TERAHERTZ METASURFACE FOR POTENTIAL LIVE CELL SENSING APPLICATION

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Outline

1. Backgrounds and motivations
2. Cell trapping experiment and THz spectral measurement
3. Metasurface design for sensing improvement
4. Conclusion and future works

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   - THz in biological / medical systems
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2. Cell trapping experiment and THz spectral measurement:
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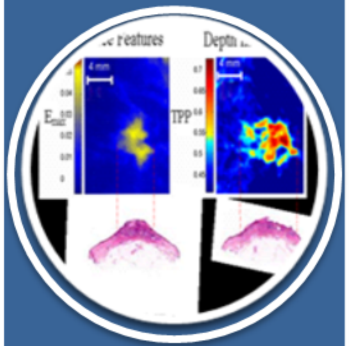
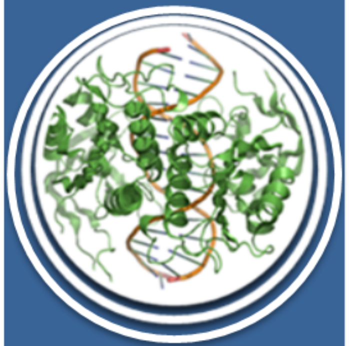
THz in biological / medical applications

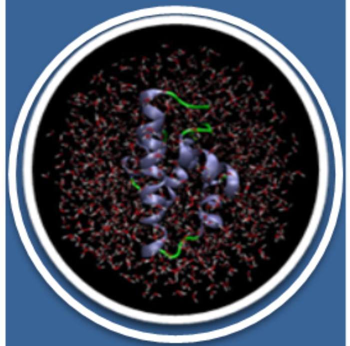
Sensing of chemicals, and drugs



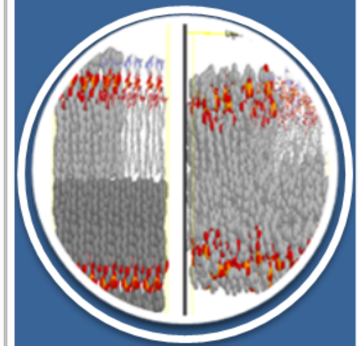
Medical imaging of skin cancer



Spectral signatures of cells and biomolecules



The role of water in biomolecule dynamics



Sensing the change in membrane permeability of liposomes

Scientific research

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Why / Why not THz?

- Vibrational modes
- Energy (meV) and timescales (picosecond)

- Not clear spectroscopic features from most samples
- Sub-wavelength cell size
- Large absorption by water
- Equipment requirements

Lack of effective tools to study

Cell trapping devices by using microfluidic techniques

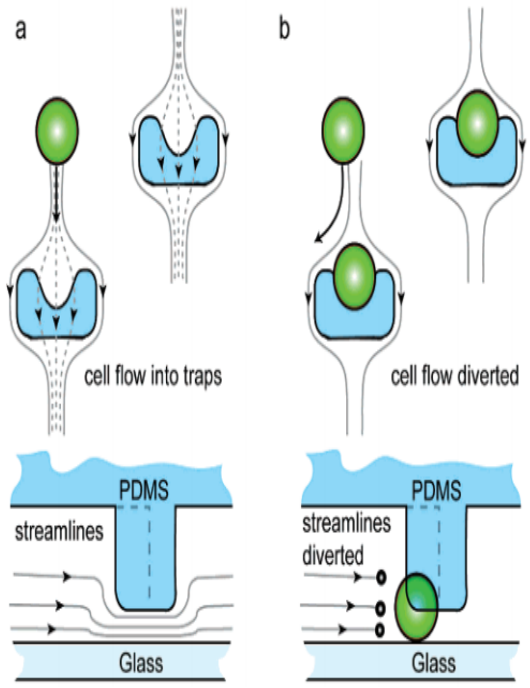
Benefits from microfluidics:

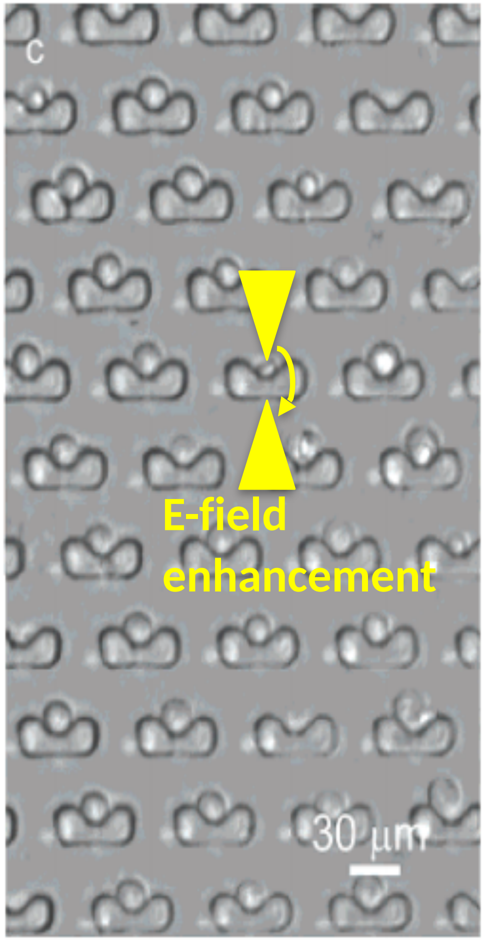
- Single cell trapping and manipulation
- Control the thickness of aqueous media
- High throughput
- Real-time measurement

Different techniques for cell trapping:

- Optical methods
- Hydrodynamics
- Electrodynamics

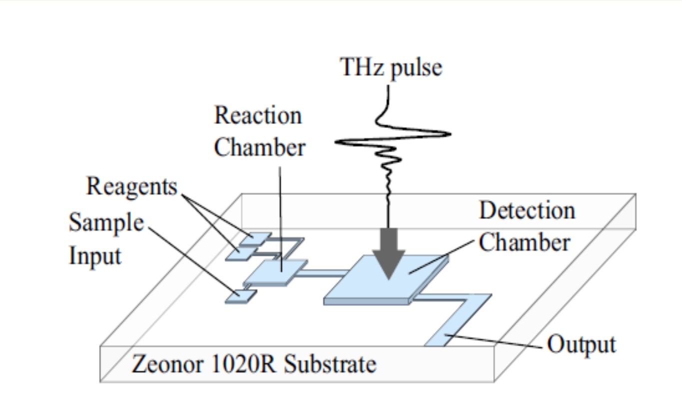
An example



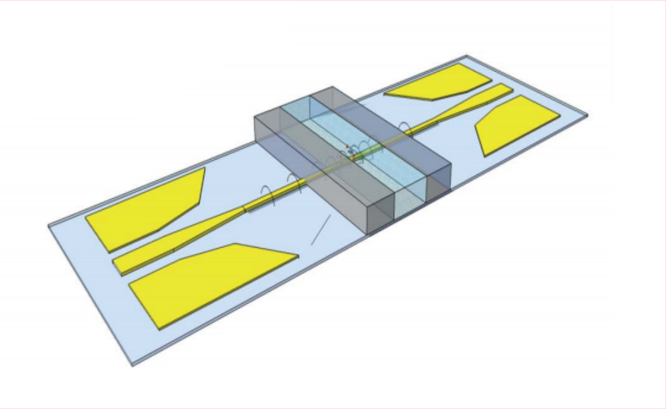


Di Carlo, D., Aghdam, N., and Lee, L. P. *Analytical Chemistry*, *78*(14), 4925-4930. (2006)

Reported THz microfluidics



- by George, P. A. *et al.*[1]
- Measure the absorption spectra of vibrational modes of bovine serum albumin (protein) from 0.5 - 2.5 THz
- Detect molecular quantities as small as 10 picomoles without integrated probes



- by Laurette, S. *et al.*[2]
- Measure the absorption spectra of BSA, lysozyme and chymotrypsine proteins
- By combining THz waveguides, the sensitivity can be down to 0.6 picomoles (5mg/mL BSA solution)

[1] George, P. A. *et al.* Microfluidic devices for terahertz spectroscopy of biomolecules. *Optics Express* **16**, 1577 (2008).

