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Biosensor based on surface plasmon interferometry independent on variations of liquid's refraction index

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Abstract

We present a surface sensitive optical sensor based on registration of the phase of surface plasmons by such a method of the phase detection that makes it possible to essentially eliminate an undesirable sensitivity to variations of refraction index of a liquid due to temperature, composition and other changes. This objective has been achieved by detecting the interference between the surface plasmon wave and a bulk wave propagating at grazing angle just above the surface. The proposed interferometric method also does not suffer from vibrational noise.

Keywords: Surface plasmon resonance; Biosensor; Optical sensor; Chemical sensor

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1. Introduction

The surface plasmon resonance (SPR) sensor technology is now leading technology in the field of direct real-time observation of biomolecular interaction.

Several methods of SPR registration are proposed and realized in biosensors. The most popular from them are Kretschmann configurations using angular and wavelength interrogation (for review see [1]).

Exploiting of a phase measurement at SPR permits to increase the sensitivity of SPR sensors by one [2] or even two orders of magnitude (using abrupt phase jump near SPR) [3] in comparison with ones which use angular and wavelength interrogation. As a rule, the phase detection is realized by measuring an interference between a reflected signal wave (which pass through the SPR cell) and a reference wave (which does not pass through the SPR cell). When some biomolecular interaction takes place at the surface of the surface plasmon (SP) supporting film, the phase velocity of the SP is changed and a change of the interference signal occurs.

But there is a general problem for all previously mentioned methods of SPR registration. It is an undesirable sensitivity of the SPR to changes in the refraction index (RI) of the liquid due to variation of the liquid temperature, composition and so on. For example, the water temperature change by 1 °C gives the RI change about 10^{-4}. So potentially very high fundamental sensitivity of SP phase detection (see Appendix A for detail) becomes meaningless without comprehensive temperature stabilization.

There is therefore a need for such a method of the phase registration which will be high sensitive to the properties of a layer deposited on the SPR supporting film, but will be insensitive to the variations of the RI of the liquid.

2. Surface plasmon interferometry between surface waves and bulk waves propagating near surface

In this paper, we present a method of the phase detection of the SP that makes it possible to decrease undesirable sensitivity to variations of the RI of the liquid and also is insensitive to vibrational noise, saving high surface sensitivity.

This method is based on the realization that the undesirable sensitivity to variations of the RI of the liquid may be suppressed when both waves—the signal wave and the reference wave (which produce an interference signal at a phase detection) will pass through the liquid cell. In this case, the change of the RI of the liquid will influence on both waves and therefore will be suppressed in the output interference signal.

This goal may be reached by the scheme presented in Fig. 1. A SP supporting film (in our case it is silver or/and gold films with total thickness >100 nm) is located on the

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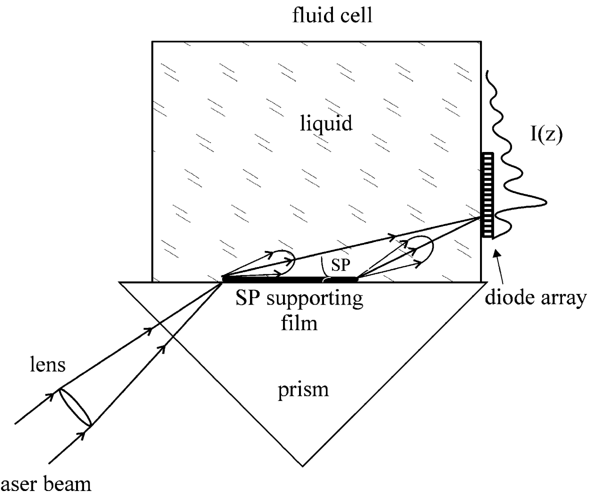

Fig. 1. Schematic illustration of the method of phase detection of the SP with suppressed (by FIF) undesirable sensitivity to variations of the RI of the liquid.

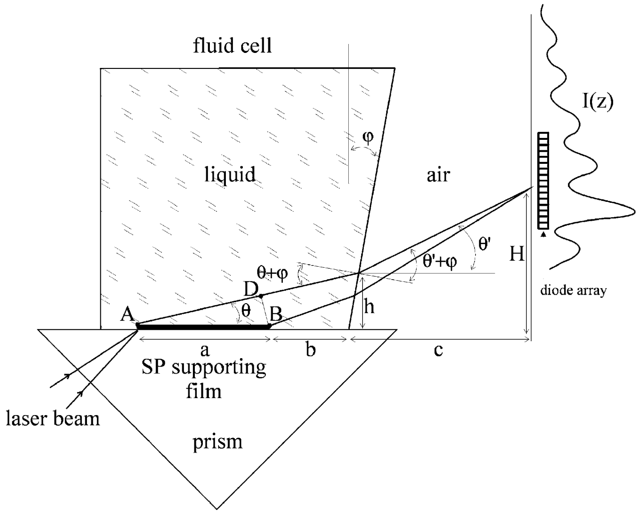

Fig. 2. Schematic illustration of the method of phase detection of the SP, which gives an additional suppression (by SIF) of the undesirable sensitivity to variations of the RI of the liquid.

base of a prism. The SP on the film–liquid interface is exited by focused laser beam at the left edge of the film under attenuated total internal reflection technique. At this so-called “edge excitation” the laser beam partially transformed to the SP and partially diffracted at the left edge of the film to a bulk radiation in the liquid (see description of the experimental setup in Section 4.1 for more details).

