

# Photothermal molecular sensing by using metal thin-film nanograting for chemical and biomedical applications

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## Abstract

We have developed a highly sensitive molecular sensor based on the heterodyne-detected third order nonlinear optical measurement with metal thin-film gratings. Pumped by an ultra-violet laser, the stripe pattern of the grating is transferred to the sample solution. The properties of the solution are detected via probe beam diffraction output from this special modulation. Time dependent signals profiles in nitrobenzene/2-propanol solution are thus obtained. The signal intensities as well as the concentrations of solute are proportional to the induced third order nonlinear electric susceptibility of solution. This technique can even detect the properties of those molecules and chemical compounds which are colorless and non-fluorescent. The merits of this method, such as simplicity, the high sensitivity, and the high speed, should be suitable for the molecular sensor of the microfluidic devices.

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**Keywords:** Photothermal molecular sensing; Metal thin-film; Nanograting; Biomedical application; Chemical application

## 1. Introduction

Recently, microfluidic technologies have been developed and applied widely in biology and analytical chemistry [1–5]. Fluorescent latex beads [2,3], DNA with fluorescent dyes [4], or colored dye solutions [5] have been used as the host objects in such fluidic channels. However, many molecules and chemical compounds have neither color nor fluorescence/phosphorescence. Highly sensitive, molecular sensing technique without human visibility is necessary for chemical and biomedical applications of microfluidic devices. In this article, we propose a highly sensitive molecular sensing technique based on the third order nonlinear spectroscopy with nano- and micrometal gratings fabricated in our laboratory in order to be applied to the monitoring of the microfluidic devices.

The nonlinear optical response can be often described by expressing the polarization  $P(t)$  as a power series in the electric field vector  $E$  as

$$P(t)/\epsilon_0 = \Sigma \chi_{ij}^{(1)} E_i + \Sigma \Sigma \chi_{ijk}^{(2)} E_i E_k + \Sigma \Sigma \Sigma \chi_{ijkl}^{(3)} E_i E_k E_l + \dots \quad (1)$$

where  $\epsilon_0$  is dielectric constant and  $\chi_{ij}^{(1)}$ ,  $\chi_{ijk}^{(2)}$  and  $\chi_{ijkl}^{(3)}$  are the tensor of the first, second and third order optical susceptibilities of materials. When the material has a symmetry center, then  $\chi_{ijk}^{(2)}=0$ . In many cases, the third order nonlinear term is the lowest nonlinear term. By using various third order nonlinear spectroscopies, the third order polarization term in Eq. (1) can be observed. It is a very useful and powerful technique for molecular sensing because third order nonlinear susceptibility [ $\chi^{(3)}$ ] of sample solution may be changed by internal dynamic processes of molecules without direct photon transfer. Examples are electron transfer, vibration, rotation, translation, thermalization, volume/structure change, clustering/aggregation, or chemical reaction, etc. [6,7]. All such molecular processes have

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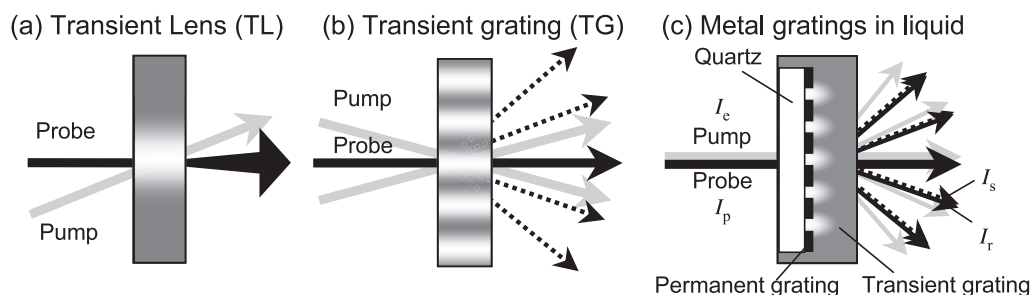


Fig. 1. Pump and probe beams alignments for (a) transient lens, (b) transient grating, and (c) present heterodyne detected transient grating with metal grating.

