HERTHA-SPONER-PREIS

# Let the molecules speak

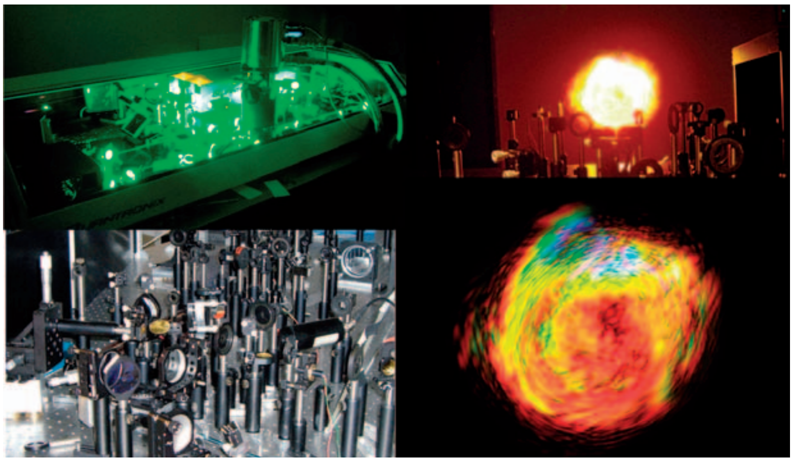
## Nonlinear optical scattering spectroscopy helps us to understand the molecular interfacial properties of micro- and nanoscopic systems.

Sylvie Roke

**How do interfaces influence the chemical and physical properties of a material? Despite the large amount of knowledge that has been uncovered in the past decades for (human-engineered) flat interfaces, the story about molecular properties of interfaces of soft matter systems, such as colloids, emulsion, vesicles, cells and other nanoscopic structures is yet to be told. This is due to the surrounding medium that forms an often impenetrable barrier. Thanks to new developments in the field of nonlinear optics, this is about to change.**

Interfaces play a key role in many processes. They play a regulating role in transport and structural phenomena in biological cells, they can determine the chemistry and phase behavior of colloidal systems, they are important for the mechanical properties of amorphous solids and they can determine the electrical properties of electronic devices. A large portion of natural matter exists on a micro- and nanoscopic scale. Living cells, organelles, colloidal systems, emulsions, micelles, and many other systems are composed of (sub)micron sized parts. For such systems, the relative interfacial area – and consequently the importance of interface atoms and molecules – increases.

The relative number of atoms and molecules present on the interface of a material increases dramatically when the material is reduced in size (**Fig. 1**). For micro- and nanoscopic systems it is well-known that the interfacial region is a dominating factor in determining the physical and chemical properties of a material [1]. For such nanoscopic systems it is known that a change of the interfacial properties results in profound changes in the physical and/or chemical properties. For example, semiconductor quantum dots are known for their exceptional fluorescence. A small change in the interfacial structure, or an increase of interfacial material (brought about by a reduction of size) can dramatically alter the color and intensity of the fluorescent light [2]. The stability of emulsions is determined by the interactions (van der Waals forces, electrostatic interaction, etc.) that occur in the interfacial region. Surface-modified beads phase separate readily upon the addition of certain proteins and enzymes and can thus be used as sensitive biochemical sensors [3]. Although we have sometimes a clear picture of what happens on the macro- and microscopic length and time scales, we do not (yet) understand the underlying molecular picture.



Left: The cryogenically cooled amplifier (top) and the type of setup needed for nonlinear optical surface spectroscopy experiments (bottom). Right: Focussed 70 fs laser pulses with 7 mJ pulse energy generate a colorful plasma in air (top). Enlarged picture of the plasma on the wall (bottom).

In this article, I will sketch some recent advances in the field of nonlinear optical spectroscopy that may lead to such a molecular picture. First, a description of this method is given, in which special emphasis is placed on the unique surface sensitivity of second-order nonlinear optical methods. This is followed by a description of the interface of a biopolymer film. Then, we move on to interfaces of micro- and nanoscopic particles embedded in condensed media. I will discuss how we can observe molecular changes at these hidden interfaces and describe an example of how molecular interfacial changes can affect macroscopic properties. Finally, I will provide an outlook to where these developments may lead in future.