[2] **Laurette, S. *et al.*** Highly sensitive terahertz spectroscopy in microsystem. *RSC Advances* **2**, 10064 (2012).

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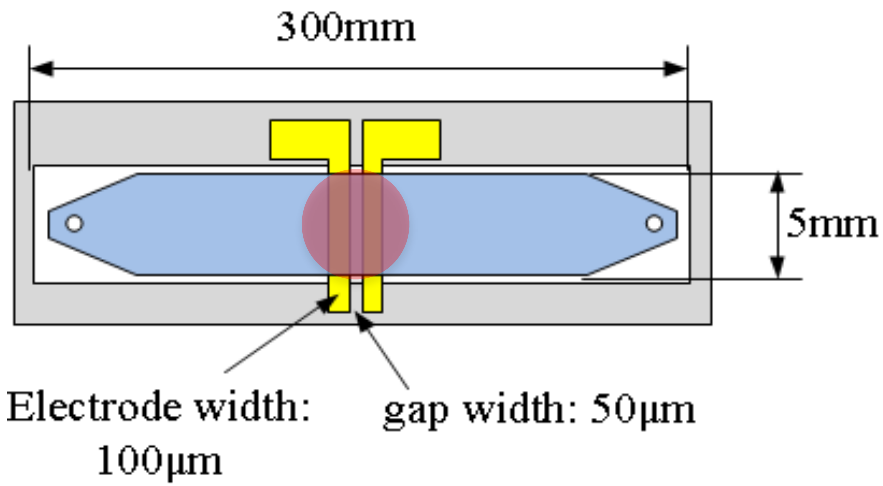
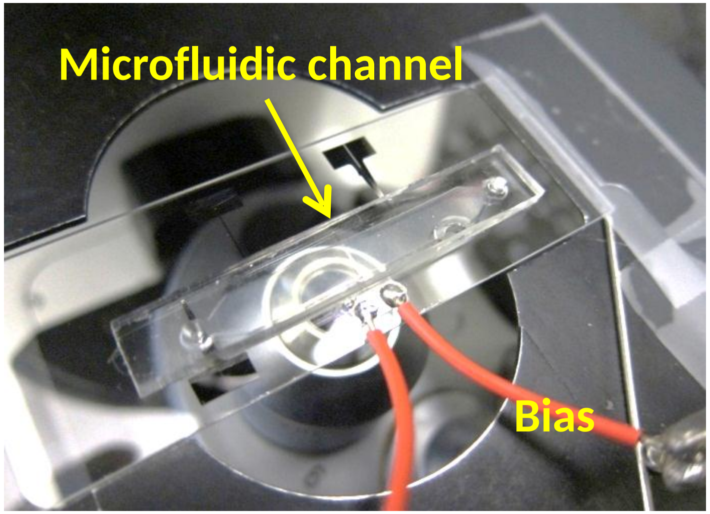
Lab-on-a-chip: Cell trapping





Channel thickness – 300 / 600 µm

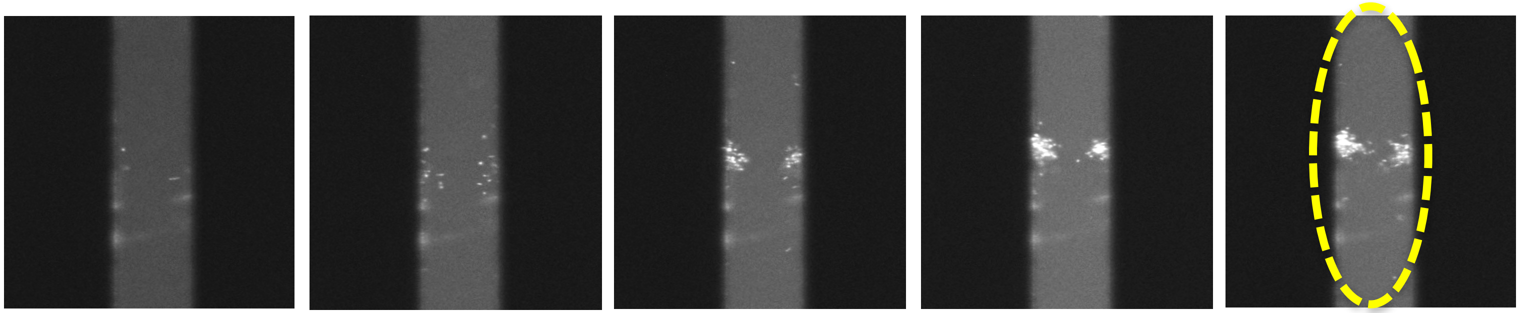
Procedure:

1. Bias the electrodes with a function generator (1 MHz, 7 V peak-to-peak square wave on electrodes);
2. Start to observe cells concentrating in the gap; frequency and voltage influence the concentration; heating of solution also contributes;
3. Mechanism: Electrokinetic forces (i.e., DEP and electrophoresis) and AC electroosmotic forces.

