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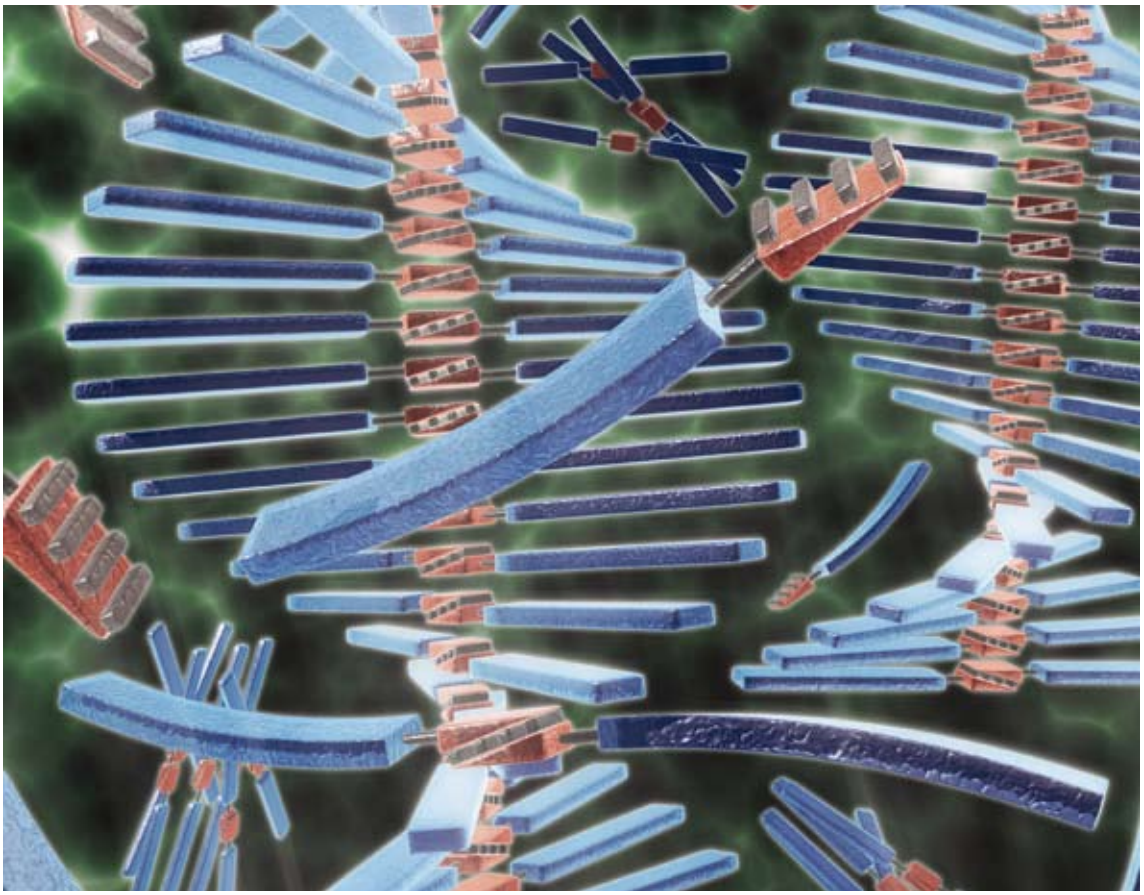

Expression of chirality in molecular layers at surfaces: insights from modelling†

Mathieu Linares,‡ Andrea Minoia, Patrick Brocorens, David Beljonne and Roberto Lazzaroni*

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This *tutorial review* illustrates how modelling can be used to understand the structure and properties of chiral surfaces formed by adsorption of molecular layers. The two major theoretical approaches for such modelling (Density Functional Theory and classical force-field methods) are briefly described and compared. A few examples of their use are given, focussing on:
(i) the expression of chirality at the local and global scale in layers of chiral molecules,
(ii) the appearance of chirality in layers of achiral molecules on achiral surfaces, and
(iii) the molecular organisation in layers formed from racemic mixtures.

Introduction

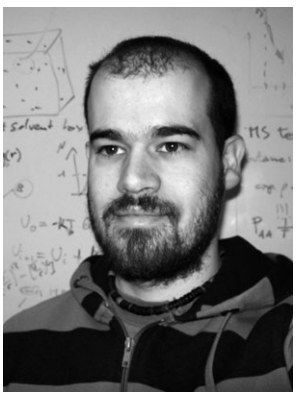
The term 'chirality' refers to the properties of an object that cannot be superimposed on its mirror image by any rotation or translation operation. Chirality is expressed both in the macroscopic world (*e.g.*, the left and right hands or the convolution of snail shells) and at the molecular level, *e.g.*, in molecules possessing at least one carbon atom with four different substituents or in helical molecular assemblies, such as the DNA double helix. Pairs of (supra)molecular objects that are non-superimposable mirror images of each other are called enantiomers. Since the most important building blocks of biological systems (sugars, amino acids, and nucleic acids) are homochiral (only one enantiomer is present), the interaction of any compound with those systems (*e.g.*, in drugs or sensing devices) is expected to be deeply influenced by the chiral character. It is therefore essential to understand the mechanisms of chiral recognition and to design strategies for generating molecular-scale systems with a well-defined chirality.

Creating a molecular-scale chiral object can be realised *via* a synthetic route (*i.e.*, asymmetric synthesis) or *via* guided molecular assembly of smaller chiral (or even achiral) units. The latter approach can be very effective when the chiral function is created at a surface. Indeed, several symmetry restrictions are intrinsically present at a surface: it has no inversion centre and the only reflection symmetry planes

Service de Chimie des Matériaux Nouveaux, Université de Mons-Hainaut, Place du Parc 20, 7000 Mons, Belgium. E-mail: roberto@averell.umh.ac.be; Fax: +32 65 37 38 61; Tel: +32 65 37 38 60
† Part of the nanoscale chirality themed issue.
‡ Present address: Department of Physics, Chemistry and Biology, IFM, Linköpings Universitet, SE-58183 Linköping, Sweden.

Mathieu Linares

Mathieu Linares obtained his PhD in Theoretical Chemistry at the Paul Cézanne University (Marseilles, France) in 2005, where he developed a valence bond method under the supervision of Prof. S. Humbel. In 2006, he joined the Laboratory for Chemistry of Novel Materials in Mons for a post-doctoral stay where he worked on the modelling of self-assembly in solution and at surfaces. Since 2008, he has been a postdoctoral researcher in the Computational Physics group at Linköping University (Linköping, Sweden) with Prof. S. Stafström. His current research interests, besides self-assembly, are valence bond theory and charge transport in organic materials.



Andrea Minoia

Andrea Minoia obtained his PhD in Chemistry at the University of Mons-Hainaut in 2008, studying (both chiral and achiral) molecular self-assembly by molecular modelling techniques. He also spent one year as a Marie Curie doctoral trainee with D. Andrienko at the Max-Planck Institute for Polymer Research in Mainz, working on coarse graining techniques. He now has a post-doc position at the Materia Nova research center in Mons; his research is focused on the morphology and electronic characterisation of supramolecular self-assemblies and carbon nanotubes dispersed in polymers, studied by a combination of quantum chemistry and force field based simulation.

possible are those perpendicular to it. It is therefore easier to generate chirality at a surface than in the bulk or in a solution.

Only a few surfaces are intrinsically chiral; for instance, this is the case for quartz or calcite.[1] It is possible however to turn an achiral surface into a chiral object by specific adsorption of a molecular overlayer. Chirality is then expressed in a variety of structures, summarised in Fig. 1.[2]

It is remarkable that chirality can originate from the adsorption of *achiral* molecules on an *achiral* substrate. That happens if the molecule is prochiral and adsorbs in such a way that reflection symmetry is lost (a chiral site is then formed), or if the arrangement of adsorbed molecules with respect to the substrate lattice is chiral (chiral domains are formed, while the individual sites are not). It must be noted however that the probability of forming the two types of enantiomeric sites or domains is equal, so that the surface is globally achiral.

