

## Stirring competes with chemical induction in chiral selection of Langmuir monolayer domains

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**Abstract.** Chirality, the absence of mirror symmetry, can be equally invoked in relation to physical forces and chemical induction processes, yet a competition between these two types of influences is rarely reported. Here, we employ Langmuir monolayers of azobenzene surfactants as a prototypical self-assembled two-dimensional system in which chiral selection is controlled by the combined independent action of a chiral dopant and vortical stirring. The two effects can be arbitrarily coupled, either constructively or destructively, leading to a situation of perfect compensation. The induced enantiomorphous excess is measured in terms of the statistical imbalance of an ensemble of sub-millimeter monolayer domains, where achiral molecules self-assemble with a well-defined orientational chirality, which is unambiguously resolved using Brewster angle microscopy.

### 1 Introduction

Besides their interest as biomimetic systems, Langmuir monolayers are interesting model systems where to study ordering in restricted dimensions [1]. The easy manipulation and monitoring of molecular ordering in monolayers provides significant advantages with respect to bulk system counterparts. One of the relevant problems that can be addressed is the control of chirality in supramolecular assemblies.

In soft matter-oriented research, control of imparted chirality is particularly valuable, both from a fundamental as well as an applied perspective [2]. A chiral modifier, chemically compatible with the host system, is often employed to imprint an achiral mesophase with a well-defined handedness [3]. For instance, using a chiral mesogenic molecule as a dopant, a nematic liquid crystal phase will convert into a chiral nematic or cholesteric phase, in which the average molecular orientation develops a spatially organized helical arrangement, with a characteristic pitch and twist sign, which depend on subtle noncovalent interactions between the modifier and the host system [4]. For a given dopant concentration, this effect is maximized when only one of the enantiomers is present, and it vanishes when the dopant consists of a racemic mixture. In Langmuir monolayers, it is well-known that the use of enantiomeric chiral surfactants typically leads to the formation of ordered domains with enantiomorphous (mirror-symmetric) chiral shapes [5]. It has also been observed that achiral

surfactants can lead to the formation of ordered domains of achiral shapes but with chiral inner textures of molecular order [6,7]. In these cases, symmetry conservation demands that domains with enantiomorphous textures be equally probable.

On the other hand, a chiral imbalance can be imparted to certain systems composed of achiral molecules or to racemic mixtures of two enantiomers by means of a suitable macroscopic chiral force, such as vortical shearing. For instance, stirring may lead to sign selection, during the formation of three-dimensional supramolecular aggregates [8]. Recently, we have demonstrated that chiral selection by vortical flow is also possible in Langmuir monolayers [9]. In spite of these results, to date it has not been possible to clearly observe chiral selection by a signed chiral force being exerted on an intrinsically chiral chemical system, presumably because of the delicate balance of cohesive forces in supramolecular chemistry.

In this contribution, we present the realization of the unambiguous coupling between a signed chiral force (vortex flow) and an intrinsically chiral chemical system during enantioselective control in Langmuir monolayers of an azobenzene derivative. We demonstrate that physical, down-scale, and chemical, up-scale, chiral influences can meet midway and their responses be arbitrarily opposed or enhanced.

