Chirality and Optical Activity

Chiral compounds exhibit a property called optical activity and are said to be optically active.

Achiral molecules are optically inactive.

Optical activity is the ability of a compound to rotate the plane of plane-polarized light.
Chirality and Optical Activity

A chiral compound rotates the plane of plane-polarized light.
A sample tube containing an optically active compound is placed between the observer and plane-polarized light. An analyzing filter allows the observer to quantitate the degree to which the plane-polarized light is rotated.
Optical Activity - The Polarimeter

No light emerges so analyser is at right angles to plane of polarization.

Plane of polarization turned by solution.

Rotated until no light emerges.

Sugar solution.
Optical Activity - Specific Rotation

The number of degrees of rotation, $\alpha$, observed for a chiral compound in a polarimeter depends upon:

- Length of the sample tube, $L$.
- Concentration of the compound, $C$.

To prevent ambiguities, the **specific rotation**, $[\alpha]$, is usually reported which standardizes the sample tube length to 1 dm, and the concentration to 1 g/ml:

$$[\alpha] = \frac{\alpha}{CL}$$

All experiments using a chiral compound will yield the same value of $[\alpha]$, thus specific rotation is a useful **physical property** for identifying compound.

Other properties not discussed here, such as solvent, wavelength used, and temperature, can also affect $[\alpha]$. 
Optical activity is the only property that distinguishes one enantiomer from the other. All other properties (MP, BP, solubility, etc.) are the same.

D-Lactic Acid  
m.p. 53 °C  
Very soluble in water  
\([\alpha] = -2.6 \, ^\circ\)

L-Lactic Acid  
m.p. 53 °C  
Very soluble in water  
\([\alpha] = +2.6 \, ^\circ\)
A chemical reaction may yield a mixture of enantiomers. The reaction actually yields a 50:50 mixture of enantiomers, which include (S)-(+)-2-butanol and (R)-(-)-2-butanol. A racemic mixture contains equal amounts of these two enantiomers.
1) The **two enantiomers** of a pair of enantiomers rotate the plane of plane-polarized light the same number of degrees but in opposite directions.

2) Rotation in the clockwise direction is called **dextrorotatory** (“+”) and in the anticlockwise direction, **levorotary** (“-”).

3) “D-” and “L-” are not directly related to (+) and (-), but are designations developed in carbohydrate chemistry to indicate a certain relationship between hydroxy groups.

4) When both the configuration and the optical rotation are known for a compound, both are indicated in the name:

   - **D- (+)-glyceraldehyde**
   - **D- (-)-fructose**

5) “**R-” and “S-” designate specific relationship** between atoms attached to a “chiral” carbon atom and are base on priority rules discussed in more detail in your text.
Most reactions in living cells are catalyzed by protein molecules called enzymes. (Enzymes are a subset of a group of biological macromolecules referred to as “receptors.”)

Enzymes are large molecules containing a surface site, called the active site, where the substrate or reactant binds. For most enzymes this site is chiral.

Chiral active sites are designed to interact strongly with one of the two possible substrate enantiomers, just as a left shoe interacts strongly with a left foot, and more or less excludes a right foot.

This phenomenon is called chiral recognition or chiral discrimination.

Other molecular properties are also used by enzymes to discriminate between substrate molecules: geometrical isomerism, size, shape, polarity, and charge.

Discrimination on these bases is called the complementarity principle.
Chiral Recognition

(R)-(-)-epinephrine
natural epinephrine

enzyme active site

enzyme–substrate complex

(S)-(+)–epinephrine
unnatural epinephrine
does not fit the enzyme’s active site
Chiral Recognition

$R$ enantiomer

$S$ enantiomer

binding site of the receptor

binding site of the receptor
Chiral Compounds - Biological Activity

R-Thalidomide (sleep-inducing)

S-Thalidomide (teratogenic)