

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

185,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



New Spectral Applications of the Fourier Transforms in Medicine, Biological and Biomedical Fields

Anca Armășelu

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/66577>

Abstract

This chapter reviews some recent spectral applications of the Fourier transform techniques as they are applied in spectroscopy. An overview about Fourier transform spectroscopy (FTS) used like a powerful and sensitive tool in medical, biological, and biomedical analysis is provided. The advanced spectroscopic techniques of FTS, such as Fourier transform visible spectroscopy (FTVS), Fourier transform infrared-attenuated total reflectance (FTIR-ATR), Fourier transform infrared-photoacoustic spectroscopy (FTIR-PAS), Fourier transform infrared imaging spectroscopy (FTIR imaging), and their biomedical applications are described. A special attention has been paid to the description of the FTVS method of commercial quantum dots like an innovative and reliable technique used in the field of nanobiotechnology.

Keywords: Fourier transform, Fourier transform visible spectroscopy, Fourier transform infrared spectroscopy, biological and biomedical applications, nanobiotechnology

1. Introduction

Fourier transform (FT) represents one of the oldest and the most powerful analytical tools in many fields such as applied mathematics, physical sciences, and engineering. Because FT helps to describe the physical mechanism of collecting and reconstructing data, it also becomes a priceless image-processing instrument in other areas which are related to biomedicine. The development of FT techniques pushed the utilization of the spectroscopic methods dramatically. So, FT methods have long been proved to be extremely useful in all fields of science and technology, such as radio-astronomy, seismology, spectroscopy crystallography, medical image processing, and signal analysis techniques.

Particularly, Fourier transform spectroscopy (FTS) has become an innovative, powerful, and extra sensitive method to study biologically important systems, varying from simple molecules to highly complex samples such as living cells and tissues. These enhanced spectroscopic methods in their modern form represent an important area of research with various applications in diverse fields of science and industry.

The main purpose of this chapter is to provide a modern review about the recent advances on FTS technique with a wide range of medical, biological, and biomedical applications. This chapter begins with a short history about FTS, followed by a description of the theoretical background of FTS with emphasis of some remarkable new results of the research of the quantum dots (QDs) based on Fourier transform visible spectroscopy (FTVS).

After a short historical presentation of the evolution of the important discoveries in the field of the Fourier transforms, the basic ideas of the FT theory are briefly reviewed. In what follows, the power of the Fourier transforms is illustrated through new spectral applications in medicine, biological, and biomedical areas.

In this present chapter, the Fourier transform spectroscopic techniques discussed in the chapter and their important physical principles will be described, that is, Fourier transform spectroscopy, such as Fourier transform visible spectroscopy, Fourier transform infrared-attenuated total reflectance (FTIR-ATR), Fourier transform infrared-photoacoustic spectroscopy (FTIR-PAS), Fourier transform infrared imaging spectroscopy (FTIR imaging), and Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS).

This review is focused on presenting new developments in FTS technique sample preparation methods, experimental conditions used in these investigations, and its useful applications in various fields of biomedical and biological research, including examples of recent advances in the area of nanobiotechnology. Among many other various products of nanotechnology, semiconductor nanocrystals or quantum dots are useful for biomedical research and applications.

Nanobiology, as an area of study, represents the fusion of the biological research with the nanotechnologies such as nanodevices and nanoparticles. This combination of nanotechnology with biology has resulted in the development of diagnostic tools, contrast agents, physical therapy applications, and targeted drug delivery vehicles [1].

Nanomedicine is the medical application of nanotechnology and involves the programs for the application of newly emerging nanotechnologies to molecular processes at the cellular level. The applications of this area of nanoscience include drug delivery, both *in vitro* and *in vivo* diagnostics, nutraceuticals, and production of biocompatible materials. An important device to achieve a series of applications is the engineered nanoparticles [2].

By grouping the study into these areas of research, the general modalities in which the nanotechnology, biology, medicine, and FTS methods are brought together for common research purposes can be noticed.

In this sense, an FTS system able to evaluate optical properties of the CdSe/ZnS core-shell QDs, produced by Evident Technologies, is presented. So, by the use of ARCSpectroHT-HR

Fourier transform spectrometer (ARCOPTIX S.A. Switzerland), the fluorescence spectra of QDs for two excitation sources (a UV laser and a blue LED) are discussed [3]. This study reveals that the FTVS of commercial quantum dots is used to show that CdSe/ZnS core-shell QDs are an example of nanomaterial that is useful such as an alternative to classical fluorochromes in order to label microbial cells.

In another research work, the FTVS is presented like a novel, rapid, and efficient technique to provide quantitative information about the QDs, including their sizes. The use of FTVS methodology for the size determination of CdSe/ZnS core-shell QDs can be easily extended to other types of QDs. Some relationships between the QD size and its corresponding fluorescence average wavelength, calculated from each emission peak of the Fourier transform spectrum, are discussed in this study [4]. The characterization of QD dimension with the help of the FTVS is important in their preparation procedures and their applications.

The reference list contains both historical and extensive analysis works together with the articles that describe several key breakthroughs in the mentioned areas of interest.

2. Advanced applications of Fourier transform methods in spectroscopy

2.1. Historical background

Integral transforms history begins in the eighteenth century, when Jean Le Rond D'Alembert used the overlapping of some sine functions in order to describe the oscillations of the violin strings. In 1822, Joseph Fourier published the book entitled "Théorie analytique de la chaleur" ("The analytical theory of heat") [5]. After James Clerk Maxwell found the equations of the electromagnetic field in 1873, the use of Fourier analysis became crucial for the study of the electromagnetic waves and their harmonic components [6].

In 1954, the French mathematician Laurent Schwartz introduced a new theory of generalized functions named distributions, using the extension of Fourier transform in the study of the tempered distributions [7].

The FT shows a powerful time-frequency duality. This property was used in 1983 by the American mathematician Charles Louis Fefferman in the paper entitled "The uncertainty principle." In his work, Fefferman deduces important results of quantum mechanics using multidimensional Fourier approach [8].

The FT has long been proved to be extremely useful as applied to spectroscopy in all research fields which require high resolution and high wavelength accuracy and broad tunability. These spectroscopic methods that use the FT are considered FTS. FTS is a well-known spectroscopic method where interferograms are collected based on measurements of the coherence of an electromagnetic radiation source in time domain or space domain and converted into the frequency domain through FT.

A Fourier transform spectrometer is a Michelson interferometer invented by Albert A. Michelson in 1880 [9] with a moving mirror at one arm. Using this instrument, Michelson

elaborated the fundamental techniques of FTS [10, 11]. The advantages of the FT spectrometers that are superior to the prism and grating ones are well known. These are the advantages of Fellgett (an increase in a signal value of signal-to-noise ratio due to the simultaneous registration of all the spectral elements [12]), Jacquinot (a greater light efficiency at a given resolution [13]), and Connes (the accuracy of the frequency determination obtained by the control of mirror displacements in the interferometer with a helium-neon laser [14, 15]).

Drs. J.E. Chamberlain, J.E. Gibbs, and H.A. Gebbie improved the Michelson interferometer equipment for molecular spectroscopy used to study the experiments on ozone and in the upper atmosphere. Their group developed the asymmetric Fourier transform spectroscopy technique for the measurement of the refractive indices of gases, liquids, and solids [16].

