THOUGHTS ON TERAHERTZ

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ELEMENT AERO, FACULTY NSF CENTER FOR BRIGHT BEAMS (CORNELL) AND THE UNIVERSITY OF NEW MEXICO

JULY 12-13 2021

THOMAS JEFFERSON NATIONAL ACCELERATOR FACILITY

THANKS FOR THE INVITATION!

- Thanks to my long-time colleague Craig Woody of BNL and the entire organizing committee for the invitation to participate.
- Great to see so many colleagues here these two days. I am looking forward to meeting in person in the Spring of 2022!

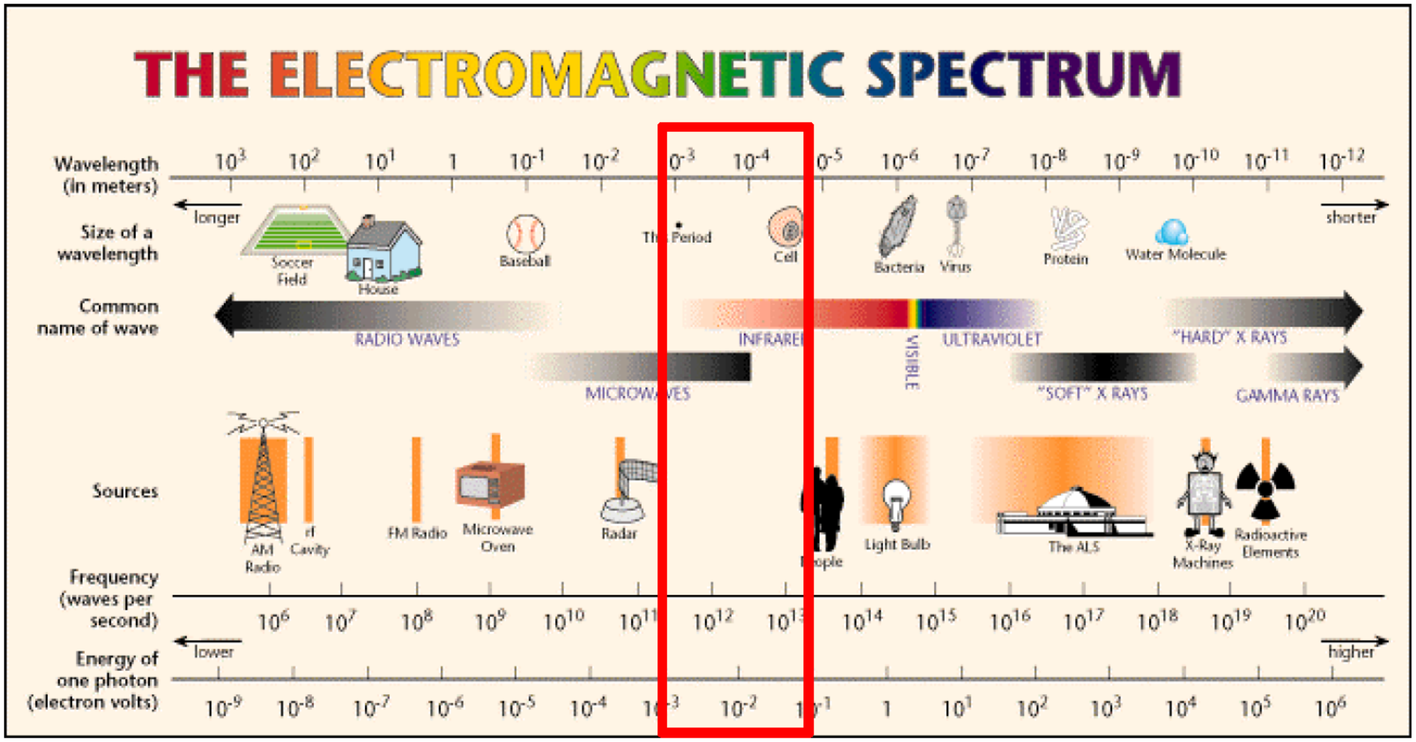


Figure 1.1 The electromagnetic spectrum. The THz frequency range discussed at this workshop lies in the middle of this diagram, between "radar" and "people" and is indicated in red. Diagram from the LBL Advanced Light Source web site (http://www.lbl.gov/MicroWorlds/ALSTool/EMSpec/EMSpec2.html).

THz lies between electronics and photonics – no existing strong sources

Electronics
- radios

Photonics
- light sources

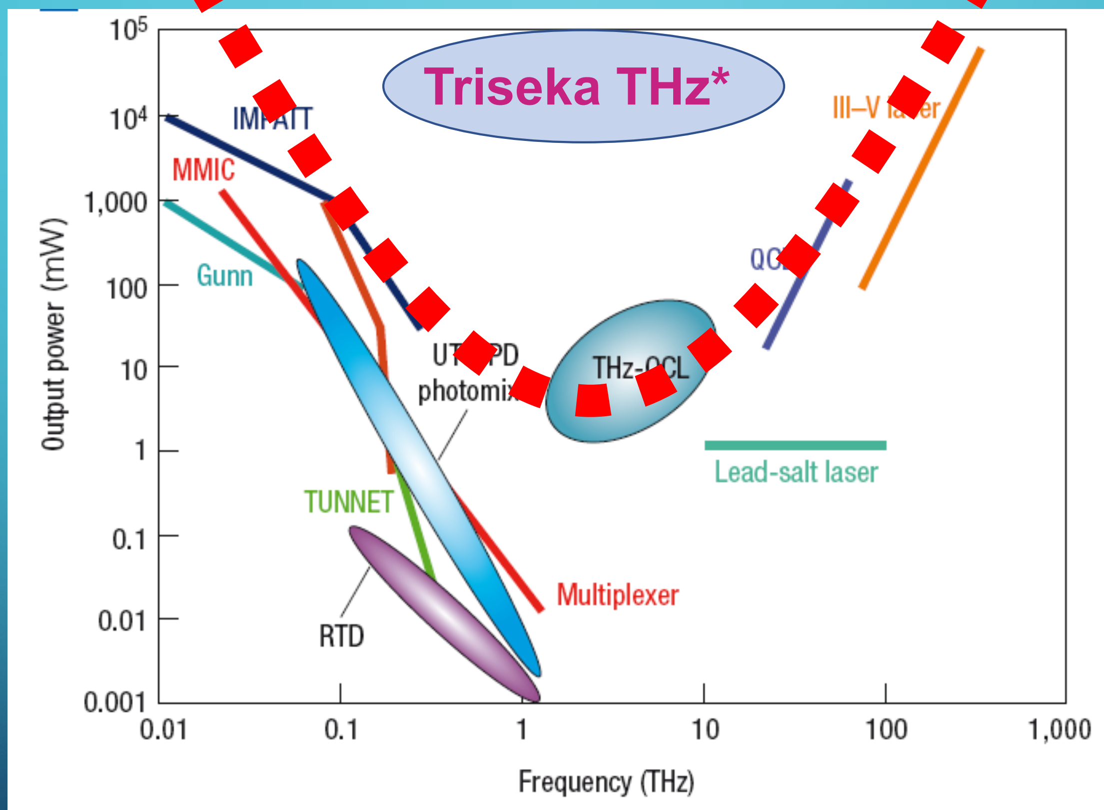


Illustration from Tonouchi Nature Photonics 1, 97 (2007)

* Triseka THz based on G.L. Carr, M.C. Martin, W.R. McKinney, K. Jordan, G.R. Neil and G.P. Williams "High Power Terahertz Radiation from Relativistic Electrons", Nature 420 153-156 (2002)

WHAT IS UNIQUE ABOUT THZ?

