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Detection in UV-visible spectrophotometry: Detectors, detection systems, and detection strategies

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ABSTRACT

A compilation of the new developments in terms of detection, detections systems and detection strategies in Ultraviolet-Visible (UV-Vis) spectrophotometry is presented and discussed. It is shown that this evolution has promoted the use of UV-Vis spectrophotometry as a simple, sensitive, reliable, and low cost technique, that allows the determination of very low concentrations of compounds, and the use of very small amounts of samples. The versatility, and the portability of the developed equipment and strategies, have also contributed for the continuous use of UV-Vis spectrophotometry, over the years.

By the examples of its use in diverse fields such as agriculture, food, clinical, pharmaceutical, and environmental is highly expectable that detection in UV-Vis spectrophotometry, continues to evolve and to promote this kind of applications.

Contents

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1. Introduction

The electromagnetic spectrum includes a wide range of energy frequencies, but the most useful is in the range between >10^{19} (γ-rays) and 10^3 Hz (radiowaves). The visible region is a small region of the spectrum and the visible light differ from the other type of radiation in the frequency of energy of its photons. The absorption of light in the UV-Vis wavelength (between ~180–800 nm) occurs frequently from many molecules such as a wide number of organic molecules. The main energy changes happen at electronic level but can also happen at vibrational quantum levels [1]. $n \rightarrow \sigma^*$ and $\sigma \rightarrow \sigma^*$ transitions need more energy and are related with absorption in the UV region and $\pi \rightarrow \pi^*$ transition with absorption in the UV–Vis region. The area of the molecule where the electronic transitions happen is called chromophore [2]. When the molecule is transparent in this region, derivatization can be used (Schiff base formation, complexation reactions, enzymatic and other catalytic reactions, azodyes derivatization, charge transfer complexation, ion-pair analysis, solid phase derivatization) [3–6]. Using the derivatization, the sensitivity and sometimes the selectivity of the UV-Vis methodology increase. The same happens when sample preconcentration/enrichment is used (based on solvent or sorbent extraction or membrane separation) [7,8]. However, these are all strategies to increase the possibility of an improved detection. During the recent past, a rapid progress in the detection processes in UV-Vis spectrophotometry has been reported, in order to improve the sensitivity, precision, and accuracy and at the same time to minimize the cost and the time of analysis. However, most part of the published papers or book chapters are focused on the basic principles of UV-Vis spectrophotometry [1,2,9,10], on its applications in specific fields such as the environment [11] or the pharmaceutical [3] or specific analytes such as organic compounds or individual elements [12] and on the treatment of spectrophotometric data [13,14]. When the instrumentation is focused, the attention is divided between light sources, monochromators, sample cells and detectors [1]. Even when the different detectors are compared [15], it has been made in an abbreviated way. In the best of our knowledge there are not any reference that compiled all the information about different kinds of detectors and, at the same time, the detection system that have been developed using the referred detector associated with other instrumentation, and the detection strategies that have been used in UV-Vis spectrophotometry. Thus, in this paper, it is intended to highlight the different and more actualized detectors, detection systems resulted from their development, and different detection strategies used in UV-Vis spectrophotometry, showing a title of example some applications in the determination of organic compounds. A flow diagram about the article structure is presented in Fig. 1 in order to guide the readers throughout the text.

2. Principles of UV-Visible (UV-Vis) spectrophotometry

Ultraviolet and Visible absorption spectrophotometry is the technique based on attenuation of electromagnetic radiation measurement by an absorbing substance [9]. This radiation, has a spectral range approximately around 190–800 nm, which also differ in terms of energy ranges, and type of excitation from other related regions (Table 1). This attenuation results from the reflection, scattering, absorption or interferences. However, accurate measurements of the attenuation can be done recording only the absorbance. Within some limits, the absorbance is proportional to

