Detection of Proteins Associated with Alzheimer's Disease using a Terahertz Chemical Microscope

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Resume of the presenter

Kohei Iwatsuki

- He received the B. E. degree from Ryukyu University in 2020.

- Currently, he is a student of the Graduate School of Interdisciplinary Science and Engineering in Health Systems, Okayama University.

- His research interests include terahertz engineering and Alzheimer's Disease.
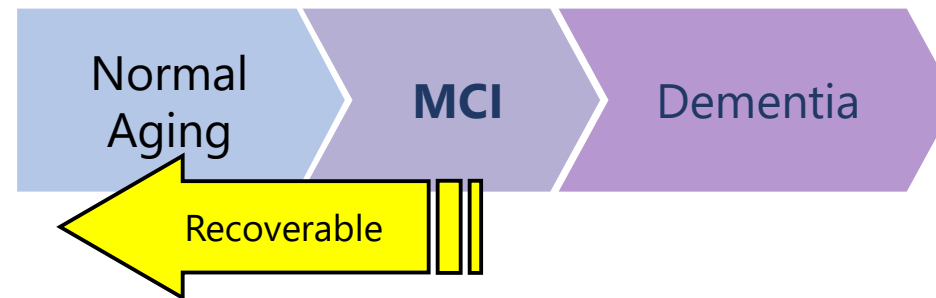
Background

Present situation

Dategorymentia · Increasing as the increase of average life expectancy
· Generally, it doesn't heal completely

Alzheimer's Disease

Accumulation of **amyloid β** in the brain

Normal Aging → **MCI** → Dementia

Recoverable

Early detection in the stage of **mild cognitive impairment (MCI)**

Purpose

Elimination of amyloid β	・Apolipoprotein AI (ApoA1) ・Transthyretin (TTR) ・Complement component 3 (C3)

Screening tests for MCI

Risk analysis based on measured blood levels of proteins

Detection method
- **Turbidimetric Immunoassay** (TIA)
- **Enzyme-Linked immunosorbent assay** (ELISA)

Sample volume
About **10mL** of blood (Serum at least **3mL**)

Terahertz Chemical Microscope (TCM)

Equipment for detecting chemical reactions in minute quantities

Application to screening tests for MCI
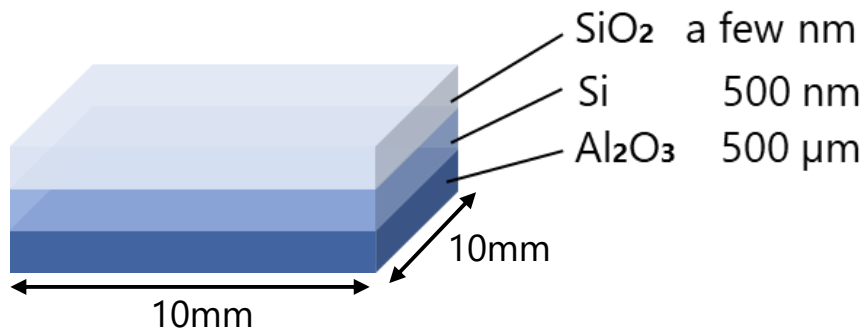
▸ **Efficiency**
Unify methods for detecting biomarkers