### IN BRIEF

- The molecular properties of interfaces of micro and nanoscopic (soft) matter systems are still not clearly understood, because the surrounding medium forms an often impenetrable barrier.
- Nonlinear optical spectroscopy helps to uncover those properties, e. g. second-order nonlinear optical spectroscopy can uniquely probe interfacial molecules.
- Information about interface molecules on micro and nanoscopic particles can be uniquely gathered with nonlinear optical scattering spectroscopy. The scattering pattern contains information on the molecular structure and the particle morphology.
- Chiral and non-chiral molecules on particle interfaces in dispersions can be probed separately.

**Dr. Sylvie Roke**, MPI für Metallforschung, Heisenbergstr. 3, 70569 Stuttgart – Plenary talk given on the occasion of the conferment of the Hertha-Sponer Prize at the DPG conference in Berlin.

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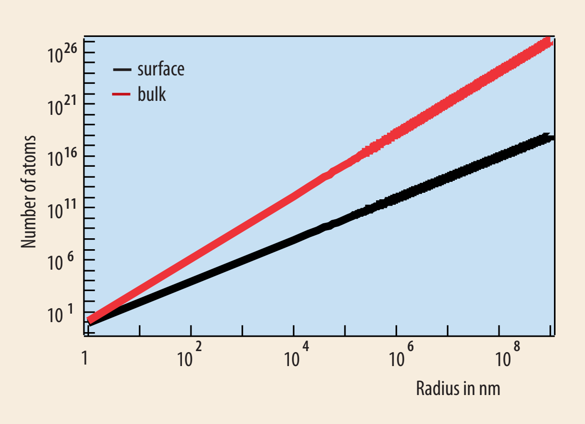

**Fig. 1:** The number of atoms situated at the interface and in the bulk of spherical particles with radius *R* are unequal.

## An interface-specific tool

During the last decades several successful attempts have been made to study flat interfaces on the molecular level and under ambient conditions. Since the second-order susceptibility vanishes in isotropic media (see **Box** "Interface Specificity"), second-order nonlinear optical spectroscopy can be used as an extremely sensitive surface probe. In such studies, the probed interfacial layer is only a few atomic diameters thick [4].

A molecular picture of an interface can be obtained by using vibrational Sum Frequency Generation (SFG) (**Fig. 2**), a method that relies on the subsequent interaction of two pulsed laser beams with an interface. The energy of one of the two incoming electric fields is tuned around the resonance of the vibrational modes of the interfacial molecules. In such a case $\chi^{(2)}_{ijk}$ is written in the following form:

$$\chi^{(2)}_{\mathrm{Res},ijk} = \frac{N\mu_k R_{ij}}{\hbar(\omega_2-\omega_{\mathrm{vib}}+i\Upsilon_{\mathrm{vib}})}. \qquad (1)$$

The vibrational motion of each chemical group in a molecule is characterized by a distinct frequency $\omega_{\mathrm{vib}}$, amplitude ($\mu_k R_{ij}$, the product of the molecular dipole moment with its polarizability), and damping constant ($\Upsilon_{\mathrm{vib}}$). The values of these observables depend on the participating atoms, the surrounding medium, and the orientation. Thus, it is possible to probe chemical composition, molecular order and orientation of parts of molecules situated on the interface.

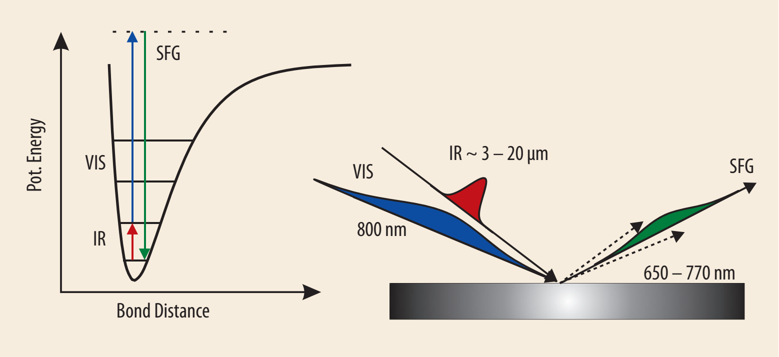

**Fig. 2** The potential energy diagram (left) shows subsequent light-matter interaction of the infrared (IR) and visible (VIS) laser pulses, which are needed to create a sum frequency photon. Sum Frequency Generation (SFG, right) was used to study flat surfaces: An infrared and a visible laser pulse are reflected from an interface. Out comes a directed sum frequency beam.

