

The added value of small-molecule chirality in technological applications

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Abstract | Chirality is a fundamental symmetry property; chiral objects, such as chiral small molecules, exist as a pair of non-superimposable mirror images. Although small-molecule chirality is routinely considered in biologically focused application areas (such as drug discovery and chemical biology), other areas of scientific development have not considered small-molecule chirality to be central to their approach. In this Review, we highlight recent research in which chirality has enabled advancement in technological applications. We showcase examples in which the presence of small-molecule chirality is exploited in ways beyond the simple interaction of two different chiral molecules; this can enable the detection and emission of chiral light, help to control molecular motion, or provide a means to control electron spin and bulk charge transport. Thus, we demonstrate that small-molecule chirality is a highly promising avenue for a wide range of technologically oriented scientific endeavours.

Chirality

The geometric property of an object (or spatial arrangement of points or atoms) of being non-superimposable on its mirror image; such an object has no mirror plane, centre of inversion or rotation—reflection axis. If the object is superimposable on its mirror image the object is achiral (non-chiral).

Enantiomers

A pair of molecular entities that are non-superimposable mirror images of each other.

Chirality is a fundamental symmetry property of elemental particles, molecules or even macroscopic objects such as human hands. Objects are defined as chiral if they exist as a pair of 'left-handed' and 'right-handed' mirror images that cannot be superimposed (BOX 1); these are known as enantiomers in the nomenclature of chemistry. Importantly, such enantiomeric forms cannot generally be differentiated by their physical properties: the chiral handedness only becomes evident when one chiral object interacts with another chiral object. Just as using your right hand to shake either the right hand (a homochiral interaction) or the left hand (a heterochiral interaction) of another person will lead to different results, the interaction of a chiral molecule with another chiral molecule and/or object will be sensitive to the stereochemistry of the interacting partners.

Small-molecule chirality has long fascinated chemists and provided an intellectually challenging exercise for selective chemical synthesis and catalysis. The value of the chiral products generated from such endeavours is well recognized in biologically relevant application areas (for example, drug and fragrance discovery, and chemical biology). Nature has evolved with a single handedness (known as homochirality), and thus biological processes are inherently chiral. Therefore, when designing a ligand (for example, a drug) for a biological receptor (for example, a drug target), chirality is often used to tune the nature (for example, the specificity) of the interaction¹. As such interactions ultimately control and/or perturb downstream biological function, the importance of chirality in a biological context is abundantly clear. Although many

case studies could be cited to support this statement, the chirality of the naturally occurring terpenoid carvone provides a fragrant example: one enantiomer of carvone (the (*R*)-enantiomer as defined using the Cahn–Ingold–Prelog (CIP) priority rules) smells like spearmint, whereas the opposite (*S*)-enantiomer smells like caraway seeds, owing to chiral recognition at the human olfactory receptors².

Despite the significant biological precedent, small-molecule chirality has not generally been a key design feature for the development of new materials for mainstream technological applications. This is surprising as the first liquid crystalline phase to be observed — which is now used in many liquid crystalline display technologies — was a chiral phase based on a chiral cholesterol organic small molecule³. In many cases, chirality has not been a requirement to achieve desired function and thus may have been regarded as more of an inconvenience. The synthesis, separation and bulk assembly of chiral materials add complexity to a process and thus may have been avoided when there is little perceived added value. New approaches to design novel materials that take chirality into account are now emerging, which is leading to new functionality in technological applications. These new applications often go beyond exploiting the interactions between two different chiral molecules — the mechanism underlying chiral biological recognition processes and sensors (BOX 2) — and include organization dependent on chiral composition, circularly polarized (CP) light and the spin of moving electrons (spintronics). This Review aims to showcase the exciting new approaches and technological applications

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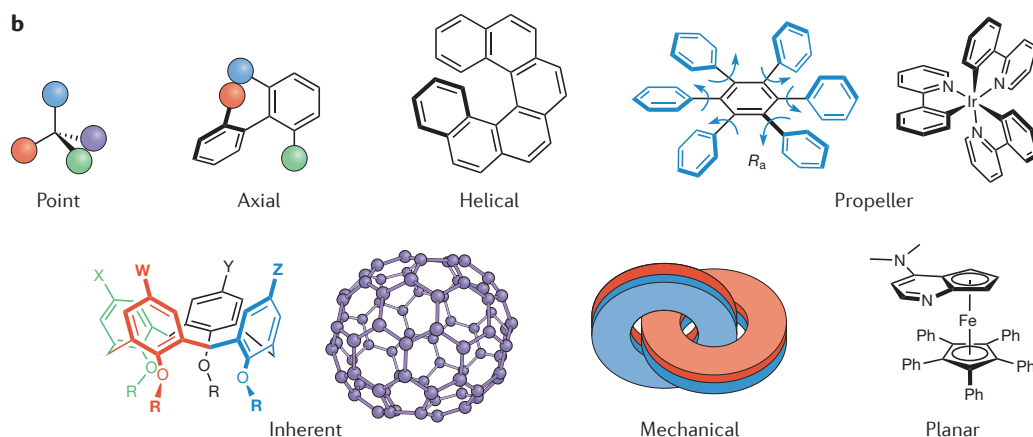
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doi:10.1038/s41570-017-0045
Published online 7 Jun 2017

Box 1 | Chirality and examples of stereogenic elements in small molecules

The word chiral is derived from the Greek word for hand, and objects are described as chiral if they exist as a pair of non-superimposable mirror images (such as hands, part **a**). Perhaps owing to its abundance in biological systems, the point chirality of a tetrahedral centre (shown superimposed on the hands in part **a**) has traditionally dominated the study and synthesis of chiral small molecules. However, the sp^3 hybridization of a carbon atom with point chirality breaks electronic conjugation through π electrons, thus decoupling the source of chirality from the conjugated system. There are many potential alternative stereogenic elements in small molecules that could induce chirality in conjugated systems and, as such, may prove to be more suitable for technological applications. Examples (shown in part **b**) include molecular frameworks in which the chirality may arise from axial chirality; helicity or curvature (for example, helical, propeller or inherent chirality); or the desymmetrization of planar systems (for example, mechanical or planar chirality).



Inherent figure (right) in part **b** is adapted with permission from REF. 93, Macmillan Publishers Limited. Mechanical figure in part **b** is adapted with permission from REF. 94, Royal Society of Chemistry.

Stereochemistry

A subdiscipline of chemistry that involves the study and manipulation of the relative spatial arrangement of atoms that form the structure of molecules.

Cahn–Ingold–Prelog (CIP) priority rules

The CIP priority rules are a set of rules to unequivocally name a stereogenic element within a molecule. CIP rules are used to assign an *R* or *S* descriptor to stereocentres (and other stereogenic elements) and an *E* or *Z* descriptor to double bonds.

Chiral composition

A chiral mixture that differs in the ratio of enantiomers (known as the enantiomeric ratio). Example chiral compositions include racemates, enantiopure substances or scalemic mixtures (see further definitions for each of these terms).

Circularly polarized (CP) light

Circular polarization of an electromagnetic wave is a polarization state in which the electric field of the passing wave does not change strength but only changes direction in a rotary manner. Circularly polarized light is chiral and can be left- or right-handed.

being realized through the design and study of chiral small molecules.

We emphasize that this article presents something of a personal viewpoint, rather than a comprehensive review, in which we select representative examples to showcase some of the areas in which we believe small-molecule chirality can have, and has had, an impact on advances in technology. We acknowledge that both the terms ‘small molecule’ and ‘technological applications’ are used loosely, in an aim to not be prohibitively bound by terms that are open to interpretation. In part, we have elected to focus on chiral small molecules as we believe this differentiates the topic under discussion from alternative application-led accounts using other chiral material sets — for example, polymers^{4,5}, nanoparticles⁶, liquid crystals⁷, highly aggregating materials⁸, metal–organic frameworks (MOFs)⁹, plasmonic nanostructures¹⁰ and nanotubes¹¹. However, limiting the discussion to small molecules is more than organizational: we believe that small molecules provide particularly exciting opportunities with respect to other approaches. Indeed, through expert chemical synthesis, one can access small molecules in high purity as a single isomer and thoroughly interrogate the molecular structure–property relationships through the synthesis and comparison of closely related derivatives. In turn, the identification of functionally

important small molecules provides huge opportunities for methodological development in (asymmetric) synthesis and catalysis. Only through the development of flexible, efficient and scalable synthetic methods will suitable quantities of chiral small-molecule materials be available for further application-led study. Thus, the opportunities presented in this Review for technologically relevant chiral small-molecule scaffolds could lead to them becoming as valid a target for synthetic chemists as biologically relevant chiral molecules.

Chiral light emission and detection

In CP light, the electric field of the wave has constant magnitude, but rotates at a constant rate in a plane perpendicular to its direction of travel. As such, the electric field vector of the wave (and a corresponding proportional magnetic field vector at 90° to the electric field vector) describes a helix along the direction of propagation, which can be either right- or left-handed. CP light can be used in many areas of technology, including in optics and filters, in spectroscopy and to encode information. Thus, it is of great interest in areas as diverse as quantum computing¹², 3D displays¹³ and bioresponsive imaging¹⁴.

