manner. On page 1896 of this issue (*2*), Yuh and colleagues report that the *Endo16* promoter of the sea urchin *Srongylocentrotus purpuratus* works remarkably like a tiny analog computer: Regulatory inputs from several promoter modules depend on a single module to integrate their status and in turn communicate directly with the basal transcription apparatus to produce a finely tuned response.

In the sea urchin embryo, transcription of *Endo16* commences shortly after gastrulation in all endodermal cells (see the figure) and remains active into late larval stages, by which time it is restricted to the midgut. This seemingly straightforward expression profile is driven by a promoter that consists of more than 30 regulatory elements dispersed through ~2.3 kb of upstream sequence (*3*). As in some other promoters, these protein binding sites are organized into distinct functional modules: three (A, B, and G) are capable of activating expression, and three (DC, E, and F) repress expression in cells that are adjacent to the gut. What makes the *Endo16* promoter so interesting, however, is the multifunctional, integrating role of module A.

Yuh *et al*. carried out an extensive series of quantitative assays that demonstrate how module A operates as the central processing unit of the *Endo16* promoter (see the figure). Its eight regulatory elements have several functions. *Transcriptional activation*: module A alone can activate transcription when one of its sites is bound by SpOtx, a homeodomain transcription factor. *Synergism*: when two other sites within module A interact with module B, transcription increases precisely by a factor of 4.2 over the level of module B alone. *Repression:* another site within module A interacts with module F to repress transcription in inappropriate cells. *Integration*: yet another site within module A interacts with the basal transcription apparatus. In this way, module A integrates and directly communicates the status of the rest of the promoter to the basal transcription apparatus. Furthermore, other experimental observations demonstrate that module A is absolutely required for modules DC, E, F, and G to have any effect on transcription.

To test their understanding of the *Endo16* promoter, Yuh and colleagues wrote a computer model that simulates these regulatory interactions. With the model, they made predictions about the consequences of specific promoter manipulations on transcription levels that were then tested experimentally. That these predictions were largely confirmed demonstrates not only an unusually complete understanding of how a particular promoter functions, but also the degree to which the *Endo16* promoter operates as an analog device. The "program" that runs this tiny computer is directly encoded in DNA as regulatory elements; its inputs are single molecules whose composition varies in time and among various cells of the embryo, and its output is a precise level of transcription.

Are other promoters equally logical? This is not the image that emerges from the literature. Many promoters appear either to have a simpler organization or to operate less logically than that of *Endo16*. On the other hand, few promoters have been examined with the many precise quantitative assays that were carried out by Yuh and colleagues. As the authors point out, only one of the eight regulatory elements within module A is concerned with spatial regulation. Nonquantitative assays would have completely missed most of the functions that the other seven elements encode. Some other promoters, such as the *even-skipped* promoter of *Drosophila*, have a clear modular organization (*4*) and may prove to operate through a single, integrating module as does *Endo16*.

Recasting the genome as thousands of simple computational devices has important implications for thinking about the evolution of genetic pathways. Little is known about how promoter structure and function evolve. To some extent, this is because the kinds of clear structure-function relations that guide our understanding of how proteins and morphology evolve are simply lacking for promoters. The results of Yuh and colleagues offer hope that the seemingly haphazard operation of animal promoters might become more comprehensible to developmental and evolutionary biologists alike.

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LIQUID CRYSTALS

Chiral Order from Achiral Molecules

Gerd Heppke and Dirk Moro

Chirality, the handedness of matter, and ferroelectricity, resulting from macroscopic electric polarization, are properties that had been believed to exist independently from each other. However, liquid crystals show a remarkable interplay between these phenomena, a fact that has great technological significance for display devices. Up to now, these ferroelectric displays use liquid crystals, which need to possess a chiral molecular structure. But in 1996, Niori *et al*. reported that a similar ferroelectric switching was observed in a liquid-crystalline phase formed by achiral molecules with a bow-shape resembling the form of a banana (*1*). Even though the molecules are achiral, these materials are able to form macroscopic chiral domains and, as Link *et al*. reported in a recent paper in *Science*, exhibit a spontaneous breaking of achiral symmetry in a bulk liquid crystal (*2*).

Max Born introduced the idea of creating a polar fluid as early as 1916 (*3*) in order to explain the formation of a nematic phase by dipolar interaction between the permanent dipoles of rodlike molecules. Although the proposed mean-field model was able to predict a transition from an isotropic phase to an anisotropic one, it had two major deficiencies. First, the dipolar interaction of the permanent dipoles of molecules forming nematic phases is too weak to produce a phase transition at room temperature, where it occurs. Worse, nematic phases are also formed by molecules that do not possess a permanent dipole at all. Second, the resulting anisotropic order of dipoles is such that, on average, the dipoles point in the same direction, so that an inherently ferroelectric fluid was predicted, but such a polar order was never found experimentally in nematic liquid-crystalline phases. Actually, the rod-shaped molecules exhibit a preferred parallel orientation, and even when the molecules bear a permanent dipole, there are, on average, as many dipoles pointing "up" as there are dipoles pointing "down."