The exited SP propagates to the opposite (right) edge of the film and also transforms to a bulk radiation in the liquid. Since these bulk waves are coherent to one another the interference fringes are appearing at the intersection of these bulk beams (for example, at the right wall of the fluid cell, as shown in Fig. 1). Thus, the sample (the film) is located in one of the arms of a double-beam interferometer. The positions of maxima and minima of the interference are dependent on the phase difference between corresponding waves, and therefore on the phase velocity v_{SP} or wavevector k_{SP} ($k_{\mathrm{SP}} = 2\pi\nu/v_{\mathrm{SP}}$) of the SP. From mathematical treatment of a series of the interferograms recording at different values of the film length a one can find the value of k_{SP} [4]. But there are no needs for such complicated (and slow) measurements at sensor applications, since only the change of k_{SP} (but not the precise value of k_{SP}) is interesting. This change—the shift of the single interferogram—may be detected in single measurement by diode array detector or by two-section photodiode (see Fig. 1).

Any biomolecular interactions which occur at the surface of the film will change the wavevector of the SP and as a result the shift of the interference fringes takes place. Any changes of the RI of the liquid will be compensated because it will affect on both ways of the interfering waves.

But in such simple configuration, the compensation is not complete. It is because the geometry of the experiment does not permit to make the path difference between the interfering waves precisely equal to zero, i.e. work in the zero order of the interference and therefore reach the complete compensation.

As it will be shown further the suppression of the undesirable sensitivity to variations of the RI of the liquid (the first improvement factor (FIF)) in comparison with ordinary SPR registration is about $|\varepsilon_{\mathrm{M}}|/n^2$, where ε_{M} is the real part of a dielectric constant of a metal (gold or silver) and n the RI of the liquid. For silver film in the water at wavelength 1.06 μm, this factor is about 30.

Further suppression of the undesirable sensitivity to variations of the RI of the liquid may be reached by using the scheme presented in Fig. 2. This approach is based on the realization that the undesirable sensitivity to variations of the RI of the liquid may be additionally suppressed when the angle between the bulk light wave and the wall of the fluid cell through which the interfering bulk waves are coming from, is properly chosen.

Further, it will be shown that for any particular interference extremum number m there is such tilted angle φ that at any variations of the RI of the liquid the position of the extremum m on the diode array (or on two-section photodiode) practically will not change (but will have the same “interferometric” sensitivity to the variation of wavevector k_{SP} of the SP). This second improvement factor (SIF) depends on the value of the deviation of the liquid’s RI from the preliminary chosen set point (the suppression of the small deviations is more intensive). As it will shown, in the case of the RI deviation from 1.327 to 1.33 (this corresponds to water cooling down by 20 °C) the SIF could be about 300. In the case of the RI deviation from 1.3270 to 1.3273 (this corresponds to water cooling down by 2 °C) this factor could be about 3000. The total improvement factor (TIF) $=$ FIF $\times$ SIF.

An additional advantage of the presented interferometric scheme also should be pointed: it is the absence of the vibrational noise (without complicated "holographic" vibrational stabilization), since the path difference does not suffer from the vibrational noise.

3. Theory

Since the film dimension a is much more less then the dimension $b+c$ (see Fig. 2), the path difference between the interfering waves and the condition for an interference extremum may be found from ABD triangle and have the form:

$$a\,(n_{\mathrm{SP}} - n\cos(\theta)) = (m+\Delta m)\lambda, \tag{1}$$

where m is the number of the extremum, which is an integer for a maximum and a half integer for a minimum, Δm the total additional phase shift between the interfering waves appearing upon the excitation and detachment of the SP at the edges of the film, λ wavelength of the light and

$$n_{\mathrm{SP}} = \sqrt{\frac{\varepsilon_{\mathrm{M}} n^2}{\varepsilon_{\mathrm{M}} + n^2}} \tag{2}$$

is the "refraction index" of the SP. In approximations $-\varepsilon_{\mathrm{M}} \gg n^2$ and $\theta \ll 1$, Eq. (1) has the form:

$$an\left(\frac{n^2}{2|\varepsilon_{\mathrm{M}}|} + \frac{\theta^2}{2}\right) \simeq (m+\Delta m)\lambda. \tag{3}$$

Since we have sum of two positive value in the parenthesis, we cannot make the path difference between the interfering waves precisely equal to zero in this geometry (i.e. work with $(m+\Delta m) \equiv 0$) and cannot obtain perfect compensation (i.e. cannot obtain FIF $\to \infty$).