- THz light passes through many materials, such as packaging material, clothing, carpet, walls.
- THz light is non-ionizing
- THz light can "recognize" and distinguish materials that x-rays cannot, such as plastics & proteins.
- THz light allows high speed & safe communications - Tera is 1000 times faster than Giga…
- THz does not pass through metal and water, and will always be complimentary to x-rays.

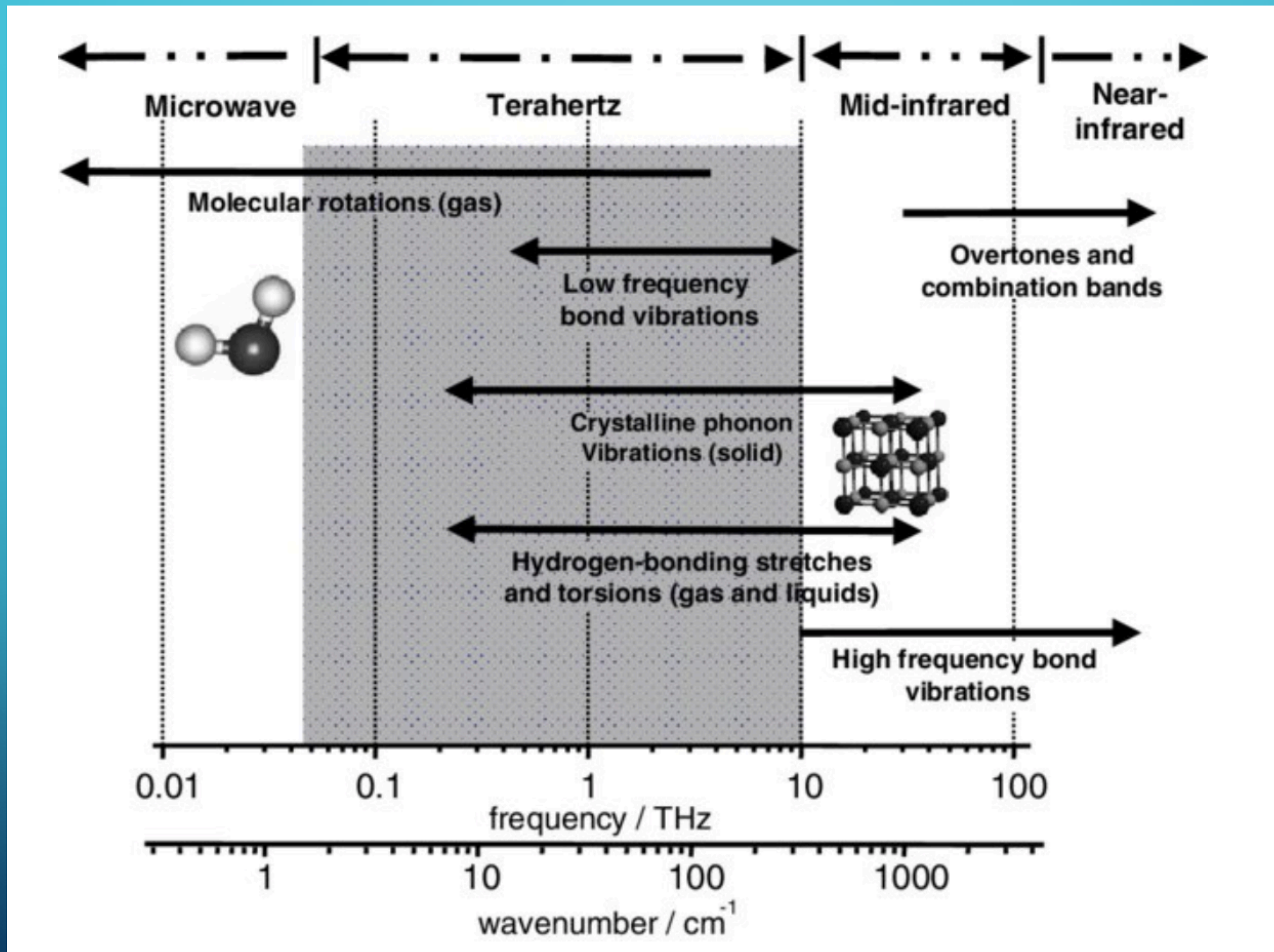
MANY APPLICATIONS

- **Medical screening (skin cancer)**
- **Security**
- **Pharmaceuticals (drug verification and testing)**
- **Non-destructive evaluation (including rebar in concrete)**
- **Environmental monitoring**
- **High speed communication**

Terahertz Waves Detect Early Corrosion in Concrete-Encased Steel

By *Ben DuBose* on 5/4/2020 1:35 PM

An abandoned building on Northern California's McAbee Beach shows the effects of corrosion on a steel-reinforced concrete structure. Photo by Per Loll, Denmark, and courtesy of NIST.



