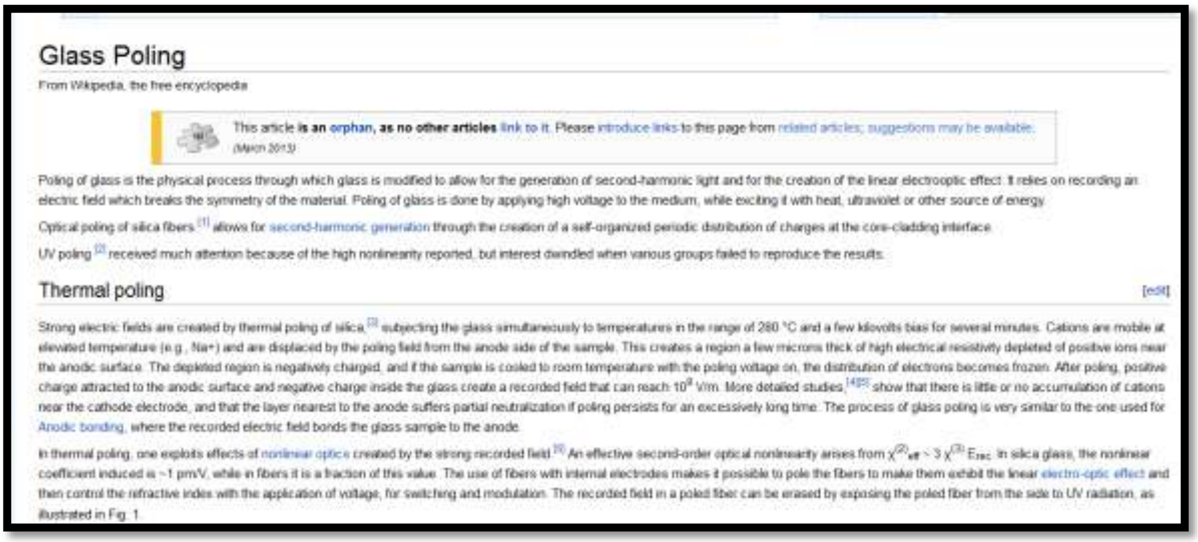
1.4 Project Public Website

The address of the website of the project CHARMING is the following: http://www.charming-project.eu/. An application page was added to the website:



A wikipedia page on glass poling has been created:
http://en.wikipedia.org/wiki/Glass_Poling.

When typing glass poling on google, it is the first link appearing.



Glass Poling

From Wikipedia, the free encyclopedia

This article **is an orphan, as no other articles** link to it. Please introduce links to this page from related articles; suggestions may be available. (March 2013)

Poling of glass is the physical process through which glass is modified to allow for the generation of second-harmonic light and for the creation of the linear electrooptic effect. It relies on recording an electric field which breaks the symmetry of the material. Poling of glass is done by applying high voltage to the medium, while exciting it with heat, ultraviolet or other source of energy.

Optical poling of silica fibers [1] allows for second-harmonic generation through the creation of a self-organized periodic distribution of charges at the core-cladding interface.

UV poling [2] received much attention because of the high nonlinearity reported, but interest dwindled when various groups failed to reproduce the results.

Thermal poling [edit]

Strong electric fields are created by thermal poling of silica,[3] subjecting the glass simultaneously to temperatures in the range of 280 °C and a few kilovolts bias for several minutes. Cations are mobile at elevated temperature (e.g., Na+) and are displaced by the poling field from the anode side of the sample. This creates a region a few microns thick of high electrical resistivity depleted of positive ions near the anodic surface. The depleted region is negatively charged, and if the sample is cooled to room temperature with the poling voltage on, the distribution of electrons becomes frozen. After poling, positive charge attracted to the anodic surface and negative charge inside the glass create a recorded field that can reach 10^9 V/m. More detailed studies,[4][5] show that there is little or no accumulation of cations near the cathode electrode, and that the layer nearest to the anode suffers partial neutralization if poling persists for an excessively long time. The process of glass poling is very similar to the one used for Anodic bonding, where the recorded electric field bonds the glass sample to the anode.

In thermal poling, one exploits effects of nonlinear optics created by the strong recorded field.[6] An effective second-order optical nonlinearity arises from $\chi^{(2)}_{eff} \sim 3\chi^{(3)} E_{rec}$. In silica glass, the nonlinear coefficient induced is ~1 pm/V, while in fibers it is a fraction of this value. The use of fibers with internal electrodes makes it possible to pole the fibers to make them exhibit the linear electro-optic effect and then control the refractive index with the application of voltage, for switching and modulation. The recorded field in a poled fiber can be erased by exposing the poled fiber from the side to UV radiation, as illustrated in Fig. 1.

A link to the CHARMING project website is included in the references of the article.

This makes it possible to artificially create an electric-field grating with arbitrary period,[7] which satisfies the condition necessary for quasi-phase-matching. Periodic poling is used for efficient frequency-doubling in optical fibers.[8] Selecting single pulses from infrared fiber lasers and frequency-doubling them with poled fibers for time-resolved spectroscopy is a main goal of EU project CHARMING.[9]

References [edit]

1. ^ U. Österberg and W. Margulis, Opt. Lett. 11, 516 (1986)

A tutorial on fluorescence microscopy is available for downloading on CHARMINGs website. Videos on fibre poling and on Fluorescence imaging principles are to be included soon.