Imaging Science Interdisciplinary Research Theme

2018 Year End Report

College of Engineering & Applied Science
UNIVERSITY OF COLORADO BOULDER

2018 Imaging Science IRT
Annual Report

IRT Scope and Mission

The Imaging Science IRT will transform society by saving lives through medical imaging, improving industrial safety and productivity through nondestructive testing, increasing integrated optoelectronics performance through fast metrology, and enabling the extraction of resources in environmentally friendly ways through seismic imaging.

In wave-based sensing and imaging, one collects information about an object by detecting the perturbation induced on the wave field by the object. The incident wave field can be, for example, electromagnetic or sound waves. In many practical cases of technological interest, the object to be imaged is buried within or behind media that distorts the wave field, scrambles object information, and hides structural features from view. This places severe limitations on sensing and imaging applications across disciplines and length scales. Optical imaging in biological tissue is restricted to the skin surface due to strong scattering induced by refractive index variations. Medical ultrasound images are distorted by fat layers, bone, and muscular tissues. Detection of cracks and defects in composite materials using ultrasonic nondestructive evaluation is hindered by strong scattering at the interfaces, and seismic imaging is complicated by the lack of knowledge of the material properties of the compound structures within the earth. Imaging in practical and often complex materials is therefore *one of the most important technological challenges of our time.*

In recent years, there have been significant developments in the understanding of wave interaction with complex media as well as in techniques to manipulate and control wave propagation. Wave fronts have been tailored to compensate for scattering using adaptive optics and time reversal mirrors. Metamaterials and photonic/phononic crystals have been designed and fabricated to produce non-intuitive physical effects such as negative refraction and super-resolution focusing. Imaging probes have been developed that produce strong and targeted responses to incident fields to enhance imaging, and inversion algorithms and compressed sensing techniques have been devised to facilitate image extraction from measured data. The Imaging Science IRT is utilizing and extending these advances to develop a new suite of imaging technologies suitable for imaging at unprecedented depth, resolution, and speed. The societal impacts of such technologies are immense. Optical imaging in deep tissue, for example, can allow for conventional biopsy and histology to be replaced by optical biopsy and permit functional information, such as blood oxygenation, to be determined with exceptional resolution. Advances in ultrasound imaging and targeted imaging probes can result in new techniques to detect, diagnose, and treat disease in areas of the body that are typically difficult to image using ultrasound, such as the brain. In nondestructive testing, the techniques will result in an improved detection of defects in composite materials with applications in the aerospace, automotive, and micro-electronics industries as well as national defense. Finally, extension of the techniques to a longer length scale will allow for advances in the detection and characterization of geological sites and find application in the energy industry.

Most Significant IRT Accomplishments in 2018

- The Imaging Science IRT faculty submitted eight provisional patents, founded or received funding for three startup companies, and have been successful at establishing new research ties with numerous companies including Teledyne Scientific, Lockheed-Martin, Medtronic, and Oculus Research.
- The Imaging Science IRT Seminar Series was established to promote new research collaborations and enhance the visibility of Imaging Science at CU.

- The Imaging Science IRT seed grant program supported ten collaborative projects. Results from these projects have led directly to one funded NIH proposal and seven pending or planned proposal submissions.
- The Imaging Science IRT faculty led four (> $1.0M) funded proposals ($8.8M total), two pending proposals ($5.0M total), and two proposals that were not funded and will be resubmitted ($5.5M total).
- The Imaging Science IRT faculty have enhanced the reputation of CU in the community through high-impact publications, keynote addresses at international conferences, conference organization, and numerous invited lectures.

Seed Grant Summary

Development of a Photoacoustic Imaging System

PI: Mark Borden (several collaborators)

- The seed grant provided funding for a research collaboration between two postdoctoral researchers at CU Boulder and a laboratory in the Department of Information Engineering at the University of Florence. The research is to design pulse sequences on an open-platform research ultrasound imaging system. Results from this research were disseminated at the 2018 Acoustical Society of America meeting in Victoria, Canada and will be presented as an invited lecture at the 2019 European Contrast Ultrasound Symposium in Rotterdam, Netherlands. **Preliminary data from this research will drive an NIH R01 grant proposal** to be submitted in June 2019.