▸ **Minimally invasive**
Reduce the amount of sample required

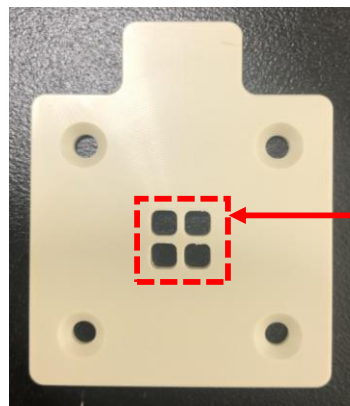# TCM : Terahertz Chemical Microscope

TCM can visualize chemical reactions on a sensing plate.
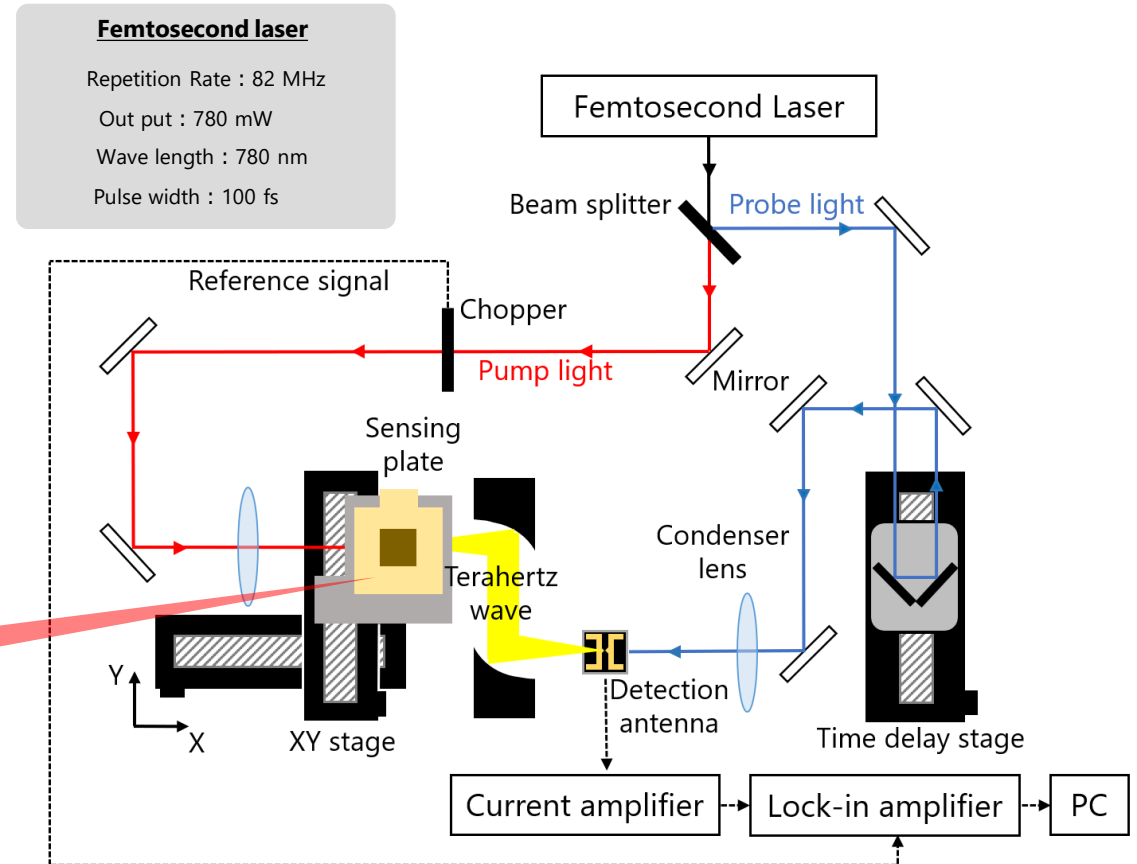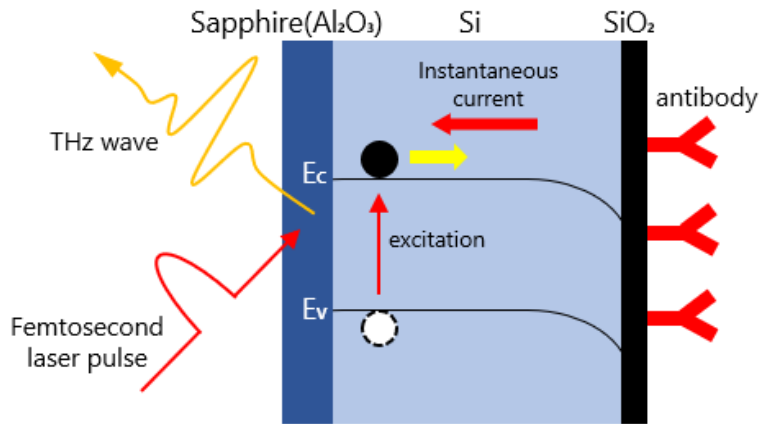
Sensing plate