## 2 Materials and Methods

### 2.1 Materials

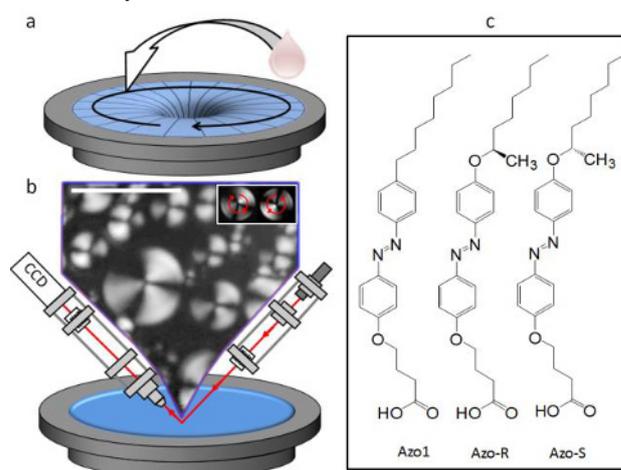
We prepare Langmuir monolayers by spreading a chloroform (Baker, p.a.) solution (1mM) of the surfactant 4-[4-[(4-octylphenyl)azo]-phenoxy] butanoic acid[7] (Azo1) that contains a 6% w/w of the chiral modifier [(S/R)-(+/-)-4-[4-[4-(1-methylheptyloxyphenyl)azo] phenoxy] butanoic acid] (Azo-S, Azo-R), either as pure S/R-enantiomers or as a racemic mixture of the two enantiomers. All surfactants were custom synthesized. See Figure 1 for a sketch of the three molecules. Earlier work with Langmuir monolayers of Azo1 revealed that the *cis* and *trans* isomers of this surfactant phase separate when spread at the air/water interface, resulting in the formation of submillimeter domains featuring orientational chirality in the molecular order (Fig. 1b). The relative composition of *cis* and *trans* isomer can be adjusted by exposing the spreading solution to light of a suitable wavelength.

### 2.2 Experimental apparatus

The experimental setup consists of a thermostatic black Delrin (polyoxymethylene) circular trough (6 cm diameter, 1.7 cm depth) filled with Milli-Q water (Figure 5). Monolayers can either be spread over a quiescent subphase or in the presence of a vortex. In the latter case, prior to monolayer spreading, a steady-state vortex flow is created in the subphase by means of a Reversible Magnetic Stirrer (J.P. Selecta, Spain) with a submerged cylindrical Teflon-coated magnetic bar (8 mm long, 3 mm diameter). The spreading solution is irradiated with UV light for 10 minutes to ensure the maximum presence of the *cis* isomer (97%). Monolayers are subsequently prepared by carefully depositing at the air/water interface one drop (2 $\mu$ l) of the chloroform surfactant solution at the outer part of the vortical funnel when the subphase is stirred at a constant rate  $\Omega$  ( $0 < \Omega < 1600$  rpm). If no vortical flow is applied, the droplet is deposited near the center of the trough. Experiments are conducted at 20°C with a surface pressure below 1 mN m<sup>-1</sup>. Stirring is applied for 35 minutes under room light. These are the optimal experimental conditions that enhance the competition between the stirring and the chiral modifier. Both with and without stirring, spontaneous *cis* to *trans* isomerization leads to the formation of isolated submillimeter elongated *trans*-rich aggregates that coalesce into circular domains with long-range order in the orientation of hydrophobic tails of Azo-1 surfactant molecules.

Monolayer observation is performed by means of a custom-built Brewster angle microscope (BAM) configured with the analyzer set at 60° counterclockwise with respect to the plane of incidence, which contains the y-axis of the images[10]. With this configuration, the orientational handedness of individual circular domains can be unambiguously determined. The microscope is equipped with an XY translation stage to be able to scan the air/water interface. This enables us to obtain data for

an extended region of the monolayer (several square centimeters). For experiments performed in the presence of vortical flow, stirring must be stopped prior to BAM image acquisition, due to the deformation caused on the interface by the vortical funnel.



**Fig. 1** (a) A single drop of chloroform surfactant solution is deposited at the outer edge of the steady-state funnel generated by a rotating magnetic bar, and is left to evolve under constant stirring for a period of time. (b) The resulting distribution of chiral submillimeter circular monolayer domains is analyzed following the arrest of stirring by means of Brewster angle microscopy. The structure of the *trans* isomer of the three azobenzene surfactant molecules is shown in (c).

