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A historical review of optical activity phenomena

> Yet each in itself – this was the uncanny, the antiorganic, the life-denying character of them all – each of them was absolutely symmetrical, icily regular in form. They were too regular, as substance adapted to life never was to this degree – the living principle shuddered at this perfect precision, found it deathly, the very marrow of death – Hans Castorp felt he understood now the reason why the builders of antiquity purposely and secretly introduced minute variations from absolute symmetry in their columnar structures.
>
> *Thomas Mann* (The Magic Mountain)

1.1 Introduction

In the Preface, an optical activity phenomenon was defined as one whose origin may be reduced to a different response of a system to right- and left-circularly polarized light. This first chapter provides a review, from a historical perspective, of the main features of a range of phenomena that can be classified as manifestations of optical activity, together with a few effects that are related but are not strictly examples of optical activity. The reader is referred to the splendid books by Lowry (1935), Partington (1953) and Mason (1982) for further historical details.

The symbols and units employed in this review are those encountered in the earlier literature, which uses CGS units almost exclusively; but these are not necessarily the same as those used in the rest of the book in which the theory of many of the phenomena included in the review are developed in detail from the unified viewpoint of the molecular scattering of polarized light. In particular, the theoretical development in subsequent chapters employs SI units since these are currently in favour internationally.

1.2 Natural optical rotation and circular dichroism

Optical activity was first observed by Arago (1811) in the form of colours in sunlight that had passed along the optic axis of a quartz crystal placed between crossed polarizers. Subsequent experiments by Biot (1812) established that the colours were due to two distinct effects: optical rotation, that is the rotation of the plane of polarization of a linearly polarized light beam; and optical rotatory dispersion, that is the unequal rotation of the plane of polarization of light of different wavelengths. Biot also discovered a second form of quartz which rotated the plane of polarization in the opposite direction. Biot (1818) recognized subsequently that the angle of rotation α was inversely proportional to the square of the wavelength λ of the light for a fixed path length through the quartz. The more accurate experimental data available to Drude (1902) enabled him to replace Biot's law of inverse squares by

$$\alpha = \sum_j \frac{A_j}{\lambda^2 - \lambda_j^2}, \qquad (1.2.1)$$

where A_j is a constant appropriate to the visible or near ultraviolet absorption wavelength λ_j. Modern molecular theories of optical rotation all provide equations of this form for transparent regions.

Optical rotation was soon discovered in organic liquids such as turpentine (Biot, 1815), as well as in alcoholic solutions of camphor and aqueous solutions of sugar and tartaric acid, the last being reported in 1832 (Lowry, 1935). It was appreciated that the optical activity of fluids must reside in the individual molecules, and may be observed even when the molecules are oriented in random fashion; whereas that of quartz is a property of the crystal structure and not of the individual molecules, since molten quartz is not optically active. As discussed in detail in Section 1.9 below, it was eventually realized that the source of natural optical activity is a *chiral* (handed) molecular or crystal structure which arises when the structure has a sufficiently low symmetry that it is not superposable on its mirror image. The two distinct forms that can exist are said to have opposite *absolute configurations*, and these generate optical rotations of equal magnitude but opposite sense at a given wavelength.

The relationship between absolute configuration and the sense of optical rotation is subtle and has exercised theoreticians for a good many years. The modern system for specifying the absolute configuration of most chiral molecules is based on the R (for *rectus*) and S (for *sinister*) system of Cahn, Ingold and Prelog, supplemented with the P (for plus) and M (for minus) designation for molecules that have a clear helical structure. The sense of optical rotation (usually measured at the sodium D-line wavelength of 589 nm) associated with a particular absolute configuration is given in brackets, for example (R)-$(-)$ or (S)-$(+)$. Eliel and Wilen (1994) may be consulted for further details. The definitive method of determining
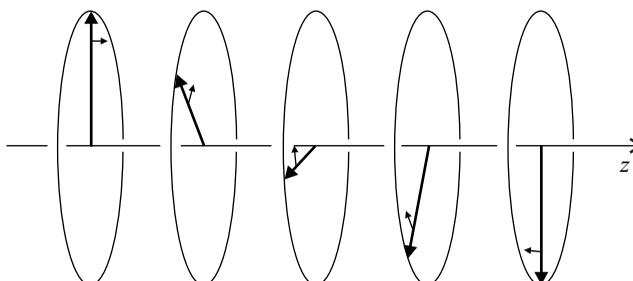
Fig. 1.1 The instantaneous electric field vectors of a right-circularly polarized light beam propagating along z. A vector in a fixed plane rotates clockwise when viewed in the $-z$ direction.

