

Structure and dynamics of amphiphilic aggregates at air/solution interfaces en route to crystal formation

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Abstract: The structure and dynamics of embryonic aggregates at the air/water or air/solution interface en route to crystal nucleation have been probed by applying a variety of techniques including stereospecific photochemistry, Second Harmonic Generation (SHG), Grazing Incidence X-ray diffraction and oriented crystallization methodologies. This approach is illustrated by three different systems: oriented crystallization of 4-Hydroxybenzoic Acid Monohydrate (HBA) by 4-Alkoxybenzoic Acid, photochemistry of 4-Methoxy-E-cinnamic acid at the air/solution interface and the induced nucleation of ice by amphiphilic alcohols.

The understanding of the dynamics of the phase transformation from a supersaturated solution into a crystalline solid requires the knowledge of the structure of the supersaturated solution at the onset of crystallization. In particular, it is of great interest to delineate the role played by structured aggregates as intermediates in crystal nucleation. In the absence of analytical tools which enable us to determine the structure and dynamics of these embryonic clusters of precritical size, we are forced to design appropriate systems, and to apply a variety of novel methodologies.

In the present lecture we shall discuss the self-assembling of amphiphilic molecules at the air/solution interface and their functionality as transient species en-route to crystal formation. A variety of analytical techniques were used including stereospecific photochemistry, Second Harmonic Generation (SHG), Grazing Incidence X-ray Diffraction (GIXD) and oriented crystallization. The approach is illustrated with some representative systems.

4-HYDROXYBENZOIC ACID MONOHYDRATE(HBA)/4-ALKOXYBENZOIC ACIDS (refs. 1,2)

In the first example we shall describe the oriented crystallization of 4-Hydroxybenzoic acid at the air/solution interface. HBA monohydrate crystallizes from aqueous solutions as elongated plate-like crystals, usually at the bottom of the crystallizing dish. Addition of 5% (wt/wt) 4-methoxybenzoic acid (MBA) to the solution induces fast nucleation of the crystals floating at the solution surface. These crystals nucleate and appear attached at the interface via a newly expressed (401) face. Additives such as benzoic acid 4-methyl, 4-fluoro, 4-isopropyl and 4-tert-butylbenzoic acids do not induce the above mentioned effect.

Analysis of the packing arrangement at the (401) crystal face (Fig. 1) reveals that the HBA molecules lie parallel to this plane forming hydrogen-bonded dimers. These dimers are interlinked by hydrogen bonds involving the phenolic-OH groups and water molecules. The induced crystallization of HBA at the air/solution interface can be explained by the formation of surface aggregates of the additive molecules whose structure mimics that at the (401) crystalline face. In such aggregates the 4-oxybenzoic moieties would lie flat on the surface so as to form the hydrogen-bonded dimer, while their aliphatic chains should emerge from the solution (Fig. 2). At first glance, such an arrangement may appear to be counter intuitive but, we propose that the specific interactions with the HBA molecules in solution should stabilize this 2-D motif.

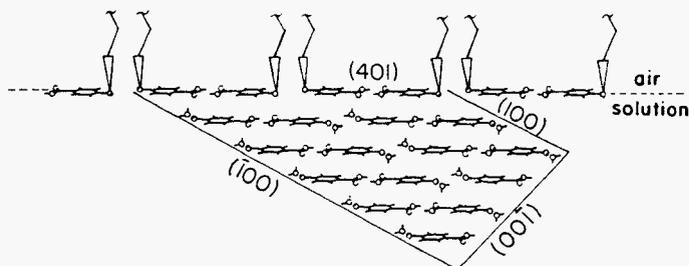


Figure 1: Packing arrangement of HBA crystal with the (401) face viewed 'edge-on', delineated by the crystal faces. The layer of molecules at the interface is the Langmuir film (represented schematically).