### 2.3 Data acquisition and analysis

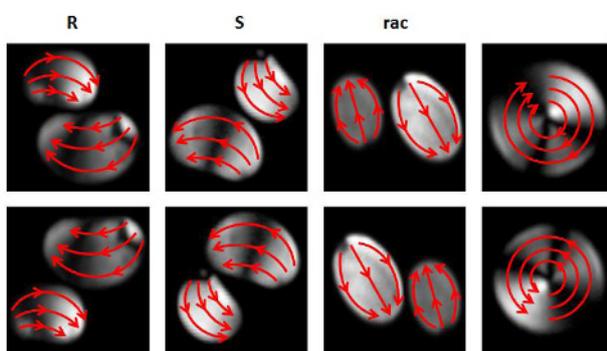
After allowing a set amount of time for self-assembly to take place (35 minutes, see above) we perform a statistical analysis of the population of circular domains of either handedness, which yields the enantiomeric excess parameter. BAM images of the monolayer are acquired during 30 min after stirring is stopped. BAM images are enhanced and analyzed by means of the software ImageJ[11].

## 3 Results and Discussion

### 3.1 Characterization of the chirally resolved Langmuir monolayer

Following previous studies, we prepare Langmuir monolayers of an azobenzene surfactant (Azo1) under conditions that lead to the formation of submillimeter ordered domains. We disperse one drop of the spreading solution with a nearly pure composition of the *cis* isomer, and let the system spontaneously transform into the *trans* isomers at constant temperature and spreading area under room light conditions. Phase separation of the two isomeric forms leads to the formation of a two-dimensional emulsion in which submillimeter circular mesophase disks, rich in the *trans* isomer, are surrounded by an isotropic continuous *cis* phase (Figure 1). After the elapsed stirring time of 35 minutes, roughly half the surface is covered by the *trans*-rich domains. BAM reflectivity patterns inside the disks unambiguously reveal that, on average, molecules are

locally tilted by the same angle along a direction parallel to the domain boundary (bend-like ordering)[7], either clockwise (CW) or counter-clockwise (CCW). This defines the two enantiomorphic configurations of the orientational order that are equally represented in absence of any chiral influence (Figure 1). Uncompensated handedness appears when we add a small amount of a chiral surfactant modifier (Azo-R or Azo-S, see Figure 1) to the Azo1 spreading solution, prior to dispersion. The signature of a chiral dominance manifests itself as a different amount of CW versus CCW bend-like domains. In quantitative terms, such a difference, normalized by the total number of counted domains, defines an enantiomorphic excess of CW domains, which we quantify by defining an enantiomeric excess parameter  $ee_{CW} = \frac{n_{CW} - n_{CCW}}{n_{CW} + n_{CCW}}$ . In our case, 6% of R-enantiomer doping leads to a robust CCW excess,  $ee_{CW} = -0.54 \pm 0.05$ , which is exactly opposite, within experimental error, to the result for the same amount of the S-form.

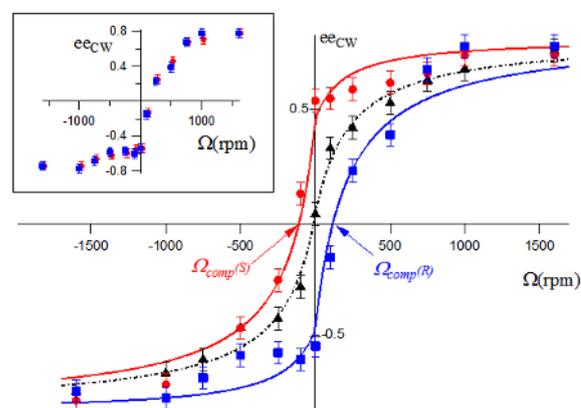


**Fig. 2.** BAM micrographs of primordial aggregates under different dopant composition. Images are  $190 \mu\text{m}$  wide, and include an overlay of the estimated field lines, giving the approximate local in-plane molecular alignment. In the presence of a chiral dopant, self-assembled elongated primordial aggregates feature enantiomorphic configurations with complete resolution for the R (6% by weight, first column) and S (6% by weight, second column) enantiomers. A racemic mixture of dopants leads to the self-assembly of achiral aggregates (third column). For all dopant composition, the spontaneous coalescence of anti-parallel aggregates results in the formation of enantiomorphic circular bend-like domains whose orientational chirality depends only on the handedness of the dimer configuration of the two parent aggregates.