absolute configuration is via anomalous X-ray scattering associated with the presence of a relatively heavy atom substituted into the molecule, first demonstrated by Bijvoet *et al.* (1951) in a study of sodium rubidium tartrate. However, many chiral molecules are not accessible to X-ray crystallography: for these cases optical activity phenomena such as optical rotation, which are intrinsically sensitive to molecular chirality, are being used with increasing success. An optical method that can differentiate between the two enantiomers of a chiral compound is referred to as a *chiroptical* technique.

Fresnel's celebrated theory of optical rotation (Fresnel, 1825) followed from his discovery of circularly polarized light. In a circularly polarized light beam, the tip of the electric field vector in a fixed plane perpendicular to the direction of propagation traces out a circle with time: traditionally, the circular polarization is said to be right handed (positive) or left handed (negative) depending on whether the electric field vector rotates clockwise or anticlockwise, respectively, when viewed in this plane by an observer looking towards the source of the light. At a given instant, the tips of the electric field vectors distributed along the direction of propagation of a circularly polarized light beam constitute a helix, as shown in Fig. 1.1. Since the helix moves along the direction of propagation, but does not rotate, the previous definition of right and left handedness corresponds with the handedness of the helix, for as the helix moves through the fixed plane, the point of intersection of the tip of the electric field vector when viewed towards the light source rotates clockwise for a right-handed helix and anticlockwise for a left-handed helix. A particularly clear account of circularly polarized light and of the pitfalls that may arise in its graphical description may be found in the book by Kliger, Lewis and Randall (1990).

Fresnel realized that linearly polarized light can be regarded as a superposition of coherent left- and right-circularly polarized light beams of equal amplitude, the orientation of the plane of polarization being a function of the relative phases of the two components. This is illustrated in Fig. 1.2*a*. He attributed optical rotation to a
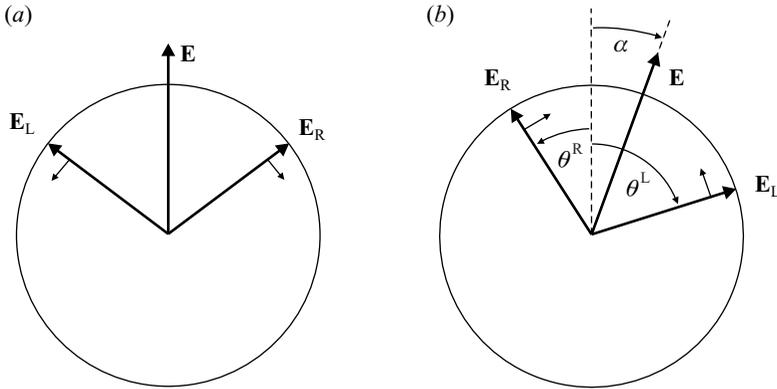
Fig. 1.2 (*a*) The electric field vector of a linearly polarized light beam decomposed into coherent right- and left-circularly polarized components. The propagation direction is out of the plane of the paper. (*b*) The rotated electric field vector at some further point in the optically active medium. Take note of Fig. 1.1 if confused by Fig. 1.2*b*.