Since the energies of the vibrational modes lie in the infrared region of the electromagnetic spectrum, infrared photons are needed to excite vibrational resonances. Also, high electromagnetic fields are required to achieve enough response from the second-order susceptibility (which is nonlinear and only occurs when pulsed lasers are used). In the last decades femtosecond laser sources have been built that can be used to generate infrared femtosecond laser pulses (with enough output energy for nonlinear optical spectroscopy) with wavenumbers in the range of 4000 – 1500 $\mathrm{cm}^{-1}$ or 2.5 – 7 µm. In this spectral range resonances of the *localized* surface chemical groups are probed, such as $CH_3$ and OH groups, so that the structure, orientation and order of small molecules can be mapped. Larger molecules such as polymers, proteins and peptides, however, are still a challenge as they have complicated three dimensional structures that cannot be deduced from measuring only localized subgroups of a larger structure.

## Increasing complexity

Three dimensional structures can be deduced by probing molecular vibrational modes that are composed of the displacement of a large number of atoms. These modes vibrate with lower frequencies, from 1500 – 500 $\mathrm{cm}^{-1}$ (7 – 20 µm). In order to generate femtosecond infrared pulses with enough energy for nonlinear optical surface spectroscopy experiments in the low frequency region of the infrared spectrum, we use a modified Ti:Sapphire laser with a cryogenically cooled additional amplifier (**Fig.** at page 57) that pumps an optical parametric amplifier combined with a difference frequency generation stage (see Ref. [5] for details).

**Fig. 3** shows the surface localized (right panel) and delocalized (left panel) modes of two forms of a complex biopolymer (poly-(lactic acid)), forms A and B [6]. This biodegradable and biocompatible compound has unique characteristics that heavily depend on the three dimensional structure of the molecule. It is an ideal candidate for use in systems and devices for drug delivery and implants. Thorough knowledge of the surface three dimensional structure is thus of great importance, since the surface constitutes a barrier to the surroundings and provides an adsorption site for chemicals. Form A consists of the same repeat units, which are both chemically and spatially identical. Form B consists of two different repeat units, which are chemically identical but spatially each others' mirror image. They are chiral mirror images. In chemistry and biology most compounds consists of chiral building blocks (e. g. 21 of the 22 amino acids in the human body are chiral). A change in chirality can completely change the chemical and biological function of a molecule, as it strongly influences the three dimensional structure of a compound. It is therefore logical to expect that the molecules at the surfaces of the A and B films have different three dimensional structures. Unfortunately, since the chemical bonds of chiral groups are identical and because we want to identify only the first layer of atoms, this is a formidable task. A task, that can be accomplished with nonlinear optical spectroscopy.

In **Fig. 3** we see the surface SFG spectra of films A and B. It shows that (1) there is only a difference in spectral shape in the low frequency region of the spectrum, so that this part clearly reveals the three dimensional structure of a complex polymer. (2) From these low frequency spectra (combined with simulation data) we can determine that the surface chains of form A adopt a helical conformation, while those of form B reside in a disordered heterogeneous state. Thus, using nonlinear optical spectroscopy to probe in particular delocalized surface vibrations is indeed very sensitive to the three dimensional structure of biopolymers in the first atomic layer of the interface. Since the A and B interfaces are clearly different, their interaction with the body will be so too.

