STRC on Real-Time Functional Imaging (STROBE)

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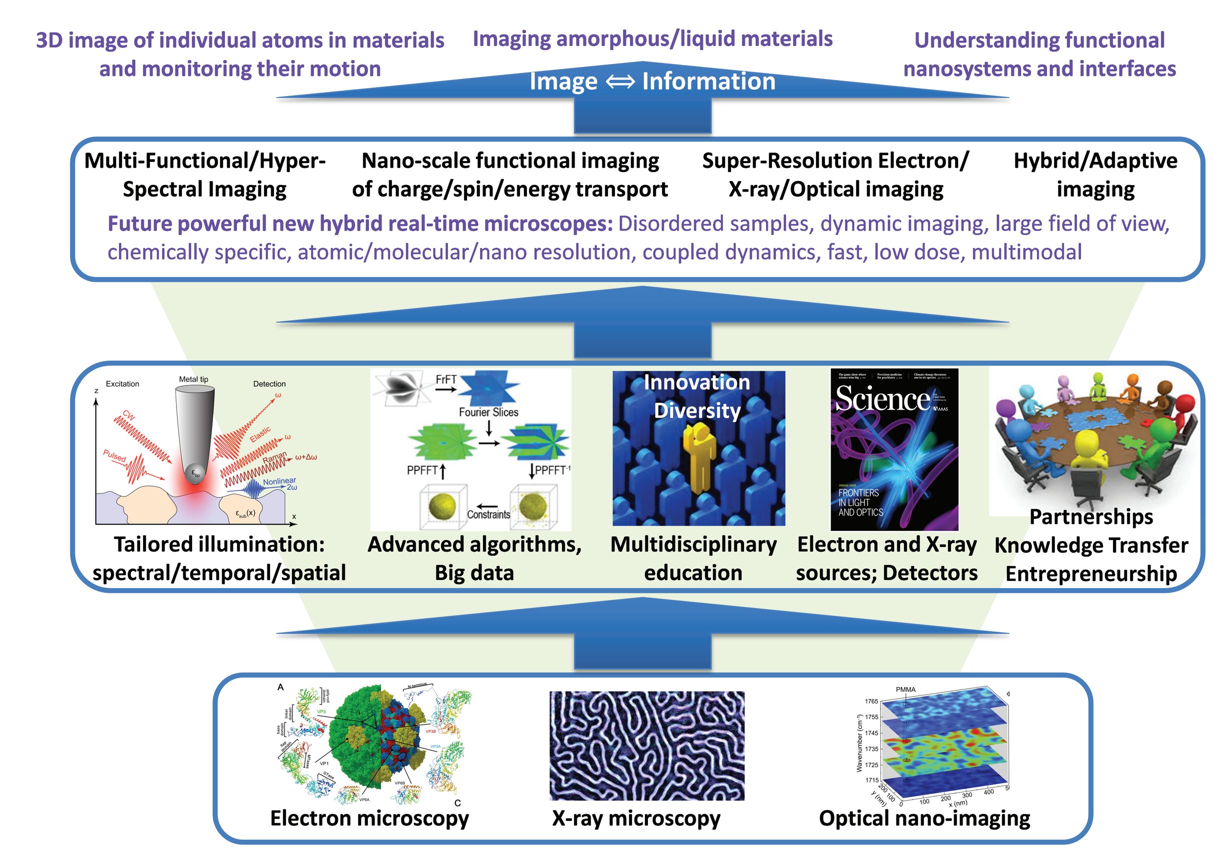
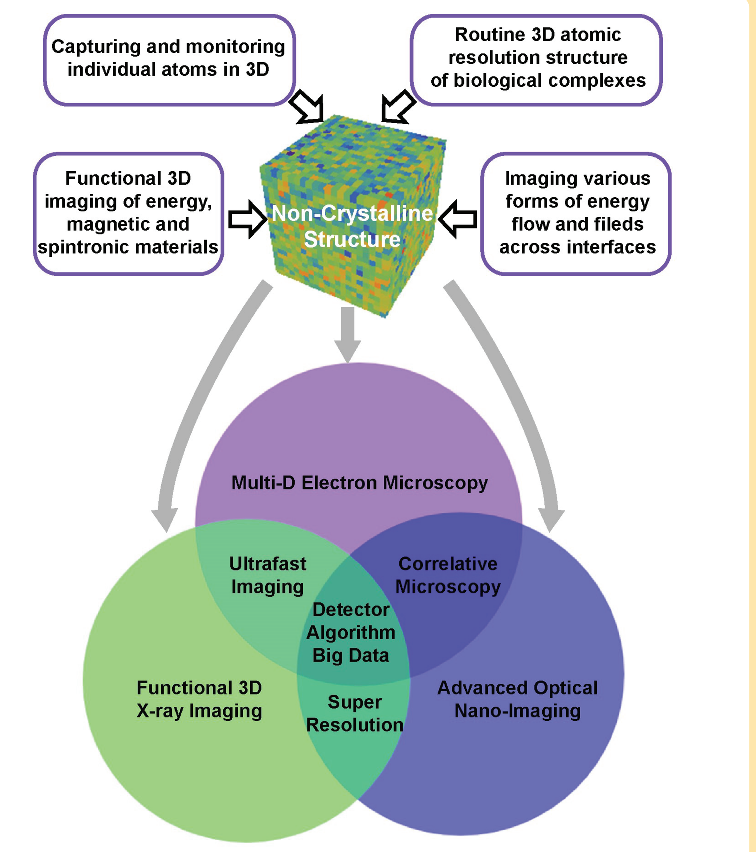
Summary

