

NSF Center for Biophotonics - Photonics for Life

Instrumentation and Ideas



Discoveries and Innovation



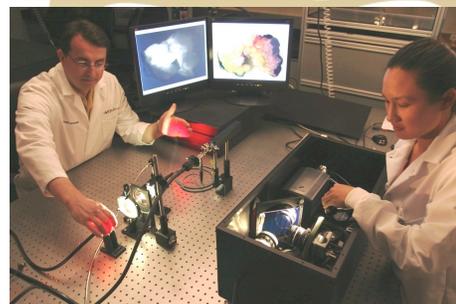
Center for
BIOPHOTONICS
Science & Technology



University of California
San Francisco



Training Future Leaders in Biophotonics



Post STC funding, CBST will live on Through Many Programs

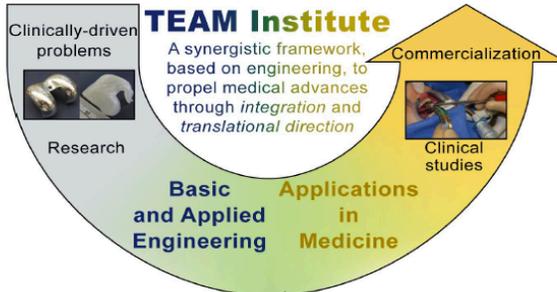
UC DAVIS
UNIVERSITY OF CALIFORNIA

The Institute of Translating Engineering Advances to Medicine (the TEAM Institute)

Lawrence Livermore National Laboratory

Sandia National Laboratories

Livermore Institute for Translational Biomed – Science, Technology, Engineering for Pharma and Medical Devices



LIVERMORE VALLEY open campus

Center for BIOPHOTONICS
Science & Technology



Center for Biology with X-ray Lasers

Center for Biophotonics Sensors and Systems (CBSS)
NSF I/UCRC



Tahoe Institute for Rural Healthcare Research

TAHOE FOREST HEALTH SYSTEM | **UC DAVIS HEALTH SYSTEM**

UC Biophotonics Alliance

your portal to biophotonics

Biophotonics World

BP4L
Worldwide Consortium

BioMedLight

Developing

Developing

Developing

Developing

Current CBST Projects Relevant to Cancer

- 1) **Point-of-care breast cancer diagnosis using multiplexed protein marker detection** (Co-developed with LLNL; Matt Coleman)
- 2) **Protein structure from coherent X-ray lasers for cancer drug discovery** (Co-developed with LLNL and others)
- 3) **IR cystoscope for cancer biopsy guidance** (Co-developed with LLNL; Stavro Demos)
- 4) **UV endoscopy for detecting esophageal cancer** (Co-developed with LLNL; Stavros Demos)
- 5) **Fluorescence lifetime imaging and spectroscopy for margin detection in neuro and gastrointestinal surgery**
(Developed by Prof. Laura Marcu, CBST, UCD/BME)
- 6) **Single cell Raman detection of leukemia, detection of cancer stem cells, and cell response to chemotherapy agents for research and microdosing** (co-developed with LLNL and the Keaton Raphael Foundation; James Chan, Doug Taylor)
- 7) **Imaging autophagy to understand chemotherapy** (Developed by CBST with Hsing-Jien Kung and Frank Chuang)
- 8) **Raman gastrointestinal endoscopy** (Developed with Christopher Contag, Stanford University)
- 9) **Rapid pathology sample imaging for intraoperative cancer assessment** (New project with S. Wachsmann-Hogiu and John Chapman (UCD/Pathology))
- 10) **Breast cancer cell characterization** (Matt Coleman, LLNL)
- 11) **Cell phone microscope based blood analysis for monitoring chemotherapy patients** (New project with S. Wachsmann-Hogiu, Denis Dwyer (UCD/Pathology), and Tahoe Forest Hospital)
- 12) **Liver cancer studies using super resolution microscopy imaging of liver endothelial cells to cancer** (New project with Thomas Huser and Mark Zern (UCD))
- 13) **Circulating cancer cell detection using light scattering** (New project co-developed with Spynsite, Inc)
- 14) **Prostate cancer detection using bioluminescence** (co-developed with C. Contag at Stanford Univ.)
- 15) **Nerve preservation in axillary lymph node dissection using Raman spectroscopy** (Planned project)