Cell trapping images

E. coli (~1−2 μm in diameter) bacteria in Luria Broth media

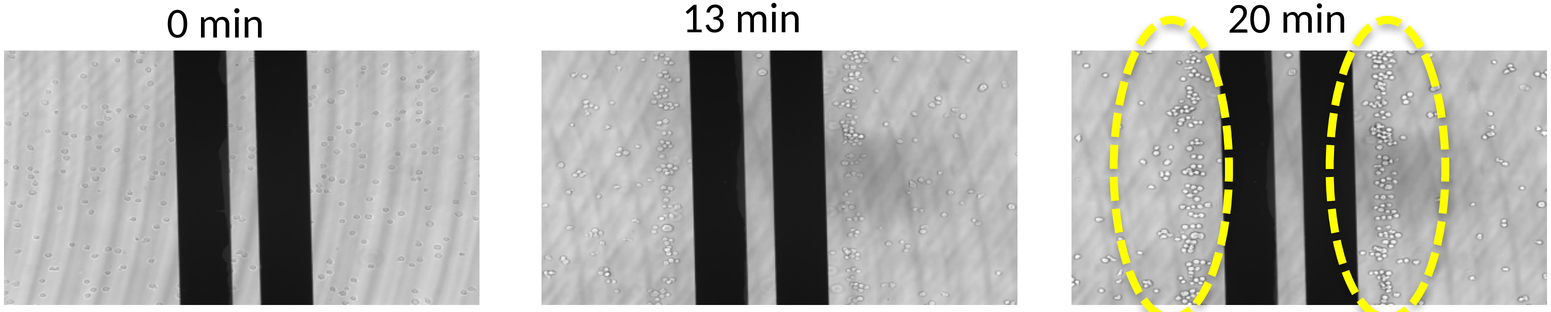
0 min 5 min 10 min 15 min 20 min



Florescent images

Jurkat cells (~12 μm in diameter) in RPMI media

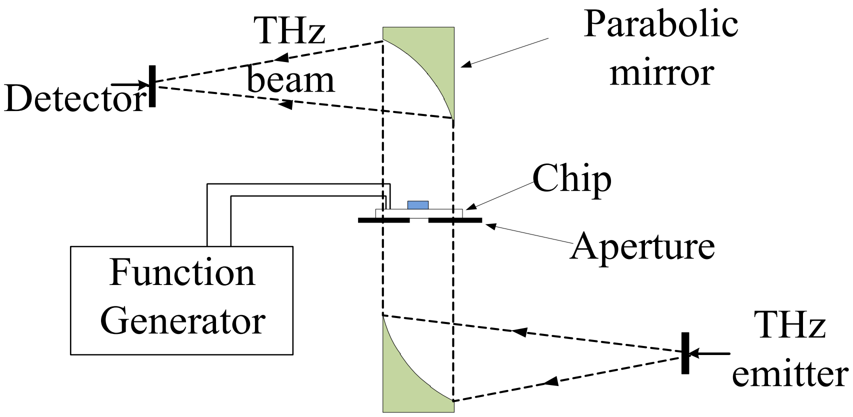
0 min 13 min 20 min

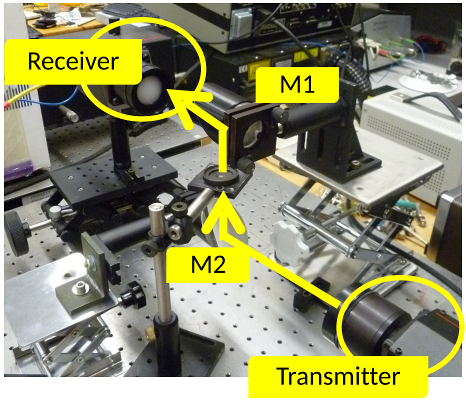


White light images

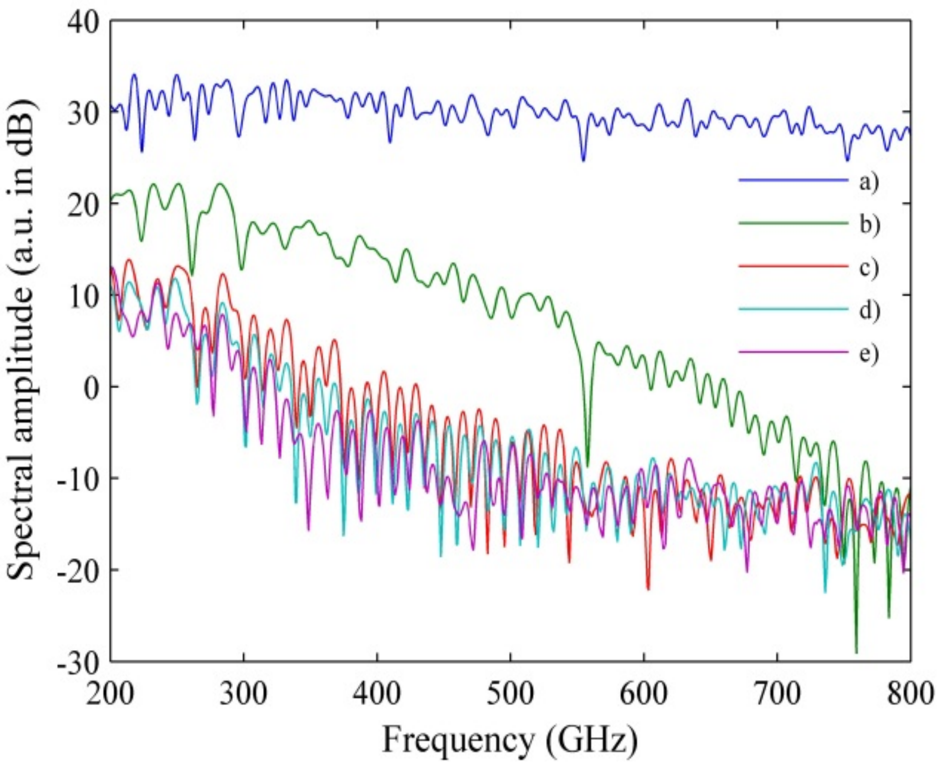
- Green, N., Ramos, A., González, A., Morgan, H., and Castellanos, A., "Fluid flow induced by nonuniform ac electric fields in electrolytes on microelectrodes. I. Experimental measurements," Physical Review E 61(4), 4011–4018 (2000).
- Wong, P. K., Chen, C. Y., Wang, T.-H., and Ho, C. M., "Electrokinetic bioprocessor for concentrating cells and molecules," Analytical chemistry 76(23), 6908-6914 (2004).

THz spectra of E. Coli bacteria (8.3×10-8 CFU/mL in LB medium)





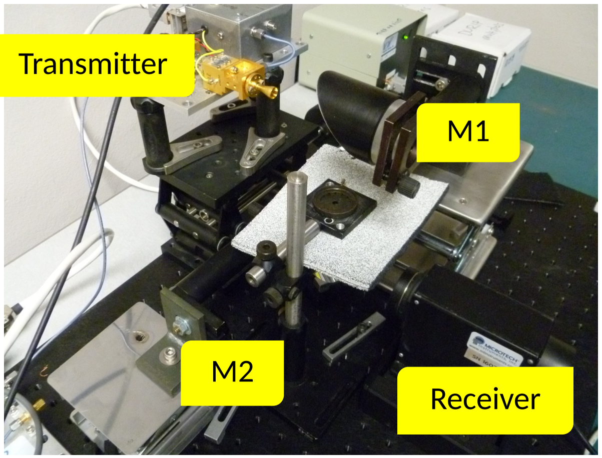
(a)T-Ray 2000® by Picometrics
(b)100 ps time-domain signals
(c)10 GHz spectral resolution