Microwave
Terahertz
Mid-infrared
Near-infrared
Molecular rotations (gas)
Low frequency bond vibrations
Overtones and combination bands
Crystalline phonon Vibrations (solid)
Hydrogen-bonding stretches and torsions (gas and liquids)
High frequency bond vibrations
0.01
0.1
1
10
100
frequency / THz
1
10
100
1000
wavenumber / cm-1

CONFESSIONS OF AN ACCELERATOR PHYSICIST

Got into THz because of security and defense

- Post 9/11, needed electronic noses for borders and in the field with ever-increasing powers

Comparison of terahertz technologies for detection and identification of explosives

May 2014 · Proceedings of SPIE - The International Society for Optical Engineering 9102:91020C · Follow journal

DOI: 10.1117/12.2050367

Conference: SPIE Sensing Technology + Applications

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[6]HÜBNER GmbH & Co. KG (Germany)
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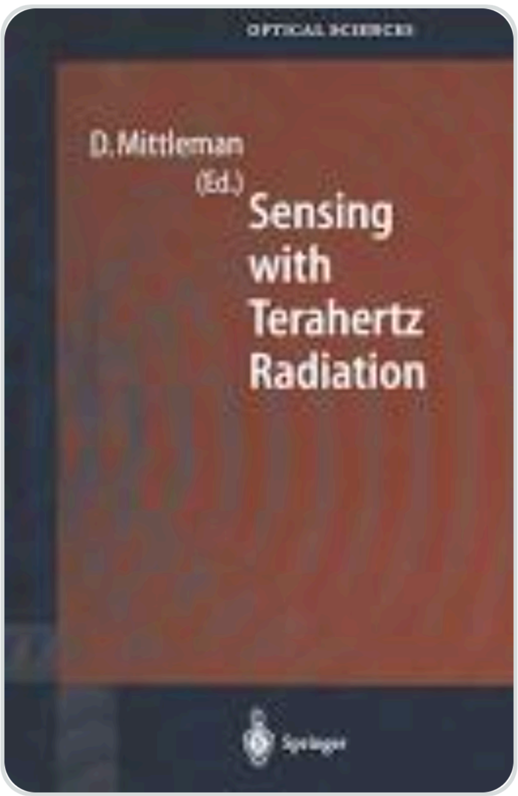
SEVERAL WAYS TO MAKE THZ – *SADLY* - EVEN WITHOUT ACCELERATORS ☺

Rather than reviewing every genre of mm-wave to THz source today, please seek out several overview papers and books, for example.



INSTITUTE OF PHYSICS PUBLISHING — JOURNAL OF PHYSICS D: APPLIED PHYSICS
J. Phys. D: Appl. Phys. 39 (2006) R301–R310 — doi:10.1088/0022-3727/39/17/R01

TOPICAL REVIEW

Biomedical applications of terahertz technology

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Online at stacks.iop.org/JPhysD/39/R301

Abstract
We review the development of terahertz (THz) technology and describe a typical system used in biomedical applications. By considering where the THz regime lies in the electromagnetic spectrum, we see that THz radiation predominantly excites vibrational modes that are present in water. Thus, water absorption dominates spectroscopy and imaging of soft tissues. However, there are advantages of THz methods that make it attractive for pharmaceutical and clinical applications. In this review, we consider applications ranging from THz spectroscopy of crystalline drugs to THz imaging of skin cancer.

(Some figures in this article are in colour only in the electronic version)

Real time THz imaging—opportunities and challenges for skin cancer detection

Cite as: Appl. Phys. Lett. **118**, 230501 (2021); https://doi.org/10.1063/5.0055259
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H. Lindley-Hatcher, R. I. Stantchev, X. Chen, A. I. Hernandez-Serrano, J. Hardwicke, and E. Pickwell-MacPherson

OVERVIEW OF TERAHERTZ RADIATION SOURCES

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Abstract
Although terahertz (THz) radiation was first observed about hundred years ago, the corresponding portion of the electromagnetic spectrum has been for long time considered a rather poorly explored region at the boundary between the microwaves and the infrared. This situation has changed during the past ten years with the rapid development of coherent THz sources, such as solid state oscillators, quantum cascade lasers, optically pumped solid state devices and novel free electron devices, which have in turn stimulated a wide variety of applications from material science to telecommunications, from biology to biomedicine. For a comprehensive review of THz technology the reader is addressed to a recent paper by P. Siegel [1]. In this paper we focus on the development and perspectives of THz radiation sources.

INTRODUCTION

Throughout this paper we will use a definition of the THz region that extends over two decades in frequency, covering the spectral range from 100 GHz to 10 THz. This should allow a better understanding of the effort in the extension of microwave electronics towards high frequencies on one side and the development of photonic devices from the optical region towards low frequencies. According to this scheme, we will first cover the state of the art of solid state oscillators and then move to gas and Quantum Cascade Lasers (QCL), which lie at the low and high frequency boundary of the THz region respectively. A brief review of laser driven THz emitters will be presented, which are the most widely used sources of THz radiation. We will also briefly discuss the physical principles of the generation of THz radiation from free electrons, describing the mechanism of Coherent Spontaneous Emission and the development of table-top Free Electron Laser (FEL) sources.

SOLID STATE OSCILLATORS

Electronic solid state sources, like oscillators and amplifiers, are generally limited in frequency due to the transit time of carriers through semiconductor junctions, which causes high frequency roll-off. High frequency Gunn, IMPATT and TUNNET diodes are being developed by several research groups [2]. They are rugged and compact devices and can operate CW at room temperature with a relatively narrow linewidth (10^{-6}). A CW power of about 100 mW can be obtained around 100 GHz. The output power falls off as $1/f^2$ and then as $1/f^3$ as the frequency increases (see Fig. 1). Frequency multipliers with two or more diodes are generally employed to reach frequencies above 200 GHz, up to about 1 THz. The average power level achievable in the region around 400 GHz is typically in the range 0.1 to 1 mW. Due to their compactness, the range of application of these sources is rapidly growing. A 200 GHz Gunn diode is being used as a source in a low cost imaging system under development at RPI-Troy for security applications [3].

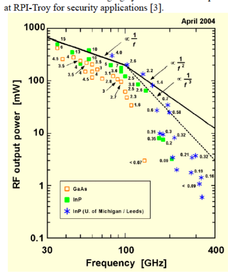


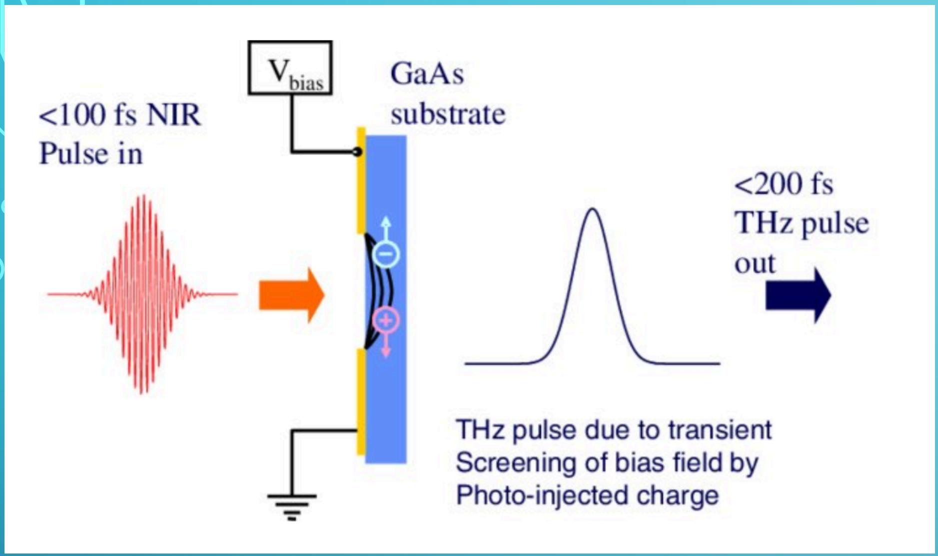
Fig. 1: State of the art results from GaAs and InP Gunn devices. Numbers next to the symbols denote dc to RF conversion efficiencies in percent (courtesy of H. Eisele, University of Leeds, UK).