Understanding the structure and evolution of matter at the nanometer and atomic scales is central for discovery and innovation in science and technology, accelerating advances in materials science, condensed matter physics, chemistry, biology, engineering, geology, and medicine. Our STC on Real-Time Functional Imaging (STROBE) will integrate different imaging modalities with underpinning technologies – advanced algorithms, fast detectors, big data manipulation, new light and electron sources, and hybrid/adaptive imaging – to tackle science grand challenges that cannot currently be addressed.

This integrative approach can fundamentally transform imaging science to enable real-time three-dimensional functional imaging that far exceed current capabilities. An expected outcome is creation and integration of a new set of powerful and broadly applicable real-time imaging modalities that can image non-crystalline systems, implement dynamic imaging with a large field of view, with chemical and magnetic contrast, and atomic/molecular/nanoscale resolution, that are applicable in situ and under environmental conditions, and are minimally invasive. Each imaging technique will be brought to reach its fundamental limits and integrated in hybrid/adaptive modalities that surpass the sum of the parts.

The center legacy will manifest through national and international leadership in cutting-edge imaging science, highly-needed diverse graduates trained in multidisciplinary science, a plethora of hybrid/adaptive imaging modalities and tabletop systems enabling new science to emerge in the upcoming decades, as well as technology transfer to industry and emerging startups in nanotechnology, imaging, and smart materials.

