

Review Article

Experimental Methods for Measuring Optical Rotatory Dispersion: Survey and Outlook

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ABSTRACT The measurement of optical rotation (OR) and optical rotatory dispersion has been finding renewed interest for some years, because of advancement in computational methods and in the performance of new experiments. Here, we shortly review the traditional and most-used experimental methods. We define and discuss the two main types of approaches in measuring OR: the intensity method and the optical null method. We report on some new results obtained by redesigning experiments based on the first approach, by adapting non-sophisticated hardware to current circular dichroism instrumentation. *Chirality* 23:711–716, 2011. © 2011 Wiley-Liss, Inc.

KEY WORDS: optical rotatory dispersion; intensity methods; optical null methods

INTRODUCTION

A commonly shared feeling among spectroscopists dealing with chiral compounds is that modern circular dichroism (CD) has developed later than optical rotation (OR) methods, in particular optical rotatory dispersion (ORD), and that, in a few years, it widely replaced the older technique. While the second statement is by sure correct, the modern CD approaches, introduced with the use of electro-optic quarter wave generators,¹ appeared more or less simultaneously to ORD spectropolarimeters and, for a few years, the two techniques have evolved in parallel.² The simpler interpretation of CD spectra, together with somehow simplified spectra collection procedures, have been for sure the main reasons of the ORD decay; nevertheless in recent years, also due to the substantial progress in the design and performance of *ab initio* calculation capabilities,^{3–5} a renewed interest in the ORD technique has manifested. In parallel, new ORD experimental procedures have been presented, often based on ideas exploited in earlier designs; in this work, we briefly review the main methods devised in the past to measure ORD, based substantially on two rather different approaches: the intensity methods and the optical null methods.

We hope that this work will help one to understand the most recent methodologies, now under development in several laboratories, often involving the simultaneous measurement of ORD and CD. This work is organized as follows: in the first two sections, we present and discuss the intensity methods and the optical null methods, respectively. In the third section, we describe the ORD accessories mounted on current CD spectrometers (that are by far the most widely used and known chiroptical instruments). We conclude with two sections that are dedicated to the future, rather than the past or present; in the penultimate section, we describe the ORD spectrometers for the near infrared (NIR) or IR range,

and in the final section, we present the novel methods and applications of ORD.

INTENSITY METHODS

OR can be measured in a very simple way by placing the sample between two polarizers with optical axes not exactly mutually orthogonal, but rather forming an angle Θ , and measuring the intensity of the radiation transmitted by the analyzer, which is the second polarizer (see Fig. 1).

According to Malus law:

$$I = I_0 \cos^2 \Theta \quad (1)$$

where I is the intensity of the light transmitted through the two polarizers and I_0 is the intensity of the beam immediately after the first polarizer. If one introduces, between the two polarizers, an optically active sample causing an OR α and not absorbing the light at the selected wavelength, then eq. 1 gets modified to:

$$I_S = I_0 \cos^2(\Theta + \alpha) \quad (2)$$

For very small α values, the \log_{10} of the (I/I_S) ratio takes the simple form:

$$\log_{10}(I/I_S) \approx k\alpha \quad (3a)$$

Equation 3a may be obtained as follows. One first takes the base 10 logarithm of Eqs. 1 and 2, then develops the ratio

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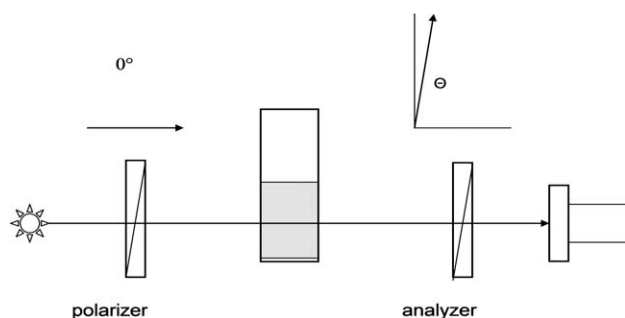