GAS AND QUANTUM CASCADE LASERS

The Far Infrared (FIR) gas laser and the quantum cascade laser (QCL) are respectively the oldest and the newest coherent source developed in the THz region. Gas lasers date back to the sixties [4]. They are optically pumped lasers, which use a CO_2 laser to excite the roto-vibrational levels of gas molecules at pressures in the mbar range. The most widely used gas is methanol, which provides a powerful (typically 100 mW) emission line at 118 μm. Gas lasers are line-tunable in the range 0.3 to 5 THz (1000 to 60 μm) although with limited power and are commercially available by several companies, among which Coherent Inc. and Edinburgh Inst. The technology of FIR lasers has seen modest development in recent years, as it has been the case of most gas lasers. However they still are ideal sources for specific applications in

accelconf.web.cern.ch/f04/papers/FRBIS02/FRBIS02.PDF

ONE FAVORITE WAYS TO MAKE THZ – LASERS!



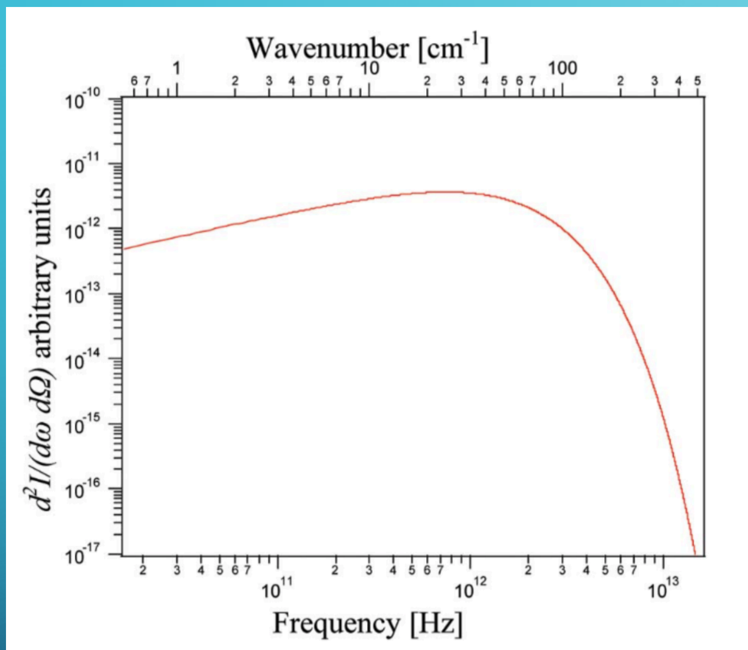
My laser-based THz system is on loan to Stuart (JLAB) for diagnosing e-beams with THz.
I think he's hoping I will leave it with him ☺

Today's commercial systems (e.g. TeraView Ltd) typically use photoconductive devices.

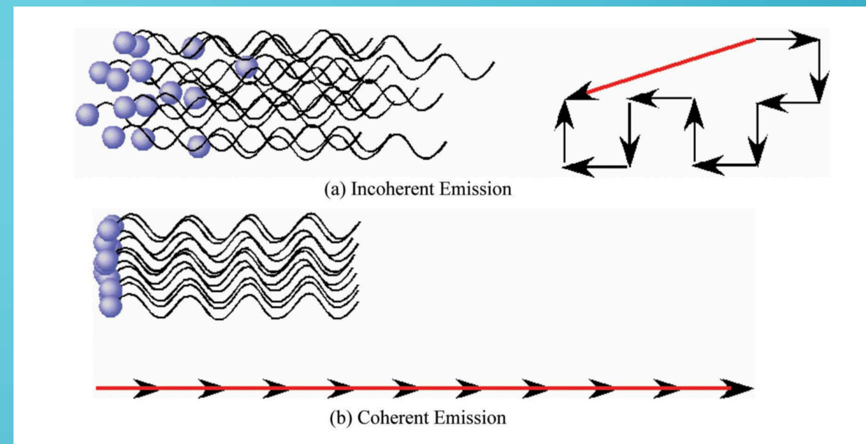
A photoconductive emitter consists of a small piece of semiconductor crystal, on which two planar metal electrodes, whose geometric design is that of an antenna, support a large electric field across its surface. Ultrafast (~100 fs) pulses of light are then focused onto the gap between the electrodes at infrared wavelengths (commonly from a Ti : Sapphire laser with a central wavelength of 800 nm); the photon energy of the 800 nm light is above the band gap of the semiconductor.

The photogenerated electron–hole pairs excited near the crystal surface rapidly change the conductance (effectively closing the optical switch). Application of a bias accelerates the electron-hole pairs and leads to a rapid change in the current density. The changing dipole produces a THz transient in the antenna that is radiated into free space. The shape of the pulse and hence the frequency distribution depend on the design of the antenna and the carrier dynamics.

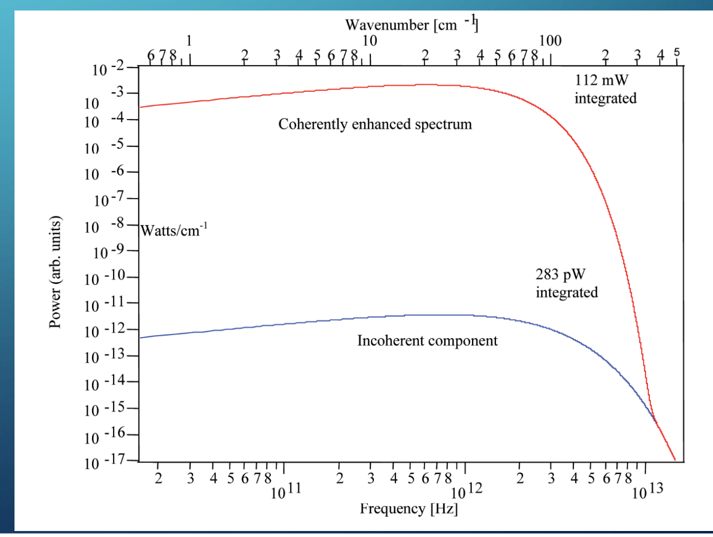
ANOTHER FAVORITE WAYS TO MAKE THZ – ELECTRON BEAMS



