# New schemes for nonlinear optical spectroscopy of solutions of chiral biological macromolecules

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(Submitted 16 February 1994)
Zh. Eksp. Teor. Fiz. **106**, 1260–1277 (November 1994)

A phenomenological analysis is carried out of nonlinear optical processes taking place in macroscopically noncentrosymmetric isotropic solutions of chiral (left–right asymmetric) macromolecules, which are the primary elements of living organisms and their metabolic products. It is shown on the basis of measurements of the frequency dispersion of the dipole nonlinear even-order optical susceptibilities of such solutions (which susceptibilities are absent in centrosymmetric liquids and racemic solutions of chiral molecules) and the quadrupole nonlinear odd-order optical susceptibilities (also present exclusively in optically active liquids and solutions) that it is possible to develop new schemes for coherent nonlinear optical spectroscopy, possessing enhanced information content and sensitivity specifically to the specularly asymmetric component of homogeneous isotropic liquid solutions. An analysis is carried out of competing nonlinear optical effects masking the manifestation of chiral-sensitive processes and means for their selective suppression are presented. Estimates are given of the expectation values of new effects, and results of the first experiments in this direction are analyzed. © *1994 American Institute of Physics.*

## 1. INTRODUCTION

One of the most universal signs of living material is the remarkable "chiral purity" of the biological macromolecules which make it up, which is expressed in the practically complete preference of living nature for one (right or left) of the two possible mirror isomers of the same biomolecule.[1–3] The reason for this cardinal bilateral asymmetry of living nature is still not clear. It is therefore of extreme importance to look for new experimental methods possessing enhanced sensitivity to the chirality of molecules which enter into the makeup of living cells and organisms or are products of their metabolic activity.

From a physical point of view, what we should be talking about here is first of all developing methods of qualitative and quantitative analysis (with possibly higher spatial and temporal resolution) of chiral biomolecules against the background of racemic mixtures of molecules of nonbiological origin—in the simplest case, this means detecting bioorganic molecules in homogeneous isotropic liquid solutions.

In the present paper we discuss some previously unexamined schemes of nonlinear laser spectroscopy, potentially possessing high sensitivity and selectivity specifically to the left–right asymmetric component of homogeneous isotropic liquid solutions. As will be shown below, by using these methods it is possible to obtain previously unavailable physical information about the magnitude and frequency dispersion of the optical hyperpolarizabilities of chiral molecules. Short reports on this account have already been published in Refs. 4–6.

Section 2 presents a phenomenological classification of possible nonlinear optical processes in nonracemic solutions of chiral molecules up to fourth order in the field, inclusive, each of which can form the basis of a corresponding spectroscopic scheme.

Presently the most well-known and most widely used spectroscopic technique—that of linear optical activity (OA) and circular dichroism (CD)—is based on the measurement of the magnitude and frequency dispersion of the real and imaginary parts of the linear optical gyration tensor of the medium.[7] Along with a large number of advantages, this spectroscopic technique possesses a number of limitations. In particular, linear OA-CD spectroscopy cannot give information about the magnitude and dispersion of the nonlinear optical hyperpolarizabilities of chiral molecules, which carry uniquely important and rich information about structure and biological activity. The nonlinear analogs of OA-CD spectroscopy working with the frequency dispersion of the optical susceptibilities of second and higher orders possess new possibilities.

A characteristic feature of homogeneous isotropic nonracemic solutions of chiral molecules is their macroscopic acentricity, which is manifested, in particular, in the presence of dipole optical susceptibilities of even orders (and also in the presence of quadrupole susceptibilities of odd orders), absent in optically inactive liquids. It is specifically on these susceptibilities that the most promising nonlinear optical schemes described in Sec. 2 are based: upconversion of infrared absorption spectra, optical rectification (OR), the scheme based on the electrooptical Pockels effect (the electric analog of the Faraday effect) with participation of the dipole quadratic susceptibility; the scheme based on second-harmonic generation (SHG) and five-photon mixing with participation of the fourth-order dipole susceptibility (the Bio-CARS scheme). We may also include here measurement of the dispersion of the rotation angle of the polarization plane of the weak probe wave induced by the more intense laser pump wave (the nonlinear optical activity (NOA) scheme), measurement of the frequency dependence of new spectral components of the probe beam (the NOA-CARS

1063-7761/94/110681-10$10.00

scheme), and measurement of the frequency dependence of two-photon circular dichroism, all engendered by the spatial dispersion of the cubic nonlinearity.

Section 3 develops a general approach to separating out the sought-after effects due to the macroscopic acentricity of the investigated isotropic medium against the background of more intense, competing nonlinear processes of lower orders on the basis of the polarization state of the recorded signal. Section 4 presents an analysis of the contribution of lower-order cascade processes to the effective nonlinear third- and fourth-order susceptibilities. As always in nonlinear optics constructed on the basis of an expansion of the nonlinear polarization of the medium into a perturbation theory series in powers of the amplitudes of the optical fields introduced into the medium, the contribution of the "direct" higher nonlinearities is commensurate with the contributions of the lower-order "cascade" nonlinearities and depends in a different way on the specific conditions of the nonlinear interaction of the light waves. This section also contains numerical estimates of the efficiency of the new spectroscopic schemes described in Sec. 2, which incorporate recent measurements[8,9] of the dipole SHG in the fourth-order nonlinearity in an optically active liquid.

## 2. PHENOMENOLOGICAL ANALYSIS

### 2.1. Even-order dipole optical nonlinearities in noncentrosymmetric media

Restricting ourselves at the outset to the electric dipole contribution to the volume polarization of the medium, induced by optical fields $\mathbf{P}^{\mathrm{D}}$, we separate the linear terms (L) from the nonlinear (NL) terms in the amplitude of the light field. In the spectral representation we can write without allowing for the spatial dispersion (see Sec. 2.4)[10,11]

$$P_i^{\mathrm{D}}(\omega_a)=P_i^{(\mathrm{L})\mathrm{D}}(\omega_a)+P_i^{(\mathrm{NL})\mathrm{D}}(\omega_a), \tag{1}$$

where

$$P_i^{(\mathrm{L})\mathrm{D}}(\omega_a)=\chi_{ij}^{(1)\mathrm{D}}(\omega_a)E_j(\omega_a) \tag{2}$$

$$\begin{aligned}P_i^{(\mathrm{NL})\mathrm{D}}(\omega_a)={}&\chi_{ijk}^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_a-\omega_b)E_j(\omega_b)E_k(\omega_a\\&-\omega_b)+\chi_{ijkl}^{(3)\mathrm{D}}(\omega_a;\omega_b,\omega_c,\omega_a-\omega_b\\&-\omega_c)E_j(\omega_b)E_k(\omega_c)E_l(\omega_a-\omega_b-\omega_c)\\&+\chi_{ijklm}^{(4)\mathrm{D}}(\omega_a;\omega_b,\omega_c,\omega_d,\omega_f=\omega_a-\omega_b\\&-\omega_c-\omega_d)E_j(\omega_b)E_k(\omega_c)E_l(\omega_d)E_m(\omega_f)\\&+\dots,\end{aligned} \tag{3}$$

where $E_j(\omega_b)$, $E_k(\omega_a-\omega_b)$, etc. are the spectral amplitudes of the corresponding vector components of the optical fields. Repeated Cartesian indices are taken to indicate summation from 1 to 3, and repeated frequencies different from $\omega_a$ are taken to indicate integration from $-\infty$ to $+\infty$.

Macroscopic symmetry imposes constraints on the nonzero components of the interesting even-order dipole susceptibility tensors $\hat{\chi}^{(2)\mathrm{D}}$ and $\hat{\chi}^{(4)\mathrm{D}}$.

Non-racemic solutions of chiral biomolecules belong to the acentric limiting symmetry class $\infty\infty$. In such solutions according to general crystallographic "selection rules"[12] the tensor $\hat{\chi}^{(2)\mathrm{D}}$ has the following form:

$$\chi_{ijk}^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_a-\omega_b)=\chi^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_a-\omega_b)\cdot e_{ijk}, \tag{4}$$

where $e_{ijk}$ is the absolute antisymmetric (pseudo)tensor of Levi–Civita and $\hat{\chi}^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_a-\omega_b)$ is a pseudoscalar.