Fig. 1. Layout of intensity method-based Instruments for measuring ORD. The simplest basic design is presented. The polarizer is horizontally oriented (0°), while the analyzer is in nearly vertical orientation (Θ close to 90°).

in Taylor's series of α , and drops all terms in α beyond first order. One thus obtains:

$$\log_{10} \frac{I}{I_S} = \log_{10} \cos^2 \Theta - \log_{10} \cos^2(\Theta + \alpha) \\ \approx -\frac{1}{\log_e 10} \frac{d}{d\alpha} [\log_e \cos^2(\Theta + \alpha)]_{\alpha=0} \alpha + \dots \quad (3b)$$

$$\log_{10} \frac{I}{I_S} \approx -\frac{1}{\log_e 10} \left| \frac{2 \cos(\Theta + \alpha) [-\sin(\Theta + \alpha)]}{\cos^2(\Theta + \alpha)} \right|_{\alpha=0} \alpha + \dots \\ = \frac{2 \tan \Theta}{\log_e 10} \alpha + \dots \quad (3c)$$

From which we may deduce the value of k in eq 3a, namely:

$$k = \frac{2 \tan \Theta}{\log_e 10} = \frac{2 \tan \Theta}{2.3026} \quad (3d)$$

Implicit in the derivation procedure, and somewhat needless to say, is the fact that α in eq. 3a is measured in radians. In conclusion, the use of the above equations allows one to obtain the OR values from a direct measurement of two intensity values on a spectrophotometer by placing two polarizers, one before and one after the sample, where Θ is the angle between the optical axes of the two polarizers. Table 1 shows the expected "absorbance" values, that is to say $\log_{10}(I/I_S)$, for some values of α , when Θ is selected at 45° ,

TABLE 1. $\log_{10}(I/I_S)$ values expected on the basis of eqs. 1 and 2 in the text for specified values of α and Θ , the latter being in correspondence with (I/I_0)

	$\Theta = 45^\circ$	$\Theta = 70^\circ$	$\Theta = 85^\circ$
I/I_0	0.5	0.117	0.0076
$\alpha = +1^\circ$	+0.0154	+0.0428	+0.1934
$\alpha = +0.1^\circ$	+0.00152	+0.0042	+0.0178
$\alpha = +0.01^\circ$	+0.000152	+0.00042	+0.0017
$\alpha = +0.001^\circ$	+0.0000152	+0.000042	+0.00017
$\alpha = 0.000^\circ$	0	0	0
$\alpha = -0.001^\circ$	-0.0000151	-0.000042	-0.00017
$\alpha = -0.01^\circ$	-0.000151	-0.000415	-0.00171
$\alpha = -0.1^\circ$	-0.00151	-0.00414	-0.0171
$\alpha = -1^\circ$	-0.0149	-0.0405	-0.158

Very similar values are obtained by use of eq. 3a.

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70° , and 85° : the values were obtained by directly using eqs. 1 and 2. Very good approximations thereof may be obtained by using eq. 3a, as one may directly verify by also keeping in mind eq. 3c, which gives $k = 0.8686$, 2.3864 , and 9.9280 , correspondingly.

There are many limitations to this simple approach: although choosing a large Θ value might be better to measure sizeable absorbance levels, the light throughput (expressed as I/I_0) of the device will be limited, resulting in poor signal to noise. In addition, any absorption of the sample at the selected wavelength will induce a reading offset, which is often much larger than the effect to be measured, and consequently difficult to compensate. Other sources of errors are the reflection losses and the nonideal quality of the polarizing elements. These limiting factors may be due to some instability of the light source, which is not compensated in a single beam experiment. In Fig. 2, we compare the ORD spectra of a 1% sucrose aqueous solution in a 10-mm pathlength cell obtained by a conventional ORD spectropolarimeter to that obtained by a device, which, according to Fig. 1, was arranged by placing an additional polarizer in the sample compartment of a JASCO J-815SE CD spectrometer. The unit was operated with the photoelastic modulator (PEM) switched off, and the absorbance spectrum was collected by measuring the direct current (DC) signal at constant high voltage applied to the photomultiplier tube (in this mode the system works as a single beam spectrophotometer). In this case, the cell absorbance offset was compensated by taking a baseline spectrum with the chiral sample placed between the analyzer and the photomultiplier tube. A similar setup has been reported recently⁶ with a diode array spectrophotometer, while the same approach had been devised in the past for high performance liquid chromatography (HPLC) OR detectors.⁷