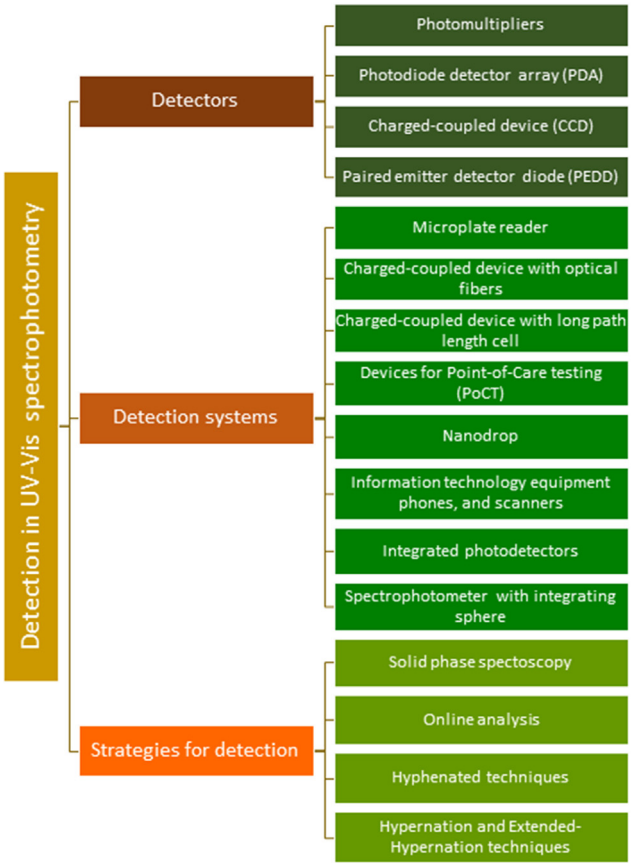

Fig. 1. Flow diagram representing the structure of the paper.

the concentration of the analyte to determine and to the distance of the light when it passes through the sample during the irradiation. This relationship is called Beer's law and it is commonly written as $A = \varepsilon \times b \times c$, where A means absorbance, ε is the molar absorbance coefficient (wavelength-dependent) in mol^{-1} L cm^{-1}, b is the path length in cm and c is the absorber concentration in mol L^{-1} [9]. This linear relationship can be influenced by different factors such as the characteristics of the spectrophotometer, photodegradation of the molecules, presence of scattering or absorbing interferences in the sample, fluorescent compounds in the sample, interactions between the analyte and the solvent, and the pH [1,9].

3. Detectors

The function of a UV-Vis detector is to convert a light signal into an electric signal. Ideally, it must respond in a wide wavelength range, respond with high sensitivity and with low noise, have a linear response range, have a fast response, allow the miniaturization and a low consumption of sample. In order to achieve an ideal detector, many detectors, that are followed described, have been developed in the last few years.

3.1. Photomultipliers

Photomultiplier tubes (Fig. 2) are composed by a photoemissive cathode, a series of electrodes (dynodes) and an anode. The cath-

Table 1
Approximate wavelengths, energies and type of excitation for different spectral regions. (Reprint from Tissue [9] with permission from the John Wiley and Sons, Copyright 2012).

Spectral region	Wavelength range (nm)	Energy range (cm^{-1})	Energy range (eV)	Types of excitation
Vacuum-UV	10–180	1×10^6-56,000	120–6.9	Electronic
UV	180–400	56,000–25,000	6.9–3.1	Electronic
Visible	400–750	25,000–13,300	3.1–1.6	Electronic
NIR	750–2500	13,300–4000	1.6–0.50	Electronic, vibrational overtones
IR	2500–25,000	4000–400	0.50–0.050	Vibrations, phonons

