

Present State of the Generalized Molecular Asymmetry Model in Liquid Crystal Physics*

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Abstract. The present state of the Generalized Molecular Asymmetry (GMA) model in liquid crystal physics is reviewed. Emphasis is made upon the recent application of this model for description of lyotropic and biological liquid crystal structures. The capacity of the model to provide a general framework for all types of liquid crystals is revealed.

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1 Multipole Model. Generalized Multipoles

The problem of relating the molecular structure and macroscopic properties of thermotropic and lyotropic liquid crystals is extremely complicated. Just a simple listing of the intermolecular amphiphile-amphiphile and amphiphile-water interactions that govern this relation displays practically all known interactions in condensed matter physics: electrostatic interactions (ion-ion, ion-dipole, dipole-dipole, etc.), dispersion interactions, hydrogen bonds, hydration forces, hydrophobic interactions, steric repulsion, protrusion forces, fluctuation forces, etc. The problem is additionally complicated by the great conformational freedom of lyomesogens. In such a situation rigorous methods of statistical physics developed for simple liquids face enormous difficulties. Even approximate methods of mean field type are usually applied for parts of the amphiphile (alkyl chains) only, while the role of polar heads is reflected in a more or less crude modelling.

Some hope for a progress in this field comes from computer modelling methods (Monte Carlo and molecular dynamics). These methods make use of rather well parametrized atomic potentials and rotational isomerization energies, and permit one to take into account a great number of conformations. The methods require

*This work is dedicated to Professor Alexander Derzhanski, DSc, Corresponding Member of the Bulgarian Academy of Sciences, on the occasion of his 70th anniversary.

powerful computers, though, and still experience problems when modelling head group-water interactions.

Therefore, looking for a general enough (although in some respects qualitative) picture, we have developed a generalized molecular asymmetry model [1,2].

We shall summarize here the existing notions about molecular asymmetry and the parameters that characterize it qualitatively and quantitatively. We will concentrate our discussion on lyotropic liquid crystals. However, some important consequences for thermotropic liquid crystals will be mentioned, too.

“Molecular asymmetry” is a synonym for *broken symmetry*. We use this term to describe the deviation of certain molecular properties from the spherical, $O(3)$, and axial, D_∞ , symmetry. We have introduced four types of Generalized Molecular Asymmetry (GMA), using multipole representation in analogy with electrostatics: (i) electric asymmetry; (ii) steric asymmetry; (iii) biphilic asymmetry; (iv) flexible asymmetry.

Clearly, in the case of molecular shape one could operate in terms of the specific symmetry of the molecule. However, molecules of different symmetry groups could be represented by the same generalized multipole, *i.e.*, they can manifest the same behaviour in the sense of our discussion. Besides, the majority of mesogen molecules are of rather low symmetry, displaying a great number of conformations. Some lipid molecules are even enantiomorphous, *viz.*, they exist as left and right enantiomers. These enantiomers demonstrate important differences in their intermolecular interaction, judging from the differences in the phase transitions of the enantiotropic phase and a racemic mixture of DPPE (dipalmitoyl phosphatidylethanolamine) at a low degree of hydration. However, these differences disappear at full hydration of the polar heads. We could then see that taking into account exact details of the molecular structure is in many cases not possible, but also not necessary. The GMA model operates with an averaged molecular structure of a higher symmetry sufficient to trace the relation between the macroscopic and molecular properties of mesophases.

We have to mention that apart from sufficiently high molecular mass, a principal feature of mesogens is a molecular shape markedly deviating from spherical symmetry. Shape anisotropy leads to anisotropic molecular polarizability and to anisotropic intermolecular interaction, respectively. We are considering the two most symmetric non-spherical shapes as basic ones: rod-like and disc-like (axial symmetry $D_{\infty h}$). They are represented in the two halves of Figure 1. Rod-like shapes are classical ones. Novel discotic mesogens, thermotropic and lyotropic ones, feature disc-like shapes. This shape asymmetry suffices to create nematic ordering of molecules above a certain packing density, even if intermolecular interactions are dominated by hard core repulsion only. Of course, such a hypothetical nematic will not display a number of properties inherent to nematic phases of lower symmetry molecules. However, such a featureless uniaxial order could be considered as a background against which molecular asymmetry effects are better outlined.

1.1 Electric asymmetry (E -asymmetry)

Quantitative expressions of E -asymmetry are various multipoles describing the distribution of electric charge along the molecule and its deviation from the spherical and axial symmetry. We restrict our discussion to the first three terms of the multipole expansion: monopole, dipole and quadrupole moment of the molecule. Their definitions in the classical and in the quantum case are well known.

The total electric charge of a mesogenic molecule, *viz.*, its “electric monopole” could be positive, negative or zero (zwitterionic amphiphiles). An electric monopole does not change the symmetry of the rod or the disc ($D_{\infty h}$) if the centre of charge coincides with the centre of mass. With an off-centre situated monopole the symmetry can be reduced to $C_{\infty v}$ for rods or to C_{2v} for discs.

The total dipole moment could be longitudinal, reducing the symmetry to $C_{\infty v}$ (Figure 1), transversal (symmetry C_{2v}) or could have both longitudinal and transversal components (symmetry C_s).

Quadrupole moment offers more possibilities. Some of them could be represented as combinations of antiparallel longitudinal dipoles, preserving $D_{\infty h}$ symmetry, or of antiparallel transversal dipoles, reducing the symmetry to C_{2h} (Figure 1). However, some quadrupolar charge distributions have no dipolar representation — *e.g.*, a positive charged core surrounded by a negative, axially deformed shell (symmetry $D_{\infty h}$).

1.2 Steric asymmetry (S -asymmetry)

We are considering S -asymmetry in connection to the orientational (or curvature) elasticity of the mesophases expressed as splay and bend deformation of the director field in nematics (calamitic and discotic) layer curvature (corresponding to the splay of the director field) in smectic A and lamellar lyotropics, and bending of columns (corresponding to a bend of the director field) in columnar discotic phases.

In the steric case it turned out that a “steric monopole” could not be consistently defined [1]. Therefore, corresponding boxes of Figure 1 are left empty and steric multipole representation starts from the dipoles. This resembles magnetostatics (no magnetic monopole).

Longitudinal “steric dipole” s_0 (symmetry $C_{\infty v}$) describes to molecules having a cone-like shape asymmetry with respect to the cylindrical or discoid shapes that are characterized by a zero steric dipole. Transversal “steric dipole” b_0 in the case of rods describes banana-like molecules (*e.g.*, some large proteins spanning the whole bilayer and inducing opposite tilt in the two monolayers); in the case of discs, non-zero b_0 means a disc with a wedge-like normal cross-section. In both cases symmetry is reduced to C_{2v} . Molecular shape can combine these

	ELECTRIC	STERIC	BIPHILIC	FLEXIBLE	ELECTRIC	STERIC	BIPHILIC	FLEXIBLE	
monopole		—				—			
dipole									
quadrupole									

Figure 1. Electric, steric, biphilic and flexible multipoles with the two basic shapes of the mesogenic molecules, rod-like and disc-like. Hatched areas in the biphilic case mark the hydrophobic portions of the molecules. The groups of molecular symmetry according to Schoenflies are also given. Note that different molecular symmetry groups belong to the same generalized multipole type. This table is a catalogue of various asymmetric mesogens with only one type of asymmetry. Combinations are described in the text.