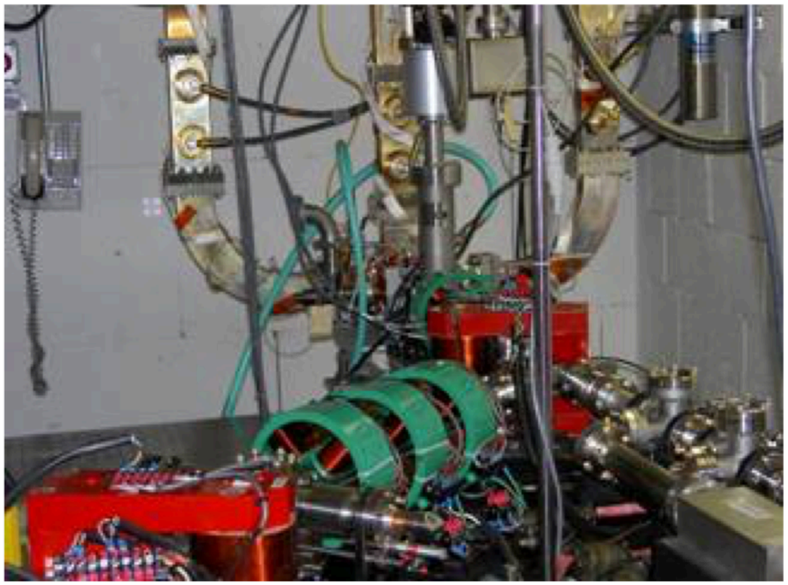
One can calculate the incoherent synchrotron radiation spectrum for a relativistic electron in circular motion. Here gamma = 5 and rho = 1 cm.

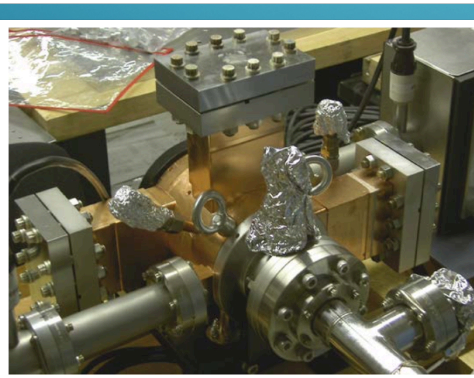


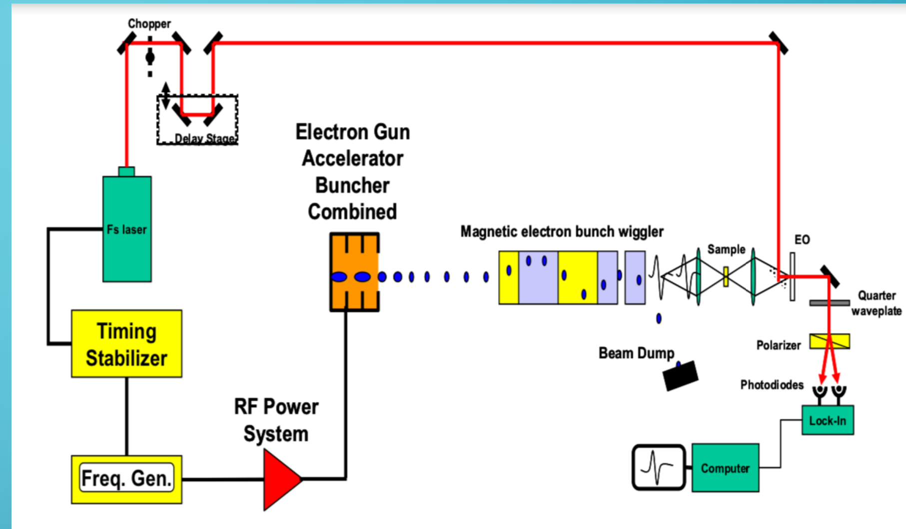
But what happens when you bunch that beam to the order of the wavelength at which you want to radiate?