Advanced Optical Microscopy for Cellular Studies at the UCD/ NSF Center for Biophotonics (CBST)

Dennis L. Matthews (Director)
Stephen M. Lane, PhD (Associate-Director)
Sebastian Wachsmann-Hogiu, PhD (Facilities Director)



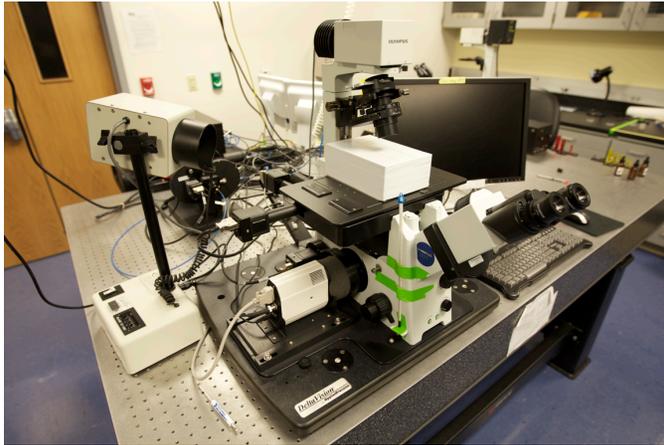
<http://cbst.ucdavis.edu>



CBST, 2700 Stockton Blvd., Suite 1400

- **Physical scientists developing new optical imaging instrumentation and then working with life scientists and physicians to solve problems in biology and medicine**
- **Science: ~20 imaging projects**
 - infectious disease
 - cancer biology
 - regenerative medicine
 - cardiovascular medicine
 - pathology
 - neuroimaging
 - optical probe development
- **Contract research: Applied Precision, L'Oreal, Becton-Dickinson, Genentech (?)**
- **Future**
 - convert to recharge facility
 - increased contract research
 - increased clinical applications (esp. pathology. e.g., new hire Vice Chair Richard Levenson)