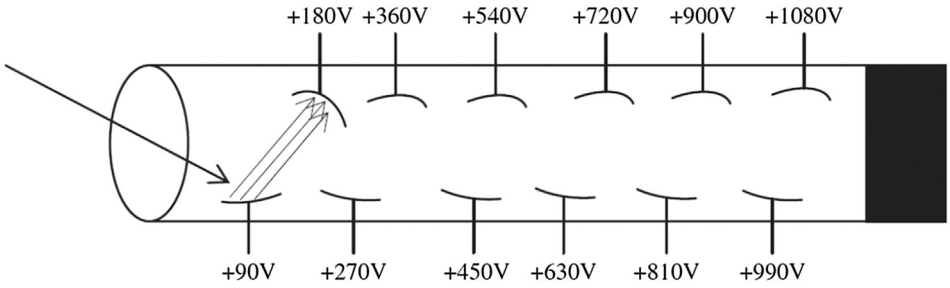

Fig. 2. A schematic diagram of a photomultiplier tube. (Reprint from Jespersen [17] with permission from the Elsevier. Copyright 2006.)

ode when stricken by a photon, emits several electrons that are accelerated towards the dynodes, since they are a release of many secondary electrons. Those ones are accelerated to the next electrode where each one releases more electrons. In the end, they are collected on the anode and consequently the final output is further electronically amplified [16].

The use of photomultipliers that are very sensitive, allow the detection of very low levels of light, and high wavelength resolution since they permit the use of narrow slit widths. They have been widely used for detections in UV and Visible regions.

3.2. Photodiode Detector Array (PDA)

The operation of a photodiode detector array is based on the fact that each diode in the array is reverse-biased. Before the exposition of the detector to the light, the diodes are completed charged through a transistor switch. When the light is reaching the PDA charge carriers will be generated in the silicon. These carriers will neutralize the stored charges that have the opposite polarity. Thus, this lost amount of charge is directly proportional to the light received by the detector and it is measured during the recharge process of each diode, measuring the amount of current need for the recharging [15].

PDA have the ability to monitor at all wavelengths. Thus, they have been widely used as multichannel detectors. In addition, they can record a complete spectrum in a very short period of time, since the movement of the diffractor does not affect the scan time. Consequently, they are able to detect transient signals, such it happens in HPLC and flow analysis [12]. Additionally, PDA present some advantages such as the ability to quantify large photon fluxes, high quantum efficiency, and the high height-to-width aspect ratio. Despite these advantages, PDA present some drawbacks, such as a relevant dark current and a high read noise [18]. The development of charged-coupled devices was performed in order to resolve these disadvantages.

3.3. Charged-Coupled Device (CCD)

The definition proposed by the Royal Society of Chemistry for the charged-coupled device is a detector that uses a silicon chip to convert light into an electric signal. The Si chip absorbs a photon and releases a single electron. The chip surface is covered by electrodes that hold the electrons in an array of wells, or pixels. The charge built up corresponds to a pattern of incident light [19]. Thus, CCD present some advantages such as a low dark count rate, a low read noise, and a high UV-Vis quantum efficiency [18], that make CCD excellent spectroscopic detectors.

3.4. Paired Emitter Detector Diode (PEDD)

The Light-Emitting Diode (LED) consists of a p-n junction that emits a narrow band of light frequencies when forward biased [20,21]. Since their development [22], LED have been used as an interesting component in optical sensors [23–25], since they are inexpensive, allow the miniaturization, the robustness and, a high efficiency. Despite their use started to be as light sources, nowadays they have been applied in a reverse mode, as detectors [26,27]. When the light is incident on the p-n junction, a current is generated. This current is proportional to the light intensity [20,21]. Thus, since they can be used as a light source and detector, several devices have been described based on Paired Emitter-Detector Diodes (PEDD) (Fig. 3).

PEDD optical sensors have shown several advantages such as the low power consumption, the reduced size, the sensitivity, the response in a large wavelength range with a high signal-noise ratio. In addition, their output is a direct pulse-duration-modulated signal, that allows the use of an expensive A/D converter unnecessary [28]. Their advantages allow their use in flow-through optical sensor used in chromatography [29,30] and in flow analysis [31,32], beyond their use in different devices for simple absorbance measurements [33,34].

4. Detection systems

Different detection systems resulted from the implementation of the different detectors described above, have been developed to be used in UV-Vis spectrophotometry, in order to increase the number of analyzed samples, the sensitivity, and selectivity, to decrease of the reagents consumption, and to allow the automation when compared with the conventional spectrophotometers.

