

## 論文の内容の要旨

論文題目     **Development of Optical Methodology  
for Extended-nano Fluidic Device Engineering**  
(拡張ナノ流体デバイス工学に向けた光学手法の開発)

氏     名     レ   ハ   ク   ホ   ウ   ン   ツ   ー

### 1. Introduction

Over the past decades, microfluidics has contributed various functional devices for analysis, synthesis, bio and related sciences and technologies. Recently, the downscaling of micro space to  $10^1$ - $10^2$  nm space, which is referred to as extended-nano space, has opened new perspectives for integrated chemical systems. As the dimensions of channels decrease to extended-nano scale, unique fluidic and transport behaviors, which are negligible or absent in micro scale, play increasingly significant roles. For example, the liquid confined in  $10^1$ - $10^2$  nm space was reported to have higher proton mobility, higher viscosity, and low dielectric constant, compared to those in bulk.<sup>[1]</sup> Various novel analytical devices have also been developed to exploit new functionality. Especially, the  $10^1$  nm space, whose scale is comparable to the characteristic length scales such as electric double layer (EDL), proton transfer layer, or the size of biomolecules promises many novel properties and devices, however the lack of fundamental methodology has limited the studies in this region of extended-nano fluidics.

Optical methodologies have been widely applied in detection, surface chemical modification, or fluidic control in microfluidics and extended-nano fluidics in  $10^2$  nm space. For example, the differential interference contrast thermal lens microscopy (DIC-TLM) is one of the ultra-sensitive optical detections applicable to nonfluorescent molecules in  $10^2$  nm space.<sup>[2]</sup> However, the introduction of optical methodologies into  $10^1$  nm space is quite challenging, as the channel size is one order smaller than the wavelength of light, and the confocal length ( $\sim\mu\text{m}$ ) that determines the detection area or the diffraction limit ( $\sim 10^2$  nm) that determines the spatial resolution of photochemical reactions. In such cases, conventional methods employing far-field light are not applicable. I focused on the optical near-field (ONF). ONF is generated on nanostructures whose sizes are much smaller than the wavelength. ONF can confine light in  $\sim 10^1$  nm spaces and it has an apparent energy higher than the energy of incident photon.<sup>[3]</sup> Therefore, the introduction of ONF into  $10^1$  nm space is expected to solve the problems of far-field light and bring new functionality. Here novel optical methodologies were developed for extended-nano fluidics in  $10^1$  nm space by device engineering and the integration of ONF. This doctoral thesis consists of three parts:

- (1) DIC-TLM detection in  $10^1$  nm space
- (2) ONF-assisted DIC-TLM detection of UV-absorbing biomolecules by visible light
- (3) ONF-assisted photochemical reactions for fabrication

## 2. DIC-TLM detection in $10^1$ nm space

### 2. 1. New channel structure for compensation of signal cancellation in DIC-TLM detection

The principle of DIC-TLM detection is based on the change of temperature ( $dT$ ), as the target molecules absorbs the excitation light, following by the change of refractive index ( $dn$ ) in the medium. Signals are detected as the phase shift of light due to the change of refractive index, thus they are very sensitive to thermo-optical coefficient  $dn/dT$  of materials. When the channel size becomes  $10^1$  nm scale, most of generated thermal diffuses to the substrates. In conventional fluidic devices,  $\text{SiO}_2$  is usually used as substrate material. The  $dn/dT$  of  $\text{SiO}_2$  is positive ( $dn/dT = +9.8 \times 10^{-6} \text{ K}^{-1}$ ), while those of value in solvents are negative. Consequently, the signal induced by solvents is cancelled out by that of  $\text{SiO}_2$  (figure 1(a)). Here, I proposed the compensation of cancellation by a new channel

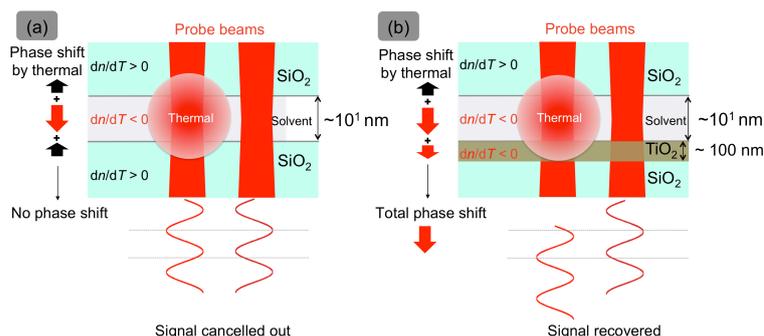


Figure. 1. (a) Signal cancellation in  $10^1$  nm  $\text{SiO}_2$ -channel and (b)  $\text{TiO}_2$ -channel structure for compensating of signal cancellation

structure using negative  $dn/dT$  material -  $\text{TiO}_2$  ( $dn/dT = -3.0 \sim 1.8 \times 10^{-4} \text{ K}^{-1}$ ), as shown in figure 1(b). The phase shift induced in the lower  $\text{TiO}_2$  substrate will compensate the phase shift in the upper  $\text{SiO}_2$  substrate, consequently the signals are recovered. The required thickness of  $\text{TiO}_2$  was determined to be 100 nm according to the calculation of thermal diffusion length in  $\text{TiO}_2$  material.