In 1964, Dr. Paul L. Richards constructed a lamellar grating interferometer which is a Michelson interferometer and proved that this instrument is a highly effective tool at low wave numbers [17]. In 1965, the invention of the fast Fourier transform (FFT) algorithm by J.W. Cooley and J.W. Tukey represented an important date for Fourier spectroscopy. The Cooley-Tukey algorithm reduces the calculation time by several orders of magnitude when compared to the classical Fourier transform [18]. In 1966, D.L. Forman published a paper that treats the implementation of the FFT algorithm in Fourier spectroscopy [19].

Only the significant historical data for the development of the FTS technique were presented here. The history of the field of the FTS shows the great utility of this promising and strongly developed instrument. The FTS method rapidly developed in the last decades. FTS is an analytic spectroscopic method with applications in astronomy, physics, physical chemistry, chemistry, chemical engineering, optics, biology, medicine, and nanotechnology.

FTS can be applied to a broad diversity of kinds of spectroscopy such as Fourier transform visible spectroscopy, Fourier transform infrared-attenuated total reflectance, Fourier transform infrared-photoacoustic spectroscopy, Fourier transform infrared imaging spectroscopy, and Fourier transform ion cyclotron resonance mass spectrometry.

2.2. New applications of Fourier transform visible spectroscopy in nanobiotechnology

In this part of the chapter, the Fourier transform visible spectroscopy of commercial quantum dots is briefly presented [3]. The fluorescence spectra of QDs produced by Evident Technologies were studied in the case of the existence of two excitation sources (a UV laser and a blue LED) with the help of ARCSpectro HT-HR Fourier transform spectrometer. Due to the quantum confinement effect, QDs are semiconductor nanocrystals which exhibit significant optical characteristics such as high photostability, fluorescence properties with broad absorption spectra, size-dependent narrow emission spectra, and slow excited-state decay rates, thus leading to major breakthroughs in microbiology, molecular and cell biology, and medical diagnostics [20–22]. Among many other various products of nanotechnology, QDs are suitable to be used in various biological and biomedical researches as the next-generation fluorescent probes for detection and imaging applications.

In addition to the research results mentioned above, a relevant biological application of CdSe/ZnS core-shell QDs as microbial labeling both for pure cultures of cyanobacteria (*Synechocystis*

PCC 6803) and for mixed cultures of phototrophic and heterotrophic microorganism was presented in the same paper [3]. Different semiconductor nanocrystals, such as CdSe/ZnS core-shell QDs dispersed in toluene with long-chain amine-capping agent, that were used in some studies, which analyze the Fourier transform spectra of these QDs [3, 4], were acquired from Evident Technologies. The QDs have the dimensions in the domain of (3–5) nm and the emission in the range (490–600) nm.

The Fourier transform spectra of QDs were studied using the experimental device shown in **Figure 1**. The experimental setup comprised the sources of excitation (a blue or a UV source), the sample (QD) containing quantum dots, the optical fiber (OF) that transmits the fluorescence signal, and the Fourier transform spectrometer which is acted by a computer [3].

ARCspectro HT-HR (ARCOPTIX S.A. Switzerland) is a Fourier transform spectrometer which is used to record the fluorescence spectra. This static Fourier transform spectrometer is based on the operating principle of the so-called common path polarization interferometer which measures the coherence function of the light. The interference image, which is formed at the output of the device, is recorded with the help of a charge-coupled device (CCD) detector array. The light spectrum is calculated using the computer with a Fourier transform algorithm and calibration tables. The ARCSpectro HT-HR shows the extraordinary advantage which is given by the fact that the high luminosity of the system is (50–100) times greater than

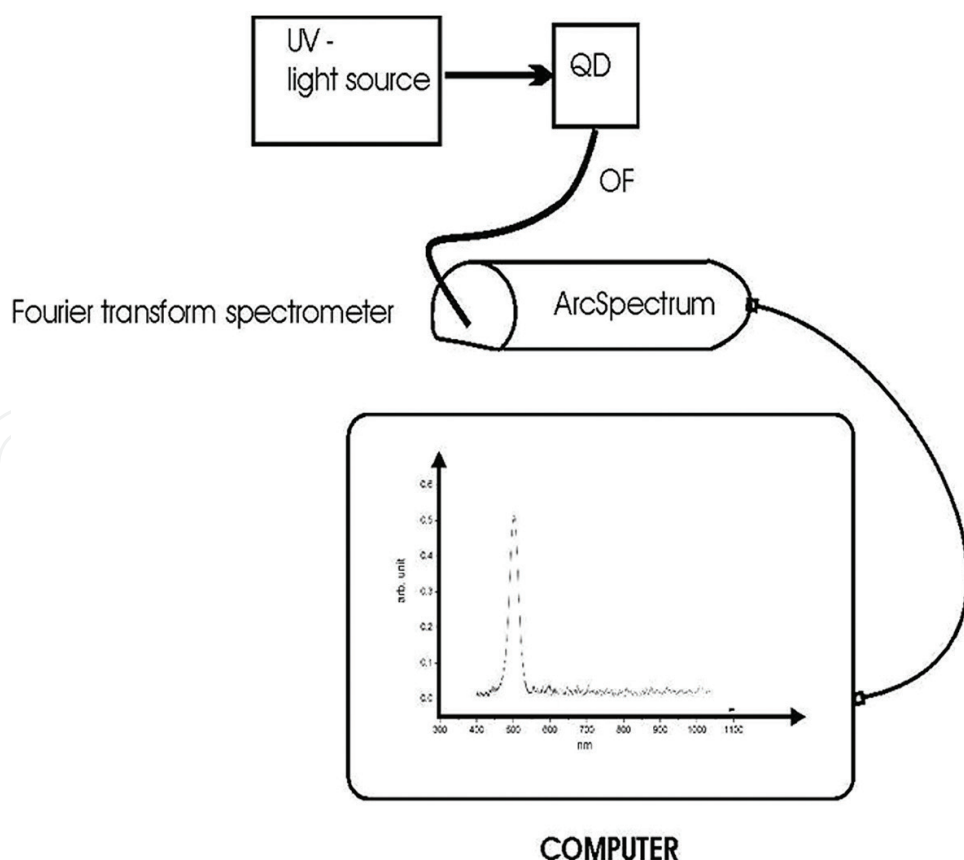


Figure 1. The schematic diagram of the fluorescent emission spectroscopy system [3].

a grating one. An advantage of this Fourier transform spectrometer, which is useful for certain applications, is the fact that fiber and collimation optics are not absolutely necessary.

Using FTVS, the emission properties of four kinds of CdSe/ZnS core-shell QDs (0490, 0520, 0560, and 0600 Evidot fluids) were analyzed and were evaluated [3, 4]. Each of **Figures 2–4** displays a Fourier transform spectrum which shows the manner in which the QDs are irradiated by the light from a NdYAG@355 nm laser or from a luminescent diode ($\lambda = 480$ nm). The calculation of the average wavelengths from each emission peak of the spectra of QDs for two excitation sources was reported [3, 4].