Given the huge commercial growth and development of organic light-emitting diode (OLED) displays,

Box 2 | Chiral recognition for sensing applications

The specificity of chiral recognition should allow for the direct sensing of chiral analytes by chiral materials in simple sensors or devices. By means of an example, methods for the determination of the enantiomeric ratio (chiral purity) for chiral substances have traditionally been dominated by chromatographic techniques (such as high-performance liquid chromatography (HPLC) and gas chromatography) using a chiral stationary phase, NMR using chiral shift or derivatizing agents (for example, Mosher's acid), or chiroptical techniques. Devices that can directly determine the enantiomeric ratio of a mixture in real time would be a valuable addition to the existing methods, owing to their potential application for in-line and point-of-care analysis, or in field studies. The basic principle for these devices is fairly similar to those for the established methods above: a sensor device (based on, for example, electrochemical^{88,89}, gravimetric, electrical or optical measurements^{90,91}) is fitted with a chiral discriminator that differentiates enantiomeric analytes through the formation of diastereomeric complexes. If the difference between the binding constants for these complexes is sufficiently large and the total concentration of analyte is known, the enantiomeric ratio can be calculated from the readout. However, this method faces a significant challenge compared with chromatographic separations: although a single interaction determines the selectivity of a device, chiral chromatography can use many consecutive interactions in the form of theoretical plates. The sum of these interactions can amplify even very small energetic differences between diastereomeric complexes. Thus, sensor devices cannot yet routinely replace the highly optimized HPLC separation methods that are currently available⁸⁹.

Chiral sensor devices were comprehensively reviewed by Torsi and co-workers⁹⁰ in 2013. Deng, Yao, Wei and co-workers⁹² later reported an interesting enantioselective vapour detector method. The addition of the (*R*)- or (*S*)-enantiomer of camphorsulfonic acid as a chiral small-molecule dopant to the conducting but non-chiral polyaniline polymer resulted in the formation of superhelical microfibrils with very strong circular dichroism of approximately 1,000 mdeg. Devices assembled from left-handed fibres showed a greater increase in resistance when exposed to 250–1,000 ppm of (*S*)-2-aminohexane compared with the (*R*)-enantiomer at identical concentrations. Conversely, right-handed fibres showed a greater increase in resistance when exposed to the (*R*)-enantiomer compared with the (*S*)-enantiomer.

one area of significant potential in CP light technologies is the development of OLEDs in which the electroluminescence is directly circularly polarized (so called CP-OLEDs; FIG. 1) — something that is only possible from a chiral emissive state. Antiglare filters commonly used for OLED displays exploit the physics of CP light to eliminate glare from external light sources (for example, sunlight), but in the process remove approximately 50% of the nonpolarized light emitted from the OLED pixel¹⁵. If the nonpolarized OLEDs were to be replaced with CP-OLEDs (with a comparable device performance), the CP light component of the correct handedness would pass through the antiglare filter, increasing the energy efficiency of the display in proportion to the increasing dissymmetry of the light.

Attempts to generate direct CP electroluminescence from fluorescent OLEDs have been dominated by the use of polymers or oligomers that bear chiral pendant alkyl side chains¹⁶ (FIG. 1a). Intense optimization of these chiral fluorescent materials led to impressive dissymmetry [g_{EL}] values of up to 0.35; this is thought to result from the formation of (helical) cholesteric stacks on top of device alignment layers¹⁷. An alternative approach would be to use a chiral additive in a polymer blend material, in which the chiral additive induces chiral emission from the polymer. In principle, this approach would be of much interest as it would allow for the existing range of

device-optimized but non-chiral fluorescent polymeric materials to be used, thus allowing for direct incorporation of the methodology into existing production lines. To date, such additive approaches have mostly been limited to the solution phase. Although translation into the solid state has been rare¹⁸, it was achieved in 2013 by Fuchter, Campbell and co-workers¹⁹ through the addition of an enantiopure helicene additive (FIG. 1b) to the well-established non-chiral polymer F8BT. Although the origin of the effect is yet to be fully determined, CP electroluminescence from the polymer was shown to be induced by the chiral helicene additive, with [g_{EL}] values of up to 0.2. A CP-OLED with a g factor of 0.2 would result in a 10% increase in efficiency relative to a comparable nonpolarized light source when used in a display with a common antiglare filter¹⁵.

Owing to spin statistics, OLEDs produce excited states of singlet and triplet multiplicity in an approximate 1:3 ratio²⁰. For fluorescent materials, only the singlet states can emit light, which limits their maximum internal quantum efficiency to 25%²¹. Higher quantum efficiencies are possible by harnessing the 75% triplet energy through radiative relaxation (phosphorescence), which is usually accomplished by exploiting the strong spin-orbit coupling of emissive metal dopants, such as iridium or platinum. Chiral complexes of such metals are capable of CP phosphorescence; however, it has been difficult to develop CP phosphorescent OLEDs (CP-PHOLEDs) that combine high dissymmetry factors with high luminance and efficiencies²². The first CP-PHOLED, reported by Di Bari and co-workers²³, achieved very high [g_{EL}] factors of 0.09–0.15 and 0.73–0.79 through the use of a chiral europium(III) complex (FIG. 1c) as the dopant; this complex exhibits an exceptional solution-phase g_{PL} of 1.38. Large solution-phase dissymmetry factors are typical for lanthanide complexes²⁴ and far exceed the values accessible with small organic molecules (which have g_{PL} values of approximately 10^{-3} – 10^{-2})²⁵. The authors noted an interesting effect in their studies: increased cathode thickness (and thus increased reflectivity) had a negative impact on the emission dissymmetry. This effect was explained in later work through two phenomena: the inversion of circular polarization upon reflection at the cathode and the attenuation of light travelling through the device, based on the recombination zone position (see FIG. 1e for a schematic representation)²⁶. Ultimately, Di Bari and co-workers were able to increase the [g_{EL}] of their CP-PHOLED up to a remarkable value of 1.0 at 595 nm; however, the comparatively weak emission from the chiral lanthanide complex limits the external quantum efficiency that can be achieved using this approach. In an alternative approach using a helical platinum(II) complex developed by Crassous, Autschbach, and Réau²⁷ (FIG. 1d), Fuchter, Campbell and co-workers¹⁵ managed to combine display-level brightness with a [g_{EL}] value of up to 0.38. Intriguingly, the [g_{EL}] of the chiral platinum(II) complex exceeds the solution [g_{PL}] by one order of magnitude²⁸, and in contrast to Di Bari's system it would appear that the reflectivity of the cathode (as shown in FIG. 1e) is less important.

Dissymmetry factor

(g factor). A measure of the dissymmetry between the left- and right-handed components of circularly polarized light; it is defined as $g = (I_L - I_R)/\frac{1}{2}(I_L + I_R)$, where I_L and I_R are the absorption or emission intensities for left- and right-handed polarized light, respectively. The parameter observed is denoted as a subscript: for example, absorption (g_{abs}), photoluminescence (g_{PL}) or electroluminescence (g_{EL}).

Enantiopure

A substance that consists of a single enantiomer, within the limit of detection.

Chiroptical

A term referring to the optical techniques (using refraction, absorption or emission of anisotropic radiation) for investigating chiral substances (for example, measurements of optical rotation at a fixed wavelength, optical rotatory dispersion, electronic circular dichroism and circular polarization of luminescence).

The left- or right-handed components of CP light can be measured using a photodetector fitted with a correctly aligned quarter-wave plate and linear polarizer¹⁵; therefore, CP light detectors can be simply engineered. The direct detection and differentiation of CP light by a (necessarily chiral) chromophore, in the context of a device, is an interesting alternative approach for CP light detection. Although solution-based approaches, in particular using chiroptical switches²⁹ (see below for more on optical switches), that detect and differentiate CP light have been reported, there has been limited translation to the solid state. Similar to the polymers used in fluorescent CP-OLEDs, the first device for the direct detection of CP light was a photodiode that used a poly(fluorene) copolymer with chiral alkyl substituents³⁰. The diode, reported by Meskers and co-workers, displayed different photocurrents upon irradiation with left- or right-handed CP light, and the authors developed a detailed optical model to account for a surprising inversion of g-factor sign at higher film thicknesses. The first small-molecule approach was reported by Fuchter, Campbell and co-workers, who fabricated organic field-effect transistors

(OFETs) from an enantiopure helicene³¹. These devices showed a tenfold higher drain current upon exposure to CP light of the correct handedness, compared with no light or light of the opposite handedness (FIG. 1f). In addition, the effect displayed fast and reversible on–off switching on the timescale of a few milliseconds. In theory, the use of a transistor architecture for such a CP light detector should allow for integration of this approach into CP-dependent electronic circuits. Finally, we note that spintronic devices (discussed further below) could be used as CP light detectors, although this has not been the central application of interest for such devices.

Optical switches and molecular machines

The ability of a molecular system to switch between two (or more) stable states in response to a stimulus is a central feature of many molecules applied in technological applications. If each stable state possesses sufficiently different properties (for example, optical or electrochemical), the measurement of these properties can serve as a readout for the state in which the molecule is in. The development of high-performance molecular switches based on these principles will be necessary for the construction