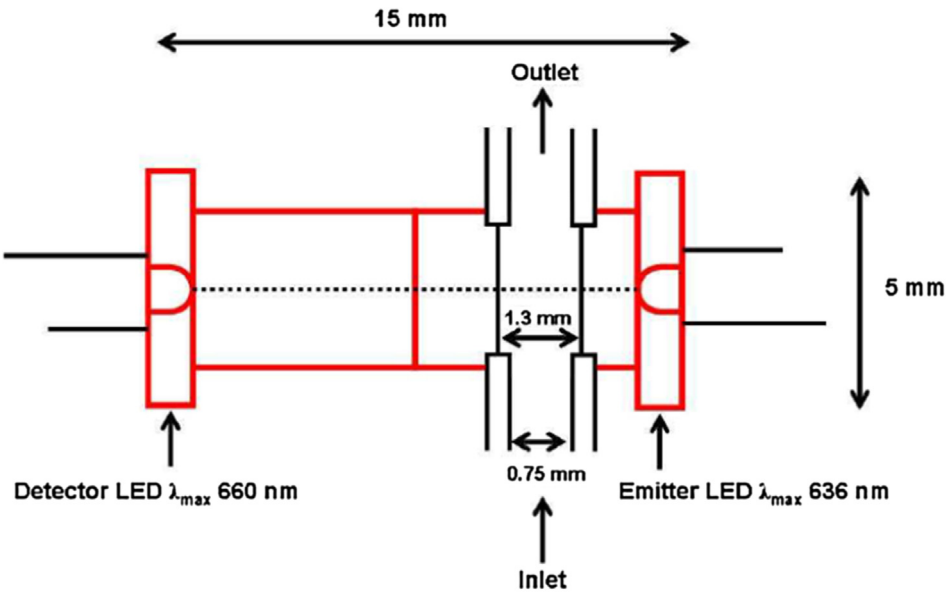

Fig. 3. A schematic of the integrated PEDD flow analysis device used for colorimetric detection. (Reprint from O'Toole et al. [28] under the Creative Commons Attribution Licence (CC BY 3.0)).

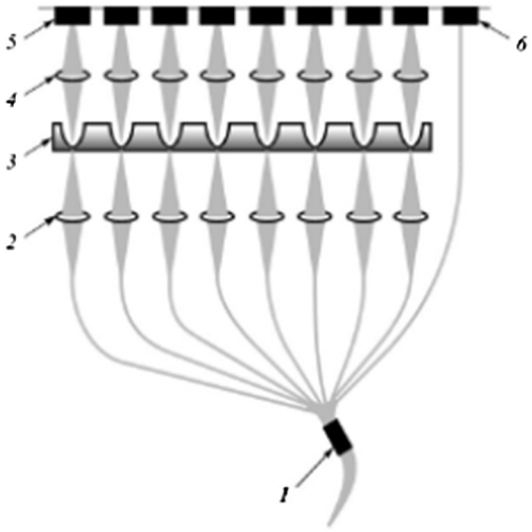

Fig. 4. Simultaneous data readout from a microplate strip: (1) fiber light guide; (2, 4) microlenses; (3) plate strip; (5) measurement channel photodiodes; (6) reference channel photodiode. (Reprint from Levin [35] with permission from the Springer Nature. Copyright 2005.)

4.1. Microplate reader

The use of a microplate optical reader results from the necessity to minimize the amount of sample and to analyze a large number of samples in a short period of time. In this kind of devices, the samples are placed in microplates pits instead of cells. The microplates usually have between 6 and 1536 pits, but the most frequently used are the microplates with 96 pits. These readers allow a thermostatic control and an orbital or a linear samples shaking before the analysis. The measurements are made moving the plate relative to the fixed probe beam, moving the latter relative to the plate or combining both strategies. More recently, it was possible to measure simultaneously an entire strip using a PDA or a CCD line [35] (Fig. 4).