Of the 243 components of the tensor $\chi_{ijklm}^{(4)\mathrm{D}}(\omega_a;\omega_b,\omega_c,\omega_d,\omega_f)$ only 60 are nonzero (of which only 6 are independent), namely those which have one index repeated three times, and with the other two different from that one and from each other:

$$\begin{aligned}\chi_{ijklm}^{(4)\mathrm{D}}(\omega_a;\omega_b,\omega_c,\omega_d,\omega_f)={}&\chi_1^{(4)\mathrm{D}}e_{ijk}\delta_{lm}+\chi_2^{(4)\mathrm{D}}e_{ijl}\delta_{km}\\&+\chi_3^{(4)\mathrm{D}}e_{ijm}\delta_{kl}\\&+\chi_4^{(4)\mathrm{D}}(e_{ikl}\delta_{jm}+e_{ikm}\delta_{jl}\\&+e_{jkl}\delta_{im}+e_{jkm}\delta_{il})\\&+\chi_5^{(4)\mathrm{D}}(e_{jlm}\delta_{ik}+e_{ilm}\delta_{jk})\\&+\chi_6^{(4)\mathrm{D}}e_{klm}\delta_{ij}.\end{aligned} \tag{5}$$

Here each of the six pseudoscalars $\chi_\alpha^{(4)\mathrm{D}}$, $\alpha=1,\dots,6$, is a function of the five frequencies $\omega_a,\omega_b,\omega_c,\omega_d,\omega_f$, where $\omega_f=\omega_a-\omega_b-\omega_c-\omega_d$. As before, $e_{ijk}$ is the Levi–Civita unit antisymmetric tensor and $\delta_{ij}$ is the Kronecker delta.

It is not hard to show that the magnitudes of the enumerated susceptibilities are proportional to the difference between the densities of the "right" and "left" isomers of the chiral molecules so that in racemic solutions they vanish. The tensor $\chi_{ijkl}^{(3)\mathrm{D}}(\omega_a;\omega_b,\omega_c,\omega_a-\omega_b-\omega_c)$ has the usual form for all isotropic media (see, e.g., Ref. 11, Ch. 2).

In the absence of dissipation at all frequencies figuring among the arguments of the susceptibility $\chi_{ijk}^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_c)$, that is, for sufficiently large separation of these frequencies from the frequencies of the allowed transitions, conservation of energy of the electromagnetic field and reversibility of the equations of motion ($T$-invariance) lead to the appearance of additional permutational relations between the tensor components of the susceptibility $\hat{\chi}^{(2)\mathrm{D}}$, known as Kleinman's permutation relations.[13]

In a dispersion-free medium they reduce to equality of all the components differing only by permutation of their Cartesian indices while preserving the order of the frequency arguments:[10,11]

$$\begin{aligned}\chi_{ijk}^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_a-\omega_b)&=\chi_{jik}^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_a-\omega_b)\\&=\chi_{kji}^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_a-\omega_b)=\dots.\end{aligned} \tag{6}$$

Since the general form of the tensor $\chi_{ijk}^{(2)\mathrm{D}}$ in interesting media of the limiting symmetry class $\infty\infty$ is given by formula (4), satisfaction of the Kleinman relations leads to the vanishing of the pseudoscalar $\chi^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_a-\omega_b)$. This fact, being a manifestation of the permutational symmetry of the Onsager kinetic coefficients in nonlinear optics, was first established by Baranova *et al.* in 1977.[14]

However, under resonance or pre-resonance conditions this prohibition of the occurrence of three-photon processes in isotropic chiral media is removed. The effect of nondegenerate three-photon mixing in an optically active solution of arabinose under pre-resonance conditions was first experimentally recorded by Rentzepis *et al.* in 1966.[15] The prohibition is also removed in the case when one of the frequencies $\omega_a,\omega_b,\omega_a-\omega_b$ vanishes and the constant-current conductivity of the medium is finite ($\mathrm{Im}\,\varepsilon(0)\neq 0$; see Refs. 14 and 17).

Permutational relations, analogous to Kleinman's relations, also hold for the tensor components of the susceptibilities of higher orders.[11,16] However, for this to occur, the lack of dissipation and dispersion at the frequencies which are arguments of the susceptibility $\chi^{(4)\mathrm{D}}_{ijklm}(\omega_a;\omega_b,\omega_c,\omega_d,\omega_f)$ is not enough. $T$-invariance and conservation of energy of the electromagnetic field in the described susceptibilities $\hat{\chi}^{(4)\mathrm{D}}$ of five-photon processes remain valid (and, consequently, the Kleinman permutation relations are fulfilled) only as long as there are no allowed transitions between the populated states of the medium that are resonant at the corresponding combinations of frequencies of the interacting optical waves. Regarding the susceptibility $\chi^{(4)\mathrm{D}}_{ijklm}(\omega_a;\omega_b,\omega_c,\omega_d,\omega_f)$, this reduces to requiring the simultaneous satisfaction of the following conditions:

there are no one-photon transitions at the frequencies

$$\omega_a,\omega_b,\omega_c,\omega_d,\omega_f;$$

there are no two-photon transitions at the frequencies

$$\omega_b+\omega_c;\omega_b+\omega_d;\omega_b+\omega_f;\omega_c+\omega_d;\omega_c+\omega_f;\omega_d+\omega_f; \qquad (7)$$

$$\omega_a-\omega_b;\omega_a-\omega_c;\omega_a-\omega_d;\omega_a-\omega_f;$$

there are no three-photon transitions at the frequencies

$$\omega_a-\omega_c-\omega_d;\omega_a-\omega_b-\omega_d;\omega_a-\omega_b-\omega_c;\omega_b+\omega_c+\omega_d.$$

If these requirements are met, then depending on the type of tensor $\chi^{(4)\mathrm{D}}_{ijklm}$ represented by formula (5), and the permutation relations, all of the components of this tensor vanish and the corresponding five-wave optical processes turn out to be forbidden.

However, with the approach of one or more of the frequencies $\omega_a,\omega_b,\omega_c,\omega_d,\omega_f$ or the combinations above to the frequency of any (one or more) of the allowed transitions, the permutation relations cease to be fulfilled, and the corresponding processes of five-wave mixing turn out to be allowed.

The prohibition is also removed if one of the frequencies $\omega_a,\omega_b,\omega_c,\omega_d,\omega_f$ or any one of their combinations enumerated in (7) vanishes. A constant current can then flow in the medium ($\mathrm{Im}\,\varepsilon(0)\neq 0$).

## 2.2. Spectroscopic schemes based on the quadratic nonlinearity

This class of spectroscopic schemes includes upconversion of infrared radiation, optical rectification (OR) and the electrooptical effect (EOE). The corresponding three-photon processes are described by the quadratic optical susceptibility tensor $\chi^{(2)\mathrm{D}}_{ijk}(\omega_a;\omega_b,\omega_a-\omega_b)$. In the presence of frequency degeneracy, i.e., when $\omega_b=\omega_a/2$, all the components of this tensor vanish as a consequence of additional permutational symmetry in the last two indices even if the Kleinman conditions are not fulfilled, so that the scheme with second harmonic generation (SHG), which is the simplest to realize in other cases, is impossible here.[18,19] All variants of mixing of nondegenerate frequencies are unrealizable in the most convenient geometry,[6,18] the collinear, since in this case the nonlinear polarization at the sum (difference) frequency $\omega_a=\omega_b+\omega_c$ ($\omega_a=\omega_b-\omega_c$) has only a longitudinal component, as follows from Eqs. (3) and (4):

$$\mathbf{P}^{(2)\mathrm{D}}(\omega_a)=\chi^{(2)\mathrm{D}}(\omega_a;\omega_b,\pm\omega_c)[\mathbf{E}(\omega_b)\mathbf{E}(\pm\omega_c)], \qquad (8)$$

and consequently cannot be a source of a free (transverse) electromagnetic wave.