The angle of a maximum of a diffraction is $\theta_{\max} = \pi/2 - \arccos(Z) \approx n/(|\varepsilon_{\mathrm{M}}|)^{1/2}$ [5], and therefore the next rough estimation may be done:

$$an\left(\frac{n^2}{|\varepsilon_{\mathrm{M}}|}\right) \simeq (m+\Delta m)\lambda. \tag{4}$$

Therefore, in this case, the situation is $|\varepsilon_{\mathrm{M}}|/n^2$ times better then in ordinary SPR schemes, where temperature and other variations affect on total optical length an (in our case only the path with dimension in several wavelengths ($(m+\Delta m)\lambda$) undergoes such variations). It is the mathematical foundation for the FIF.

As we have pointed earlier, the interference rays refract at wall of the fluid cell before fall on the photodetector. This fact permits to obtain additional suppression of undesirable sensitivity to variations of the index of refraction subject to proper choice of the angle between interference rays and the wall of the fluid cell. (In other words, it permits to make an optical path length equalization of interference rays in liquid for particular extremum m.) The mathematical foundation for this SIF is derived further.

The angle θ, which determinates the direction on the extremum m may be derived from (1):

$$\theta = \arccos\left(\frac{n_{\mathrm{SP}}}{n} - \frac{(m+\Delta m)\lambda}{an}\right) \tag{5}$$

(note that this angle depends on n and it decreases when n increases). But the angle θ' (see Fig. 2) is associated with θ by Snell's law:

$$n\sin(\theta+\varphi) = \sin(\theta'+\varphi), \tag{6}$$

where φ is the tilted angle of the cell's wall. One can see that according to (6), θ' increases when n increases.

Therefore, there is such an angle φ that variations in n will not be reflected in θ'. This angle may be found by solving equations:

$$\frac{\partial}{\partial n}(n\sin(\theta+\varphi)) = 0, \tag{7}$$

in respect of φ.

The solution is:

$$\varphi_m = \arctan\left(\frac{(m+\Delta m)\lambda - a n_{\mathrm{SP}}^3/\varepsilon_{\mathrm{M}}}{\sqrt{a^2n^2 - (a n_{\mathrm{SP}} - (m+\Delta m)\lambda)^2}}\right) - \arccos\left(\frac{a n_{\mathrm{SP}} - (m+\Delta m)\lambda}{an}\right). \tag{8}$$

At such tilted angle φ a small variation in the n will not change the direction θ' on the extremum number m. But the sensitivity to the variations of k_{SP} will be the same; because, in this case, only the angle θ will change (without simultaneous changes of the n of the liquid).

The "reverse" problem also may be solved. We may fix the tilted angle φ (for example, at the most convenient value $\varphi = 0$; the right-angled wall) and find the extremum number m_{opt}, which will not move when the liquid's RI changes. The approximated solution is:

$$m_{\mathrm{opt}} \simeq 2\frac{an^3}{\lambda|\varepsilon_{\mathrm{M}}|}. \tag{9}$$

The most interesting quantity—the angle θ_{opt}, that points to the extremum m_{opt} is:

$$\theta_{\mathrm{opt}} = \arccos\left(\left(\frac{\varepsilon_{\mathrm{M}}+n^2}{\varepsilon_{\mathrm{M}}}\right)^{3/2}\right) \approx \sqrt{\frac{3}{|\varepsilon_{\mathrm{M}}|}}\,n. \tag{10}$$

In our case, $\varepsilon_{\mathrm{M}} = -53$, $n = 1.326$ (at $\lambda = 1.06\,\mu\mathrm{m}$), $\theta_{\mathrm{opt}} \approx 0.315\,\mathrm{rad} = 18^\circ$. As a rule the interference extremum m_{opt} (and $\theta_{\mathrm{opt}} \approx 18^\circ$) is reachable and it is possible to work with the right-angled wall of the fluid cell.

The expressions taken into account the finite dimensions of b and c are more complicated than (8)–(10), but also may be obtained (in this case φ should be $>\varphi_m$ and so on). The calculated variation of the z-position of the interference extremum with number m is shown in Fig. 3 (in this example we take $m = 17$, $\Delta m = +0.5$, $a = 200\,\mu\mathrm{m}$, $\lambda = 1.06\,\mu\mathrm{m}$, $\varepsilon = -53$, $\varphi = 0$, $b = 5\,\mathrm{mm}$, $c = 90\,\mathrm{mm}$). From this figure,