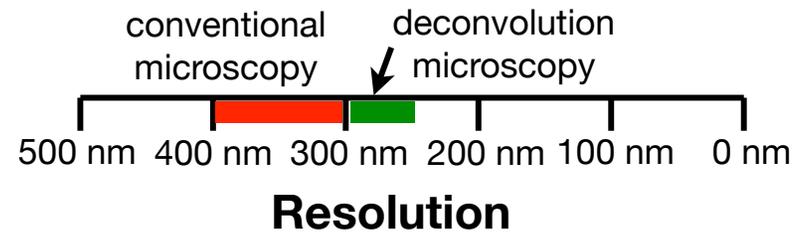
Deconvolution fluorescence microscopy



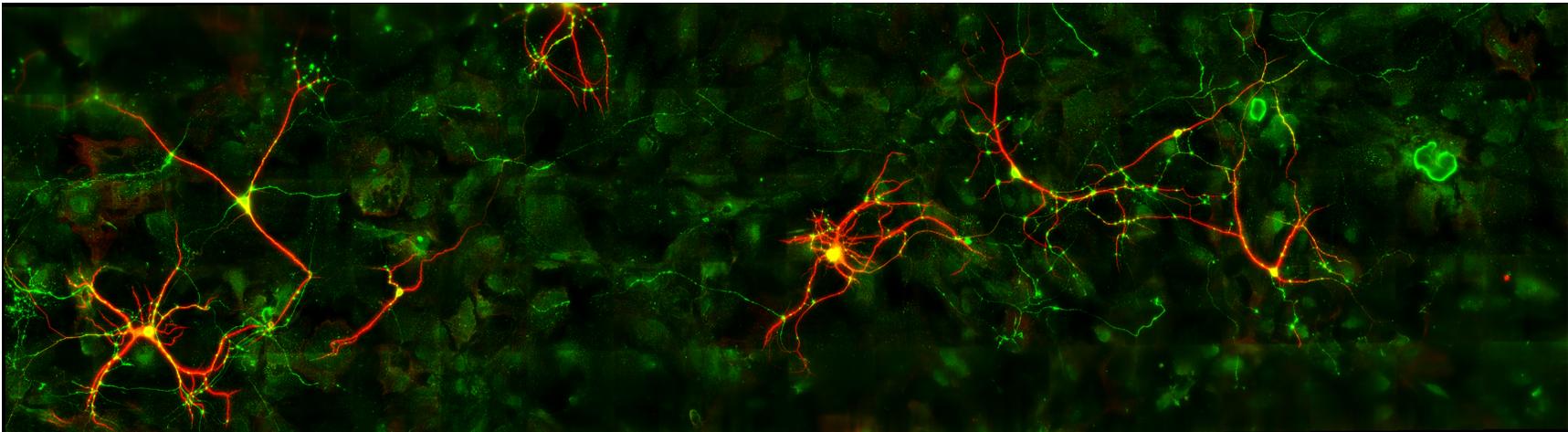
AppliedPrecision®

personal DeltaVision microscope

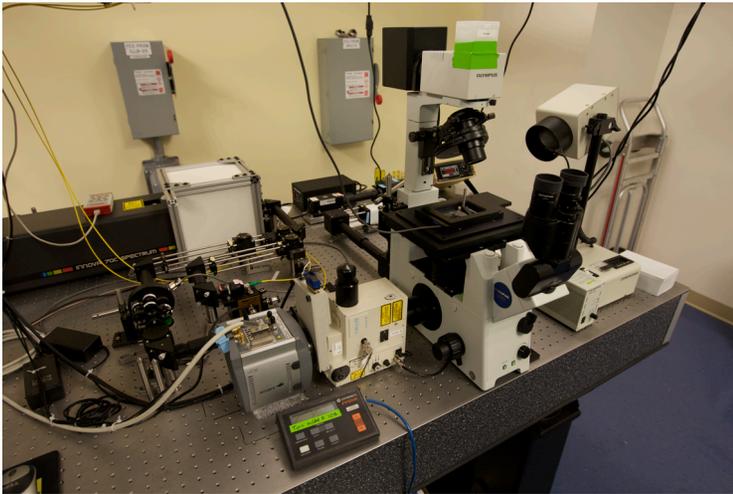
- ✓ 3D
- ✓ large field-of-view
- ✓ 250 nm resolution
- ✓ live cell
- ✓ 4 color channels
- ✓ user friendly



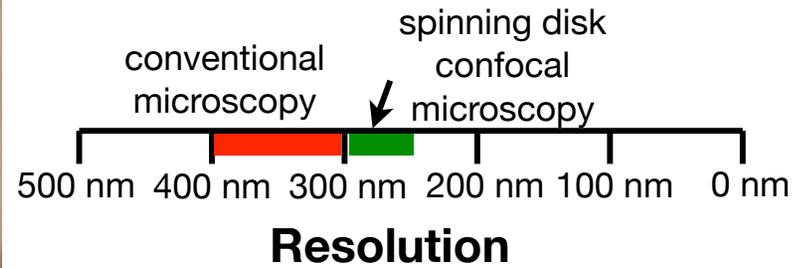
rat neurons (red) and astrocytes (green) 1839 μm X 527.5 μm