Alternative approaches based on the use of two polarizers and changing their relative orientation in the sample compartment of a single beam spectrophotometers were reported many years ago.^{8,9} In the apparatus by Keston et al., which

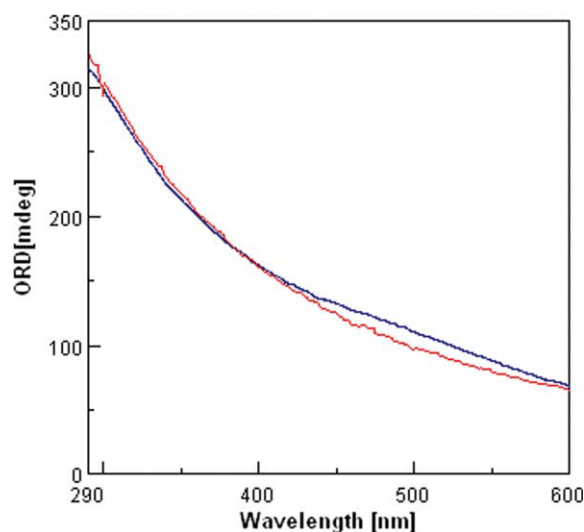


Fig. 2. Comparison of 1% (w/v) aqueous solution sucrose ORD spectra obtained in a 1-cm pathlength cell, measured through the accessory built with the basic design described in the text and mounted in Brescia on a JASCO J-815SE CD machine (red curve) with the corresponding ORD spectra in the same conditions obtained using a conventional optical null spectropolarimeter (blue curve).

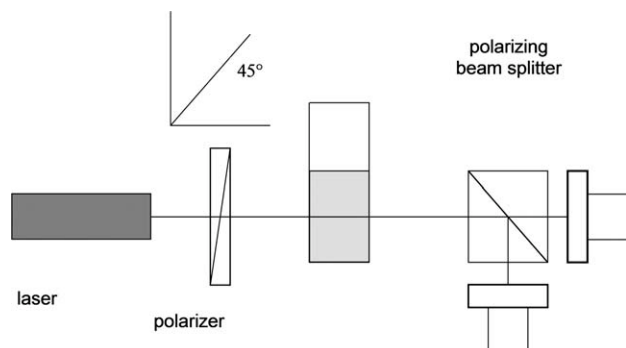


Fig. 3. Layout of a corner-cube polarizer-based intensity method apparatus for measuring ORD. An accessory based on a quite similar design was built and made to work in Brescia.

was developed as an accessory of the Beckman DU single beam spectrophotometer, at that time very popular, two measurements are carried out by rotating the analyzer at two angles $+\Theta$ and $-\Theta$, close to $\pm 90^\circ$, with respect to the first polarizer. The ratio between the two intensities:

$$\frac{I_{S1}}{I_{S2}} = \frac{\cos^2(\Theta + \alpha)}{\cos^2(-\Theta + \alpha)} \approx 1 - 4 \cdot \alpha \cdot \tan \Theta \quad (4a)$$

provides data related to α (the third term of eq. 4a may be obtained by Taylor expansion of the second term in the same equation, as done above for deriving eqs. 3a and 3c). This accessory was produced in several exemplars for a few years by the company Standard Polarimeter Co. and its calibration had been subject of several papers.^{10–13}

A double beam version of the Keston accessory was introduced by Woldbye.¹⁴ Two alike Keston units were placed, respectively, in the sample and in the reference compartment of a Cary 11 spectrophotometer, with the analyzers oriented at $+\Theta$ and $-\Theta$, respectively. ORD spectra of acceptable quality could be collected by placing two identical cuvettes filled with the sample in both beams. An accessory based on the same idea was produced for a few years also by Perkin-Elmer for their Model 450 spectrophotometer. It pays to mention that today this approach would not be as good as in the past, as the Cary 11 apparatus made use of a double prism monochromator, immune from Woods anomaly, and of parallel sampling beams in the external optics; all this is quite different from the current technology used in double beam UV-Vis spectrophotometers.