Figure 2 shows the Fourier transform spectra of the 0490 Evidot fluid, for two situations. First situation treats the case of the enlightenment the probe with the laser light from an NdYAG@355 nm, obtaining the fact that the maximum of the peak intensity corresponds to an average wavelength calculated at 500 nm. The second situation presents the case where the fluorescence wavelength, which corresponds to a maximal value of the intensity, has the value of 511 nm, when the sample is illuminated with a luminescent diode ($\lambda = 480$ nm) [3].

For the Fourier transform spectra of the 0520 Evidot, it was observed that for UV laser excitation, the average fluorescence wavelength was 510 nm, while for the excitation with blue LED light, the corresponding average wavelength of fluorescence was calculated at 525 nm [4].

The Fourier transform spectra of the 0560 Evidot in **Figure 3** illustrate that for the illumination with laser light, the average fluorescence wavelength was 572 nm and for the excitation with blue LED light, the corresponding average wavelength of fluorescence was the 588 nm [3].

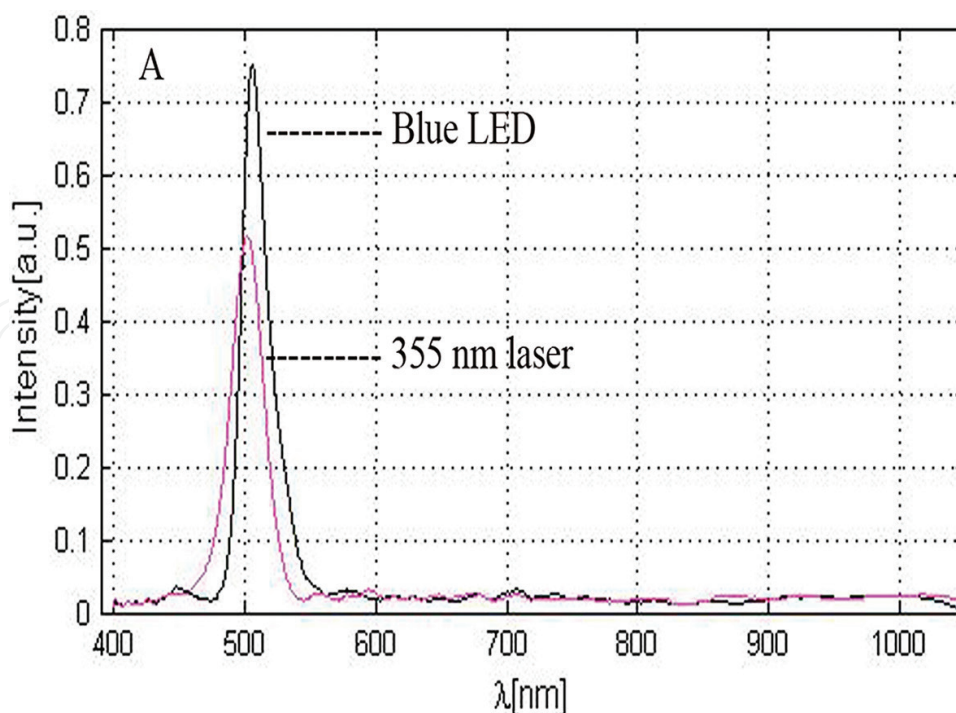


Figure 2. The Fourier transform spectra of CdSe/ZnS core-shell QDs of the 0490 Evidot fluid type in the case of two excitation sources: a laser (NdYAG@355 nm) and a luminescent diode ($\lambda = 480$ nm) [3].

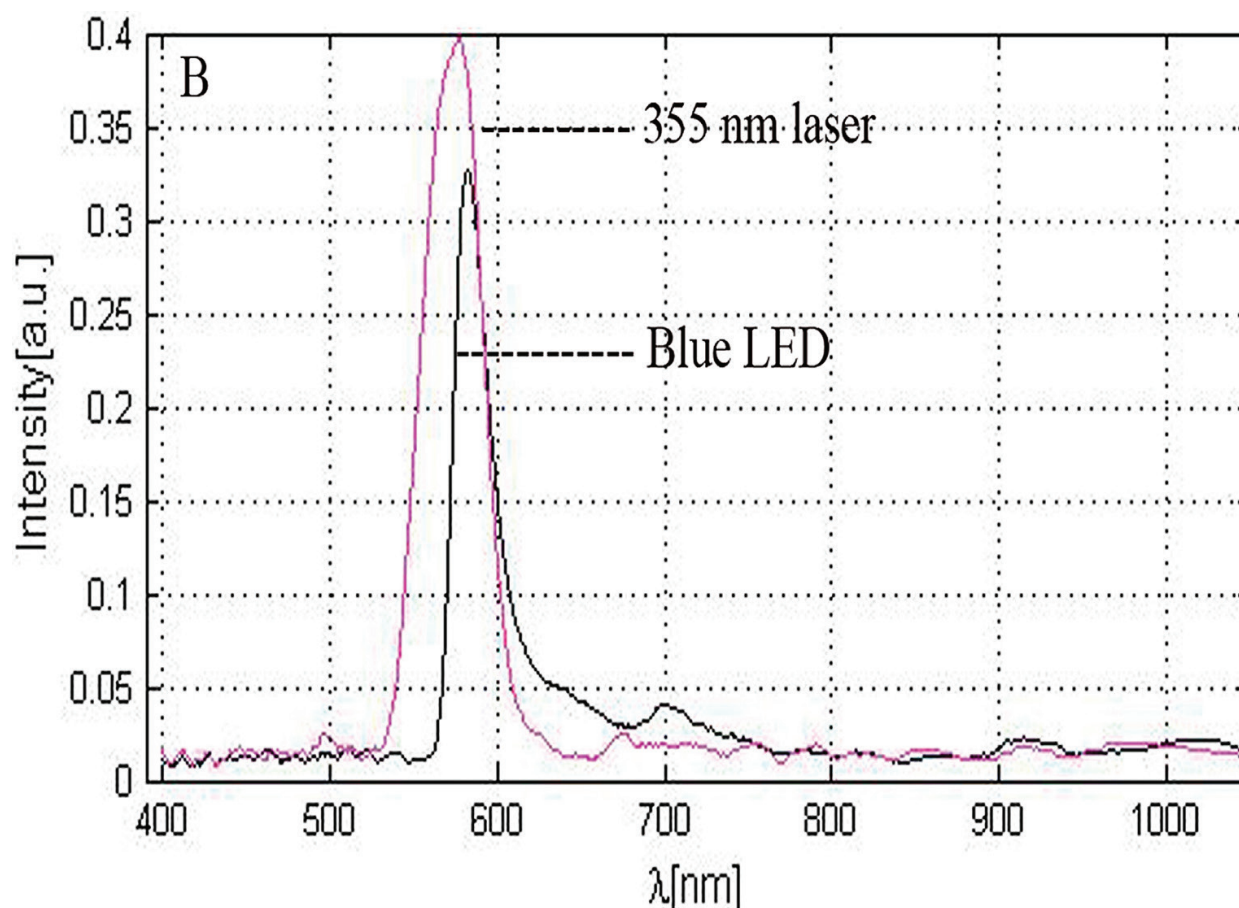


Figure 3. The Fourier transform spectra of the 0560 QDs fluid in the situation of two excitation sources: a laser (NdYAG@355 nm) and a blue LED [3].