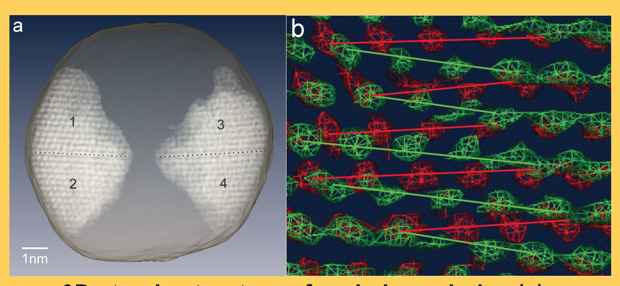




Research

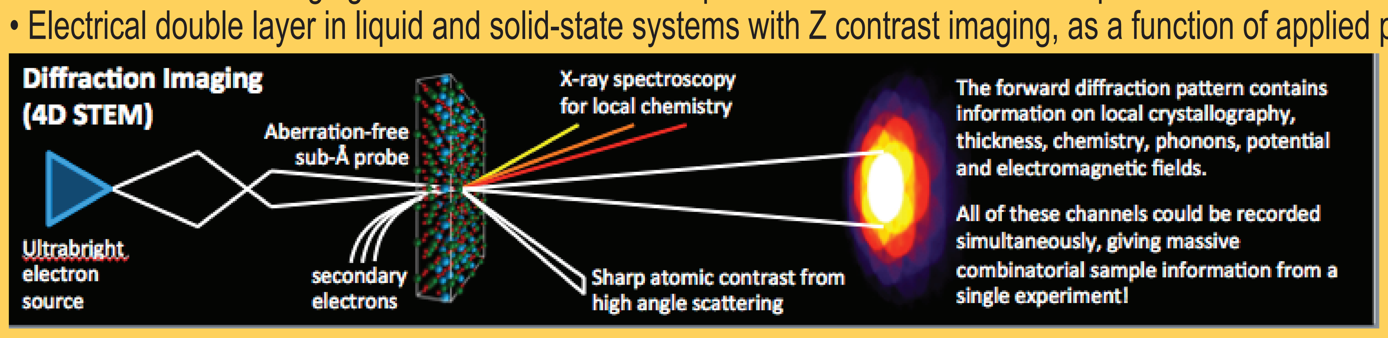
Thrust I *Multi-Dimensional Electron Microscopy (EM) at Atomic Resolution*

1. Capturing the 3D position of individual atoms in non-crystalline materials, and monitoring their motion using atomic electron tomography (AET)
- High-quality tilt series from the electron aberration-corrected microscope (TEAM) at LBL
- Sparsity-based advanced de-noising and/or mathematical regularizations, atom tracing and refinement
- Acquisition of a tilt series of phase maps using the transport of intensity equation and electron holography

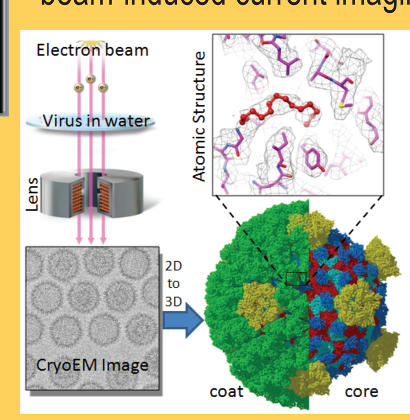


3D atomic structure of grain boundaries (a) and a screw dislocation (b) revealed by AET

2. Multimodal, correlative EM for atomic-resolution imaging of liquid and solid-state systems
- High speed atomic-resolution EM and spectroscopy in simultaneous collection of multiple signals at once
- Atomic resolution imaging of nucleation events with precise measurements of sample and environmental conditions
- Electrical double layer in liquid and solid-state systems with Z contrast imaging, as a function of applied potential, distance from the electrode, bulk salt concentration, pH, ion type and valence
- In-situ mapping via electron beam-induced current imaging

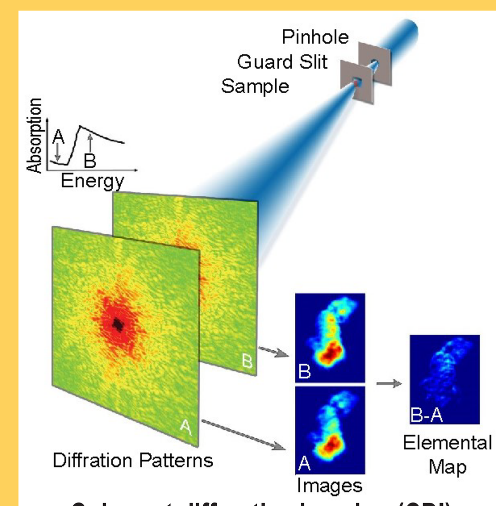


3. Unraveling the 3D structure of biological complexes at the single atom level
- Single particle cryoEM for 3D structure determination of biomolecules at near atomic resolution
- Building backbone models - sometimes even full atomic models of these systems
- Increasing the resolution to the single atom level (<2Å) by combining advanced fast direct electron detectors with state-of-the-art cryoEM, harnessing the big data expertise, and developing advanced image reconstruction algorithms tailored to the specific properties of the resulting images