SiO₂ a few nm
Si 500 nm
Al₂O₃ 500 μm

10mm
10mm

Substrate

Well size: 3.5mm × 3.5mm

Configuration of TCM

Femtosecond laser

Repetition Rate : 82 MHz
Out put : 780 mW
Wave length : 780 nm
Pulse width : 100 fs

Femtosecond Laser

Beam splitter   Probe light
Reference signal   Chopper
Pump light   Mirror
Sensing plate
Terahertz wave   Condenser lens
Y   Detection antenna   Time delay stage
X   XY stage
Current amplifier → Lock-in amplifier → PC
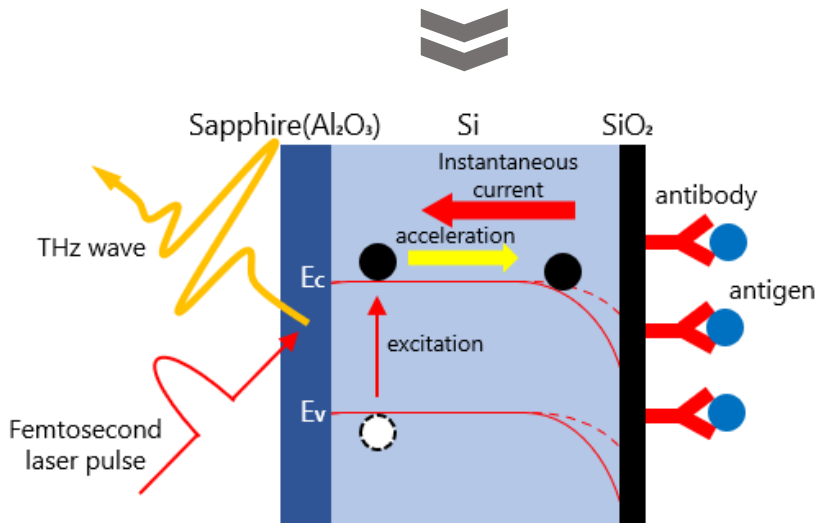
Measurement by TCM

Measurement principle

Principle of THz wave generation

Carrier is excited by laser irradiation

Carrier acceleration by depletion layer electric field

Instantaneous current is generated

Terahertz wave is generated

Measurement of antigen-antibody reaction
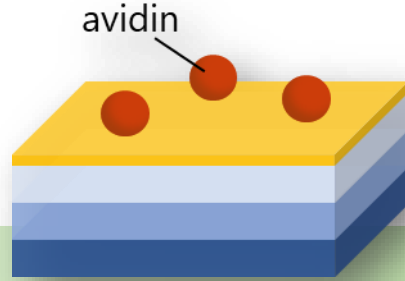
Binding of antigen and antibody　⟩　Change of electric field　⟩　**Change in the intensity of terahertz wave**
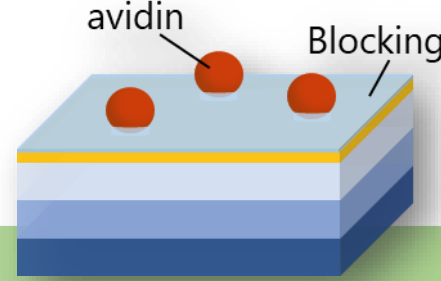
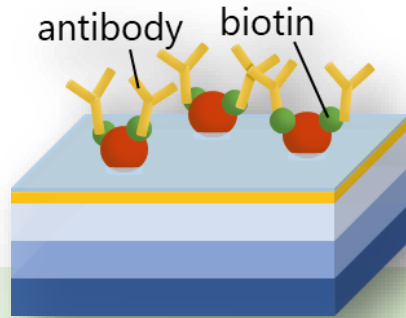# Measurement by TCM