ANOTHER FAVORITE WAYS TO MAKE THZ – ELECTRON BEAMS

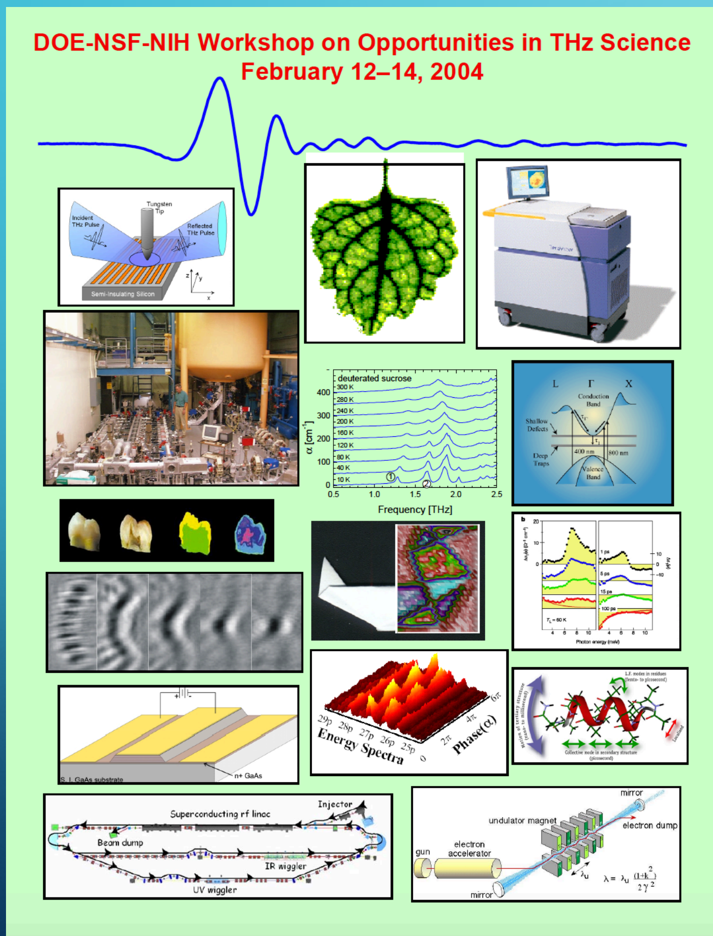






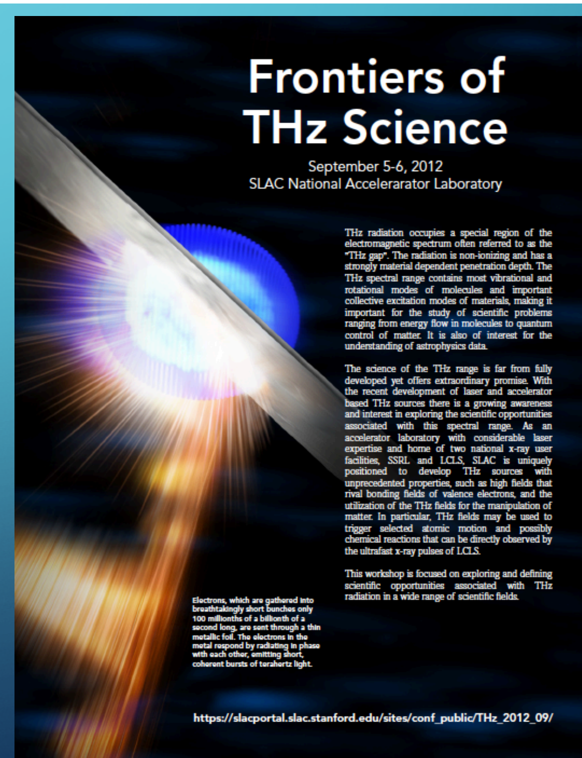
Parameter	*Value*
γ	5
Electron Beam Energy (MeV)	2.6
σ_z (μm)	50
Charge per Bunch (pC)	100
Useful duration of RF pulse (μs)	2
RF Frequency (MHz)	2856
RF repetition rate (Hz)	60
Radius of Curvature (cm)	1
Magnetic Field (T)	0.9

TERAHERTZ THROUGH THE AGES
REPORTS AND WORKSHOPS THAT ARE STILL RELEVANT!



THz Workshop

Workshop on Terahertz Sources for Time Resolved Studies of Matter
July 30-31, 2012
Argonne National Laboratory, Argonne, IL, USA



ONE EXAMPLE FROM THE DOE-NSF-NIH WORKSHOP

There are opportunities with regard to protein structure and dynamics. It is currently possible to distinguish many amino acids based on their THz spectrum, particularly in the crystalline form. Future work will characterize secondary and tertiary structure. There have been many theoretical predictions of the vibrational frequencies of alpha helices, for example, but still no convincing experimental evidence. Linear and nonlinear THz spectroscopy will allow dynamics to be studied on a variety of time scales ranging from milliseconds to sub-picosecond.

Several recent papers have demonstrated the ability to detect single and double stranded DNA sequences. Refinement of this work will lead to label-free sensors based on complementary DNA hybridization. The THz spectra of the individual DNA base pairs have been obtained. There is an extraordinary range of opportunities with regard to DNA dynamics and conductivity.

Ultimately, much larger systems than proteins and DNA strands will be accessible, particularly with the coupling of THz science with near-field probes. One envisions label-free measurement of protein-protein interactions as cellular activity is occurring in live cells.

IMAGING EXAMPLE

Status: One of the best examples of the current state of the art of THz science in medical applications is shown in Figure 7.1. As described in the caption, and later in the chapter, it is possible to determine the extent and depth of a basal cell carcinoma tumor non-invasively through reflectance mode THz imaging. In addition to imaging features and sub-surface on skin, as shown here, other groups have demonstrated that it is possible to detect dental caries that are not evident in x-ray images, although not *in vivo*. Furthermore, 3-dimensional imaging of bone, again, not *in vivo*, has recently been demonstrated at the level of proof-of-principle.