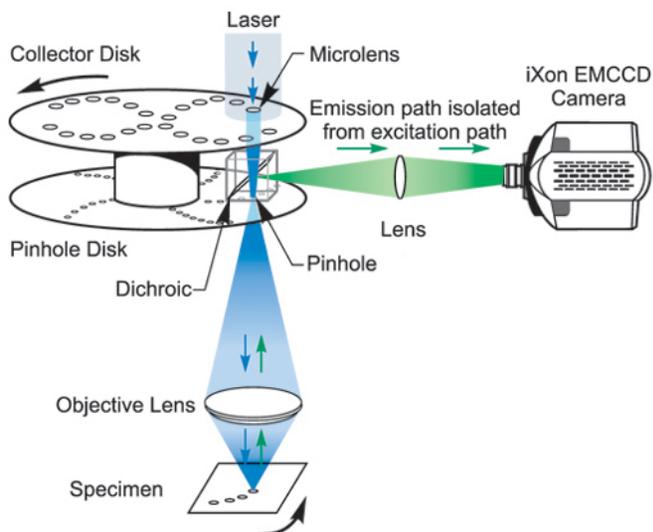
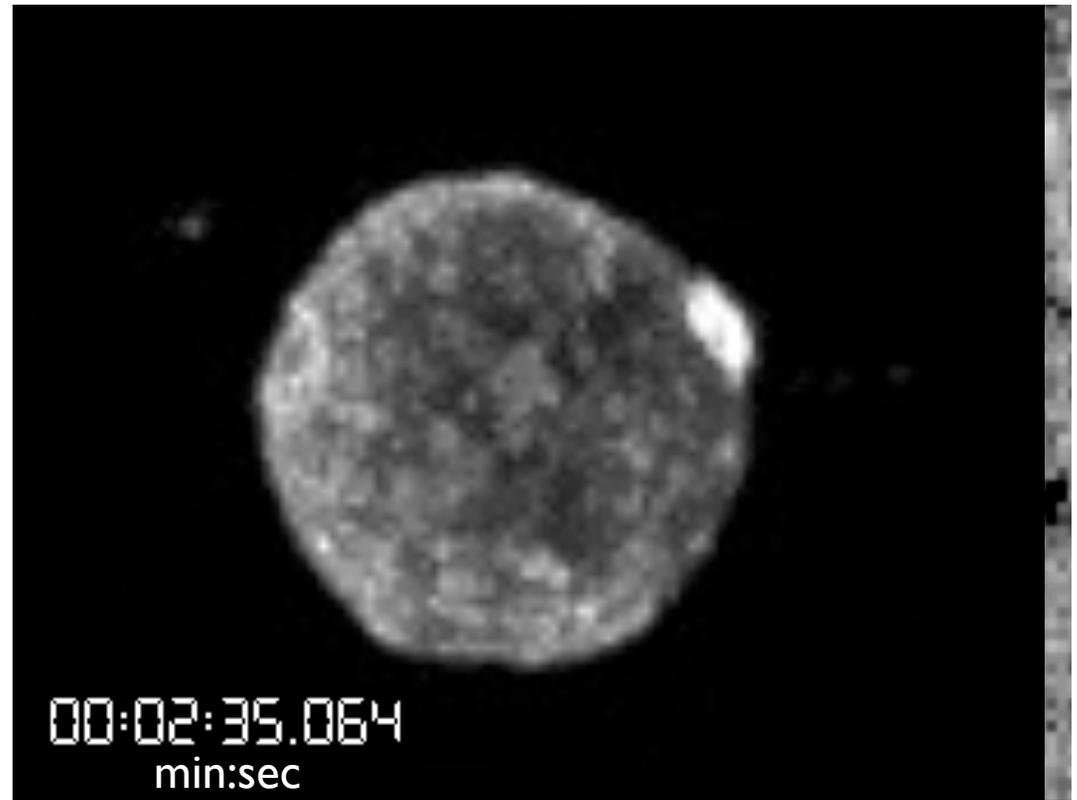
Spinning disk confocal fluorescence microscopy