Development and Validation of Photoacoustic Contrast Agents with Nonlinear Response for Continuous Wavefront Shaping through Scattering Media

PIs: Andrew Goodwin, Jennifer Cha, Rafael Piestun

- The seed grant was successful in its aims. First, preliminary data was obtained showing nonlinear response of the photoacoustic agents. This preliminary data **led to an NIH R21 submission which was just funded**. The R21 money will be used to build data for a larger R01 proposal with other members of the imaging IRT.

A Transformative Approach to Super-Resolution Microscopy: Fiber-Coupled Stimulated Emission Depletion Microscopy

PIs: Juliet Gopinath, Robert McLeod

- Our seed grant enabled us to gather super-resolution imaging data from HeLa cells that will be **used in an MRI proposal as well as an NIH R01 proposal**. We are also writing up an Optica paper on the results, and will submit this in the next few weeks. In addition, I attended the OSA incubator this summer on OAM, where I was able to present some of the results on the seed grant.

Correlation Between Nonlinear Dispersion and Harmonic Generation in Thin Elastic Solids: An Integrated Theoretical and Experimental Approach for Enhanced NDT

PIs: Mahmoud Hussein, Mark Ablowitz

- We developed a new method for band-structure calculation for elastic wave propagation in a highly nonlinear rod, and are currently extending this work to experimental validation on beams; formed new collaborations with Todd Murray (ME) and Mark Ablowitz (Applied Math). **Submitted a $1.25 million proposal to the NSF Leap Hi Program** (with Sedat Biringen as co-PI). Planning to submit a >$1 million proposal to the NSF DMREF program in January 2018 (in collaboration with

NIST). Planning to submit a white paper to AFOSR in January 2018 to apply our concept of "phononic subsurface" to hypersonic flow.

A Transformative Approach to Microscopy Imaging that Links Breakthroughs in Nanoparticles Contrast Agent Development to Innovations in Computational Optical Super-Resolution Imaging
PIs: Carol Cogswell, Stephen Becker, Won Park

- The Cogswell-Becker group started a new collaboration with Park's group to explore the possibility of using up-conversion nanoparticles (UCNPs) as a super-resolution optical microscopy contrast agent. We have proven the concept that UCNPs can be used in optical microscopy to achieve super-resolution imaging. We are currently beginning discussions regarding large scale funding on this new super-resolution paradigm with **the NSF IIBR** (in a new collaboration with CU biologist James Orth).

Real-Time Imaging and Characterization of Advancing Anomalies in Complex Composites
PIs: Fatemah Pourahmadian, Richard Regueiro

- The aim of this research was to develop imaging indictors for real-time reconstruction of evolving anomalies in unknown backgrounds using boundary or far-field data. We have successfully completed the computational and analytical tasks described in the proposal in the frequency domain which **resulted in a manuscript** entitled "Differential imaging of evolution in elastic domains with unknown micro/macrostructure" by FP and Houssem Haddar of Ecole Polyte in France which is currently under review by SIAM Journal of Imaging Sciences. We have also made efforts to develop a laboratory platform to demonstrate the capabilities of these next-generation imaging indictors in the context of some simple laboratory experiments.

High Definition Live 3D Deep Tissue Nonlinear Microscopic Tomography
PIs: Shu-Wei Huang, Juliet Gopinath

- **A joint NSF proposal is being drafted** for submission at the end of January to the **NSF Biophotonics** program. Mid-infrared light source and parametric wavelength conversion, two key components in the proposed imaging system, were successfully developed and characterized. Preliminary imaging of egg shell and small fish is currently in progress in our lab.

Soft Computational Optics
PIs: Robert McLeod, Carol Cogswell

- We are using the funds to acquire hardware for a preliminary experiment. Our goal is to demonstrate volumetric 3D printing based on a time-reversal of the computed tomography algorithm. When applied to index-responsive polymers developed by our group for holography, this will enable 3D gradient index "soft optics" - a new class of deep tissue imaging system. We have worked for some time to finalize the design and are thus just ordering parts now.

Fourier Telescopic Imaging through Turbulence: Self-Cal vs TAFT
PIs: Kelvin Wagner, Daniel Feldkhun, Stephen Becker

- **A 9-month phase 1 proposal (called SPISTAR) was submitted** to continue funding the collaboration between Profs. Wagner and Becker initiated under this imaging IRT program on Fourier Telescopic Imaging through Turbulence. If successful, **this Phase 1 effort would allow us to apply for the limited submission multi-million-dollar phase 2 project**. To improve the chances of award for a resubmission of this SPISTAR proposal, with the support of the imaging IRT we are acquiring a telescope through which we can project optically modulated fringes on a far field

target through a turbulent atmosphere, but this equipment has not yet arrived, but is expected shortly.