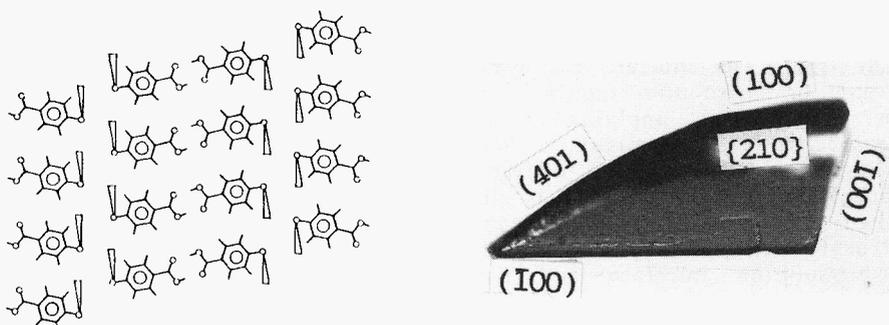


Figure 2: (left) Proposed aggregate structure viewed perpendicular to the HBA subphase; (right) Photograph of HBA crystals.

In order to elucidate the mechanism by which the nucleation occurs, we studied the oriented crystallization of HBA as induced by model amphiphilic molecules 1-6 (Table 1), forming monolayers at the air/solution interface.

Table 1

No.	Name	Structure
1.	4-(hexadecyloxy)benzoic acid	HOOC-Ph-O-(CH ₂) ₁₅ -CH ₃
2.	4-(hexadecylamino)benzoic acid	HOOC-Ph-NH-(CH ₂) ₁₅ -CH ₃
3.	4-(hexadecanoyloxy)benzoic acid	HOOC-Ph-OCO-(CH ₂) ₁₄ -CH ₃
4.	4-(hexadecyloxy)phenylacetic acid	HOOC-CH ₂ -Ph-O-(CH ₂) ₁₅ -CH ₃
5.	3-[4-(hexadecyloxy)phenyl]propionic acid	HOOC-(CH ₂) ₂ -Ph-O-(CH ₂) ₁₅ -CH ₃
6.	Octadecyl-4-hydroxybenzoate	HO-Ph-COO-(CH ₂) ₁₇ -CH ₃

Analogous to the case of the soluble additive 4-methoxybenzoic acid, (401) oriented nucleation of HBA crystals was also induced at the air/solution interface when amphiphiles 1,2 or 3 were spread on the supersaturated solutions. On the other hand amphiphilic molecules 4,5 and 6, of a slightly different structure, did not induce HBA crystallization at the interface.

In order to understand the different effects on the crystallization imparted by the various monolayers 1-6 we have studied their behavior at the air/solution interface. The presence and orientation of the amphiphilic molecules as a function of HBA concentration were determined by Second Harmonic Generation (SHG) and Surface Pressure-Area isotherms.

The significant change in the π -A isotherm of the amphiphilic 2 as a function of HBA concentration in the subphase is shown in Fig. 3.

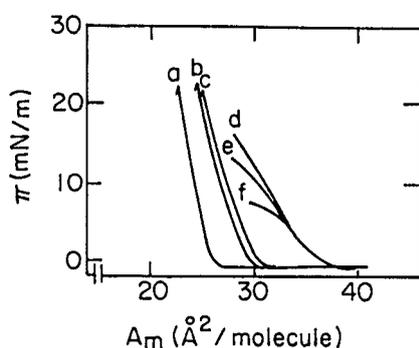


Figure 3: π -A isotherms of 4-(hexadecylamino)benzoic acid monolayer spread on various subphases: a) water; b) 14.2 mM HBA; c) 20 mM; d) 28.4 mM; e) 56.8 mM f) 80.5 mM (solution for crystallization).

Second Harmonic Generation is a surface specific technique which can determine the presence and orientation of surface adsorbates on centrosymmetric and isotropic substrates. The experimental set-up for SHG is depicted in Fig. 4.

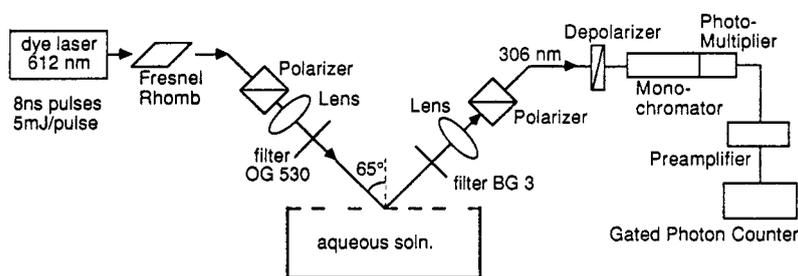


Figure 4: SHG experimental set-up.