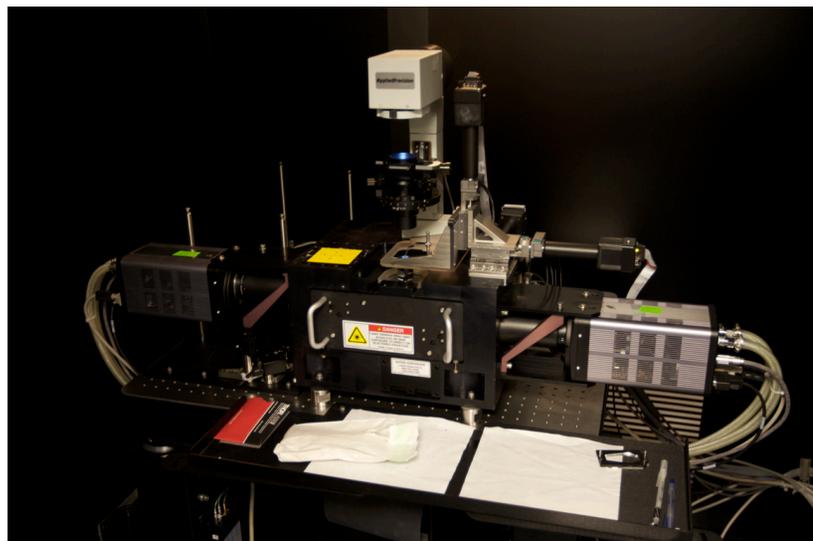
Yokogawa / Andor / Olympus system



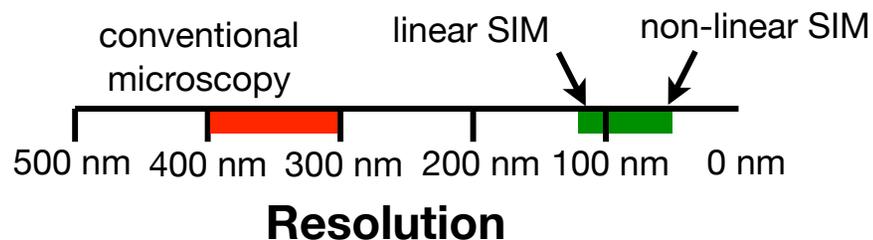
- ✓ 3D
- ✓ dynamic
- ✓ live cell
- ✓ optical trapping
- ✓ 3 color channels



Super-resolution structured-illumination microscopy (SIM)



- ✓ super-res
- ✓ 3D
- ✓ dynamic
- ✓ live cell
- ✓ 3 color channels (2 simultaneous)
- ✓ currently only commercial system in world



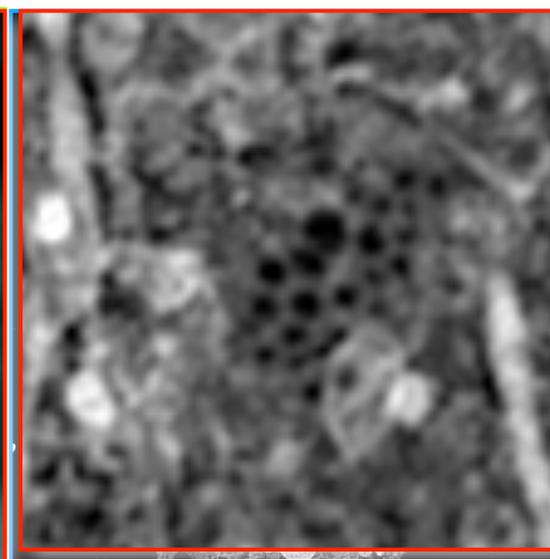
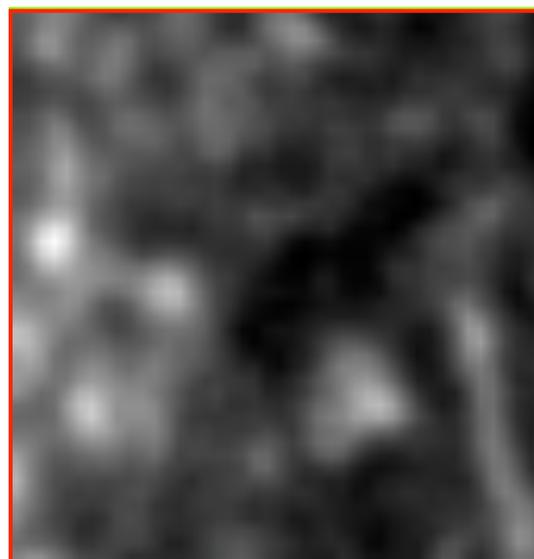
Applied Precision®

