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InGaAs/InP single-photon avalanche diode operated in gated mode for time-resolved diffuse optical spectroscopy up to 1700 nm

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Summary. — Time-domain diffuse optical spectroscopy is being applied with increasing success to study highly scattering media, mainly in the fields of non-invasive medical diagnostics and quality assessment of food and pharmaceutical products. The region beyond 1100 nm is still largely unexplored by time-domain techniques, probably due to the difficult combination of tunable pulsed sources and suitable single-photon detectors. We extend the spectral range up to 1700 nm thanks to a pulsed supercontinuum laser and a time-gated InGaAs/InP single-photon avalanche diode, with potential applications in medical diagnostics and in the study of scattering materials. A first application on lipids is shown.

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Nowadays optical spectroscopy of turbid media is an increasingly applied technique for the characterization of a variety of highly diffusive materials both of biological and non-biological interest such as collagen and lipids on the one hand and starch and lignin on the other.

One of the main problems when dealing with turbid media is that the diffusive properties of the sample heavily affect the optical signal and therefore light attenuation is not only due to the absorption but it is influenced by the scattering properties as well. As a result, in a normal measurement based on Continuous Wave (CW) illumination it is not possible to disentangle the contributions of the absorption and diffusion coefficients. Since the absorption is related to the chemical composition of the sample and the scattering is connected to its internal structure, uncoupling these two coefficients might prove

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of great interest for a variety of fields, such as medicine, biology and for applications of quality assessment of food and pharmaceutical products. A possible way to achieve this result is working with pulsed light, *i.e.* using time-resolved techniques, since while propagating into the medium the shape of the injected light pulse is modified differently by the absorption and scattering properties, respectively: the absorption coefficient alters the slope of the time-resolved curve, while the scattering coefficient behaves like a delay and a broadening of the photon temporal distribution.

Up to now only a few spectroscopic data are available in the spectral region beyond 1100 nm, even if in this part of the light spectrum more marked differences are expected to characterize the different structures and tissues of biological samples and also other constituents of non-biological interest could show a higher relevance in this range rather than for shorter wavelengths. In the spectral region 600–1100 nm a few broad-band spectroscopy studies have been carried on, based on multidistance CW systems [1, 2], on a combination of frequency domain measurements at few discrete wavelengths and spectral CW acquisition [3, 4] and on time-domain techniques. Only quite recently a system based on multidistance CW illumination was developed [5]. Furthermore, till now the region beyond 1100 nm is still largely unexplored by time-domain spectroscopic techniques, maybe due to the uneasy combination of tunable pulsed sources and suitable single-photon detectors. Only lately, initial tests on phantoms were performed with a first tunable time-resolved system working up to 1400 nm and based on a supercontinuum laser source and a cooled Micro-Channel Plate photomultiplier tube [6].

This work shows the use of a single-photon avalanche diode (SPAD) detector with active surface in InGaAs/InP for time-resolved diffuse optical spectroscopy in the spectral region 1100–1700 nm.

The set-up for time-resolved diffuse optical spectroscopy up to 1700 nm is based on a supercontinuum fibre laser emitting pulsed radiation from 450 nm to 1750 nm; pulses have a duration of tens of ps and their repetition rate is 40 MHz. Spectral selection is achieved through a prism, the rotation of which is controlled by a computer. To accomplish a better spectral selection, diffused light is focused onto an adjustable slit; light is therefore sent to the sample by means of a 100 μm core graded-index optical fibre, while a 1 mm core step-index multimodal fibre collects light which has been diffused through the sample and takes it to the detector. The detector, developed by Dipartimento di Elettronica e Informazione of Politecnico di Milano, is a time-gated InGaAs/InP SPAD, sensitive over the spectral range 900–1700 nm. The active area is very small, only 25 μm in diameter, but it has a quantum efficiency higher than 20% over the whole sensitivity range. It is a compact device, characterized by a low polarization voltage and by around 1000 dark counts per second when operated at 230 K [7]. Time-correlated single-photon counting (TCSPC) boards are employed to collect and elaborate electronic signals. The system is fully automated for what concerns both data acquisition and analysis.

The full-width at half maximum (FWHM) of the spectra in the range 1100–1700 nm, obtained with a spectrometer, is in the order of a few tens of nm, with a maximum value of less then 40 nm at 1700 nm; the spectral width increases for increasing wavelengths due to the dispersion characteristic of the prism. The power of the spectra, measured with a powermeter, is in the order of a few mW per wavelength.