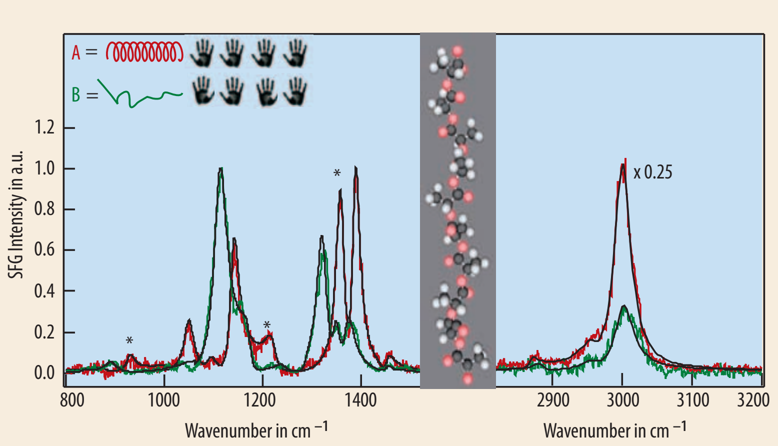

**Fig. 3** Vibrational sum frequency generation spectra of the first few atomic layers of the interfaces of chemically identical biopolymer films A (red trace) and B (green trace). The black lines are fits to the data in which all contributions to the reflected electrical sum frequency field are added (Eq. (1)). Left: The delocalized surface modes of A and B. The modes indicated with a * are representative of helices. Middle: Illustration of chiral mirror images. Molecular model of the biopolymer. Right panel: The localized surface modes of A and B. As can be seen they are insensitive to the 3-dimensional structure.

## Molecules on particle interfaces

The nonlinear optical methods described thus far in this article can give a very detailed description of interface processes on flat surfaces, because a directional reflected beam is needed. This means that it is not suited for the investigation of micro- and nanoscopic objects embedded in other media, such as colloids in dispersions, droplets in emulsions, micelles and vesicles. Consequently, the interface molecules of systems like colloids, vesicles, micelles and emulsions have never been observed in-situ and non-invasively. Thus, compared to flat surfaces a molecular picture is still missing. Therefore, it would be highly desirable if one could obtain molecular structural and dynamical properties in-situ of particles immersed in liquid or solid phases, so that molecular interfacial properties of the above mentioned systems can be probed.

Recently it has been shown that a surface molecular picture of particles embedded or dispersed in solid or

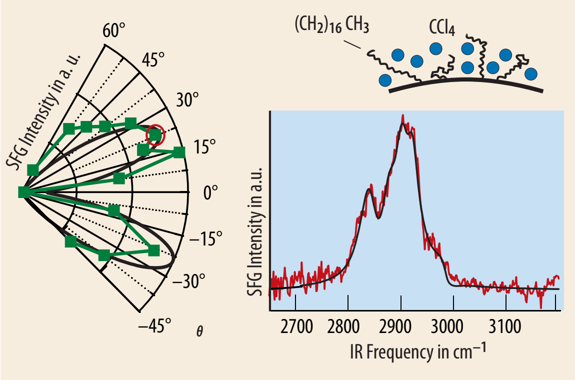

**Fig. 4** Nonlinear scattering spectroscopy data of 300 nm glass particles covered with carbohydrate chains, dispersed in apolar solvent (CCl$_4$). Left: The angular distribution of the scattered sum frequency photons. The black line is a fit using nonlinear scattering theory [8,10]. Right: One of the corresponding spectra as a function of infrared frequency obtained at a scattering angle of 22°, which displays the disordered surface structure of the particle/solvent interface (sketched in the inset).

### INTERFACE SPECIFICITY

Second-order nonlinear optical processes rely on the interaction of two electromagnetic fields, $\mathbf{E}_2(\omega_2)$, and $\mathbf{E}_1(\omega_1)$, with a medium. The fields induce a charge oscillation in a medium, the nonlinear optical polarization, $\mathbf{P}^{(2)}(\omega_0)$, which can occur at the sum (or difference) of the frequencies of the incoming beams ($\omega_0=\omega_1+\omega_2$). $\mathbf{P}^{(2)}(\omega_0)$ is a source for radiation of frequency $\omega_0$ and its magnitude can be described by:

$$P_i^{(2)}(\omega_1+\omega_2)=\chi_{ijk}{}^{(2)}(\omega_1+\omega_2)E_{1,j}(\omega_1)E_{2,k}(\omega_2) \qquad (2)$$

The radiated field can be found by inserting the source term into the appropriate Maxwell equations and applying the correct boundary conditions [4].

$\boldsymbol{\chi}^{(2)}$ is the second-order susceptibility, which describes the response of the medium, analogous to $\boldsymbol{\chi}^{(1)}$, the linear response, but more specific towards molecular symmetry.