UC DAVIS
UNIVERSITY OF CALIFORNIA

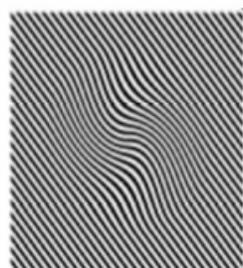
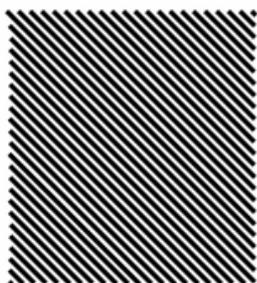
UCSF

Deconvolution

Structured Illumination

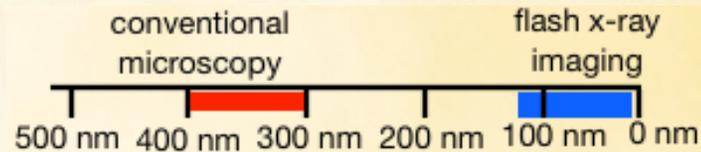


illumination



sample

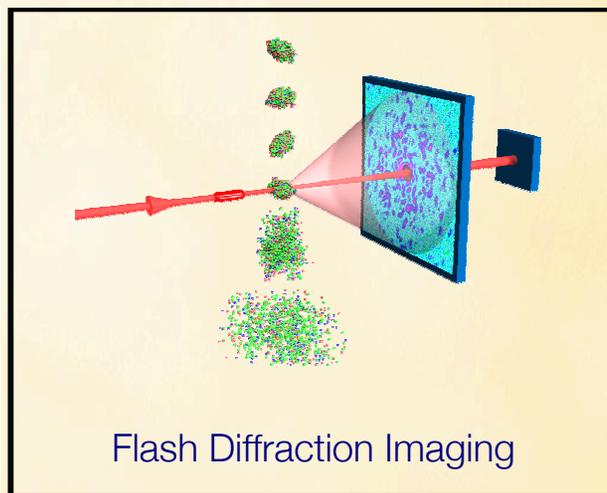
Flash X-ray imaging at LCLS: Towards single molecule structure measurements using X-FEL



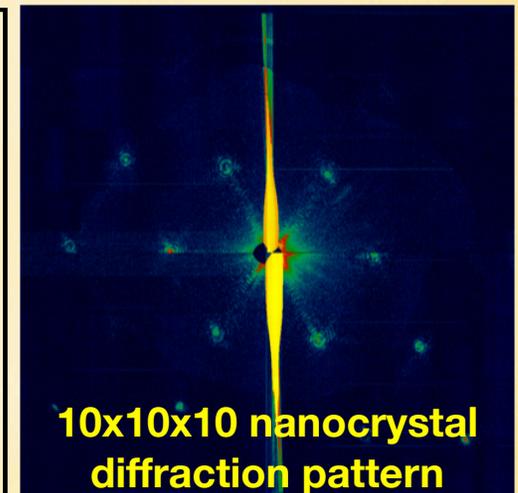
- ✓ atomic - res
- ✓ 3D, membrane proteins



Linac Coherent Light Source (LCLS) at SLAC



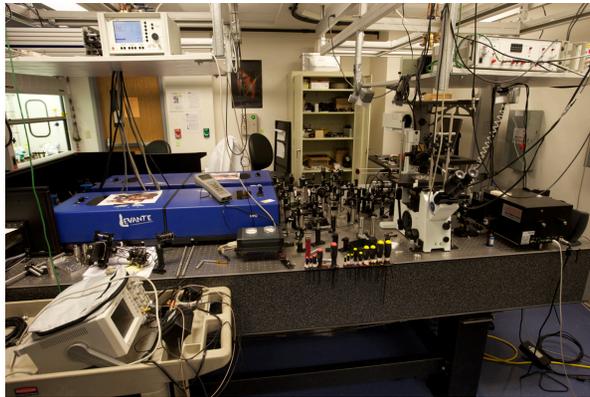
Flash Diffraction Imaging



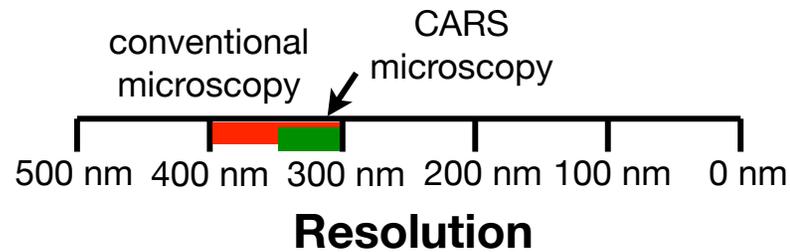
10x10x10 nanocrystal diffraction pattern