Noncollinear schemes for three-wave mixing are ineffective because of strong phase mismatching. Nevertheless, it was specifically in this noncollinear geometry that the first nonlinear optical effect of the quadratic dipole nonlinearity of a liquid under pre-resonance conditions was recorded more than 25 years ago—the generation of the sum frequency attendant to mixing in a solution of arabinose of the fundamental frequency of a ruby laser and its second harmonic.[15]

Most promising spectroscopically is the scheme for studying optically active liquids based on frequency summing in a variant of infrared upconversion: the infrared radiation ($\omega_b$) being retuned in frequency, thereby scanning the vibrational infrared resonances of the chiral molecules, is mixed in acentric molecules with laser radiation at the fixed frequency $\omega_c=\omega_a-\omega_b\geqslant\omega_b$ and is thereby upconverted into the visible or ultraviolet range: $\omega_a=\omega_b+\omega_c$. The dependence of the intensity of the sum-frequency signal $I_a$ on the frequency of the infrared radiation $\omega_b$ is recorded; this dependence, after correcting for dispersion of the linear optical characteristics (the absorption coefficient and the coherence length) in the region of infrared resonances, reflects the frequency dispersion of the quadratic nonlinear susceptibility of the solution due exclusively to the left–right asymmetric biomolecules:

$$I_a(\omega_b)\sim|\chi^{(2)\mathrm{D}}(\omega_a;\omega_b,\omega_c)|^2. \qquad (9)$$

This dispersion is determined by the presence of vibrational resonance transitions in the chiral molecules under study and does not contain any contributions from resonances of molecules of the isotropic nonchiral solvent. Thereby a selective (with respect to the chiral biomolecules) upconversion of their infrared absorption spectra is realized; these spectra are rich in information about their structure, conformational variations, and biological activity. It is usually extremely difficult to carry out direct measurements of the infrared absorption spectra of biomolecules in solution because of strong masking absorption over practically the entire near and middle infrared range due to the solvent molecules (usually water). The technique of upconversion has turned out to be extremely informative and practical in other branches of spectroscopy, for example, in the study of the vibrational spectra of molecules adsorbed onto the surfaces of solid bodies or molecular monolayers on the surface of a liquid.[10,20]

Other experimentally easily realizable schemes of spectroscopic analysis of chiral liquids based on quadratic optical nonlinearities are the schemes of optical rectification (OR) (described by the susceptibility $\chi_{ijk}^{(2)\mathrm{D}}(0;\omega,-\omega)$, Ref. 4) and the electrooptical effect (EOE), that is to say, the electrical analog of the Faraday effect,[14] which is described by the susceptibility $\chi_{ijk}^{(2)\mathrm{D}}(\omega;\omega,0)$.

Up until now, the OR effect in chiral liquids has not been discussed in the literature (with the exception of brief reports by the author[4,6]), nor has it been experimentally observed. A physically similar situation arises in noncentrosymmetric crystals during the observation of the photovoltaic (photogalvanic) effect.[21,22] It is useful to distinguish the physically distinct situations that can obtain in real chiral liquids when observing OR.1)

1) The medium is not electrically conducting and has no photoconductivity (absorption of light takes place by virtue of bound-bound electronic transitions in chiral molecules).

2) The medium is not electrically conducting in the absence of light, but demonstrates photoconductivity when absorbing light with frequency $\omega$.

3) The medium is initially electrically conducting, but has no photoconductivity; in this case two subcases are possible:

3a) absorption of light at frequency $\omega$ is absent;

3b) the chiral molecules absorb light at frequency $\omega$.

4) The medium is electrically conducting in the absence of light, and also possesses photoconductivity.

As noted in Sec. 2.1, the optical rectification effect in a chiral liquid described by the nonlinear susceptibility $\chi^{(2)\mathrm{D}}(0;\omega,-\omega)$ can be observed only upon violation of the Kleinman conditions, i.e., in the presence of optical absorption and/or constant-current conductivity (or photoconductivity). Therefore, in the above cases, there is no case in which the investigated liquid is simultaneously electrically nonconducting and optically transparent.

The phenomenological analysis in Sec. 2.1 is directly applicable to case 1. For this case the static polarization in the OR scheme, referring to Eqs. (3) and (4), has the following form:

$$\mathbf{P}^{(2)\mathrm{D}}(0)=\chi^{(2)\mathrm{D}}(0;\omega,-\omega)|A|^2[\mathbf{ee}^*]+\text{c.c.}, \tag{10}$$

where $\mathbf{e}$ is the complex unit polarization vector of the light wave $\mathbf{E}(\omega)$ and $\mathbf{A}$ is its amplitude. If $\mathbf{E}(\omega)$ is an elliptically polarized plane wave with arbitrary orientation of its semimajor ($a$) and semiminor ($b$) axes in the $xy$ plane, then

$$\mathbf{P}^{(2)\mathrm{D}}(0)=2|A|^2\sin 2\gamma\cdot\mathrm{Im}\,\{\chi^{(2)\mathrm{D}}(0;\omega,-\omega)\}\mathbf{e}_z, \tag{11}$$

[where $\gamma=\pm\mathrm{arctg}(b/a)$], so that on the plates of the capacitor introduced into the measuring cuvette along the direction of propagation of the plane wave (intensity $I$) (see Fig. 1) there arises the potential difference

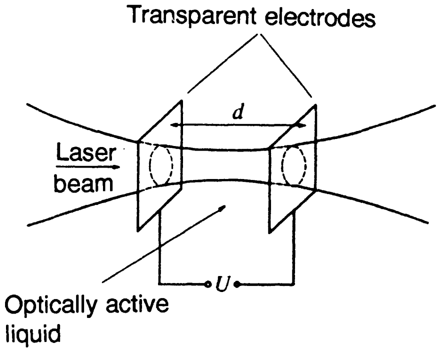

FIG. 1. Diagram of a proposed experiment on optical rectification in an optically active liquid.

$$U_{\max}\approx[64\pi^2\,\mathrm{Im}\,\chi^{(2)\mathrm{D}}/c(\varepsilon(0)-1)n(\omega)]Id\sin 2\gamma, \tag{12}$$

where $n(\omega)$ is the index of refraction, $\varepsilon(0)$ is the static dielectric constant, and $d$ is the distance between the capacitor plates. The OR signal is sensitive to the sign of the chirality of the medium (this latter is related to the sign of the imaginary part of $\chi^{(2)\mathrm{D}}$) and to the sign of the chirality of the light wave (determined by the sign of $\gamma$). This signal is nonzero and can be recorded by tuning the frequency of the light wave $\omega$ over the absorption band of the chiral molecules where, according to Sec. 2.1, the complex pseudoscalar $\chi_{ijk}^{(2)\mathrm{D}}(0;\omega,-\omega)$ is nonzero.

In the analysis of cases 2–4, it would be more correct to formally expand the optically induced current $j$ in powers of the amplitudes of the incident light field, but not expand the dielectric polarization of type (3). In the present article I do not carry out such a formally distinct, phenomenological analysis, rather leaving it for later publications. However, the general conclusion of the presence of the OR effect in cases 2–4 remains valid when the photocurrent is formally expanded in powers of the electromagnetic field amplitudes.

To complete the picture, we present expressions which follow from Eqs. (3) and (4) for the previously discussed[14] electrooptical effect (EOE) in chiral liquids.

In the EOE scheme, the nonlinear polarization has the form

$$\mathbf{P}^{(2)\mathrm{D}}(\omega)=\chi^{(2)\mathrm{D}}(\omega;0,\omega)AE_0[\mathbf{ee}_0], \tag{13}$$

where $E$ and $\mathbf{e}_0$ are the amplitude and unit direction vector of the static electric field, respectively. If $\mathbf{e}_0=\mathbf{e}_z$ and $\mathbf{e}=\mathbf{e}_x$, then $\mathbf{P}^{(2)\mathrm{D}}(\omega)$ describes an additional (beyond the linear effect of optical activity) rotation of the polarization plane of the light wave, since in the light wave $\mathbf{E}(\omega)$, a component appears along the $y$ axis:

$$E_y=i[8\pi^2/\lambda n(\omega)]\chi^{(2)\mathrm{D}}AU, \tag{14}$$

where $U=E_0d$ is the voltage on the capacitor plates. The effect is of course linear in the amplitude of the light wave and is present only in absorbing ($\mathrm{Im}\,\chi^{(2)\mathrm{D}}\neq 0$) media and in conducting media ($\mathrm{Im}\,\varepsilon(0)\neq 0$), where the condition of

$T$-invariance breaks down.[14] To record this effect, it is convenient to modulate the electrostatic field and synchronously detect the optical signal.