According to Neumann's principle, every tensor that describes a physical property must be invariant under the symmetry operations ($T$) of the point group of a material. If a medium possesses spatial inversion symmetry, we may choose $T$ to be the inversion symmetry operator ($T_{ij}=-\delta_{ij}$). Applying this $T$ gives:

$$\boldsymbol{\chi}^{(2)}_{lmn}{}' = T_{li}T_{mj}T_{nk}\boldsymbol{\chi}^{(2)}_{ijk} \quad \xrightarrow{T_{ij}=-\delta_{ij}} \quad \boldsymbol{\chi}^{(2)}_{ijk}{}' = -\boldsymbol{\chi}^{(2)}_{ijk}=0 \qquad (3)$$

This means that media that possess spatial inversion symmetry (or randomness on an atomic scale, like liquid water) cannot generate sum frequency photons in the bulk. The consequence is that sum frequency photons can only be generated at the interface of such a medium (as there is no inversion symmetry there) so that second-order nonlinear optical spectroscopy can be used uniquely to probe interfacial molecules. It contrasts starkly with linear spectroscopy in that the average structure of (e. g.) a film is not detected but only the first monolayer situated at the interface.

The method is specific towards chiral mirror image molecules. Such molecules consist of the same type of bonds (so that they are chemically identical), but are spatially mirror images. They have therefore an identical $\boldsymbol{\chi}^{(1)}$. Their $\boldsymbol{\chi}^{(2)}$ components, however, are different so that chiral molecules can be distinguished from each other by measuring their nonlinear optical responses.

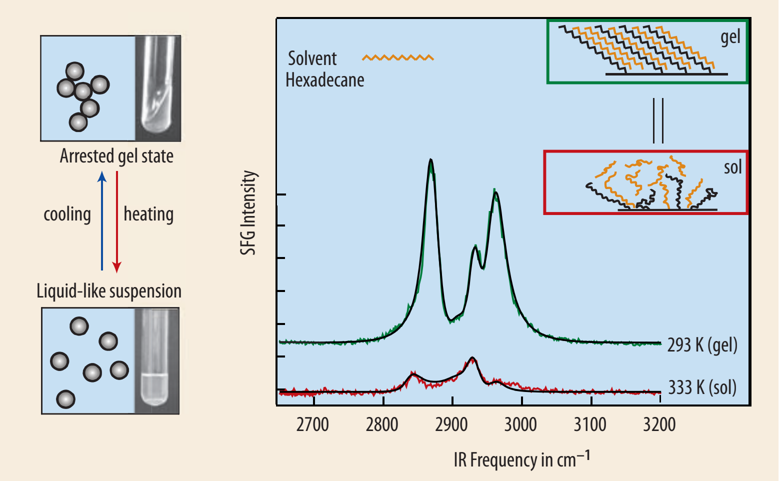

**Fig. 5** The highly viscous gel state transforms into a liquid-like one upon increase of temperature (left). This process happens for coated silica particles dispersed in hexadecane. Right: Nonlinear scattering spectra ($\theta$=51°) of the highly viscous gel state (293 K) and the liquid-like suspension (333 K) of colloids dispersed in hexadecane. The corresponding surface state of the particle interfaces as determined from the spectra are also shown.

liquid phase can be obtained by performing nonlinear optical *scattering* spectroscopy (NLSS). That is a combination of light scattering and nonlinear optical spectroscopy [7]. In such experiments the infrared and visible laser pulses are overlapped (in time and space) in a dispersion of particles. The incoming beams generate a nonlinear optical polarization ($P^{(2)}$) at the particle interface. Since the particle size is of the same order as the sum frequency wavelength, the sum frequency light is scattered. As the surface polarization is the source of the scattered sum frequency light, the scattering pattern contains information on both the molecular structure as well as the particle morphology (**Box** "Inversion Symmetry").

