Ultrasensitive Multi-Photon Nonlinear Laser Methods for Environmental and Biomedical Applications

William Tong, Distinguished Professor
Head, Department of Chemistry and Biochemistry
San Diego State University, San Diego, California 92182, USA
william.tong@sdsu.edu

We have developed novel nonlinear multi-photon laser methods for chemical analysis with zeptomole-level (10^{-21} mole) or sub-parts-per-quadrillion-level detection sensitivity for a wide range of areas including biomedical, environmental and security applications. The TongLab has been funded by various funding agencies including the National Science Foundation, National Institutes of Health (R01), National Institute of General Medical Sciences, U.S. Department of Defense, U.S. Department of Homeland Security and various corporate funding sources for studies in analytical chemistry, bioanalytical chemistry, environmental chemistry, physical chemistry and biophysics.

Laser wave mixing offers comparable or better detection sensitivity levels for biomolecules as compared to widely used fluorescence-based methods and yet our wave-mixing methods can detect both fluorescing and non-fluorescing molecules with excellent sensitivity levels. Hence, biomolecules could be detected in their native form without using tags or labels (more convenient), with fluorophore tags (using existing labels and procedures) or with chromophore tags (more widely available). The laser probe is very small (picoliter) and it can be positioned precisely inside the analyte (e.g., a single bio cell) for 2D and 3D spatial mapping. The input laser beams create dynamic laser gratings at the atomic or molecular scale and the resulting nonlinear optical effect produces a strong signal beam that propagates out of the analyte. Unlike currently available techniques such as fluorescence methods, our laser methods produce a strong coherent laser-like signal beam, and hence, it is easy to detect with excellent signal-to-noise ratios. Picoliter-level probe volumes offer effective interfacing to sensors, microchannels, microarrays, lab-on-a-chip, chip-based electrophoresis systems and microfluidic devices that are suitable for studying mechanisms and dynamics of important chemical and biological processes.

Our patented laser wave-mixing methods can distinguish not only large biomolecules but also small isotopes. Our laser-based detectors are more portable and less expensive than isotope-capable high-resolution mass spectrometers. Wave-mixing laser methods yield hyperfine profiles (atomic fingerprints), and hence, unambiguous isotope information from both stable and radioisotopes. Hence, one could use stable isotopes as biotracers instead of radioactive biotracer isotopes. We have also studied fast laser-powered pyrolysis with laser-induced diagnostic real-time monitoring of reaction rates, intermediate species and mechanisms of semiconductor materials for better understanding of fundamental physical and chemical processes. We use a wide range of lasers with wavelengths from UV (solid-state lasers) and visible (tunable external cavity diode lasers) to mid-IR (tunable quantum cascade lasers). Potential applications of our ultrasensitive nonlinear laser methods include earlier detection of diseases (Parkinson’s, Alzheimer’s, Multiple Sclerosis, etc.), more sensitive detection of biomarkers, cancer cells and viruses (HPV, HIV), better design of cleaner drugs, more sensitive detection of pollutants and chemicals both inside the human body and in the environment, remote standoff detection of chem/bio agents, and even authentication of paintings and art objects.

About the Speaker:

Bill Tong, Distinguished Professor, joined SDSU in 1985 as an associate professor after his postdoctoral research at the Oak Ridge National Laboratory, U.S. Department of Energy. In 1989, five years after receiving his Ph.D., he was promoted to full professor. He has supervised 22 Ph.D. (University of California San Diego and San Diego State) and many more Masters and postdoctoral students and visiting scientists/professors. He has been awarded major grants by the National Science Foundation, NIH (R01), National Institute of General Medical Sciences, U.S. Department of Defense, U.S. Department of Homeland Security, U.S. Army Research Office, Lockheed Martin, Beckman, Johnson and Johnson and other funding agencies. He holds various patents on nonlinear laser methods. He regularly serves on NIH and NSF review panels and study sections and reviews for research journals.

He was named the 2003 Distinguished Scientist (San Diego Region) by the American Chemical Society (2 of the 20 winners of this award won the Nobel Prize in Chemistry later). He was named Distinguished Professor of Chemistry and Biochemistry in 2005. He received the Albert Johnson University Research Award, SDSU’s top research award, in 2005, the 2017 SDSU Faculty Diversity Award, and the 2005 Distinguished Achievement Award from the Sigma Xi Research Society. He also received the 2008 SDSU President Leadership Award. He was awarded Outstanding SDSU Faculty Awards in 1990, 1991 and 2000, and the SDSU Technology Innovation Award in 2002. His research projects have been reported and highlighted by *Analytical Chemistry, Applied Spectroscopy* (cover story), San Diego Union-Tribune (front page) and San Diego TV stations (ABC, CBS, NBC, Fox, KUSI, KPBS, UCSD-TV and University of California-TV).