Due to the capacity to analyse a large number of samples using small volumes of these samples, the microplate reader have been used in different fields such as in environmental analysis, for example in the determination of biochemical oxygen demand using 2,6-dichlorophenolindophenol (DCIP) as a redox colour indicator [36]. It has also been used in clinical analysis, for example in the quantification of bacterial pathogens' virulence on the insect model Galleria mellonella [37], in pharmaceutical field such as in the determination of olmesartan medoxomil in tablets [38] or in food analysis, for example in the evaluation of antioxidant compounds in fruits [39].

4.2. Charged-coupled device with optical fibers

Charged-coupled devices have been used in association with two optical fibers in order to miniaturize the detection system. One of these fibers connect the light source to the cell holder (where the sample is placed) and the other one connects this cell to the CCD detector. This detection system is frequently used in association with flow systems for the spectrophotometric quantification of organic compounds such as glucose [40] or for the evaluation of enzymes activity such as the evaluation of peroxidase activity in fruits [41] or the evaluation of glutathione reductase activity in order to predict the toxic effect of ionic liquids [42].

4.3. Charged-coupled device with long path length cell

In order to improve the sensitivity of the method, a liquid waveguide capillary cell with a long path length, have been coupled with CCD detectors, in flow analysis manifolds. This cell is made of a fused silica tubing coating outside with a low refractive index polymer. The liquid sample is guided through the hole of the capillary and consists in the core of the waveguide. This kind of cell combines the use of small sample volumes (between 2.4 μL and 3 mL) with an increase in the optical path length (between 10 and 500 cm) [43]. This kind of strategy has been frequently used for the evaluation of some elements such as bismuth in well waters [44], cadmium in waters [45], and manganese in seawaters [46], but it has also been used to evaluate organic compounds such as

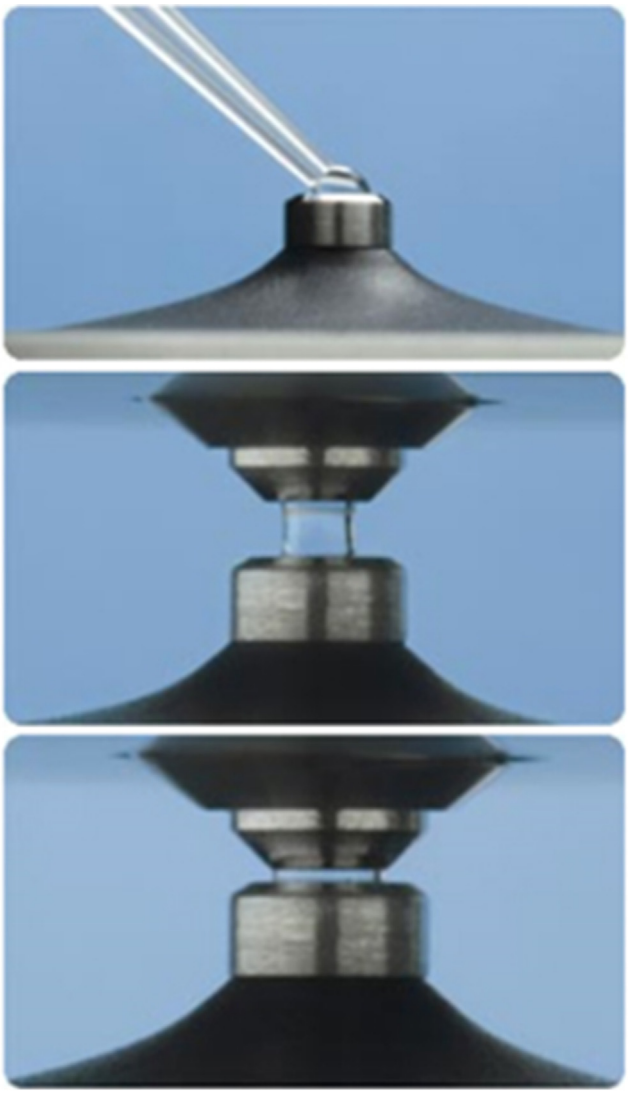

Fig. 5. The Nanodrop sample retention system. (a) one microliter of sample is loaded directly onto the lower measurement surface. (b) The sample is engaged an upper optical surface and retained by surface tension during the measurement. (Reprint from ThermoFisher Scientific web page [96]).

phenols in drinking waters [47], or Tc-99, an artificial compound widely used in nuclear medicine for diagnostic tests [48].