The orientation of the major nonlinear optical axis (here the polar $\text{XC}_6\text{H}_4\text{COOH}$ head group) of the amphiphile relative to the surface normal can be determined [3] from two independent SHG measurements - such as from the ratio of the s- and p-polarized SHG signals generated by a 45° polarized input laser (I_{45-s} and I_{45-p} respectively). From these measurements we can obtain the value of β , the second order nonlinearity per molecule.

Amphiphiles 1,2 and 6 spread on water all exhibited SHG signals considerably stronger than that of the bare water subphase, and $\langle\theta\rangle$ values in the range 24° - 47° (Table 2). The bare HBA subphase had an SHG intensity similar to that of water. The SHG signal of 6 spread on HBA solution was the same as on water, while full monolayers of 1 and 2 on HBA behaved differently. The total SHG signal in these two cases was about the same as that of the bare HBA solution. This is entirely consistent with our model since the lack of SHG from the compounds 1 and 2 means that their polar moiety $\text{XC}_6\text{H}_4\text{COOH}$ lies flat ($\theta = 90^\circ$) on the HBA solution surface [4].

Table 2
SHG signals and orientations for monolayers on various subphases

Monolayer	ON WATER				ON HBA		
	I_{45-s}	I_{45-p}	$\theta(^{\circ})$	$\beta(\text{esu})$	I_{45-s}	I_{45-p}	$\theta(^{\circ})$
Bare Subphase	1	0.6			0.4	0.8	
1	10	40	24	2×10^{-30}	same as subphase		90
1 80% cov.	7	30	24	2×10^{-30}	7	30	24
2	450	150	42	7×10^{-30}	same as subphase		90
6	150	40	47	3×10^{-30}	150	40	47

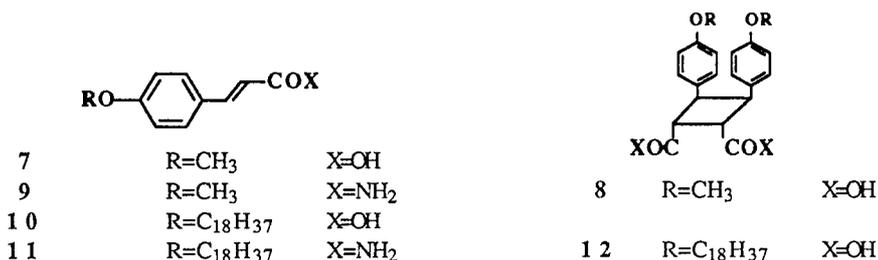
The absence of SHG signals from these monolayers on HBA could in principle arise from another reason - the formation of a bilayer (at any angle to the surface), between one HBA molecule from the solution and an amphiphile molecule, leading to cancellation of their nonlinearities. This might be possible (at least in principle) for the monolayer of 1 but can be discounted for 2 due to the large difference in β values of the 4-hydroxybenzoic and 4-aminobenzoic chromophores. Thus the SHG results can only be explained by monolayers of 1 and 2 lying flat ($\theta = 90^\circ$) on the solution surface. At 80% of the full monolayer coverage the $\langle\theta\rangle$ value of 1 spread on HBA is the same as on water, implying that its interaction with solute molecules at this coverage density is insufficient to change the orientation.

The fact that the HBA subphase can drastically alter the surface alignment of monolayers of 1 and 2 but not the closely related monolayer of 6 demonstrated how specific the solute-amphiphile interactions can be. We have further demonstrated this by checking the SHG of 1 spread on an aqueous solution of 4-hydroxyphenylacetic acid (HO-Ph-H₂-COOH). Over this solution, the monolayer of 1 shows exactly the same SHG signal strength and $\langle\theta\rangle$ value 24° as on pure water, indicating the loss of the strong solution/amphiphile interaction with a minor change of the solute molecule.