### 2. 2. Verification of compensation of cancellation and DIC-TLM detection in $10^1$ nm channel

The microchip using  $\text{TiO}_2$  was successfully fabricated. The DIC-TLM measurements in  $\text{TiO}_2$ -channels with various channel depth  $d$  ranging in  $10^1 - 10^2$  nm were investigated, using Sunset Yellow dye as analyte and ethanol as solvent. The result in figure 2(a) clearly shows that sensitivity in  $\text{SiO}_2$

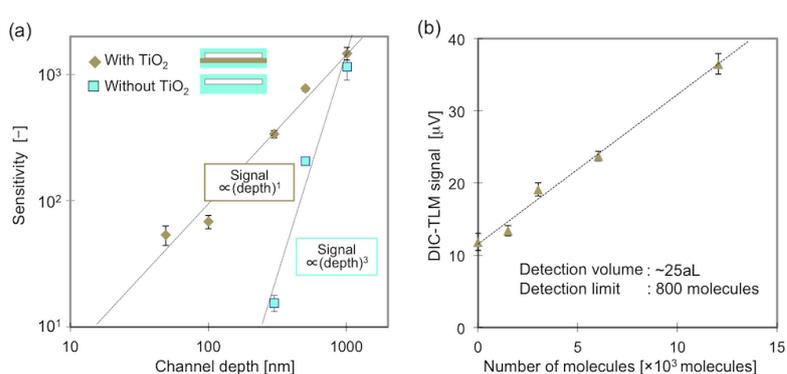


Figure. 2 (a) Dependency of sensitivity on depth in  $\text{TiO}_2$  and  $\text{SiO}_2$ -channel and (b) Calibration curve of dye in  $\text{TiO}_2$ -channel (depth = 50nm)

channel was proportional to  $(\text{depth})^3$ , while in  $\text{TiO}_2$  channel, it was proportional to  $(\text{depth})^1$ . It indicated that the signal cancellation was successfully compensated in  $\text{TiO}_2$ -channel, because without cancellation, the sensitivity should be proportional to  $(\text{depth})^1$  or the detection volume. The DIC-TLM detection was also successfully demonstrated in 50 nm-deep  $\text{TiO}_2$ -channel. The limit of detection (LOD) reached to zeptomole in a detection volume of 25 aL (figure 2(b)).

### 3. ONF-assisted DIC-TLM detection of UV-absorbing biomolecules by visible light

#### 3.1 Principle of ONF-assisted DIC-TLM

In ONF-assisted DIC-TLM, the nanostructures were fabricated in  $10^1$  nm channel (nano-in-nano structures) by top-down nanofabrication for the ONF generation. As visible light was irradiated, the ONF was generated as an integrated light source (figure 3). The ONF with apparent higher energy photon allowed the absorption of UV-absorbing analyte molecules,

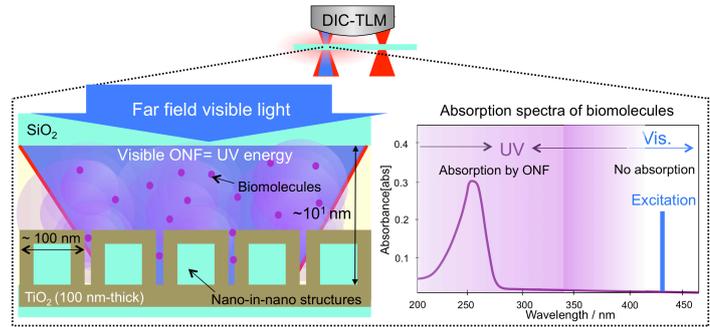


Figure 3. Principle of ONF-assisted DIC-TLM detection of UV-absorbing biomolecules by visible light in  $10^1$  nm space

even though the energy of incident photon was lower than the absorption energy of analyte. The light absorption was then sensitively detected by DIC-TLM. Here, the channel consisted of TiO<sub>2</sub>-nanostructures on the lower substrate, and the upper substrate of SiO<sub>2</sub>, was used for DIC-TLM detection in  $10^1$  nm space (using the result of chapter 2).

#### 3.2 Principle verification and detection of UV-absorbing protein by visible light

The proposed ONF-assisted DIC-TLM principle was verified using channels with nanostructures (for example, width (213±16) nm × gap (69±9) nm × height (50±2) nm) integrated. Target protein (lysozyme) in phosphate buffer solution was used as analyte, and 405 nm visible light (intensity: 4mW) was used as the excitation beam. Although lysozyme has absorption band at ~240 nm and no absorption at 405 nm light, the calibration curve in figure 4 clearly showed that signals derived from lysozyme were detected in channel with nanostructures integrated, while in flat channel (without nanostructures), no signals derived from analyte were detected. The dependency of signals on excitation intensity showed that signal was proportional to (intensity)<sup>1</sup>, which excluded the possibility of signal induced from the non-linear two photon absorption. The principle was verified. The detection of UV-absorbing biomolecules in  $10^1$  nm space with visible excitation was successfully realized by the assistance of ONF. Even under the low excitation intensity of 4 mW, the detection limit of ~220 molecules, which was three orders lower than conventional non-label detection methods in micro/nanofluidics, was achieved.

