microflora for which they provide evidence are highly unlikely to alter gastrointestinal function or endanger human health. I would conclude, however, that whereas this may be true for the construct examined by Gilbert's group, it may not be true in other cases, such as genes that encode resistance to antibiotics used in human medicine.

Netherwood *et al.* call on risk assessors to consider the possibility of trans-kingdom gene flow in the future safety assessment of GM foods[1]. I endorse that conclusion and would extend it by adding that every case must be considered on its own merits.

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Label-free detection becomes crystal clear

Paul S Cremer

Liquid crystalline platforms offer fast, simple and inexpensive detection of incoming analytes on two-dimensional fluid biomembrane mimics.

The binding of ligands to cell membrane–bound receptors plays a critical role in a wide range of fields from cell-cell signaling and lymphocyte trafficking to the immune and inflammatory responses[1–2]. For example, the initial step in pathogen attack on a human host usually involves the binding and rearrangement of cell surface moieties by the incoming virus or protein toxin. Moreover, it is generally estimated that half of prescription drugs target membrane-bound receptors[3]. Only a handful of widely applied techniques are available for monitoring ligand-receptor binding. Most of them either require a label to be attached to the incoming analyte or involve complex optical and surface patterning methods for readout. This has motivated the search for label-free assays to rapidly detect protein-membrane interactions without requiring special optics, temperature control or thin film metal surfaces. As a step toward this goal, Brake *et al.*[4] report in *Science* the use of a thermotropic liquid crystal, 4′-pentyl-4-cyanobiphenyl, as a responsive support for phospholipid monolayers.

Phospholipid monolayers and bilayers are becoming ubiquitous for modeling the complex biophysical mechanisms of protein-cell membrane interactions[5]. They have significant potential for use as sensor devices to detect pathogens in clinical settings or even as continuous monitors of biological warfare agents. The advantage of these systems lies in their maintaining many of the properties of natural cellular membranes without the complications arising from using whole cell assays. One of the most important properties that phospholipid bilayers and monolayers share with whole cells is their two-dimensional fluidity. Individual lipid molecules are free to diffuse around the surface and membrane-bound ligands can reorganize in the presence of a protein, viral or bacterial analyte that contains multiple binding sites. Indeed, such multivalent ligand-receptor binding is a dominant motif of protein-cell membrane interactions[6–8].

Brake *et al.* have combined such phospholipid monolayers with a thermotropic liquid crystal to create a device that can rapidly detect incoming analytes. Their liquid crystal belongs to the same class of molecules that are found in digital watches and liquid crystal displays. The liquid crystal sensor device directly transmits information on protein binding from the thin phospholipid film to the outside world. The method works by reorienting the liquid crystal molecules beneath the portion of the monolayer at which proteins bind (see **Figure 1**).

In their report, the authors demonstrate that assays based on liquid crystals can easily be used to detect ligand-receptor interactions. For example, the binding of phospholipase A_2 (PLA_2) to phospholipid membranes was fol-

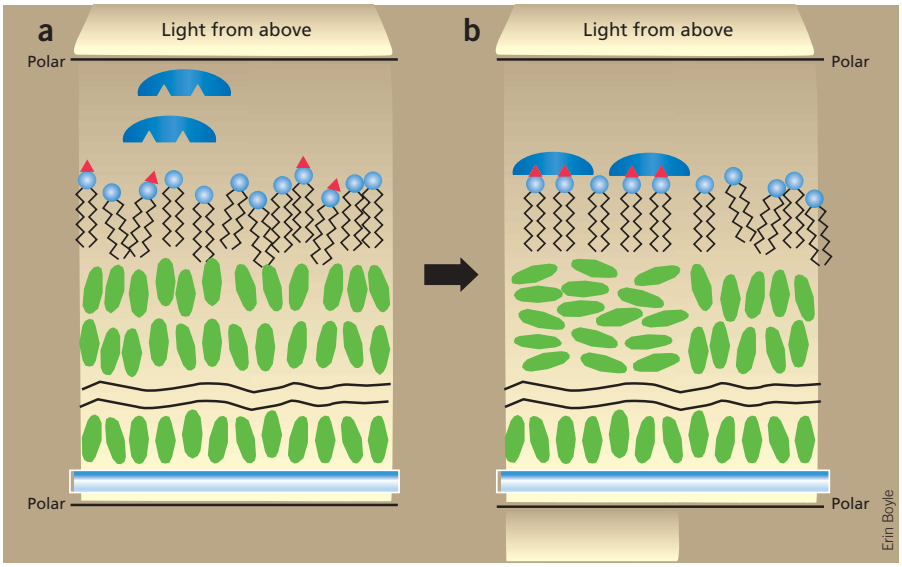

Figure 1 Molecular interactions at a phospholipid coated surface on a liquid crystal.(**a**) Proteins approach a surface containing a thermotropic liquid crystal reservoir coated with a lipid monolayer. (**b**) The membrane contains specific ligands (shown in red) that specifically bind to the incoming protein (blue). This causes the liquid crystal molecules beneath the bound proteins to realign. Light sent through crossed polars passes through the region where the realignment took place, whereas the areas containing the vertically aligned species remain dark.

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lowed with high specificity in the presence of only nanomolar concentrations of this enzyme. It was even possible to obtain rudimentary kinetic information on the hydrolysis of L-α-dilauroyl phosphatidylcholine (DLPC) to its lysophospholipid products by enzymatic action, a process that took place over tens of minutes.

The authors also show that the ubiquitous biotin-neutravidin interaction can be monitored. This very tight ligand-receptor interaction leads to two-dimensional protein crystallization on lipid monolayers through the organization of neutravidin molecules into dendritic patterns at the interface[9]. In fact, the same patterns of protein crystals were found using the liquid crystal detection scheme as are seen through the more common fluorescence imaging method.

The mechanism by which the liquid crystal detection scheme operates is still not completely clear. However, in the case of PLA_2 binding, the tilt angle of the lipid alkyl chains is attenuated as a result of an increase in the packing density of the phospholipid monolayer[10]. This conformational change must somehow lead to a change in orientation in the liquid crystals. A similar process presumably occurs upon the crystallization of neutravidin.

Future studies will be important to determine the exact mechanism by which binding information is transmitted from the protein analytes to the liquid crystal layer. It will also be necessary to test this detection mechanism against other ligand-receptor interactions to determine whether it can be considered universal. Another significant step for this technique will be to find its lower detection limit. Even if it doesn't ultimately prove to have single molecule capabilities like fluorescence, it will be highly convenient if merely 10^8 proteins/cm^2 can be followed.

It will also be interesting to test the platform in other applications. One potential use for the liquid crystal system would be to follow lipid raft formation because the liquid-condensed domains of the raft consist of less tightly packed lipid molecules than the surrounding liquid-expanded regions. Finally, it would be valuable to see if this method could be expanded to phospholipid bilayers as these systems are usually necessary for the presentation of transmembrane proteins at the sensor interface.

The technology described by Brake *et al.* represents a first step toward the development of new approaches for studying interface processes and for detecting the presence of specific biological species in aqueous environments. Similar to many other areas of human endeavor, liquid crystals may be set to transform the way we go about biological detection.

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