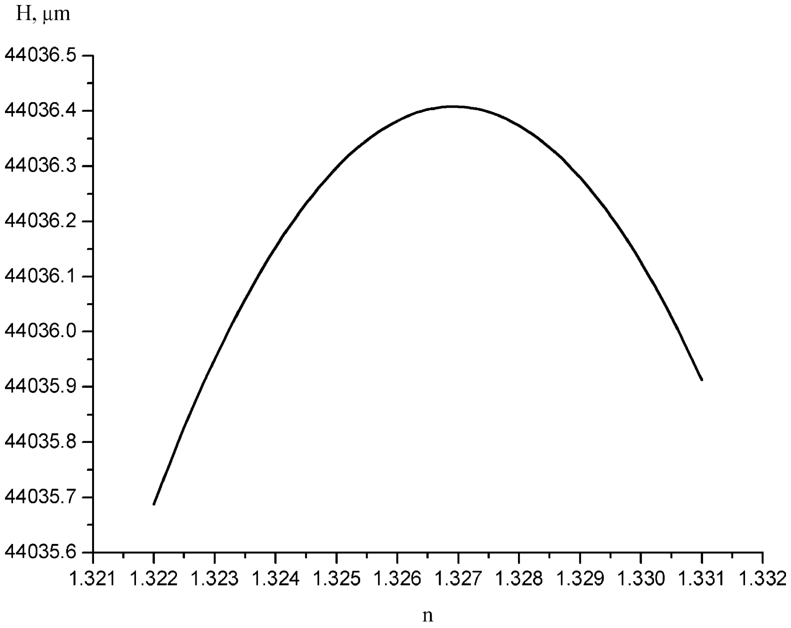

Fig. 3. Calculated variation of the z-position of the interference extremum with number $m = 17$ vs. RI of the liquid (see text for details).

one can see that very small RI variations, near preliminary chosen value $n \simeq 1.327$, do not change a position of the extremum at all. One can also see that at RI variations from 1.324 to 1.33 the variations in z-position of the extremum do not exceed $\Delta H \simeq 0.3\,\mu\text{m}$.

When there is no refraction on the cell's wall (for example, $b = 95\,\text{mm}$, $c = 0$, i.e detector is located immediately on the cell's wall as in Fig. 1) the variations in z-position of the extremum exceed 100 μm at the same RI variations. Therefore, the SIF is ∼300 in this case. To obtain total improvement factor of this scheme in comparison with ordinary Kretschmann scheme, this quantity must be multiplied on FIF. For given above values (i.e. at $m = 17$), FIF is $an/((m + \Delta m)\lambda) \simeq 13.5$, i.e. TIF $\simeq 4000$. At smaller RI variations the SIF is increased due to quadratic dependence of $H(n)$ near chosen n (see Fig. 3).

4. Experiment

4.1. Experimental setup

We have performed our experiments in configuration with right-angled cell's wall ($\varphi = 0$) near optimal extremum m_{opt}. The scheme of our experiment is shown in Fig. 4.

Metal films were deposited on part of the hypotenuse surface of a heavy flint glass prism. A mask for obtaining of sharp edges of the metal films was made by putting a 5 μm thick polymeric film on the prism before metal deposition. Metal films were prepared by thermal evaporation at the pressure 7×10^{-4} Pa at a room temperature. The thickness of metal films was measured using a quartz crystal monitor disposed near the base of the prism.

The structure of the metal films is shown in the inset of Fig. 4. 2 nm thick sublayer of Cr was deposited first for better adhesion of the following metal layers. It should be noted here that the presence of such Cr sublayer does not deteriorate the quality of this SP supporting film, because the film in our configuration is much more thick than at Kretschmann configuration. Following 170 nm thick Ag layer was protected from air and water deterioration by deposition of 10 nm thick Au layer on the top of it. The presence of such layer protect Ag film very well [6] and only slightly decrease an SP quality of the Ag film in near-infrared region.

A cw Nd–YAG laser beam ($\lambda = 1.06\,\mu\text{m}$) focused by a lens is directed through the prism at such an angle that total internal reflection takes place from the hypotenuse surface of the prism. It is well known [7] that during total internal reflection on a boundary with a less dense medium, the electromagnetic field decays exponentially with increasing distance from the interface, and the reflected ray is displaced somewhat relative to the incident ray. If the edge of a metal film is placed between the “entrance” and “exit” points of the ray, the condition for total internal reflection is violated, and the radiation is partially transformed into an SP and bulk radiation, which propagates above the surface of the metal. The surface plasmon wave excited on the left edge of the metal film propagates over its outer surface (at the boundary with liquid) and reaches the opposite (right) edge of the film (or an edge of an additional Cr layer as shown in the inset of Fig. 4), where it is transformed back into bulk radiation.

There are several methods for such transformation into bulk radiation at the right edge of the film. One of them was presented in Figs. 1 and 2, where the total film length is equal to a. The efficiency of the SP transformation into bulk