3D Super-Resolution via Multiple-Scattering Waves
PI: Rafael Piestun

- We have **submitted a NIH R21 proposal with a new international collaborator** and developed a novel approach for imaging through scattering with excellent resolution.

Next Steps and Anticipated Milestones

The following strategic activities are planned for the coming year:

- Seed grant program: the next round of seed funding will support new collaborative efforts that have the potential to lead to large scale funding opportunities. Proposals will be due at the end of January and the funding decisions made in early February.
- Imaging science faculty hire: the Imaging Science Seminar Series will host faculty candidates for the Imaging Science search. Once the search process is complete, the seminar series will continue to host external speakers from industry, academics, and government for the remainder of the year.
- Team forming/ research blitz workshops: two events are planned for each semester to promote new collaborations and team forming for large-scale proposal opportunities. Additional meetings of the IRT leadership will be called as necessary.
- Industry conference/workshop: A conference/ workshop designed to promote collaboration with industry is planned for late summer/early fall.
- Several trips to visit relevant program managers are anticipated throughout the year (this process will be facilitated by connections made through Lewis Burke and Associates)

IRT Performance Metrics

Industry Collaboration

New external collaborations

- Svenja Knapp established a new collaboration with **Teledyne Scientific**
- Mahmoud Hussein received a seed grant from **Boeing** to jointly experimentally validate the concept of a "phononic subsurface" which he co-developed with Sedat Biringen
- Kelvin Wagner: Member of Scientific Advisory Board for **Fathom Computing**, an optical Deep Learning company.
- Kelvin Wagner Initiated collaboration with Dr. Charles Garvin at **Lockheed-Martin** Coherent Technologies division in Lafayette on Si-Photonics LIDAR.
- Kelvin Wagner is in discussions with **Ball Aerospace** related to Silicon Photonics LIDAR.
- Kelvin Wagner Initial collaboration discussion with Sriram Vishwanath at **GenXComm** on Optical Deep Learning.
- Kelvin Wagner: Consulting with **QuantaSpec** on the LWIR polarimetric imaging capabilities of uniaxial anisotropic wedge interferometers.
- Kelvin Wagner Consulting with **Lambdametrics** on analyzing and mitigating speckle in multibeam LIDAR imaging.

- Carol Cogswell has an ongoing collaboration with a microscope R&D company in Denver called "**Intelligent Imaging Innovations** (3i)." This work is funded in part by a Colorado Advanced Industries Accelerator award (2017-2018).
- Mark Borden: 3-Party agreement put in place between CU Boulder, University of Florence and **X-Phase** for research using an open-platform ultrasound system (ULA-OP)
- Mark Borden started a research collaboration with **Acertara**, Longmont, CO.
- Mark Borden started a research collaboration with **Medtronic**, Boulder, CO.
- Bob McLeod: **AlignTech**, world's largest user of 3D printing, is part of an NSF GOALI proposal and has started licensing discussions.
- Bob McLeod is working with **Oculus Research** on materials for augmented reality.
- Todd Murray established a new collaboration with **LLNL**, was a partner on an internal proposal (LDRD), and received funding to develop new inspection techniques for advanced manufacturing

Technology transfer, IP generation, and start-ups

Patents

- Carol Cogswell: provisional patent filed: European National Phase Application Based on PCT Patent Application No. PCT/US2017/022600 Entitled "Super-Resolution Imaging of Extended Object" (2018)
- Won Park: patent awarded: W. Park, T. Flaig, X. Yang, L.-J. Su and K. Emoto, "Multifunctional nanomaterials for treatment of cancer", United States Patent 10,052,393 (Aug. 21, 2018)
- Svenja Knapp filed provisional patent application on "High-resolution magnetographic camera based on optically-pumped magnetometer"
- Todd Murray was granted a patent "Non-destructive acoustic metrology for void detection" US 9991176
- Mahmoud Hussein submitted two provisional patents
- Ted Randolph: We have filed for a patent on our machine learning algorithms. Currently, two companies are in late stage negotiation with tech transfer to license the inventions in the pharmaceutical and clinical arenas. We have signed CDAs with two additional companies interested in the technology.
- Rafael Piestun filed 3 new patent applications
- Mark Borden submitted a provisional patent application on click chemistry ligand conjugation to microbubble ultrasound molecular imaging probes