been detectable by using various third order nonlinear spectroscopies. Probably, the simplest setup of the third order nonlinear spectroscopy was the transient lens (TL) spectroscopy [8,9] (Fig. 1a). In this method, both pump and probe beams were focused together onto the sample. The Gaussian shaped spatial distribution of optical properties due to the pump beam was detected by focus/defocus of the probe beam. Transient grating (TG) spectroscopy [10–14] was also one of the useful methods of such nonlinear spectroscopies (Fig. 1b). In this method, bright and dark stripe-patterned modulations of the sample medium were created by the crossing of two pump beams and were detected by the diffraction of the probe beam. There were many reports of the TG technique to observe many molecular processes with broad time scales [10–14]. The setup of the TG technique was complicated but the sensitivity was high and S/N ratio was much better than the TL technique. However, the signal intensities were still too weak to apply to the molecular sensing in microfluidic devices and some high-sensitive detector or signal amplification technique has become necessary. In 1995, optical heterodyne detection of stimulated Raman [15] and Rayleigh [16] scattering were reported. After that, optical heterodyne detected transient grating (OHDTG) technique has been developed and reported by several groups [17–24]. The signal intensities were dramatically enhanced by using OHDTG techniques but experimental setups has been much too complex. More recently, Katayama et al. [25,26] developed technique of the lens-free OHDTG for easy alignment and repeatability.

Here, we describe a novel and convenient technique of third order nonlinear spectroscopy by using the direct pattern transfer from nano-fabricated metal film grating to the sample solution (Fig. 1c). This method has the same advantage as the OHDTG technique of the past. Moreover, the optical configuration and tuning are much simpler and easy to use.

## 2. Experimental details

The schematic diagram of our photothermal molecular sensor using thin-film grating is shown in Fig. 2. Time-modulated (50–400 Hz) InGaN laser (405 nm, 5 mW) is used as pump beam for frequency dependence measurement. A cw-He–Ne laser (633 nm, 0.05 mW) is used as

probe beams. Both beams are focused by a lens onto the sample solution. Diffraction limited probe beam passes through a pinhole and a glass filter and projected to an InGaAs photodetector. A frequency-tripled Nd:YAG laser (355nm) is also used as a pump beam for the time resolved measurement. The pulse width, power and repetition rate of the pump beam are 10 ns, 0.3 mJ/pulse and 3 Hz, respectively. Microfluidic devices can use similar structures as in Ref. [1–5], but a quartz sample cells is used here for our first test operation. Metal gratings of nano- and micrometer scale are fabricated by chromium evaporation on quartz substrates, patterned by electron beam lithography, and chemical etching. Microscopic image of the grating with 1:1 and 1:2 metal/window ratios are shown in Fig. 3a,b. The smallest width and period of the grating are 333 nm and 1  $\mu\text{m}$ , respectively. The fabricated metallic grating is suspended in the sample solution.

The sample solution we choose is nitrobenzene in 2-propanol (5 vol.%). Unlike other cases, whose solute molecule could only be detected though the fluorescence, phosphorescence, or photochemical reaction by UV irradiation, this nitrobenzene is one of the well-known molecules which have no fluorescence, no phosphorescence, and also no photochemical reaction by UV irradiation. Nitrobenzene molecules absorb UV light whose energy pumps molecular electrons to excited states, which is immediately converted to

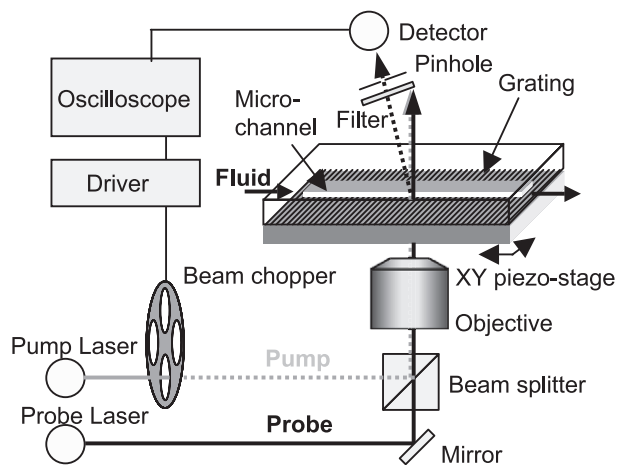


Fig. 2. Experimental setup of photothermal molecular sensor with grating for microfluidic devices.