4-METHOXY-E-CINNAMIC ACID (MCA) (ref. 5)

In order to throw additional light on the nature of the early self-aggregates of MCA at the air/water interface, we have probed their structure by topochemical photodimerization.

It could be shown, by two entirely independent techniques, that MCA 7 solute molecules are sufficiently hydrophobic to accumulate at the air/solution interface. Surface tension measurements as a function of solution concentration result in the surface accumulation parameter, using the Gibbs equation. The SHG signal from the surface of a saturated MCA solution which, unlike HBA, is significantly greater than that of water, can be compared to that generated by a Langmuir monolayer of the long chain analog 10. The average value of the surface coverage in a saturated MCA solution obtained using these two methods was ~30% [6].



Structural considerations, based on packing modes of molecules in crystals, suggest that the MCA molecules should form at the air/solution interface, close-packed stacks of "translationally" related molecules, separated by 4.0Å, stabilized by aromatic ring interactions and coulombic forces between the carboxyl groups. This organization should influence the photochemical behavior of these molecules as was established from photoreactivity in the crystalline state. Thus while MCA trans-cis photoisomerizes in the bulk solution, as do all (E)-cinnamic acids, the self-organized molecules at the interface are expected to undergo a $2\pi+2\pi$ photodimerization leading to the mirror-symmetric cyclobutane, 4,4'-dimethoxy- β -truxinic acid 8.

In order to differentiate between products formed in the bulk of the solution and at the interfaces, aqueous solutions of MCA were irradiated in two different experimental setups: closed glass vessels completely filled with solution and open glass vessels with a large solution/air interface (Fig. 5). Irradiation of the solution in the closed vessel resulted in a trans:cis ratio of about 1:3, whereas the open vessel yielded, in addition, formation of 5-20% of the photodimer 8, depending upon the exposure time. The molecular organization at the surface could be gradually removed by addition of EtOH (35%) to the solution, as made manifest of the formation of only traces of the photodimer 8.