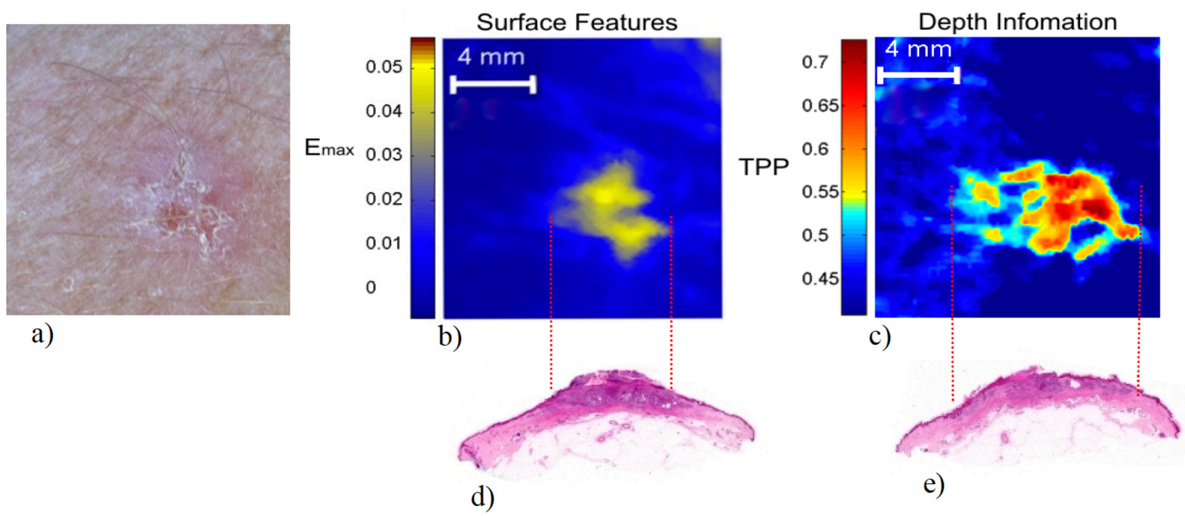


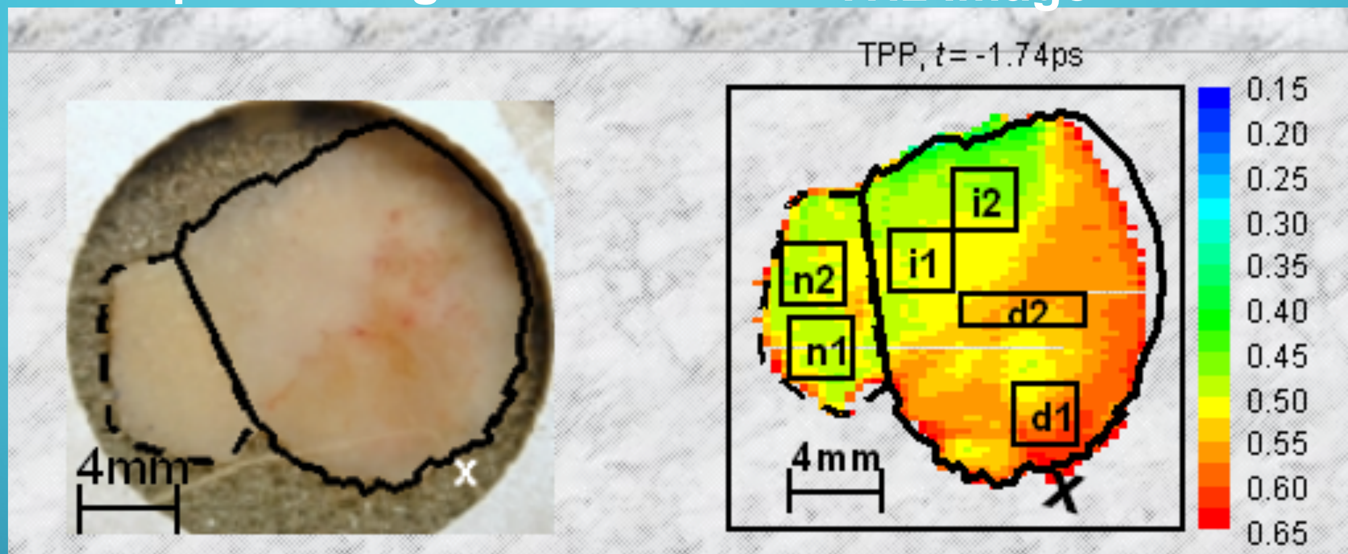
Figure 7.1. An *in vivo* measurement of a nodular BCC with an invasive component. Image a) is a clinical photograph of lesion, b) is a THz image formed by plotting the THz value at E_{min} showing surface features, c) is a THz image that indicates the extent of the tumor at depth (~250µm), d) is a representative histology section showing acute inflammatory crust corresponding to THz image b) and e) is a representative histology section showing lateral extent of tumor corresponding to THz image c). Images courtesy of TeraView Ltd, Cambridge, UK.

TERAHERTZ THROUGH THE AGES
REPORTS AND WORKSHOPS THAT ARE STILL RELEVANT!

- DOE NIH NSF meeting -> https://digital.library.unt.edu/ark:/67531/metadc889765/
- Argonne 2012 -> https://www.aps.anl.gov/Accelerator-Systems-Division/Meetings-Workshops/THz-Workshop
- SLAC workshop 2012 -> https://portal.slac.stanford.edu/sites/conf_public/THz_2012_09/Pages/default.aspx

Skin cancer screening

Optical Image THz Image



Basal cell carcinoma shows malignancy in red. Teraview Ltd.*
- contrast mechanism likely water, but molecular resonances also exist in the THz region.

Eliminates biopsy and Mohs – sees margins directly

1 mW source images 1 cm^2 in 1 minute

100 W source would image whole body (50 x 200cm) in few seconds

* R.M. Woodward, V.P. Wallace, D.D. Arnone, E.H. Linfield and M. Pepper, "Terahertz Pulsed Imaging of Skin Cancer in the Time and Frequency Domain", J. Biol. Phys. 29 257 (2003).

THZ TO DISRUPT

Research Article Vol. 10, No. 10 / 1 October 2019 / *Biomedical Optics Express* 4931

Biomedical Optics EXPRESS

Effective demethylation of melanoma cells using terahertz radiation

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Abstract: Terahertz (THz) demethylation is a photomedical technique applied to dissociate methyl-DNA bonds and reduce global DNA methylation using resonant THz radiation. We evaluated the performance of THz demethylation and investigated the DNA damage caused by THz irradiation. The demethylation rate in M-293T DNA increased linearly with the irradiation power up to 48%. The degree of demethylation increased with exposure to THz radiation, saturating after 10 min. Although THz demethylation occurred globally, most of the demethylation occurred within the partial genes in the CpG islands. Subsequently, we performed THz demethylation of melanoma cells. The degree of methylation in the melanoma cell pellets decreased by approximately 10–15%, inducing ~5–8 abasic sites per 10^5 bp; this was considerably less than the damaged DNA irradiated by the high-power infrared laser beam used for generating THz pulses. These results provide initial data for THz demethylation and demonstrate the applicability of this technique in advanced cancer cell research. THz demethylation has the potential to develop into a therapeutic procedure for cancer, similar to that involving chemical demethylating agents.

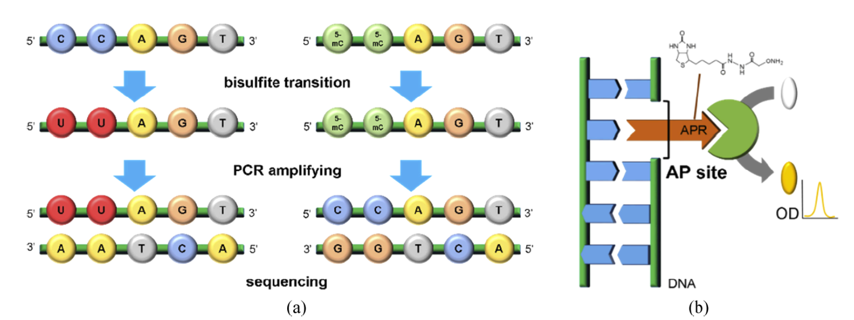


Fig. 3. Biological methods for verifying THz demethylation. (a) Bisulfite sequencing to quantify the degree of DNA methylation in partial genes. (b) Investigation of DNA damage by measuring AP sites, indicating the locations of missing nucleobases.

> Terahertz radiation is coming into a variety of applications today, and it is important to come to a full understanding of its effect on biological tissues, both to gauge any risks and to look for potential applications."
>
> *Chiko Otani, Leader of the Research Group, RIKEN*

Source:

RIKEN

Journal reference:

Yamazaki, S., *et al*. (2020) Propagation of THz irradiation energy through aqueous layers: Demolition of actin filaments in living cells. *Scientific Reports*. doi.org/10.1038/s41598-020-65955-5.

They considered the possibility that it was caused by a rise in temperature but found that the small rise, of around 1.4 degrees Celsius, was not sufficient to explain the change, and concluded that it was most likely caused by a shockwave.

To further test the hypothesis, they performed experiments in living cells and found that in the cells as in the solution, the formation of actin filaments was disrupted. However, there was no sign that the radiation caused cells to die.

According to Shota Yamazaki, the first author of the study, published in *Scientific Reports*, "It was quite interesting for us to see that terahertz radiation can have an effect on proteins inside cells without killing the cells themselves. We will be interested in looking for potential applications in cancer and other diseases."