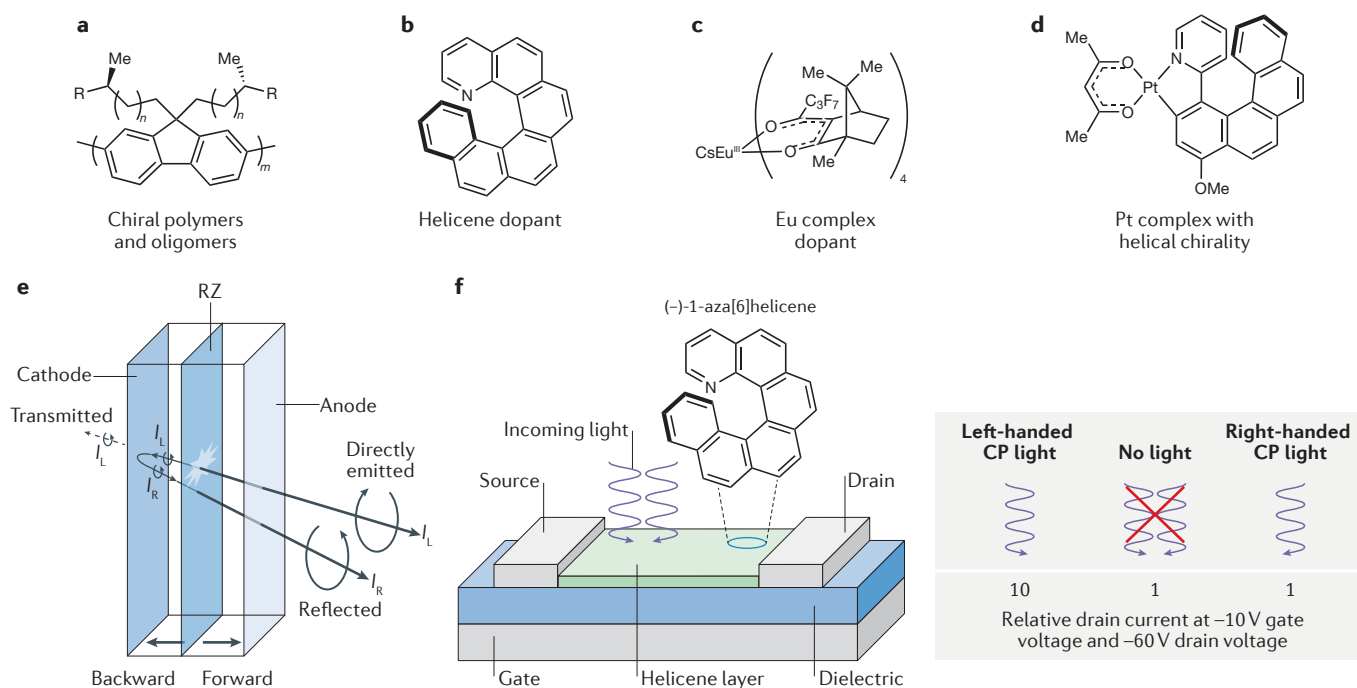


Figure 1 | Direct emission and detection of CP light. Examples of chiral materials used in the production of organic light-emitting diodes that emit circularly polarized light (CP-OLEDs): chiral fluorescent polymers¹⁷ (part a), a helicene¹⁹ (part b) and chiral phosphorescent dopants (parts c and d)^{15,23}. A schematic representation of the Di Bari model for the influence of cathode reflectance and recombination zone (RZ) position on the dissymmetry factor $|g_{EL}|$ of circularly polarized electroluminescence is shown in part e; as the light handedness is reversed upon reflection, a lower cathode reflectance leads to a higher ratio of directly emitted light (as opposed to reflected light) and thus to a higher observed $|g_{EL}|$. Similarly, $|g_{EL}|$ can be increased by moving the RZ closer to the anode, which lengthens the distance that the reflected light has to travel and thus increases its attenuation.³¹ I_R and I_L are the intensities of the right- and left-handed polarized light. An illustration of an organic transistor fabricated from a chiral helicene film is shown in part f; the device that uses the left-handed helicene semiconductor displays a tenfold current increase at the region of the turn-on voltage when exposed to left-handed CP light, compared with no light or right-handed CP light. When the right-handed helicene enantiomer is used, the device responds to right-handed light²⁶. Part e is adapted with permission from REF. 26, Wiley-VCH. Part f is adapted with permission from REF. 31, Macmillan Publishers Limited.

of molecular logic gates and memory devices, which is crucial to achieve molecular-scale electronics³². Chiral molecular switches allow the chirality of CP light to be exploited as an additional parameter, either as the stimulus or as the readout mechanism. Switches with a chiroptical readout have been shown to change their chiroptical properties upon exposure to a range of stimuli, including pH, electrochemical potential or light²⁹. For technological applications, switching induced by changes in electrochemical potential (redox switching) is of great interest, and, in part owing to their exceptionally strong chiroptical properties, many recent studies have focused on helicene-based chiroptical switches³³. Typically, such switches function via simple, reversible redox reactions with little or no significant structural change of the helicene. The redox properties can be tuned through changes in the helicene structure or substitution, or through the inclusion of redox active metallic centres. One particularly exciting example of such chiroptical switches is an organometallic iron helicene reported by Crassous and Autschbach³⁴ (FIG. 2a). Upon oxidation of the iron centres, this system undergoes a significant change in sign of the molar optical rotation at a wavelength of 1.54 μm , which is reversed upon reduction. Such long wavelengths are in a spectral region suitable for telecommunication via fibre-optic cables, and the chiroptical nature of the signal would, in principle, allow for the transmission of encoded information. Therefore, such approaches hold much promise once further developed and validated in solid-state device prototypes.

In contrast to the simple molecular switches described above, molecules that undergo significant structural changes between their stable states can be used to convert their molecular motion into macroscopic work, thus distinguishing them as molecular machines³⁵. A range of potential applications have been, and continue to be, explored for such molecular machines^{35,36}; however, the integration of such systems into real-world technologies is only at an early stage³⁷. Although there are well-known examples of structural changes in molecular switch components, including the interconversion of double bond isomers (for example, as observed in the ubiquitous azobenzenes³⁸) or changes in helicity (for example, as observed in the cyclization of dithienylethenes³⁹), any chirality present in such situations is often unimportant, irrelevant or overlooked. However, chirality has provided a basis for one of the most topical areas of molecular motion upon exposure to an external stimulus: the area of unidirectional rotary molecular motors, which constitutes part of the 2016 Nobel prize-winning field of molecular machines⁴⁰. The research of one of the recipients of this award, Ben Feringa, has led to a range of unidirectional molecular motors that exploit chirality as a means to control motion. Whether the precise rotary axle consists of a crowded single or double bond, control of motion is most often provided by a molecular design that contains two stereogenic elements — one labile and one stable. As is well known, the combination of more than one stereogenic element into a molecule gives rise to a series of possible stereoisomers. For example, two stereogenic elements in a molecule will give rise to a maximum of four possible

stereoisomers: two diastereoisomers, each of which can exist as two enantiomers (however, the total number of isomers may be lower than the theoretical maximum if meso isomers exist). Although enantiomers are energetically equivalent, diastereoisomers are not. Thus, the rotary motors designed by Feringa and co-workers often exploit diastereomeric energy differences to control the conformational preference of a given state and then use an additional stimulus to switch between states. The sum of these events gives rise to unidirectional motion.

One recent example of such a motor exploits the stable point chirality of a sulfoxide group and the labile axial chirality of a biaryl single bond; this system demonstrates unidirectional rotary motion, powered by a chemical fuel⁴¹ (FIG. 2b). Although many stimuli, including electrochemical energy⁴², have been reported to drive synthetic molecular motors, those that operate through the consumption of a chemical fuel^{41,43,44} represent an exciting advance in the field, given that the biological motors that often inspire such machines are powered by chemical energy. It should be noted however that although molecular chirality can control unidirectional rotation and its translation into macroscopic work (see below), it is not an absolute requirement for unidirectional molecular motion, as demonstrated in an alternative design for a chemically fuelled rotary motor⁴³. In this design, Leigh and co-workers report a small interlocked macrocyclic ring that is continuously transported in a single direction around a cyclic molecular track when powered by a chemical fuel (FIG. 2c). Although two chiral centres are present in this alternative motor design and a chiral catalyst is used to power the motor, the authors demonstrate that it is not the chirality of the system that controls the unidirectional motion. However, we note that although such a design clearly does not require chirality to achieve unidirectional rotation, chirality should aid the translation of rotary molecular motion into macroscopic work. Chirality can facilitate the directional alignment of multiple motors; for example, it can enable the rotation of a micrometre-sized glass rod⁴⁵. It is hard to imagine how a comparable alignment of rotational direction could be achieved for non-chiral materials.

Control of spin

There is a close relationship between magnetism and chirality; for example, magnetic fields can influence the absorption of nonpolarized light by chiral molecules (known as magneto-chiral dichroism)⁴⁶ or lead to enantiomer-dependent electrical resistance of chiral conductors (termed electrical magneto-chiral anisotropy)⁴⁷. Intriguingly, the equation that governs electrical magneto-chiral anisotropy can also describe the interactions between chirality and electron spin⁴⁷, which have been most thoroughly explored in relation to the field of spintronics (spin transport electronics). In spintronics, the spin of the electron can be used in addition to the electronic charge as a degree of freedom to drive electronic switches or processes. The higher degree of freedom of an informational system that involves both charge and spin, together with the low energy required for spin flips, could lead to spintronic devices with higher power densities and

Stereogenic elements

Groupings within molecular entities that give rise to stereoisomerism. Some stereogenic elements can be interconverted between the two possible configurations in a selective (that is, stereospecific) or unselective manner (for example, racemization) upon exposure to stimuli such as light, heat or chemical reagents. For the purpose of this Review, we differentiate between stereogenic elements that can interconvert under the selected conditions (labile) and those that cannot (stable).

Stereoisomers

Isomers that differ in the spatial arrangement of atoms without any differences in connectivity or bond multiplicity. Enantiomers and diastereoisomers are examples of stereoisomers.

Diastereoisomers

Stereoisomers that are not related as mirror images. Diastereoisomers are characterized by differences in physical properties and by some differences in chemical behaviour.

Meso isomers

Achiral members of a series of diastereoisomers in which at least one isomer is chiral.