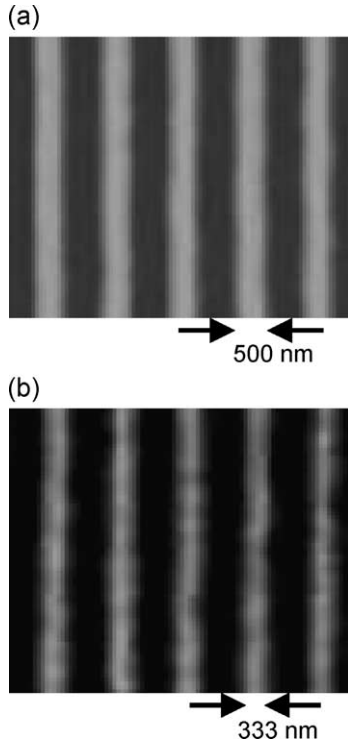


Fig. 3. Microscopic images of fabricated metal grating with 1:1 (a) and 1:2 (b) metal/window ratios.

the molecular vibrational energy, then to molecular translational energy, and finally randomized as the heat energy. Such the non-radiative relaxation processes of nitrobenzene are completed within very fast time-scale (a few hundred picosecond) [27]. Therefore, nitrobenzene has no coloration, and shows neither fluorescence nor phosphorescence. Moreover, nitrobenzene does not have a known photochemical reaction at UV irradiation. Because of these characteristics, nitrobenzene has been used as a fluorescence quenching agent [28,29] or an optical heating source [30,31], but molecular photoresponse of nitrobenzene has rarely shown.

### 3. Results and discussion

Fig. 4 shows the waveforms of (A) a pump beam modulated by a beam chopper (100 Hz), (B) a diffraction signal of nitrobenzene in 2-propanol, and (C) that of only 2-propanol all with 1  $\mu\text{m}$  period grating. The signal (B) has two constituents; the large background offset ( $I_r$ ) and the time modulated signal ( $I_s$ ). The waveform of  $I_s$  component is similar to that of the pump beam ( $I_e$ ). Similar waveforms are obtained with 1:1 and 1:2 metal/window ratios but the former signal amplitude is much larger than the latter signal amplitude. The analyses of the signals are as follows.

The UV excitation pump beam ( $I_e$  in Fig. 1c) is irradiated at the grating in the solution and the grating pattern is transferred to the sample solution. This mechanism is similar to photolithography but, in this case, the sample material is not a solid

substrate but is a liquid solution. Transferred spatial modulation of the optical intensity ( $\delta I_e$ ; optical grating) induced the spatial modulations of the excited medium; including population of excited states ( $\delta P$ ; population grating), temperature ( $\delta T$ ; temperature grating), and density of solvent ( $\delta \rho$ ; density grating). These transient gratings modulate the refractive index ( $\delta n$ ; phase grating) and absorbance ( $\delta k$ ; amplitude grating) of sample materials. All can be detected by the diffraction of the probe beam ( $I_p$ ). There are two types of signals: one diffracted by the permanent metal grating ( $I_r$ ) and the other by the transient grating ( $I_s$ ).

According to the nonlinear optics theory [6,7], the time profile of the electric field of signal diffracted by transient grating [ $E_s(t)$ ] is given by,

$$E_s(t) = \chi^{(3)}(t)E_e E_e E_p \quad (2)$$

where  $E_e$  and  $E_p$  are the electric field intensities of the pump and probe beams calculated from  $I_e = A|E_e|^2$  and  $I_p = A|E_p|^2$  ( $A$ : constant), respectively. In the case of homodyne detected TG technique, signals were attributed to this term, but the signal intensities were very weak. In the case of our setup,  $E_s(t)$  can be coupled to another electric field intensity ( $E_r$ ;  $I_r = A|E_r|^2$ ) of the diffracted signal by metallic grating because both signal are coherent and superimposed on each other. Thus, detected total output signal intensity ( $I_{\text{total}}$ ) can be described by [17–24]

$$I_{\text{total}} = A|E_r + E_s(t)|^2 = I_r + 2a \left[ \chi^{(3)'}(t) \cos \Delta \phi + \chi^{(3)''}(t) \sin \Delta \phi \right] I_e I_p + |\chi^{(3)}(t)|^2 I_e I_e I_p \quad (3a)$$

in which

$$E_r = a \exp(i\Delta \phi) E_p \quad (3b)$$

where  $\chi^{(3)'}(t)$  and  $\chi^{(3)''}(t)$  are the real and imaginary parts of  $\chi^{(3)}(t)$ , respectively,  $a$  is a real constant. Physically,  $\chi^{(3)'}(t)$

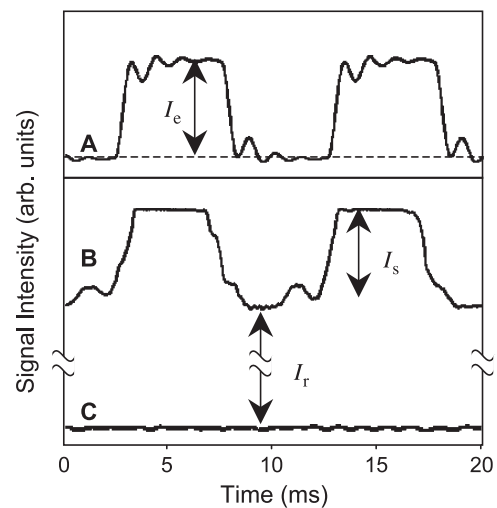


Fig. 4. Waveforms of the pump beam (curve A) modulated by beam chopper (100 Hz), diffraction signal of nitrobenzene in 2-propanol (curve B), and that of only 2-propanol (curve C) all with 1  $\mu\text{m}$  period's grating.