When chiral molecules are adsorbed, chirality first stems from the preservation of molecular chirality in the adsorbate. In addition to that, the arrangement of the molecules can also be chiral, with the formation of only one type of enantiomeric domain, so that chirality is expressed at both the local and the global scale. Finally, one may imagine a system in which the chiral molecules are arranged in domains that *appear to be* reflection images of each other (but are not, because of the intrinsic chirality of the molecules), and the system is chiral overall; this last type of organisation has not yet been observed experimentally.

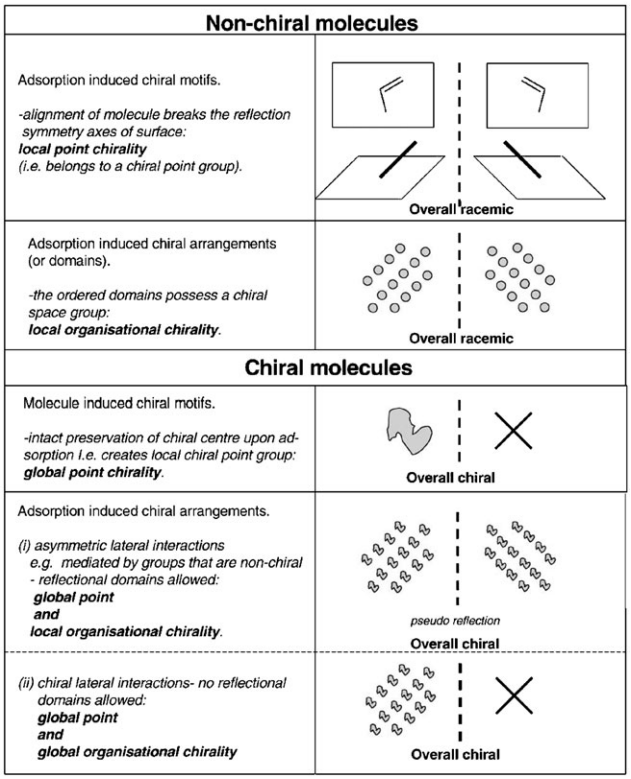
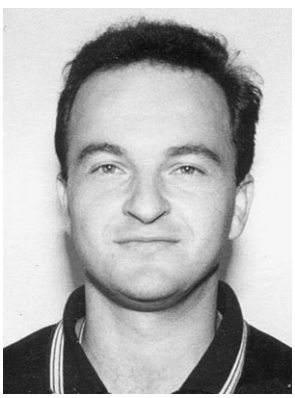


Fig. 1 Manifestations of chirality at surfaces upon the adsorption of a molecular layer (from S. M. Barlow, R. Raval, *Surf. Sci. Rep.*, 2003, **50**, 201; with permission of Elsevier).

The generation of chiral surfaces is of prime interest for a wide range of applications, the most relevant ones being

Patrick Brocorens

Patrick Brocorens obtained his PhD in Chemistry at the University of Mons-Hainaut in 2002, studying the morphology of dendrimers by molecular modelling techniques. He now holds a permanent 'research and teaching' position in Mons; his research interests center on the organisation and morphological properties of liquid crystals, conjugated polymers, and clay/polymer composites, studied by a combination of simulation techniques and atomic force microscopy.



David Beljonne

David Beljonne got his PhD in Chemistry at the University of Mons-Hainaut in 1994. After post-doctoral stays at the Universities of Cambridge (with Prof. Friend) and Rochester (with Prof. Mukamel), he went back to Mons where he is now a Research Director of the Belgian National Science Foundation (FNRS). He is also a Visiting Principal Research Scientist at the Georgia Institute of Technology in Atlanta. Co-author of about 200 scientific publications, his research activities deal with the modelling using classical and quantum-chemical approaches of the interplay between the supramolecular organisation and the opto-electronic properties of conjugated materials.

Roberto Lazzaroni

Roberto Lazzaroni obtained a PhD in Chemistry at the University of Namur in 1987. After post-doctoral stays at the University of Linköping (with W.R. Salaneck) and CNR-Bologna (with C. Taliani), he joined the University of Mons-Hainaut where he is now professor at the Chemistry Department. He is also scientific director at the Materia Nova research center in Mons. His research interests mostly deal with the structure and electronic properties of organic and hybrid supramolecular structures, constructed by self-assembly of functional (macro)molecules.

enantioselective catalysis (the specific formation of one enantiomer),[3] chiral sensing (the specific detection of one enantiomer),[4] enantiomer resolution (the separation of enantiomers)[5] and non-linear optical materials (as the even-order non-linear optical responses require a non-centrosymmetric medium).[6] Nevertheless, research on chiral surfaces has developed only recently, mostly because of the difficulty in probing chirality at a surface. With the advent of scanning tunnelling microscopy (STM), which opened the possibility of investigating surfaces with atomic-scale resolution, the direct observation of chiral patterns of adsorbed molecules became possible and many important results were obtained for a large variety of molecular adsorbates on very diverse surfaces (for reviews, see ref. 2, 7–9).

Chiral patterns in adsorbed layers can appear upon both chemisorption and physisorption. Chemisorption implies the presence of a reactive (usually metal) surface, which must be prepared and kept clean prior to adsorption. Therefore, those studies are most often conducted in ultra-high-vacuum (UHV) conditions, which also allow precise control of the amount of deposited adsorbate and variation of the substrate temperature during and after deposition (*i.e.*, thermal annealing). The combination of STM and low-energy electron diffraction (LEED) data provides a detailed description of the system in terms of the structure and orientation of the overlayer with respect to the substrate lattice, as well as the molecular organisation in the overlayer.

In contrast, most studies of chirality in physisorbed layers deal with liquid–solid interfaces. The layer forms on a surface (most often, atomically-flat graphite or MoS_2) that is in contact with a saturated solution of the adsorbate. Such a situation is interesting in that it is closer to real-life conditions with respect to UHV, but it does not allow for control of surface coverage or for large variations of substrate temperature. The latter point can be considered as a minor problem, because the dynamic nature of the system (the molecules can continuously exchange between the layer and the overlaying solution) probably drives it towards an equilibrium structure. The reversible character of physisorption also permits determination of the orientation of the overlayer with respect to the substrate lattice in a single STM experiment: after imaging the molecular layer, one can modify the measurement conditions so that the tip is brought closer to the surface. It then 'brushes the molecules away' and the substrate surface can be visualised. Upon restoration of the initial conditions, the tip retracts and the physisorbed layer readily forms again.

The scanning probe-based studies provide important information on the structure of (chiral) molecular layers at surfaces. However, they seldom reach atomic-scale resolution at room temperature; molecules most often appear as individual objects with very little discernible internal structure. Some types of substituents usually show very little contrast (*e.g.*, alkyl side groups) and the exact orientation of functional groups (including those around stereogenic centres) can hardly be determined. It is important to stress that STM views the electronic density at a given potential and probing distance of the ensemble formed by the monolayer and the underlying substrate, which might not be readily related to the geometric structure of the molecular layer. To bridge the gap and propose/refine structural models that reproduce the STM results, atomistic modelling (*i.e.*, theoretical methods that explicitly consider all atoms) is needed. This implies a strong feedback between measurement and modelling: the experimental adsorption patterns can be used as input for the calculations. The geometry of the system is then optimised towards a stable (*i.e.*, low energy) situation and the theoretical results are finally confronted with the original data for consistency checks. Combined with the STM data, the results of the calculations then yield a full structural description of the adsorbed molecular layers. Examples of this joint 'STM-modelling' approach will be given in the following sections.