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two asymmetries; a steric dipole will then have both components s_0 and b_0 (symmetry C_s).

Some “steric quadrupoles” could also be considered as antiparallel combinations of longitudinal ($D_{\infty h}$) or transversal (C_{2h}) steric dipoles, both in the rod-like and disc-like case (Figure 1). These may again be relevant to some integral protein shapes. Typical steric quadrupoles provide the shapes of the double-swallow-tailed mesogens.

We want to stress explicitly that the effective molecular shape, as it comes into our model, is determined not only by the hard core repulsive steric interactions but also by the electric intermolecular interactions. Relationships accounting for the charge of a lipid polar head or its longitudinal electric dipole could be used in calculating the effective size of the lipid head group of an ionic or zwitterionic lipid, *i.e.*, in determining its resulting conical asymmetry (see below).

It is clear then, that S -asymmetry is a dynamic characteristic of membrane molecules. It can be varied by variations of the temperature, polar head hydration and conformation, pH, ionic strength, etc.

1.3 Biphilic asymmetry (B -asymmetry)

B -asymmetry is determined by the distribution of hydrophilic and hydrophobic groups along or across the long molecular axis. A “positive” biphilic monopole is supposed to characterize the solubility of the whole molecule in water: a monopole having a higher value has better solubility. Analogically, good solubility in oil as a whole is characterized by a “negative” B -monopole. The B -monopole is a property attributed to the molecular surface by a specific surface energy (see below). Hydrophilicity is related mainly to charged or polar groups capable of forming hydrogen bonds with water (oxygen, sodium, *etc.*) while hydrophobicity means a lack of such groups. In Figure 1 a positive B -charge is denoted by hatching in the corresponding area.

Biphilic molecules (soaps, lipids, proteins) display a difference in water solubility between the two halves of the molecule. This feature has not been recognized in investigations of surface phenomena for a long time [3]. We describe such molecules as B -dipoles, longitudinal (symmetry $C_{\infty v}$) and transversal (symmetry C_{2v}).

B -quadrupoles then represent certain amphiphiles with two hydrophilic groups at the two ends of an alkyl chain (α, ω -amphiphiles forming a lamellar phase of single layers [4]) and integral membrane proteins spanning the whole membrane. The term B -quadrupole is also ascribed to rod-like molecules with a hydrophilic central part and two hydrophobic alkyl end substituents (thermotropic mesogens) and to disc-like molecules with a hydrophobic core and a hydrophilic periphery (lyotropic discotics) or *vice versa* (thermotropic discotics). All such structures belong to $D_{\infty h}$ symmetry.

The B -monopole could be defined as proportional to the molecular surface times a specific value of the surface energy depending also on the water/oil ratio in the environment (see below). The B -dipole could be assumed equal to the value of the monopole times the vector between the centre of mass of the opposite monopoles, etc.

Let us especially stress a basic property of B -monopoles: contrary to the electric case, equal B -monopoles attract each other while opposite ones repel. This is, in fact, the basic property of the hydrophobic effect of Tanford [3], leading to a decrease of the free energy of the system when like associates with like. According to this point, the analogy with electrostatics should take into account the inversion of sign of the interaction, *e.g.*, adjacent parallel dipoles will attract each other, while antiparallel will repel. This is not the case with S -asymmetry; there the analogy with electrostatics (or, more precisely, magnetostatics) is complete.

Recently, an important extension of the biphilic concept was made by introducing polyphilic molecules [5-8]. Besides aromatic and hydrocarbon segments, along the full length of the molecule they also contain a fluorocarbon segment. Each one of the three segments has a chemical affinity to be in contact with like ones, leading to layered and polar molecular arrangement. A B -dipole for such a molecule could be defined by Eq. (9) below. These polyphilics were synthetically realized, and proved to be longitudinal ferroelectrics, as suggested in [9].

To sum up, we should mention that although the three types of asymmetry considered up to now are not entirely independent of one another, and the last two are in a way connected to the electric asymmetry, for the time being it does not seem possible to express all of them in terms of electric charge distribution. The separate definition of three types of asymmetry of mesogens and consideration of their numerous combinations proved very convenient for a joint discussion of many volume and surface effects in thermotropics and lyotropics [1].

1.4 Flexibility asymmetry (F -asymmetry)

Lattice model calculations [10] have shown that there is a tendency for space separation of the rigid and flexible molecular segments in liquid crystals in such a way that flexible packs with flexible and rigid with rigid. This explained in particular the arising and disappearance of translational order in smectic phases.

In our language, rigid or flexible segments (*e.g.*, cholesterol skeleton or its alkyl tail) could be called F -monopoles. They can be combined in F -dipoles, F -quadrupoles, *etc.* Some examples are shown in Figure 1.

Let us note that flexible segments are often hydrophobic as well, so that in many cases F -monopoles and B -monopoles coincide. However, in most lipids and non-ionic detergents hydrophilic parts are also flexible. F -asymmetry and B -asymmetry are similar in the sense that in both cases like monopoles attract

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while unlike repel. In the case of F -asymmetry this is due to the finding that a rigid segment in a flexible environment restricts the conformational freedom of adjacent flexible segments, reduces their entropy and increases the free energy of the system, being as a result expelled from this environment. The situation with a flexible segment in a rigid environment is analogous, this time its own free energy being increased.

F -monopoles could be assigned a value proportional to their length. F -dipoles could be defined as equal to the monopole times the vector between the centre of mass of the opposite monopoles, *etc.*

1.5 Summary

In general, all four types of molecular asymmetry introduced above are dynamic characteristics of mesogenic molecules. GMA can be varied by variations of the temperature, polar head hydration, pH, ionic strength, etc. Eventually, it might be possible to trace a relationship between molecular symmetry change and the symmetry aspects of various liquid crystal and gel phases, as well as the order of the phase transitions in the field of the complex lipid polymorphism at lower temperature and degree of hydration, following the general method of Landau and Lifschitz [11] and its extension for the smectic polymorphism [12,13].

Closing this section, let us mention that several of the molecular structures predicted by us on the basis of GMA model in 1982 [1] were very soon synthetically created:

Cone-shaped, or pyramidal discotics [14,15] are characterized in our language as a combination of S -dipole and E -dipole along the symmetry axis of the cone (symmetry C_{3v}). This assures conditions for permanent electric polarization of the whole column of cones or pyramids piled one over another [16].

Discotic amphiphiles [17] represent B -quadrupoles with a hydrophilic periphery and a hydrophobic flat core. These amphiphiles in water display a lyonematic phase with a remarkably broad stability range. This is because shape asymmetry does not allow formation of bilayer aggregates and the transition to lamellar phase is forbidden. At further increase of the amphiphile concentration a hexagonal phase of columnar type is formed, water being situated between the columns. This is the same aggregation principle as in thermotropic discotics, but here driven by the B -field instead of F -field.

Some other newly synthesized mesogens like flexible core discotics or flexible super-discs [18,19], phasmids [15] and biforked mesogens [20] can also be described in terms of F -multipoles [21,2].