4.4. Devices for Point-of-Care Testing (PoCT)

The development of point-of-care testing has increased in the last decades. They intend to be easier-to-use devices and allowing the performance of low-cost analysis in a non-laboratory environment. There are two major categories of PoCT. The first one is composed of small handheld devices, used either to qualitative or to quantitative analysis. Glucose biosensor strips and lateral flow strips for the determination of cardiac markers and infectious pathogens using immobilized antibodies are the most used technologies in this group. The second category is composed of larger devices that result from the reduction in size and complexity of laboratory instruments. In this category are included critical care analyzers, immunology and small hematology analyzers [49]. In order to promote, even more, the development of patient-centered devices, the miniaturization of electronics and increasing computing power have been taking place. Smart holograms [50], for example, has already been presented as a future device.

4.5. Nanodrop

The NanoDrop technology is based on the development of a patented sample- retention system that allows the use of very small volumes of sample (around 1 μL). In these microvolume spectrophotometers, the sample is placed between two optical surfaces, and the surface tension of the sample allows the formation of a liquid column with a path length, mechanically controlled (Fig. 5). This control allows the use of a wide range of concentrations, eliminating the need for dilutions. The surface tension of the sample promotes the creation of its own container, dispensing the use of cuvettes, microcells or capillaries. This kind of devices has been used for absorbance measurements in nucleic acids and proteins analysis [51]. It has been used, for example, to evaluate the integrity of genomic DNA isolated from whole blood [52], for the quantification of cell-free DNA(cfDNA) in malignant melanoma and prostate cancer patients [53], or for the analysis of gold nanoparticle-oligonucleotide conjugate to detect the sequence of a lung cancer biomarker [54].

4.6. Information technology equipment (Digital cameras, video cameras and webcams, mobile phones and scanners)

The use of information technology equipment (mobile phones, digital and video cameras, scanners and, webcams), have been recently used as detection devices for colorimetric chemistry. They have been applied using Microfluidic Papers based Analytical Devices (μPADs), well plate reaction vessels and indicator papers. The use of these devices is simple, the cost per analysis is low, and the portability allows their implementation in point of care diagnosis and in-situ determinations in different fields [55]. For example, a digital camera has been used for the evaluation of 2,4,6-trinitrotoluene in soil extracts [56] or brilliant green in wastewaters [57], a mobile phone for the determination of sulfadiazine and sulfasalazine in pharmaceutical and veterinary formulations [58] and a webcam for the monitoring of hydrochloric and phosphoric acids in aqueous solutions [59].

4.7. Integrated photodetectors

The integration of photodetectors in lab-on-chip has been reported for the development of photonic biosensors. This integration allows an increment of the sensitivity, label-free and real-time detection, promotes the automation and minimize the operator intervention. To develop a photonic lab-on-chip device in the same platform it should be included the photonic sensor, the valves, the pumps, the flow cell, the light source and the detector (a miniaturized CCD camera or a PDA), the processing electronics and the firmware and software. This integration could be considered monolithic if all the components are in the same chip or hybrid if they are divided for different chips [60]. This integration has allowed the development of portable and easy-to-use devices for example for the evaluation of phenolic compounds [61], antimicrobial metabolites [62], peptides [63] and drugs [64].