In **Figure 4**, the Fourier transform spectra of the 0600 Evidot are shown. When the probe was irradiated with the laser light, the average value of the emitted light was 614 nm and in the case of the blue LED the average wavelength was 634 nm [3].

Figure 5 presents five Fourier transform spectra obtained in the case of a probe of 0520 Evidot suspension with the concentration 23 ml QDs in 3 ml toluene in a quartz container for the following values of the energy emitted by the laser: 1, 3, 8, 18, and 25 mJ, respectively [3].

In this section, several important aspects of previous research studies of the author of this chapter regarding the investigation of the optical properties of QDs and their role as fluorescent probes for different biological and medical applications using an FTVS system that helps to study the spectral characteristics of the fluorescence emission have been revised.

Another significant research direction in this review, which must be mentioned in this study, is the discovery of some fast and reliable methods for the determination of the QD size. Such a method, which assists at the evaluation of the diameter of commercial CdSe/ZnS core-shell QDs, is FTVS technique. Due to the high sensitivity and simplicity, FTVS has numerous performance advantages over conventional methods, in providing qualitative and quantitative information about QDs, including their sizes.

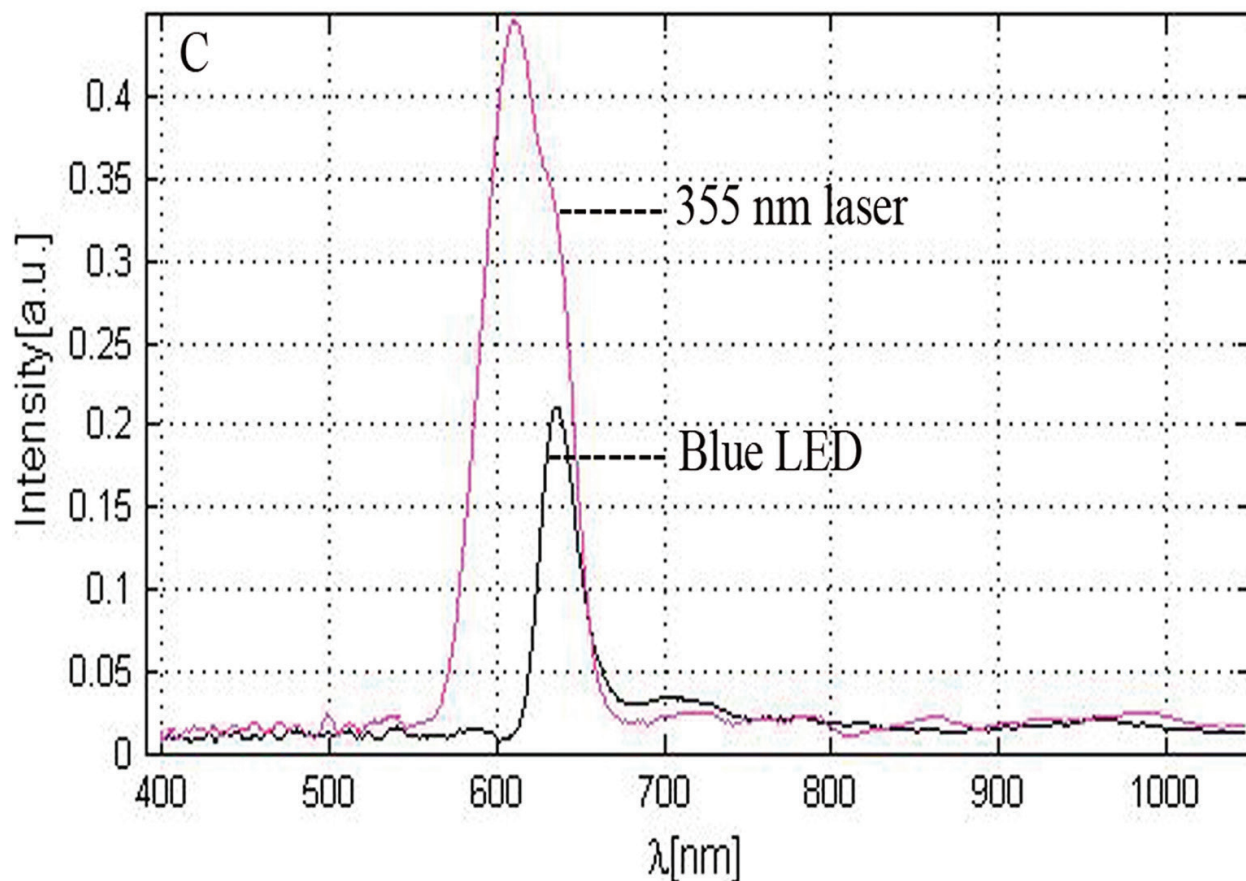


Figure 4. The Fourier transform spectra of the 0600 QDs fluid for two excitations sources that were used in the research paper [3].

In Ref. [4], the relationship between the QD size and its calculated fluorescence average wavelength of corresponding Fourier transform spectrum is discussed. So, the dependence of the dimension of the QDs and excitation conditions of the maxima of the fluorescence emission were analyzed with the help of FTVS. In this research, the empirical equations that fit these dependences aiming to elaborate a simple and trustworthy technique for the determination of the dimension of QDs, besides conventional techniques, were obtained.

The measurements required for FTVS method were made by means of the ARCSpectro HT-HR (ARCOPTIX S.A. Switzerland) Fourier transform spectrometer. The major components of the experimental system were elaborately presented in [3, 4]. This investigation method proposed in [4] helps to estimate the dimensions of core-shell CdSe/ZnS QDs of a certain type and their fluorescence features which are determined by the wavelength of each peak of fluorescence.

In **Figure 6**, a triplet of the fitting curves of the QD size with their emission wavelength is represented. The fitting functions of the curves (a)–(c) from **Figure 6** were built by utilization of the interpolating polynomials from Mathematica software.