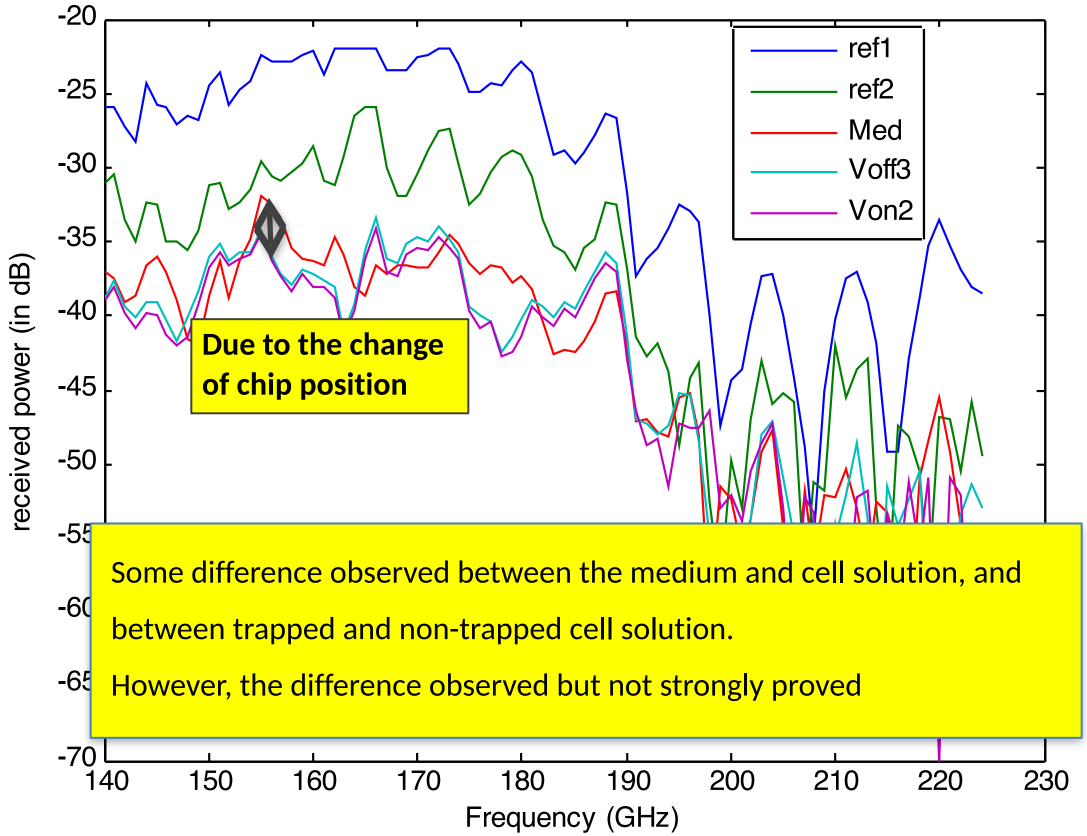
(a) Aperture reference;
(b) Empty chip;
(c) Medium;
(d) E. coli in medium;
(e) Trapped E. coli in medium

[1] Q. Tang, M. Liang, Y. Lu, P. K. Wong, G. J. Wilmink, H. Xin, *"Development of terahertz (THz) microfluidic devices for 'Lab-on-a-Chip' applications"*. Proc. SPIE 8585, Terahertz and Ultrashort Electromagnetic Pulses for Biomedical Applications, 858506 (February 23, 2013)

THz spectra of Jurkat cells (5.4×10⁵ cells/mL in RPMI medium)



- VDI-MixAMC-S117: Multi-band Amplified Multiplier Chain
- Freq. range: 140-225GHz
- Freq. resolution: 1GHz



Some difference observed between the medium and cell solution, and between trapped and non-trapped cell solution.

However, the difference observed but not strongly proved

- **Ref1: Aperture reference;**
- **Ref2: Empty chip;**
- **Med: Medium;**
- **Voff3: Jurkat in RPMI medium;**
- **Von2: Trapped Jurkat cells in RPMI medium**

[2] not published

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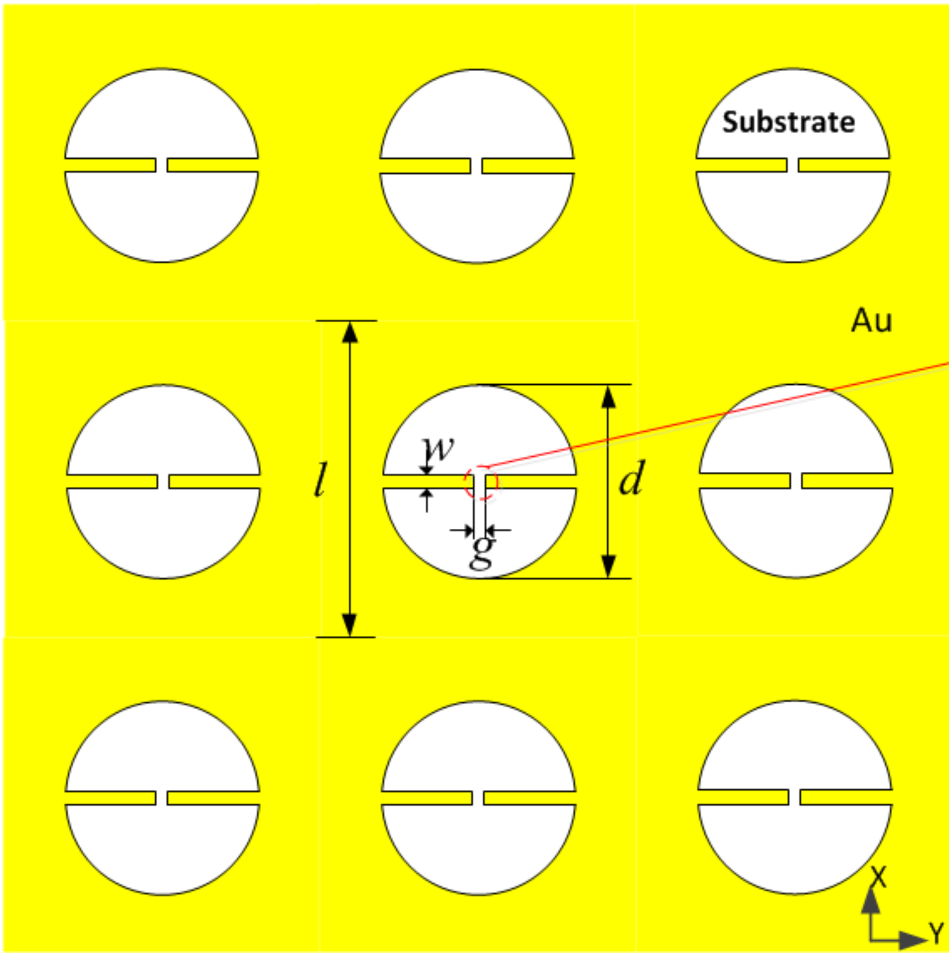
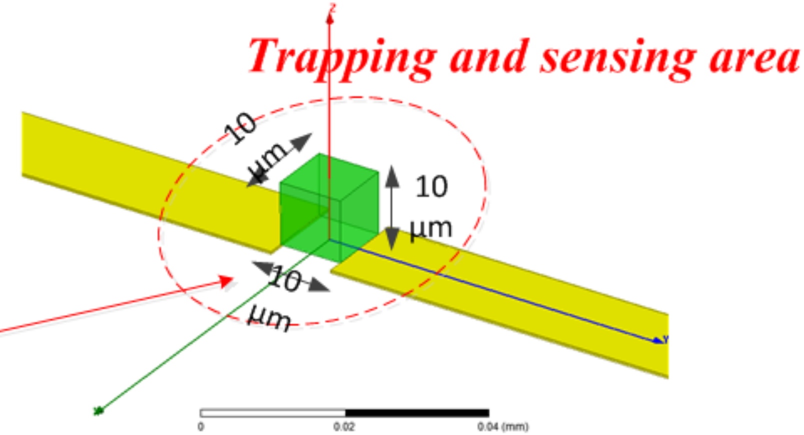
- **Metasurfaces:**
  - Artificially structured metallic surfaces whose electromagnetic response can be deliberately designed;
  - Widely used for filtering, modulation, sensing, and many other.
  - Passive and periodic.