difference in the velocity of propagation of the left- and right-circularly polarized components of the linearly polarized beam in the medium, for the introduction of a phase difference between the circularly polarized components would change the orientation of the plane of polarization, as shown in Fig. 1.2*b*. Suppose that a linearly polarized light beam of angular frequency $\omega = 2\pi c/\lambda$ enters a transparent optically active medium at $z = 0$. If, *at a given instant*, the electric field vectors of the right- and left-circularly polarized components at $z = 0$ are parallel to the direction of polarization of the linearly polarized light beam, then *at the same instant* the electric field vectors of the right- and left-circularly polarized components at some point $z = l$ in the optically active medium are inclined at angles $\theta^R = -2\pi cl/\lambda v^R$ and $\theta^L = 2\pi cl/\lambda v^L$, respectively, to this direction, where v^R and v^L are the velocities of the right- and left-circularly polarized components in the medium. The angle of rotation in radians is then

$$\alpha = \tfrac{1}{2}(\theta^R + \theta^L) = \frac{\pi cl}{\lambda}\left(\frac{1}{v^L} - \frac{1}{v^R}\right). \tag{1.2.2}$$

Since the refractive index is $n = c/v$, the angle of rotation in radians per unit length (measured in the same units as λ) can be written

$$\alpha = \frac{\pi}{\lambda}(n^L - n^R), \tag{1.2.3}$$

and is therefore a function of the *circular birefringence* of the medium, that is the difference between the refractive indices n^L and n^R for left- and right-circularly polarized light.

In the chemistry literature, the medium is said to be *dextro rotatory* if the plane of polarization rotates clockwise (positive angle of rotation), and *laevo rotatory* if the plane of polarization rotates anticlockwise (negative angle of rotation), when viewed towards the source of the light. The path of a linearly polarized light beam in a transparent optically active medium is characterized by a helical pattern of electric field vectors, since the orientation of each electric field vector is a function only of its position in the medium, although its amplitude is a function of time.

The form of the Drude equation (1.2.1) follows from (1.2.3) if an expression for the wavelength dependence of the refractive index such as

$$n^2 = 1 + \sum_j \frac{C_j \lambda^2}{\lambda^2 - \lambda_j^2} \qquad (1.2.4)$$

is used, where C_j is a constant appropriate to the visible or near ultraviolet absorption wavelength λ_j. This is a version of Sellmeier's equation (1872). Thus if the C_js are slightly different for right- and left-circularly polarized light, an expression for $(n^L)^2 - (n^R)^2$ is found. But $(n^L)^2 - (n^R)^2 = (n^L - n^R)(n^L + n^R)$, and since n^L and n^R are close to n, the refractive index for unpolarized light, the value of $(n^L + n^R)$ may be taken as $2n$, and Drude's equation (1.2.1) is obtained with $A_j = \pi\lambda(C_j^L - C_j^R)/2n$. This simple argument serves to illustrate how optical rotation can be generated if a mechanism exists giving $C_j^L \neq C_j^R$.

Since refraction and absorption are intimately related, an optically active medium should absorb right- and left-circularly polarized light differently. This was first observed by Haidinger (1847) in amethyst quartz crystals, and later by Cotton (1895) in solutions of copper and chromium tartrate. Furthermore, linearly polarized light becomes elliptically polarized in an absorbing optically active medium: since elliptically polarized light can be decomposed into coherent right- and left-circularly polarized components of different amplitude, as illustrated in Fig. 1.3, the traditional theory ascribes the generation of an ellipticity to a difference in the absorption of the two circular components. The *ellipticity* ψ is obtained from the ratio of the minor and major axes of the ellipse, which are simply the difference and sum of the amplitudes of the two circular components:

$$\tan \psi = (E_R - E_L)/(E_R + E_L). \qquad (1.2.5)$$

When $E_R > E_L$, ψ is defined to be positive, corresponding to a clockwise rotation of the electric field vector of the elliptically polarized beam in a fixed plane. The attenuation of the amplitude of a light beam by an absorbing medium is related to the absorption index n' and path length l by

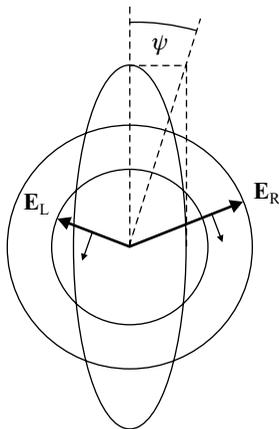$$E_l = E_0 e^{-2\pi n' l/\lambda}. \qquad (1.2.6)$$

Fig. 1.3 Elliptical polarization, specified by the angle ψ, resolved into coherent right- and left-circular polarizations of different amplitude.