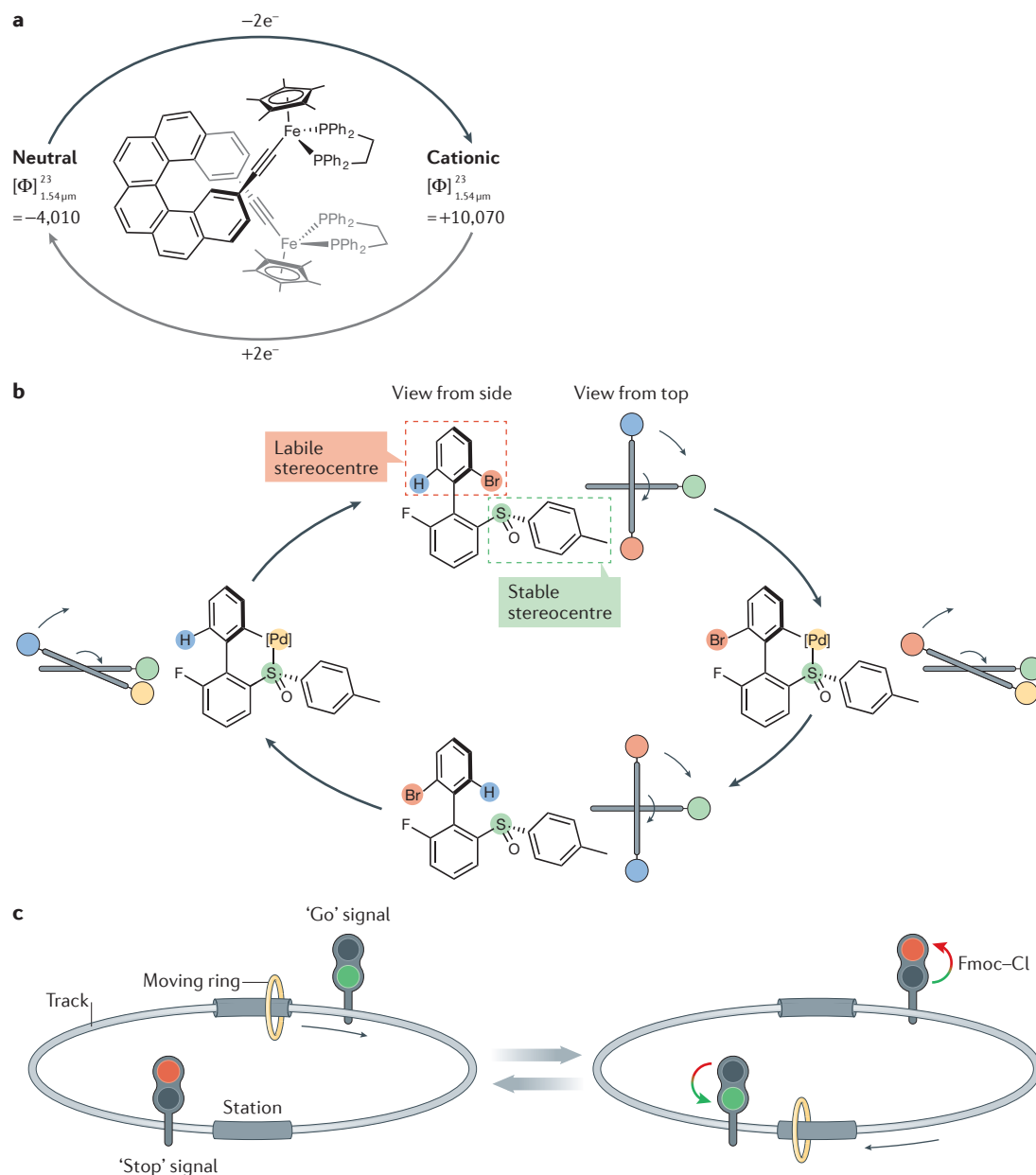


Figure 2 | Chiroptical switches and molecular machines. a | An iron alkynyl helicene that allows chiroptical switching at long wavelengths. Oxidation of the iron centres leads to a reversible inversion in the sign of the molar rotation at $1.54\ \mu\text{m}$, which could potentially allow the encoding of information at a wavelength suitable for telecommunication via transport in fibre-optic cables³⁴. **b** | A chiral unidirectional molecular motor incorporating a rotating axle connecting two aryl rings⁴¹. One ring acts as a rotor, with a hydrogen atom in one *ortho* position and a bromine atom in the other. The other ring is a stator and has a (chiral) sulfoxide group in one *ortho* position and a fluorine atom in the other. The rotation cycle of the system begins with the rotor and stator perpendicular to each other. Addition of a palladium(II) reagent, and the subsequent C–H cyclometallation chemistry, allows one ring to pass the other; this is followed by reductive cleavage of the palladacycle, which affords Pd(0) and allows the rings to relax to the alternative perpendicular arrangement. The addition of a phosphine ligand effects the oxidative addition of Pd(0) into the C–Br bond and another 90° rotation. The final 90° rotation occurs upon reductive elimination of the C–Br bond. Unidirectional rotation is governed by selective binding of the palladium centre to give diastereomeric metal complexes. **c** | A unidirectional molecular motor in which a small molecular ring moves between two hydrogen-bonding stations on a large ring (the track)⁴³. The movement between the stations is blocked by bulky chemical 9-fluorenyl-methoxycarbonyl (Fmoc) groups — the 'stop' signal; removal of Fmoc allows the small ring to move between the stations — the 'go' signal (left). Although the smaller ring moves in a dynamic equilibrium between the stations, it is preferentially ratcheted to the second, more advanced position owing to steric interactions: attachment of the Fmoc group is faster when the moving ring is further away. Cleavage of the second Fmoc group then completes the rotation (right) and, combined with the ratcheting 'go signal', net unidirectional movement is achieved. Part **b** is adapted with permission from REF. 41 and REF. 44, Macmillan Publishers Limited. Part **c** is adapted with permission from REF. 44, Macmillan Publishers Limited.

improved processing speeds in addition to lower power consumption than conventional, purely charge-driven, semiconductor devices^{48,49}. Organic materials are of particular interest in spintronic devices: the small spin–orbit coupling of organic molecules greatly increases the spin relaxation time compared with typical heavy-atom doped inorganic semiconductors, thus allowing long-range spin transport^{50,51}. By contrast, the small spin–orbit coupling of organic materials means that they cannot generally be used for spin injection, which instead requires the use of ferromagnetic electrodes^{51,52}. However, an exciting new opportunity to use chiral organic molecules for the creation of spin-polarized electrons without the use of magnets was established through the seminal work of Naaman and co-workers in 2011 (REFS 53–56) (FIG. 3A). In the chiral-induced spin selectivity (CISS) effect^{49,57,58}, chiral molecules can achieve spin filtering more than two orders of magnitude larger than would be expected, equivalent to a pseudomagnetic field of hundreds of Tesla⁵³. Although several theoretical models for the CISS effect exist^{59–62}, an intuitive explanation can be obtained by considering an electron moving in a chiral electrostatic potential, in which it experiences an effective magnetic field oriented along the propagation axis. Within the effective magnetic field, one electron spin is favoured, which lifts the degeneracy of the electron spin states. Thus, the CISS effect couples the linear momentum and the spin of the electron: if parallel spin in one direction is energetically favoured, travel in the opposite direction is favoured with antiparallel spin^{49,57} (FIG. 3A; opposite enantiomers of the spin filter result in opposite spins being favoured). Although most measurements of CISS have used DNA or peptides^{63,64}, the viability of small molecules as CISS spin filters was demonstrated by Naaman, Lacour and co-workers⁶⁵ using cationic helices. The potential applications for the CISS effect are far reaching; for example, the coupling of an electron's spin to its transport direction could eliminate backscattering and thus lead to dissipationless transport^{66,67}. In addition, the CISS effect has been implied in biological processes⁶⁸ and has been demonstrated in emerging technological applications, such as those outlined below.

Paltiel and co-workers have reported several cases in which they successfully generated magnetization by exploiting the CISS effect. For example, current flowing through an α -helix L-polyalanine spin filter at low temperature was shown to generate magnetization in a nickel layer that was equivalent to the application of an external magnetic field of 0.4 T (REF. 69) (FIG. 3B). Importantly, at low temperatures and low voltages the magnetization was independent of the current direction: electrons flowing through the spin filter into the nickel layer are spin polarized parallel to the electron's velocity and thus increase the majority spin population. When the voltage is reversed, electrons travelling in the opposite direction — from nickel through the spin filter — can only pass through with an antiparallel alignment (FIG. 3A), thus depleting the minority spin state. The authors demonstrate a memory effect for the device and suggest that the use of two ports with spin filters of opposite chirality could also generate an XOR logic circuit: current flow through neither or both ports would result in a non-magnetic sample.

By contrast, current flow through exactly one port would result in magnetization.

Naaman and co-workers have illustrated that the CISS effect may also be applied to control the outcome of electrochemical reactions. The generation of hydrogen through water splitting could have vast importance for future energy storage applications and liquid fuel production. However, it is limited by the oxidation half reaction, which usually requires a significant overpotential to proceed, thus lowering the overall efficiency. Naaman and co-workers⁷⁰ were able to show that control of the electron's spin alignment could reduce the overpotential in the photoelectrochemical oxidation of water: electrodes coated with achiral organic molecules displayed overpotentials of 0.5–0.7 V, whereas those coated with chiral molecules displayed overpotentials of only 0.0–0.2 V. The authors suggest that the overpotential could be lowered in two different ways. First, the spin-selection processes form the spin-aligned ground state, $^3\text{O}_2$, rather than the higher-energy antiparallel spin state, $^1\text{O}_2$. Second, the inefficient formation of the possible intermediate, hydrogen peroxide, can be avoided through spin control, as shown in a later study by Naaman, Meijer and co-workers⁷¹. For anodes coated with achiral semiconductors, the lack of spin control leads to the formation of $\cdot\text{OH}$ radicals that can recombine to form hydrogen peroxide (FIG. 3C, left). By contrast, chiral semiconductor coatings allow the selective removal of electrons with the same spin, which leads to spin-aligned $\cdot\text{OH}$ radicals that cannot recombine without spin flipping⁷¹ (FIG. 3C, right).