All this demonstrates that the GMA model could be very useful in the directed molecular design of mesogens. The examples above do not exhaust its predictive capabilities. Figure 1 serves as a catalogue of the asymmetric molecular structures of both rod-like and disc-like mesogens. At present, most examples shown

in this catalogue can be considered realized, with a few exceptions. However, these are (so to say) pure asymmetric types, when a molecule could be classified as a single generalized multipole. Taking all possible combinations of two generalized multipoles per one molecule yields

$$\binom{11}{2} = 55 \text{ combinations,}$$

i.e., 55 possible molecular types for each of the two basic form of mesogens (rods or discs) separately. Taking combinations by three yields

$$\binom{11}{3} = 165 \text{ combinations, } \textit{etc.}$$

Of course, not all of the possible combinations could be meaningful, but still the large number of possibilities is quite impressive and a systematic synthetic chemistry approach for their realization is worth trying.

Another promising field of research is offered by various new effects arising from combinations of generalized multipoles in generalized fields (see below).

2 Generalized Potentials and Fields

The concept of generalized multipoles is inherently coupled to the concept of generalized potentials and fields. Each type of multipole interacts with a corresponding type of field listed below. Examples of mixed interactions are also possible.

2.1 Electric field

The case of E -multipoles is most simple. Here a generalized field is the electric field \mathbf{E} itself as a gradient of the scalar electric potential U :

$$\mathbf{E} = -\text{grad } U. \quad (1)$$

An E -monopole q experiences a force \mathbf{F} proportional to the field: $\mathbf{F} = q\mathbf{E}$ and an E -dipole of modulus μ — to the field gradient: $\mathbf{F} = \mu \text{grad}|\mathbf{E}|$. On the other hand, a dipole μ experiences a torque \mathbf{M} equal to its vectorial product with the field vector, $\mathbf{M} = \mu \times \mathbf{E}$ while a quadrupole's torque is equal to the vectorial product of the quadrupole tensor Θ with the vector-gradient of the field, $\mathbf{M} = \Theta \cdot \text{Grad } \mathbf{E}$.

2.2 Steric field

We have argued [1] that in the steric case it is natural to apply the invariant expressions of the two basic deformations in a nematic: splay \mathbf{S} and bend \mathbf{B}

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vectors introduced first by Meyer [22]:

$$\mathbf{S} = n \operatorname{div} \mathbf{n}, \quad (2)$$

$$\mathbf{B} = -\mathbf{n} \times \operatorname{curl} \mathbf{n}, \quad (3)$$

where \mathbf{n} is the director. We noted that two separate fields have to be considered in this case, and they cannot in general be represented as gradients of a scalar potential. That was a reason not to introduce S -monopoles and potentials.

Consequently, the lowest order forces proportional to the fields are absent and the first non-zero effects on steric dipoles are torques. Expressions for the orientational energy of S -dipoles in deformed nematics are given by Petrov [23] and Gruler [24]. These expressions contain, as in electrostatics, scalar products $\mathbf{s}_0 \cdot \mathbf{S}$ and $\mathbf{b}_0 \cdot \mathbf{B}$, where steric dipoles are defined as above. In the general case of non-ideally oriented nematics (with a degree of order less than unity) crossed terms $\mathbf{s}_0 \cdot \mathbf{B}$ and $\mathbf{b}_0 \cdot \mathbf{S}$ arise as well [25]. These results easily yield expressions for the torques upon S -dipoles.

In the case of smectics A and lamellar lyotropics (described as regularly organized interfaces with biphilic molecules localized over them), bend deformation of the director is not allowed and only splay field \mathbf{S} is active. We remind here the definitions regarding just that case.

For an arbitrary curved lipid monolayer where \mathbf{n} coincides with the layer normal it holds that

$$\operatorname{div} \mathbf{n} = (c_1 + c_2) \mathbf{n} = \left(\frac{1}{R_1} + \frac{1}{R_2} \right) \mathbf{n}. \quad (4)$$

Therefore, in view of (2)

$$\mathbf{S} = (c_1 + c_2) \mathbf{n}. \quad (5)$$

The steric dipole \mathbf{s}_0 of biphilic molecules can be defined analogically to nematogens [26] by considering the macroscopic monolayer deformation, in case all steric dipoles are unidirectionally oriented and the monolayer is left to deform freely to a state where elastic torques relax to zero. Consulting curvature elastic energy expression of Helfrich [27] we could immediately see that this is the phenomenological spontaneous curvature c_0 of the monolayer.

This phenomenological definition of c_0 can be translated into molecular terms by making use of the model of Petrov and Derzhanski [28]. It describes a lipid molecule by two equilibrium cross sections (Figure 2): H , of polar head, and C , of hydrophobic part (chain or chains). If a cross-section in the middle of the chain length is considered, then the distance between the two sections is $b/2$, where b is the monolayer thickness. In general, this distance is also a model parameter, δ . It was shown before that the spontaneous curvature of a monolayer of such model molecules is given by

$$c_0 = \frac{1}{\delta} \frac{H - C}{A_0}, \quad (6)$$

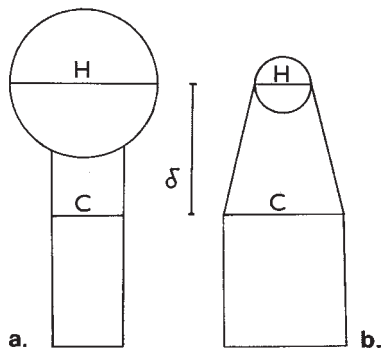


Figure 2. Models of asymmetric lipid molecules. H is the equilibrium cross section of polar head and C is the equilibrium cross-section of hydrophobic part (chain or chains). δ is the distance between the effective surfaces of head and chain interaction. (a) Positive asymmetry, direct cone ($H > C$). Examples: lysolecithin, gangliosides, phosphatidic acids, soaps. (b) Negative asymmetry, inverse cone ($H < C$). Examples: cholesterol, phosphatidylethanolamine, cardiolipin, Aerosol OT.

where A_0 is the equilibrium area per molecule in a flat monolayer state (being a weighted average of H and C). We see that with symmetric cylindric molecules ($H = C$, *i.e.*, zero steric dipole) $c_0 \equiv 0$; with $H > C$, $c_0 > 0$ and with $H < C$, $c_0 < 0$. Eq. (6) expresses quantitatively the steric asymmetry if molecular parameters H and C are known. At this point we are able to make qualitative conclusions concerning the effect of: charging a head group by varying pH (increasing H); head group hydration (increasing H); rising of ionic strength (decreasing H); introducing divalent ions (decreasing H); temperature rise (increasing C); the presence of double bonds (increasing C); the enzymatic cleavage of lipid chains (decreasing C), *etc.* Most of these factors were recently discussed in details [29,30]. Another way of increasing H is to graft a PEG chain to the lipid head group [31].