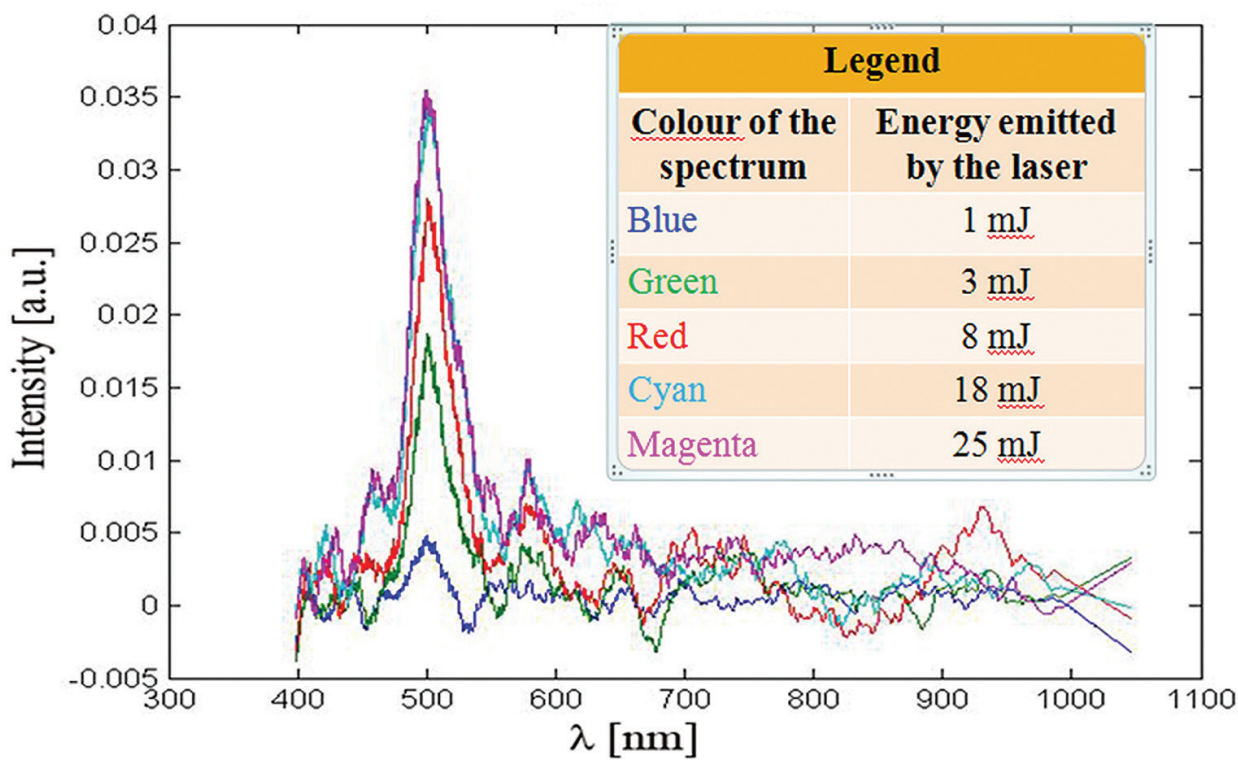


Figure 5. Five presented smoothed Fourier transform spectra for the case of increasing values of the laser energy. The height of the main peaks grows and the main fluorescence band considerably broadens with the increasing of the values of the laser energy [3].

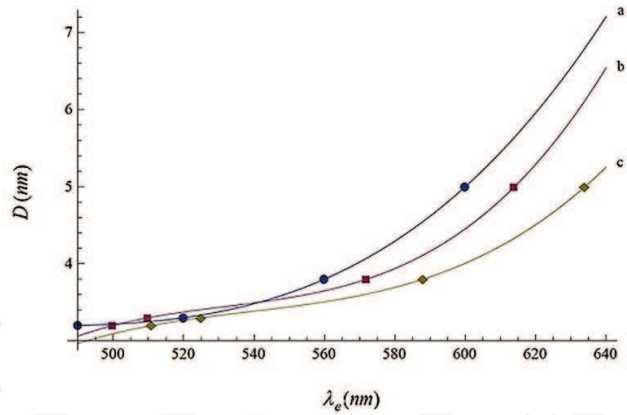


Figure 6. Sizing curves for CdSe/ZnS core-shell QDs. Solid lines (a–c) represent the fitting curves illustrated by Eqs. (1)–(3), while the symbols used for points (circles, squares, and rhombs) on curves refer to the catalog data (curve a) and experimental data (curves b and c) [4].

Eq. (1), which represents the fitting function of curve (a) from **Figure 6** and was constructed by fitting the known diameters, D , of CdSe/ZnS QDs versus the values of the emission wavelengths, λ_{e_s} , from the Evident Technologies catalog specifications, is given by

$$D_{CdSe/ZnS} = (7.9816 \times 10^{-7})\lambda_{e_s}^3 - (1.12216 \times 10^{-3})\lambda_{e_s}^2 + (5.25882 \times 10^{-1})\lambda_{e_s} - 78.9545 \quad (1)$$

By fitting the known sizes of different CdSe/ZnS core-shell QDs versus the experimental data of the emission wavelengths found in [3, 4] with the help of FTVS method for QDs enlightened by the laser light from a NdYAG@355 nm (curve b) or by the blue LED (curve c), the empirical fitting functions of curves (b) and (c) were obtained as can be seen in **Figure 6**.

$$D_{\text{CdSe/ZnS}} = (1.96547 \times 10^{-6})\lambda_{e_b}^3 - (3.13626 \times 10^{-3})\lambda_{e_b}^2 + (1.67384)\lambda_{e_b} - (295.338) \quad (2)$$

$$D_{\text{CdSe/ZnS}} = (1.27001 \times 10^{-6})\lambda_{e_c}^3 - (2.05218 \times 10^{-3})\lambda_{e_c}^2 + (1.11082)\lambda_{e_c} - (198.023) \quad (3)$$

In Eqs. (2) and (3), $D_{\text{CdSe/ZnS}}$ (nm) denotes the diameter of the core-shell QDs and λ_{e_b} , λ_{e_c} (nm) represent the values of the fluorescence average wavelengths, calculated from each emission peak of the Fourier transform spectra for those two excitation sources that were used [3, 4].

It should be pointed that unlike other studies the obtained empirical formulae refer to the whole core-shell QD diameter and comprise both the thickness of CdSe hard-core and the thickness of ZnS shell. In Ref. [4], it has been proved that FTVS is a simple, rapid, and efficacious technique for the size evaluation of the core-shell QDs. The procedure analyzed could be developed for the dimension determination of other fluorescent nanoparticles.

2.3. Recent applications of Fourier transform infrared spectroscopy in medical, biological, and biomedical sphere

Fourier transform infrared spectroscopy represents a fundamental and a reliable technique, with many potential useful applications in the area of biology and medicine, thanks to its nonperturbative and highly sensitive features.

FTIR spectroscopic method analyzes the wavelength of the light absorbed by the probe at certain vibrational frequencies. The spectrum produced in this way, which is peculiar for the biological material exposed to radiation in this method, represents a “molecular fingerprint.” More exactly, the biological materials such as carbohydrates, proteins, lipids, nucleic acids, biomembranes, animal tissues, microbial cells, plants, and clinical samples possess unique structures leading to the obtaining spectral fingerprints according to their functional groups, bends, and molecular structure [22]. So, FTIR can be used to detect structural changes of individual amino acid residues, backbone peptides, binding ligands, chromophores, and internal water molecules [23]. The application of FTIR to biological problems is continuously extending, thus evolving from the study of isolated biological molecules to the study of more sophisticated and complex systems, such as diseased tissues.

Also, FTIR is a suitable and a well-established standard technique utilized to study nanoparticles coupled with molecules in order to use them for drug delivery systems, for targeting strategy, or for bioimaging scopes [24].

Recent methods of FTIR are Fourier transform infrared-attenuated total reflectance, Fourier transform infrared-photoacoustic spectroscopy, Fourier transform infrared imaging spectroscopy, and Fourier transform infrared microspectrometry (FTIR microspectrometry).

In the late 1980s and 1990s, Nauman and his collaborators [25, 26] reinsert the FTIR techniques in order to analyze *in situ* the bacterial cells and to identify, differentiate, and classify bacteria [27]. Since then, FTIR spectroscopy has been proved to be a preferred and a valuable tool for characterization and for differentiation of microorganisms. The FTIR spectra furnish highly accurate spectroscopic fingerprints of microbial strains permitting a rapid and reliable identification at both species and subspecies level [28].