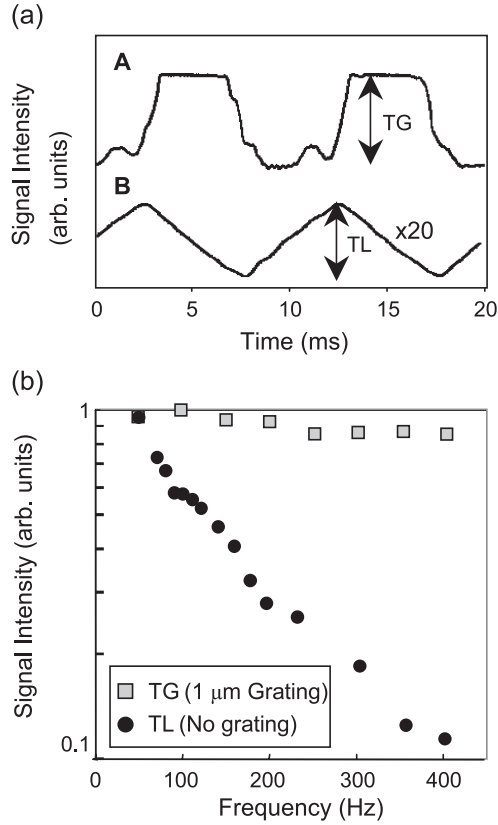


Fig. 5. (a) Chopped waveforms of the TG signal with 1  $\mu\text{m}$  grating (A) and the TL signal without grating (B) with 100 Hz chopping frequency. (b) Optical chopping frequency dependence of the TG signal intensity with 1  $\mu\text{m}$  grating (squares) and the TL signal intensity without grating (circles).

and  $\chi^{(3)''}(t)$  are the refractive index change  $[\delta n(t)]$  and the absorbance change  $\delta k(t)$  induced by the transient grating, respectively. In this case,  $\delta k(t)=0$  because this sample has no absorption at the probe wavelength (633 nm). The third term in Eq. (3) is negligible because of the relationship  $E_r \gg E_s(t)$  ( $I_r \gg I_s$  in Fig. 4),  $\Delta\phi$  is the phase difference between  $I_r$  and  $I_p$ . For OHDTG techniques, an unstable  $\Delta\phi$  has been a very serious problem for the experimental setup. In order to control  $\Delta\phi$ , between  $I_r$  and  $I_p$  must be tuned within the wavelength scale. This has been the main difficulty of the setup and operation of OHDTG technique in the recent past. However, in our setup,  $\Delta\phi$  is due only to the properties and structure of the metal grating and is very stable. Thus, a proportional relationship is obtained between  $I_s(t)$  and  $\delta n(t)$ .

Small quantities of  $\delta n(t)$  should be induced by the temperature grating and density grating at this frequency scale (100 Hz) because the lifetime of the electron excited states of nitrobenzene is very short. The initial refractive index change ( $\delta n_0$ ) just after excitation can be described by [32]

$$\delta n_0 = \left[ \left( \frac{\partial n}{\partial \rho} \right)_T \left( \frac{\partial \rho}{\partial T} \right) + \left( \frac{\partial n}{\partial T} \right)_\rho \right] \frac{Q}{\rho C_p} \delta I_e [C] \quad (4)$$

where,  $Q$ ,  $C_p$ , and  $[C]$  are the heat energy released from unit molecules, specific heat capacity, and the molecular concen-

tration of solute in the sample solution. The first and the second terms of this equation exhibit the density grating and temperature grating, respectively. This equation shows that the signal intensity is proportional to the molecular concentration, which suggests that the solute molecular concentration can be detected by this technique.

