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SERS measurement of cancerous cells with optical fiber sensor

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Received April 15, 2014; accepted May 15, 2014; posted online September 11, 2014

The optical fiber nanoprobe is prepared using spark fused taper and acid corrosion methods. With 3-aminopropyltrimethoxysilane coupling, gold nanoparticles are solidified onto the surface of fiber optic and then the optical fiber sensor is prepared using the surface-enhanced Raman spectroscopy (SERS) measurement of the cell solution. The SERS of the esophageal cancer cell solution is measured by direct detection and fiber detection methods. Similar results are obtained by both detection methods. SERS measurement of tissues and organs is done using the optical fiber sensor.

OCIS codes: 170.5660, 170.1530, 280.1415.
doi: 10.3788/COL201412.S23002.

The surface-enhanced Raman spectroscopy (SERS) is a useful analysis method in analytical chemistry, which provides the molecular vibration spectrum with label-free information\(^5\). It is widely used in many fields such as biomedical\(^2\), environmental science\(^8\), and pharmaceutical industry\(^6\).

A cell composed of proteins, nucleic acids, sugar, lipids, and vitamins is the basic composition unit which constitutes a complex life\(^3\). In the process of cell canceration, the malignancy multiplication of the cells leads to the abnormal metabolism, for example, the increase in synthesis and decomposition of proteins. Compared with the normal cells, cancer cells have many differences in chemical composition, configuration, and conformation of molecules. Raman spectroscopy can provide highly detailed chemical information about a tissue sample and is being preferred as an objective method for the diagnosis of diseases in tissues\(^6\). In the stokes scattering process, a laser light interacting with the molecules gets inelastically scattered, some of its energy gets transferred to the molecular vibrational excitations in the sample. The health condition of an organ can be detected from the cells which contain certain types of bio-molecules. And the unique composition of the bio-molecules also has a unique vibrational band representing the vibrational motions of these bio-molecules. Therefore, the changes in the proteins caused by canceration can be seen from the SERS comparison of normal and cancerous cells.

In the recent years, the development of optical fiber detection technology has greatly promoted the development of biomedical research, especially the innovation of biological detection means\(^7\). On the basis of optical fiber sensor, with the near-field optical microscopy and nanoprobe preparation technologies, the fiber nanosensors have developed rapidly and have been widely used\(^9\). By combining the optical fiber sensor nanotechnology with Raman spectroscopy, the Raman spectra of the cells were measured for studying the difference of normal and cancerous cells in the molecular level. It will be useful for the early diagnosis of the diseases and in vivo cancer detection\(^11\).

Here, the SERS of a single esophageal cancer cell was detected through direct focusing on the cell. The fiber detecting method and the direct detecting method of the SERS of esophageal cancer cells suspension were studied, and we also analyzed the major assignment of Raman peaks.

Esophageal cancer cells were seeded in high-glucose Dulbecco’s modified Eagle medium supplemented with 10% fetal calf serum, 100 units/mL penicillin, and 100 mg/mL streptomycin in a 5% CO\(_2\) incubator at 37°C. After approximately 24 h in exponential growth condition, cells were washed with phosphate buffered saline (PBS) for three times, digested, and suspensions were transferred to 1.5 mL centrifuge tubes. Then the suspensions were centrifuged at 1000 rpm for 5 min. The cell cluster on the bottom of the tubes was re-suspended in PBS and then centrifuged at 1000 rpm for 5 min. This process was repeated more
than three times, then the esophageal cancer cells suspension sample was prepared.

In order to measure the SERS of the esophageal cancer cell suspension, the objective lens of the microscope on the core of the optical fiber were focused, and the nanoprobe was placed in the centrifuge tube. The fiber used in the experiment was a multimode fiber with a cladding of 125 $\mu$m and a core of 50 $\mu$m. The SERS spectra of fiber end were detected with Renishaw microscopic confocal Raman spectrometer under 633 nm laser excitation. The output laser power was about 10 mW and the SERS spectra were measured in a collection time of 10 s. Raman signals were collected in the spectral range from 200 to 2000 cm$^{-1}$. The experimental setup is shown in Fig. 1.

Figure 2 shows the optical fiber of about 8 cm long for the fiber detection SERS. In Fig. 2, curves a and b indicate the SERS of the suspension without esophageal cancer cells and with esophageal cancer cells, respectively. Many characteristic peaks of esophageal cancer cells can be seen in Fig. 2.

Five 8 cm long optical fiber nanoprobes were prepared and then under the same experimental condition (633 nm laser excitation, the output laser power 10 mW, and 10 s collection time), the fiber detection SERS of esophageal cancer cells were measured with five probes. The spectra are shown in Fig. 2.

Before the fiber detection, the SERS of a single esophageal cancer cell was measured with the direct detection method. In Fig. 3, spectrum a indicates the SERS of fiber detection and spectrum b indicates SERS of direct detection. When compared with the SERS of direct detection (spectrum b), the SERS of fiber detection (spectrum a) showed many similar Raman peaks, although some peaks disappeared. This may be due to the attenuation of the transmission in optical fiber.

The SERS detected by direct and fiber methods have many Raman characteristic peaks, and each peak represents a specific molecular vibration, and the peak assignment of SERS are listed in Table 1.

In conclusion, the fiber detection SERS of the esophageal cancer cells are measured using the optical fiber sensor. Similar result is obtained using the direct detection method, and the SERS measurement with the optical fiber has important significance for the detection of in vivo Raman spectra of tissues or organs in future.

This work was financially supported by the National Natural Science Foundation of China (Nos. 61027015, 61177088, and 61107076), the National 973 Program of China (No. 2012CB723405), and the Key Laboratory of Specialty Fiber Optics and
Table 1. Peak Position and Major Assignment

<table>
<thead>
<tr>
<th>Peak Position(cm$^{-1}$)</th>
<th>Vibrational Mode</th>
<th>Major Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>657</td>
<td>(C–C ) Twisting Mode</td>
<td>Thymine</td>
</tr>
<tr>
<td>855</td>
<td>(C–C) Stretching Mode</td>
<td>Proline</td>
</tr>
<tr>
<td></td>
<td>(CCH) Ring Bending Mode</td>
<td>Tyrosine</td>
</tr>
<tr>
<td>1031</td>
<td>(C–H) Stretching Mode</td>
<td>Phenylalanine</td>
</tr>
<tr>
<td>1152</td>
<td>(C–H) Stretching Mode</td>
<td>Proteins</td>
</tr>
<tr>
<td>1322</td>
<td>(CH$_3$CH$_2$) Twisting Mode</td>
<td>Collagen</td>
</tr>
<tr>
<td>1445</td>
<td>(CH$_2$, CH$_3$) Bending Mode</td>
<td>Collagen</td>
</tr>
<tr>
<td>1470</td>
<td>(CH$_2$) Bending Mode</td>
<td>Collagen</td>
</tr>
<tr>
<td>1552</td>
<td>(C=C) Stretching Mode</td>
<td>Tryptophan</td>
</tr>
</tbody>
</table>

Optical Access Networks (Nos. SKLSFO2012-01 and SKLSFO2013-02).

References