### 2.3. Spectroscopy of a chiral isotropic medium, based on five-photon processes

This spectroscopic scheme is based on the measurement of the fourth-order dipole nonlinearity $\chi^{(4)\text{D}}_{ijklm}(\omega_a;\omega_b,\omega_c,\omega_d,\omega_f)$.

The basic expression for the fourth-order nonlinear polarization vector $\mathbf{P}^{(4)\text{D}}$, describing the nondegenerate five-photon process in an isotropic, homogeneous, acentric medium $\omega_a=\omega_b+\omega_c+\omega_d+\omega_f$, where $\omega_f=\omega_a-\omega_b-\omega_c-\omega_d$, is obtained by direct summation in the last term of expression (3), allowing for the symmetry properties of the tensor $\chi^{(4)\text{D}}_{ijklm}$ (5). The result can be put in the following invariant form:

$$\begin{aligned}P^{(4)}(\omega_a)=DA_bA_cA_dA_f\{&\chi^{(4)\text{D}}_{23111}[\mathbf{e}_b\mathbf{e}_c](\mathbf{e}_d\mathbf{e}_f)\\&+\chi^{(4)\text{D}}_{31121}[\mathbf{e}_c\mathbf{e}_d](\mathbf{e}_b\mathbf{e}_f)+\chi^{(4)\text{D}}_{31112}[\mathbf{e}_d\mathbf{e}_f](\mathbf{e}_b\mathbf{e}_c)\\&+\chi^{(4)\text{D}}_{13112}\mathbf{e}_d(\mathbf{e}_b[\mathbf{e}_c\mathbf{e}_f])+\chi^{(4)\text{D}}_{13121}\mathbf{e}_f(\mathbf{e}_b[\mathbf{e}_c\mathbf{e}_d])\\&+\chi^{(4)\text{D}}_{11123}\mathbf{e}_b(\mathbf{e}_d[\mathbf{e}_f\mathbf{e}_c])\},\end{aligned}\tag{15}$$

where $\omega_a$ is the frequency of the new wave generated in the nonlinear medium by the interaction of the four incident plane waves with frequencies $\omega_b,\omega_c,\omega_d,\omega_f=\omega_a-\omega_b-\omega_c-\omega_d$; $\mathbf{e}_b,...,\mathbf{e}_f$ are the unit polarization vectors, $A_b,...,A_f$ are the amplitudes of the optical fields and $\chi^{(4)\text{D}}_{23111}$, etc. are the six nonzero independent components of the fifth-rank nonlinear polarization tensor [they are expressed in an obvious way in terms of the pseudoscalars $\chi^{(4)\text{D}}_{\alpha}$ $\chi^{(4)\text{D}}_{\alpha}$, $\alpha=1,...,6$, introduced in Eq. (5)]; the factor $D$ reflects possible degeneracy of the frequencies $\omega_b,\ldots,\omega_f$ (in the case when all the frequencies are different, $D=4!=24$; if only three out of four are different, then $D=3!=6$, etc.). Square brackets denote a vector product, and parentheses denote a scalar product.

The unit vectors $\mathbf{e}_b,...,\mathbf{e}_f$ ($|\mathbf{e}_i|^2=1$, $i=a,\ldots,f$) are in general complex and describe the possible states of elliptic polarization of the incident beams. In the simplest case of noncollinear SHG with this nonlinearity participating, when two interacting beams with the same frequency $\omega$ interact according to the scheme $\omega_{\text{SH}}=\omega+\omega+\omega-\omega$, in a medium with normal linear dispersion the synchronous regime (see Fig. 2)[4,8,9]

$$\mathbf{k}_{\text{SH}}=3\mathbf{k}-\mathbf{k}'$$

is possible, where $\mathbf{k}$ and $\mathbf{k}'$ are the wave vectors of the intersecting beams with frequency $\omega$, and $\mathbf{k}_{\text{SH}}$ is the wave vector of the generated second-harmonic wave. Here the nonlinear polarization at the second-harmonic frequency has the form

$$\mathbf{P}^{(4)\text{D}}(2\omega)=4\chi^{(4)\text{D}}_{31112}A^3A'^*[\mathbf{e}\mathbf{e}'^*](\mathbf{e}\mathbf{e}),\tag{16}$$

$A,A',\mathbf{e},\mathbf{e}'$ are the complex amplitudes and unit polarization vectors of the intersecting beams with frequency $\omega$. As can be seen, the nonlinear polarization (16) vanishes for circular polarization of the wave $\mathbf{E}(\omega)$. The choice of linear polarization for the waves $\mathbf{k}$ and $\mathbf{k}'$ is optimal, and only the geometry in which both vectors $\mathbf{e}$ and $\mathbf{e}'$ are normal to the plane containing $\mathbf{k}$, $\mathbf{k}'$, and $\mathbf{k}_{\text{SH}}$ is undesirable—in this case we again have $\mathbf{P}^{(4)\text{D}}(2\omega)=0$.

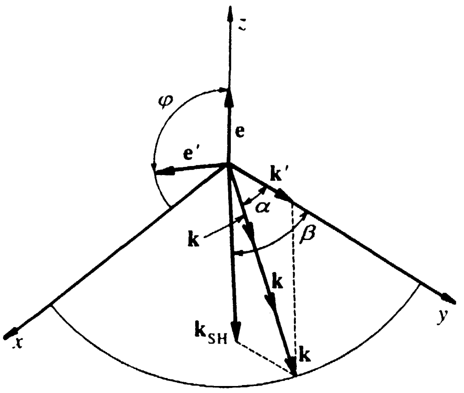

FIG. 2. Vector diagram of synchronous SHG: $2\omega=\omega+\omega+\omega+\omega-\omega$, $\mathbf{k}_{\text{SH}}=3\mathbf{k}-\mathbf{k}'$.

We can easily write out an expression for the pulsed power of the second-harmonic signal, $\mathscr{P}_{\text{SH}}$, in the direction of the phase-matching generated by the intersecting focused beams with frequency $\omega$ and power $\mathscr{P}$, each of which has the same beam waist $w_0$:

$$\begin{aligned}\mathscr{P}_{\text{SH}}&\approx\pi w_0^2I_{\text{SH}}=\frac{cw_0^2n}{8}|E_{\text{SH}}|^2\\&\approx\frac{\pi^2w_0^2\omega^2}{2c^2n}\left(\sin\alpha\,\frac{2w_0}{\text{tg}\,\alpha}\right)^2|\mathbf{P}^{(4)\text{D}}(2\omega)|^2\\&\approx\frac{2^{15}\pi^4|\chi^{(4)\text{D}}_{31112}|^2\mathscr{P}^4}{\lambda_\omega^2c^3n^4w_0^4n_\omega}\sin^2\varphi\,\sin^2\beta.\end{aligned}\tag{17}$$

Here we have assumed that $\alpha\ll1$, so $\sin\alpha\approx\tan\alpha$; $n$ is the index of refraction, the angles $\varphi$ and $\beta$ are defined in Fig. 2. Of course, in a purely collinear geometry ($\alpha=\beta=0$) the effect is completely absent. We have not allowed for the influence of linear absorption, which can be present at one or both of the frequencies $\omega$, $2\omega$.

By tuning the frequency $\omega$ over the interval of interest and recording the relative intensity of the second harmonic, the experimenter gains the capability of measuring the dispersion $|\chi^{(4)\text{D}}_{31112}(2\omega)|^2$, in whose frequency dependence are represented not only the one-photon resonances but also the two-photon resonances of the medium.