At this point we should note that steric dipoles of lipids were historically the first expression (1976) of the so-called “shape concept”. We remind the reader that the sign of the spontaneous curvature of a lipid monolayer is assumed positive when it is convex towards water and negative when convex towards its hydrophobic core. Consequently, we divided lipid molecules into “positive asymmetry” and “negative asymmetry” types (Figure 2), depending on the sign of the difference between H and C [28]. Other authors employing subsequently shape concept in the same sense as we do used the notion of Type I and Type II lipids according to the type of hexagonal phase they possess, direct (H_I) or inverse (H_{II}) [32], or “bilayer” and “nonbilayer” lipids [30,33]. In the packing approach of Israelachvili *et al.* [34] lipid shape is described in terms of a “packing parameter” v_0/a_0l_c , v_0 being the volume of the hydrophobic part, a_0 the head group area, and l_c the length of the extended alkyl chain. Largely neglecting membrane curvature elasticity, the packing approach is not appropriate for our aims.

The lateral elastic force acting on a steric dipole s_0 in a curved membrane is [35]

$$\mathbf{f} = AK(\text{div } \mathbf{n} - s_0)\text{grad div } \mathbf{n}, \quad (7)$$

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where A is the area of the steric dipole. As in the electric case this force is proportional to $\text{grad } S$ and in a membrane with variable curvature it drags steric dipoles to a point where $\text{div } \mathbf{n} = s_0$. This is demonstrated, *e.g.*, in the accumulation of integral proteins over curved membrane domains over the surface of microvillae [36].

On the other hand, by introducing steric dipoles in a membrane each one of them becomes a source of a steric field that brings about long-range elastic interactions between them. Parallel will repel each other while antiparallel will attract ([24,37]).

2.3 Biphilic field

GMA approach. The way to introduce the biphilic potential and the biphilic field employing the electrostatic analogy is to use a small probe biphilic monopole (*e.g.*, a molecule of H_2O or CH_4) and to look for its standard free energy as a function of its position in the liquid (lyotropic or thermotropic) crystal [1]. Steep variations of the biphilic potential can be observed at water/oil interfaces and at the interfaces between the hydrophilic and hydrophobic regions in membranes. Those are just the surfaces where strong biphilic field \mathbf{B} is supposed to act along their normals.

An easy way to obtain the biphilic potential $u(x)$ and the biphilic field as its first derivative du/dx is to employ the water concentration profile across an oil/water interface $c(x)$ (in molar units).

The water profile in lipid bilayers can be measured at present by neutron scattering [38-41]. It has also extensively been modelled by molecular dynamics simulations [42-46]. Such simulations demonstrate a quite diffusive character of the interface when the lipid is in liquid crystal phase: the thickness of 10–90% water zone is found to be 1.3 nm compared to 3.0 nm thickness of the hydrophobic core [42] or 1 nm compared to 4.6 nm total bilayer thickness [46]. Water molecules penetrate up to the region of the ester groups linked to the glycerol backbone [46]. This is confirmed by neutron diffraction experiments [38,39,41] which show that water penetrates up to 1.5 nm from the middle of the bilayer, near the acylester groups. Taking twice the value 1.3 nm (both interfaces) this means that more than 40% of the total bilayer belongs to the interfacial region where the biphilic field is concentrated.

The biphilic potential $u(x)$ is measured by the free energy of transfer of a water molecule to the point x . If the molecule under consideration is not water then we could model [1] the free energy of transfer $u(x)$ following [47] in such a manner as to define simultaneously the biphilic charge of the molecule and the biphilic potential at the given point. We proposed to consider $u(x)$ proportional to the product of the molecular surface area a and a specific surface energy $\gamma(x)$ which depends on the local water concentration in the point x of the interfacial

zone:

$$u(x) = \alpha a \gamma(x). \quad (8)$$

The coefficient α takes the value of +1 for a completely hydrophilic molecular surface (H₂O) and -1 for a completely hydrophobic one (CH₄). For larger, more complicated molecules (*e.g.*, hydrophilic glycerol or hydrophobic benzene) α could take intermediate values between these limiting ones. Recently, excess chemical potentials of methane and fluoromethanes across water-membrane and water-hexane interfaces were obtained by molecular dynamics simulation [48]. Molecular surface area could be measured over the lateral molecular surface composed by spherical segments constructed with the van der Waals radii of the outer atoms of the molecular skeleton. Alternatively, the solvent-accessible surface area could be used; this is defined as the area over which the centre of a solvent molecule (*e.g.*, a water molecule of radius 0.14 nm) can move while maintaining unobstructed contact with the molecular surface [49]. This specification is important, because $\gamma(x)$ depends on the way molecular surface is chosen.

In this model B -monopole of a molecule is given by the value αa and is measured in area units, the sign being controlled by α .

A B -dipole can be quantified by a separation of its molecular surface into two parts with respect to their biphilic charges $\alpha_1 a_1$ and $\alpha_2 a_2$, where $\text{sign } \alpha_1 = -\text{sign } \alpha_2$ and $|\alpha_1 a_1| = |\alpha_2 a_2|$. The dipole itself could be defined as

$$\beta = \alpha_1 a_1 \mathbf{l}, \quad (9)$$

where \mathbf{l} is the vector, connecting the centres of mass of the two monopoles. An analogous procedure could be performed with quadrupoles.

In Eq. (8) $\gamma(x)$ is the biphilic potential having the meaning of a position-dependent surface energy. For convenience, one can assign to it a zero value at the point with a maximum slope $d\gamma/dx$, *i.e.*, at the point where *biphilic field* B is a maximum:

$$\mathbf{B} = \frac{d\gamma}{dx} \mathbf{n}. \quad (10)$$

For an oil/water interface the difference between the asymptotic values of γ should be close to the interfacial tension $\sigma_{o/w}$: $\gamma(-\infty) - \gamma(\infty) = 50$ mN/m.

We have established [2] a complete analogy of B -monopoles' distribution to the well-known Boltzmann distribution of charges in an external electric field. The electrostatic analogy can further be followed with the next biphilic multipoles. The result about the dipoles' orientation is a trivial paraphrase of the experimentally observed amphiphile orientation in monolayers. Their location at the plane where the force acting on them is vanishing ($\beta dB/dx \propto d^2\gamma/dx^2 = 0$) perhaps is not trivial. The result about the quadrupoles predicting the formation of two layers on both sides of the ($d^2\gamma/dx^2 = 0$)-plane with mutually orthogonal orientation is certainly novel.

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Comparison to other approaches. Our concept of biphilic multipoles can be compared to the familiar HLB-concept in colloid chemistry ([50,51]. Taking the well-known Davies formula

$$HLB = 7 + 0.36 \ln (c^\alpha / c^\beta) \quad (11)$$

and substituting for the ratio of the concentrations in the water/oil phase we obtain

$$HLB = 7 + 0.36 \frac{\alpha a \gamma}{k_B T}. \quad (12)$$

That means that we can use extensively tabulated *HLB*-numbers in order to evaluate the total *B*-charge of any amphiphile according to

$$\sum (\alpha a) = \frac{(HLB - 7) k_B T}{0.36 \gamma}. \quad (13)$$

This relationship tells us that pure *B*-dipoles (zero *B*-charge) are amphiphiles with $HLB = 7$. When $HLB < 7$ the amphiphile is a combination of a lipophilic charge plus *B*-dipole; when $HLB > 7$ it carries a hydrophilic charge and a *B*-dipole, respectively. This could explain the localization of the amphiphile with respect to the interface and its effect as an emulsifier (Table 1). However, we could see now that *B*-multipoles offer a more detailed description of amphiphiles, *e.g.*, various pure *B*-dipoles differing in length and value correspond to the same $HLB = 7$.