A 3.3Å cryoEM structure of an aquareovirus primed for 'fusion' to enter host cells

Thrust II *Real-Time Functional 3D X-ray Imaging of Advanced Materials*

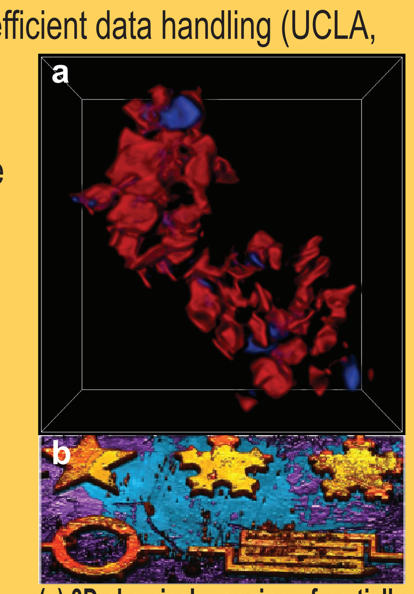


Coherent diffractive imaging (CDI) with elemental specificity

1. Real-time 3D Coherent Diffractive Imaging (CDI) of materials with elemental/chemical specificity
- Co-develop two world leading X-ray ptychographic microscopes with wavelength limited spatial resolution (0.5-5 nm) and chemical/magnetic specificity
- Coherent X-ray light sources at Berkeley (ALS, ns time resolution) and Boulder (tabletop HHG, fs time resolution), and combine these with advanced algorithms (UCLA, Berkeley), efficient data handling (UCLA, Berkeley), fast detectors (LBNL) and ultrastable scanning systems (LBNL)
- Capture nano and mesoscale energy, charge and spin transport in inhomogeneous, nanostructured, and interface-dominated systems, which are currently inaccessible to either experiment or theory.

2. Functional X-ray hyperspectral imaging at multiple atomic sites
- A new form of CDI – hyperspectral imaging – allows retrieving an image at several different wavelengths simultaneously
- Capture and image the instantaneous charge and spin states, spin dynamics, as well as correlations and couplings in opaque magnetic/catalytic/spintronic/quantum systems in 3D in real time, on all relevant time and spatial scales
- Shining a few-fs burst of coherent supercontinuum X-rays onto a sample, and recover an image at each wavelength simultaneously, providing spatial resolutions <5nm and temporal resolutions <10 fs

3. Super-resolution X-ray imaging beyond the wavelength limit
- Super-resolution (SR) techniques from optical imaging to move X-ray imaging below the wavelength limit
- New X-ray microscopes with structured illumination to push the resolution limits and enable adaptive functional imaging
- Use of X-ray sources, compressive sensing and advanced algorithms to develop SR X-ray imaging beyond the wavelength limit