Besides the structural information, atomistic modelling is most useful to get a deep insight on the energetics of the systems under study. First, it is possible to calculate the binding energy of a given molecule to the surface; this implies, for instance, the energetics of metal–molecule bonding in the case of chemisorption, or weak CH–π or π–π interactions for systems physisorbed on graphite. Second, the internal cohesion of the adsorbed layer can be evaluated, by computing the molecule–molecule interaction energy; this includes van der Waals interactions, as well as H-bonding or π–π interactions. Third, one can compare different molecular organisations, and identify the most probable one on the basis of the energy criterion. Fourth, since energy barriers can also be calculated, the occurrence of transitions can be assessed at the molecular scale (*e.g.*, between different conformations) or at the supramolecular scale (*e.g.*, between different supramolecular arrangements).

It is however essential to realise that the accurate description of the adsorbed layers, in terms of structure and energy, requires that an appropriate theoretical approach be selected, depending on the nature and strength of the surface–molecule interactions. When chemisorption is concerned, a proper representation of chemical bonding is needed, which can only be provided by *ab initio* quantum-mechanical methods. Among those, density functional theory (DFT)-based techniques are clearly the most reliable and efficient to describe the chemisorption of molecules on metal surfaces, because they take into account electron correlation, which is notoriously important in metal systems, while still being tractable for large-size systems. The DFT calculations yield detailed information on all aspects of chemical bonding: the bonding site(s), the electron density redistribution between the adsorbate and the surface, the atomic orbitals involved (provided a localised basis set is used), as well as theoretical vibrational spectra. The DFT approach can also be used to simulate STM images and to interpret scanning tunnelling spectroscopy (STS) data.

In contrast, most DFT techniques provide a rather poor description of intermolecular interactions, which are central to physisorbed systems. In those cases, a radically different theoretical approach must be used. It is based on an empirical 'force-field' that represents all the interatomic and intermolecular interactions present in the system. When properly parameterised, such force fields are very accurate for the description of the structure and energetics of physisorbed supramolecular systems. For instance, it is possible to evaluate the relative strength of different contributions to the stability

of the layer (*e.g.*, H-bonding *vs.* dipole–dipole *vs.* dispersion forces) and so obtain a detailed description of the interplay between the different intermolecular interactions.

Because they are generally less computationally demanding, force-field methods can be applied to very large systems (*i.e.*, several thousand atoms) while DFT techniques are usually restricted to a few hundred atoms. With the former approach, it is therefore possible to model physisorbed layers in the presence of solvent molecules, a situation that is very close to the actual conditions in the STM experiments (note that considering simply the molecular adsorbate and the metal surface, as done with DFT, is also close to the UHV conditions in which chemisorbed systems are studied). Finally, the dynamics of the adsorbed layers (*i.e.*, the time evolution of the system at a given temperature) can also be investigated theoretically. In practice, such studies are very often computationally intractable at the quantum-mechanical level but can be carried out with a force-field approach. The time scale that such atomistic molecular dynamics (MD) simulations can span is typically in the nano to microsecond range; this means that only fast processes can be followed (*e.g.*, the adsorption or desorption of a molecule or molecular segment) whereas 'large scale' cooperative processes (*e.g.*, the formation of a well-ordered domain of chiral molecules from solution) are presently out of reach.

In this tutorial review, we will illustrate how modelling can be used to shed light on the structure and properties of chiral surfaces. These theoretical studies typically address the following questions: (i) what is the nature of the intermolecular interactions at play in chiral molecular layers at surfaces? (ii) what are the mechanisms by which the chirality at the molecule level is expressed in the two-dimensional system? In other words, what is the link between local chirality and global chirality? and (iii) what is the structure of the layer when the surface is exposed to a racemic mixture? Do the enantiomers form separate domains or do they mix at the molecular scale?

The manuscript is organised as follows: the two major modelling approaches (DFT and force-field techniques) are described in the following section. The central part of the paper is devoted to the description of a few typical modelling studies for both physisorbed and chemisorbed systems, focussing on: (i) the expression of chirality in layers of chiral molecules; (ii) the formation of chiral patterns by adsorption of achiral molecules on achiral surfaces; and (iii) the molecular organisation in layers formed upon adsorption of racemic mixtures. Finally, a few prospects for improved modelling of chiral molecular layers are proposed.

Modelling protocols

The first step in molecular modelling consists in selecting a method to best describe the behaviour of the molecules and molecular systems under study. Although computer hardware and calculation algorithms keep improving, quantum-chemical methods are intractable for systems exceeding thousands of atoms, and can be advantageously substituted by force-field methods. This is not only due to the gain in calculation time (several orders of magnitude faster with respect to *ab initio* quantum-chemical techniques), but also because the non-bonded interactions, which play a critical role in physisorbed systems, are extremely difficult to reproduce accurately with quantum-mechanical methods.

A Force-field techniques

While it is usual in quantum mechanics, according to the Born–Oppenheimer approximation, to study the electronic structure in the field of frozen nuclei, the opposite approach is used in force-field-based methods. The electrons are not explicitly treated and are assumed to surround the nuclei appropriately, generating a potential field in which the nuclei are located. The energy changes that appear when modifying the nuclei positions define a Born–Oppenheimer surface, also called a potential energy surface (PES), which governs many properties of the system, such as the molecular structures, energetics, and dynamics. Investigating these properties requires a way to reproduce and explore the PES. The first task is devoted to a force-field, which is a set of equations whose mathematical form is derived from classical mechanics. Atoms are approximated as soft spheres bonded to each other with springs. Once a force-field is parameterised to correctly reproduce experimental or quantum-chemical results, the PES can be explored to find the lowest energy situations; this is done by means of algorithms that can be divided into two categories: (i) local algorithms, namely molecular mechanics (MM), explore the energy landscape downhill. Whatever the starting geometry, the algorithm optimises the geometrical parameters leading to an energy minimum located in the same PES valley as the initial structure; (ii) in contrast, global algorithms allow overcoming potential barriers and finding different energy minima away from the starting geometry. In this category, the most popular approaches are the Monte Carlo and molecular dynamics (MD) methods.

A.1 Force-fields. A force-field is a mathematical translation of the old basic idea that bonds and angles between atoms in a molecule tend to have "natural" values. The interatomic interactions are mimicked by a set of empirical formulas, and the accuracy of the results depends on the way the parameters and functional forms of the energy expression have been chosen. Practically, a force-field is tuned to best reproduce experimental or calculated data of a series of simple molecules, and its applicability domain is then assumed to extend to other similar systems according to the principle of transferability of the parameters.

$$V = \sum V_{\text{bond}} + \sum V_{\text{angle}} + \sum V_{\text{torsion}} + \sum V_{\text{inversion}} + \sum V_{\text{crossterms}} + \sum V_{\text{elec}} + \sum V_{\text{vdW}} + \sum V_{\text{Hbond}}$$

A force-field is broken down into valence terms and non-bonded terms. The valence terms include bond stretching, angle bending, torsion, and inversion contributions. Bond stretching and angle bending interactions are often considered as hard degrees of freedom, as they require significant energies to be modified from their reference value, and are thus very commonly approximated by a harmonic potential. The torsion term is a soft degree of freedom and, along with non-bonded terms, is responsible for the largest conformational changes *via* potential barrier crossing. More attention has thus to be paid to select proper parameters and functions. A cosine series

expansion with up to six terms is generally used. The inversion or 'out-of-plane' terms describe the propensity of an atom I bonded to three other atoms J, K, L to lie in or depart from the JKL plane and can be described by a cosine Fourier expansion. Some force-fields also include cross terms reflecting the coupling between internal coordinates. Generally, only the interactions between two internal coordinates having atoms in common are considered, as they usually provide the largest contributions. The van der Waals and electrostatic interactions between pairs of atoms form the non-bonded terms, and are typically expressed as functions of some inverse power of the distance, as in the best known van der Waals expression, the 6-12 Lennard-Jones potential. In some force-fields, a specific term is included to describe hydrogen bonds.