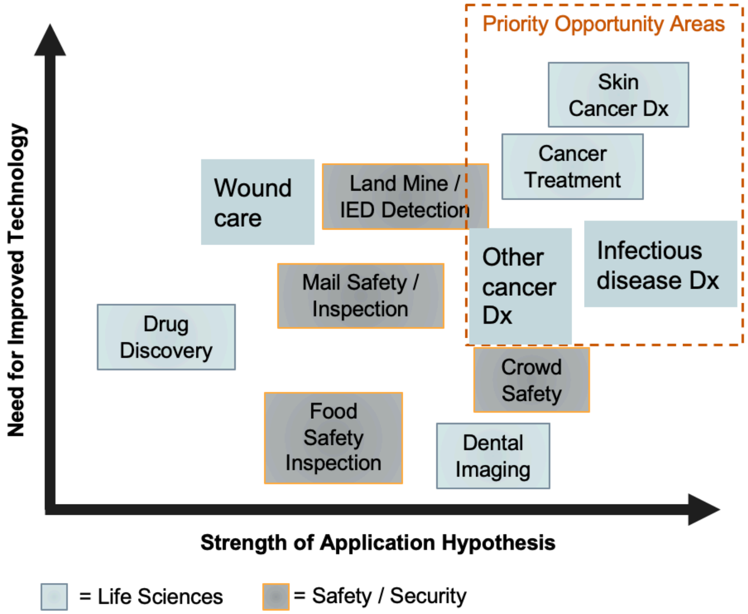
LOTS OF WORK AT LONGER WAVELENGTHS FOR BIOEFFECTS

- See, for example, Journal of Directed Energy, MMW/Bio-effects issue of the Journal, Volume 6, Number 4

This technology is based on non-lethal impact on human skin, which in other words does not kill, but scare off people from locations where their presence is unwanted. The technique employs millimeter waves at the frequency of 95 GHz that considerably heat up the very thin top layer of human skin (only down to 0.4mm deep) up to a temperature of approximately 53-54 °C. Such heat ray impact generated by this stand-off deterrent system lasts only for a couple of seconds (or use series of burst 2-sec long), but it's more than enough to achieve the sought result - disperse the crowd. A targeted persons cannot tolerate such effect even for a few seconds, which in its turn forces them to seek escape from its influence and move away.

Potential Applications Analysis - THz

Triseka is building a compact high powered THz source for life sciences applications



Need for Improved Technology

- Because of the unique properties of THz, there are a number of areas where it could fill unmet needs, either because there is no existing technology in that space or because of significant limitations associated with those technologies.

Strength of Application Hypothesis

- A significant body of research has developed over the last 20 years on the use of THz technology for a number of applications, with many of those falling with life sciences. We highlight a few here.
- All of these rely upon the availability of a robust, reliable, high-power source.

For more information visit: www.triseka.com

THOUGHTS FOR THE FUTURE – FROM A STILL-RELEVANT REPORT

7.0 Executive summary

Opportunities: Major opportunities abound for THz science in medicine. Improving spatial resolution and data acquisition rates are one example. A better understanding of THz pulse propagation through complex media is another. Development of endoscopic ability to provide access to internal epithelial surfaces is a third. After THz methods have been proven and appear likely to be adopted, safety guidelines must be established.

7.5 Suggested areas for focus and development

In order to advance imaging applications of THz radiation in medicine several critical steps should be considered.

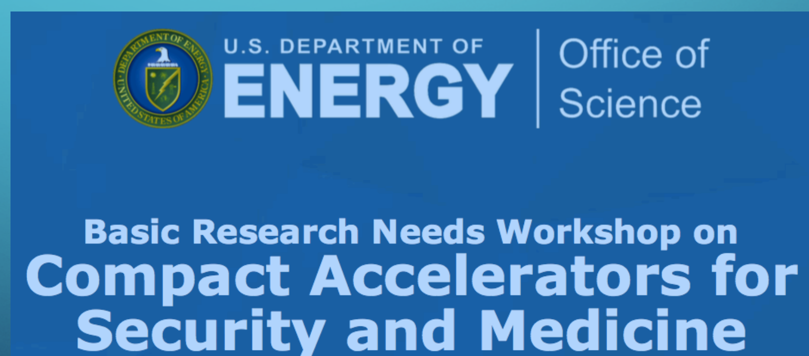
1. Multidisciplinary teams with physicists, chemists, engineers, imaging scientists, biologists and pathologists are required for progress.
2. Methodical investigations to optimize sources, pulse sequences, detector and image generation are the key to scientific progress.
3. Exploration of THz propagation through tissue and improved modeling of the propagation process will help optimize instrumentation and improve imaging techniques. Both reflection and transmission measurement will play a role in understanding the basis for biologic contrast mechanisms.
4. Advances in quantum cascade lasers, fiber lasers, multiple wavelength sources and time-domain techniques suggest rapid progress can be expected. Also, advances in high powered tabled top accelerator based systems may prove useful.
5. Development of expertise in imaging can be accomplished at 3 levels a) at large highly specialized centers with dedicated beams lines from synchrotrons or FELs. b) Regional core laboratories with table-top systems supported by local networks of investigators and c) highly focused specific projects at multiple institutions. Large scale facilities can help identify optimal parameters. Regional centers can provide rich resources of both instrumentation and expertise to a broad range of investigators. A network can help link individual investigators and rapidly address common problems. None of theses facilities are mutually exclusive and all can play a role in developing THz imaging.
6. Collaboration with industry should be encouraged, coordination of effort between centers and industry are likely to produce significant progress. Development of turnkey THz imaging systems which can be placed in a broad range of institutions will enlarge the research community and allow access to technology. The growth of the technology maybe similar to that of MRI and OCT instrumentation.
7. Although THz radiation is non-ionizing, safety considerations for both medical imaging and users should be investigated. No specific guidelines exist for THz radiation. European studies have shown that THz radiation has no effect on cell growth or differentiation. However, tissue damage thresholds, and potential impact on biologic systems are not known. These issues should be addressed for both the imaging applications and for investigators who may be exposed to THz radiation.

RECENT EVENTS HIGHLIGHTING SOURCES AND INTELLIGENT TECHNIQUES INCLUDING IN CONTROL

THESE WILL CERTAINLY LEAD TO OPPORTUNITIES IN THZ AS WELL

Invite-only summit lunched the AI office in DOE with members of industry, government, labs, and academia

Four town halls are being conducted to collect input on the needs and visions of the community. Several of my team members and I attended the meetings at Argonne and LBL and tried provided view points of the controls and scientific facilities communities.



Several of the accelerator facility community were part of the controls, computing mad design cross-cut panel.

e.g. Colleagues in Derek Abbott's group in Adelaide used Support Vector Machines for THz imaging analysis as early as 2006!

LET'S EXPLORE THZ MORE

Thanks to colleagues for many collaborations in THz - Stephen Milton, John Lewellen, Mark Neice, Gian Piero Gallerano, Andrea Doria, Emilio Giovenale, Giovanni Messina, and Ivan Panov Spassovsky, John Noonan, Matt Virgo, John Schneider, Laura Skubal, N. Gopalsami, Yuelin Li, Peter M.J. van der Slot, and Triseka - Katy van Pelt, Gywnn Williams, George Neil, Mary Anne Powles

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