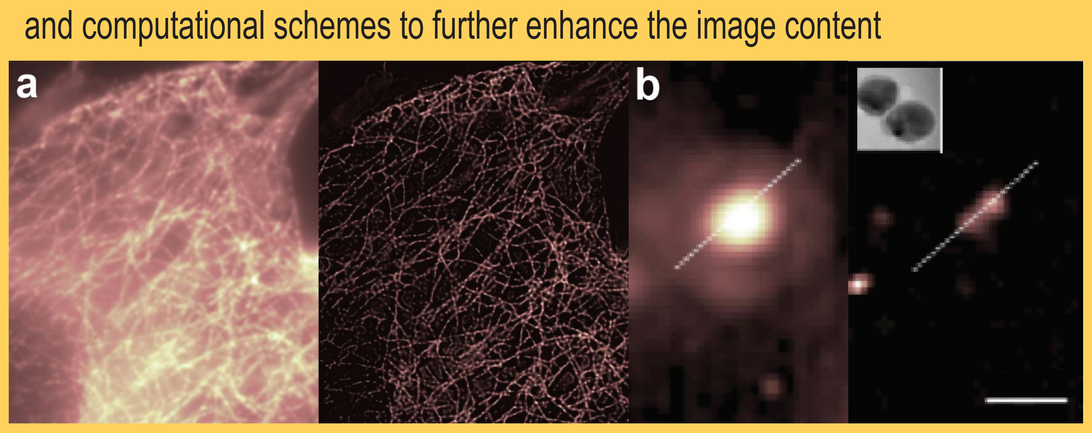


(a) 3D chemical mapping of partially delithiated $LiFePO_4$ nanocrystals at 11nm resolution ($FePO_4$ in blue and $LiFePO_4$ in red). (b) High contrast 3D image of a surface using tabletop HHG, with spatial resolution 1.3λ horizontally (40 nm) and 5Å axially.

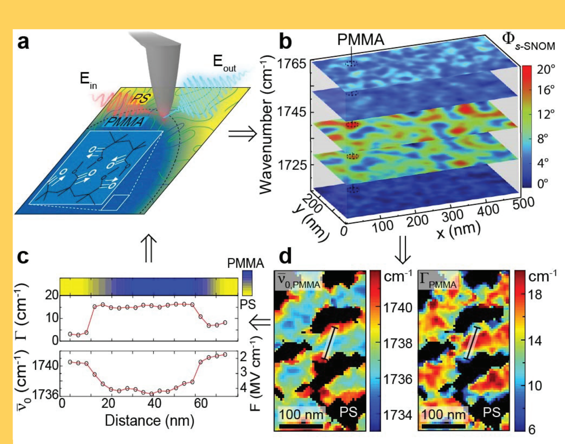
Thrust III *Advanced Optical Nano-Imaging*

1. Super-resolution beyond fluorescence imaging
- Compressive methods (experimental and numerical) to significantly increase the allowable label density in fluorescence super resolution (SR) imaging, combined with SR optical fluctuation imaging (SOFI), which blindly disentangles stochastically fluctuating signals through correlation analysis
- Further develpment would allow imaging without metal particles labels
- High speed, high throughput 3D nano-images using Raman, Stark-effect, and re-orientation of probes, re-orientation of molecules inside probes, local heating, or surface charge fluctuations

2. Nanoscale probing of intermolecular coupling, structure and dynamics
- Complementary scattering scanning near-field microscopy (s-SNOM) also allows label-free contrast agent density
- New molecular-level insight with unprecedented near-single-protein sensitivity achieved via probing amide resonances
- Extending to broadband and coherent ultrafast, chemical IR and Raman s-SNOM, and combine with new optical antenna tip-geometries, detection, and computational schemes to further enhance the image content

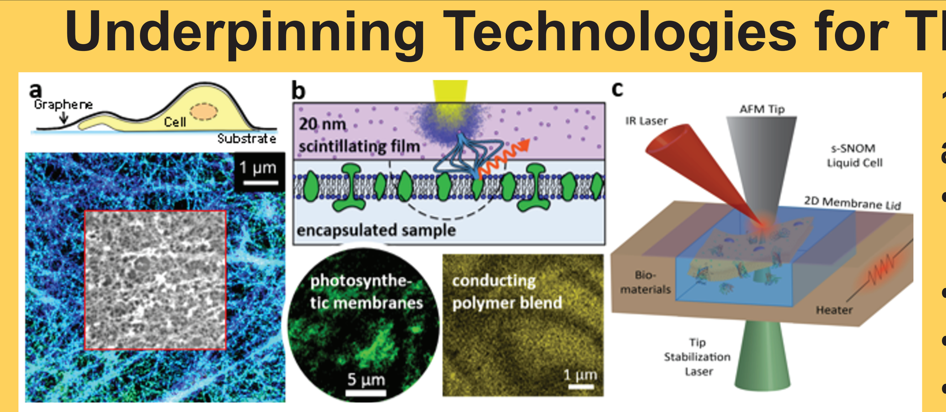


a, Conventional and SOFI images of quantum-dot labeled microtubules in a cell. b, Non-fluorescence SOFI, resolving two nano-plasmonic particles with peak-to-peak distance of 300nm.



