Enhancing the Detection Sensitivity of Terahertz Spectroscopy for Biomolecules using Metasurfaces

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Terahertz Time-Domain Spectroscopy (THz-TDS) has been recognized as an emerging optical biosensing technique, based on the observation that the intermolecular vibration frequencies of major biomolecules have resonances in the Terahertz (THz) region. THz-TDS emits low-energy, non-ionizing radiation and can be performed non-invasively, giving it extensive applicability in the biomedical field. That being said, it is often limited by a weak and broad detection, characterized by a low Q-factor. THz metasurfaces serve as a promising solution to this issue by interacting with the THz wave at a sub-wavelength scale. This ultimately allows us to achieve high local electric field enhancement and increase the molecular absorption cross section. In our experiment, we fabricated three different gold metasurfaces by photolithography to use in conjunction with the THz system. By using metasurfaces, we anticipate heightening the system's ability to discern a spectral shift correlated with modifications to the refractive index of creatinine solutions. Serum and urine creatinine levels are widely used to evaluate renal health and abnormally high concentrations tend to indicate kidney disease. A multitude of creatinine measurement techniques currently exist, of which isotope dilution mass-spectrometry (IDMS) is regarded as the primary reference method. IDMS and other creatinine assays, however, involve tedious and expensive preparation steps. Comparatively, THz-TDS has much higher throughput and eliminates the need for expensive reagents. As such, the THz-TDS/metasurface combination has the potential to become a valuable addition to the existing landscape of diagnostic practices available for analyzing creatinine and many other biomolecules.

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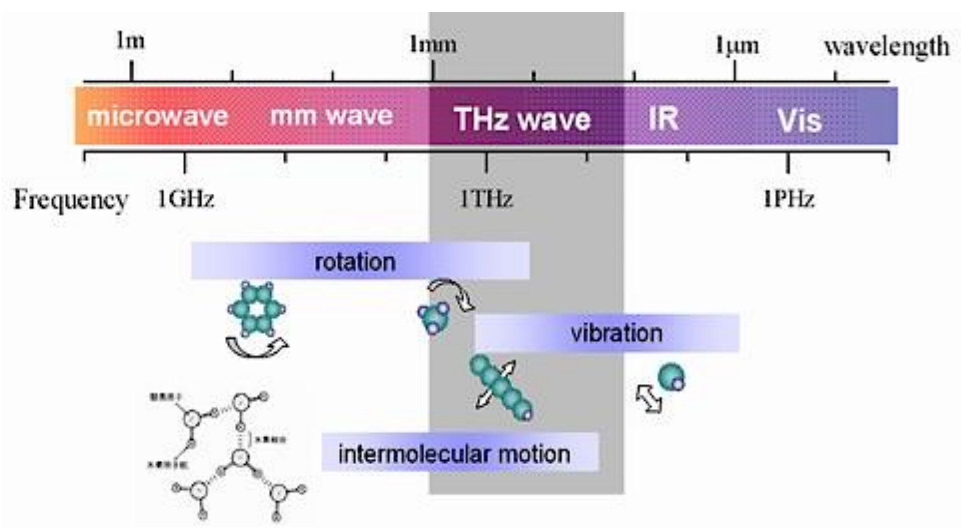
Introduction

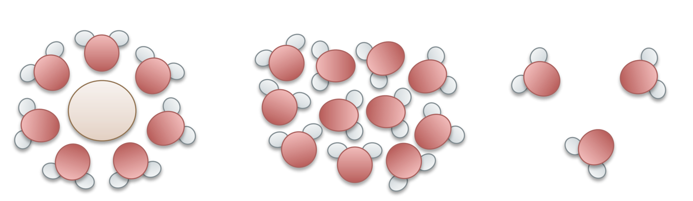
Terahertz Time-Domain Spectroscopy (THz-TDS) for Biomedical Applications

- **Non-invasive**
- **Label-free**
- **Low energy, non-ionizing radiation**
- **Low cost**
- **High throughput**
- **User-friendly**