Here, I want to describe briefly a proof of principle experiment in which NLSS is performed on a dispersion of small glass particles covered with chemically linked carbohydrate chains (**Fig. 4**). These particles are well documented and it is known that in apolar solvents they undergo a gelation transition when the temperature is decreased. Despite all the literature available, it is not known what the surface structure is and how it may play a role in the gelation transition. Nonlinear scattering spectroscopy provides a unique insight into these issues. The NLS pattern displays two lobes, which can be described by a nonlinear optical scattering model that relies on solving the wave equation using a Greens function method and applying the far field approximation [8]. From the fit, the elements of the second-order susceptibility can be extracted as well as the particle size and shape. From the spectrum the molecular order and orientation of the chemically linked groups can be inferred. It turns out that the interfacial chains are not at all a densely packed layer as was assumed [9], but rather one with a chain density of only 30 %. It implies that the chemical preparation is not as efficient as thought and that most carbohydrates bind in the interior of the porous silica particle instead of at the surface.

When these porous surface-modified silica particles are dispersed in apolar solvents they can undergo a gelation transition. As can be seen in **Fig. 5** (left panel), upon heating the dispersion changes from a solid-like arrested, highly viscous state into a fluid-like free flowing one with a low viscosity. The explanation of such a phase transition is that the van der Waals interaction between the particles becomes attractive at lower temperatures due to a temperature-dependent change in dielectric constant. This macroscopic picture does not explain the observation that for some apolar solvents (like hexadecane) the transition is accompanied by a large calorimetric heat effect. This discrepancy has been debated in literature and a wide variety of possible explanations was suggested.

The reason for the mysterious heat effect was found by performing nonlinear optical scattering spectroscopy during several stages of the gelation transition

## INVERSION SYMMETRY

Although spheres do possess inversion symmetry it is possible to generate sum frequency photons from a surface of a sphere (as demonstrated in **Fig. i**). This seemingly contradictory observation can be explained by considering the size of the sphere: As the incoming fields propagate through the sphere they experience a phase shift. The result is that the polarization has a different relative phase on different parts of the interface. The total scattered light originates from the interference of all fields across the particle surface. The radiated sum frequency field ($\mathbf{E}_{\mathrm{SFG}}(\theta)$ with wave vector $k_0$) at scattering angle $\theta$ can be found by solving the wave equation with $\mathbf{P}^{(2)}$ as a source term. Using a Greens function method the field can be expressed as:

$$\mathbf{E}_0(\mathbf{r}) \propto \frac{1}{\varepsilon}\nabla\times\nabla\times\oint \mathrm{d}^2\mathbf{r}' \frac{e^{ik_0|\mathbf{r}-\mathbf{r}'|}}{|\mathbf{r}-\mathbf{r}'|}\mathbf{P}_0^{(2)}(\mathbf{r}')$$

Depending on the type of material (metal or dielectric) and the size range of the particle (compared to $\lambda_{\mathrm{SFG}}$) several approximations are possible. Depending on the material, sizes down to $a \sim 5-10$ nm can be measured. From using the reciprocity principle [13] it follows that the scattered field (at the detector position $r_0$ in the far field) from a particle can be expressed as follows [8]:

$$\mathbf{E}_{i,\mathrm{SFG}}(\theta) \propto \frac{k_0^2\, e^{ik_0r_0}}{r_0}\, \Gamma_{ijk}^{(2)}[\boldsymbol{\chi}^{(2)},R,\theta]\mathbf{E}_{j,\mathrm{IR}}\, \mathbf{E}_{k,\mathrm{VIS}}$$

It means that the sum frequency field emerges in a wide angular distribution, so that a scattering pattern is observed. The amplitude is determined by the incoming fields as well as the response of the surface molecules. $\Gamma^{(2)}$ is the particle susceptibility which contains the surface susceptibility ($\boldsymbol{\chi}^{(2)}$) as well as the particle morphology. Thus, by measuring a scattering pattern it is possible to extract the local surface susceptibility elements as well as the molecular structure, orientation, order and chirality [10].

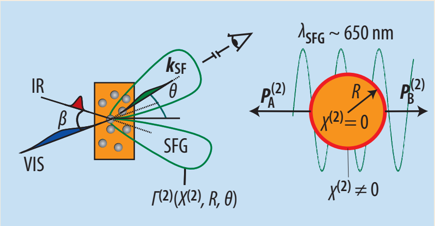

**Fig. i** In a nonlinear light scattering (NLS) experiment the incoming beams generate a nonlinear optical polarization at the interface of a particle ($\mathbf{P}^{(2)}$). The polarization is the source of the scattered sum frequency light. The magnitude and spectral shape of the scattered field are determined by the molecular properties of the interface, which are contained in the surface second-order nonlinear susceptibility ($\boldsymbol{\chi}^{(2)}$). The angular distribution reflects both the value of the second-order susceptibility as well as the size of the particle.