The identification of microorganisms in a rapid and simple way is a vital task for the food safety and quality in a processing retail, or production environment. Conventional plating, biochemical, and serological tests represent traditional techniques that have several stages and that can last a long period of time until the obtaining of the confirmatory results. Because of the fact that FTIR techniques produce biochemical fingerprints of bacteria in a short period of time, there is therefore an encouragingly large goal for study on the use of FTIR spectroscopy in the area of food microbiology.

FTIR methods combined with various chemometric analyses procedures [28–30] can be applied to the field of medical applications, pharmaceutical industry, and food microbiology, comprising the detection of bacteria from culture and food, discrimination between various microbial species and strains, classification of a diversity of microorganisms at genus, species, and subspecies levels, bacteria viability analysis, characterization growth-dependent phenomena and cell-drug interactions, investigation *in situ* intracellular components or structures such as inclusion bodies (IBs), storage materials, or endospores [31]. Because in biological and in medical field, protein aggregation represents an important issue encountered in the expression of recombinant proteins in bacterial cells in the form of IBs and in some diseases, the monitoring *in vivo* of the kinetics of protein aggregation in *Escherichia coli* within intact cells using the FTIR spectroscopy methods constitutes a fast and a facile technique used to acquire structural information on proteins within IBs [32].

Due to its rapidity, simplicity, and high sensitivity, FTIR spectroscopy technique can also be utilized for the identification and differentiation of the most frequent yeast species isolated from infected human mouth/vagina, chronic disease cows, crop mycosis in chicken, and soil contaminated with pigeon droppings [33]. Based on the research results published by some authors, the feasibility of FTIR for identification of *Candida*, *Cryptococcus*, *Trichosporon*, *Rhodotorula*, and *Geotrichum* isolated from humans and animals [33–35] has been proved.

The FTIR-attenuated total reflection technique is based on the interaction between IR light and an absorbing sample at its interface. ATR is a specialized sampling technique where the sample is situated in contact with an ATR crystal which has a high refractive index material. As a result of the phenomenon of total intern reflection of light produced at the interface between the ATR crystal and a sample of lower refracting index, an evanescent wave is formed which extends into the sample. The sample absorbs at discrete IR frequencies which leads to the attenuation of the incident IR light. Therefore, the infrared spectra of solid or liquid samples in their native state are obtained by combining ATR with FTIR [36, 37].

The release of the drugs in semisolid and solid formulations, the penetration of the drug into artificial and biological membranes, and the influence of penetration modifiers *in vivo* studies are investigated with the FTIR-ATR method [36, 38]. FTIR-ATR is utilized for the examination

of the structure of the stratum corneum (SC) at the molecular level for the estimation of the penetration enhancers which grow the permeation of the drugs through the human SC and for the analysis of its lipids, proteins, and water content [36, 39].

Genistein (GEN; 4, 5, 7-trihydroxyisoflavone), which is also known as phytoestrogen because it has similar structure with the human hormone 17β -oestradiol, represents a powerful tyrosine kinase inhibitor that has been widely utilized in order to prevent and to cure many diseases and disorders such as cardiovascular disease, osteoporosis, and cancer [39, 40]. Recent results [40, 41] have shown that using FTIR-ATR technique helps to discover new ways for the improvement of the transdermal transport of a lyotropic liquid crystal genistein-based formulation (LLC-GEN). In order to increase the transdermal drug transport, LLC-GEN was coupled with electroporation (EP). So, in Ref. [40] the synergistic effect of EP in the case of the hairless mouse skin with the help of FTIR-ATR has been proved.

The FTIR-ATR method is among characterization techniques of surfaces used to investigate new properties of the nanomaterials for various biomedical applications including the implant applications. In this sense, in order to investigate the interactions of nanomaterials with biological systems such as proteins, FTIR-ATR is used to provide information about the changes in the surface chemistry after certain nanotechnology-based chemical or physical after treatments are applied with the aim of the contribution to the regeneration of the different tissues (such as those of bone, cartilage, vascular, and neural systems) [42, 43].

The potential of the FTIR method combined with photoacoustic spectroscopy and diffuse reflectance spectroscopy (DRS) was exploited for the applications in the detection of the fungi and the mycotoxins which represent a severe cause of food poisoning in humans and animals. More exactly, there are some recent studies that show the usefulness of FTIR-PAS technique for the identification of corn kernels infected with fungi *Fusarium moniliforme* and *Aspergillus flavus* [44].

FTIR-PAS also provides the possibility to obtain information about the drug mechanism and the barrier function of SC in order to implement them to the biomedical and cosmetic applications [36, 45].

Recently, by coupling the FTIR techniques with imaging methods, a correlation of the biochemical information such as protein misfolding and metal homeostasis was reached, which has resulted in understanding of the mechanism of the neurodegenerative protein misfolding disease including Alzheimer's disease, Parkinson's disease, Huntington's disease, and multiple sclerosis [46, 38].

Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) represents one of the most advanced and complex techniques of mass analysis and detection. FTICR-MS is a powerful tool which can be utilized to find masses with high accuracy. Many applications of FTICR-MS utilize the mass accuracy like a very important parameter in order to find the composition of the molecules based on accurate mass. FTICR-MS has been shown to provide important clues regarding the nontargeted metabolic profiling and functional characterization of novel genes [47, 48]. The compilation of the high mass accuracy and the ultra-high-resolving power of FTICR-MS is ideal for the resolving of the analytical problems of the complex-mixed analyses encountered in proteomics [49, 50] and petroleomics [50, 51].

Electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry (ESI FTICR-MS) represents an emerging method which helps to analyze the biological macromolecules, like in the case of the investigation of non-covalent interactions of proteins [52].

Electron capture dissociation (ECD) represents a relatively new technique used for the analysis of peptides and proteins and is a method utilized for inducing fragmentation in FTIR-MS [50]. ECD combined with FTIR-MS represents a powerful and useful technique in proteomic studies.

In some successful advanced works [51, 53], new techniques are described for the deployment of the improved electron injection methods. So, in Ref. [53, 54] the improvement of the overlap of ion, photon, and electron beams in the ICR ion trap is reported, using the compressed hollow electron beam injection technique.

Collision-induced dissociation (CID) and infrared multiphoton dissociation (IRMPD) are traditional methods that are used to induce fragment spectra in tandem mass spectrometry analyses. CID and IRMPD generate the dissociation of the peptides by breaking the backbone amide linkages [55]. When applying ECD fragmentation technique, co- and post-translational modifications within the peptide and protein sequence are maintained, as opposed to the using of those two methods, namely CID and IRMPD, which may provoke dissociation of post-translational modifications [55]. This fact is important for the application of ECD to glycosylation [56, 57], sulfation [56, 57], and phosphorylation analysis [56, 58].

3. Conclusions

This chapter represents a reference review for Fourier transform methods as they are applied in spectroscopy. More exactly, the work concerns an overview of the current status, of the recent achievements in FTS spectroscopy, and some selected new applications of FTS in the medical, biological, and biomedical fields, with the emphasis on the own work done by the author of this chapter.