### 3.2 Self-assembly pathway to the formation of chiral domains

Exploration of the early stages of domain formation reveals that *trans* molecules arising from the spontaneous isomerization of the *cis* azobenzene assemble into elongated aggregates in which the molecular field has a dipolar order with elongated (head-tail asymmetric) molecules featuring an average orientation along the longest dimension. Circular bend-like domains arise through the spontaneous coalescence of these aggregates [12]. The shape and inner configuration of these aggregates depend on the enantiomeric excess of chiral dopant: while they are elliptical for a racemic mixture of the chiral dopant, they

acquire a bean-like shape for an imbalance of one of the enantiomers (Figure 2). Line tension at the boundary with the *cis* phase prompts the spontaneous merging of a pair of aggregates with anti-parallel polarity, resulting in the formation of a circular domain whose orientational chirality corresponds to that of the dimer formed by the two parent aggregates. Although circular domains of both chiralities are always formed, doping with opposite enantiomers introduces opposite imbalances in their enantiomorphic excess.

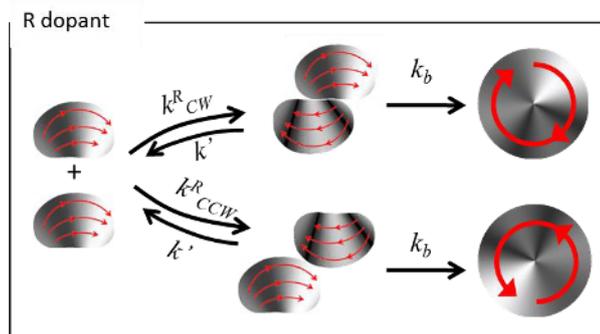


**Fig. 3.** Enantiomorphic excess,  $ee_{CW}$ , quantifying the statistical bias of CW bend-like domains as a function of the vortical stirring rate in the presence of different enantiomeric compositions of the chiral dopant: 6% of S-enantiomer (red circles), 6% of R-enantiomer (blue squares), and racemic mixture (3%+3%) of R and S enantiomers (black triangles). Error bars correspond to 5% of the full-scale value of  $ee_{CW}$ . Solid lines are a fit to the model proposed in the text. In the inset, data for  $ee_{CW}^R(\Omega)$  are plotted along  $-ee_{CW}^S(-\Omega)$ .

### 3.3 Competition of chiral influences

We have shown [9] that vortical shearing can effectively be employed to imbalance the enantiomeric excess of bend-like domains, so that the magnitude and sign of  $ee_{CW}$  change as a function of the signed stirring rate  $\Omega$ . In that work, we argued that surface shearing couples to the spontaneous coalescence of elongated aggregates and introduces a kinetic bias for the formation of bend-like domains of a certain handedness. Given that the presence of chiral dopants and subphase stirring have a similar influence on the chirality of bend-like domains, we proceed to couple the two influences by spreading the doped monolayer while gently stirring the aqueous subphase. Results plotted versus  $\Omega$  (clockwise is arbitrarily taken as positive) are summarized in Figure 3, which unveils the concept of chiral coupling from disparate origins. In particular, the data certify the possibility of exact compensation between a chemical chiral influence and an opposing vortical shear. At equal concentration (6% by weight) of either enantiomer (R or S), the compensation stirring rate exhibits the required symmetry ( $\Omega_{\text{comp}}^{(R)} = 120 \pm 25 \text{ rpm}$ ,  $\Omega_{\text{comp}}^{(S)} = -110 \pm 20 \text{ rpm}$ ), interpolated from the data by using the model detailed below. Finally, the robustness of the

phenomenon is clearly evidenced by the perfectly symmetric racemic data (obtained with the same amount of total doping equally distributed among the R and S forms of the chiral modifier) and by the congruent asymmetry of the data series for the two enantiomers (See inset in Figure 3).