A.2 Molecular mechanics methods. When building complex molecules, the default geometrical parameters are very approximate and must be refined. This geometry optimisation is performed by MM algorithms, which use either the first-derivatives (GRADIENT methods) or the first- and second-derivatives (NEWTON methods) of the energy function *versus* the coordinates to minimise the energy. This is an iterative process that goes on until some convergence criteria are reached, typically when the energy or geometry changes after an iteration are less than a threshold value. As the march on the PES occurs only in a downhill direction, only the minimum located in the valley containing the starting geometry will be found; minima located in nearby potential wells (however deep) will not be reached, since this would require the overcoming of an energy barrier (however small).

For finding other minima, a new reasonable starting geometry has to be built before repeating the energy minimisation procedure. Several simulation procedures may help to drive the search towards specific morphologies or low energy regions. For instance, in a grid scan conformational search, the PES is scanned systematically by modifying selected torsion angles over a grid of equally spaced values.

A.3 Molecular dynamics methods. Molecular dynamics methods (MD) calculate the time-dependent behaviour of a molecular system. The starting point is Newton's equation of motion. The force is expressed here as the gradient of the potential energy E simulated by the force-field. Integrating these equations provides the positions, velocities, and accelerations of the atoms as they vary with time; this collection of data constitutes the trajectory, which is a source of information at the microscopic level, from which macroscopic observables (internal energy, pressure...) can be extracted. The initial positions usually correspond to an energy minimum that has been obtained by MM, while the initial velocities are often chosen from a Maxwell–Boltzmann distribution reflecting the temperature at which the simulation is performed. The velocities vary during the simulation, as kinetic energy is changed into potential energy and *vice versa*, and temperature also changes. Hence, different temperature control methods periodically adjust the velocities to maintain the temperature, while reproducing the correct statistical ensemble (NVE, *i.e.*, constant number of particles, volume and energy is called the microcanonical ensemble; NVT, the canonical ensemble; NPT, the isobaric–isothermal ensemble).

The integration of Newton's laws of motion is solved numerically on the basis of the finite-difference method. The positions, velocities, and accelerations are determined at a time $t + \Delta t$ from their values at time t. Ideally, the time step should be large, in order to generate as much trajectory time as possible for a given computational effort, but it must also be shorter than the typical time for the fastest atomic movements. Typically, a time step of 10^{-15} s is chosen, *i.e.*, ten times shorter than a C–H vibration. With such a small time step, MD simulations can be very time consuming and computationally expensive, depending on the time scale of the dynamic process investigated. Among the fastest processes are the local motions (0.01 to 5 Å, 10^{-15} to 10^{-1} s) such as atomic fluctuations, the motion of short molecular segments and loop motions in proteins. At longer time scale, there are the rigid-body motions (1 to 10 Å, 10^{-9} to 1 s), *i.e.*, the motion of molecular parts that are locally organised, such as the helices and domains in proteins. Finally, the large-scale motions (>5 Å, 10^{-7} to 10^{4} s), for instance protein folding or unfolding processes, the dissociation/association of molecular complexes, or the helix–coil transitions, are the slowest and are still out of reach of atomistic MD simulations.

B Density functional theory methods

When the electronic properties of a material have to be studied, the force-field techniques are inappropriate and must be replaced by quantum-mechanical methods. Among them, the DFT methods are very popular as they are less computationally intensive than other *ab initio* methods with similar accuracy. DFT is most useful for studying electronic properties (namely the density of electronic states), and is also particularly appropriate for describing chemisorption phenomena (force-field techniques are unable to treat the building and breaking of bonds occurring during chemisorption).

The central concept of DFT is that the *electronic* energy of a system can be determined from the electron density $\rho(r)$ rather than from the wavefunction, through the following relation:

$$E[\rho(r)] = \int \rho(r) v_{\text{ext}}(r) + F_{\text{HK}}[r]$$

$v_{\text{ext}}(r)$ is the external potential generated by the nuclear configuration and $F_{\text{HK}}[r]$ is a universal functional, which is not known exactly and is not associated to any external potential. To define a practical functional, Kohn and Sham described the electronic density in terms of mono-electronic molecular orbitals $\psi_i(r)$:

$$\rho(r) = \sum_{i=1}^{\text{occ}} |\psi_i(r)|^2$$

The total electronic energy of the system is expressed as the energy of a system of non-interacting electrons plus a new energy term E_{xc}, called exchange–correlation energy:

$$E[\rho(r)] = \sum_{i}^{\text{occ}} \int \psi_i^*(r) \left(-\frac{\nabla^2}{2}\right) \psi_i(r)\, \mathrm{d}r + \int v_{\text{ext}}(r)\rho(r)\, \mathrm{d}r + \frac{1}{2} \iint \frac{\rho(r)\rho(r')}{|r - r'|}\, \mathrm{d}r\mathrm{d}r' + E_{\text{xc}}[\rho(r)]$$

Approximations are required in order to compute the exchange–correlation energy. The most common one is the so-called local density approximation (LDA). In this case the exchange correlation term E_{xc} is calculated from the exchange–correlation energy for a homogeneous gas of electrons having a density, ρ, equal to the local density $\rho(r)$. The LDA approximation yields reliable molecular geometries and vibrational frequencies, but overestimates the bond energies. To overcome this problem, the exchange–correlation term can be decomposed in separate exchange and correlation contributions. This allows combining the advantages of Hartree–Fock methods (which account for the exact exchange) and DFT methods (which include electron correlation). This combined approach relies on hybrid functionals: the exchange is calculated in part with Hartree–Fock and in part with DFT and the correlation is calculated with DFT.

Geometry optimisation algorithms can also be coupled to DFT calculations in order to obtain the most stable structure for the system under study. Because DFT describes the electron density, it can intrinsically account for changes due for instance to strong, chemical interactions between a molecule and a metal surface.

From the modelling point of view, a molecular layer on a surface is a quasi-infinite two-dimensional system. To treat it computationally, two approaches are possible:

(i) one can consider that the adsorbed layer is a perfectly regular 2D system for which a structural unit cell can be defined. Periodic boundary conditions (PBC) can then be applied, both at the DFT and force-field levels; the calculations then deal only with one elementary cell surrounded by equivalent cells, which strongly reduces the complexity of the problem and bypasses finite size effects. In order to define the unit cell, this approach requires that the adsorbate and the surface are commensurate, which is always the case for chemisorbed systems, but may not be the case for physisorbed systems.

(ii) a fragment can be 'carved off' the system and the calculations can be carried out on that fragment. In this approach, the atoms and molecules in the periphery of the fragment are not representative of the actual situation because they miss neighbouring sites; this is called the 'edge effect'. For the results to be relevant, the fragment should therefore be large enough so that its central part can be considered as unaffected by the edges. Because no unit cell is defined, the advantages of this approach are that the commensurability problem mentioned above does not exist and that specific situations (*e.g.*, the presence of defects) can be taken into account.

Modelling of chiral molecular monolayers

A Physisorbed systems

In this section, we will present a few case studies to illustrate how a force-field modelling approach can be used not only to support experimental results, but also to develop and propose models to explain the expression of chirality from the molecular to the global scale in monolayers of physisorbed molecules, be they chiral or achiral.