1THz = 300μm = 4.2meV

Intermolecular vibration frequencies that arise between biomolecules have resonances in the THz region, notably those of hydrogen bonding (1)



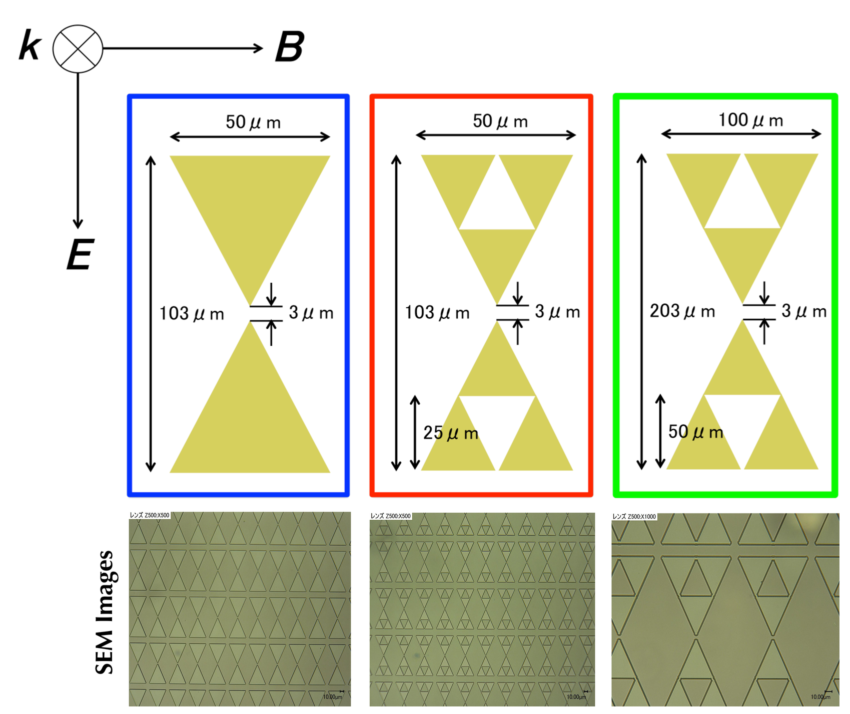
Goal: observe distinct spectral shift correlated with varying solution concentration

Problem

- Low-sensitivity
- Weak/broad detection
- Low Q-factor

THz Metasurfaces

- Sub-wavelength design
- Anomalous transmission of THz wave
- High near-field enhancement
- **Increase THz detection sensitivity**



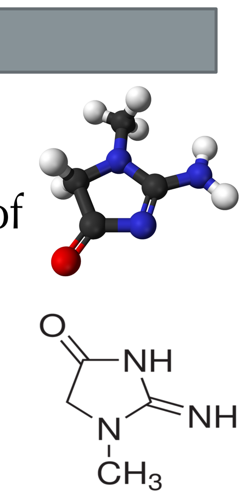
Biomolecules: Glucose and Creatinine

Glucose

- Monosaccharide carbohydrate
- Essential for metabolism and cellular communication
- Used to **demonstrate viability of methodology** – previously studied by Lee, D.-K. *et al.* (2)