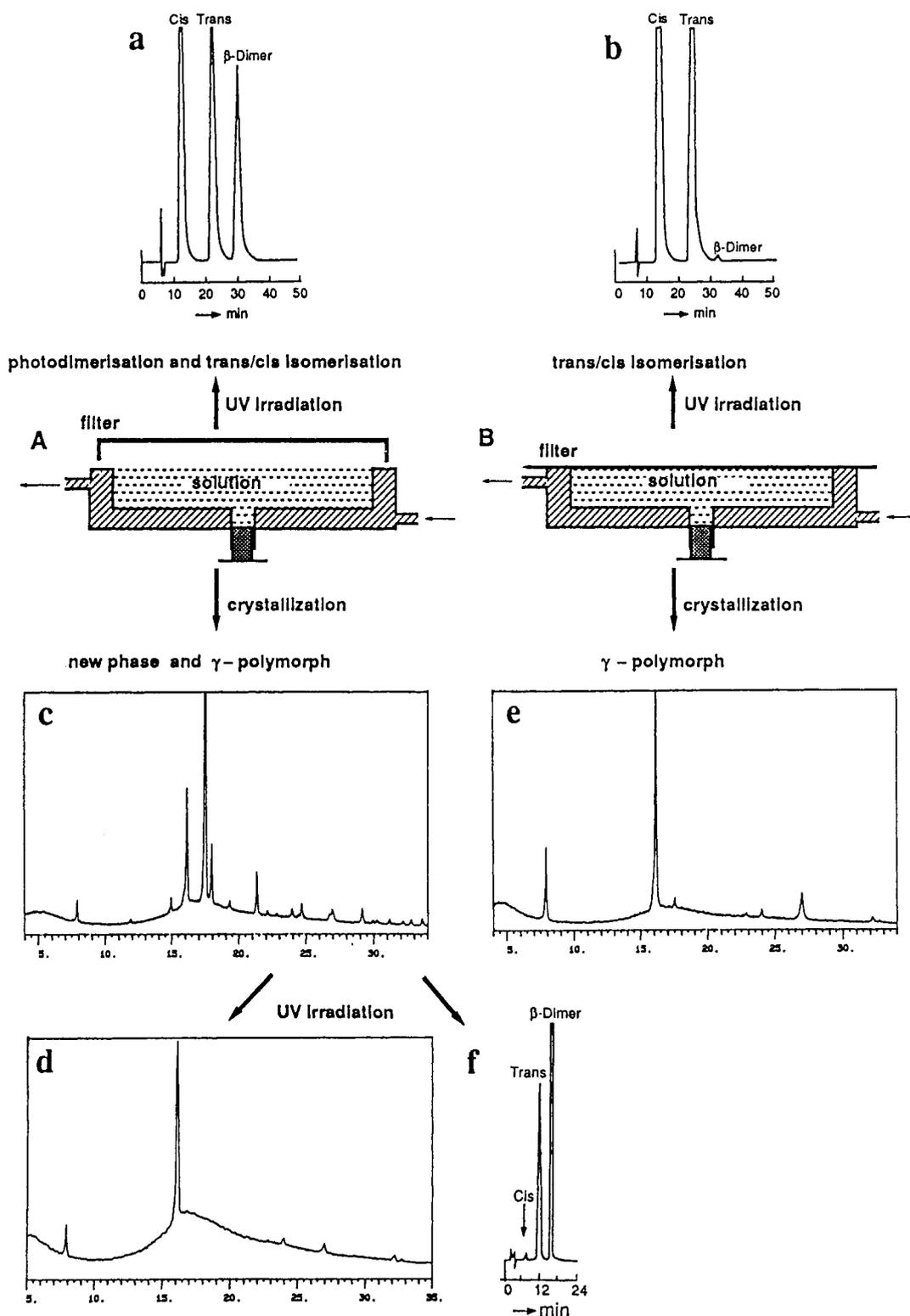


Figure 5: Schematic drawing of the two experimental set-ups: A) open vessel; B) closed vessel. HPLC analyses of the solution irradiated in the two types of vessels. a) sample from open vessel; b) sample from closed vessel, X-ray powder patterns of the crystalline materials; c) sample precipitated in the open vessel; d) sample as in (c) after solid-state irradiation; e) sample precipitated in the closed vessel; f) HPLC analysis of the sample as in (d).

A similar structural analysis of the 4-methoxy E-cinnamamide 9 implies that it should organize, at the interface, into two-dimensional clusters within which the molecules form close-packed stacks interlinked by N-H...O=C hydrogen bonds. Because the hydrogen-bonding repeat distance is about 5.5Å, in this arrangement the C=C double bonds will be separated by too large a distance to allow photodimerization. Indeed, irradiation of aqueous solution of 4-methoxy-E-cinnamamide in the two experimental setups yielded only trans/cis isomerization in a ratio of 1:3.5.

Similar photochemical behavior was observed with the use of insoluble amphiphilic analog 4-octadecyloxy-E-cinnamic acid 10 and amide 11 spread on water subphase in a Langmuir trough, either in the compressed or in the uncompressed state with a surface coverage of 50-80%. Here again, while the acid yielded about 10% of the mirror dimer 12 and ~16% of the cis isomer, the amide monolayer underwent only a trans/cis isomerization in both the compressed and the uncompressed states.

In order to probe the role played, if any, by the ordered self-aggregates of MCA at the interface in promoting the formation of new crystalline forms, this material was precipitated from aqueous solutions, by cooling, in the two experimental setups. The crystallization experiments in the open vessel yielded a new crystalline phase, which precipitated together with the known phase, previously defined as the γ -form. Such samples display four new and distinct diffraction peaks with d-spacings of: 6.0, 5.1 and 4.2Å.

Solid-state U.V. irradiation of the mixture of the crystalline phases yielded the mirror photodimer 8. This dimer must arise from the new crystalline phase because the γ -form is light stable and the diffraction peaks associated with the new phase disappear upon irradiation.

From the crystallization experiments performed in the closed vessels, the γ -phase precipitates, either in pure crystalline form (50% of experiments) or with only small amounts of the new phase.

The formation of the mirror-symmetric β -dimer from irradiation of the solutions in the open vessel and from the solid precipitated in the same vessel strongly suggests the formation of ordered two-dimensional aggregates at the air/solution interface. Furthermore, the common feature of the mirror molecular symmetry of the dimer implies that the molecules are stacked by "translation symmetry" within the clusters at the interface and in the new polymorph.