A.1 Chiral assembly of chiral molecules. A quite relevant example for the chiral assembly of chiral molecules is the monolayer self-assembly on graphite of the chiral mesogen (*R*)- or (*S*)-[4′-(1-methylheptyloxy)-3′-nitrobiphenyl-4-yl] 4-(*trans*-5-decenyloxy)benzoate (1-MHNBDB) (Fig. 2). STM images show the formation of a crystalline monolayer with packing chirality in two dimensions.[10] The presence of chirality is detected by the fact that the molecular orientation in the layer is systematically tilted with respect to one reference direction of the substrate lattice. The data also show that the tilting is reversed when switching the molecular chirality, *i.e.*, clockwise (CW) and counterclockwise (CCW) for (*R*)- and (*S*)-1-MHNBDB, respectively. MD simulations were then used to investigate the mechanism of chirality induction from the molecular to the supramolecular level.[11] The graphite surface is modelled by a single square graphene sheet in a 'frozen' geometry (*i.e.*, the surface atoms are kept fixed); this is commonly done for the sake of modelling efficiency and relies on the assumption that physisorption, in contrast to chemisorption, does not strongly affect the structure of the surface. All the simulations were conducted in ambient conditions, *i.e.*, at 300 K.

At first, the role of the stereogenic center in the presence of the surface is assessed, by studying the stability of domains of (*R*)- and (*S*)-1-MHNBDB with the same initial packing pattern. The results show that the initial structure of the well-ordered domain is rapidly lost in the case of (*R*)-1-MHNBDB, while it is maintained in the case of (*S*)-1-MHNBDB. This is due to the relative orientation of the methyl group attached to the stereogenic center of the molecules: the C*–CH_3 bond is directed towards the graphite surface in the initial (*R*)-1-MHNBDB assembly, and away from the surface in the (*S*)-1-MHNBDB assembly. In the former system, the time-dependent evolution of the orientation of the C*–CH_3 bonds with respect to the surface shows that a major reorientation occurs around the stereogenic center, with the C*–CH_3 bonds tending to point upwards; such large conformational modification destroys the order present in the initial structure. Those

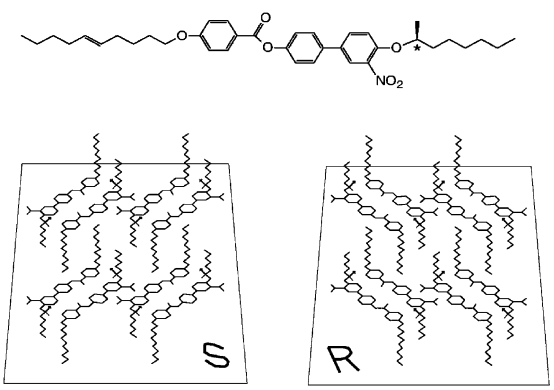


Fig. 2 Chemical structure of 1-MHNBDB (here the *S* enantiomer). Simulated molecular packing of the *S* (left) and *R* (right) enantiomers, with the nitro groups on adjacent molecules close to each other and the methyl group of the stereogenic centers pointing upwards. These structures show opposite tilting in the orientation of the layer (adapted from M. Yoneya *et al.*, *J. Chem. Phys.*, 2001, **114**, 9532, with permission of the American Institute of Physics).

simulations are important to clarify the role of the surface in the adsorption behaviour of the molecules.

MD simulations have also been used to shed light on the origin of the rotation (tilt direction) of the monolayers. This tilt appears to be dependent on the relative positions of the nitro groups on adjacent molecules. This conclusion has been reached by comparing the self-assembly of two different models, consisting of molecular dimers that are the elementary structural units for the monolayer. In the first type of dimer (not shown here), the nitro groups of adjacent molecules are far apart; no clear tilting is observed and thus it is impossible to reproduce the CW or CCW orientation of the monolayer. In the second model, the nitro groups are close to each other (as represented in Fig. 2) and their steric hindrance and electrostatic interaction lead to a molecular organisation that produces a well-defined tilting in the monolayer orientation. So, the joint effect of the breaking of: (i) the monolayer up–down symmetry due to the orientation of the methyl group on the stereogenic center; and (ii) the tilt-direction symmetry due to the interaction of the nitro groups explains the one-to-one correspondence between the absolute molecular chirality (*R* or *S*) and the monolayer 2D chirality (CW or CCW tilt direction) observed with STM. In the proposed model, the coupling between the two origins of symmetry breaking is defined by the geometrical conformation of the molecule. It must be noted that such MD simulations can also be used to go beyond the interpretation of experimental data, in order to predict the modifications in the layer chirality upon variations in the molecular structure, *e.g.*, when moving the stereogenic center from one carbon to the next along the alkyl chain.

Along the same line, we recently modelled the self-assembly of an enantiopure (*R*,*R*,*R*,*R*) functionalised tetraphenyl porphyrin at the interface between graphite and 1-heptanol.[12] STM images show self-assembly over large domains, forming a layer that is globally chiral (in other words, all domains show the same, non-zero tilt angle, $+13 \pm 2^{\circ}$, with respect to the reference direction of the substrate). Again, the aim of the modelling work was to understand the transfer of chirality from the molecule to the surface. Because the molecular structure is quite complex, we chose a stepwise approach, starting with an MM/MD analysis of the conformation of a single molecule adsorbed on the surface (two sheets of graphite without any solvent). This conformational study allowed us to identifying the most stable situation for the adsorbed molecule, with a detailed description of key aspects, such as the relative position and orientation of the phenyl, the position of the methyl groups attached to the stereogenic centers, and the orientation of the amide group with respect to the surface. The resulting conformers were subsequently used to build 2D assemblies.

As the starting situation, we built an eight-molecule assembly in a periodic cell matching the packing density observed with STM. Upon MD simulation, we found 2D lattice parameters ($a = 1.92 \pm 0.12$ nm, $b = 4.20 \pm 0.14$ nm, and $\gamma = 87.4 \pm 4.7^{\circ}$) in good agreement with the STM values ($a = 1.9 \pm 0.1$ nm, $b = 4.0 \pm 0.1$ nm, and $\gamma = 80 \pm 2^{\circ}$). However, at that stage, no relevant information can be obtained on the tilting angle between the molecular orientation and the substrate lattice. This is an intrinsic drawback of simulations done under periodic boundary conditions (PBC): because the layer and the substrate lattice are part of the same periodic cell, their relative orientation is constrained, and subtle effects like the tilting we aim at understanding are suppressed. To solve this problem, it is necessary to lift the periodic boundary conditions and consider a large molecular cluster on the surface. Here we built a sixteen-molecule assembly on a large slab of graphite (with the molecular packing obtained from the PBC simulation), and then optimised the structure with a MM/MD run. Except for slight fluctuations at the borders due to open boundary conditions, these calculations yield similar molecule–molecule relative arrangements. Yet, as the registry between the monolayer and the substrate is no longer enforced, the porphyrin monolayer adopts a preferred orientation on the graphite: the porphyrin molecules form rows that are tilted by $+12.2 \pm 0.4^{\circ}$ with respect to the graphite axes, in excellent agreement, both in term of sign and in term of absolute value, with the deviation observed by STM (Fig. 3a).