Chirality-dependent organization

The development of stereochemistry as a discipline has its origins in the chirality-dependent assembly of chiral molecules in the solid state: Louis Pasteur's optical resolution of the chiral salt ammonium sodium tartrate into a conglomerate of homochiral crystals in 1848 allowed him to assign an opposite sense of optical activity to aqueous solutions of opposite-handed crystals⁷²; this laid the groundwork for the identification and understanding of molecular chirality. It should be highlighted, however, that conglomerates of homochiral crystals — such as those observed by Pasteur — are a minority; racemic solutions most often crystallize as racemates, with identical numbers of both enantiomers in the unit cell. Therefore, when comparing the solid-state structures of different chiral compositions, an enantiopure chiral substance generally crystallizes into a different bulk structure than its corresponding racemate; thus, assembly in the solid state is sensitive to the chiral composition. Although this statement may seem obvious to many chemists, we believe that this phenomenon is widely overlooked when considering the technological potential of chiral organic materials. It is essential to emphasize that key to successful and high-performance organic devices is the need to link the well-understood characteristics of an isolated molecule (that is, molecular properties such as the highest occupied and lowest unoccupied molecular orbital energy levels, and molecular structure) into the collective behaviour of multiple units in the bulk (that is, material properties such

Racemates
Equimolar mixtures of enantiomer pairs.

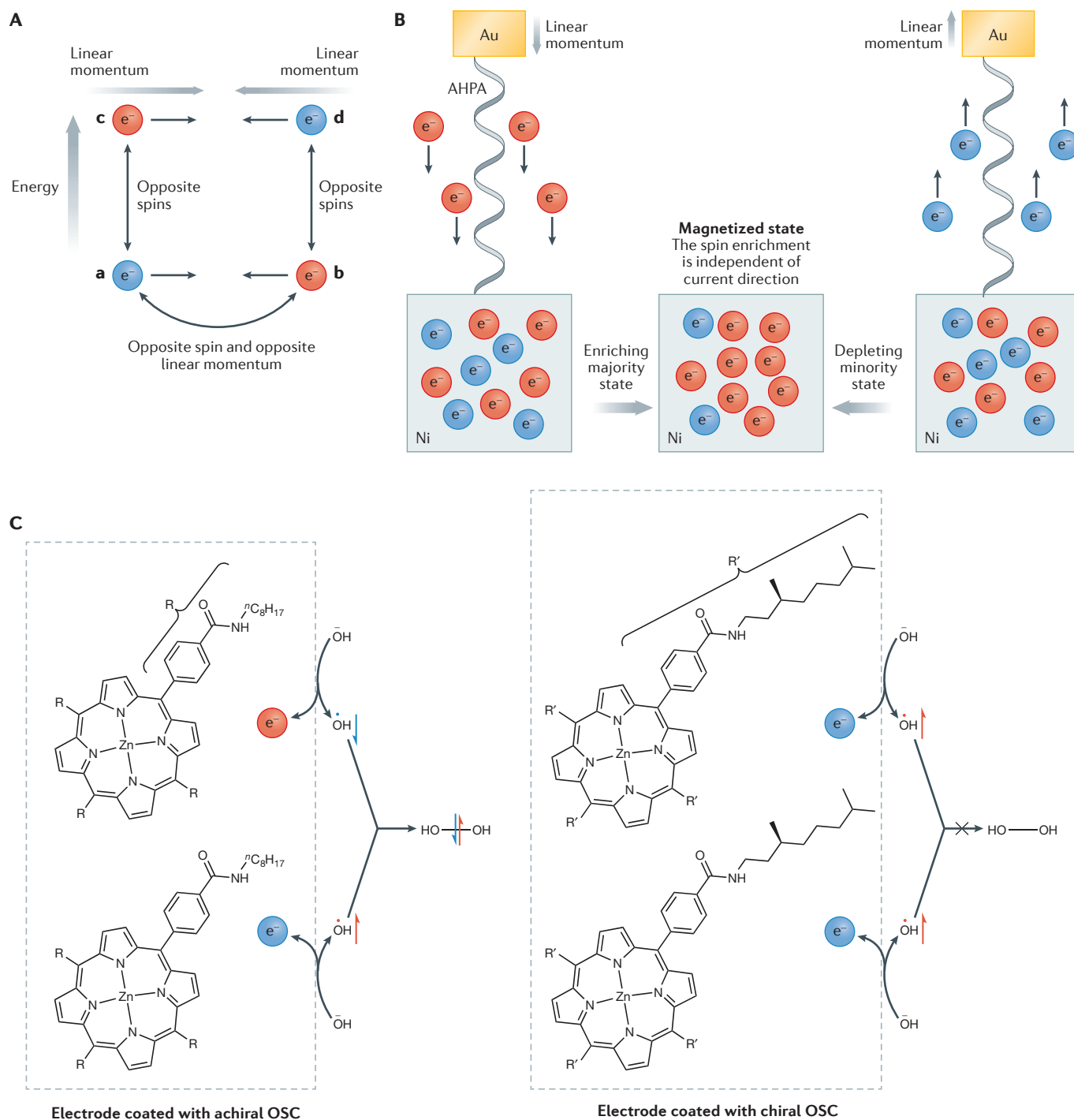


Figure 3 | Controlling and exploiting electron spin. **A** | Energy diagram that demonstrates the principle that underlies the chiral-induced spin selectivity (CISS) effect: in a chiral environment, the spin and linear momentum of an electron are coupled. From an energetically favoured state (part **Aa**), inversion of either spin (part **Ac**) or linear momentum (part **Ad**) requires energy; only inversion of both spin and linear momentum generates the other low energy state (part **Ab**). Opposite enantiomers result in opposite spins being favoured. **B** | Magnetization of a nickel layer by use of α -helix L-polyalanine (AHPA) as a spin filter. The magnetization is independent of the current direction; both injection of the majority spin (left panel) and ejection of the minority spin (right panel) lead to spin enrichment, and thus magnetization (middle panel)⁶⁹. As the spin alignment increases, injecting electrons into the nearly completely filled majority spin state becomes increasingly difficult and the resistance increases. **C** | The photoelectrochemical oxidation of water usually produces undesired hydrogen peroxide (left panel). However, electrodes coated with enantiopure chiral molecules can suppress this peroxide formation owing to the CISS effect⁷¹. The chiral electrode coating allows the selective removal of electrons with one spin state (right panel); the remaining spin-aligned $\cdot\text{OH}$ radicals cannot recombine without flipping the spin. OSC, organic semiconductor.

as charge transport and morphology)⁷³. Different chiral compositions (for example, racemic versus enantiopure) of a chiral organic electronic material will have exactly the same molecular properties but very different material properties. Thus, it should be possible to modify the performance of chiral organic materials solely through alteration of the chiral composition without any change to their molecular structure.

Mostly, studies involving chiral organic materials use the material as either the racemate or the enantiopure form, and rarely compare the two. However, several preliminary studies have compared different chiral compositions. Pu and co-workers⁷⁴ studied the conductivity of oligo(arylene-ethynylene)s containing a chiral 1,1'-binaphthyl unit (FIG. 4a) in a nanowell device architecture. They found that devices assembled from enantiopure materials (either *R* or *S*) exhibited median currents significantly (up to ≈ 80 -fold) larger than those assembled from racemic and scalemic mixtures (specifically, *R:S* ratios of 80:20, 50:50 and 20:80). However, chiral composition-dependent effects are not limited to axially chiral materials. Helicenes, for example, have proved excellent systems for the investigation of chiral intermolecular recognition and self-assembly at surfaces⁷⁵ — an intermediate means to understand chiral intermolecular recognition and self-assembly in the bulk — and therefore should be prime candidates for the study of assembly in the bulk. Hatakeyama, Nakamura and co-workers⁷⁶ have shown that photoinduced charge transport for bulk films of azaboradibenzo[6]helicene (FIG. 4b) is sensitive to the chiral composition, even in the absence of circular polarization (see above). They reported that bulk films of the racemic material exhibited hole mobility ($4.6 \times 10^{-4} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$) but a transient photocurrent for electron mobility could not be measured, whereas enantiopure films exhibited both hole ($7.9 \times 10^{-4} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$) and electron mobility ($4.5 \times 10^{-3} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$). This effect was attributed to differences in the packing of the racemic and enantiopure azaboradibenzo[6]helicene crystals, which in turn affects the electronic coupling between molecular units in the bulk. As a final example, Avarvari and co-workers reported that chiral derivatives of radical cation tetrathiafulvalene (TTF) salts (specifically, DM-EDT-TTF salts, FIG. 4c) — important contributors to the field of molecular electronics⁷⁷ — have conductivities that are highly dependent on the chiral composition used. Enantiopure salts of DM-EDT-TTF were found to exhibit semiconducting behaviour (with a conductivity of $10^{-5} \text{ S cm}^{-1}$ at room temperature and ambient pressure), whereas the racemic salts had metallic conductivity (with a conductivity of 250 S cm^{-1} at room temperature and ambient pressure). This differential conductivity was attributed to the very different crystalline packing of the two forms⁷⁸. Notably, this outcome differed from a previous study on an alternative chiral TTF salt, in which the two chiral compositions were found to crystallize with similar unit cell parameters⁷⁹. In this earlier study, the differential conductivity between the compositions (with the outcome inverted relative to DM-EDT-TTF —

the enantiopure salt was more conducting) was attributed to occupational disorder observed in the unit cell of the racemic salt⁷⁹.

While preparing this Review, two further studies on chirality-dependent organization were reported. In the first, Favereau, Blanchard, Cabanetos, Crassous and co-workers⁸⁰ reported organic photovoltaic devices consisting of the polymer P3HT blended with a chiral helicene small-molecule additive; enantiopure additives showed a fivefold higher power conversion efficiency than racemic additives. The second report by Oh and co-workers⁸¹ showed that the performance of organic phototransistors was influenced by the pendant chirality of perylene diimides in self-assembled crystalline nanowires, with homochiral aggregates displaying an improved electron mobility.