Recently in our laboratory the first experiment was performed on recording the above-described effect of dipole second-harmonic generation at a fourth-order nonlinearity under pre-resonance conditions.[8,9]

The SHG scheme can be generalized to the nondegenerate case, in which noncollinear beams with different frequencies $\omega_b$, $\omega_c=3\omega_b-\omega_a$ interact, and the five-photon process

$$\omega_a=2\omega_b-\omega_c=\omega_b+\omega_b+\omega_b-\omega_c.\tag{18}$$

$$\begin{aligned}\mathbf{P}^{(4)\text{D}}(\omega_a)=&4\chi^{(4)\text{D}}_{31112}(\omega_a;\omega_b,\omega_b,\omega_b,-\omega_c)\\&\times A_b^3A_c^*[\mathbf{e}_b\mathbf{e}_c^*](\mathbf{e}_b\mathbf{e}_b)\end{aligned}\tag{19}$$

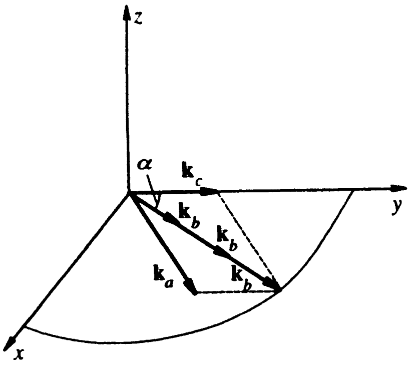

FIG. 3. Vector diagram of synchronous frequency-nondegenerate five-wave mixing according to the BioCARS scheme: $\omega_a = 3\omega_b - \omega_c$, $\mathbf{k}_a = 3\mathbf{k}_b - \mathbf{k}_c$.

feeding into the susceptibility $\chi^{(4)\mathrm{D}}_{ijklm}(\omega_a;\omega_b,\omega_b,\omega_b,-\omega_c)$ is recorded.

This noncollinear scheme can also be made to be synchronous in a medium with normal dispersion by a suitable choice of the angle $\alpha$ between the beams $\omega_b$, $\omega_c = 3\omega_b - \omega_a$ (Fig. 3). In some sense this scheme is analogous to the widely used scheme of coherent anti-Stokes Raman scattering (CARS), based on the four-photon interaction $\omega_a = \omega_b + \omega_b - \omega_c$ (Ref. 11). As in CARS, in the five-photon process it is possible to investigate resonances not only at the harmonics of the investigated frequencies, but also at difference and combination frequencies. Here these are $\omega_b - \omega_c$, $2\omega_b - \omega_c$, $3\omega_b - \omega_c$ (and in the scheme $\omega_a' = \omega_c + \omega_c + \omega_c - \omega_b$ this also includes $2\omega_c - \omega_b$, $3\omega_c - \omega_b$). In what follows, for brevity we will call this five-photon scheme BioCARS since it is of greatest interest for studies of chiral biomolecules in solution.

It is convenient to choose the wave whose frequency is being tuned (let it be $\omega_c$) in the BioCARS scheme to be circularly polarized. Then upon scanning its frequency over the one-photon absorption bands, the dispersion of the linear optical activity will not manifest itself. This latter can contribute to the dispersion of the five-photon signal in the case of linear polarization of the wave being tuned.

The resonances in the BioCARS scheme at the difference frequency $\omega_b - \omega_c$ will take place if the Raman resonance condition $\omega_b - \omega_c = \Omega_\alpha$ is fulfilled and, simultaneously, in accordance with Eq. (18), also the condition of hyper-Raman resonance $\omega_a - 2\omega_b = \Omega_\alpha$, where $\Omega_\alpha$ is the frequency of any normal vibration of the chiral molecule with index $\alpha$, simultaneously allowed in Raman scattering (RS), i.e., at the two-photon transition, and in hyper-Raman scattering (HRS), i.e., at the three-photon transition. Similarly, resonances at the frequency combination $2\omega_b - \omega_c = \Omega_\alpha$ (and, according to Eq. (18), $\omega_a - \omega_b = \Omega_\alpha$) will be represented in the BioCARS spectrum when the normal mode of the molecule $\alpha$ is simultaneously manifested in HRS and RS. Resonances of the form $3\omega_b - \omega_c = \Omega_\alpha$ ($\omega_a = \Omega_\alpha$) will be represented in BioCARS spectra when the mode $\alpha$ is simultaneously allowed in one- and four-photon transitions. A more detailed microscopic treatment of the selection rules of BioCARS spectra will be published separately.[23]

### 2.4. Spatial dispersion of nonlinear optical susceptibilities

A more complete description of nonlinear optical processes in nonracemic solutions of chiral molecules should include an account of effects of spatial dispersion of the nonlinear susceptibilities. Of greatest interest for the spectroscopy of chiral molecules is the dispersion of the cubic nonlinearity which describes four-wave processes of the form $\omega_a = \omega_b + \omega_c + \omega_d$. A term should now be added to expansion (1) (we will arbitrarily call it the quadrupole term, Q, although it also has a magnetic dipole component), which depends on spatial derivatives:[24,25]

$$\begin{aligned}P_i^{(\mathrm{NL})\mathrm{Q}}(\omega_a) = {} & D_2\chi^{(2)\mathrm{Q}}_{ijkl}(\omega_a;\omega_b,\omega_a-\omega_b)\nabla_l E_j(\omega_b)E_k(\omega_a \\ & -\omega_b) + D_3\chi^{(3)\mathrm{Q}}_{ijklm}(\omega_a;\omega_b,\omega_c,\omega_a-\omega_b \\ & -\omega_c)\nabla_m E_j(\omega_b)E_k(\omega_c)E_l \\ & \times(\omega_a-\omega_b-\omega_c)+\ldots \end{aligned} \tag{20}$$

($D_2$ and $D_3$ are factors which take account of possible frequency degeneracy). For plane waves, taking the derivative reduces to direct vector multiplication by $-ik_m$, where $k_m$ is the $m$th component of the wave vector of the corresponding light wave. The susceptibility $\chi^{(2)\mathrm{Q}}_{ijkl}$ is nonzero in all media, whereas $\chi^{(3)\mathrm{Q}}_{ijklm}$ is nonzero only in acentric media.

The spectroscopic scheme based on the nonlinear optical activity effect (NOA) operates with the third-order quadrupole susceptibility $\chi^{(3)\mathrm{Q}}_{ijklm}(\omega;\omega_\mathrm{L},\omega,-\omega_\mathrm{L})$ ($\omega$ and $\omega_\mathrm{L}$ are the frequencies of the probe beam and the pump beam, respectively) and consists in measuring the dispersion of the rotation angle of the polarization plane of the probe beam ($\omega$) induced by the stronger optical field of the pump beam ($\omega_\mathrm{L}$) by tuning the latter. In fact, the action of the nonlinear optical activity reduces to a renormalization of the linear gyration due to the nonlinear term, which is proportional to the intensity of the pump wave $\omega_\mathrm{L}$. The invariant expression for the nonlinear quadrupole polarization vector is obtained by direct summation of the corresponding term in expression (20), taking account of the general form of the tensor $\chi^{(3)\mathrm{Q}}_{ijklm}$ in an isotropic medium, which coincides with expression (5):

$$\begin{aligned}\mathbf{P}^{(3)\mathrm{Q}}(\omega) = {} & \mathrm{i}6|\mathrm{A_L}|^2 A\{\chi^{(3)\mathrm{Q}}_{23111}[\mathbf{k}\mathbf{e}_\mathrm{L}](\mathbf{e}\mathbf{e}^*_\mathrm{L}) + \chi^{(3)\mathrm{Q}}_{31121}[\mathbf{e}_\mathrm{L}\mathbf{e}] \\ & \times(\mathbf{k}\mathbf{e}^*_\mathrm{L}) + \chi^{(3)\mathrm{Q}}_{31112}[\mathbf{e}\mathbf{e}^*_\mathrm{L}](\mathbf{k}\mathbf{e}_\mathrm{L}) + \chi^{(3)Q}_{13112}\mathbf{e}(\mathbf{k}[\mathbf{e}_\mathrm{L}\mathbf{e}^*_\mathrm{L}]) \\ & + \chi^{(3)\mathrm{Q}}_{13121}\mathbf{e}^*_\mathrm{L}(\mathbf{k}[\mathbf{e}_\mathrm{L}\mathbf{e}]) + \chi^{(3)\mathrm{Q}}_{11123}\mathbf{k}(\mathbf{e}[\mathbf{e}^*_\mathrm{L}\mathbf{e}_\mathrm{L}])\}. \end{aligned} \tag{21}$$

Here $\mathbf{k}$ is the wave vector of the probe wave, $A$, $A_\mathrm{L}$ and $\mathbf{e}$, $\mathbf{e}_\mathrm{L}$ are the amplitudes and unit polarization vectors of the waves with frequencies $\omega$, $\omega_\mathrm{L}$, respectively.

