Twin-focus thermal lens microscopy: A theoretical description

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Sensitive and specific detection of trace nonfluorescent targets in microanalytical devices is the foremost task in chemical and biological analyses. Conventional thermal lens microscopy (TLM) can realize sensitive detection of nonfluorescent analytes down to a nanoparticle and is insensitive to scattering background [1]. However, the conventional TLM (usually working in time-domain intensity-modulation mode) suffers low detection performance when there exists a large background absorption, which could come from interferents in light path, such as pollutants on optical elements or absorptive agents (nanoparticles, surface coatings, etc. [2]) within and around the micro space. When the intensity of excitation laser is modulated, the background absorption will introduce an undesired background noise, which can prevail over the real TL signal from the analyte. One direct way to remove these background noises is to keep the excitation laser running continuously without modulation, which will however suppress the conventional TLM signal of analyte as well. To overcome this contradiction, we must employ a new TLM scheme, which can eliminate the background noise while keeping the TL signal from the analyte in target region unaffected.

Here, I introduce a twin-excitation-focus thermal lens microscopy (TF-TLM). Instead of modulating the excitation intensity in time domain in conventional TLM, the excitation focus is modulated back and forth between the positive and negative signal zones of TF-TLM (Fig. 1, left), which can produce a periodic signal from the analyte of target with little contribution from the background interferents. The axial excitation focus modulation can be realized by a beam-parameter-adjustment unit, which consists of an electro-optic modulation, a polarization beam splitter and four reflecting mirrors.

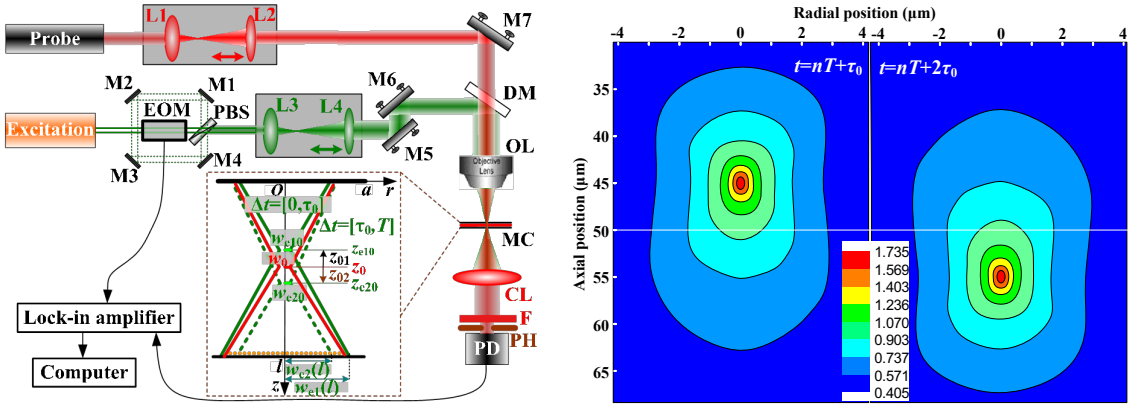

Fig. 1. Schematic of TF-TLM (left). CL: condenser lens; DM: dichroic mirror; EOM: electro-optic modulator; F: interference filter; L0-L4: lenses; M1-M7: mirrors; MC: microfluidic chip; OL: objective lens; PBS: polarization beam splitter; PD: photodiode; PH: pinhole. And temperature profiles in sample at the end of 1st and 2nd excitation half-cycles in one modulation cycle (right), with w_{e0}=0.42 μm and f=10 kHz

The theoretical model of TF-TLM is similar to conventional TLM, except that the temperature distribution should be rededuced under excitation of a quasi-continuous twin-focus excitation. Detailed description of the temperature and photothermal signal model will be given elsewhere. I first simulated the temperature profiles at the end of the 1st and 2nd excitation half-cycles in one modulation cycle (Fig. 1, right). When the excitation focus shifts from the positive to negative signal zone, the temperature around z_{e10}=45 μm shows an increase in the 1st excitation half-cycle and a decrease in the 2nd excitation half-cycle, while the temperature around z_{e20}=55 μ m shows an opposite change during these two excitation durations. This temporally and spatially periodic change of photothermal effect can result in a periodic change of probe beam intensity at the detector.

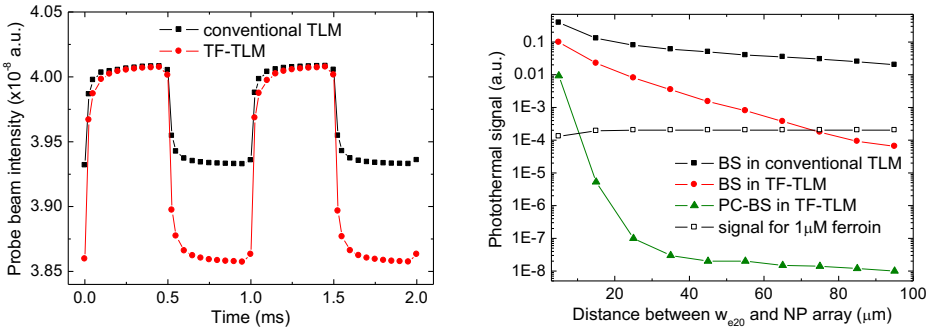

Fig. 2. Temporal change of photothermal signal of an ensemble sample at (z_{e10}=45 μ m and z_{e20}=55 μ m) and at (z_{e10}=48 μ m and z_{e20}=52 μ m) (left). And change of the photothermal signal with the distance (z_{23}) between w_{e20} and gold nanoparticle array at the bottom of the sample cell(right). BS: background signal; PC-BS: power-compensated background signal.

Figure 2 (left) gives the temporal intensity change of probe beam, whose beam waist is at the center of two excitation foci, namely z_{01}=z_{02} (Fig. 1, left). Following the temperature change, the intensity takes on a periodic change. In the 1st excitation half-cycle, the probe beam shows an increase, while a decrease is observed in the 2nd excitation half-cycle when the excitation focus shifts to the negative signal zone. In comparison with the conventional TLM, the intensity change is nearly doubled in TF-TLM, which will induce a two-fold increase in TLM detection sensitivity. Figure 2 (right) shows the impact of background absorption on the TLM. When the gold nanoparticle (NP) array on the sample-cell wall absorbs the excitation light intensity, temperature gradient occurs around the array. While the lateral phase shows a periodic change in conventional TLM, the phase changes slightly between the 1st and 2nd excitations. The small difference comes from the discrepant excitation light intensities (due to the inconsistency in $w_{e1}(l)$ and $w_{e2}(l)$). In comparison with the signal of sample, the background signal in conventional TLM is 1000-fold higher while the background signal in TF-TLM is only 10-fold higher. By adjusting the power of one of the excitation beams (EB1 or EB2), the background signal can be greatly suppressed or even eliminated. For example, when the power of EB2 (dashed line around EOM) is reduced to 9 mW, the background signal will disappear. This is quite promising for weak absorption detection when a background absorption cannot be ignored.

In conclusion, this novel TF-TLM, which shows twice higher sensitivity and moreover a nearly background-free detection in comparison with conventional TLM, provides a robust tool for sensitive detection of trace analytes in complex micro spaces.

References

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