Eisenberg *et al.* [53] independently developed the idea of the helical hydrophobic moment as a measure of the amphiphilicity of a protein helix. Originally they used the numerical values of the hydrophobicities of 20 amino acid residues based on a “consensus scale”. Later on, Eisenberg and McLachlan [54] adopted an approach based on atomic solvation parameter (ASP) of each atom accessible to water. They expressed the free energy of transfer of atom *i* from the interior of a protein to aqueous solution ΔG_i as

$$\Delta G_i = \Delta \sigma_i A_i, \quad (14)$$

where A_i is the accessible surface area of the atom (*v. supra*) and $\Delta \sigma_i$ is its atomic solvation parameter. The total free energy of transfer is then the sum of

Table 1. The relationship between the hydrophylic-lipophilic balance of the emulsifier, *R*-value of Winsor and the emulsion type [52]

<i>HLB</i> -interval	<i>R</i> -value	Emulsion type
16–20	$\ll 1$	Micellar solution in water
12–15	< 1	Oil-in-water emulsion
8–10	≈ 1	Inversion point; plane
4–6	> 1	Water-in-oil emulsion
1–4	$\gg 1$	Inverse micelles in water

individual contributions (14). In this way they estimated 5 ASP values of the atoms C (carbon), O⁻ (charged oxygen), N⁺ (charged nitrogen), N/O (neutral nitrogen and oxygen) and S (sulphur) forming amino acid residues (except hydrogens) using accessible areas [55] and free energies of transfer from n-octanol to water [56].

This ASP approach is very similar to ours. Eisenberg and McLachlan's definition of a hydrophobic moment as an atomic property of a group of atoms (**a**) is the following:

$$\mathbf{m}_a = \sum_{\text{atoms } i} \Delta\sigma_i A_i \mathbf{r}_i - \langle \Delta\sigma A \rangle \sum_{\text{atoms } i} \mathbf{r}_i, \quad (15)$$

in which \mathbf{r}_i is a vector from any origin to the position of atom i , and where the brackets indicate the mean value for all atoms of the group. The second term ensures that the value of \mathbf{m}_a is independent of the choice of origin. It is identically zero if the total biphilic charge of the group is vanishing. Note then the close analogy between (8) and (14): our α is equivalent to the ratio $-\Delta\sigma/N_A\gamma$, where $\gamma = 50$ mN/m is the interfacial tension oil/water. Values of α corresponding to $\Delta\sigma$ are given in column 2 of Table 2.

Thermodynamic parameters of peptide-bilayer interaction have been related to structural parameters obtained by diffraction methods [57]. An experimentally determined hydrophobicity scale for proteins at membrane interfaces has been introduced [58,59]. This scale is complete, as it includes all 20 natural amino acids in proteins and also the contribution of the peptide bond. The need for modifying the values [56] of the solvation energies of Asp, Glu and Cys was established. Hydrophobicities in both water/octanol and water/POPC membrane were measured and compared. They were found to be strongly correlated, but the membrane values are generally about one-half those observed for n-octanol [59]. This should be kept in mind for an eventual revision of Table 2 in a membrane-relevant sense.

Interaction of biphilic multipoles. Our considerations [1] have shown that biphilic multipoles interact in general *via* biphilic potentials of a screened Coulomb type, *i.e.*, in most cases they are short-range. An exponentially decaying molecular hydrophobicity potential was recently introduced in [60] and

Table 2. Column 1: atomic solvation potentials (after Eisenberg and McLachlan [54]); column 2: biphilic charge coefficients $\alpha = -\Delta\sigma/N_A\gamma$, where $\gamma = 50$ mN/m (after Derzhanski and Petrov [1])

$\Delta\sigma(\text{C}) = 67 \pm 8 \times 10^{20} \text{ Jm}^{-2}\text{mol}^{-1}$	$\alpha = -0.222$
$\Delta\sigma(\text{N/O}) = -25 \pm 17 \times 10^{20} \text{ Jm}^{-2}\text{mol}^{-1}$	$\alpha = 0.083$
$\Delta\sigma(\text{O}^-) = -100 \pm 42 \times 10^{20} \text{ Jm}^{-2}\text{mol}^{-1}$	$\alpha = 0.332$
$\Delta\sigma(\text{N}^+) = -209 \pm 38 \times 10^{20} \text{ Jm}^{-2}\text{mol}^{-1}$	$\alpha = 0.694$
$\Delta\sigma(\text{S}) = 88 \pm 42 \times 10^{20} \text{ Jm}^{-2}\text{mol}^{-1}$	$\alpha = -0.292$

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was used for the classification of lipid-associating protein helices, determining in this way the mode of their interaction with membranes. An important result of the work [60] is also the determination of the individual atomic transfer energy contributions of 7 types of atoms (including two types of hydrogen), which may also be utilized in defining B -multipoles.

2.4 Flexibility field

F -potential and F -field could be defined in layered mesophases where spatial separation into rigid and flexible regions exists [2]. The F -potential of a flexible monopole could be identified with its standard free energy having low value in a flexible environment and a higher one in a rigid environment due to the entropy reasons discussed above. Interfaces between flexible and rigid domains are just the locations where strong F -fields are considered to act in a normal direction. F -field is the first derivative of the F -potential and determines the force acting on an F -monopole and the torque on an F -dipole. The force acting on an F -dipole is equal to the first derivative of the F -field, *viz.*, to the second derivative of the F -potential, *etc.*

The notion of flexibility asymmetry can be of importance in discussing smectic induction in mixtures of nematic mesogens. This notion tells us that F -dipoles should be more effective in the smectic induction than F -quadrupoles. This is so because the longitudinal force acting on the quadrupoles becomes zero just at the interface. In comparison, the force acting on the quadrupoles (being proportional to the second derivative of the F -field) becomes zero below and above the interface. Consequently, the density wave maxima describing a one-dimensional translational smectic order should be sharper in the case of F -dipoles compared to F -quadrupoles. The higher efficiency of F -dipoles than of F -quadrupoles was demonstrated in the thorough studies of smectic induction [61].

Simultaneous consideration of biphilic and flexible asymmetry is very convenient for a common description of thermotropic and lyotropic systems in the framework of the GMA-model. In thermotropics the role of the B -field is dominated by the F -field. From the discussion above a close analogy between the two fields can be established. Consequently, the existence in both systems of lamellar, cubic and columnar types of ordering appears quite natural, being determined by the combination of B - and S -asymmetry in lyotropics or F - and S -asymmetry in thermotropics, respectively.

3 Molecular Asymmetry, Intermolecular Interactions and the Structure of Liquid Crystals

As we already noted above, molecular asymmetry is not generally a necessary condition for liquid crystal alignment. The attempt of M. Born [62] to describe

nematic ordering as a result of the interaction of electric dipoles was in disagreement with the experimental situation of non-polar molecular ordering. In contrast, successful models of uniaxial order, the basic orientational characteristic of the liquid crystal state, use as sufficient the requirement for axially symmetric molecular shapes (rods or discs) or anisotropically polarizable molecules [63]. It is worth mentioning that the anisotropy of electronic polarizability is inherent to axially symmetric molecules.