4.8. Spectrophotometer with integrating sphere

The combination of an integrating sphere with a UV-Vis spectrophotometer is useful for high precision reflectance and scattered transmittance measurements. This allows the characterization of solid samples, and photometric analysis of translucent, turbid and colloidal samples. The analysis of this kind of samples in a conventional spectrophotometer results in significant

photometric errors and high variation between samples since the light is lost before to reach the detector. The use of an integrating sphere avoids this behavior since it collects all the light which has passed through the sample [65,66]. Thus, it is very useful, for example to evaluate the optical properties of biological tissues such as the mucosa and submucosa of human colon tissue [67], to characterize powders with encapsulated active pigments, such as the yellow miraxanthin V and the violet betanidin, used in food applications [68], to measure the ultraviolet/visible transmission of intraocular lenses [69], or to evaluate the concentration cells such as cyanobacterium Anabaena variabilis [70].

5. Strategies for detection

5.1. Solid phase spectroscopy

The solid phase spectroscopy (SPS), is a photometric procedure, firstly described by Yoshimura et al. [71] that is based on the immobilization of an analyte or a reaction product on a solid phase. As solid phase, it can be used microbeads of non-polar or polymeric materials or ion-exchange resins. After the obtained equilibrium between the sorbent active sites and the target species, the beads are collected and placed in a cell with a few mL of a solution to be measured as a suspension. The optical measurement is proportional to the analyte concentration in the sample. The analyte retention on the solid support allows the analyte preconcentration, resulting in a high sensitivity and selectivity of this procedure. However, to obtain this enhanced sensitivity, it is crucial to use a high volume of sample (between 100 and 1500 mL). Additionally, the consumption of solid support is also high since it is discarded at every determination. However, when the batch concept is replaced by the implementation of a SPS in flow-analysis systems, the solid phase starts to be regenerated after each determination, performing successive measurements. Using this approach, the sorbent is placed inside the flow cell and the retention, the preconcentration, and the detection of the analyte are performed in the same place (the flow cell). The first time that SPS was performed in association with flow analysis was in 1985 by Ruzicka et al. [72]. Since then, it has been reported the association of SPS with different kinds of flow systems (flow injection analysis, sequential injection analysis, multi-syringe flow injection, and multicommutation) [40,73]. This promotes the association of different features such as the miniaturization with a subsequent reagent and sample consumption and waste generation, the automation, the re-use of the solid phase (except in bead injection approach), the versatility, the high sensitivity and selectivity [74].

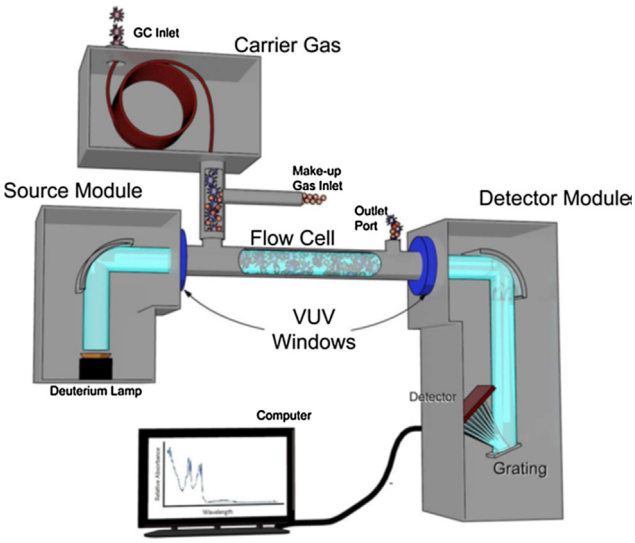

Fig. 6. Schematic (not to scale) of the GC-VUV instrument. (Reprint from Schug et al. [97] with permission from the American Chemical Society. Copyright 2014.)