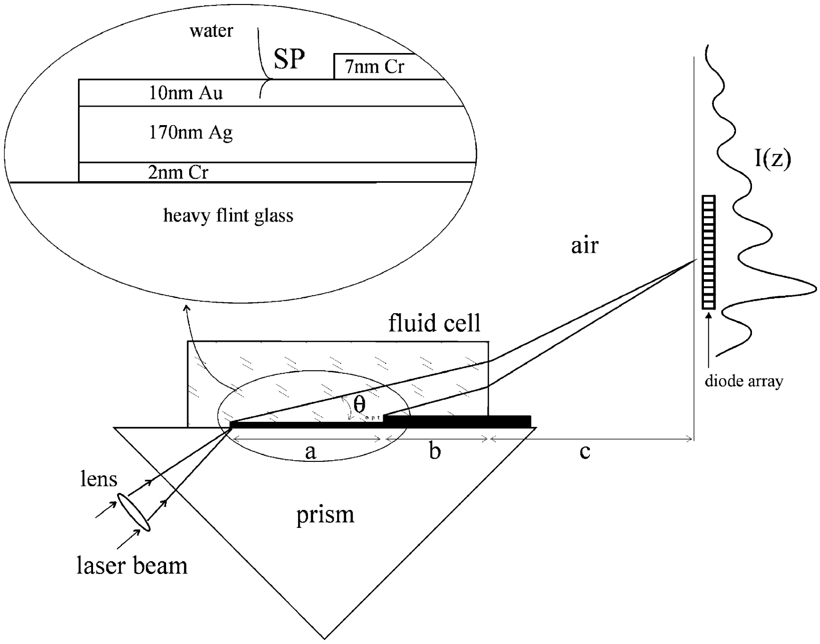

Fig. 4. The scheme of the experiment. In the inset, the structure of the metal films is shown.

radiation in this method is very good, but strong precautions must be made from diffraction of the initial laser beam at the right edge of the film (i.e. a size of the focal spot of the laser beam must be much less than *a*), because such diffraction is produced "false" interference pattern on the photodetector. Another method is the deposition of a thin layer of a dielectric or a metal (which does not support the SP propagation in the spectral range of interest) at the distance *a* from the left edge of the film. The conversion efficiency into bulk radiation in such method is lower, but such method is totally free from any "false" interference patterns. We used both methods in our experiments with similar results. To use the second method we deposited an additional 7 nm thick layer of Cr at the distance *a* from the left edge of the film. The distance *a* may be three to five times larger than mean free path of the SP in the water L_{SP} (see Appendix A for details) and in our experiments the length *a* was in 150–200 μm range. Interference pattern was detected by 512-pixel Hamamatsu diode array. The measurement time for one interferogram was 1 s. Mathematical treatment of the recorded interferogram was made during measurements by personal computer.

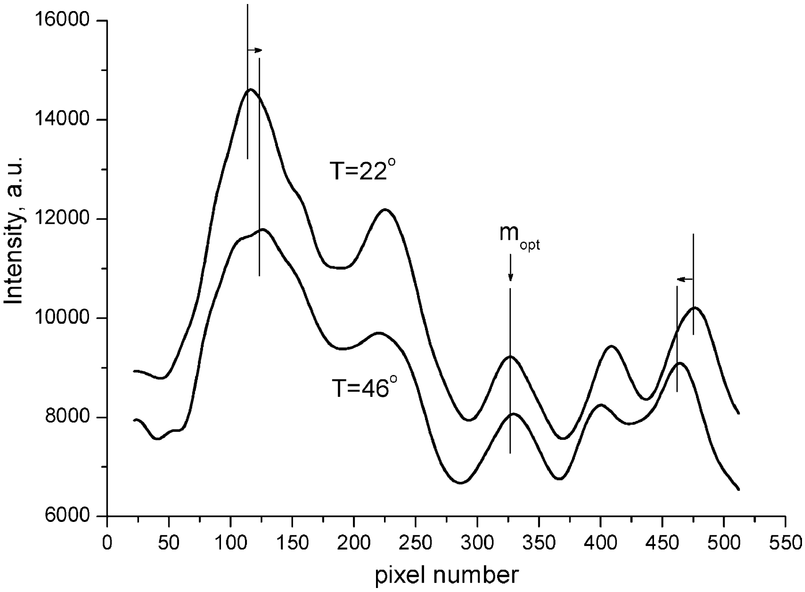

Fig. 5. Interferograms recorded at two different temperatures: 22 and 46 °C (the 46 °C interferogram is shifted down by 2000 a.u.).

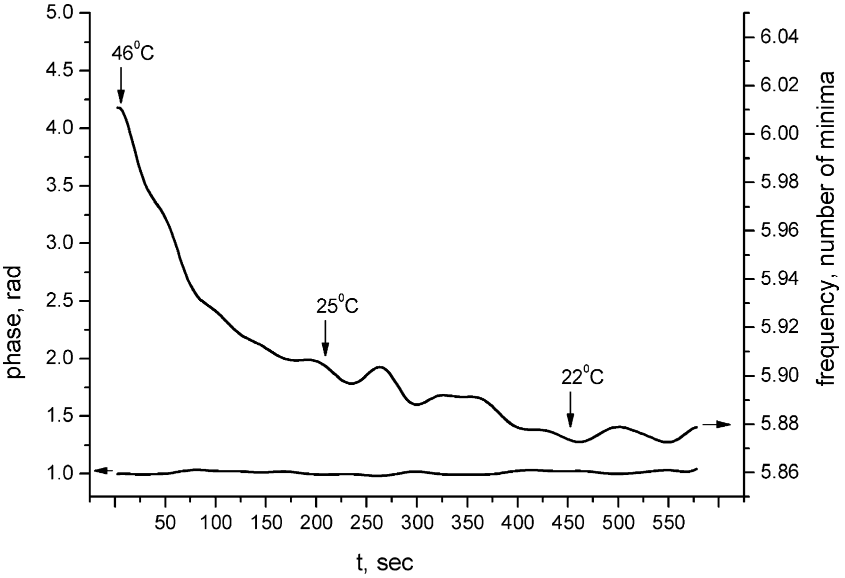

Fig. 6. The change of the “phase” and “frequency” of the interferograms during water cooling down from 46 °C to room temperature. One can see that the “phase” is not sensitive to the change of the liquid’s RI, while “frequency” is.