The ellipticity is then

$$
\begin{aligned}
\tan \psi &= \frac{\mathrm{e}^{-2\pi n'^{\mathrm{R}} l/\lambda} - \mathrm{e}^{-2\pi n'^{\mathrm{L}} l/\lambda}}{\mathrm{e}^{-2\pi n'^{\mathrm{R}} l/\lambda} + \mathrm{e}^{-2\pi n'^{\mathrm{L}} l/\lambda}} \\
&= \frac{\mathrm{e}^{\pi(n'^{\mathrm{L}} - n'^{\mathrm{R}})/\lambda} - \mathrm{e}^{-\pi l(n'^{\mathrm{L}} - n'^{\mathrm{R}})/\lambda}}{\mathrm{e}^{\pi l(n'^{\mathrm{L}} - n'^{\mathrm{R}})/\lambda} + \mathrm{e}^{-\pi l(n'^{\mathrm{L}} - n'^{\mathrm{R}})/\lambda}} \\
&= \tanh \left[\frac{\pi l}{\lambda}(n'^{\mathrm{L}} - n'^{\mathrm{R}}) \right],
\end{aligned}
\tag{1.2.7}
$$

where n'^{L} and n'^{R} are the absorption indices for left- and right-circularly polarized light. For small ellipticities, in radians per unit length (measured in the same units as λ),

$$
\psi \approx \frac{\pi}{\lambda}(n'^{\mathrm{L}} - n'^{\mathrm{R}}).
\tag{1.2.8}
$$

The ellipticity is therefore a function of $(n'^{\mathrm{L}} - n'^{\mathrm{R}})$, the *circular dichroism* of the medium.

Apart from the fact that they are signed quantities, circular dichroism and optical rotatory dispersion have wavelength dependence curves in the region of an electronic absorption very similar to those for conventional absorption and refraction, respectively. These are illustrated in Fig. 1.4. Circular dichroism, together with the anomalous optical rotatory dispersion which accompanies it in the absorption region, are known collectively as the *Cotton effect*. The ellipticity maximum coincides with the point of inflection in the curve of optical rotatory dispersion, which ideally coincides with the maximum of an electronic absorption band at λ_j. The ellipticity
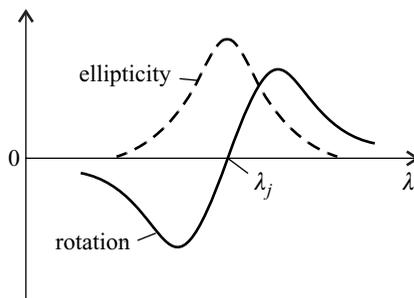
Fig. 1.4 The ellipticity and anomalous optical rotatory dispersion in the region
of the electronic absorption wavelength λ_j. The signs shown here correspond to a
positive Cotton effect.

and optical rotatory dispersion curves always have the relative signs shown in
Fig. 1.4 for an isolated absorption band in a given sample. At wavelengths far re-
moved from any λ_j, the rotatory dispersion is given by the Drude equation (1.2.1),
but in the anomalous region the Drude equation must be modified to remove the
singularity and to allow for the finite absorption width. If there are several adjacent
absorption bands, the net Cotton effect will be a superposition of the individual
Cotton effect curves.