Therefore, we shall consider molecular asymmetry effects on the background of a liquid crystal order provided by the basic rod-like or disc-like structure of the molecules. Doing that, we shall explain the specificity of molecular ordering in various mesophases as a deviation from this background order caused by a certain type of molecular asymmetry (or a combination of these) as well as by external field influence.

3.1 Electric asymmetry

Monopoles. In thermotropics, the influence of electric charge upon intermolecular interactions is usually negligible because of the low charge densities and the essentially non-orientational character of these interactions. In lyotropic molecules electrically charged groups are usually asymmetrically situated – they are localized in one of the ends of the molecule (Figure 1). In ionic amphiphiles, head group charges largely determine the effective size of the head (*i.e.*, its steric asymmetry). Indeed, if we resort to the “capacitor approximation” of the double layer of polar heads and counterions [34] then the specific double layer electric energy per polar head will be

$$f_{el} = \frac{(\beta e)^2 \lambda_D}{2\varepsilon\varepsilon_0} \frac{1}{a}, \quad (16)$$

where a is the area per head, β is the degree of dissociation of the head, e is the electron charge, ε_0 is the absolute dielectric permittivity of free space, ε is the dielectric constant of the electrolyte close to the interface and λ_D is the Debye length (χ is the inverse of Debye length):

$$\lambda_D = \chi^{-1} = \sqrt{\frac{\varepsilon\varepsilon_0 k_B T}{2nz^2 e^2}}, \quad (17)$$

where n is the volume electrolyte concentration (ions/m³) and z is the ion valence. In combination with the hydrophobic energy γa , where γ is the interfacial energy between the hydrophobic and hydrophilic zones, the free energy per polar head takes the form [34]:

$$f = \gamma a + \frac{(\beta e)^2 \lambda_D}{2\varepsilon\varepsilon_0} \frac{1}{a}. \quad (18)$$

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The minimum of this expression then defines the so-called “optimal area per polar head” a_0 (having the same meaning as our equilibrium area H):

$$a_0 = \beta e \sqrt{\frac{\lambda_D}{2\gamma\epsilon\epsilon_0}}. \quad (19)$$

At small variations of a around a_0 the free energy f variations follow a parabolic law, *i.e.*, the head group system shows elastic behaviour.

Eq. (19) demonstrates that a_0 depends in a linear fashion on the partial charge of the head βe . An estimation with $\beta = 1$, *i.e.*, $\beta e = 1.6 \times 10^{-19}$ C and $\gamma = 20$ mN/m [64], $\epsilon = 30$ (a value obtained by molecular dynamics simulation [46]), $\lambda_D = 10$ nm yields $a_0 = 4.9$ nm², *i.e.*, a value substantially exceeding the steric size of the head (usually less than 1 nm²). If we substitute $H = a_0$ in our spontaneous curvature expression (6) we shall see how (at fixed C) the charge of the head group influences the structure of the lyotropic phase by changing the spontaneous curvature of the amphiphile monolayer. In lyomesophases a number of possibilities for such changes exist: pH variations changing β , electrolyte concentration variations changing λ_D , *etc.* The transition from lyonematic I (rod-like micelles, higher a_0) to lyonematic II (disc-like micelles, lower a_0) by increasing electrolyte concentration [65] can be discussed on this basis. Another example of this type is the formation of lamellar structures from micellar solutions of single chain ion amphiphiles (fatty acids) by titration, neutralizing the head group charge [66].

A detailed development of the thermodynamics of ion amphiphile aggregates with lamellar, cylindrical and spherical geometry is given in [64] and [67].

Dipoles. The electrostatic interaction of permanent dipolar moments often leads to compensation for the dipolar asymmetry of mesogens by means of an appropriate mutual orientation of neighbouring molecules. In this way the resulting mesophase is non-polar, *i.e.*, with a higher symmetry ($D_{\infty h}$) than the constituent molecules ($C_{\infty v}$ or C_{2v}). In nematics the antiparallel orientation of the longitudinal dipoles, creating antiferroelectric short range order, is well known [68].

Until recently there was no real example in liquid crystals of ferroelectric order due to dipole-dipole interaction. We already noted our prediction that the combination of columnar order of discotics and a dipole moment normal to the disc plane could bring about permanent polarization of the column along its axis [1]. This prediction seems to be realized with the pyramidal discotics [69] of symmetry C_{3v} , where an electric dipole is also coupled to a longitudinal steric dipole (Figure 1).

Strong evidence of permanent ferroelectric polarization exists also in polyphilic liquid crystals [9,5,6].

If intermolecular interactions are dominated by biphilic asymmetry (as at the water/oil interfaces in lyotropics) then a high degree of parallelism of both biphilic and electric dipoles of molecules takes place. In this case dipole moments of polar heads of zwitterionic lipids (at zero net charge) would also determine to a great extent the equilibrium area per head, *viz.*, the steric asymmetry. Longitudinal dipoles with fixed orientation (due to the hydrophobic effect) will result in a higher head group area because of their electrostatic repulsion. This effect can also be estimated from the “capacitor approximation”. For permanent dipoles μ_z with a length d and charge $\pm\beta e$ we can write

$$f = \gamma a + \frac{\mu_z^2}{2\delta\epsilon\epsilon_0} \frac{1}{a}, \quad (20)$$

i.e.,

$$a_0 = \frac{\mu_z}{\sqrt{2\delta\epsilon\epsilon_0}}. \quad (21)$$

Estimations with Eq. (21) demonstrate that with a supposed length of the dipole $\delta = 0.1$ nm and other values like the above, a value of $a_0 = 0.10$ nm² is obtained for a dipole moment μ_z of 1 Debye = 3.33×10^{-30} C.m. This means that dipole-dipole interactions can entirely determine observed areas per head of about 0.60 to 0.70 nm² at a value of the dipole μ_z above 6 Debye, *i.e.*, 20×10^{-30} C.m.

Results from conformational analysis of polar heads of phosphatidyl choline and phosphatidylethanolamine [70] combined with quantum-chemical calculations of the partial electric charges in the polar head [71] yield dipole moment components of the polar head μ_z and μ_x (for the most favourable head group conformations) and a total dipole moment μ ($\mu = \sqrt{(\mu_x^2 + \mu_z^2)}$) in the following ranges:

Phosphatidylethanolamine:

$$\begin{aligned} \mu_z &= 0 \dots 16.7 \times 10^{-30} \text{ C.m} \\ \mu_x &= 40 \dots 77.0 \times 10^{-30} \text{ C.m} \\ \mu &= 40 \dots 80.0 \times 10^{-30} \text{ C.m} \end{aligned} \quad (22)$$

Phosphatidylcholine:

$$\begin{aligned} \mu_z &= 10.0 \dots 32.0 \times 10^{-30} \text{ C.m} \\ \mu_x &= 58.3 \dots 80.0 \times 10^{-30} \text{ C.m} \\ \mu &= 61.7 \dots 84.7 \times 10^{-30} \text{ C.m} \end{aligned} \quad (23)$$

These data demonstrate that with phosphatidylethanolamine the dipole-dipole interaction of μ_z is not essential in determining the equilibrium area of the head group, while with phosphatidyl choline it is essential for some of the conformations in the upper end of μ_z range.