A variant of the above approach was explored by Rouy¹⁵: the sample was irradiated in alternation, through a rotating chopper system, by two linearly polarized beams, whose polarization plane formed angles $\pm\Theta$ with respect to the analyzer axis. Despite very favorable acceptance,¹⁶ the unit never went into actual production. In an earlier attempt, Gould¹⁷ designed an ingenious system using a double beam system with rotating analyzer and a phase detector. A triple beam OR and absorption was patented by Chiratech Inc.,¹⁸ but also in this case we are not aware of any actual production and availability on the market.

To complete this part of our review dealing with the intensity detection methods, we now consider the use of splitting polarization analyzers. Figure 3 shows the layout of a simple, easy to assemble, laser source polarimeter, which contains a corner cube beam splitter as analyzer. As the polarisation

axis of the incident beam is oriented at 45° with respect to the analyzer axis, we will have, with no sample, identical vertical and horizontal I_v and I_h light intensities on the two detectors at the same λ , but if the sample is optically active:

$$\frac{I_{S1}}{I_{S2}} = \frac{\cos^2(45 + \alpha)}{\cos^2(-45 + \alpha)} \approx 1 - 4\alpha \quad (4b)$$

(α here is in radians). Defining a pseudo-absorbance A from I_v/I_h , one may derive a relation between A and α , as follows:

$$A = \log_{10}\left(\frac{I_v}{I_h}\right) \approx \frac{4 \cdot \pi}{\log_e 10 \cdot 180^\circ} \alpha^\circ \quad (4c)$$

Inverting eq. 4c, one has the relation:

$$\alpha^\circ \approx 0.03 A \quad (4d)$$

which may be obtained online with a ratio log amplifier (we have added the superscript $^\circ$ to mean that the units for angles are degrees). This mode to measure OR, which compensates intensity fluctuations of the light source and sample absorbance, has been implemented in a few commercial HPLC detectors, in NIR polarimeters,¹⁹ and in the advanced cavity ring down polarimeter for gas phase samples.²⁰

In Figure 4, we report the ORD spectra obtained for a Λ -Co(en)₃Cl₃:H₂O standard solution on a quickly assembled accessory, allowing us to measure ORD spectra following this approach. As in the case of Figure 2, a J-815SE with PEM switched off was used, placing a Rochon polarizer with the

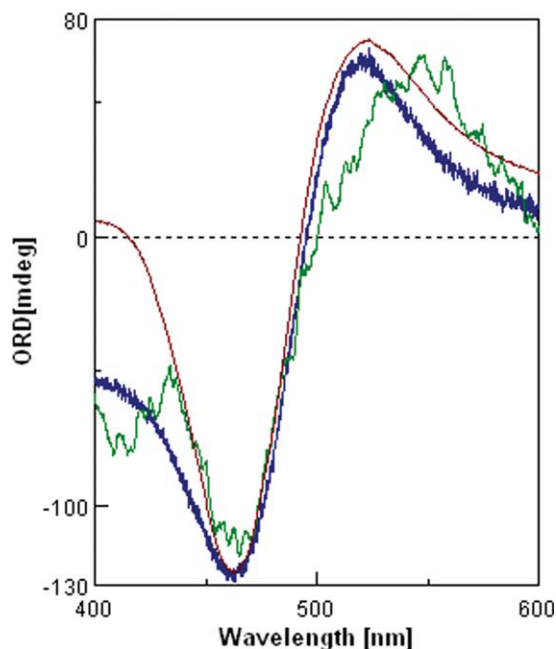


Fig. 4. Comparison of ORD spectra for aqueous solution of Λ -Co(en)₃Cl₃:H₂O (0.16% w/v) in a 1 cm quartz cell as obtained: on a JASCO CD-815SE with an accessory according to Fig. 3 (green line), on a old J-20 optical null ORD spectropolarimeter (blue line), and applying Kramers-Kronig (KK) transform of the CD spectrum obtained with the same J-815SE (red line). The KK conversion is simple to perform, but while signal to noise is very good, the intrinsic accuracy is restricted by the limited wavelength range used for calculation (600–300 nm in this case).