An extension to this concept would be to consider the different material properties of a selection of stereoisomers for a chiral molecule, for example, the comparison of two diastereoisomers. However, care must be taken, because diastereoisomers do not have exactly the same molecular properties; two diastereoisomers are, in effect, two different compounds. However, for the chiral conjugated materials in which the source of chirality is remote from the conjugated core — the region of the molecule that determines optoelectronic molecular properties — it is possible to argue that an analogous conceptual framework is in place: identical conjugated cores give rise to identical molecular optoelectronic properties, whereas pendent chiral side chains control chirality-dependent assembly and thus material properties. Two excellent cases in point can be found in the studies of Nguyen and co-workers⁸², and Xue and Castellano and co-workers⁸³, both of which studied the effect of 2-ethylhexyl side chain stereochemistry on the properties of small-molecule organic semiconductors (FIG. 4d). Typically, conjugated organic (small-molecule and polymer) materials append alkyl side chains to the conjugated core in order to improve solubility and (solution) processability. Such side chains are frequently branched; the 2-ethylhexyl side chain comes pre-installed on many commercially available building blocks for π -conjugated materials. The isomeric complexity of products made from these building blocks, given the point chirality of the branch point, is, however, generally ignored. Nguyen and co-workers⁸² studied the stereoisomers of DPP(TBFu)₂ (FIG. 4d), comparing the enantiomeric *R,R* and *S,S* isomers with the achiral *meso* *R,S* isomer (which is diastereomeric with respect to the *R,R* or *S,S* isomers), and with the statistical isomeric mixture that would be obtained from a synthesis involving the racemic side chain. As would be expected from the analysis above, all isomers, and the mixture, were found to have identical absorption properties in solution but different structural and spectroscopic characteristics in the solid state. Most notably, they found that for OFETs fabricated from annealed materials, the *meso* *R,S* isomer exhibited a hole mobility ($2.8 \times 10^{-3} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$) that was three to four times larger than that of the *R,R* or *S,S* isomers, both of which exhibited the same mobility ($\approx 9 \times 10^{-4} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$), as would be expected. The origin of

Scalemic mixtures

Mixtures of enantiomers at a ratio other than 1:1.

Organic semiconductors

A class of conjugated organic materials that combine the electronic advantages of semiconducting materials with the chemical and mechanical benefits of organic compounds such as plastics. Their charge transport properties can be induced to lie between an insulator and a semiconductor.

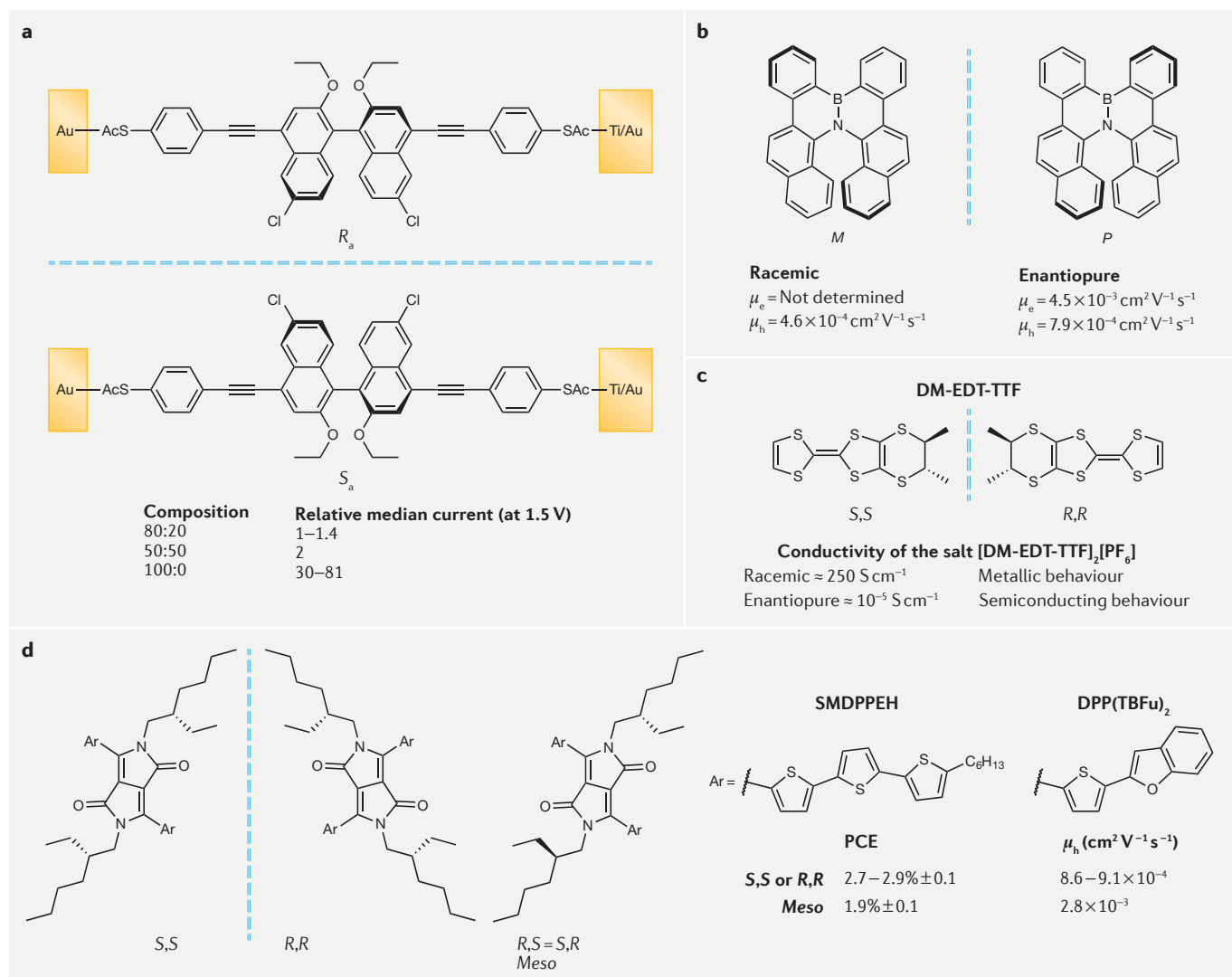


Figure 4 | Control of bulk electronic properties by stereochemical composition. **a** | Examples of materials that exhibit chiral composition-dependent changes of bulk properties. Molecular structures of oligo(arylene-ethynylene)s that contain a chiral 1,1'-binaphthyl unit⁷⁴. The enantiopure nanowires show current up to 80 times higher than those of other chiral compositions. The compositions of the mixtures refer to R:S and S:R. **b** | Chemical structure of azaboradibenzo[6]helicene⁷⁶. The film obtained from the racemic mixture of this molecule displays higher hole mobility (μ_h) than electron mobility (μ_e), whereas the opposite was observed for the enantiopure film. **c** | Structure of the tetrathiafulvalene (TTF) derivative dime-thyl-ethylenedithio-TTF (DM-EDT-TTF)⁷⁸. Single crystal conductivity measurements of the [DM-EDT-TTF]₂[PF₆]₂ salt show metallic conductivity when the racemic mixture is used and semiconducting behaviour for the enantiopure crystal. **d** | Examples of materials that exhibit stereochemical composition-dependent effects through differences in the bulk film properties of diastereomeric isomers. When DPP(TBFu)₂ is used in organic field-effect transistors, the *meso* isomer shows higher hole mobility than the S,S or R,R isomers⁸². When SMDPPEH is used as a donor in bulk heterojunction photovoltaic cells, the devices with either the S,S or R,R blend have higher power conversion efficiency (PCE) than the *meso* blends.⁸³

the improved hole mobility for the *meso* R,S isomer was attributed to the higher crystallinity of this compound. Xue and Castellano and co-workers⁸³ conducted a similar study on SMDPPEH (FIG. 4d), although in this case they examined the performance of bulk heterojunction photovoltaic devices fabricated with different stereoisomeric compositions and PCBM as the acceptor. Compared with the statistical composition, the more crystalline *meso* R,S isomer film showed weaker external quantum efficiency across the whole visible spectrum and consequently lower power conversion efficiency. By contrast,

the enantiopure film displayed a slightly blue-shifted external quantum efficiency without significant impact on the power conversion efficiency.

Conclusions

Through representative examples, we have highlighted cases in which small-molecule chirality has provided opportunities for and had an exciting impact on areas of technological relevance. Although highly promising, many of the examples described remain at an early stage of technological development and much

work is needed to further translate proof-of-concept results into real-world applications. In such endeavours, it is worth considering how the precise chiral framework used (BOX 1) affects key performance characteristics, and whether a certain type of chirality, or a certain type of chiral framework, could outperform others. Although chirality is often described as having a Boolean logic — an object is either chiral or it is not — efforts have been made to quantify chirality^{84–86}. However, these methods are not routinely applied to real molecules or to link such chirality indices to macro-properties of relevance to the examples presented here (for example, circular dichroism, CP-photoluminescence and CISS)⁸⁷. Thus, efforts to increase, for example, the dissymmetry of chiroptical effects are mainly empirical, which illustrates the need for an overarching theoretical framework that would allow advancement beyond the current trial-and-error stage. Of course, the identification of any privileged chiral structure need not be limited to a chiral small molecule; there are many alternative chiral

materials — for example, polymers^{4,5}, liquid crystals⁷ and plasmonic nanostructures¹⁰ — under active study. However, we believe that the examples presented here clearly demonstrate that from an application-led standpoint chiral small molecules can be competitive with other materials. Furthermore, small molecules have key advantages over many alternative material sets: through synthesis such materials are available in a highly pure, single composition and can be systematically derivatized and studied. Ultimately, we believe that in order to fully exploit the opportunities of small-molecule chirality there needs to be more collaboration between scientists in different disciplines; for example, between those who can measure the effects described herein, or understand a given application need (but may be unfamiliar with chirality), and those scientists who synthesize chiral molecules (but are unfamiliar with the effects and/or measurements). We hope that this Review, in part, helps to seed and stimulate such collaborations, driving further development in this burgeoning area.