Along with the frequency dispersion of the NOA angle, we can also investigate the frequency dispersion of a new spectral component of the probe beam, e.g., the anti-Stokes component $\omega_a = 2\omega_\mathrm{L} - \omega$ [as in ordinary CARS on the cubic dipole nonlinearity $\chi^{(3)\mathrm{Q}}_{ijklm}(\omega_a;\omega_b,\omega_b,-\omega_c)$], generated by the nonlinear source:

$$\mathbf{P}^{(3)\mathrm{Q}}(\omega_a)=i3A_{\mathrm{L}}^{2}A^{*}\{\chi_{23111}^{(3)\mathrm{Q}}[\mathbf{k}_a\mathbf{e}_{\mathrm{L}}](\mathbf{e}_{\mathrm{L}}\mathbf{e}^{*})$$
$$+\chi_{31112}^{(3)\mathrm{Q}}[\mathbf{e}_{\mathrm{L}}\mathbf{e}^{*}](\mathbf{k}_a\mathbf{e}_{\mathrm{L}})$$
$$+\chi_{13112}^{(3)\mathrm{Q}}\mathbf{e}_{\mathrm{L}}(\mathbf{k}_a[\mathbf{e}_{\mathrm{L}}\mathbf{e}^{*}])\}. \qquad (22)$$

Here $\mathbf{k}_\alpha=2\mathbf{k}_{\mathrm{L}}-\mathbf{k}$ is the wave vector of the signal wave under phase-matching conditions.

The spectrum of the coherent anti-Stokes signal generated by this phase matching displays resonances of the form $\omega_b-\omega_c=\Omega_\alpha$, where, as before, $\Omega_\alpha$ is the frequency of the normal vibrational mode $\alpha$ of the chiral molecule, which made this time should be allowed only in Raman scattering. Hence it follows that the scheme for coherent spectroscopy of chiral biomolecules considered here should be compared with spectroscopy of the optical activity of chiral molecules (which has recently gained widespread use) manifested in spontaneous Raman scattering, or as it is customarily called, spontaneous Raman spectroscopy. It is logical to call the coherent variant of the latter spectroscopic scheme, generated by the nonlocal nonlinear source (22) NOA-CARS. NOA-CARS spectroscopy was discussed earlier on the basis of the more direct analogy with the spontaneous scheme and an attempt was undertaken (so far unsuccessful) to experimentally observe the NOA-CARS effect.[27] However, a complete phenomenological analysis of this effect has yet to be carried out. Expression (22) for the nonlinear source in the NOA-CARS scheme was first obtained here.

### 2.5. Two-photon circular dichroism

In addition to linear circular dichroism (different absorption of circularly polarized light beams with left and right rotation of the polarization plane in a chiral medium), its nonlinear analog is also possible, i.e., the experimenter can measure the difference in the two-photon absorption of circularly polarized waves with opposite directions of rotation.

The phenomenological effect is due to the nonzero imaginary part of the susceptibility $\chi_{ijklm}^{(3)\mathrm{D}}(\omega;\omega_{\mathrm{L}},-\omega_{\mathrm{L}},\omega)$, where $\omega$ is the frequency of the probe beam, in which, in the presence of the pump wave with frequency $\omega_{\mathrm{L}}$, an additional absorption is induced. The expression for two-photon absorption (TPA) at the frequency $\omega$ has the form

$$W_{\mathrm{TPA}}(\omega,\omega_{\mathrm{L}})=-E\,\overline{\frac{\partial P^{(3)\mathrm{Q}}}{\partial t}}=\frac{\omega}{2}\,\mathrm{Im}\,[E^{*}P^{(3)\mathrm{Q}}(\omega)], \qquad (23)$$

where $P^{(3)\mathrm{Q}}$ is the nonlocal nonlinear polarization at the frequency $\omega=\omega_{\mathrm{L}}-\omega_{\mathrm{L}}+\omega$. For beams with left (−) and right (+) circular polarization, and the same frequency of the probe and pump waves ($\omega=\omega_{\mathrm{L}}$), the expression for two-photon circular dichroism, according to Eqs. (20), (22), and (23), has the form

$$W_{\mathrm{TPA}}^{(\pm)}(\omega,\omega)=-\frac{\omega}{2}\,|A|^{4}\{(\chi_{1122}^{(3)\mathrm{D}''}+\chi_{1212}^{(3)\mathrm{D}''})\pm k(\chi_{23111}^{(3)\mathrm{Q}''}$$
$$+\chi_{13112}^{(3)\mathrm{Q}''})\}, \qquad (24)$$

where $\chi_{1122}^{(3)\mathrm{Q}''}$, etc. are the imaginary parts of the corresponding components of the quadrupole susceptibility tensors, $k=|\mathbf{k}|$.

As in other spectroscopic schemes using two-photon absorption, it should be possible in experiments on two-photon circular dichroism (TPCD) to record the effect by means of the fluorescence accompanying two-photon absorption, i.e., record the difference in the intensity of the fluorescence excited by two-photon absorption of the right- and left-polarized light waves. Bearing in mind the inevitable smallness of the TPCD effect against the fluorescence background created by dipole two-photon absorption [the first term in braces in expression (24)], it would be best in such an experiment to resort to synchronous detection by periodic switching of the direction of rotation of polarization of the light wave and tuning the synchronous detector recording the fluorescence intensity to the modulation frequency of the polarization.

## 3. POLARIZATION DISCRIMINATION OF SIGNALS FROM CHIRAL MOLECULES AGAINST A BACKGROUND OF MASKING EFFECTS FROM THE SOLVENT

Effects associated with the nonlinear optical response of chiral molecules can take place against a background of uninformative processes involving the solvent molecules, the window material, etc., The most universal masking processes of such kind arise as a consequence of the spatial dispersion of the quadratic optical nonlinearity described by the quadrupole susceptibility $\chi_{ijkl}^{(2)\mathrm{Q}}$, which is nonzero in all media, even centrosymmetric media. The corresponding quadrupole nonlinear polarization within the context of the optical rectification scheme (Sec. 2.2) has the form

$$\mathbf{P}^{(2)\mathrm{Q}}(0)=2|A|^{2}\ \mathrm{Im}\,\{\chi_{1122}^{(2)\mathrm{Q}}\}\mathbf{k}(\mathbf{e}\mathbf{e}^{*}).$$

However, the signal generated by this source is quite weak because of its quadrupole nature: for pure optically active liquids it can be 3–4 orders of magnitude less than the signal from the dipole optical rectification effect. It is possible to gain an additional reduction in this signal by using a standing-wave geometry: the quadrupole signal disappears, and the dipole signal doubles. In an analogous way it can also be used to discriminate the electrooptical effect.