- **Goal:** Rapidly produce atomic resolution structures of biological macromolecules without the need for high-quality crystals in order to accelerate biological understanding and drug discovery.
- **International consortium:** DoE, SLAC, LLNL, LBNL, CBST, Max Planck Inst, U of Hamburg, U of Melbourne, U of Uppsala
- **Current status:**
 - Achieved 6 nm diffraction-limited resolution with photosystem-I nanocrystals using 100 fs pulses of 2.8 keV X-rays (Chapman et al., Nature 470, 73 (2011)).
 - In Jan, 2011, used 9.5 keV X-rays to get molecular scale resolution (0.3 nm) (M. Hunter and J. Spence)

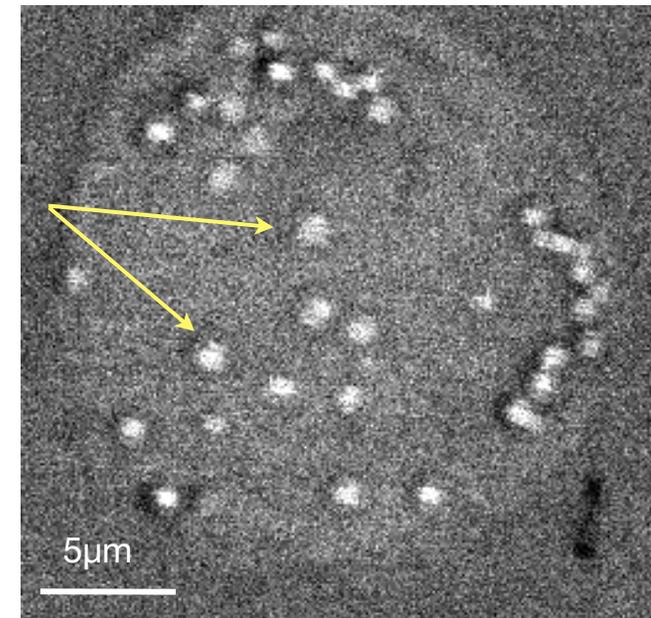
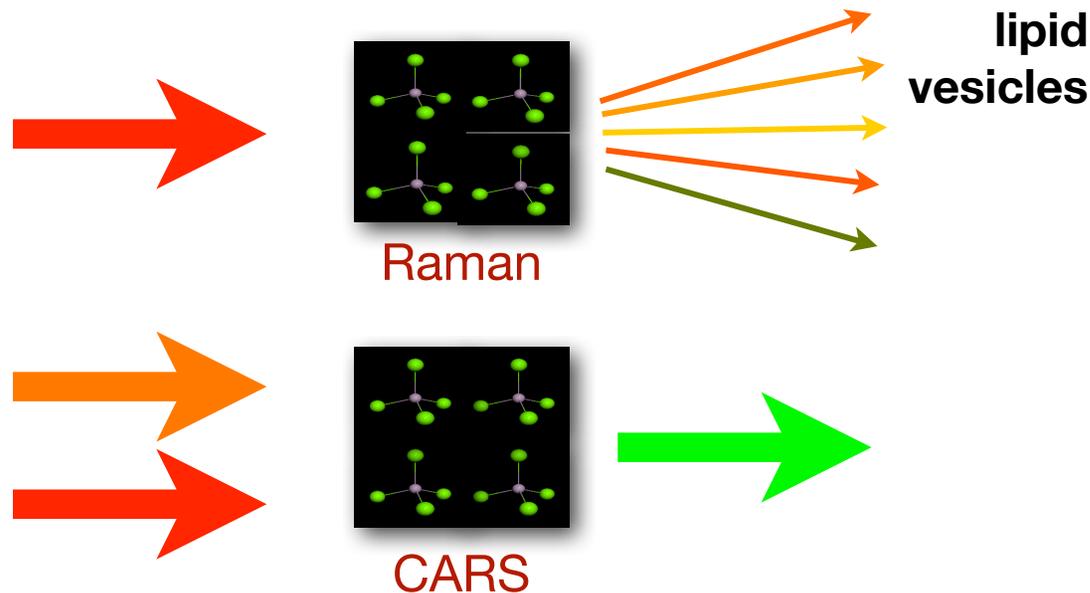
Coherent anti-Stokes Raman scattering (CARS) label-free microscopy