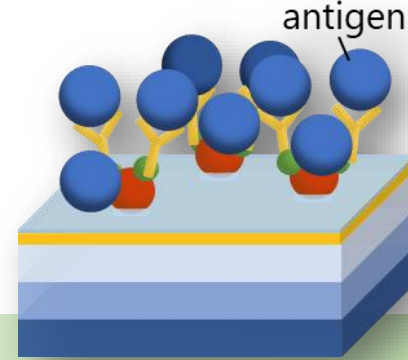**Reaction process on a sensing plate**

Chemical modification → Fix avidin → Blocking → React biotin-labeled antibody → React with antigen (protein) → Remove excess antigen by washing
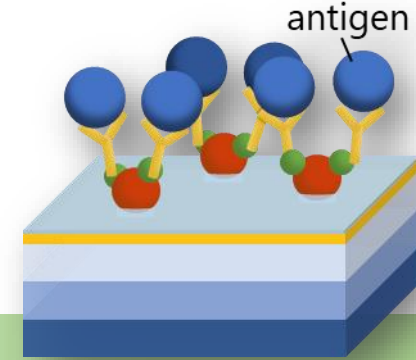
Avidin-Biotin Interaction

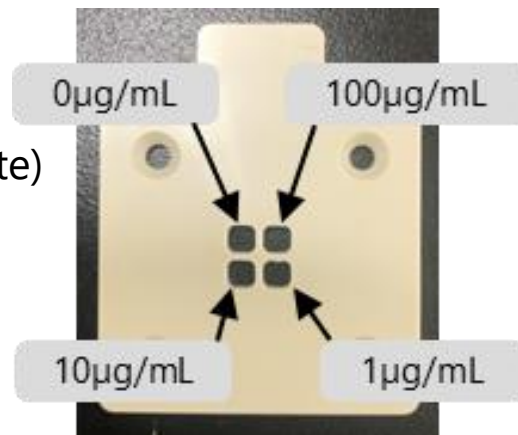Before → Measurement using TCM → After

Measurement by TCM

Sample

C3 and **ApoA1** were measured.

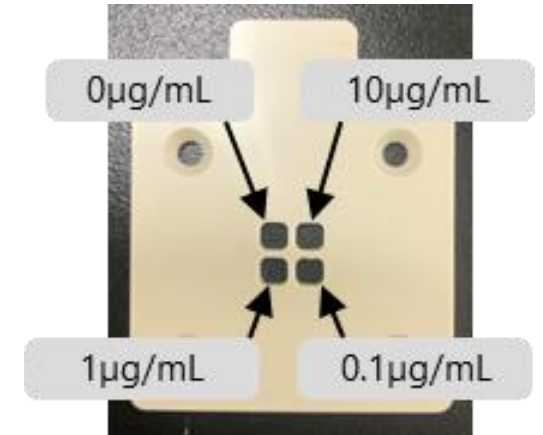We prepared **three samples** of each.

C3

Concentration of C3

・Antibody
(Rabbit, Polyclonal, Biotin conjugate)