Optical rotation measurements are usually presented as the *specific optical ro-
tatory power* (often called simply the *specific rotation*)

$$[\alpha] = \frac{\alpha V}{ml}, \tag{1.2.9}$$

where α is the optical rotation in degrees, V is the volume containing a mass m of
the optically active substance, and l is the path length. In much of the chemistry
literature, CGS units are used and l is specified in decimetres. Similarly, circular
dichroism measurements are usually presented as the *specific ellipticity*

$$[\psi] = \frac{\psi V}{ml}, \tag{1.2.10}$$

where ψ is measured in degrees. Circular dichroism is now usually obtained directly
by measuring the difference in the decadic molar extinction coefficients

$$\epsilon = \frac{1}{cl} \log \frac{I_0}{I_l}, \tag{1.2.11}$$

where I is the intensity of the light wave and c is the concentration of absorbing
molecules in moles per litre, of separate left- and right-circularly polarized light
beams, rather than via the ellipticity induced in an initially linearly polarized light
beam. Since the intensity of a wave is proportional to the square of the amplitude,
the relationship between extinction coefficient and absorption index is obtained

from (1.2.6) and (1.2.11) by writing

$$I_l = I_0 e^{-2.303\epsilon cl} = I_0 e^{-4\pi n'l/\lambda}, \tag{1.2.12}$$

from which it follows that

$$n' = \frac{2.303\lambda c\epsilon}{4\pi}. \tag{1.2.13}$$

The following expression, giving the relationship between the ellipticity in degrees and the decadic molar circular dichroism, is often encountered in the chemistry literature:

$$[\theta] = 3300(\epsilon^L - \epsilon^R) = 3300\Delta\epsilon. \tag{1.2.14}$$

This obtains from (1.2.8), (1.2.10) and (1.2.13) if CGS units are used and it is remembered that the path length is specified in decimetres.

A useful dimensionless quantity is the *dissymmetry factor* (Kuhn, 1930)

$$g = \frac{\epsilon^L - \epsilon^R}{\epsilon} = \frac{\epsilon^L - \epsilon^R}{\frac{1}{2}(\epsilon^L + \epsilon^R)}, \tag{1.2.15}$$

which is the ratio of the circular dichroism to the conventional absorption. The constants that arise in the determination of absolute absorption intensities therefore cancel out, and g often reduces to simple expressions involving just the molecular geometry. Since circular dichroism is of necessity always determined in the presence of absorption, g is also an appropriate criterion of whether or not circular dichroism in a particular absorption band is measurable, given the available instrumental sensitivity.

Although optical rotatory dispersion and circular dichroism have been known for more than 100 years, until the middle of the twentieth century most applications in chemistry utilized just the optical rotation at some transparent wavelength, usually the sodium D line at 589 nm. Then in the early 1950s a revolution in the study of optically active molecules was brought about through the introduction of instruments to measure optical rotatory dispersion routinely: this was possible as a result of developments in electronics, particularly the advent of photomultiplier tubes, so that the recording of visible and ultraviolet spectra no longer depended on the use of photographic plates. Steroid chemistry was one of the first areas to benefit, mainly as a result of the pioneering work of Djerassi (1960). Instruments to measure circular dichroism routinely were developed in the early 1960s when electro-optic modulators, which switch the polarization of the incident light between right and left circular at a suitable frequency, became available, and this technique is now generally preferred over optical rotatory dispersion because it provides better discrimination between overlapping absorption bands (the circular

dichroism lineshape function drops to zero much more rapidly than the optical rotatory dispersion lineshape function).

Conventional optical rotation and circular dichroism utilize visible or ultra-violet radiation: since this excites the electronic states of the molecule, these techniques can be regarded as forms of polarized electronic spectroscopy. Thus it is the spatial distribution of the electronic states responsible for a particular circular dichroism band, for example, that is probed. This can often be related to the stereochemistry of the molecular skeleton in ways that are elaborated in later chapters. It is often stated that optical rotatory dispersion and circular dichroism are used to look at the stereochemistry of the molecule through the eyes of the chromophore (the structural group absorbing the visible or near ultraviolet radiation). The first successful application of this anthropomorphic viewpoint was the celebrated *octant rule* of Moffit *et al.* (1961), which relates the sign and magnitude of Cotton effects induced in the inherently optically inactive carbonyl chromophore by the spatial arrangement of perturbing groups in the rest of the molecule. The theoretical basis of the octant rule is discussed in detail in Chapter 5.