Thus it is reasonable to deduce that clusters formed at the interface are nuclei en route to crystal formation.

INDUCED NUCLEATION OF ICE BY AMPHIPHILIC ALCOHOLS (ref. 7)

In the previous two studies the formation and dynamics of the structured clusters has been deduced indirectly. The recent availability of the new method of grazing incidence X-ray diffraction (GIXD) using bright monochromatic and highly collimated light from synchrotron sources provides an entry into the structure of 2-D crystalline aggregates, almost at the atomic level. In the next example of the induced nucleation of ice we shall illustrate this approach [7,8].

Water-soluble alcohols generally reduce the freezing point of water. In contrast, we expected, on the basis of GIXD studies of compressed Langmuir films of heneicosanol (C₂₁H₄₃OH) [9], that insoluble amphiphilic alcohols at the air/water interface might form 2-D crystalline domains with structure akin to that of hexagonal ice and thus act as ice nucleators. The unit cell of the crystalline monolayer at temperatures just above 0°C, is distorted hexagonal with axes $a=b=4.5\text{Å}$, $\gamma=113^\circ$, and area per molecule $a^2\sin\gamma=18.6\text{Å}^2$. Thus the arrangement of the OH head groups of the alcohol at the water surface would appear to mimic or complement the (001) face of hexagonal ice since the ice has unit cell dimensions $a=b=4.5\text{Å}$, $\gamma=120^\circ$. The proposed structural match between the monolayer and the layer of ice in the ab plane, suggested that such a monolayer should be an efficient nucleator of ice.

Indeed this expectation was confirmed experimentally by measuring the freezing points of supercooled water drops covered by aliphatic alcohol monolayers [8]. Comparative measurements were done using the alcohols and the corresponding acid as a

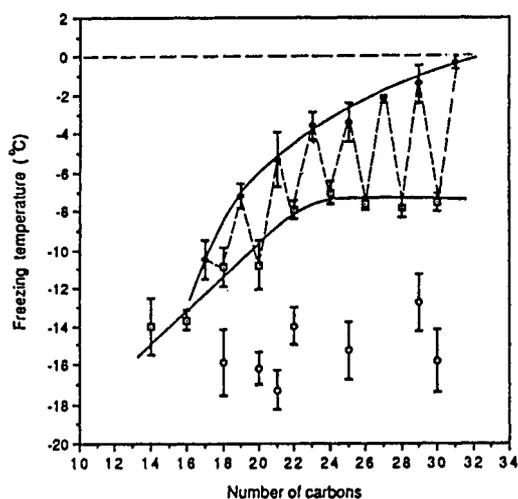


Figure 6: Freezing points of drops of supercooled water covered by monolayers of alcohols $C_nH_{2n+1}OH$ (n even \square and odd \diamond) and carboxylic acids (\circ).

reference. Fig. 6 summarizes some results of freezing points induced by amphiphilic alcohols and acids. The freezing point is sensitive to the length and parity of the chain. The curve for the n -odd series increases asymptotically with chain length, approaching 0°C for $n=31$. The n -even series behaves differently, the freezing point curve reaches a plateau of about -8°C for n in the range 22 to 30.

Grazing angle X-ray diffraction measurements on several monolayer alcohols ($n=23,30,31$) and on one acid ($n=30$) over pure water at 5°C , were performed in uncompressed state at $\sim 70\%$ surface coverage. Diffraction peaks observed for all films indicated the formation of self-aggregated crystalline domains with anisotropic coherence lengths of ~ 300 and 1000\AA [10].

The cell dimensions (Table 3) show a good lattice match between the ab lattice of ice and the lattices of the alcohols (Fig. 7) but not with the acid monolayer. However, at present we cannot account for the observed differences in ice nucleation from the minor differences in cell dimensions and molecular tilt angles between the various odd and even alcohols.