For application of this molecular sensor to the microfluidic devices, high sensitivity and high speed operation are necessary. Recently, a similar molecular sensor by using the transient lens (TL) technique has already been reported and applied to microfluidic channel [33,34]. In this technique, Gaussian shaped spatial distribution of sample properties ( $\delta T$  and  $\delta\rho$ ) were due to the irradiation of Gaussian shaped pump beam (Fig. 1a). Such a TL signal was equivalent to using our setting without grating and shown in Fig. 5a with a 100 Hz optical chopping frequency. We have found that the TG signal intensity in our setup with metal grating has been about 20 times larger than those of the TL signal without grating. Moreover, signal rise and decay slopes of our technique are much sharper due to the facts the signal rise and the decay times are determined here by the diffusion length of heat energy. By using microscopic grating, we can shorten and control the diffusion length by changing the grating periods. This property is advantageous for the high speed operation. Fig. 5b shows the frequency dependence of both the TL signal without grating and the TG signal with 1  $\mu\text{m}$  period grating, where signal intensities were normalized to 1 at 50 Hz. We concluded that our setting is much better for the high speed operation. By the use of nano-grating to control both the phase and the spatial frequency of molecular responses, we have improved the signal to noise ratio by an order of magnitude or more.

In order to observe the actual time dependence of the relaxation of transient grating, we investigate the time-resolved measurement. Fig. 6 shows the time profiles of the diffracted signal of nitrobenzene in 2-propanol with 1  $\mu\text{m}$

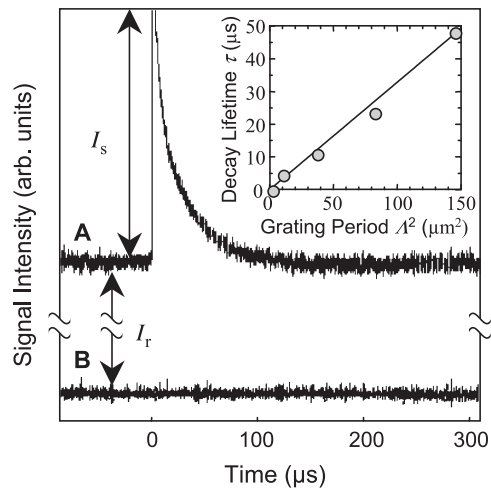


Fig. 6. Time profile of the diffracted signal of nitrobenzene in 2-propanol excited by nanosecond pulse beam. Inset shows the relationship between the decay lifetime and the square of the grating periods.

period grating excited by a nanosecond pulse laser beam. This signal is also built by two components;  $I_r$  and  $I_s(t)$ . The signal decay should be attributed to the relaxation processes of the temperature and density grating by the heat conduction in the solution. By solving Fourier's diffusion equation, the time and spatial profile of  $\delta n(t, x)$  is given by [35,36]

$$\delta \hat{n}(t, q) = \delta n_0 \exp(-D_{th} q^2 t) \quad (5)$$

where  $\delta \hat{n}(t, q)$  is the spatial Fourier component of  $\delta n(t, x)$ .  $D_{th}$  is the thermal diffusion coefficient of the solvent.  $q$  is the intensity of the grating vector and described by the grating period ( $A$ ) as  $q=2\pi/A$ . Thus, signal decay lifetime of the signals ( $\tau$ ) obtained by the exponential fitting is described by

$$\tau = \frac{A^2}{D_{th} 4\pi^2} \quad (6)$$

The inset in Fig. 6 shows a linear plot between  $\tau$  and  $A^2$  at each grating. We find a good linear relationship and  $D_{th}$  value is derived from the slope as  $D_{th}=7.0 \pm 0.7 \times 10^8 \text{ m}^2 \text{ s}^{-1}$ .  $D_{th}$  is also given by the thermal conductivity ( $\kappa$ ) as  $D_{th}=\kappa/\rho C_p$ . The calculated  $D_{th}$  value (by using the values of  $\kappa$ ,  $\rho$ , and  $C_p$  of 2-propanol in the literature) is  $D_{th}=6.8 \times 10^8 \text{ m}^2 \text{ s}^{-1}$  [35]. This excellent agreement between experimental and calculated values of  $D_{th}$  demonstrates the validity of the signal through our analysis.

#### 4. Conclusions

In conclusion, we have developed a new technique for the third order nonlinear optical spectroscopy by using the fabricated nano- and microgratings. This method has many advantages in comparison to traditional techniques such as: (1) simple setting and easy alignment, (2) high sensitivity and high S/N ratio (heterodyne detection), (3) high speed (high frequency) detection, and (4) ease of analysis (linear relationship between signal intensity and molecular concentration). This technique is expected to become a powerful tool to monitor the molecules in nano- and microfluidic devices.

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