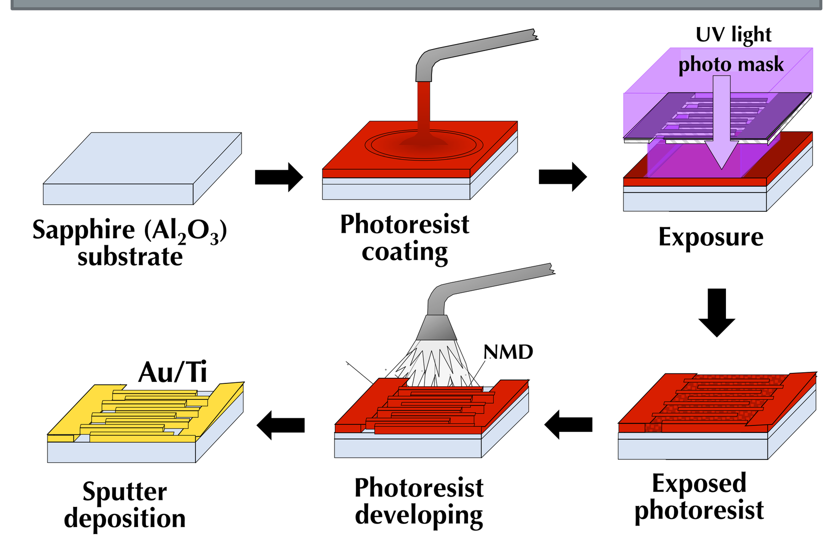
Creatinine

- Byproduct of muscle metabolism
- Serum and urine levels indicative of renal health
- Variations in measurement methodology affect diagnosis (3)
- **More reliable and efficient measurement techniques are necessary**