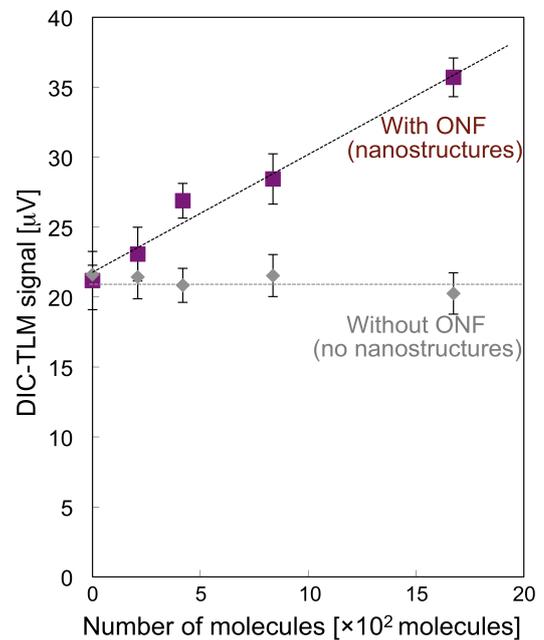


Figure 4. Calibration curve of lysozyme under 405 nm excitation

## 4. ONF-assisted photochemical reactions for fabrication

### 4. 1 Partial surface modification by ONF

Photochemical surface modification is an important technique in functionalization of devices such as patterning of biomolecules for molecular capture, hydrophobic/hydrophilic patterning for fluidic control, etc. However, in  $10^1$  nm space, as the channel size is much smaller than the wavelength, the conventional far-field techniques are not applicable due to the diffraction limit of light. Here, new partial surface modification on  $10^1$  nm scale by ONF was proposed, as described in figure 5(a). As  $\text{TiO}_2$  nanostructures were irradiated with visible (488 nm) light, ONF was generated and enhanced at the edges of nanostructures. This ONF allows the excitation of  $\text{TiO}_2$ , leading to the photocatalytic decomposition of modifying chemicals (e.g. hydrophobic octadecylsilane (ODS)) at the edges of nanostructures, even though the light energy (visible) is lower than the bandgap of  $\text{TiO}_2$  ( $\sim 380$  nm). As a result, pattern sizes on scale of ONF ( $\sim 10^1$  nm) can be achieved. SEM images in figure 5(b), (c) verified the ODS decomposition at the edges or nanostructures, while the centers remained untreated. At minimum, 40 nm ODS-decomposed (hydrophilic) patterns were achieved (figure 5(c)). Importantly, the pattern size could be easily controlled on  $10^1 - 10^2$  nm scale by irradiation intensity.

### 4. 2 Visible response photocatalytic water splitting by ONF

The ONF-assisted photochemical reaction was also applied to the photocatalytic water splitting by visible light. The result showed a two orders enhancement in visible response of water splitting in nanostructures  $\text{TiO}_2$  compared to  $\text{TiO}_2$  flat film without nanostructure.<sup>[4]</sup> The reaction is promising for fuel (hydrogen) generation in integrated energy devices.

## 5. Conclusion

In summary, novel optical methodologies such as DIC-TLM detection, surface modification, etc. were successfully introduced to extended-nano fluidics in  $10^1$  nm space by device engineering and the integration of ONF. This study has contributed fundamental tools that may accelerate the studies on fluidic behavior, or properties of liquid confined in  $10^1$  nm space, and the development of functional devices employing those unique properties. The combination of nanophotonics and extended-nano fluidics also promises many novel spectroscopies in extremely small spaces.

## 6. References

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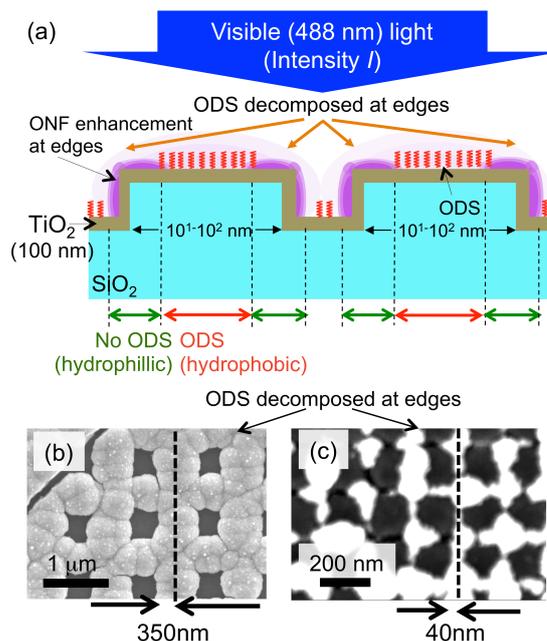


Figure 5(a) Principle of partial surface modification by ONF,  
(b) (c) ODS decomposed at edges on  $10^1 - 10^2$  nm scale verified