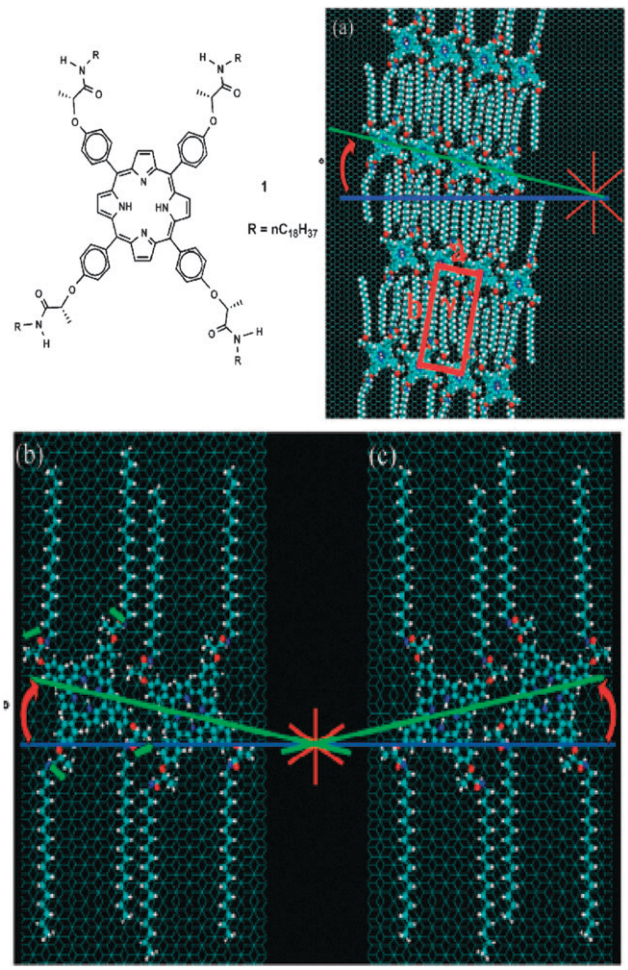


Fig. 3 Molecular structure of the chiral amide-substituted tetraphenyl porphyrin. (a) MD-simulated structure of a sixteen-molecule cluster of the *R*,*R*,*R*,*R* molecule on a graphite surface, showing a tilting angle of $+12^{\circ}$ between the orientation of the molecular row (green line) and the reference axis of the substrate (blue) line. (b, c) Comparison of assemblies of *R*,*R*,*R*,*R* (left) and *S*,*S*,*S*,*S* (right) enantiomers (from M. Linares *et al.*, *Langmuir* 2008, **24**, 9566, with permission of the American Chemical Society).

From the detailed analysis of that structure, one can understand the origin of the tilt: the methyl groups attached to the stereogenic centers are exclusively pointing counterclockwise with respect to the porphyrin core (see the four small green pointers around the molecule on the left of Fig. 3b). Once a molecule is lying on the surface, its neighbour has to shift in the direction perpendicular to the reference axis (the blue line), so that one of its methyl groups can accommodate in the empty space along the core of the first molecule. This shift induces a deviation of the molecular row with respect to the substrate lattice and the direction of the deviation (hence the sign of the deviation) is unequivocally determined by the configuration of the stereogenic center. Consistently, for the enantiomer with the (*S*,*S*,*S*,*S*) configuration, a deviation in the opposite direction is found from the model (Fig. 3c).

Finally, to further improve the quality of the model and check the stability of the monolayer structure, we added a thick layer of solvent molecules on top of the porphyrin assembly. The 1-heptanol molecules are found to interact specifically with the amide groups, *via* hydrogen bonding, thanks to the favourable orientation of the C═O bonds away from the surface. These interactions do not disturb significantly the molecular organisation and further stabilise the formation of the monolayer.

A.2 Chiral assembly of achiral molecules. As mentioned in the introduction, chiral self-assembled monolayers can be formed by molecules that are not chiral themselves. An example of such situation has been proposed recently by Katsonis *et al*. for diarylethene compounds.[13] In their open form, diarylethene molecules are free to adopt a number of energetically similar conformations, among which are helical structures. Depending on the sign of the helix, the conformers are denoted *P* and *M* (Fig. 4). In solution at room temperature there can be interchange between *P* and *M* conformers, the two conformers are equivalent and the system is not chiral. Interestingly, when those molecules are adsorbed on a surface from the solution, they are locked in their *P* or *M* conformation, because the surface suppresses the *P*–*M* rotational interconversion and helical chirality emerges.

STM images reveal the formation of a well-ordered monolayer containing two types of domains that are mirror image of each other and feature opposite orientation with respect to the graphite lattice (Fig. 4a). In each of these domains, the elementary structural units are composed of pairs of molecules (Fig. 4b) whose conformation, *i.e*., *P* and *M*, cannot be determined from the measurements. To understand how the chirality that appears in the molecule upon adsorption is transferred to the self-assembled monolayer, it is important to have a detailed model for the intermolecular interactions acting within the molecular dimers and between dimers. The proposed model for the formation of the dimers is based on molecular shape recognition and locking of helicity (Fig. 4c). Since the molecular chirality arises when molecules are adsorbed, two different types of dimers can form at the surface: the first one is composed by molecules having the same helicity, *i.e*., *PP* or *MM*, while the second one is formed by molecules with opposite helicity, *i.e*., *PM* or *MP*. The main difference is that while the *PP* (or *MM*) dimer is

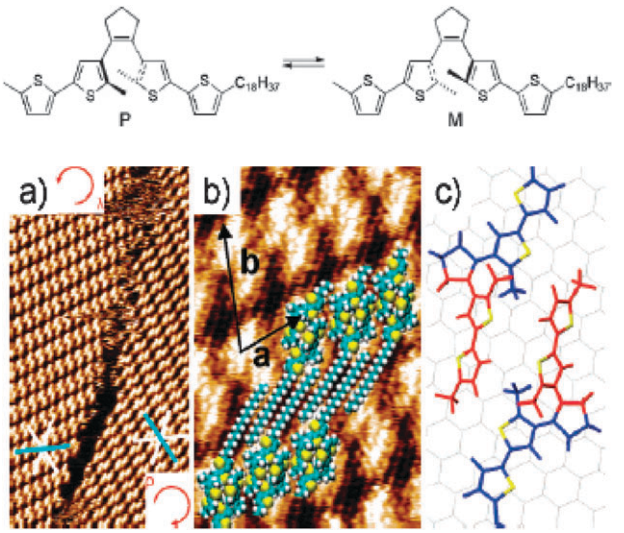


Fig. 4 Molecular structure of the diarylethene compound under study. (a) Enantiomorphic domains in a monolayer on the graphite surface; the orientations of the main crystallographic axes of graphite are schematically represented by white lines. The relevant reference axis for the respective domains is indicated in blue. (b) High-resolution image and proposed packing model obtained by force-field calculations. (c) A dimer adsorbed on graphite; the blue parts of the molecules are those directly in contact with the surface, the red ones are not directly adsorbed (From N. Katsonis *et al*., *J. Am. Chem. Soc*., 2008, **130**, 386, with permission of the American Chemical Society).

chiral, the *PM* (or *MP*) is not; we will refer to the first type as chiral dimer, and to the second as racemic dimer. Both dimers are compatible, in size and shape, with the STM results, and MD calculations are crucial to investigate the stability of those dimers.

MD simulations for chiral and racemic dimers on the surface, both in 'wet' and 'dry' conditions (*i.e*., with or without explicit solvent molecules in the MD model), show that the racemic dimer is not stable and rapidly dissociates, while the chiral dimer remains stable. This different stability suggests that only the chiral dimers can form the monolayer domains. This hypothesis has been confirmed by comparing the geometry of the modelled domains and that observed experimentally. A good match between theory and experiment is only found for chiral dimers. This is a further strong indication that the layers are formed of diarylethene molecular dimers in the *PP* (and *MM*) configuration, giving rise to the enantiomorphic domains.

In this case, as well as in other similar cases,[14] the chiral assembly forms at the surface thanks to specific interactions between achiral molecules. Another possibility can occur, in which it is a specific interaction with the surface that induces chirality in the self-assembly monolayer. For example, using a combination of MM and MD simulations, thiophene–fluorenone conjugated oligomers[15] have been shown to assemble in a chiral way because of a specific adsorption of the thiophene ring on the graphite substrate.