axis at 45° in the sample compartment. Detection of the two linearly polarized components was performed by a pair of Si diodes linked to the electronics of a JASCO Uvidec-100V HPLC detector, able to output the ratio log output of the intensities. We superimpose our ORD data to the theoretical Kramers-Kronig (KK) curve obtained from the CD spectrum run on the same J815SE instrument, with the prescriptions of reference.³ We also superimpose the real ORD spectrum obtained on a conventional optical null spectropolarimeter. It should be noted that the two experimental ORD curves are similar and differ from the KK curve at shorter wavelengths. A very interesting ORD spectrometer using this approach was announced by J&M in 1993, based on one Machler patent.²¹ The unit featured two diode array polychromators connected by optical fibers to the two outputs of the beam splitter prism, allowing real-time ORD spectra collection in the 200–600 nm range with 1.5 nm resolution. This interesting instrument, designed also as chiral HPLC detector, did not pass the prototype stage. In all cases, OR or ORD systems based on intensity measurements call for calibration all over the available spectral range; this can be typically achieved using a sucrose solution as reference standard.

OPTICAL NULL METHODS

The replacement of mere inspection methods with photoelectric unambiguous detection methods has been for a long time the goal of optical null polarimetry. A few examples are reported here: although obsolete in their practical construction, yet they are based on valid principles and some of them are still used today.

In the Peck patent of 1944,²² a Kerr cell was used to rotate back the plane of the polarization vector that had been rotated by the sample, and the detection was performed by a photocell looking for maximum light intensity, as the polarizer and the analyzer axis were kept parallel in that design. In the Levy design,²³ a photoelectric servo-system was used, which alternated, through a rotating sector, the two halves of “half-shade” images of a conventional polarimeter to feed a photomultiplier detection tube. The demodulated signal was used to rotate the analyzer to the null point. A rather similar design had been used in the commercial JASCO DIP-4 digital polarimeter manufactured in the seventies. Saltzman et al.²⁴ presented a polarimeter suitable for use in industrial plants with two analyzers crossed each other at 90° and two detectors. The misbalance signal was used to rotate the analyzer to reach the null position. In their 1961 patent,²⁵ Hyde and Tubbs introduced an optical null polarimeter including a quarter wave plate and a rotating analyzer.

There is no doubt that the development which gave origin to the modern ORD spectropolarimeter was the symmetric angular oscillation method proposed by Rudolph.²⁶ The polarizer oscillates a few degrees on either side of the crossed position at a frequency f . When the polarizer and the analyzer are crossed and the sample is not optically active, the detector will receive just a signal at the frequency $2f$. If an optically active sample is inserted in the path, a component at f frequency will appear: this signal is synchronously rectified to generate a DC voltage, with intensity proportional to the rotation angle to be balanced, and polarity according to the sign of the rotation. This voltage able to rotate, by a suitable servo loop, the analyzer to null the f component and in this way the physical rotation, is thereby measured. In the

original Rudolph design the analyzer was oscillating, while the polarizer was rotating to reach the new null point, but this obviously gives the same results as described above. It pays to mention that the Rudolph spectropolarimeters had a relevant role in the early application of chiroptical techniques for conformation studies of biomolecules and opened the way to further developments.