CBST custom CARS microscope

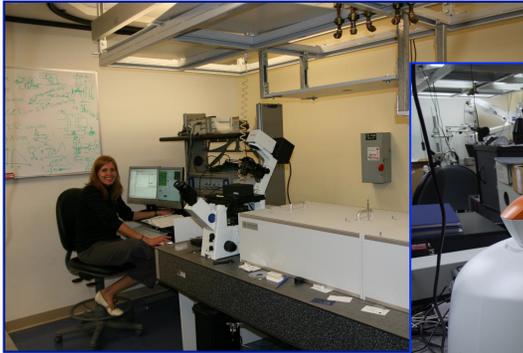


- ✓ 3D
- ✓ label free chemical mapping
- ✓ improved CARS variants
- ✓ biofuel applications



CARS imaging of circulating monocytes scavenging lipid particles in the bloodstream.

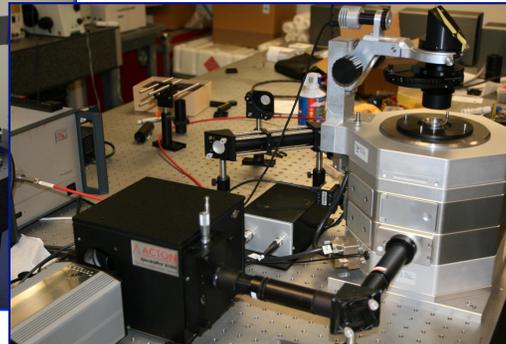
Other imaging capabilities



**Picoquant
fluorescent lifetime
microscope**

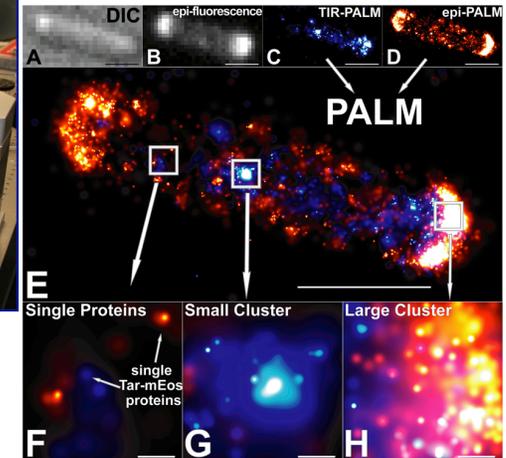


**Renishaw Raman
microscope**



Till robotic microscope

- \$6.5M total investment in imaging instrumentation
- CBST has 15 high-end microscopes (3 in educational area)



**Localization microscopy
(10-20 nm resolution)**

Potential Funding Sources for LLNL/ UCD Cancer CTR collaborations

- ***Fitzpatrick Estate Funds*** -- Amy will discuss shortly
- Pre-competitive industry-sponsored research: ***The Center for Biophotonics Sensors and Systems*** (an NSF Industry University Cooperative Research Center involving Boston U and CBST)
 - Need a company to sign up with a \$50k annual membership
 - Need proposals from researchers at UCD and in collab with LLNL
- Industry Partnered commercialization via the ***NSF Ecosystem for Biophotonics Innovation***
 - Need a corporate sponsor for your commercialization
- Keaton Raphael Memorial Foundation, St. Baldrick Foundation
- LLNL SMS, LDRD funds
- UC/Lab Fees Research Grants
- UC President Postdoctoral Fellowships
- UC Davis Chancellor's Postdoctoral Fellowships (2/yr, one in the SOM, Nov 1 deadline!)
- Other ideas??