The confluence of Fourier transform spectroscopy methods with nanotechnology, biology, and medicine opens new opportunities for the detection and handling of the atoms and molecules using nanodevices, with potential for a large variety of biological and medical applications at the cellular level.

Author details

Anca Armășelu

Address all correspondence to: anca_armaselu@yahoo.com

Faculty of Electrical Engineering and Computer Science, Department of Electrical Engineering and Applied Physics, Transilvania University of Brasov, Brasov, Romania

References

- [1] Alharbi KK, Al-Sheikh YA. Role and implications of nanodiagnostics in the changing trends of clinical diagnosis. *Saudi J. Biol. Sci.* 2014; 21(2): 109–117. DOI: 10.1016/j.sjbs.2013.11.001
- [2] Tibbals HF. *Medical Nanotechnology and Nanomedicine*. Ed. CRC Press: Taylor & Francis Group; 2010. 528 p. DOI: 10.1201/b10151
- [3] Damian V, Ardelean I, Armășelu A, Apostol D. Fourier transform spectra of quantum dots. *Proc. SPIE*, 2010; 7469. DOI: 10.1117/12.862053
- [4] Armășelu A. Determination of quantum dot size by Fourier transform visible spectroscopy. *Optoelectr. Adv. Mater. Rapid Commun.* 2015; 9(3): 531–536.
- [5] Fourier JBJ. *The analytical theory of heat*. Paris: Chez Firmin Didot, Père et Fils; 1822. 638 p.
- [6] Maxwell JC. *A Treatise on Electricity and Magnetism*, vol. 1, Clarendon Press, Oxford; 1873, 534 p.
- [7] Schwartz L. On the impossibility of the multiplication of distributions. *C. R. Acad. Sci. Paris* 1954; 239: 847–848.
- [8] Fefferman CL. The uncertainty principle. *Bull. Amer. Math. Soc.* 1983; 9(2): 129–206. Available from: <http://projecteuclid.org/euclid.bams/1183551116>
- [9] Michelson AA. On the application of interference methods to astronomical measurements. *Philos. Mag.* 1890; 30(182): 1–21.
- [10] Fowles GR. *Introduction to Modern Optics*. 2nd ed. New York, NY: Dover Publications; 1989. 336 p. ISBN: 9780486659572
- [11] Bell RJ. *Introductory Fourier Transform Spectroscopy*. New York, NY: Academic Press; 1972.
- [12] Fellgett PJ. A contribution to the theory of the multiplex interferometric spectrometer. *J. Phys. Radium.* 1958; 19: 187. DOI: 10.1051/jphysrad:01958001903018700.
- [13] Jacquinot P. New developments in interference spectroscopy. *Rep. Prog. Phys.* 1960; 23: 267–312.
- [14] Connes P, Connes J, Maillard JP. *Atlas of Near Infrared Spectra of Venus, Mars, Jupiter, and Saturn*. Paris: Editions Du Centre National de Recherche Scientifique; 1969.
- [15] Connes J. Spectroscopic studies using Fourier transformations. *Rev. Opt. Theor. Instrum.* 1961; 40: 45, 116, 171, 231.
- [16] Chamberlain JE, Gibbs JE, Gebbie HA. The determination of refractive index spectra by Fourier spectroscopy. *Infrared Phys.* 1969; 9: 185.

- [17] Richards PL. High-resolution Fourier transform spectroscopy in the far infrared. J. Opt. Soc. Amer. 1964; 54(12): 1474-1484. Available from: <https://doi.org/10.1364/JOSA.54.001474>
- [18] Cooley JW, Tukey JW. An algorithm for the machine calculation of complex Fourier series. Math Comput. 1965; 19: 297.
- [19] Forman ML. Fast Fourier transform technique and its application to Fourier spectroscopy. J. Opt. Soc. Amer. 1966; 56: 978.
- [20] Parak WJ, Pellegrino T, Plank C. Nanotechnology. 2005; 16: 9.
- [21] Delehanty JB, Mattoussi H, Medintz IL. Anal. Bioanal. Chem. 2009; 393: 1091.
- [22] Bhattacharyya S. Fourier transform infrared spectroscopy: applications in medicine. J. Phys. Chem. Biophys. 2015; 5: 4. DOI: 10.4172/2161-0398.1000e128
- [23] Kenneth RJ. The early development and application of FTIR difference spectroscopy to membrane proteins. A personal perspective. Biomed. Spectrosc. Imaging. 2016; 5: 231–267. DOI: 10.3233/BSI-160148
- [24] Kumar A, Mansour HM, Friedman A, Blough ER, editors. Nanomedicine in Drug Delivery. CRC Press: Taylor & Francis Group, LLC; 2013. 469 p. ISBN 13:978-1-4665-0617-6
- [25] Naumann D, Fijala V, Labischinski H. The rapid differentiation and identification of pathogenic bacteria using Fourier Transform spectroscopic and multivariate statistical analysis. J. Mol. Struct. 1988; 174: 165–170.
- [26] Naumann D, Helm D, Labischinski H. Microbiological characterizations by FT-IR Spectroscopy. Nature. 1991; 35181: 2.
- [27] Gomez MA, Perez MAB, Gil FJM. Identification of species of *Brucella* using Fourier transform infrared spectroscopy. J. Microbiol. Meth. 2003; 55: 121–131.
- [28] Maquelin K, Kirschner C. Identification of medically relevant microorganism by vibrational spectroscopy. J. Microbiol. Meth. 2002; 51: 255–271.
- [29] Al-Qadiri HM, Al-Holy MA, Lin M, Alami NI, Cavinato AG, Rasco BA. Rapid detection and identification of *Pseudomonas aeruginosa* and *Escherichia coli* as pure and mixed cultures in bottled drinking water using Fourier transform infrared spectroscopy and multivariate analysis. J. Agric. Food Chem. 2006; 54(16): 5749–5754.
- [30] Al-Qadiri HM, Lin M, Al-Holy MA, Cavinato AG, Rasco BA. Detection of sublethal thermal injury in *Salmonella enterica* serotype Typhimurium and *Listeria monocytogenes* using Fourier transform infrared (FT-IR) spectroscopy (4000 to 600 cm^{-1}). J. Food Sci. 2008; 73: M54–M61.
- [31] Davis R, Mauer LJ. Fourier transform infrared (FT-IR) spectroscopy: a rapid tool for detection and analysis of foodborne pathogenic bacteria. In: Méndez-Vilas A, editor.

Current Research, Technology and Education Topics in Applied Microbiology and Microbial Biotechnology. Formatex Research Center: Badajoz, Spain. 2010; 2:1582-1594.