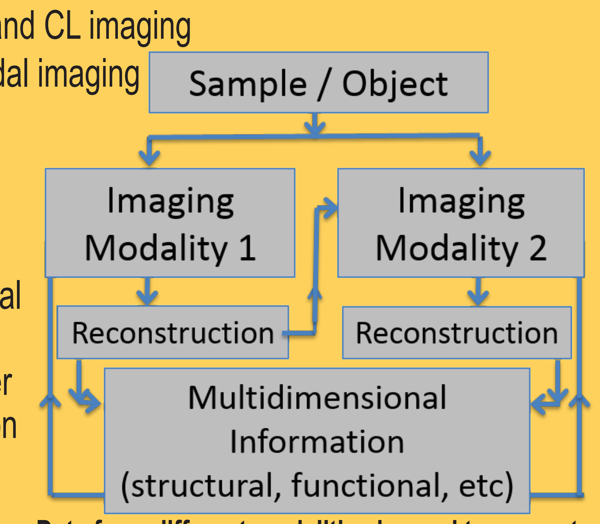
Intermolecular coupling from spatio-spectral computational nano-IR imaging of a disordered phase-separated polymer hetero-structure based on solvatochromic vibrational Stark shifts

Underpinning Technologies for Thrusts I, II, III



Integrative imaging approaches. a, Graphene protection of wet cells for correlated STORM and EM of actin. b, A scanning electron beam converted to a nm-scale optical spot. c, In situ s-SNOM, SOFI, and CL imaging with an ultrathin IR-transparent cover.

1. Integrative high-resolution dynamic imaging of heterogeneous, soft and bio-materials
- Graphene protection for correlative stochastic optical reconstruction micros copy (STORM) and EM.
- Noninvasive cathodoluminescent (CL)-activated imaging
- Integrated IR-s-SNOM, SOFI, and CL imaging
- Smart-scope adaptive multimodal imaging



Data from different modalities is used to generate quantitative sample information, which is fed back to iteratively re-configure each modality.

2 Advanced algorithms for electron, X-ray and adaptive optical nanoimaging
- Integrating algorithm development and image reconstruction activities across electron, X-ray and optical imaging.
- Iterative algorithms using constraints such as atomicity, positivity, sparsity, dictionary learning and other regularizations to achieve i) multi-D EM, ii) real-time functional 3D X-ray imaging and iii) SR beyond conventional fluorescence imaging, via GPU processing, parallel computing and more efficient algorithms.

3. Fast detectors and data acquisition methods for real-time functional imaging
- Develop 4D functional microscopes that both capture and display reconstructed images in real-time
- Adding new capabilities such as elemental/chemical identification of functioning systems
- Design computational methods for each imaging modality to enable efficient and fast data acquisition and processing