- Brooks, H. W., Guida, C., W. & Daniel, G. K. The significance of chirality in drug design and development. *Curr. Top. Med. Chem.* **11**, 760–770 (2011).
- Leitereg, T. J., Guadagni, D. G., Harris, J., Mon, T. R. & Teranishi, R. Chemical and sensory data supporting the difference between the odors of the enantiomeric carvones. *J. Agr. Food Chem.* **19**, 785–787 (1971).
- Reinitzer, F. Beiträge zur Kenntniss des Cholesterins [German]. *Monatsh. Chem.* **9**, 421–441 (1888).
- Kane-Maguire, L. A. P. & Wallace, G. G. Chiral conducting polymers. *Chem. Soc. Rev.* **39**, 2545–2576 (2010).
- Song, C. *et al.* Optically active particles of chiral polymers. *Macromol. Rapid Commun.* **34**, 1426–1445 (2013).
- Kumar, J., Thomas, K. G. & Liz-Marzán, L. M. Nanoscale chirality in metal and semiconductor nanoparticles. *Chem. Commun.* **52**, 12555–12569 (2016).
- Davis, E. J. & Goodby, J. W. in *Handbook of Liquid Crystals* Vol. 1 Ch. 7 (Wiley, 2014).
- Liu, M., Zhang, L. & Wang, T. Supramolecular chirality in self-assembled systems. *Chem. Rev.* **115**, 7304–7397 (2015).
- Bisht, K. K., Parmar, B., Rachuri, Y., Kathalikattil, A. C. & Suresh, E. Progress in the synthetic and functional aspects of chiral metal–organic frameworks. *CrystEngComm* **17**, 5341–5356 (2015).
- Valev, V. K., Baumberg, J. J., Sibilia, C. & Verbiest, T. Chirality and chiroptical effects in plasmonic nanostructures: fundamentals, recent progress, and outlook. *Adv. Mater.* **25**, 2517–2534 (2013).
- Liu, B., Wu, F., Gui, H., Zheng, M. & Zhou, C. Chirality-controlled synthesis and applications of single-wall carbon nanotubes. *ACS Nano* **11**, 31–53 (2017).
- Wagenknecht, C. *et al.* Experimental demonstration of a heralded entanglement source. *Nat. Photonics* **4**, 549–552 (2010).
- Kim, D.-Y. Potential application of spintronic light-emitting diode to binocular vision for three-dimensional display technology. *J. Korean Phys. Soc.* **49**, S505–S508 (2006).
- Heffern, M. C., Matosziuk, L. M. & Meade, T. J. Lanthanide probes for bioresponsive imaging. *Chem. Rev.* **114**, 4496–4539 (2014).
- Brandt, J. R., Wang, X., Yang, Y., Campbell, A. J. & Fuchter, M. J. Circularly polarized phosphorescent electroluminescence with a high dissymmetry factor from PHOLEDs based on a platinum-helicene. *J. Am. Chem. Soc.* **138**, 9743–9746 (2016).
A diagrammatic explanation of the inherent inefficiency of anti-glare filters used in conjunction with OLEDs that emit non-polarized light can be found in the supporting information of reference 15.
- Peeters, E. *et al.* Circularly polarized electroluminescence from a polymer light-emitting diode. *J. Am. Chem. Soc.* **119**, 9909–9910 (1997).
- Geng, Y. *et al.* Origin of strong chiroptical activities in films of nonfluorenes with a varying extent of pendant chirality. *J. Am. Chem. Soc.* **125**, 14032–14038 (2003).
- Shikoh, E., Fujiwara, A., Ando, Y. & Miyazaki, T. Spin injection into organic light-emitting devices with ferromagnetic cathode and effects on their luminescence properties. *Jpn J. Appl. Phys.* **45**, 6897–6901 (2006).
A rare example of CP light emission by spin injection into a non-chiral OLED.
- Yang, Y., da Costa, R. C., Smilgies, D.-M., Campbell, A. J. & Fuchter, M. J. Induction of circularly polarized electroluminescence from an achiral light-emitting polymer via a chiral small-molecule dopant. *Adv. Mater.* **25**, 2624–2628 (2013).
- Baldo, M. A., O'Brien, D. F., Thompson, M. E. & Forrest, S. R. Excitonic singlet–triplet ratio in a semiconducting organic thin film. *Phys. Rev. B* **60**, 14422–14428 (1999).
- Yang, Z. *et al.* Recent advances in organic thermally activated delayed fluorescence materials. *Chem. Soc. Rev.* **46**, 915–1016 (2017).
An elegant method to improve fluorescence quantum yields is described in this Review on thermally activated delayed fluorescence.
- Li, T.-Y. *et al.* Circularly polarised phosphorescent photoluminescence and electroluminescence of iridium complexes. *Sci. Rep.* **5**, 14912 (2015).
- Zinna, F., Giovanella, U. & Di Bari, L. Highly circularly polarized electroluminescence from a chiral europium complex. *Adv. Mater.* **27**, 1791–1795 (2015).
- Zinna, F. & Di Bari, L. Lanthanide circularly polarized luminescence: bases and applications. *Chirality* **27**, 1–13 (2015).
- Sánchez-Carnerero, E. M. *et al.* Circularly polarized luminescence from simple organic molecules. *Chem. Eur. J.* **21**, 13488–13500 (2015).
- Zinna, F. *et al.* Design of lanthanide-based OLEDs with remarkable circularly polarized electroluminescence. *Adv. Funct. Mater.* **27**, 1603719 (2017).
- Norel, L. *et al.* Metallalhelixes: easily accessible helixene derivatives with large and tunable chiroptical properties. *Angew. Chem. Int. Ed.* **49**, 99–102 (2010).
- Shen, C. *et al.* Straightforward access to mono- and bis-cycloplatinated helixenes that display circularly polarized phosphorescence using crystallization resolution methods. *Chem. Sci.* **5**, 1915–1927 (2014).
- Browne, W. R. & Feringa, B. L. in *Molecular Switches* 121–179 (eds Browne, W. R. & Feringa, B. L.) (Wiley, 2011).
- Gilot, J. *et al.* Polymer photovoltaic cells sensitive to the circular polarization of light. *Adv. Mater.* **22**, E131–E134 (2010).
- Yang, Y., da Costa, R. C., Fuchter, M. J. & Campbell, A. J. Circularly polarized light detection by a chiral organic semiconductor transistor. *Nat. Photonics* **7**, 634–638 (2013).
- Xiang, D., Wang, X., Jia, C., Lee, T. & Guo, X. Molecular-scale electronics: from concept to function. *Chem. Rev.* **116**, 4318–4440 (2016).
- Isla, H. & Crassous, J. Helicene-based chiroptical switches. *C. R. Chim.* **19**, 39–49 (2016).
- Shen, C. *et al.* Iron alkynyl helixenes: redox-triggered chiroptical tuning in the IR and near-IR spectral regions and suitable for telecommunications applications. *Angew. Chem. Int. Ed.* **55**, 8062–8066 (2016).
- Coskun, A., Banaszak, M., Astumian, R. D., Stoddart, J. F. & Grzybowski, B. A. Great expectations: can artificial molecular machines deliver on their promise? *Chem. Soc. Rev.* **41**, 19–30 (2012).
- Kay, E. R., Leigh, D. A. & Zerbetto, F. Synthetic molecular motors and mechanical machines. *Angew. Chem. Int. Ed.* **46**, 72–191 (2007).
- Steuerman, D. W. *et al.* Molecular-mechanical switch-based solid-state electrochromic devices. *Angew. Chem. Int. Ed.* **43**, 6486–6491 (2004).
An example of a (non-chiral) rotaxane used in a prototype electrochromic device.
- Bandara, H. M. D. & Burdette, S. C. Photoisomerization in different classes of azobenzene. *Chem. Soc. Rev.* **41**, 1809–1825 (2012).
- Irie, M. Diarylethenes for memories and switches. *Chem. Rev.* **100**, 1685–1716 (2000).
- Leigh, D. A. Genesis of the nanomachines: the 2016 Nobel Prize in Chemistry. *Angew. Chem. Int. Ed.* **55**, 14506–14508 (2016).
- Collins, B. S. L., Kistemaker, J. C. M., Otten, E. & Feringa, B. L. A chemically powered unidirectional rotary molecular motor based on a palladium redox cycle. *Nat. Chem.* **8**, 860–866 (2016).
- Kudernac, T. *et al.* Electrically driven directional motion of a four-wheeled molecule on a metal surface. *Nature* **479**, 208–211 (2011).
An example of the use of electrochemical energy to drive a molecular motor.
- Wilson, M. R. *et al.* An autonomous chemically fuelled small-molecule motor. *Nature* **534**, 235–240 (2016).
- Clayden, J. No turning back for motorized molecules. *Nature* **534**, 187–188 (2016).
- Eelkema, R. *et al.* Molecular machines: nanomotor rotates microscale objects. *Nature* **440**, 163–163 (2006).
- Train, C., Gruselle, M. & Verdager, M. The fruitful introduction of chirality and control of absolute configurations in molecular magnets. *Chem. Soc. Rev.* **40**, 3297–3312 (2011).
- Pop, F., Auban-Senzier, P., Canadell, E., Rikken, G. L. J. A. & Avarvari, N. Electrical magnetochiral anisotropy in a bulk chiral molecular conductor. *Nat. Commun.* **5**, 3757 (2014).