- [32] Natalello A, Ami D, Gatti-Lafranconi P, Ario de Marco, Lotti M and Doglia SM. Kinetics of aggregation and structural properties of proteins in inclusion bodies studied by Fourier transform infrared spectroscopy. *Microb. Cell Fact.* 2006; 5 (Suppl 1): S10. DOI: 10.1186/1475-2859-5-S1-S10
- [33] Taha M, Hassan M, Essa S, Tartor Y. Use of Fourier transform infrared spectroscopy (FTIR) for rapid and accurate identification of Yeast isolated from human and animals. *Int. J. Vet. Sci. Med.* 2013; 1: 15–20. Available from: <http://dx.doi.org/10.1016/j.ijvsm.2013.03.001>
- [34] Salem EZ, Shahin IM, Yaser FM, Hamed MA, Abdel Hamid MF, Emam H et al. Applicability of Fourier transform infrared spectroscopy for rapid identification of some yeast and dermatophytes isolated from superficial fungal infections. *J. Egypt Women Dermatol. Soc.* 2010; 7: 105–110.
- [35] Allam AA, Salem JM. Evaluation of rapid molecular identification of clinically important *Candida* spp. isolated from immuno-compromised patients using RF-PCR. *J. Am. Sci.* 2012; 8: 463–468.
- [36] Dole MN, Patel PA, Sawant SD, Shedpure PS. Advance applications of Fourier transform infrared spectroscopy. *Int. J. Pharm. Sci. Rev. Res.* 2011; 7(2): 159–166. Article-029. ISSN 0976-044X
- [37] Dougan AJ, Kazarian GS. Fourier transform infrared spectroscopy imaging of live cells. *Spectrosc. Eur.* 2013; 25(5): 6–12.
- [38] Krafft C, Sergo V. Biomedical applications of Raman and infrared spectroscopy to diagnose tissues. *Spectroscopy* 2006; 20: 195–218. DOI: 10.1155/2006/738186
- [39] Balász B, Sipos P, Danciu C, Avram Ș, Soica C, Deheleanu C, Varju G, Erős G, Budai-Szücs M, Berkó S, Csányi E. ATR-FTIR and Raman spectroscopic investigation of the electroporation-mediated transdermal delivery of a nanocarrier system containing an antitumour drug. *Biomed. Opt. Express.* 2016; 7(1): 67–78. Available from: <https://doi.org/10.1364/BOE.7.000067>
- [40] Pawlikowska-Pawlega B, Misiak LE, Zarzyka B, Paduch R, Gawron A, Gruszecki WL. Localization and interaction of genistein with model membranes formed with dipalmitoylphosphatidylcholine (DPPC). *Biochim. Biophys. Acta* 2012; 1818(7): 1785–1793. DOI: 10.1016/j.bbamem.2012.03.020
- [41] Mbah CJ, Uzor PF, Omeje EO. Perspectives on transdermal drug delivery. *J. Chem. Pharm. Res.* 2011; 3(3): 680–700. ISSN No: 0975-7384 CODEN (USA): JCPRC5. Available from: www.jocpr.com
- [42] Khaizan NA, Wong WT. Microwave: effects and implications in transdermal drug delivery. *Progr. Electromag. Res.* 2013; 141: 619–643.

- [43] Lin PC, Lin S, Wang PC, Sridhar R. Techniques for physicochemical characterization of nanomaterials. *Biotechnol. Adv.* 2014; 32(4): 711–726. DOI:10.1016/j.biotechadv.2013.11.006
- [44] Sarah De Saeger, editor. *Determining Mycotoxins and Mycotoxigenic Fungi in Food and Feed*. Woodhead Publishing Series in Food Science, Technology and Nutrition. Cambridge, UK: Woodhead; 2011. No 203. 427 p. ISBN: 9781845696740
- [45] Chauchan A, FTIR: a novel bio-analytical technique. *J. Anal. Bioanal. Tech.* 2012; 3: e107. DOI: 10.4172/2155-9872.1000e107
- [46] Severcan F, Haris PI, (Eds). *Vibrational Spectroscopy in Diagnosis and Screening*. Amsterdam: IOS Press; 2012. 432 p. DOI: 10.3233/978-1-61499-059-8-118
- [47] Jack C (Ed) (Ewing's) *Analytical Instrumentation Handbook*, Third Edition. Ed. CRC Press Taylor & Francis Group: Taylor & Taylor Group; 2004. 1064 p.
- [48] Ohta D, Kanaya S, Suzuki H. Application of Fourier-transform ion cyclotron resonance mass spectrometry to metabolic profiling and metabolic identification. *Curr. Opin. Biotechnol.* 2010; 21(1): 35–44. DOI: 10.1016/j.copbio.2010.01.012
- [49] Bogdanov B, Smith RD. Proteomics by FTICR mass spectrometry: top down and bottom up. *Mass Spectrum. Rev.* 2005; 24(2): 168–200. DOI: 10.1002/mas.20015
- [50] Nikolaev EN, Kostyukevich YI, Vladimirov GN. Fourier transform ion cyclotron resonance (FTICR) mass spectrometry: theory and simulations. *Mass Spectrum. Rev.* 2016; 35: 219–258. DOI: 10.1002/mas.21422
- [51] Creese AJ, Cooper HJ. Liquid chromatography electron capture dissociation tandem mass spectrometry (LC-ECD-MS/MS) versus liquid chromatography collision-induced dissociation tandem mass spectrometry (LC-CID-MS/MS) for the identification of proteins. *J. Am. Soc. Mass Spectrom.* 2007; 18(5): 891–897. DOI:10.1016/j.jasms.2007.01.008
- [52] Barrow MP, Burkitt WI, Derrick PJ. Principles of Fourier transform ion cyclotron resonance mass spectrometry and its application in structural biology. *Analyst.* 2005; 130: 18–28. DOI: 10.1039/B403880K
- [53] Tsybin YO, Quinn JP, Tsybin OY, Hendrikson CL, Marshall AG. Electron capture dissociation implementation progress in Fourier transform ion cyclotron resonance mass spectrometry. *J. Am. Soc. Mass Spectrom.* 2008; 19(6): 762–771. DOI: 10.1016/j.jasms.2008.02.007
- [54] Marshall AG, Chen T. 40 years of Fourier transform ion cyclotron resonance mass spectrometry. *Int. J. Mass Spectrom.* 2015; 377: 410–420. DOI: 10.1016/j.ijms.2014.06.034
- [55] Scigelova M, Hornshaw M, Giannakopoulos A, Makarov A. Fourier transform mass spectrometry. *Mol. Cell. Proteom.* 2011; 10(7): M111.009431-M111.009431. DOI: 10.1074/mcp.M111.009431
- [56] Leach FE, Wolff JJ, Xiao Z, Ly M, Laremore TN, Arungundram S, Al-Mafraji K, Venot A, Boons G-J, Linhardt RJ and Amster IJ. Negative electron transfer dissociation Fourier

transform mass spectrometry of glycosaminoglycan carbohydrates. *Eur J. Mass Spectrom* (Chichester, Eng.). 2011; 17(2): 167–176. DOI: 10.1255/ejms.1120

- [57] Zhou W and Hakansson K. Electron capture dissociation of divalent metal-adducted sulfated N-glycans released from bovine thyroid stimulating hormone. *J. Am. Soc. Mass Spectrom.* 2013; 24(11): 10.1007/s13361-013-0700-3. DOI: 10.1007/s13361-013-0700-3
- [58] Creese AJ and Cooper HJ. The effect of phosphorylation on the electron capture dissociation of peptide ions. *J. Am. Soc. Mass Spectrom.* 2008; 19(9): 1263–1274. DOI: 10.1016/j.jasm.2008.05.015