In the wavelength range 1100–1700 nm water absorption is very high [8] and the absorption of the other main constituents of biological tissues (*e.g.*, lipids [5], collagen) and of other materials of practical interest (*e.g.*, lignin, cellulose) is supposed to be high as well: since in this regime the diffusion model may not work properly, data were analyzed with a method based on Monte Carlo (MC) simulations, in which a curve with

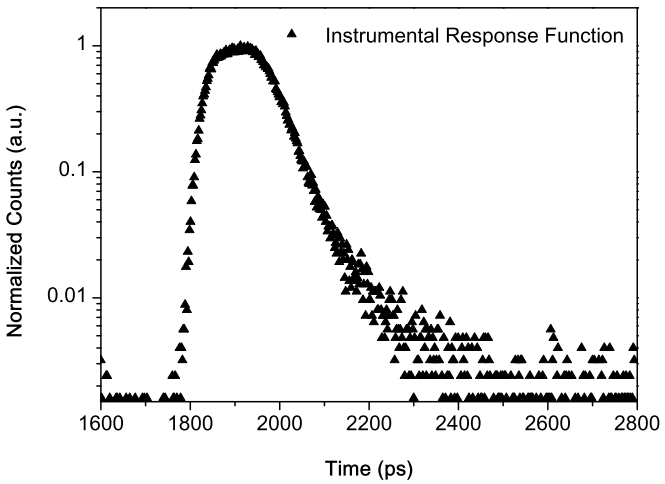

Fig. 1. – Example of a typical instrumental response function of the system.

a fixed absorption and scattering coefficient is generated with a CUDA® accelerated MC code [9] and then it is fitted to the data with a Levenberg-Marquardt optimization routine [10]. Before the fitting procedure, the simulated curve is convoluted to the Instrumental Response Function (IRF) of the system, which takes into account its finite width (affected by the width of the light pulse, the dispersion of the optical fibres and the response of the detector). Figure 1 shows the photon temporal distribution of a typical IRF: its full with at half maximum is around 150 ps with steep rising and falling edges, especially important when dealing with samples characterized by high absorption values.

Since in the spectral region beyond 1100 nm we figured very high absorptions, to test our system over a wide range of absorption values a linearity measurement at 1100 nm was performed on a solution of water and Intralipid, a milky substance usually employed as a scatterer. Calibrated quantities of ink were added to simulate samples with increasing absorption coefficient. Figure 2 reports the absorption coefficient (in the top panel) and the scattering coefficient (in the bottom panel) as a function of the ink concentration of the solution. In these graphs, the straight lines represent respectively the linear interpolation and the mean of the first seven data points, the ones characterized by the lowest absorption values, and correspond to the theoretical values of absorption and scattering we expect. Usually the absorption in the 600–1000 nm range is much lower than $1\,\mathrm{cm}^{-1}$ and so far there has been no need to explore much higher values. It was unexpected to retrieve a linear behaviour of the absorption coefficient up to very high ink concentration, as the linearity is well preserved up to $1.5\,\mathrm{cm}^{-1}$. Another important aspect to be noted here is that no saturation effect is present: this feature assures us that peak positions are not shifted because of an underestimation of the absorption coefficient. For what concerns the scattering coefficient, the higher the ink concentration the worse its recovery, as expected.

As a first example of application, we measured lipids in a solid state (pig fat) in the spectral range 1100–1700 nm. Lipids are an important constituent of biological tissues. Since in the range 600–1100 nm their absorption features are less relevant with respect to other constituents (*e.g.*, water), the knowledge of its spectrum as well as of the spectrum