4.2. Temperature dependence near optimal extremum

At first, in our experiments we checked the temperature dependence of the interference pattern near m_{opt}. According to our theoretical consideration in Section 3, the extremum number m_{opt} will not move at temperature (i.e. the refraction index) variations, but extrema with greater and lesser numbers m will move in opposite directions. In Figs. 5 and 6, one can see the results that confirm these conclusions. Fig. 5 presents two interferograms recorded at two different temperatures: 22 and 46 °C (for better view we shifted the 46 °C interferogram down by 2000 a.u.). One can see that maximum m_{opt} in the center of the interferogram practically does not move during the water heating, while right and left extrema move to opposite directions (to the center of the interferogram, in our case). This means that “phase” of the interferogram practically does not change, but “spatial frequency” of the interferogram (that is the effective number of the extrema on the diode array) increases. Our computer program derives these quantities (“phase” and “frequency”) from recorded interferograms in real-time regime and in Fig. 6 one can see “phase” and “frequency” of

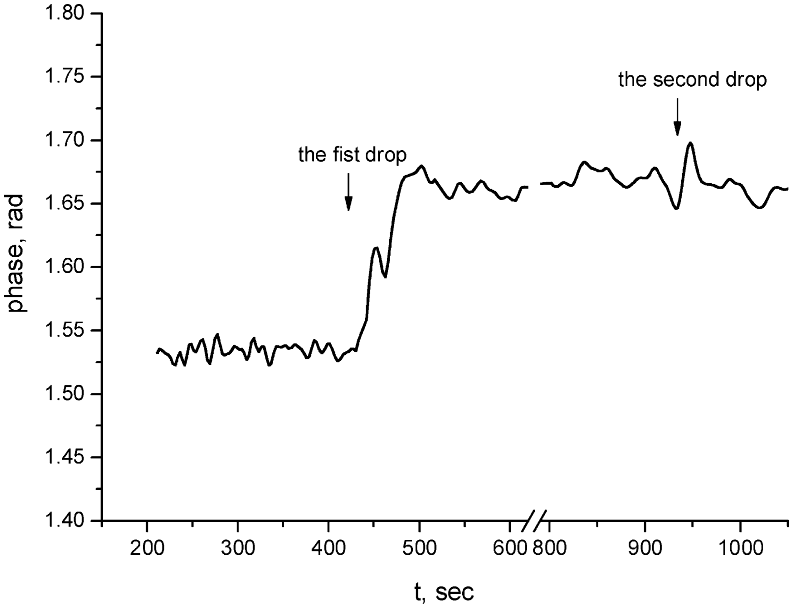

Fig. 7. The deposition of the SAM of 2-mercaptoethanol on gold surface. The RI change after the second drop of the thiol is the same as after the first one ($\Delta n \simeq 0.0033$). But the SAM was built up after the first drop and only this surface change is detected by the “phase” signal.

the interferograms during water cooling down from 46 °C to room temperature. From these results, it is clearly seen that the change of the liquid's refraction index does not change the position of the m_{opt} (i.e. the interferogram "phase"). In the next section we will demonstrate that any changes on the surface of the SP supporting film lead to shift of the interferogram as a whole, i.e. lead to change of the "phase" of the interferogram.

4.3. Deposition of SAM on the surface

We used the deposition of a self-assembled monolayer (SAM) of 2-mercaptoethanol to demonstrate the surface sensitivity of our method. 2-Mercaptoethanol is a small thiol molecule. Its molecular formula is C_2H_6OS, its molecular weight is equal to 78.13 and its RI is equal to 1.5.

Thiol was added dropwise into the fluid cell contained 1 ml of pure water. One drop was about 0.02 ml. From the phase curve depicted in Fig. 7, one can see that creation of thiol's SAM on the gold surface leads to change of the "phase" of the interferogram. To make sure that such phase signal change is associated with a process that occurs on the surface but not into the volume of liquid (so after the first thiol drop the liquid's RI is changed from 1.326 to 1.3293), we fall the second drop of the thiol when SAM is already created (and no additional changes on the surface can occur). The second drop of the thiol leads to approximately the same change of the liquid's RI (up to 1.3325—note that $\Delta n \simeq 0.0033$ corresponds to change of the water temperature $\Delta T \simeq 22\,^{\circ}\mathrm{C}$), but after initial perturbation of the phase signal it returns to the same value. The same initial perturbation was occurred after the first thiol drop (see Fig. 7). We believe that such perturbations take place because the liquid becomes irregular in optical thickness during an initial stage of the mixing. When all fluctuations expire the signal returns to its stationary value. The registered phase shift is appropriate to the deposition of a thin layer with optical thickness $n_d d \approx 1.5 \times (3.1 \pm 0.1)$ Å (i.e. if the RI of the layer is $n_d = 1.5$, so its thickness is $d = (3.1 \pm 0.1)$ Å).