A.3 Self-assembly of racemic mixtures: enantiopure or enantio-mixed domains? Ilan and coworkers[16] have modelled the self-assembling properties of the chiral (*R*)/(*S*)-2-bromohexadecanoic

acid, $CH_3(CH_2)_{13}CH(Br)COOH$, on graphite surface. The basis for that work is the STM study of the formation of monolayers from mixtures of (*R*) and (*S*)-2-bromohexadecanoic acid with hexadecanoic acid at the solvent–substrate interface. The calculations are aimed at assessing the relative stability of the enantiopure (*i.e.*, the enantiomers assemble in separate domains) and enantio-mixed (*i.e.*, the enantiomers mix at the molecular scale) layers for the racemic mixture of 2-bromohexadecanoic acid on graphite. The results show that the orientation of the bromine atom of the stereogenic center with respect to the graphite surface plays a very important role. The notations *R*(u)/*R*(d) and *S*(u)/*S*(d) are used to represent the *R* or *S* isomers with the C–Br bond either pointing upward (u) or downward (d) with respect to the substrate surface. The lower potential energy of the enantio-mixed configurations strongly suggests that at the solid–vacuum interface, the self-assembled domains of the racemic mixture of (*R*)/(*S*)-2-bromohexadecanoic would not be enantiopure domains, but rather *R*(u)/*S*(d) or *R*(d)/*S*(u) enantio-mixed domains. It must be noted however that the solvent is expected to play a significant role here (in contrast to what described in subsection A.1), because of better interactions with the bromine atoms pointing upwards.

B Chemisorbed systems

B.1 Chiral assembly of achiral molecules. A typical example of the formation of chiral domains by chemisorption of achiral molecules is 1,2,4-benzenetricarboxylic acid on Cu(100).[17] The formation of monolayers of that compound has been studied with a combination of spectroscopy (XPS and NEXAFS), scanning probe microscopy, and DFT calculations. The DFT calculations provide a detailed description of the molecule–surface interactions and, more importantly in this case, of the molecule–molecule interactions, which are responsible for the formation of chiral domains. Upon adsorption, deprotonation occurs at one carboxylic group and a copper–carboxylate bond is formed (site a in Fig. 5a). The two remaining carboxylic acid moieties (b, c: in *para* positions with respect to each other) are then available to form an intermolecular network of hydrogen bonds (Fig. 5c). Depending on the global orientation of the molecule on the copper surface, two types of domains form that are mirror images of each other (Fig. 5b).

B.2 Chiral assembly of chiral molecules. Tartaric acid adsorbed on the Cu(110) surface provides a nice illustration of the use of modelling to understand the formation of chiral surfaces from chemisorbed chiral molecules. In 2000, Raval and co-workers initially reported on the formation of long-range self-assemblies of enantiomerically pure (*R*,*R*) and (*S*,*S*) tartaric acid molecules.[18] After deprotonation, the bitartrate form is chemically bonded to the surface, each oxygen atom being linked to a copper atom. The STM images show groups of three aligned bitartrate molecules, which pack parallel to each other and form long chains (Fig. 6). Those rows constitute chiral domains along the $\langle 1\ \bar{1}\ 4 \rangle$ direction; they are separated by channels in which the metal atoms are not coordinated by the tartaric acid molecules and are thus still available as catalytic sites. Because the groups of tartaric acid

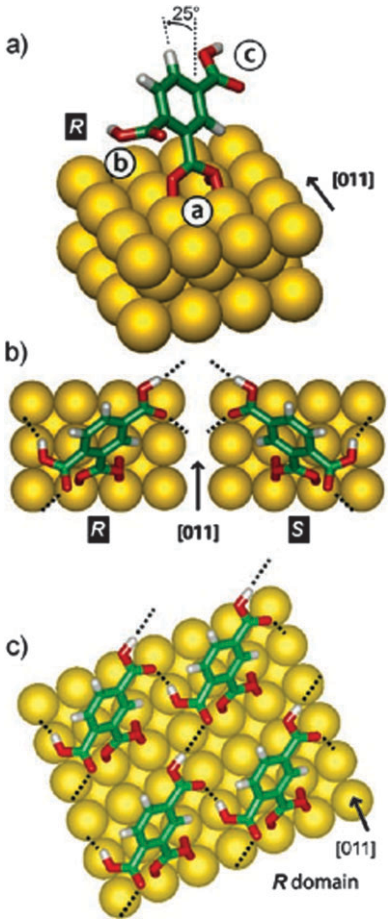


Fig. 5 DFT-calculated structure of 1,2,4-benzenetricarboxylic acid on Cu(100). (a) Formation of a carboxylate–Cu bond. (b) Representation of the two possible molecular orientations, corresponding to enantiomeric domains. (c) Formation of a 2D H-bond network (from A. Dmitriev *et al.*, *ChemPhysChem*, 2006, **7**, 2197, with permission of Wiley Interscience).

molecules are chiral, those empty sites also possess chirality, so that enantioselective catalysis becomes possible. The specific arrangement of the (*R*,*R*) and (*S*,*S*)-tartaric acid molecules was thought to be due to the difference in the spatial orientation of their OH groups and it was assumed that this spatial orientation leads to intermolecular hydrogen-bonding interactions networks, not only along a row but also in between the three rows.

However, in 2001, DFT calculations performed by Barbosa and Sautet[19] showed that the specific orientation of the (*R*,*R*) and (*S*,*S*)-bitartrate moieties is due to a specific adsorption on the surface, rather than to the formation of intermolecular hydrogen bonds. For the sake of simplicity, the isomers were optimised on the same type of surface domain (the type corresponding to the (*R*,*R*) assembly). The chemisorption energy was calculated to be larger for the (*R*,*R*)-isomer than for the (*S*,*S*)-isomer by 10 kJ mol^{-1}, which is consistent with the experimental observation that it is the (*R*,*R*)-isomer that assembles on that type of domain. Because of such energy difference, only a given isomer is expected to assemble on a given type of domain and the chemisorption of the racemic

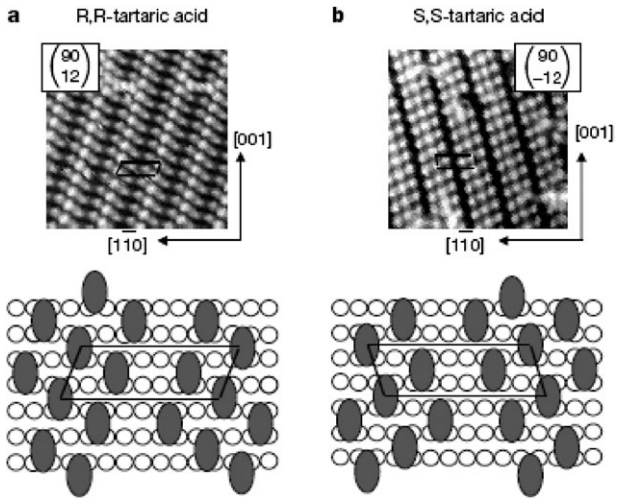


Fig. 6 Top: STM images of (*R*,*R*) (left) and (*S*,*S*)-tartaric acid on Cu(100) showing mirror image patterns. Bottom: sketch of the organisation of the molecules with respect to the metal substrate (from M. Ortega Lorenzo *et al*., *Nature* 2000, **404**, 376, with permission of Nature Publishing Group).

mixtures must give rise to the formation of two types of chiral domains. Moreover, a detailed analysis of the geometries shows the formation of *intramolecular* hydrogen bonds between the hydroxyl and the carboxyl groups, rather than *intermolecular* H-bonds. These intramolecular hydrogen bonds induce distortions in the molecule, which are different for the different isomers on a given domain, and explain the calculated stability difference.

At that stage, two points remained unexplained: why are the molecules assembled in groups of three? What is the origin of the empty channel between the rows? In 2004, a theoretical study addressed those questions by a combination of DFT calculations and kinetic Monte Carlo simulations.[20] Those calculations showed that the co-adsorption of more than three bitartrate molecules next to each other causes a surface stress. Consequently a decrease in binding energy by about 5 kJ mol^{-1} (*i.e*., a destabilisation) is observed. To reduce that stress, it is preferable to leave an empty channel, along the $\langle 1\ \bar{1}\ 4\rangle$ direction, between the groups of bitartrate molecules. The peculiar surface pattern formed upon chemisorption of tartaric acid on the Cu(110) surface is therefore fully understood, based on those calculations and comparison with the experimental data.