5.2. Online analysis

Nowadays, the flow analysis techniques, such as Flow Injection Analysis (FIA) [75], Sequential Injection Analysis (SIA) [76], Multicommutation Flow Injection Analysis (MCFIA) [77], Multisyringe Flow Injection Analysis (MSFIA) [78], and Multi-Pumping Flow System (MPFS) [79] have shown to be great tools in the laboratories. This kind of flow systems present several advantages comparing with batch procedures, such as, the increment of sample throughput, allow the reduction of sample and reagents consumption and consequently the reduction in the cost per analysis and the waste generation, allow the automation, reducing the operator intervention, the errors and the time spent per analysis, allow online sample pretreatment (including dialysis, gas diffusion, digestion, separation, dilution or preconcentration). The miniaturization of these flow systems resulted in Lab-On-Valve (LOV) [80] systems as well as microfluidic devices that allow the development of new microflow analytical systems. In addition, these systems can integrate different kinds of detectors, improving the selectivity and the sensitivity [81,82]. However, UV-Vis spectrophotometry is the most common choice, frequently associated with chemical derivatization, due to the simplicity and adequate selectivity [82]. In some cases, some strategies can be used to decrease the detection limit such as using long pathlength cells, as it happens in the determination of pesticides in milk [83] or antibiotics in honey [84].

5.3. Hyphenated techniques

Hyphenation consists in the combination between a spectroscopic detection with a separation technique with the objective to obtain structural information about the analytes [85,86]. Liquid Chromatography-Mass Spectrometry (LC-MS), and Gas Chromatography-Mass Spectrometry (GC-MS) are hyphenated techniques frequently used [86]. However, sometimes, complementary information is required. Thus, LC and GC are hyphenated with other kinds of detection, including the use of a PDA. The LC-UV hyphenation has been used for example, in the pharmaceutical, biomedical, environmental and food analysis [86]. The UV spectrophotometry is rarely used as CG detection since there are a reduced number of GC amenable compound that absorb in the UV range, however, this number is enhanced in the Vacuum Ultraviolet (VUV) region (80–190 nm) [87] (Fig. 6).

The VUV spectrophotometer was developed in order to overcome some limitations presented by other detectors and it performs the deconvolution of co-eluting analytes, allowing qualitative and quantitative analysis [87]. The CG-VUV hyphenation has been used in different applications, such as, in the multiclass pesticide determination [88], in natural gas characterization [89], and in fatty acid methyl esters (including saturated, monounsaturated and polyunsaturated fatty acids) analysis [90].

5.4. Hypernation and extended-hypernation techniques

A combination of different hyphenated techniques in the same setup is called hypernation and sometimes is an option for solving some analytical problems [86]. The hypernation use is advantageous in terms of runtime, data correlation, and sample size but it presents the disadvantage of the use of diverse and expensive spectrophotometers [86]. Recently, it has been developed hypernation techniques that combine UV, Inductively Coupled Plasma-MS (ICP-MS), MS, Nuclear Magnetic Resonance (NMR), and Fourier

Transform Infrared (FTIR), detectors with LC-based operations. The hypernation LC/UV/MS has been referred as useful to distinguish several sub-classes of flavonoids [91] and in the investigation of phytochemical products, when additional information is crucial [92,93]. The combination of VUV detection with a GC × GC has been reported for the measurements of volatile organic compounds in bread gas [94] and for hydrocarbon fuels analysis [95], in order to complement the selectivity of a mass spectrometer.

6. Conclusions

A high evolution in the UV-Vis detection has happened in the last years. The development of different kinds of detectors have been occurring in order to increase the detection capacity and to minimize some particular drawbacks. Coupling these detectors with other instrumentation, such as optical fibers or long path length cells, some new detection systems have appeared. New strategies of detection, such as the solid phase spectroscopy or the hyphenation with some other techniques were also described in the last years.

All the detectors, detection systems or detection strategies were developed in order to promote simple and low cost analysis, the decrease in the detection limits, and the increase in the sensitivity of different methodologies of analysis. Thus, it is not possible to elect the best detector, detection system or detection strategy, since each one has particular characteristics that can be useful in different situations according for example with the analyte, with analyte concentration in the sample, the reaction involved in the determination, the available sample volume, the sample matrix, or the necessity of portability.

In the future, it is highly expectable that detection in UV-Vis spectrophotometry continues to evolve in order to keep up with the necessity to determine very low concentrations of compounds and to promote the quantification in samples available in very small quantities. The portability, the versatility, and the simplicity of the equipment, and its mode of use will always be present during the development of new detectors and new strategies of detection.

Conflicts of interest

There are no conflicts of interest to declare.

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