has a selectivity similar to the antagonists now described although it is considerably less potent. The Sandoz researchers first synthesized analogues of serotonin and discovered compounds that selectively mimicked its effects on neurones or on smooth muscle. This knowledge was used to synthesize antagonists with selective action on neurones in which the serotonin side-chain nitrogen is incorporated in a tropane ring, as in cocaine (see figure).

Interest in serotonin pharmacology has been particularly strong in the past few years. New generations of antidepressant agents are emerging that act by inhibiting the re-uptake of serotonin after its release from synaptic terminals in brain, thus enhancing its synaptic actions[7]. It has also been reported recently that novel anti-anxiety drugs of the buspirone type may act by selective stimulation of serotonin receptors in brain, although the precise category of sites involved remains unclear[8]. Receptors for serotonin of the type that are blocked by the new antagonists have not yet been identified in the central nervous system but their presence there would not be surprising.

As so often in pharmacology, the discovery of novel drugs with selective antagonist actions will undoubtedly allow rapid progress to be made in defining the occurrence and functional significance of a hitherto obscure class of monoamine receptors. □

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Surface structure

X-ray reflection from liquids

from Stuart A. Rice

In an important paper in *Physical Review Letters*, A. Braslau *et al.* report measurements of the surface roughness of water deduced from the scattering of X rays reflected from the surface[1]. To do so, they have introduced a new way to interpret the reflectivity data. This and related advances are beginning to revolutionize the understanding of liquid surfaces.

For two decades there has been a steady stream of improvements in the scope and sensitivity of techniques with which to study the atomic and electronic structures of surfaces. Many of these techniques use electrons as probes, or detect electrons, or both. Unfortunately, because electrons interact very strongly with the atomic charge distribution, the interpretation of electron-scattering data usually requires removal of the contributions to the signal from multiple scattering processes, which cannot at present be carried out for liquid surfaces. Unlike electrons, X rays are weakly scattered by the atomic charge distribution, and two X-ray techniques have recently been introduced to study surfaces: X-ray reflectivity as a function of angle of incidence, and grazing incidence X-ray diffraction. Both can be used to study liquids as well as solids.

That X rays will be totally reflected from a condensed medium if the angle of incidence is less than some critical value was predicted and first demonstrated by A.H. Compton in the 1920s[2]. The thrust of the work in the following decade was concerned with the determination of the refractive index of matter at X-ray frequencies, assuming the sample to be homogeneous up to a planar surface, treated as a geometrical discontinuity. It was not until 1954 that L.G. Parratt suggested inverting the analysis and interpreting X-ray reflectivity as a function of angle of incidence via models of the inhomogeneous surface-density distribution[3]. This suggestion lay dormant for twenty years, until B. C. Lu and S. A. Rice[4] adapted it to provide information about the surface structure of liquid mercury. Other applications[5,6] are rare.

X-ray reflectivity as a function of angle of incidence is sensitive to the distribution of density perpendicular to the surface; the greater the range of incident angles for which measurements can be made, the more accurate will be the inferences drawn about the surface density profile. The dynamic range required for such experiments is large — of the order of 10^7 to 10^8 — so synchrotrons are the favoured X-ray sources. The data can be interpreted by two means. In one, a model of the surface-density distribution is assumed and the predicted X-ray reflectivity is compared with that observed. Alternatively, the data can be interpreted in terms of some model-independent parameter that is characteristic of the density profile.

It is the second means of interpretation that has been introduced by Braslau *et al.* They show that the reflectivity data they obtain can be interpreted in terms of the mean square roughness of the surface without prescribing the molecular mechanism by which the roughness is generated. The value they obtain for this measure of the surface density profile is 3.24 ± 0.05Å. A molecular dynamics simulation of a rigid charge distribution model of water[7] shows that the density falls smoothly through the liquid–vapour interface with a characteristic width of 3.56Å; the deviation between these values provides one measure of the inadequacy of the model potential used in the molecular dynamics simulation.

As expected, total external reflection of X rays is accompanied by fluorescence and, very recently, this has been exploited to study the properties of solid and liquid surfaces. Smirnov[8] has shown that measurement of the fluorescence intensity as a function of angle of incidence of the exciting X rays can be used to infer the density distribution perpendicular to the surface — in his case, for a film of germanium deposited on glass. In an independent development, Bloch *et al.*[9] have used the same kind of measurement to infer the concentration profile of a dissolved polymer in the solution–vapour interface.

To date, the only reported application of grazing incidence X-ray diffraction to a liquid is by J. Als-Nielsen and P. S. Pershan[10] who measured the interplanar spacing perpendicular to the surface of a smectic-A liquid crystal. The interpretation of the X-ray diffraction pattern in terms of the in-plane distribution of molecules in a liquid–vapour interface is more difficult than for a solid, because removal of the contribution to the X-ray scattering from atoms below the surface requires knowledge of their distribution as a function of density. Whereas the atomic distribution in a crystal substrate is substantially the same up to the outermost plane of atoms, the variation in distribution in the 2–3-atom thick, inhomogeneous liquid–vapour interface is important. Nevertheless, guided by computer simulations, it should be possible to obtain useful information about the in-plane distribution of atoms and molecules in a liquid-vapour interface.

The availability of powerful tunable X-ray sources is likely greatly to increase our information base and understanding of liquid surfaces. A few of the possibilities we can expect in the next few years are studies of the structure of films supported on liquids and of phase transitions in those films; measurements of the influence of oxidation on the structure of the liquid surface; and investigations of the spatial distribution associated with the excess surface concentration of a component of a mixture. □

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