Different commercial ORD spectropolarimeters used different ways to oscillate the polarization vector: for example, in the Rudolph units of the JASCO ORD-UV5 and J-20 instruments and in the Perkin Elmer P23 instrument, the polarizer was mechanically oscillating, while in the Cary 60²⁷ and in the Carl Zeiss REMP-12 apparatuses a Faraday cell was used to modulate the linear polarization feeding the sample. The other two ORD units which had been commercially available for some time (the Bendix Polarmatic 62²⁸ and the FICA Spectropol 1) worked on a different principle. The optical null condition was not achieved by rotating the analyzer but by fitting a DC-controlled Faraday cell in the light path. In this way, the optical null conditions were met feeding the Faraday cell with a current of suitable intensity and proper polarity. That approach gave a few important benefits, such as response speed and cost reduction but the intrinsic accuracy and the need of calibration were clear drawbacks. The use of Faraday cells not only to modulate the polarization but also to achieve optical null conditions is still pursued today in some OR HPLC detectors. As a further way to simplify the instruments, it has been suggested to keep the analyzer and the polarizer crossed and to detect OR directly by the intensity and the phase of the f component. This approach is valid only for small rotation angles and had been and is still used in a few OR HPLC detectors.

As a matter of fact ORD spectropolarimeters, among which only the Cary 60 and the various JASCO models had a real commercial success, soon disappeared from the market, as users soon switched to CD as the main, almost unique, chiral technique. Only the JASCO J-20 had been covering the ORD market with no competition, but with marginal sales, for nearly 15 years, when production was stopped in 1987.

ORD ACCESSORIES FOR CURRENT CD SPECTROMETERS

Since for several years no dedicated ORD spectropolarimeter has been built and made available for commercial purposes, manufacturers introduced ORD accessories to CD spectrometers. JASCO and Applied Photophysics are currently offering accessories based on the design by Shindo²⁹ (ORDE-402 and ORD.3, respectively); very recently also Bio-Logic started the promotion of a similar accessory for their MOS450/CD spectrometer. In the JASCO accessory, a quartz Rochon polarizer is inserted just after the sample with its optical axis oriented at 45° , the photomultiplier tube is spaced far away not to detect the extraordinary beam of the Rochon unit. The PEM driving program is set to generate linear polarizations at twice its running frequency (50 kHz). A 100 kHz lock-in amplifier is used to demodulate the signal. In the ORD.3 case a Calcite polarizer is used, so there is no need to put the photomultiplier tube at a certain distance, but the accessible wavelength range is more limited in the far UV. This approach is another example of intensity methods discussed above, but with polarization modulation and phase-linked detection. Calibration can be performed by collecting a spectrum of sucrose

TABLE 2. Comparison of characteristics for ORDE and ORDM accessories mounted on JASCO J-700/800 CD instruments

	ORDE	ORDM
Wavelength range (nm)	185–700	185–700
Angular range (°)	±1	±45
Accuracy (%)	±1	±0.5
Root mean square (RMS) noise SBW 1 nm, integration time 16 sec		
500 nm (mdeg)	0.2	0.5
300 nm (mdeg)	0.15	0.5
200 nm (mdeg)	1	1
Baseline stability (mdeg/h)	3	3

solution to be ratioed with reference data to generate a suitable curve to correct experimental data.

JASCO is additionally offering the ORDM-401 accessory, which is a real optical null polarimetric head added to the basic system; when the CD unit is turned to this modality, it operates as a genuine rotating analyzer ORD unit, in which the modulation function is assigned to the photoelastic element already used for CD.

Table 2 compares the main specifications of both ORDE and ORDM accessories. What is not written here is that ORDE allows much faster spectra acquisition, but the stated accuracy is not absolute and intrinsically lower even after calibration.

ORD IN THE NEAR INFRARED AND INFRARED RANGE

While seldom investigated, even caused by intrinsic difficulties in the measurements, ORD spectra in the NIR and IR range are presently attracting more interest, due to the increased *ab initio* computational capabilities. A NIR ORD spectrometer based on an acousto-optical tunable filter, acting as wavelength dispersive system, as well as linear polarization splitter, has been recently described.³⁰ The unit makes use of two InGaAs detectors; overtone spectra of camphor enantiomers have been presented in the 1000–1300 nm range.