Quadrupole polarization in the noncollinear SHG scheme has the form

$$\mathbf{P}^{(2)\mathrm{Q}}(2\omega)=i2AA'[\chi_{1122}^{(2)\mathrm{Q}}(\mathbf{k}+\mathbf{k}')(\mathbf{e}\mathbf{e}')+\chi_{1212}^{(2)\mathrm{Q}}(\mathbf{e}'(\mathbf{k}'\mathbf{e})$$
$$+\mathbf{e}(\mathbf{k}\mathbf{e}'))]. \qquad (25)$$

However, in a medium with normal dispersion, no direction of phase-matching of this polarization with the free second-harmonic wave exists, although in the direction $\mathbf{k}+\mathbf{k}'$ the phase mismatch is minimal. (The experiments reported in Refs. 8 and 9 probably detected exactly this parasitic effect.) As can easily be seen from expression (25), in this direction of polarization of the nonlinear source the phase mismatch is determined by the normal component of the vector on the right in expression (25), multiplied by $\chi_{1212}^{(2)\mathrm{Q}}$, and does not depend on the properties of the medium. Consequently, by correct alignment of the polarization-phase analyzer it is possible to suppress this component of the nonlinear source. The equation for the complex unit vector $\mathbf{p}$ prescribing such orientation of the analyzer is

$$(\mathbf{pe}')(\mathbf{k}'\mathbf{e})+(\mathbf{pe})(\mathbf{ke}')-\frac{2(\mathbf{k}'\mathbf{e})(\mathbf{ke}')}{(\mathbf{k}+\mathbf{k}')^2}\,(\mathbf{k}+\mathbf{k}',\mathbf{p})=0. \tag{26}$$

The SH radiation passing through the analyzer set up in the described way no longer contains a contribution from the quadrupole quadratic nonlinearity, but is now wholly determined by the "chiral" nonlinearity $\hat{\chi}^{(4)\mathrm{D}}$.

In the scheme based on the nondegenerate five-photon process, in addition to the "direct" process described in Sec. 2.3 there are also competing cascade processes involving the dipole quadratic susceptibility $\hat{\chi}^{(2)\mathrm{D}}$ and the dipole cubic susceptibilities $\hat{\chi}^{(3)\mathrm{D}}$ (see Sec. 4 below).

Nonlinear optical processes competing with NOA and NOA-CARS and possessing similar characteristics are the optical Kerr effect (OKE) and ordinary CARS (Ref. 11) with participation of the third-order dipole susceptibility, i.e., four-photon processes of the type $\omega=\omega_\mathrm{L}+\omega_\mathrm{L}-\omega_\mathrm{L}$ (OKE) and $\omega=\omega_a+\omega_b-\omega_c$ (CARS). One indicator that can conveniently discriminate the target effect of the chiral molecules against the background of these generally much more intense signals is, as before, the polarization state of the various nonlinear sources.

It can be shown that there exist two polarization configurations in which the "dipole" optical Kerr effect does not perturb the linear polarization state of the probe wave. In both configurations the NOA effect is not canceled out.

Let us choose, for definiteness, the $x$ axis along the vector $\mathbf{e}$, and the $z$ axis, along the vector $\mathbf{k}$. Then for the above conditions we have

$$\begin{aligned}
&\text{a)}\ \ \mathbf{e}=\mathbf{e}_\mathrm{L}=\mathbf{e}_x,\\
&P_y^{(3)\mathrm{D}}(\omega)=0,\\
&P_y^{(3)\mathrm{Q}}(\omega)=i6|A_\mathrm{L}|^2A\chi_{23111}^{(3)\mathrm{Q}}k.
\end{aligned} \tag{27}$$

$$\begin{aligned}
&\text{b)}\ \ \mathbf{e}=\mathbf{e}_x,\quad \mathbf{e}_\mathrm{L}=\mathbf{e}_y,\\
&P_y^{(3)\mathrm{D}}(\omega)=0,\\
&P_y^{(3)\mathrm{Q}}(\omega)=i6|A_\mathrm{L}|^2A\chi_{12131}^{(3)\mathrm{Q}}k.
\end{aligned} \tag{28}$$

Polarizational suppression of the ordinary-CARS signal in the NOA-CARS scheme is possible in three polarizational configurations:

$$\begin{aligned}
&\text{a)}\ \ \mathbf{e}_b=\mathbf{e}_c=\mathbf{e}_x;\quad \mathbf{k}_a=k_a\mathbf{e}_z,\\
&P_y^{(3)\mathrm{D}}(\omega_a)=0,\\
&P_y^{(3)\mathrm{Q}}(\omega_a)=i3A_b^2A_c^*k_a\chi_{23111}^{(3)\mathrm{Q}}
\end{aligned} \tag{29}$$

$$\begin{aligned}
&\text{b)}\ \ \mathbf{e}_b=\mathbf{e}_x,\quad \mathbf{e}_c=\mathbf{e}_y,\quad \mathbf{k}_a=k_a\mathbf{e}_z,\\
&P_y^{(3)\mathrm{D}}(\omega_a)=0,\\
&P_y^{(3)\mathrm{Q}}(\omega_a)=i3A_b^2A_c^*k_a\chi_{13112}^{(3)\mathrm{Q}}.
\end{aligned} \tag{30}$$

$$\begin{aligned}
&\text{c)}\ \ \mathbf{e}_b=\frac{1}{\sqrt{2}}\,(\mathbf{e}_x\mp i\mathbf{e}_y),\\
&\mathbf{e}_c=(\mathbf{e}_x\cos\alpha\pm i\mathbf{e}_y\cos\alpha\mp i\mathbf{e}_z\sin\alpha)/\sqrt{1+\cos^2\alpha},\\
&\mathbf{k}_b=k_b\mathbf{e}_z,\quad \mathbf{k}_c=k_c(\mathbf{e}_y\sin\alpha+\mathbf{e}_z\cos\alpha),\\
&\mathbf{k}_a=k_a(\mathbf{e}_y\sin\gamma+\mathbf{e}_z\cos\gamma)
\end{aligned} \tag{31}$$

(here $\alpha$ and $\gamma$ are the angles between the wave vectors $\mathbf{k}_b$ and $\mathbf{k}_c$, $\mathbf{k}_b$ and $\mathbf{k}_a$, respectively).

In this configuration it is possible to completely suppress the CARS signal:

$$\mathbf{P}^{(3)\mathrm{D}}(\omega_a)=0.$$

The component of the quadrupole polarization orthogonal to $\mathbf{k}_a$ has the following form:

$$\begin{aligned}
\mathbf{P}_\perp^{(3)\mathrm{D}}(\omega_a)&=3A_b^2A_c^*k_a\,\frac{\sin\alpha\sin\gamma}{2\sqrt{1+\cos^2\alpha}}\,(\chi_{31112}^{(3)\mathrm{Q}}+\chi_{13112}^{(3)\mathrm{Q}})\\
&\times(\mathbf{e}_x\mp i\mathbf{e}_y'\cos\gamma),
\end{aligned} \tag{32}$$

where $\mathbf{e}_y'$ is the unit vector orthogonal to $\mathbf{e}_x$ and $\mathbf{k}_a$.

## 4. INTERFERENCE OF "DIRECT" AND "CASCADE" PROCESSES IN NONLINEAR OPTICAL SCHEMES. NUMERICAL ESTIMATES

In spectroscopic schemes involving nonlinearities of higher than second order, along with the "direct" processes of signal generation discussed in Secs. 2 and 3, two- and three-step "cascade" processes involving lower nonlinearities are also allowed.

In particular, for the NOA-CARS scheme, two successive processes in cascade are possible:

a) first a difference-frequency electromagnetic wave is generated in the infrared, $\Omega=\omega_b-\omega_c$, and then a wave at the frequency $\omega_a=\omega_b+\Omega$ (or $\omega_c=\omega_b-\Omega$);

b) at the first step, a sum-frequency light wave, $\omega'=\omega_b+\omega_c$ (or $\omega''=\omega_b+\omega_c$) is generated, and then a wave with frequency $\omega_a=\omega_b+\Omega$ (or $\omega_c=\omega_b-\Omega$).

The general scheme and resulting formulas for solution of the problem of cascade signal generation in processes of types $a$ and $b$ are well known in nonlocal nonlinear optics (see Ref. 28 and Ch. 4 of Ref. 11).