- **Design requirements**
  - Band-pass (rather than band-stop): transmission mode (instead of reflection mode).
  - Field enhancement: increase sensitivity.
  - Spectral difference with different dielectric properties of small particles.

Structure design





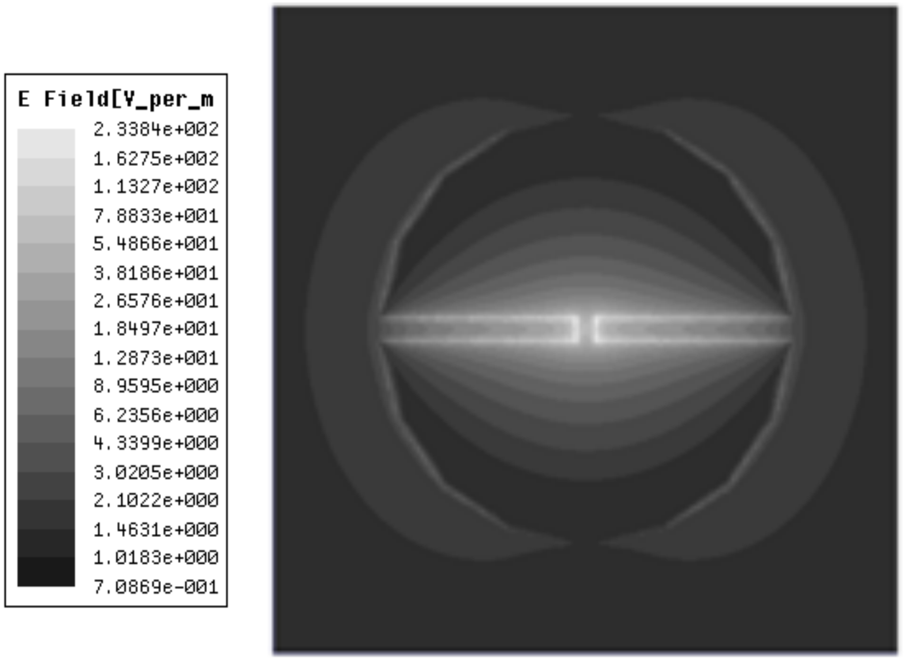
l= 300 μm
d= 200 μm
w= 10 μm
g= 10 μm

Assumed effective dielectric properties of live cells is similar to water.

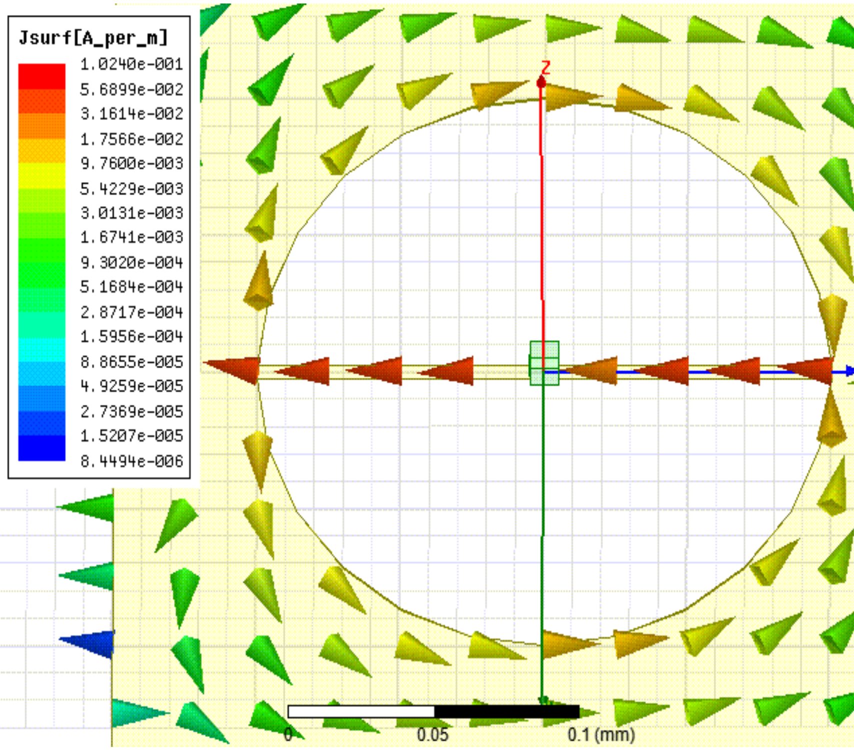
E-field direction

Field enhancement

- The E-field distributon in a unit cell of the freestanding metasurface with a 1 V/m incident E-field intensity at 0.49 THz.