5. Conclusion

In this paper we proposed and realized the optical sensor based on the registration of the interference between the surface plasmon wave and a bulk wave propagating at grazing angle just above the surface. We shown theoretically and experimentally that the proposed method is insensitive on variations of refraction index of a liquid due to temperature, composition and other changes. Suppression of these undesirable variations of liquid's RI is more strong for the small variations. For example, according to theoretical estimation the total improvement factor in comparison with ordinary Kretschmann configuration is TIF = 4000 in the case of the RI deviation from 1.327 to 1.33 (this corresponds to water cooling down by 20 °C), and TIF = 40,000 in the case of the RI deviation from 1.3270 to 1.3273 (this corresponds to water cooling down by 2 °C).

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Appendix A. Fundamental limit for detection of thin films on the surface by SPI technique

As it was pointed in [2,3], the use of the phase detection technique may increase the sensitivity of the SPR sensors by one to two orders of magnitude in comparison with ordinary SPR methods. The main obstacle for exploiting of such high sensitivity was the undesirable sensitivity to variations of the liquid's RI. If these variations are successfully suppressed it is naturally to bring up the question about fundamental, ultimate sensitivity to the thin layer deposition by the phase detection in SPI.

As a rule in articles devoted to SPR sensors the sensitivity is expressed in terms of minimal detected change of RI of liquid. Our method is insensitive to this quantity, and we will express the sensitivity in terms of deposition of a mass in pg on an area in mm^2.

At first let us give the expression, which show how the "RI" of the SP, (2) is changed when a thin homogeneous film with the thickness d and the RI n_d is deposited on the SP supporting film [8]:

$$\Delta n_{\text{SP}} = 2\pi \frac{d}{\lambda} \frac{n^3}{\sqrt{|\varepsilon_{\text{M}}|}} \left(1 - \frac{n^2}{n_d^2} - \frac{n_d^2}{\varepsilon_{\text{M}}}\right), \qquad \text{(A.1)}$$

where n is the RI of liquid, and ε_{M} the real part of the dielectric constant of the SP supporting metal film.

When the optical path change is equal to one wavelength: $a\Delta n_{\text{SP}} = \lambda$, the phase change of one interference ray (and change of the "phase" of interferogram) is equal to 2π. A minimal detectable phase change is the quantum uncertainty of the phase of light in the coherent state:

$$\delta\phi_{\text{shot noise}} \simeq \frac{1}{2\sqrt{N_{\text{el}}}} = \frac{1}{2}\sqrt{\frac{\hbar\omega}{\eta P t_m}}, \qquad \text{(A.2)}$$

where N_{el} is the number of photoelectrons at the photodetector during the measurement time t_m, P the total light power at the photodetector, η the photodetector quantum efficiency, and $\hbar$ the Plank's constant. Therefore, the minimal detectable thickness (caused by a quantum uncertainty) of absorption layer $d_{\min}$ is:

$$d_{\min} \approx \frac{\lambda^2}{8\pi a\sqrt{N_{\mathrm{el}}}}\left(\frac{\sqrt{|\varepsilon_{\mathrm{M}}|}}{\pi n^3}\frac{n_d^2}{(n_d^2-n^2)}\right), \qquad (A.3)$$

where we have made approximation $n_d^2/|\varepsilon_{\mathrm{M}}| \ll 1$.

One pixel of our photodiode array has a well capacity about 10^8 electrons, the number of pixels is 512, therefore in our case $N_{\mathrm{el}} = 5.12 \times 10^{10}$ (for one readout) and the minimal detectable change of layer thickness in our case is:

$$d_{\min} \simeq 6 \times 10^{-5}\,\text{Å} \qquad (A.4)$$

(we have taken the given above values $\varepsilon_{\mathrm{M}} = -53$, $n = 1.326$, $n_d = 1.5$, $\lambda = 1.06\,\mu\mathrm{m}$, $a = 150\,\mu\mathrm{m}$). The sensitivity of our setup is about three order worse. The reasons are an unaccounted above readout noise of the diode array and an excessive laser power noise. Efforts are now underway to reach the fundamental sensitivity limit, and results will be published elsewhere [9]. We emphasize here again that in this section we take into account only absolute fundamental limit caused by quantum fluctuation of laser light in coherent state. We neglect here, for example, any thermodynamic fluctuations inside and nearby of the adsorption layer, which also can deteriorate the sensitivity limit.