The amplitude of the "induced" electromagnetic wave of intermediate frequency (let it be $\omega'$), generated at the first step, can be expressed in terms of the amplitude of the quadratic polarization $\mathbf{P}^{(2)}(\omega')$:

$$\mathbf{E}(\omega')=-\frac{4\pi\omega'^2}{c^2(k'^2-q^2)}\left\{\mathbf{P}^{(2)}(\omega')-\frac{\mathbf{q}(\mathbf{qP}^{(2)}(\omega'))}{k'^2}\right\}, \tag{33}$$

where $\mathbf{q}$ is the wave vector of the polarization wave and $k'=\omega'/c\sqrt{\varepsilon(\omega')}$ is the wave number of the "free" electromagnetic wave with frequency $\omega'$.

At the second step, the field $\mathbf{E}(\omega')$, interacting with the field $\mathbf{E}_\mathrm{L}$ or $\mathbf{E}$, excites a nonlinear polarization in the medium at the frequency of the detected signal. The polarization, being expressed in terms of the amplitudes of the waves introduced into the medium, $A_\mathrm{L}$ and $A$, is the "cascade" cubic polarization, and we may call the corresponding fifth-rank (or sixth-rank) tensor coupling the components of the vector amplitudes of the three fields and the one wave vector (or two) with the "cascade" nonlinear polarization vector the "cascade" cubic nonlinearity tensor of quadrupole (or dipole, or mixed) type.

The corresponding general expressions for the case of arbitrary mutual orientation of the unit polarization vectors and wave vectors of the interacting waves are quite lengthy, and we will not reproduce them here.

By way of example, we display the simplest expression for the cascade polarization of "mixed" type in the NOA-CARS scheme at the frequency $\omega_a = 2\omega_b - \omega_c$ in the polarization configuration in which the ordinary dipole CARS signal is suppressed:

$$\begin{aligned} &\mathbf{e}_b = \mathbf{e}_c = \mathbf{e}_x, \quad \mathbf{k}_a = 2\mathbf{k}_b - \mathbf{k}_c = k_a \mathbf{e}_z, \\ &P^{(3)\mathrm{QD}}_{y\ \mathrm{casec}} = 3A_b^2 A_c^* \frac{4\pi}{\varepsilon(\Omega)} \chi^{(2)\mathrm{Q}}_{1122}(\Omega; \omega_b, \\ &\qquad - \omega_c) \chi^{(2)\mathrm{D}}(\omega_a; \omega_\mathrm{L}, \Omega_c)(\mathbf{e}_b \mathbf{e}_c^*)[\mathbf{e}_b \mathbf{q}]_y. \end{aligned} \tag{34}$$

It is possible, generally speaking, to amplify "cascade" processes if the conditions of phase matching are satisfied at the first step of the cascade, i.e., $|\mathbf{q}| = |\mathbf{k}'| = \omega'/c\sqrt{\varepsilon(\omega')}$.

To estimate the efficiency of a "direct" or "cascade" process of the type under consideration, it is sufficient to estimate the magnitude of the corresponding dipole, quadrupole, or mixed nonlinear susceptibility.

From the experimental data of Ref. 15, in a concentrated solution of chiral molecules of arabinose under pre-resonance conditions $|\chi^{(2)\mathrm{D}}| \approx 10^{-10}$ cgs Oe units, making the order-of-magnitude assumption for the optical rectification scheme $\mathrm{Im}\,\chi^{(2)\mathrm{D}} \approx |\chi^{(2)\mathrm{D}}| \approx 10^{-10}$ cgs Oe units, we have according to formula (12) for $I = 1$ MW/cm$^2$, $\varepsilon(0) = 10$, $n(\omega) = 1.5$, $d = 2$ cm, $\lambda = 1$ $\mu$m, $S = 1$ cm$^2$, and a circularly polarized light wave ($\nu = \pm\pi/4$):

$$u_{\max} \approx 0.6 \text{ mV}.$$

In the EOE scheme for $U = 1$ kV, $\lambda = 0.5$ $\mu$m, $n(\omega) = 1.5$, $|\chi^{(2)\mathrm{D}}| \approx 10^{-10}$ cgs Oe units, we have $|E_y/A| \approx 0.3 \cdot 10^{-3}$.

From general considerations, we can estimate that the order of magnitude of $|\chi^{(3)\mathrm{Q}}k|$ is the same as that of $|\chi^{(3)\mathrm{D}}|a/\lambda$, where $a/\lambda$ is the spatial dispersion parameter ($a$ is the characteristic dimension of the molecule, $\lambda$ is the wavelength). For the visible range $a/\lambda = 10^{-2}-10^{-4}$. Typical values of the "background" dipole susceptibility $\chi^{(3)D}$ are of the order of $10^{-14}$ cm$^3$/erg, so $|\chi^{(3)\mathrm{Q}}k| \approx 10^{-16}-10^{18}$ cm$^3$/erg (direct measurements of the ratio $|\chi^{(3)\mathrm{Q}}k/\chi^{(3)\mathrm{D}}|$, so far as we know, have not been carried out). The sensitivity of modern nonlinear spectrometers in the study of condensed matter allows one to record signals from nonlinearities $\chi^{(3)\mathrm{D}}$ as low as $10^{-21}-10^{-23}$ cm$^3$/erg. Therefore the magnitude of the NOA-CARS signal is more than adequate for reliable detection (of course, under conditions of essentially complete suppression of the competing CARS signal).

The fourth-order dipole susceptibility of a concentrated solution of chiral molecules can be roughly estimated from the condition $|\chi^{(4)\mathrm{D}}/\chi^{(3)\mathrm{D}}| \sim |\chi^{(3)\mathrm{D}}/\chi^{(2)\mathrm{D}}|$, and for $|\chi^{(2)\mathrm{D}}| \approx 10^{-10}$ cgs Oe units and a typical value of the cubic susceptibility $|\chi^{(3)\mathrm{D}}| \approx 10^{-14}$ cgs Oe units we have $|\chi^{(4)\mathrm{D}}| \approx 10^{-18}$ cgs Oe units. On the other hand, from the direct measurement of the dipole fourth-order nonlinearity of a condensed medium (a crystal of lithium formate)[24] (such measurements are unique to our laboratory)[8,9] we obtain the estimate $|\chi^{(4)\mathrm{D}}| \approx 10^{-21}$ cgs Oe units in the transmission band. Our experiments[8,9] on dipole SHG on the nonlinearity $\chi^{(4)\mathrm{D}}$ in a concentrated (2.46 M) aqueous solution of varabinose under pre-resonance conditions give a value of the fourth-order nonlinearity that is still two orders of magnitude smaller: $|\chi^{(4)\mathrm{D}}| \approx 10^{-23}$ cgs Oe units. This result was obtained from the approximate formula (18) by substituting into it experimentally measured values of the parameters.

Here it should be borne in mind that in the experiments reported in Refs. 8 and 9, the fundamental-frequency wave ($\lambda = 532$ nm) lay within the transmission band of the solution, and the second-harmonic wave ($\lambda_{\mathrm{SH}} = 266$ nm) lay at the edge of the ultraviolet absorption band of arabinose.

The unexpectedly low value of the fourth-order dipole nonlinearity of the optically active liquid, estimated in Refs. 8 and 9 from the experimental measurements, was probably due to incomplete removal of the prohibition put in place by fulfillment of the Kleinman relations in the transmission band (see Sec. 2.1).

## 5. CONCLUSION

It appears likely that the nonlinear optical spectroscopic schemes proposed in this paper can be realized experimentally. The spectroscopic information obtained with their help on the magnitude and dispersion of the even dipole and odd quadrupole hyperpolarizabilities of chiral molecules cannot be extracted from the data obtained by linear optical methods. It is possible to choose those experimental schemes in which the detected signals are generated by the chiral molecules, and the undesirable contribution from the specularly symmetric solvent molecules is suppressed.

The author is grateful to the late S. A. Akhmanov, and also to Yu. P. Svirko, V. A. Makarov, A. P. Shkurinov, V. S. Solomatin, T. M. Il'inova, and V. F. Kamalov for helpful discussions of the results.

This work was partly supported by Grant 93-02-15026 of the Russian Foundation for Fundamental Research and Grant MCGOOO of the International Scientific Fund.

[1)] The author is grateful to B. Ya. Zel'dovich for the suggestion of giving this classification of chiral liquids.

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Translated by Paul F. Schippnick