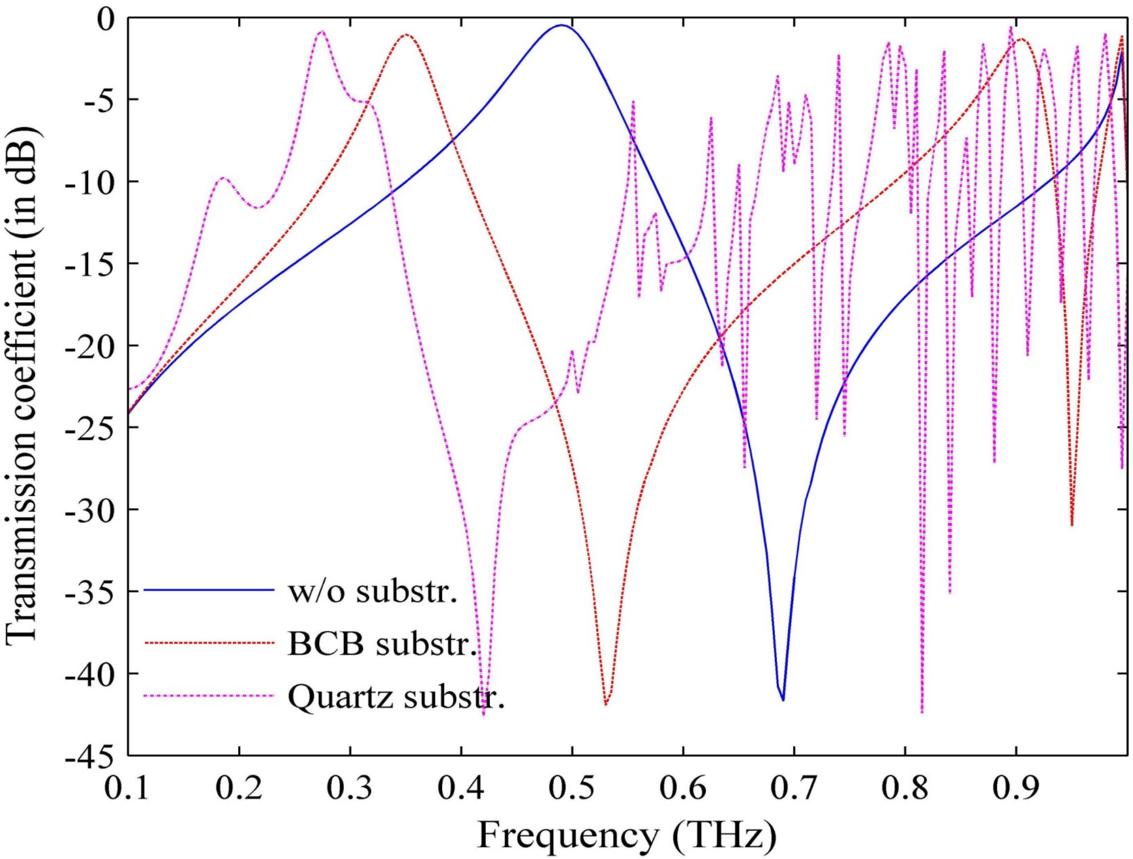


- Current distribution on the surface



Maximum field enhancement by a factor of 200 at the center

Substrate selection

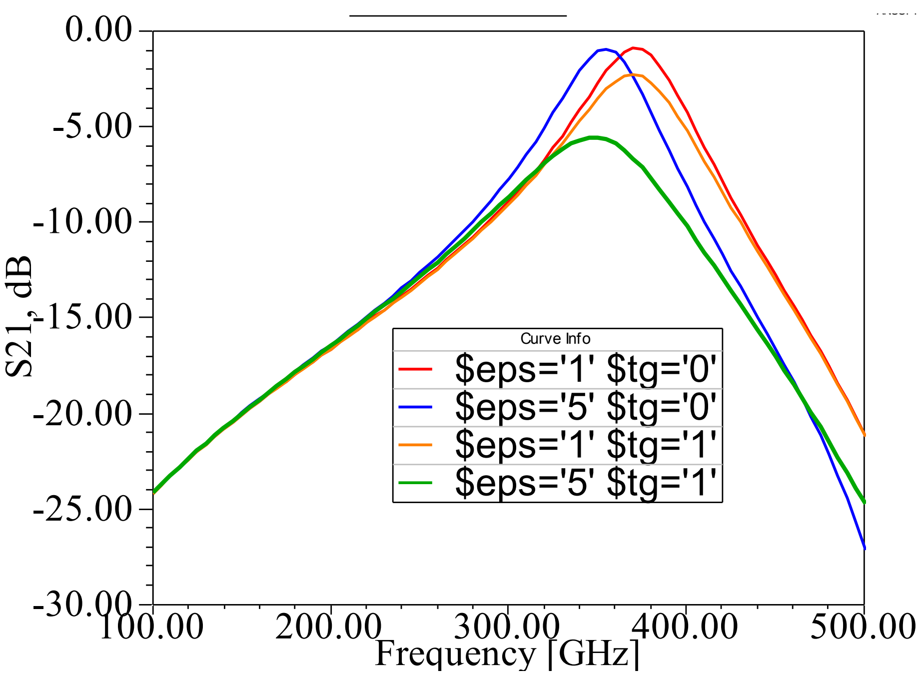


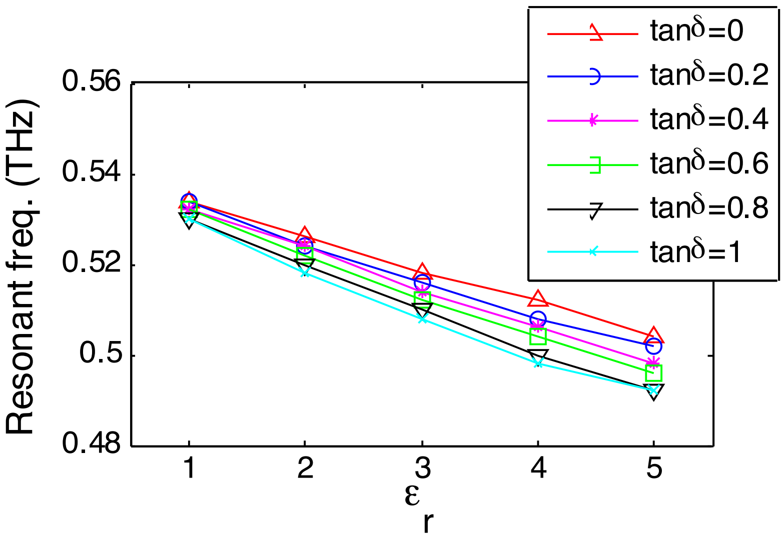
- 26-µm-thick benzocyclobutene (BCB)
  $\varepsilon_r = 2.65$
  $\tan\delta = 0.01$.
- 500-µm-thick quartz
  $\varepsilon_r = 4.64$
  $\tan\delta = 9.7\times10^{-5}$

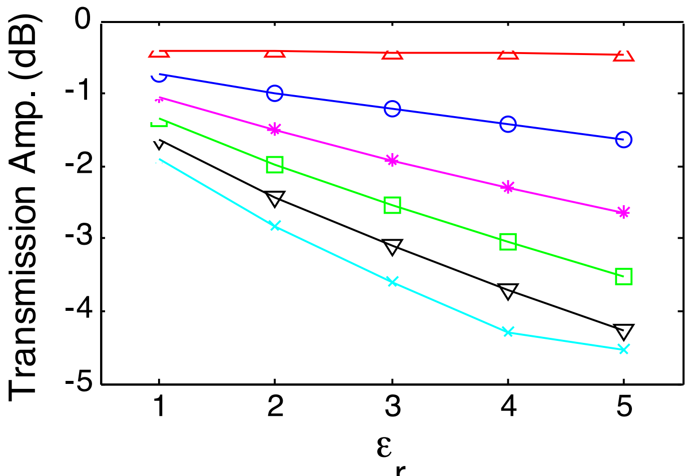
Some other choices:

- coverslides (very thin glass) on polymer Petri dish

Sensitivity results (BCB substrate)

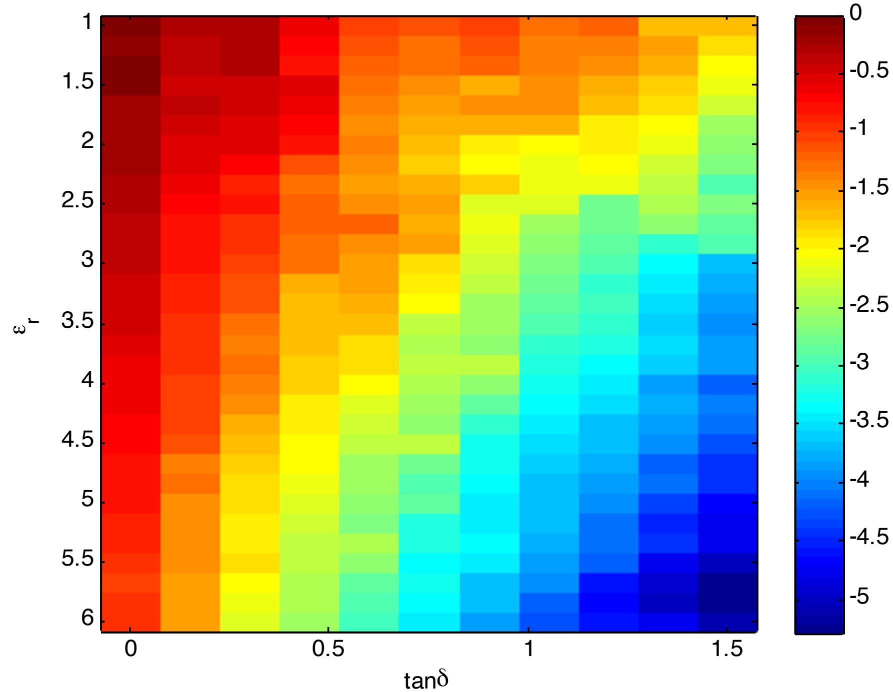






- Resonant frequency and transmission coefficient as a function of ε_r and tanδ

Both ε_r and tanδ influence the amplitude of transmission coefficient. The influence by ε_r is caused by frequency shift.