B.3 Chemisorption of racemic mixtures: enantiopure or enantio-mixed domains? Rankin and Sholl have modelled with a DFT approach the adsorption of enantiopure and racemic alanine ($NH_2CH_3CHCOOH$) on Cu(110).[21] To understand the details of the molecule–surface bonding, a simple model containing a single alanine molecule was considered. It turned out that the result of the geometry optimisation process was strongly dependent on the starting point. A systematic study combining MD and DFT, in order to explore fully the potential energy surface, would be cumbersome. Consequently, the approach that was used to acquire a reliable picture of the adsorbed geometry was to try numerous different binding configurations, to optimise each of them, and to identify the one with the lowest energy.[22] This tedious procedure leads to the following binding scheme: as in the tartaric acid, the binding of the alanine molecule occurs after deprotonation of the carboxylic group. In addition, the lone pair of the amino group also binds to the surface. By comparison with the achiral equivalent molecule, glycine (NH_2CH_2COOH), the authors show that the introduction of the stereogenic center does not influence the binding geometry of the molecule, because the methyl group is pointing away from the surface. When considering the adsorption of a mixture of the *R* and *S* enantiomers of alanine, the calculations indicate that there is only a small energy difference between enantiopure and enantio-mixed domains on the copper surface. Consequently it was concluded that if a racemic mixture of alanine is deposited on Cu(110), large chiral domains are unlikely to form, and the surface would remain achiral even on the local scale.

Concluding remarks

As illustrated throughout this review, the detailed understanding of the expression of chirality in molecular layers adsorbed on surfaces most often relies on a proper combination of experimental data (in most cases, STM results) and modelling, with either a quantum-chemical DFT approach or a force-field approach. While both theoretical approaches can provide important physico-chemical information, their domains of application tended to be mutually exclusive: DFT is needed for the description of chemical bonding, in particular for chemisorbed layers of metal surfaces, but is computationally intense and usually fails in reproducing weak intermolecular interactions. In contrast, the most common force-field techniques properly describe physisorbed systems and can be applied to large systems, but are not appropriate for processes occurring at metal surfaces.

Recent trends in the modelling of molecular adsorbates are clearly directed towards lifting this dichotomy: on one hand, the quantum-chemical description of intermolecular interactions is constantly being improved, as recently reviewed,[23] in particular by the development of specifically-designed DFT techniques. One such scheme consists in adding to the density-functional a semi-empirical dispersion term (DFT-D), *i.e*., a long-range attractive pair-potential (proportional to R^{-6}) that is shut off at short range.[24,25] This has recently led to an accurate description of the adsorption of DNA elementary segments on the graphite surface[26] and clearly opens the way to studying the type of physisorbed systems reported in this paper.

On the other hand, force-field techniques are being developed to provide accurate descriptions of molecular adsorbates on metal surfaces. This implies the design of specific force-fields that can take into account the polarisability of the metal surface and changes in the electron density upon adsorption.[27] Recently, this approach has been successfully applied to the modelling of the structure and dynamics of functionals thiols in self-assembled monolayers[28,29] and the mechano-chemistry of a polymer on the gold surface.[30]

Finally, other important methodological developments, based on the 'coarse-grain' approach, in which molecules are

represented as simple objects interacting with each other and with the surface,[31] are expected to further improve the modelling of chiral molecular adlayers towards larger systems and longer time scales.

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References

1 J. D. Orvath and A. J. Gellmann, *Top. Catal*., 2003, **25**, 9.
2 S. M. Barlow and R. Raval, *Surf. Sci. Rep*., 2003, **50**, 201.
3 R. Raval, *CATTECH*, 2001, **5**, 12.
4 M. Matsunaga, T. Nakanishi, T. Asahi and T. Osaka, *Chirality*, 2007, **19**, 295.
5 V. J. Mayani, S. H. R. Abdi, R. I. Kureshy, N. H. Khan, S. Agrawal and R. V. Jasra, *J. Chromatogr., A*, 2008, **1191**, 233.
6 O. K. Kim, L. S. Choi, H. Y. Zhang, X. H. He and Y. H. Shih, *Thin Solid Films*, 1998, **327**, 172.
7 S. De Feyter and F. C. De Schryver, *Chem. Soc. Rev*., 2003, **32**, 139.
8 S. De Feyter and F. C. De Schryver, *J. Phys. Chem. B*, 2005, **109**, 4290.
9 K. H. Ernst, *Top. Curr. Chem*., 2006, **265**, 209.
10 F. Stevens, D. J. Dyer and D. M. Walba, *Angew. Chem., Int. Ed. Engl*., 1996, **35**, 900.
11 M. Yoneya and H. Yokoyama, *J. Chem. Phys*., 2001, **114**, 9532.
12 M. Linares, P. Iavicoli, K. Psychogyiopoulou, D. Beljonne, S. De Feyter, D. B. Amabilino and R. Lazzaroni, *Langmuir*, 2008, **24**, 9566.
13 N. Katsonis, A. Minoia, T. Kudernac, T. Mutai, H. Xu, H. Uji-i, R. Lazzaroni, S. De Feyter and B. L. Feringa, *J. Am. Chem. Soc*., 2008, **130**, 386.
14 S. Lei, M. Surin, K. Tahara, J. Adisoejoso, R. Lazzaroni, Y. Tobe and S. De Feyter, *Nano Lett*., 2008, **8**, 2541.
15 M. Linares, L. Scifo, R. Demadrille, P. Brocorens, D. Beljonne, R. Lazzaroni and B. Grevin, *J. Phys. Chem. C*, 2008, **112**, 6850.
16 B. Ilan, B. J. Berne and G. Flynn, *J. Phys. Chem. C*, 2007, **111**, 18243.
17 A. Dmitriev, H. Spillmann, S. Stepanow, T. Strunskus, C. Wöll, A. P. Seitsonen, M. Lingenfelder, N. Lin, J. V. Barth and K. Kern, *ChemPhysChem*, 2006, **7**, 2197.
18 M. Ortega Lorenzo, C. J. Baddeley, C. Muryn and R. Raval, *Nature*, 2000, **404**, 376.
19 L. A. M. M. Barbosa and P. Sautet, *J. Am. Chem. Soc*., 2001, **123**, 6639.
20 C. G. M. Hermse, A. P. van Bavel, A. P. J. Jansen, L. A. M. M. Barbosa, P. Sautet and R. A. van Santen, *J. Phys. Chem. B*, 2004, **108**, 11035.
21 R. B. Rankin and D. S. Sholl, *Surf. Sci*., 2005, **574**, L1.
22 R. B. Rankin and D. S. Sholl, *Surf. Sci*., 2004, **548**, 301.
23 See special issue of *Phys. Chem. Chem. Phys*., 2008, **10**, on the theoretical description of stacking interactions and references therein.
24 C. Morgado, M. A. Vincent, I. H. Hillier and X. Shan, *Phys. Chem. Chem. Phys*., 2007, **9**, 448.
25 M. Pavone, N. Rega and V. Barone, *Chem. Phys. Lett*., 2008, **452**, 333.
26 J. Antony and S. Grimme, *Phys. Chem. Chem. Phys*., 2008, **10**, 2722.
27 R. Baxter, G. Teobaldi and F. Zerbetto, *Langmuir*, 2003, **19**, 7335.
28 S. Rapino and F. Zerbetto, *Small*, 2007, **3**, 386.
29 S. Alkis, P. Jiang, L. L. Wang, A. E. Roitberg, H. P. Cheng and J. L. Krause, *J. Phys. Chem. C*, 2007, **111**, 14743.
30 A. S. Duwez, S. Cuenot, C. Jérôme, S. Gabriel, R. Jérôme, S. Rapino and F. Zerbetto, *Nat. Nanotechnol*., 2006, **1**, 122.
31 G. Srinivas, S. O. Nielsen, P. B. Moore and M. L. Klein, *J. Am. Chem. Soc*., 2006, **128**, 848.