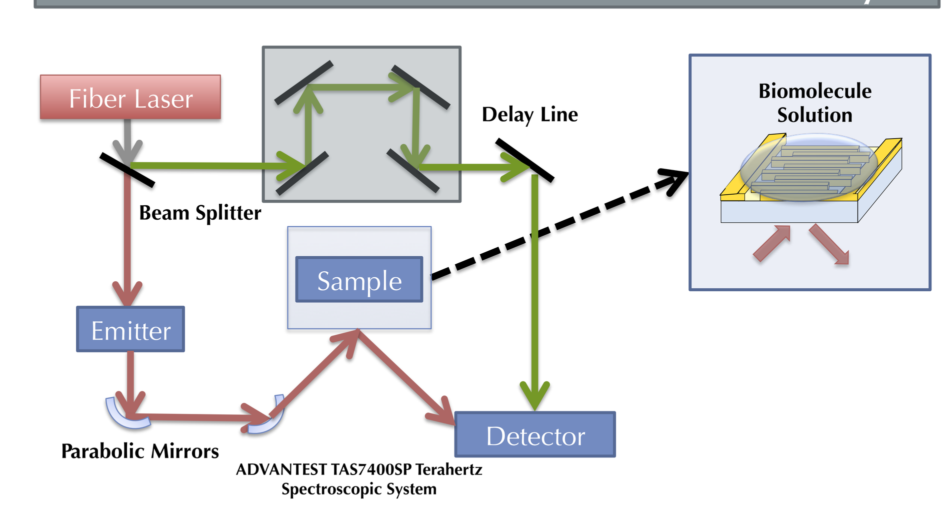


Experimental Setup

Metasurface Fabrication

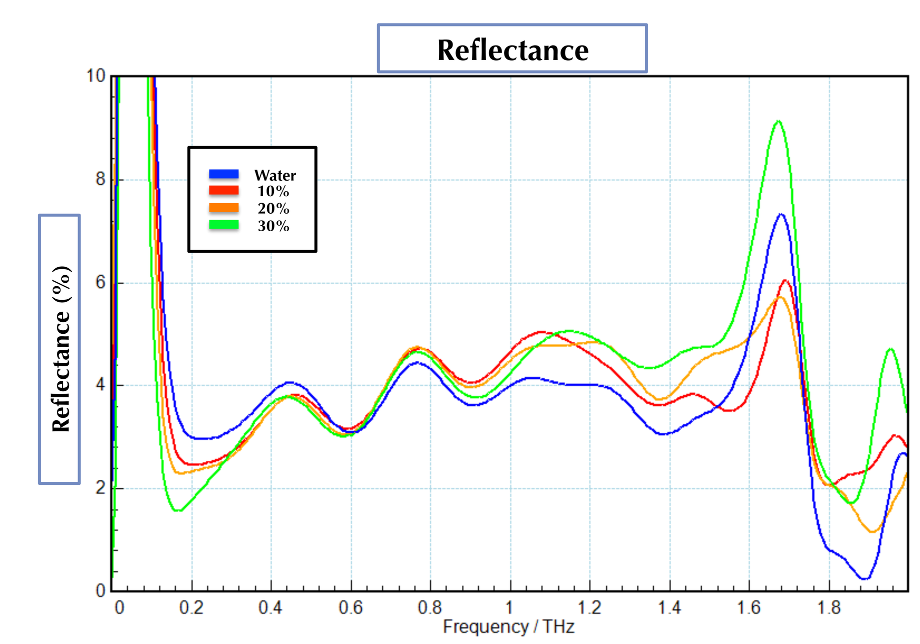


THz – TDS – Reflection Geometry

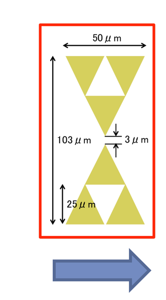


Results and Analysis

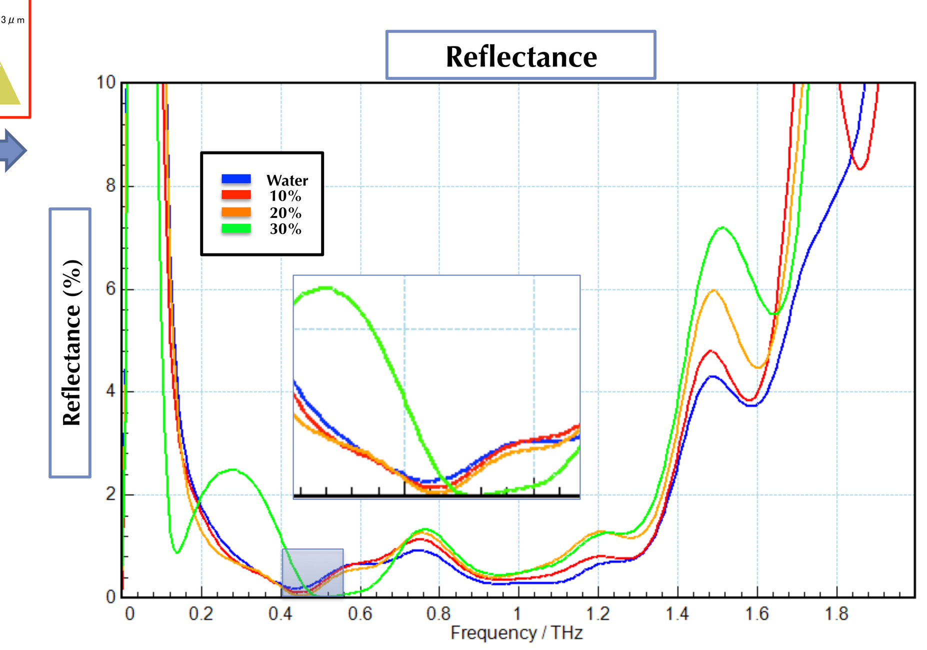
Glucose on Sapphire



Random – no clear indication of concentration differences

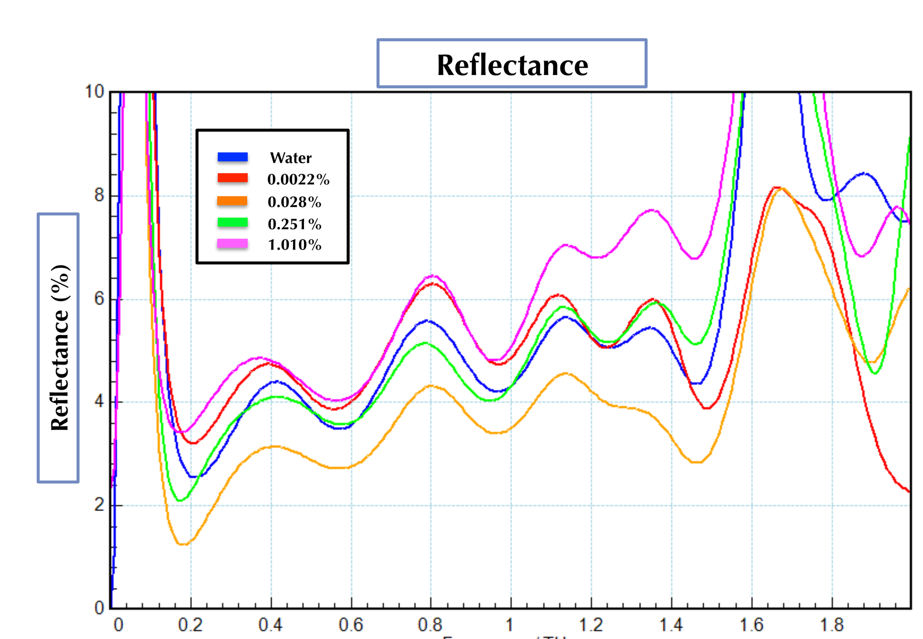


Glucose on Metasurface



- Decreasing reflectance from 0% - 30% glucose at 0.45 THz
- Distinct blue-shift occurs as concentration increases in 1.40 – 1.60 THz range

Creatinine on Sapphire



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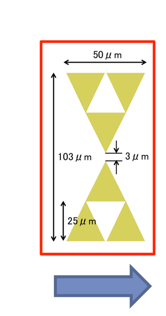
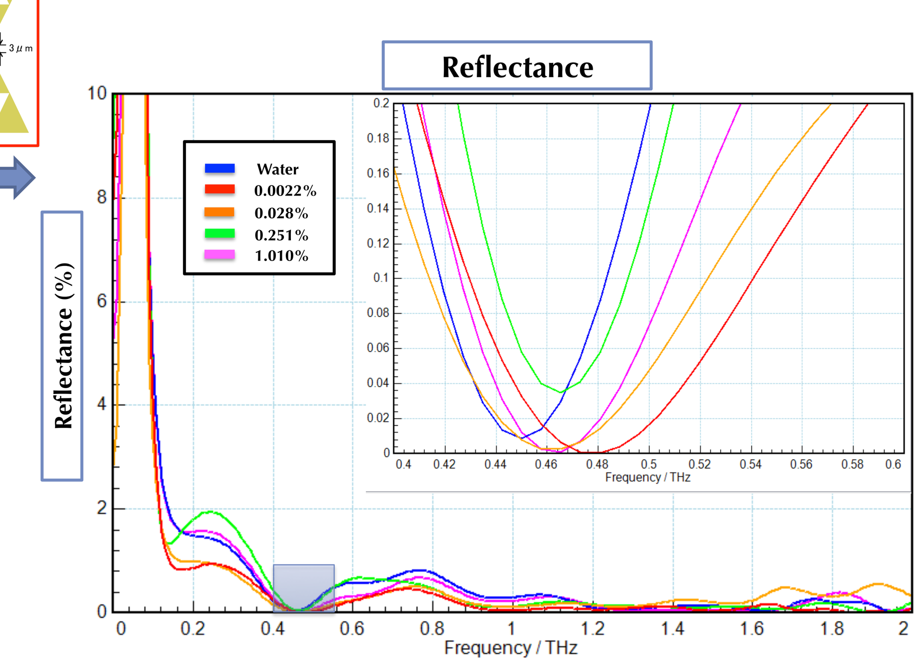


Creatinine on Metasurface



- Significant decrease in reflectance from 0.45 THz – 0.48 THz
- Disordered arrangement of reflectance dips

Conclusion

Glucose

Metasurface produces notable linearity in 1.4 THz – 1.60 THz region

Creatinine

Low concentration possible cause of disordered data

Future Work

- Maintain consistent solution droplet size for uniform distribution on metasurface
- Sufficiently eliminate humidity to increase signal intensity
- Develop method to quantify concentration changes from spectrum data
- Repeat experiment with other metasurfaces

References

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Acknowledgements

This research project was conducted as part of the 2016 Nakatani RIES Fellowship for U.S. Students with funding from the Nakatani Foundation. For more information, please visit http://nakatani-ries.rice.edu/. I would like to thank Tabata-sensei, Uematsu-san, Lili-san, Yamahara-san, and Endo-san for all of their help on this research project. Special thanks also to Professor Stanton, Kono-sensei, Sarah Phillips, Packard-san, Ogawa-san, Endo-san, and Takarada-san for making this program possible and for all of their support and guidance.