69 **先端TERS顕微鏡の開発と早期がん検出への応用**

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Cancer is a global health challenge that requires innovative early detection techniques. The presence of various biomolecules and their concentrations on cell membranes serve as early indicators of cancer, which must be investigated at the nanoscale under the native conditions of cells. This research aimed to develop a modified tip-enhanced Raman scattering (TERS) imaging system to study the various biomolecules on a cell membrane at the nanoscale in water. The challenges include TERS measurement in a liquid environment, achieving stronger enhancement of the Raman signal from the weak-scattering biomolecules, and ensuring ultra-stable TERS measurement. In this project, we have addressed all these challenges. We started by improving our existing TERS system with a home-built feedback system (Fig.1a) for ultra-stable measurement. Separate feedback systems for vertical and horizontal stabilization were introduced. Stabilization in the vertical direction was achieved using a piezo-controlled objective scanner and a laser-reflection sensing scheme, and stabilization in the horizontal direction was achieved by employing a laser scanning-assisted technique. We confirmed nanoscale stabilization in all directions. We further upgraded the TERS system with a liquid AFM (Fig.1b) for measuring cell membranes in water. We successfully achieved TERS measurement in water, which was validated by measuring carbon nanotubes as a test sample. We then proceeded to measure lipid bilayers, which are essential components of a cell membrane. Figure 1c shows an AFM image of the lipid bilayer, on which we performed Raman and TERS measurements. A strong enhancement in the TERS spectrum relative to the corresponding Raman spectrum of the lipid bilayer is demonstrated in Fig.1d. The spatial resolution of this measurement was 20 nm. With this, a major part of this research was successfully finished. However, at this point, we could not complete the final objective of TERS imaging of various biomolecules on the cell membrane due to time constraints, but we are close to achieving that goal and plan to conduct the experiment soon, even after this funding period is finished, and will write a journal article upon completion of the task.

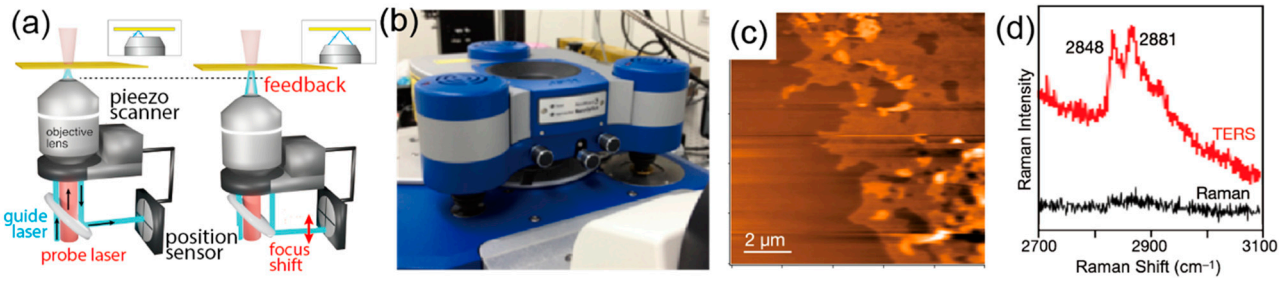


Figure 1: (a) Schematics of a home-built feedback system for ultra-stable measurements, (b) AFM head that operates in liquid, (c) an AFM image of a lipid bilayer sample, and (d) a normal Raman and TERS spectrum of the lipid bilayer.