According to this picture of the nematic phase, it was accepted for a long time that macroscopic polar order could not exist in liquid-crystalline phases in general. However, this view had to be revised when Meyer *et al*. (*4*) showed by a simple symmetry argument that layered liquid-crystalline

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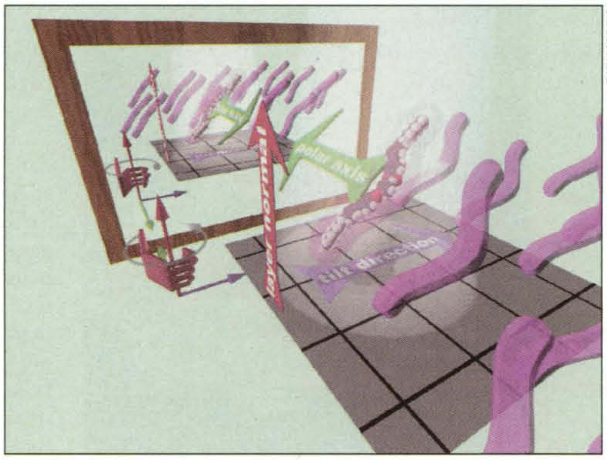
phases consisting of molecules that are tilted in the layer with respect to the layer normal show ferroelectricity if the molecular structure is chiral. Symmetry allows the occurrence of a spontaneous electric polarization along a direction perpendicular to both the layer normal and the tilt direction. Enantiomeric molecules (that is, molecules that are mirror images of each other) generate a spontaneous polarization of same magnitude but pointing in opposite directions. Thus, in racemic mixtures, which contain both enantiomers in equal amounts, the electric polarization vanishes. Obviously, the electric polarization is directly connected with molecular chirality in these ferroelectric liquid crystals.



DIRK MORO

All in a row. Schematic representation of one polar chiral layer consisting of achiral bent-core molecules (purple rods). The molecules are parallel to each other, the long axis being tilted with respect to the layer normal (vertical red arrow). Owing to the bent core of the molecules, each one possesses a dipole moment (green arrow) in the molecular plane and perpendicular to the long axis of the molecules. The layer normal, tilt direction (blue arrow), and the polar axis define a right-handed coordinate system (denoted by curled fingers), whereas in the mirror image, these vectors define a left-handed system, demonstrating the chirality of the layer structure.

The liquid-crystal community was fascinated with the possibility of creating a polar fluid from chiral molecules. When high-speed bistable electro-optic switching was demonstrated with this type of liquid (*5*), hundreds of chiral ferroelectric liquid crystals were synthesized. Ferroelectric liquid crystals have turned into a major liquid-crystal subfield, and flat-panel displays with a high information content made with these materials are currently commercialized. It became widely accepted that polar order in liquid-crystalline phases is possible, but only if the molecules are chiral.

Although several attempts were undertaken to achieve polar order with achiral molecules—by making bowl-shaped molecules that intrinsically stack into polar columns, or by means of chemical segregation of distinct chemical subspecies (polyphilicity) or even more complex systems, such as polymers with side-chains organized in a fishbone geometry—it was only when Niori *et al.* presented evidence for ferroelectric switching in a layered liquid-crystalline phase consisting of achiral bent-core molecules (*1*) that polar order in fluids in the absence of chirality were the focus of interest again. Motivated by this observation, several groups throughout the world started to work on these materials. Recently, Link *et al.* proposed a structural model (see figure) based on the spontaneous formation of chiral layers in a liquid-crystalline phase consisting of achiral molecules (*2*). At a workshop (*6*) held in Berlin last December, it turned out that the model is consistent with the observations obtained with different experimental techniques.

Because of the bent-core of this new type of liquid-crystalline molecule, a steric packing is favored, where all molecular "bows" point in the same direction, thereby defining a polar axis. Similar to normal smectic liquid-crystalline phases, the position of the molecules in space is periodically modulated along one direction, resulting in a layered structure of the fluid. Additionally, the common direction of the molecular long axis within these layers is tilted with respect to the layer normal. Now, each layer as a whole is chiral (see figure), despite the fact that the individual molecules are achiral. This ordering means that for a given tilt direction, two equivalent layer structures with antiparallel polar axes can exist, such that they are mirror images of each other. Because no molecular chirality is present, both enantiomorphic structures are realized with equal probability. Yet surprisingly, it was found that rather large macroscopic domains of same chirality are formed. This observation establishes for the first time a spontaneous breaking of achiral symmetry in bulk liquid crystal.

The tilt direction is arbitrary in the absence of an external field, but because an electric polarization exists perpendicular to the tilt direction and layer normal in each layer, the polar axis, and thereby the tilt direction, can be controlled by application of an electric field. Indeed, such ferroelectric switching was confirmed experimentally and moreover is found to be a hundred times faster than conventional nematic liquid-crystalline mixtures used for display applications. Domains of opposite chirality switch in opposite directions, which is easily seen under a polarizing microscope.

It should be noted that even before the discovery of ferroelectricity in liquid crystals, de Gennes mentioned in his famous textbook (*7*) a generalized type of a tilted smectic phase that would differ from its mirror image; if the constituent molecules were achiral, they would build up enantiomers. The achiral bent-core molecules can be regarded as a manifestation of this theoretically discussed phase, and moreover, they show ferroelectric switching. The chirality in these materials is a consequence of the polar order induced by the steric packing of the bent-core molecules, whereas in the ordinary ferroelectric liquid-crystalline phases (*4*), polar order is a consequence of the molecular chirality.

But this remarkable circular odyssey between ferroelectricity and chirality in liquid-crystals research is not the whole story: one more point should be added. Generally, in liquid-crystalline phases, the presence of molecular chirality leads to the formation of helical superstructures, essentially characterized by a spiraling of the mean orientation of the molecules around an axis. Such an induced twist was not observed for achiral molecules.

Again, the bent-core molecules show an unexpected behavior. Although the molecules do not possess a chiral structure, circular dichroism and optical rotation is observed in a certain phase exhibited by these molecules (*8*), indicating the presence of a helical superstructure, which is also directly revealed by atomic force microscopy. It seems that the chirality of individual molecules is here replaced by the chirality of the layer, now acting as a whole as a chiral object, which induces the helical superstructure. Altogether, these bent-core molecules have demonstrated that chirality in soft condensed matter means more than just a chiral center in a molecule.

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