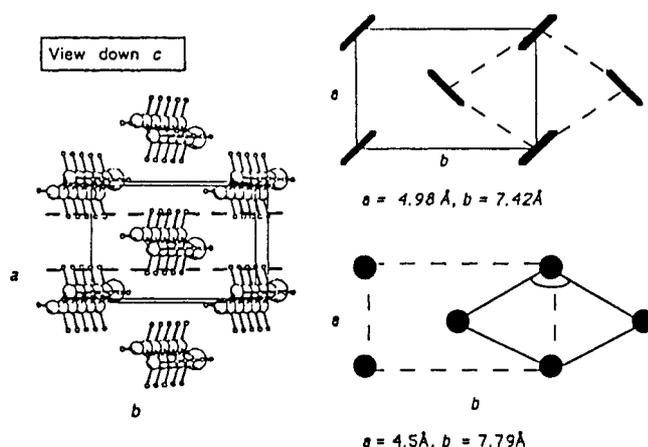


Figure 7: Packing arrangement viewed perpendicularly to the water surface of models of alcohol monolayers in crystallites formed at 5°C over pure water (left). Schematic representation of orthogonal packing of the hydrocarbon chains (right top). Schematic representation of the ab lattice of hexagonal ice (right bottom).

Table 3 Cell constants of uncompressed monolayers over pure water at 5°C

Monolayer	$a = b(\text{\AA})$	$\gamma(^{\circ})$	$ab \sin\gamma(\text{\AA}^2)$
$C_{23}H_{47}OH$	4.54	113.0	19.0
$C_{30}H_{61}OH$	4.50	112.8	18.7
$C_{31}H_{63}OH$	4.52	113.1	18.8
$C_{29}H_{59}CO_2$	4.65	106.3	20.7
$C_{19}H_{39}CO_2C_9H_{18}OH^*$	4.69	104.6	21.3
$C_{19}H_{39}CO_2C_{10}H_{20}OH^*$	4.69	104.6	21.3

*Cell constants measured at 2°C .

In order to determine the role played by the orientation of the -OH groups at the water surface, the induction of ice nucleation by several long chain ester alcohols has been studied [11]. When 9-hydroxy-nonyl eicosanoate (9-HNE) or its higher homologue 10-hydroxy-decyl eicosanoate (10-HDE), were spread on water drops they induce ice nucleation at -10°C and -4°C respectively; i.e. 10-HDE induces ice nucleation at a temperature elevated by 6°C as compared to 9-HNE. Grazing incidence X-ray diffraction patterns measured at $+2^{\circ}\text{C}$ and supported by theoretical calculations on both uncompressed monolayers, gave unit cells that are almost identical to each other $a=5.53\text{\AA}$, $b=7.44\text{\AA}$ and with tilt angle around 29° . This identity implies that the polar ester groups fix the orientation of the hydrocarbon chains and consequently fixing the relative orientation of the hydroxyl groups at the water surface. While for 10-HDE the hydroxyl group points almost perpendicularly to the water surface, in the 9-HNE the hydroxyl group lies in a parallel orientation. Furthermore, although the lattice match of the ester to the ice crystal is poorer than that of C_{30} alcohol, the induced freezing point of ice by the ester is elevated by 4°C . This result implies that the arrangement of the hydroxyl groups at the interface or the reorientation of these groups at the onset of crystallization, as observed in the 4HBA system shown previously, may be as important as the match between the alcohol and ice lattices. Parallel studies with other alcohols are in accord with these conclusions.

OUTLOOK

In the present study we presented some preliminary insight into the structure and dynamics of embryonic aggregates formed en-route to crystal nucleation. In these systems the induced nucleation depends upon parameters such as coherence length of the crystallites, structural and lattice match between the crystallites and the to-be-grown 3-D crystal. Most of the efforts at present are directed towards the understanding of the process of clustering at the air/water interface. Similar processes of self-assembling are also expected for molecules at other interfaces such as the solid/liquid, however, novel analytical tools have to be invented to probe these clusters which reside at surfaces much rougher than the liquid/air interface.

Finally, once the structure of these clusters will be assigned it will become possible to design "tailor-made" auxiliary molecules which will enable us to control crystal growth processes in a more rational way. Studies along these lines are reported elsewhere.

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