For biomolecular interaction it is more convenient to present the fundamental sensitivity in term of absorbed mass on mm^2. In this case, the Eq. (A.3) has the form:

$$\left(\frac{m}{S}\right)_{\min} \approx \rho\frac{\lambda^2}{8\pi a\sqrt{N_{\mathrm{el}}}}\left(\frac{\sqrt{|\varepsilon_{\mathrm{M}}|}}{\pi n^3}\frac{n_d^2}{(n_d^2-n^2)}\right). \qquad (A.5)$$

Eqs. (A.3) and (A.5) are the main result of this section. Although (A.3) and (A.5) were obtained for the phase detection technique, the ultimate sensitivity of any technique exploiting the SPR will be the same.

For $\rho \simeq 1$ g/ml one can obtain from (A.4), the value 0.006 pg/mm^2. It should be noted that if one will detect the signal not by diode array, but (for example) by two-section photodiode, one may increase the light power P (and so N_{el}) on photodetector by many orders of magnitude and therefore decrease the fundamental limit (A.3) by several orders of magnitude.

In conclusion, it is worth to compare fundamental SP phase detection sensitivity (A.3) with fundamental sensitivity of (non-SPR) biosensors based on registration of a change of a thickness of a glass plate due to biomolecular interaction on the surface of the plate [10,11]. In such methods, the ultimate sensitivity will be the same (or worse) like the ultimate sensitivity of Michelson interferometer:

$$d_{\mathrm{M}} \approx \frac{\lambda}{8\pi\sqrt{N_{\mathrm{el}}}}. \qquad (A.6)$$

In (A.3), the value in the parenthesis (for our values) is $B(n, n_d, |\varepsilon_{\mathrm{M}}|) \simeq 4.5$. One can see (from comparison of (A.3) and (A.6)) that at the fundamental level SP sensors at least in $a/(\lambda B)$ ($\sim$30 in our case) more sensitive than the thickness sensors (subject to the same registration energy $P\eta t_m$ in both configuration). The advantage of the SP sensors increases while the distance a increases.

The length a in our method can be $a \sim (3-5) \times L_{\mathrm{SP}}$, where the mean free path of SPs L_{SP} is [12]:

$$L_{\mathrm{SP}} = \frac{\lambda}{2\pi}\frac{|\varepsilon'_{\mathrm{M}}|^2}{\varepsilon''_{\mathrm{M}}}\left(\frac{\varepsilon'_{\mathrm{M}}+n^2}{\varepsilon'_{\mathrm{M}}n^2}\right)^{3/2} \approx \frac{\lambda}{2\pi}\frac{|\varepsilon'_{\mathrm{M}}|^2}{n^3\varepsilon''_{\mathrm{M}}}. \qquad (A.7)$$

On the other hand, in Kretschmann configuration, at optimal film thickness, a real plasmon free path is halved due to leakage of the energy into prism side [12], i.e the SP free path $a_{\mathrm{Kr}} \sim L_{\mathrm{SP}}/2$. Therefore, our configuration is by order of magnitude more sensitive than Kretschmann configuration.

References

[1] J. Homola, S.S. Yee, G. Gauglitz, Surface plasmon resonance sensors: review, Sens. Actuators B 54 (1999) 3–15.

[2] S.G. Nelson, K.S. Johnson, S.S. Yee, High sensitivity surface plasmon resonance sensor based on phase detection, Sens. Actuators B 35–36 (1996) 187–191.

[3] A.V. Kabashin, P.I. Nikitin, Surface plasmon resonance interferometer for bio- and chemical sensors, Opt. Commun. 150 (1998) 5–8.

[4] Yu.E. Petrov, E.V. Alieva, G.N. Zhizhin, V.A. Yakovlev, Phase measurements of surface electromagnetic waves on silver with excitation through substrate, Tech. Phys. 43 (1998) 323–326.

[5] V.N. Konopsky, E.V. Alieva, Dispersion relation of surface plasmons near photonic band gaps: influence of the interaction with light, J. Mod. Opt. 48 (2001) 1597–1615.

[6] V.A. Yakovlev, A. Poleshaeva, private communication.

[7] N.J. Harrick, Internal Reflection Spectroscopy, Interscience, New York, 1967.

[8] G.N. Zhizhin, M.A. Moskalova, E.V. Shomina (Alieva), V.A. Yakovlev, Surface electromagnetic waves propagation on metal surfaces, in: V.M. Agranovich, D.L. Mills (Eds.), Surface Polaritons, North-Holland, Amsterdam, 1982.

[9] V.N. Konopsky, E.V. Alieva, in press.

[10] P.I. Nikitin, B.G. Gorshkov, M.V. Valeiko, S.I. Rogov, Spectral phase interference method for detection of biochemical reaction on a surface, Kvantovaya Electronika 30 (2000) 1099–1104 (in Russian).

[11] P.I. Nikitin, M.V. Valeiko, B.G. Gorshkov, New direct optical biosensors for multi-analyte detection, Sens. Actuators B 90 (2003) 46–51.

[12] H. Raether, Surface Plasmons, Springer Tracts in Modern Physics, vol. 111, Springer-Verlag, Berlin, 1988, p. 36.