For the IR range, the group of Korte presented different optical designs based on dedicated single beam or commercial double beam dispersive spectrophotometers^{31,32}; the single beam device contained a continuously rotating wire-grid polarizer and a fixed analyzer placed, respectively, before and after the sample, thus causing a sinusoidal modulation of the sampling beam reaching the detector after being dispersed by a monochromator.³³ An optically active sample induces a phase shift of the radiation proportional to the OR. Sensitivity down to 0.01° was reported in favorable cases.

Another FT/IR polarimeter was reported³⁴ and patented³⁵; the unit had capabilities to measure the sample Mueller matrix, but here sensitivity for ORD spectra of organic compounds was low. More recently, probably for the first time, ORD spectra in the IR range have been reported by the group of Lombardi and Nafie,³⁶ obtained on a VCD interferometric spectrometer, which was used with 45° analyzer as in the Shindo approach.

NOVEL ORD METHODS AND APPLICATIONS

Multiphoton ORD measurements were reported in 1987³⁷ for 10% aqueous solutions of camphorsulfonic acid in the

450–470 nm region with an excimer-pumped dye laser and an optical null analyzer. In 1995, Kliger and coworkers³⁸ applied the Keston method to measure ORD changes into the nanosecond time scale. The setup included a Xenon flash lamp, an actinic light source consisting of a 532 nm laser and a polichromator with a gated array detector.

Dressler et al.³⁹ reported polarimetry of chiral surfaces by near-field scanning optical microscopy; in the same field a patent has been awarded.⁴⁰

Above we mentioned the innovative cavity ring down polarimetry introduced by Vaccaro and coworkers²⁰ which opened new opportunities for probing chirality in the gas phase; sensitivity enhancement inserting a cavity (Fabry-Perot interferometer) between crossed polarizers had been discussed previously,^{41,42} and the use of multipass cells had also been proposed for OR HPLC detectors.⁴³

Ghosh and Fischer suggested a new approach to polarimetry and spectropolarimetry,⁴⁴ which consists of measuring the relative difference in the direction of propagation of two circularly polarized light components that refract or reflect at an interface in the presence of an optically active sample. This approach does not require long path cells and operates with a position sensitive detector. The brilliant idea has been recently patented⁴⁵; potential applications in material science are many, but sensitivity is probably a concern.

An innovative Vis–NIR spectropolarimeter using liquid crystals to polarize and modulate radiation has been recently patented in France⁴⁶ by Horiba Jobin-Yvon together with CNRS and Ecole Polytechnique. The instrument is able to acquire a series of measurements to compute the Mueller matrix of the sample and it is mainly devoted to ellipsometric measurements.

Gibbs and Beebe⁴⁷ patented heterodyne optical systems with a modulated light source coupled to a chiroptical system with further modulation at a different frequency: radiation passes through the sample cell and then through a linear polarizer before reaching the detector. Intermodulated side bands are outputted and processed to extract the OR data with very high sensitivity. Spectroscopic polarimetry in a static way using retarders between the polarizers and the analyzers were introduced by Oka and Kato⁴⁸ and have been widely developed at Tokyo University of Agriculture and Technology.⁴⁹

Quite recently Helbing and Bonmarin⁵⁰ has been using alternating left- and right-handed mid-infrared laser pulses synchronized with a PEM to collect CD and ORD spectra in the IR CH-stretching region; changing polarizer and analyzer orientation (similarly to what indicated in Table 1) signal enhancement was achieved. Finally, as window wide open into the future, we wish to mention the work by Cho and coworkers,⁵¹ whereby a “direct phase-and-amplitude measurement of the electric field of a chiroptical signal over time” monitored by laser radiation is proposed. The method uses cross-polarized analyzers to carry out heterodyne spectral interferometry. Advantages are described there in removing achiral background signals. The method enables the simultaneous characterization of VCD and vibrational ORD spectra. Not only does this work opens new experimentation paths, in terms of time-resolved phenomena, but it also spurs new theoretical approaches, based in the time-domain rather than in the energy-domain and allowing to characterize bandwidths in addition to frequencies and rotational strengths.^{51–53}

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