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Recent Monte-Carlo simulations of polar group statistics in lipid bilayers and monolayers of phosphatidylethanolamine and phosphatidylcholine, taking into account non-local electrostatics of hydrogen-bonded water clusters [72], did not find any significant difference between the averaged values of μ_z components of both lipids in the fluid phase. From these results, represented in bond lengths taking a maximum value of the dipole of 66.6×10^{-30} C.m, we infer:

Phosphatidylethanolamine:

$$\begin{aligned}\mu_z &= 14.4 \times 10^{-30} \text{ C.m} \\ \mu_x &= 47.9 \times 10^{-30} \text{ C.m}\end{aligned}\tag{24}$$

Phosphatidylcholine:

$$\begin{aligned}\mu_z &= 13.8 \times 10^{-30} \text{ C.m} \\ \mu_x &= 46.3 \times 10^{-30} \text{ C.m}\end{aligned}\tag{25}$$

i.e., averaged μ_z components are not sufficiently high to be of importance.

On the other hand, the transversal dipole components μ_x being rather substantial in value and free to reorient around a long molecular axis may adopt some antiparallel mutual orientation and by virtue of their attraction may contribute to a decrease of the equilibrium area per head (below the values conditioned by μ_z).

Quadrupoles. The role of electric quadrupoles in thermotropics is relatively well understood [73]. The interaction of adjacent quadrupoles composed by two antiparallel longitudinal dipoles favours, by means of longitudinal displacement, pair correlations of the type middle-end, *viz.*, a nematic phase or a smectic *C* with a large tilt [74]. On the other hand, interaction between adjacent transversal quadrupoles favours pair correlations middle-middle, *viz.*, a smectic A or a low tilt smectic *C* in a case when antiparallel dipoles have longitudinal components, too [75].

In discotics transversal quadrupoles would favour relative positions of the centre-periphery type, *viz.*, a tilted columnar phase. A longitudinal quadrupole would oppose columnar ordering and give rise to discotic nematics. The same conclusions could be drawn about discotic amphiphiles.

In rod-like amphiphiles the role of quadrupoles is not well understood. Being as a rule of a polar symmetry (C_∞) they usually exclude quadrupoles of the thermotropic type (composed of antiparallel dipoles). An exception is provided by some α, ω -amphiphiles (*e.g.*, archaeobacterial lipids [76,77] which are biphilic quadrupoles at the same time. They could display electric quadrupole effects similarly to the thermotropic case. Interestingly, the *B*-field of an air-water interface on a Langmuir trough “polarizes” these lipids, *i.e.*, forces them to lose

their quadrupolar asymmetry assuming a U-shape anchored to the interface with both polar groups, *i.e.*, becoming a *B*-dipole [78].

Uniaxially ordered quadrupolar moments of the alkyl chains and polar heads contribute to the flexoelectric coefficients of lipid bilayers, because a gradient of the quadrupolar density induced by an orientational deformation of quadrupoles is equivalent to electric polarization [79]. The same could be claimed about the contribution of integral proteins of high quadrupole moment in biomembranes with high protein concentration (*e.g.*, purple membranes).

3.2 Steric asymmetry

Monopoles. We have not introduced steric monopoles.

Dipoles. In non-deformed structures steric dipoles of adjacent molecules are, as a rule, antiparallel, thus compensating for the steric asymmetry of single molecules. This corresponds to a minimum of the orientational elastic energy of the liquid crystal. Because steric dipoles are most often coupled to electric ones, that also leads to antiferroelectric short range order, but this time sterically conditioned [26].

Biphilic mesogens combining biphilic and steric dipoles provide a case in which steric asymmetry is most fully demonstrated, as the decisive role of the biphilic field in the orientation of biphilic dipoles excludes the possibility of a compensation of steric dipoles by antiparallel orientation. Some compensatory possibility offers only the interdigitation of alkyl chains of the two monolayers of a bilayer that could compensate substantial positive steric asymmetries ($H > C$, Figure 3a) keeping a flat monolayer configuration at the same time. This possibility is mainly realized in the gel phases of single-chain soaps. In double-chain lipid gel phases such positive asymmetry is compensated by a tilt of the chains.

In mesophases with molten chains steric asymmetry of the dipolar type leads, according to Eq. (6), to a spontaneous monolayer curvature or to internal stresses if constrained flat. Such stresses create conditions for the arising of different kinds of defects. The changes in mesophase states as related to the variations of the areas of the hydrophilic and hydrophobic parts of the molecule under the influence of different factors (temperature, hydration, admixtures of different steric asymmetry) and connected changes of the monolayer curvature carefully followed before (the *R*-theory of Winsor [80]; the polymorphism of interfaces of Charvolin [81]).

From the viewpoint of the spontaneous curvature and its molecular interpretation, Eq. (6), we can make (Table 3) a classification of the lyotropic phases in terms of the steric asymmetry of the molecule (bearing in mind that $\delta \approx b/2$, where b is the monolayer thickness, *i.e.*, about the alkyl chain length).

With steric asymmetries having intermediate values between those listed above

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Table 3. Classification of lyotropic mesophases in terms of spontaneous monolayer curvature c_0 and steric asymmetry, expressed by the PDM-model parameters H , head group area, and C , chain area. δ is the distance between the two planes, where H and C are measured

Spontaneous curvature c_0	Steric asymmetry H vs. C	Mesophase type
$c_0 \approx 2/\delta$	$H \approx 3C$	micellar phase
$c_0 \approx 1/\delta$	$H \approx 2C$	hexagonal phase
$c_0 \approx 0$	$H \approx C$	lamellar phase
$c_0 \approx -1/\delta$	$H \approx C/2$	inverse hexagonal
$c_0 \approx -2/\delta$	$H \approx C/3$	inverse micellar

defect phases would be observed, the defects having a structure of the next possible phase. It has been established by systematic shape variation that some amount of negative steric asymmetry ($H < C$) is a prerequisite for the formation of stable bilayers: amphiphiles are able to create planar BLMs up to 1 mm in diameter only if $C/H = 1.6 \div 2.4$ [82].

Cubic phases with saddle type curvature require a positive modulus of saddle curvature $\bar{K} > 0$, which in turn requires a higher negative steric asymmetry $H - C < 0$.

Of course, if a developing spontaneous curvature at S -dipole variation (*e.g.*, by increasing head group hydration) is expected to create elastic stresses that would make the phase with lower c_0 energetically unfavourable, it is also necessary for the curvature elasticity modulus K of the monolayer to have a high enough value. At a lower K the geometry of the monolayer is unstable against thermal fluctuations.

Quadrupoles. Steric interaction of longitudinal steric quadrupoles favours middle-end pair correlations (just like electric ones), *viz.*, a nematic or smectic phase of high tilt [73], while the interaction of adjacent transversal quadrupoles favours middle-middle and end-end correlations, *viz.*, a smectic A or smectic C phase of low tilt [83].

With discotic mesogens transversal quadrupoles again favour middle-end correlations, *viz.*, a tilted columnar phase. Longitudinal quadrupoles prevent columnar phase formation.