・C3, Human

ApoA1

Concentration of ApoA1

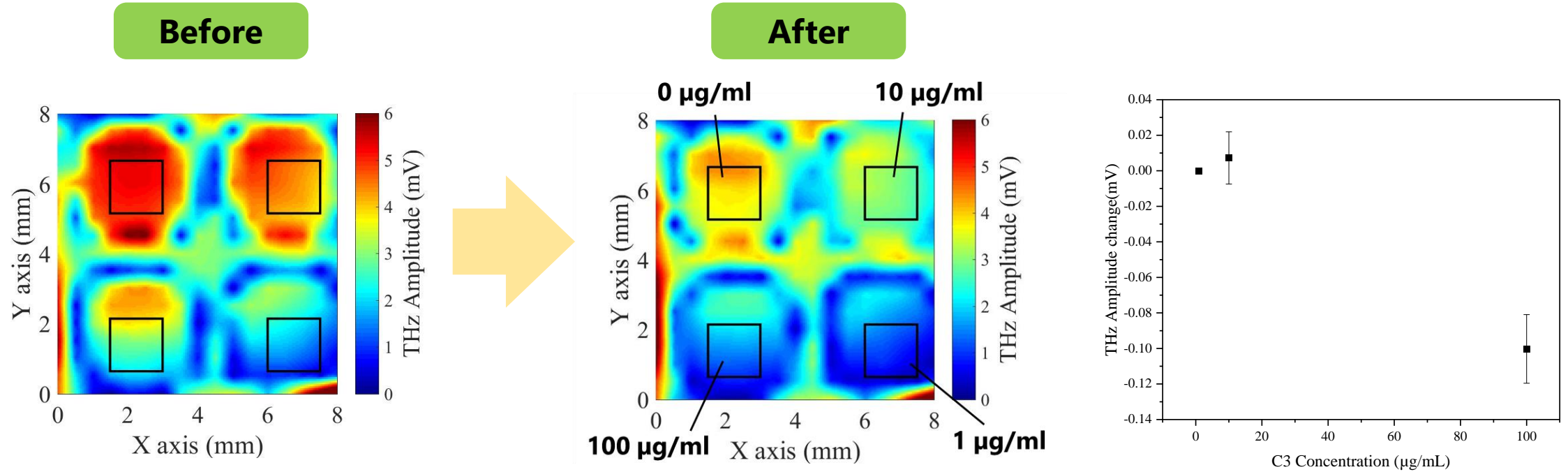・Antibody
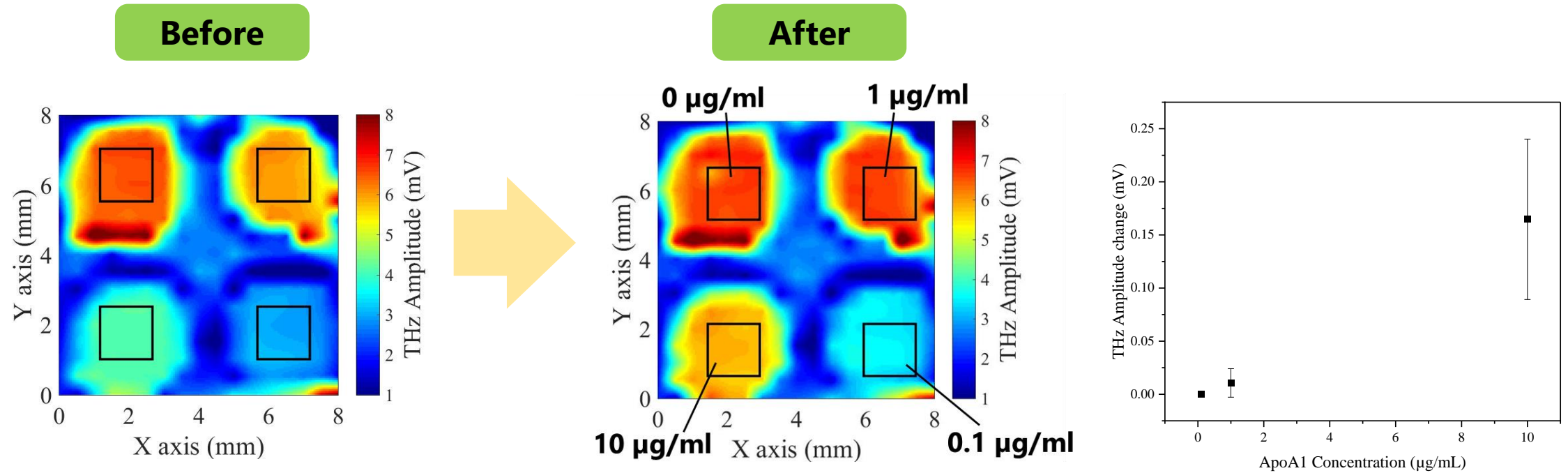(Goat, Polyclonal, Biotin conjugate)

・Apolipoprotein A-I, Human

C3

The intensity of terahertz waves changes with the concentration of C3(0, 1, 10, 100μg/mL)

Result

ApoA1

Before

After

The intensity of terahertz waves changes with the concentration of ApoA1(0, 0.1, 1, 10μg/mL)

Conclusion and Future Work

The TCM has been proposed for early diagnosis of AD by measuring several types of biomarkers.

Antibodies (**Anti-C3** and **Anti-ApoA1**) were immobilized on the sensing plate using avidin-biotin conjugation to measure the **C3** and **ApoA1**, respectively.

The change in the amplitude of terahertz wave from the sensing plate depended on the concentration of biomarkers.
‣ protein concentration［C3 ➡ 1～100μg/mL , ApoA1 ➡ 0.1～10μg/mL］

Future Work

・**Measurement of TTR**

・Simultaneous measurement of three proteins (C3, ApoA1, TTR)

・Improvement of detection sensitivity

・Measurement of protein in serum