48. Wolf, S. A. Spintronics: a spin-based electronics vision for the future. *Science* **294**, 1488–1495 (2001).
49. Naaman, R. & Waldeck, D. H. Chiral-induced spin selectivity effect. *J. Phys. Chem. Lett.* **3**, 2178–2187 (2012).
50. Watanabe, S. *et al.* Polaron spin current transport in organic semiconductors. *Nat. Phys.* **10**, 308–313 (2014).
51. Devkota, J., Geng, R., Subedi, R. C. & Nguyen, T. D. Organic spin valves: a review. *Adv. Funct. Mater.* **26**, 3881–3898 (2016).
52. Geng, R., Daugherty, T. T., Do, K., Luong, H. M. & Nguyen, T. D. A review on organic spintronic materials and devices: I. Magnetic field effect on organic light emitting diodes. *J. Sci. Adv. Mater. Devices* **1**, 128–140 (2016).
53. Göhler, B. *et al.* Spin selectivity in electron transmission through self-assembled monolayers of double-stranded DNA. *Science* **331**, 894–897 (2011).
Conclusive proof that chiral organic materials can be used to generate spin-polarized electrons. See also references 53–55.
54. Mayer, S. & Kessler, J. Experimental verification of electron optic dichroism. *Phys. Rev. Lett.* **74**, 4803–4806 (1995).
55. Blum, K. & Thompson, D. G. in *Advances in Atomic, Molecular and Optical Physics* Vol. 38 (eds Bederson, B. & Walther, H.) 39–86 (Elsevier, 1998).
56. Ray, K., Ananthavel, S. P., Waldeck, D. H. & Naaman, R. Asymmetric scattering of polarized electrons by organized organic films of chiral molecules. *Science* **283**, 814–816 (1999).
57. Naaman, R. & Waldeck, D. H. Spintronics and chirality: spin selectivity in electron transport through chiral molecules. *Annu. Rev. Phys. Chem.* **66**, 263–281 (2015).
58. Michaeli, K., Varade, V., Naaman, R. & Waldeck, D. H. A new approach towards spintronics — spintronics with no magnets. *J. Phys. Condens. Matter* **29**, 103002 (2017).
59. Eremko, A. A. & Loktev, V. M. Spin sensitive electron transmission through helical potentials. *Phys. Rev. B* **88**, 165409 (2013).
A theoretical model of the CISS effect, see also reference 60–62.
60. Matityahu, S., Utsumi, Y., Aharoni, A., Entin-Wohlman, O. & Balseiro, C. A. Spin-dependent transport through a chiral molecule in the presence of spin–orbit interaction and nonunitary effects. *Phys. Rev. B* **93**, 75407 (2016).
61. Varela, S., Mujica, V. & Medina, E. Effective spin–orbit couplings in an analytical tight-binding model of DNA: spin filtering and chiral spin transport. *Phys. Rev. B* **93**, 155436 (2016).
62. Pan, T.-R., Guo, A.-M. & Sun, Q.-F. Spin-polarized electron transport through helicene molecular junctions. *Phys. Rev. B* **94**, 235448 (2016).
63. Zwang, T. J., Hürlimann, S., Hill, M. G. & Barton, J. K. Helix-dependent spin filtering through the DNA duplex. *J. Am. Chem. Soc.* **138**, 15551–15554 (2016).
An interesting example of the influence of helix handedness on spin filtering. See also reference 68.
64. Aragonès, A. C. *et al.* Measuring the spin-polarization power of a single chiral molecule. *Small* **13**, 1602519 (2017).
65. Kiran, V. *et al.* Helicenes — a new class of organic spin filter. *Adv. Mater.* **28**, 1957–1962 (2016).
66. Qi, X.-L. & Zhang, S.-C. The quantum spin Hall effect and topological insulators. *Phys. Today* **63**, 33–38 (2010).
67. Carmeli, I., Kumar, K. S., Heifler, O., Carmeli, C. & Naaman, R. Spin selectivity in electron transfer in photosystem I. *Angew. Chem. Int. Ed.* **53**, 8953–8958 (2014).
68. Michaeli, K., Kantor-Uriel, N., Naaman, R. & Waldeck, D. H. The electron's spin and molecular chirality — how are they related and how do they affect life processes? *Chem. Soc. Rev.* **38**, 188–229 (2016).
69. Ben Dor, O., Yochelis, S., Mathew, S. P., Naaman, R. & Paltiel, Y. A chiral-based magnetic memory device without a permanent magnet. *Nat. Commun.* **4**, 2256 (2013).
70. Mtangi, W., Kiran, V., Fontanesi, C. & Naaman, R. Role of the electron spin polarization in water splitting. *J. Phys. Chem. Lett.* **6**, 4916–4922 (2015).
71. Mtangi, W. *et al.* Control of electrons' spin eliminates hydrogen peroxide formation during water splitting. *J. Am. Chem. Soc.* **139**, 2794–2798 (2017).
72. Pasteur, L. Recherches sur les relations qui peuvent exister entre la forme cristalline: la composition chimique et les sens de la polarisation rotatoire. *Ann. Chim. Phys.* **24**, 442–459 (in French) (1848).
73. Henson, Z. B., Müllen, K. & Bazan, G. C. Design strategies for organic semiconductors beyond the molecular formula. *Nat. Chem.* **4**, 699–704 (2012).
74. Zhu, Y. *et al.* First optically active molecular electronic wires. *Org. Lett.* **8**, 355–358 (2006).
75. Ernst, K.-H. Stereochemical recognition of helicenes on metal surfaces. *Acc. Chem. Res.* **49**, 1182–1190 (2016).
76. Hatakeyama, T., Hashimoto, S., Oba, T. & Nakamura, M. Azaboradibenzof[6]helicene: carrier inversion induced by helical homochirality. *J. Am. Chem. Soc.* **134**, 19600–19603 (2012).
77. Brunetti, F. G., López, J. L., Atienza, C. & Martín, N. π -Extended TTF: a versatile molecule for organic electronics. *J. Mater. Chem.* **22**, 4188–4205 (2012).
78. Pop, F. *et al.* Chirality driven metallic versus semiconducting behavior in a complete series of radical cation salts based on dimethyl-ethylenedithio-tetrathiafulvalene (DM-EDT-TTF). *J. Am. Chem. Soc.* **135**, 17176–17186 (2013).
79. Madalan, A. M. *et al.* Order versus disorder in chiral tetrathiafulvalene-oxazoline radical-cation salts: structural and theoretical investigations and physical properties. *Chem. Eur. J.* **16**, 528–537 (2010).
80. Josse, P. *et al.* Enantiopure versus racemic naphthalimide end-capped helicene non-fullerene electron acceptors: impact on organic photovoltaics performance. *Chem. Eur. J.* **23**, 6277–6281 (2017).
81. Shang, X. *et al.* Supramolecular nanostructures of chiral perylene diimides with amplified chirality for high-performance chiroptical sensing. *Adv. Mater.* <http://dx.doi.org/10.1002/adma.201605828> (2017).
82. Liu, J. *et al.* Effects of stereoisomerism on the crystallization behavior and optoelectrical properties of conjugated molecules. *Adv. Mater.* **25**, 3645–3650 (2013).
83. Zerdan, R. B. *et al.* The influence of solubilizing chain stereochemistry on small molecule photovoltaics. *Adv. Funct. Mater.* **24**, 5993–6004 (2014).
84. Buda, A. B. & Mislav, K. A Hausdorff chirality measure. *J. Am. Chem. Soc.* **114**, 6006–6012 (1992).
85. Alvarez, S., Alemany, P. & Avnir, D. Continuous chirality measures in transition metal chemistry. *Chem. Soc. Rev.* **34**, 313–326 (2005).
86. Yewande, E. O., Neal, M. P. & Low, R. The Hausdorff chirality measure and a proposed Hausdorff structure measure. *Mol. Phys.* **107**, 281–291 (2009).
87. Neal, M. P., Solymosi, M., Wilson, M. R. & Earl, D. J. Helical twisting power and scaled chiral indices. *J. Chem. Phys.* **119**, 3567–3573 (2003).
A study that links the chiral indices of liquid crystals to their helical twisting power.
88. Trojanowicz, M. & Kaniewska, M. Electrochemical chiral sensors and biosensors. *Electroanalysis* **21**, 229–238 (2009).
89. Trojanowicz, M. Enantioselective electrochemical sensors and biosensors: a mini-review. *Electrochem. Commun.* **38**, 47–52 (2014).
90. Manoli, K., Magliulo, M. & Torsi, L. Chiral sensor devices for differentiation of enantiomers. *Top. Curr. Chem.* **341**, 133–176 (2013).
91. Tiwari, M. P. & Prasad, A. Molecularly imprinted polymer based enantioselective sensing devices: a review. *Anal. Chim. Acta* **853**, 1–18 (2015).
92. Zou, W. *et al.* Biomimetic superhelical conducting microfibers with homochirality for enantioselective sensing. *J. Am. Chem. Soc.* **136**, 578–581 (2014).
93. Ettl, R., Chao, I., Diederich, F. & Whetten, R. L. Isolation of C₇₆, a chiral (D₂) allotrope of carbon. *Nature* **353**, 149–153 (1991).
94. Neal, E. A. & Goldup, S. M. Chemical consequences of mechanical bonding in catenanes and rotaxanes: isomerism, modification, catalysis and molecular machines for synthesis. *Chem. Commun.* **50**, 5128–5142 (2014).

Acknowledgements

The authors thank the chirality community for the fruitful discussions that inspired this Review, acknowledge their long-standing collaboration with A. Campbell and thank the Engineering and Physical Sciences Research Council (EPSRC) for funding (EP/L014580/1, EP/L016702/1, and EP/P000525/1).

Competing interests statement

The authors declare no competing interests.

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How to cite this article

Brandt, J. R., Salerno F. & Fuchter M. J. The added value of small-molecule chirality in technological applications. *Nat. Rev. Chem.* **1**, 0045 (2017).