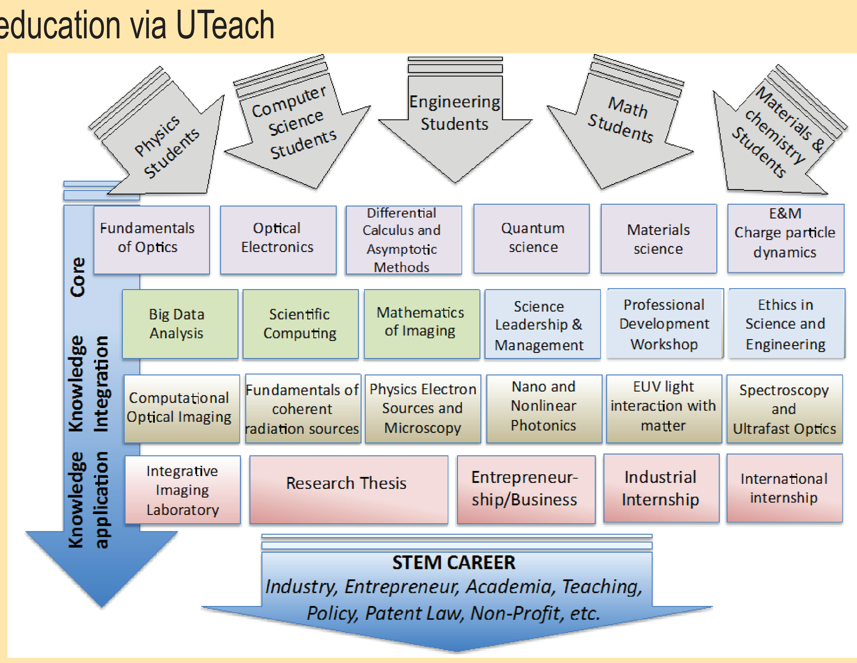
4. Big data: handling, analysis, and visualization
- Computational imaging methods to both reduce the amount of data collected and to improve algorithm efficiency for data analysis
- Managing big data and implementing large-scale algorithms: parallelizing algorithms, GPU processing, supercomputing

Education and Human Resources

1. Student Training for the Innovation STEM Careers
- New multi-disciplinary Ph.D. programs in imaging science
- Team-oriented multi-campus/national laboratory/industry/international projects
- Professional development programs for students

2. High School Teacher Education & Development
- Enhanced high school teacher education via UTeach
- Professional development and research programs for teachers
- Professional development programs for students

3 Engaging K-12, Public
- New STEM track at high school level
- Partner with local schools (CA, CO, Miami Dade)
- Science Discovery, Lawrence Hall of Science, Frost Science Museum



Broadening Participation

1. Pathways to STEM for Diverse Group of Students
- Partner with local diverse K-12 populations of CO, CA, FL
- Research projects with societal impact
- Evidence-based teaching: Modeling Instruction, Learning Assistants
- Research for diverse STEM undergrads at Fort Lewis, Florida Internat.
  - Skill sets and mentoring via STROBE team with SMART, REU, and HHMI-style/ course based undergraduate research
  - Long-term freshman-to-senior relationships with URM students
  - Specialized APS bridge programs, mentoring & role models

2. Women and Minorities in STEM Careers
- STROBE postdoctoral fellowship program for faculty track
- Professional development programs for students/postdocs for all careers
- Entrepreneurship programs and networks for women and minorities
- STROBE web page with student, postdoc resumes

Participants	Total	Females		Minorities	
Faculty	30	13	(43%)	7	(20%)
Postdocs	49	14	(29%)	21	(45%)
Graduates	91	26	(29%)	28	(31%)
Undergraduates	57	21	(37%)	22	(39%)
Scientists	2	0	(0%)	1	(50%)
Industry	5	1	(20%)	1	(20%)
Total	**234**	**75**	**(32%)**	**80**	**(34%)**

Strong diversity of STROBE team

Knowledge Transfer

1. Past Knowledge Transfer Successes of STROBE Team

KMLabs Inc. is a JILA spin-off company that was first to provide a commercial tabletop coherent extreme ultraviolet (EUV) source at wavelengths from 10 to 40nm

STROBE tech transfer success: Commercial tabletop coherent EUV source

2. New Light Source, Imaging and Detector Technologies
- Soft X-ray beams on a tabletop, spanning the entire electromagnetic spectrum from the UV to the keV region, also planning for tabletop X-ray to infrared sources
- Fast CCD designs optimized for large-scale sources, a promising avenue for commercialization

3. Industry Partnerships

Industry partners include Intel, IBM, Anasys, SRC, GlobalFoundries, ASML, IMEC KMlabs, Anasys, and can be expanded further to meet student interest and demand

4. STROBE instruments as core facilities

Each of our academic institutions has existing successful and highly-utilized core facilities that attract users from all over the world, greatly facilitating knowledge transfer