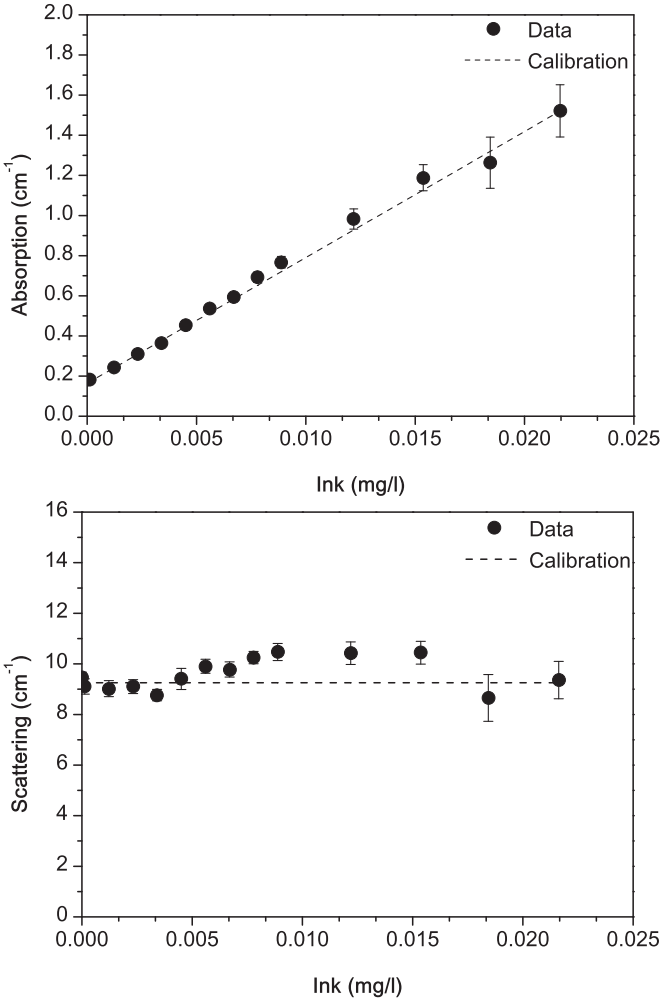

Fig. 2. – Results of the linearity test: calibrated quantities of ink were added to a solution of intralipid and water. In the top panel we report the absorption coefficient as a function of the ink concentration and the straight line represents the linear interpolation of the first seven data points; in the bottom panel the scattering coefficient *vs.* increasing values of ink concentration is displayed; here the straight line is the mean of the first seven data points.

of the other biological chromophores beyond 1100 nm may prove useful for a more accurate recovery of the quantitative composition of tissues. Moreover, the main peaks of lipids around 930 nm and 1030 nm are partially overlapped with those of collagen: hence, a more exact measure of lipid content is also significant for collagen quantification. This task is important since a recent work on mammary tumours in mice showed how an increasing collagen density implies a higher risk to develop mammary cancer [11]; the correct quantification of collagen content based on optical techniques might thus prove a powerful diagnostic tool for non-invasive assessment of cancer risk.

Figure 3 shows the lipid spectrum measured with our system. Three major peaks can be identified around 1200 nm, 1400 nm and 1680 nm. The maximum absorption value is

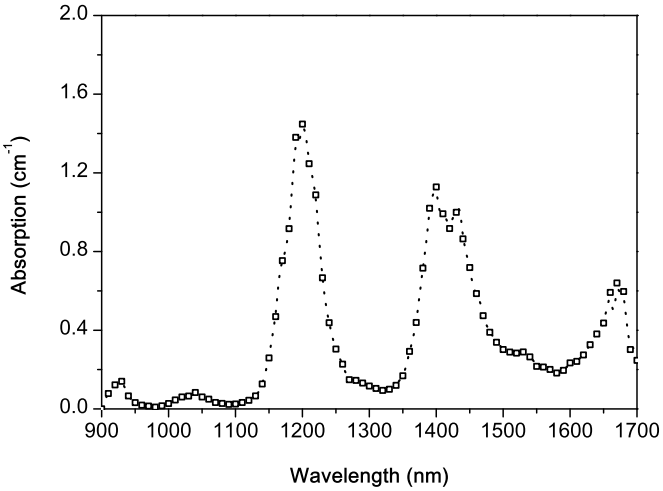

Fig. 3. – Absorption spectrum of lipids as a function of wavelength.

around $1.4\,\mathrm{cm}^{-1}$, reached in correspondence of the peak around 1200 nm. The scattering coefficient is rather flat, with values between $5\,\mathrm{cm}^{-1}$ and $1\,\mathrm{cm}^{-1}$.

In conclusion, we developed a system for time-domain diffuse optical spectroscopy able to work in the spectral range 1100–1700 nm. The system is based on a supercontinuum fibre laser, emitting pulsed white light, and on a time-gated single-photon avalanche diode with active surface in InGaAs/InP. A prism is used for light dispersion. The capacity of the system for working in the spectral range beyond 1100 nm has been proved performing a test on a calibrated liquid phantom: the measurements showed how the system is linear up to high values of absorption (*i.e.* $1.5\,\mathrm{cm}^{-1}$). A first example of application has been presented on lipids: its spectrum reaches up to an absorption value of $1.4\,\mathrm{cm}^{-1}$ around 1200 nm and it is characterized by other two major peaks around 1400 nm and 1680 nm.

As future work, we plan to further improve the spectral resolution of the system and to test the system feasibility for *in vivo* measurements.

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