**Fig. 4.** Scheme of the kinetic model for chiral selection in the presence of R dopant. Following *cis-trans* isomerization, antiparallel bean-shaped *trans* aggregates may associate following two distinct parallel pathways, with stirring-dependent rate constants, corresponding to the pair of enantiomorphically different dimer configurations. We propose that the kinetics of formation of the dimers is the rate-limiting step, described by stirring-dependent rate constants.

### 3.4 Kinetic model

Similarly to our earlier proposition that a kinetic bias in the pathway leading to circular domains is introduced by vortical shearing, we propose that the two complementary coalescence events are also kinetically biased due to the asymmetric shape of the parent aggregates (Figure 2). In fact, our experiments indicate that chiral dopants favor the pathway involving dimers of bean-shaped domains that face their convex sides.

We have introduced a mechanism [13] that translates into a chemical-kinetics-like model (Figure 4). The formation of bend-like domains stems from the formation of dimer entities of antiparallel bean-like elongated primordial aggregates, *B*. We denote as  $D_{CW}$  and  $D_{CCW}$  the dimer of each handedness. Let us consider the case of the coupling between vortical flow and doping with the Azo-R enantiomer. An equivalent analysis could be performed with the Azo-S enantiomer. We consider the kinetics of formation of the dimer entities to be described by stirring-dependent rate constants  $k_{CCW}^R(\Omega) = k_1 + k_1^{st}(\Omega)$ , and  $k_{CW}^R(\Omega) = k_2 + k_2^{st}(\Omega)$ . Here,  $k_1^{st}(\Omega)$  and  $k_2^{st}(\Omega)$ , which vanish under quiescent (no flow) conditions, correspond to the hydrodynamic influence in the chiral selection process, and  $k_1 = k_{CCW}^R(0)$  and  $k_2 = k_{CW}^R(0)$  correspond to the chemical influence due to the presence of a chiral dopant. We also include a relaxation and a disaggregation constant, which we consider smaller than the dimer formation constants. By applying the quasi-steady state approximation to the dimer entities, we can express  $ee_{CW}$  as [13]

$$ee_{CW} = \lambda \frac{[D_{CW}] - [D_{CCW}]}{[D_{CW}] + [D_{CCW}]} = \lambda \frac{k_2^{st}(\Omega) - k_1^{st}(\Omega) - (k_1 - k_2)}{k_2^{st}(\Omega) + k_1^{st}(\Omega) + (k_1 + k_2)}$$

In this expression,  $\lambda$  is a parameter,  $0 < \lambda < 1$ , accounting for the loss of circular bend-like domains due to the different processes involved in the evolution of the monolayer, such as the coalescence of CW and CCW domains, the absorption of bend domains by larger non-circular domains, etc. [12].

By selecting a linear, yet asymmetric ansatz for the rate constants,  $k_1^{st}(\Omega) = -\theta(-\Omega)\gamma\Omega$ , and  $k_2^{st}(\Omega) = \theta(\Omega)\gamma\Omega$ , where  $\theta(\Omega)$  is the Heaviside function, the final expression is  $ee_{CW} = \lambda(\Omega - \Omega_{comp}) / (|\Omega| + a)$ , where  $a$  is a fit parameter related to the average rate of the two parallel pathways (Fig. 4). The above expression captures the experimental results reported in Figure 3 [13]. The effect of the dopant is captured by  $\Omega_{comp}$ , which takes opposite values for the two enantiomers.

## 4 Conclusions

In this paper, the principle of chiral superposition from two independent sources has been unambiguously reported, mechanistically interpreted and modelled using Langmuir monolayers. Earlier studies aimed at exploring such superposition had been reported on different soft matter systems, but they all failed to provide clear experimental evidences. The ease of manipulation, control, and characterization of Langmuir monolayers has significantly contributed to our results. We would like to stress the remarkable finding that a three-dimensional physical force (vortical stirring), operating in centimeter-length scales can couple to the chemical effect of a supramolecular level modifier. Our contribution should also be envisaged, upon transference of the monolayer onto a solid support [14], as a new strategy for stereocontrol of chemical reactions and responses at chiral surfaces.

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