There are two topics closely related to circular dichroism that should be mentioned, namely circular polarization of luminescence, and fluorescence detected circular dichroism. The latter is simply an alternative method of measuring circular dichroism in samples, usually biological, with poor transmission, and involves measurement of a difference in the fluorescence intensity excited by right- and left-circularly polarized incident light with wavelength in the vicinity of an electronic absorption band (Turner, Tinoco and Maestre, 1974). The former refers to a circularly polarized component in the light spontaneously emitted from an optically active molecule in an excited state. The well-known relationship between the Einstein coefficients for absorption and spontaneous emission suggests that the circular dichroism and circular polarization of luminescence associated with a particular molecular electronic transition will provide identical structural information. However, differences between these observables will occur when the structure of the molecule in the ground electronic state differs from the structure in the excited luminescent state. Thus circular dichroism is a probe of ground state structure and circular polarization of luminescence is a probe of excited state structure. Under certain conditions, circular polarization of luminescence can be used to study aspects of excited state molecular dynamics such as photoselection and reorientational relaxation. A detailed development of these topics is outside the scope of this book, and the interested reader is referred to reviews by Richardson and Metcalf (2000) and Dekkers (2000).

An interesting variant of fluorescence detected circular dichroism has been mooted: circular differential photoacoustic spectroscopy (Saxe, Faulkner and Richardson, 1979). In conventional photoacoustic spectroscopy, light energy is

absorbed by a sample, and that portion of the absorbed energy which is subse-
quently dissipated into heat is detected in the following manner. If the exciting
light is modulated in time, the sample heating and cooling will also be modulated.
The resulting temperature fluctuations lead to the transformation of the thermal
energy into mechanical energy carried by sound waves in the sample which are
detected with a microphone. In circular differential photoacoustic spectroscopy,
the polarization of the incident light is modulated between right- and left-circular
and the intensity of any sound waves detected at the modulation frequency will
be a function of the circular dichroism of the absorbing chiral sample. It could be
more widely applicable than fluorescence detected circular dichroism because a
fluorescing chromophore is not required, and could be particularly attractive for
studying molecules on surfaces.

As well as their general importance in stereochemistry, natural optical activity
techniques, especially ultraviolet circular dichroism, have become central physical
methods in biochemistry and biophysics since they are sensitive to the delicate
stereochemical features that determine biological function (Fasman, 1996; Berova,
Nakanishi and Woody, 2000).

1.3 Magnetic optical rotation and circular dichroism

Faraday's conviction of the connection between electromagnetism and light led him
to the discovery of the rotation of the plane of polarization of a linearly polarized
light beam on traversing a rod of lead borate glass placed between the poles of an
electromagnet (Faraday, 1846). A Faraday rotation is found when light is transmitted
through any medium, isotropic or oriented, in the direction of a magnetic field.
The sense of rotation depends on the relative directions of the light beam and
the magnetic field, and is reversed on reversing either the direction of the light
beam or the magnetic field. Thus magnetic rotatory power differs from natural
rotatory power in that the rotations are added, rather than cancelled, on reflecting
the light back through the medium. It was soon discovered that magnetic optical
rotation varies inversely with the square of the wavelength, in accordance with
Biot's law for natural optical rotation; although it was subsequently found that a
better approximation is provided by a formula similar to Drude's equation (1.2.1).

The quantitative investigations of Verdet (1854) are summarized in Verdet's law
for the angle of rotation per unit path length in a magnetic field **B** making an angle
θ with the direction of propagation of the light beam:

$$\alpha = VB\cos\theta, \tag{1.3.1}$$

where V is the Verdet constant for the material for a given wavelength and temper-
ature. For light passing through the medium in the direction of the magnetic field
(north pole to south pole) most diamagnetic materials rotate the plane of polarization