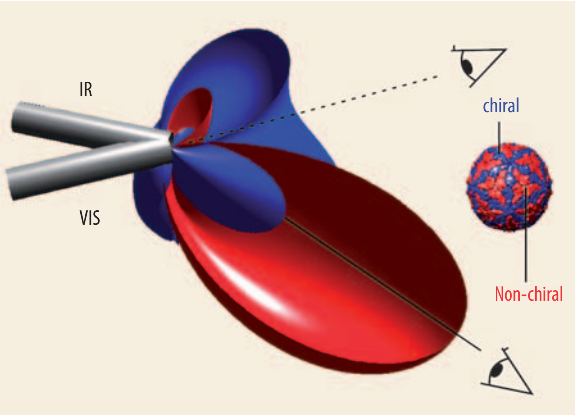

**Fig. 6** Calculated scattering pattern of a 200 nm particle (which, for example, could be a virus) containing both chiral (blue) and non-chiral (red) groups. It can be seen that both groups generate a distinctly different NLS pattern that points in different directions, so that they can be measured separately.

in hexadecane. **Fig. 5** shows scattering spectra for the gel and liquid-like state in hexadecane (upper traces). The upper (gel) spectra can be traced back to originate from an ordered film of alkane chains. The lower (fluid) spectrum belongs to a disordered film. In order to form an ordered film (with a chain tilt angle of 52°) the chemically linked alkane chains need to interact with the solvent molecules. Because hexadecane has a similar structure as the surface-crafted films, it can intercalate with the surface chains and hence form a nicely ordered, crystalline-like film. The formation of such a film explains the poorly understood discrepancy in the observed heat effects: In fluid suspension in hexadecane at high temperatures, the interfacial molecules are in a liquid-like state of conformational disorder. As the temperature is lowered, the onset of gelation is identified by macroscopic phenomena, including changes in turbidity, heat release and diverging viscosity. At the molecular level, the onset of this transition coincides with straightening of the carbon-carbon backbones of the interfacial molecules and the formation of an ordered layer of both solvent molecules and interface-grafted molecules. Solvents such as benzene that cannot intercalate with the surface-grafted chains do not interact with the chains on the particle surface [11,12].

This is an example of a phase transition that has been thoroughly investigated on the macro- and microscopic scales, but not on the molecular scale. Since many systems and processes depend on interface-solvent interactions it can be expected that many more important relations and effects will be uncovered in future.

## How far can we go?

Nonlinear optical scattering methods combine the surface sensitivity of nonlinear optical interface spectroscopy with the ability to study in-situ and non-invasively the molecular interface properties of micro- and nanoscopic systems. It can be expected that it will soon be used to answer biologically relevant questions that relate molecular structural properties to chemical and biological function. As was mentioned above, the chiral molecules are difficult to distinguish from each other (as well as from similar non-chiral ones) as the set of chemical bonds in such molecules are identical. However, it is often a single chiral form of an amino-acid, protein, peptide or polymer that is responsible for a specific chemical reaction or biological functionality.

**Fig. 6** shows the sensitivity of nonlinear scattering spectroscopy towards chiral molecules. It shows the scattering patterns of chiral and non-chiral surface molecules on a 200 nm particle [10]. Since the chiral molecules have different non-zero elements of $\chi^{(2)}$ to the non-chiral ones, they also lead to different responses of $\chi^{(2)}$ and hence give rise to different scattering patterns. Thus, it is possible to distinguish between chiral molecules on particle interfaces in dispersions (in-situ and non-invasively). Because most biologically relevant systems consist primarily of chiral groups, which are difficult to identify, this observation will prove to be very useful.

In this article I have demonstrated that a wealth of new phenomena can be observed at interfaces of micro- and nanoscopic sized material. Understanding these phenomena will enable us to tailor material properties on a more advanced level.

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