- Total transmission difference as a function of ε_r and tanδ at single frequency (320 GHz).

Substr. material	frequency shift as ε_r change from 1 to 5 with tanδ = 0
Air	30 GHz
BCB	15 GHz
Quartz	2 GHz

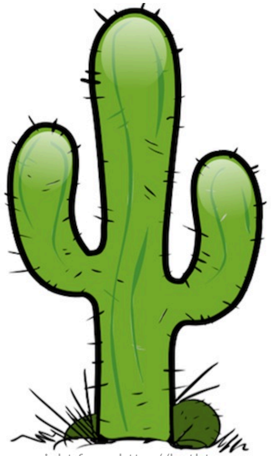
Conclusion and future works

- A microfluidic chip designed and live cells trapped.
- THz transmission spectra measured and compared
- Not significant enough spectral difference to discriminate cells and aqueous medium.
- The feasibility of using metasurfaces to sense small dielectric particles at THz frequencies proved.
- Different substrates including BCB film and quartz evaluated.

- Integration of this kind of metasurfaces and microfluidic structures in future works.
- Further improvement by using low loss substrate and channel material and optimizing structure dimensions.

Acknowledgement

- **Yi Lu, Tingting Liu, and Prof. Pak Kim Wong,** the systematic bioengineering lab, the department of Aerospace and Mechanical Engineering, University of Arizona;
- **Prof. Donna Zhang,** the department of Pharmacology and Toxicology, University of Arizona;
- **Abram Young**, the department of Physics, University of Arizona;
- **Dr. Gerald J. Wilmink,** Air Force Research Laboratory, Radio Frequency Bioeffects Branch, Fort Sam, Houston, TX, USA



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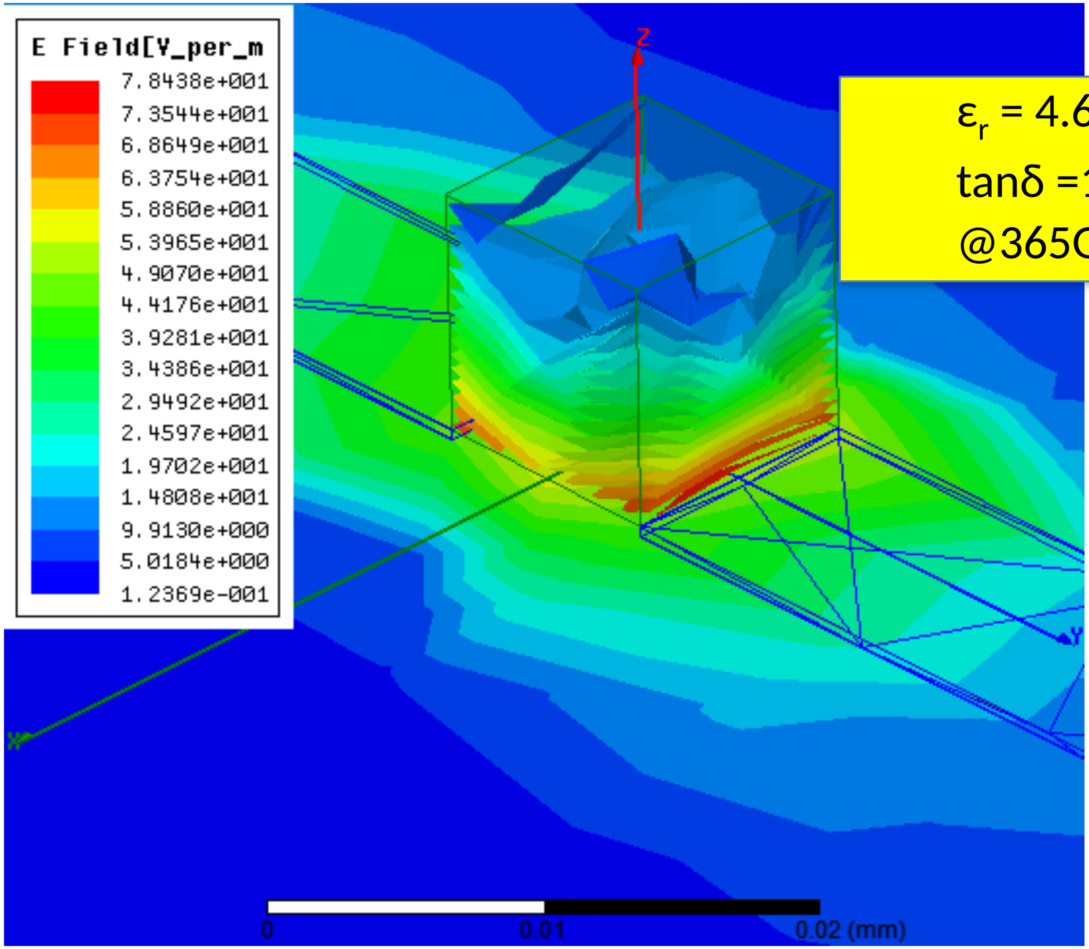
QUESTIONS?