Analogous to the electric case, the energy of uniaxially ordered quadrupoles depends on the derivatives of the generalized field, *e.g.*, on $\text{div } \mathbf{S}$. This means that quadrupolar steric asymmetry contributes to the higher order elastic moduli (like K_{13} in nematics). A typical example of the effect of S -quadrupoles on molecular ordering gives a smectic phase of mutually interdigitated smectic layers, having a symmetry plane of slip normal to the smectic layers with a translation $\Delta d = d/2$, where d is the layer thickness [84].

In lyomesophases quadrupolar asymmetry may be of importance with α, ω -amphiphiles and integral proteins.

3.3 Biphilic asymmetry

Monopoles. They define the overall hydrophilicity of thermotropic liquid crystals and their ability to dissolve polar or non-polar admixtures. In lyotropics the monopoles are also admixtures, partitioned by the B -field between polar and non-polar zones of the mesophase. The most typical example provides the solubilization phenomenon: hydrophobic monopoles of lower B -charge (*e.g.*, benzene) are localized nearer to the oil/water interface than paraffins. The association of hydrophobic monopoles with the hydrophobic part of B -dipoles (*i.e.*, the solvation of alkyl chains) may change S -asymmetry of the amphiphile and lead to negative spontaneous curvature, *viz.*, inverse phases.

Dipoles. Due to the basic property of B -charges (attraction of equals, repulsion of opposites) the favourable mutual orientation of longitudinal biphilic dipoles is already parallel for lateral neighbours and antiparallel for the longitudinal ones. Besides lamellar lyotropics such interactions are probably important for bilayer smectics A formation: when a strong polar group is situated in one end of the molecule [85], *viz.*, when in a smectogen molecule a separation of a hydrophilic and a hydrophobic part exists. Bilayer structure is simultaneously antiferroelectric.

If the non-polar part of the smectogen is rather bulky (a combination of B -dipole and S -dipole) the appearance of a thermotropic inverse cubic phase (called smectic D) is possible [86,87]. Eventually, one can also search for an inverse hexagonal phase in mixtures with non-polar nonmesogenic substances (hydrophobic monopoles).

An example of antiparallel orientation of neighbours in the longitudinal direction is the dimerization of alkoxybenzoic acids. Hydrophilic groups of these acids (-COOH groups) form dimers by hydrogen bonding [88]. This is a typical hydrophilic interaction. The dimer itself becomes already a B -quadrupole.

As a possible relationship between B -asymmetry (in terms of HLB) and S -asymmetry (in terms of the R-theory) we can consider the correlation of HLB-number and the emulsifying action of detergents [89,52](see Table 1). As we noted, at $HLB \neq 7$ the amphiphile possesses a also non-zero B -charge (according to our notion).

Quadrupoles. The association between longitudinal biphilic quadrupoles of the type middle-middle and end-end is responsible for the monolayer lamellar phases of α, ω -amphiphiles and for the incorporation of integral proteins in membranes in such a way that their two hydrophilic parts are in contact with the two opposing monolayers of the membrane.

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We have suggested [1] that the association of discotic thermotropic mesogens in columns is also connected to the biphilic interactions: hydrophilic centres \leftrightarrow hydrophobic peripheries (in view of the fact that central fragments of discotics are more hydrophilic than alkyl peripheral substituents). However, taking into account the fourth element of generalized asymmetry in our scheme, the F -asymmetry, we are rather of the opinion now that this association is due to the interaction of discotic F -quadrupoles (rigid centre — flexible periphery, see Figure 1). On the other hand, biphilic interaction of B -quadrupoles is certainly specific for the association of discotic amphiphiles [17] in a water environment.

A peculiar example of a rod-like B -quadrupole with rigid hydrophobic boundary, $-\text{COO}^-$ group at one end and $-\text{CF}_3$ group at the other is provided by the antirheumatic drug molecule diethylammonium salt of fluphenaminoacid [90]. These molecules aggregate in bilayers, with $-\text{COO}^-$ groups facing water but, interestingly, the central zone of the bilayers is also hydrophilic (containing a thin layer of hydrated $-\text{CF}_3$ groups). These bilayers contain a large number of defects (pores).

3.4 Flexible asymmetry

The role of this asymmetry for thermotropic liquid crystals was demonstrated earlier [91]. In lyotropics which are, as a rule, entirely flexible this asymmetry has a limited role. In biomembranes it is demonstrated with molecules that combine B -dipoles with F -dipoles (cholesterol) or B -quadrupoles with R -monopoles (integral proteins). Such molecules rigidify their immediate alkyl chain environment, creating a “lipid halo” with a modified orientational order parameter. According to the notion of F -field there will be a tendency for the expulsion of rigid hydrophobic monopoles from the flexible hydrophobic core of the lipid bilayer. In the case of cholesterol (an F -dipole) this tendency is weaker, being dependent on the gradient of F -field. In an earlier investigation of the interaction of the antihelminthic drug Droncit (*i.e.*, 2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4H-pyrazino[2,1-a]isochinolin-4-on) with lamellar phases and liposomes of egg lecithin by various NMR methods (^{31}P -NMR, ^{13}C -NMR, ion permeability for shifting NMR reagents: Eu^{3+} ions) a somewhat strange result of complete rejection of the otherwise fully hydrophobic Droncit molecule by lipid lamellae was obtained (Klose, Gawrisch, Sprinz and Petrov, 1980, unpublished). Presently, we can explain this result by the marked conformational rigidity of Droncit (R -monopole).

4 Conclusion

Let us summarize. We counted above the number of asymmetric combinations of one, two and three elements of generalized asymmetry as a total of

$$11 + 55 + 165 = 231 \text{ asymmetric molecular structures}$$

for rods and discs separately. Here we will count additionally the number of possible field effects. In principle, the 11 elements of asymmetry (E -, S -, B - and F -multipoles) for each of the two basic mesogen shapes (Figure 1) taken separately and by twos in combination with 4 generalized fields lead to

$$4 \times 11 + 4 \times \binom{11}{2} = 264 \text{ field effects.}$$

Even more combinations are possible, *e.g.*, by threes of asymmetries as well as the employment of generalized tensorial fields. By including higher order multipoles (octupoles) such a scheme could also be applied to the description of chiral effects [92].

In conclusion, the generalized multipole model makes it possible to consider a large number of asymmetric molecular structures and a large number of effects created by molecular asymmetry (some familiar and some novel ones) as elements of a common picture. We could see that some combinations do not lead to meaningful effects, while some others may have an equivalent macroscopic manifestation (like flexoelectricity), but a very different molecular background. This, of course, makes it difficult to use some relationships (considered earlier as unequivocal) between measurable macroscopic parameters (like flexocoefficients) and molecular characteristics. Experimental confirmation of predicted novel structures and effects may prove the importance of the generalized multipole model. Three such predictions (pyramidic, amphiphilic and flexible-core discotics) have already been confirmed. This model is also very useful for a unified description of rod-like and disc-like mesogens and of thermotropic and lyotropic liquid crystals. Thus, in a natural way the GMA-model (first proposed in 1981 – [93]) provides a versatile framework for future studies.

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