Supplementary results



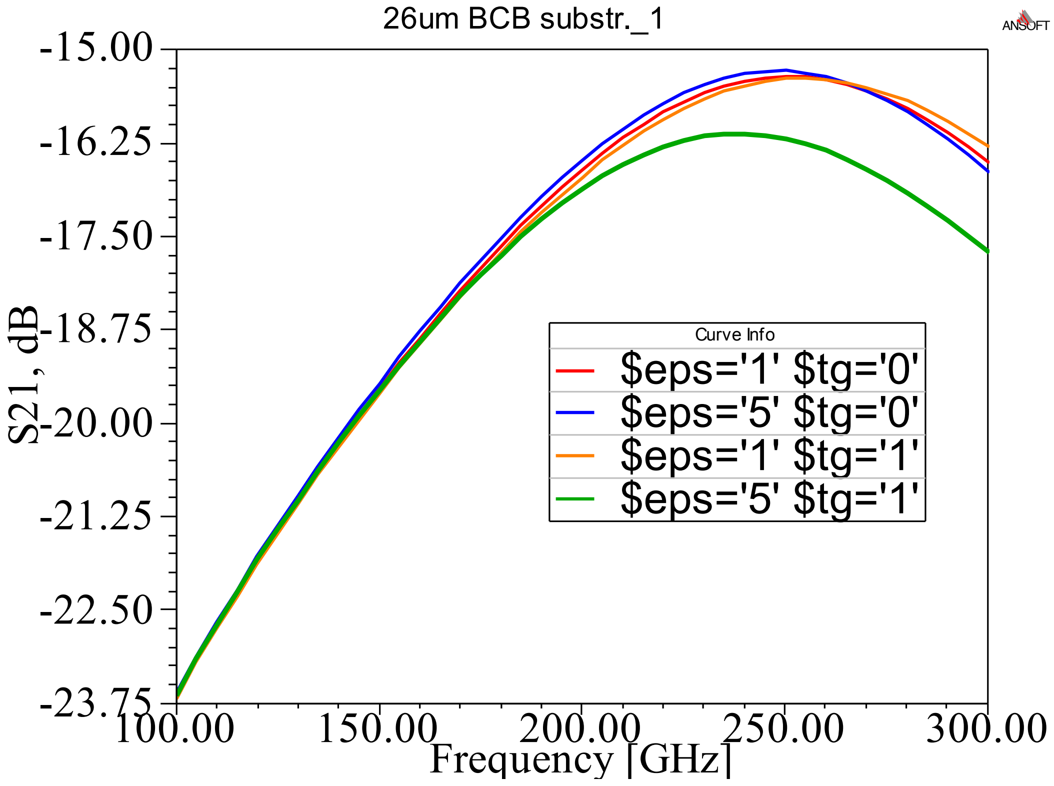
$\varepsilon_r = 4.64$

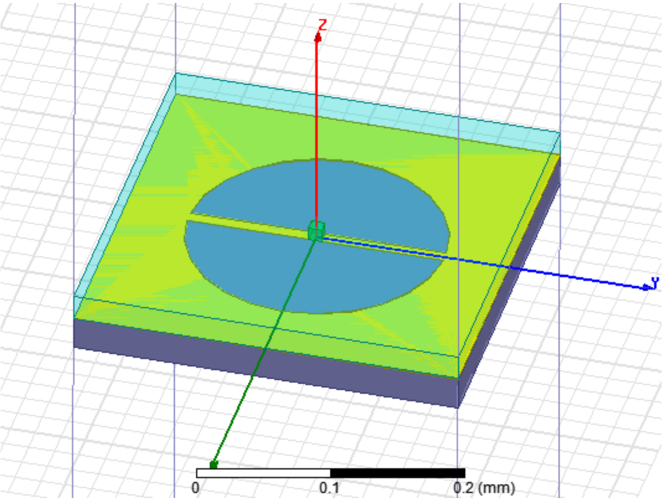
$\tan\delta = 1$

@365GHz

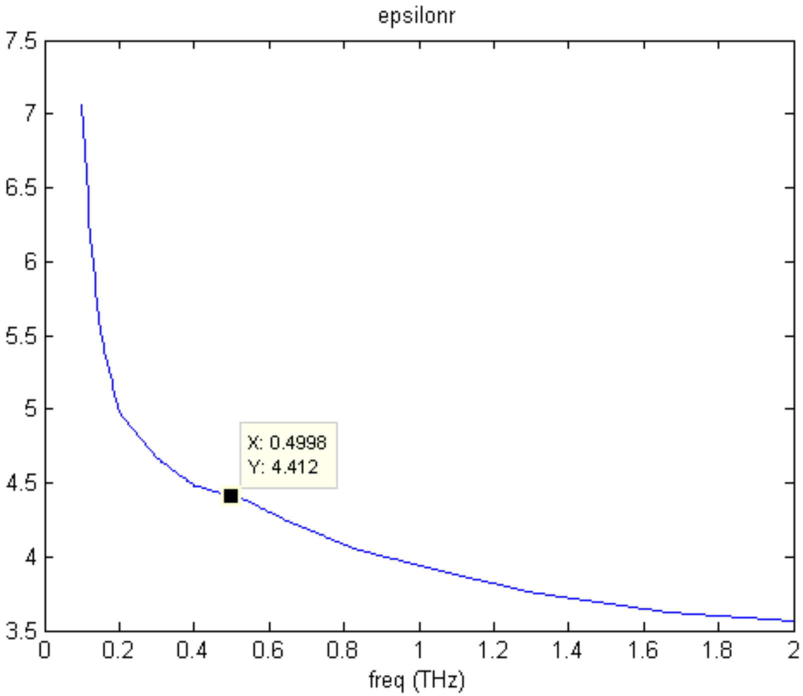
Supplementary results

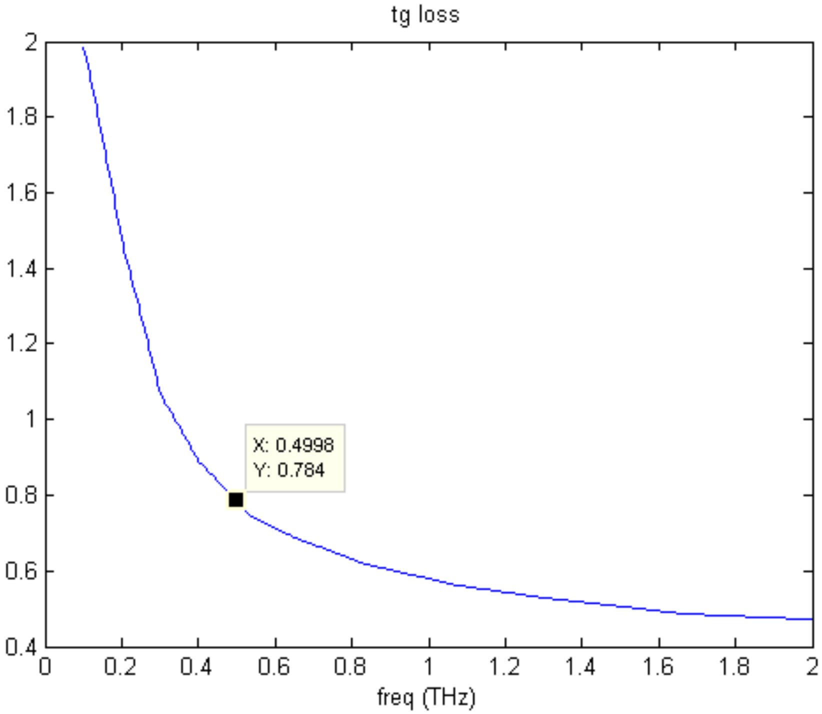
- 20 µm thick water layer, 15GHz shift ε_r from 5 to 1.





Supplement: Water dielectric properties





APPENDIX II

1. http://ec.europa.eu/enterprise/sectors/chemicals/specific-chemicals/drug-precursors/index_en.htm
2. http://labrat.fieldofscience.com/2010/12/molbio-carnival-is-here.html
3. http://www.hfsp.org/frontier-science/hfsp-success-stories/water-and-biological-molecules-probed-terahertz-spectroscopy
4. http://biowiki.ucdavis.edu/Biochemistry/Lipids/Dynamics_of_Membrane_Lipids
5. http://www.ee.cuhk.edu.hk/~emma/SHIAEmma.htm