Start-ups

- Svenja Knapp Founded startup company Fieldline Inc.
- Svenja Knapp Received Lab Venture Challenge funds from TTO
- Mahmoud Hussein received funding from Kairos Ventures (venture capital company) to fund his research on "nanophononic metamaterials"
- CU spinoff company Double Helix llc (out of Piestun lab) awarded Luminate award, Rochester NY. $1 million investment.
- Mark Borden became Chief Scientific Officer, Respirogen Inc., Boulder, CO.
- Mark Borden: Patent License, Respirogen Inc., Boulder, CO

Reputation

National/International Recognition

- Ted Randolph's work on machine learning strategies for analysis of flow microscopy images of aggregated protein within therapeutic protein formulations and the relationships of these aggregates with clinical safety profiles won the Ebert Prize. The Ebert Prize, established in 1873, is the oldest pharmacy award in existence in the United States. They have been asked not to announce this award until the American Pharmacist Association makes the official announcement early next year, but there will be some press coverage at that point.
- Mahmoud Hussein is the Founding Vice President of the International Phononics Society (IPS)
- Mahmoud Hussein was Elected Fellow of ASME
- Rafael Piestun delivered Keynote talk at LANE conference in Germany.
- Rafael Piestun co-chaired the Gordon Conference on Image Science
- Rafael Piestun co-organized and chaired the workshop Optics for Information Processing in the 21st century. Florence, Italy
- Todd Murray was selected to serve on the External Advisory Panel for the Rosalind Franklin Institute: a new national institute, funded by the UK government through UK Research and Innovation, dedicated to bringing about transformative changes in life science through interdisciplinary research and technology development.
- Carol Cogswell received a "Certificate of Appreciation, 25 Years of Service" from the Society of Photo-optical Instrumentation Engineers (SPIE), for Chairing the Photonics West Conference on Three-Dimensional and Multidimensional Microscopy, annually from 1994 through 2018.

Selected High Impact Publications Enhancing Visibility of Imaging Science at CU

- Tzang, Omer, Antonio M. Caravaca-Aguirre, Kelvin Wagner, and Rafael Piestun. "Adaptive wavefront shaping for controlling nonlinear multimode interactions in optical fibres." *Nature Photonics* (2018): 1.
- Haiyan Wang, R Piestun, "Dynamic 2d implementation of 3D diffractive optics" *Optica* (2018)
- M. Brasino, S. Roy, A. H. Erbse, L. He, C. Mao. W. Park, J. N. Cha,* and A. P. Goodwin.* "Affibodies with Site-Specific Photocrosslinker Incorporation Show Both Directed Target-Specific Photoconjugation and Increased Retention in Tumors." *J. Am. Chem. Soc.* (2018)
- D. Feldkhun, O. Tzang, K.Wagner, R. Piestun, Instantaneous focus formation and scanning through scattering media in microseconds. Forthcoming, *Optica*.
- *Article Featured on Cover:* Hussein, M.I. and Khajehtourian. R., "Nonlinear Bloch waves and balance between hardening and softening dispersion," *Proceedings of the Royal Society A* (2018).
- Ananda Das, Chenchen Mao, Suehyun Cho, Kyoungsik Kim & Wounjhang Park "Over 1000-fold enhancement of upconversion luminescence using water-dispersible metal-insulator-metal nanostructures," *Nature Communications* (2018).

Examples of Recognition by Peer Institutions

- Andrew Goodwin started a new symposium on Acoustically-Active Colloids for Imaging and Therapy for the 259th ACS National Meeting and Exposition, March 22-26, 2020, Philadelphia, PA.
- Svenja Knapp gave an invited lecture at the Innovation Symposium on Optically Pumped Magnetometers, 2018, Scottland/UK, "Microfabricated Optically Pumped Magnetometers for non-invasive Brain Imaging"

- Svenja Knapp gave an invited lecture at the Kolloquium des Institutes für Microsystemtechnik der Universität Freiburg/Germany, 2018, “Magnetic Imaging with Microfabricated Optically Pumped Magnetometers”
- Svenja Knapp gave an invited lecture at the International Workshop on Advanced Magnetometry for Defense Applications, 2018, Adelaide/Australia, “Microfabricated optically-pumped magnetometers for imaging applications”
- Bob McLeod: Invited talk at LLNL on “Transport effects in photo responsive polymer gels”
- Bob McLeod: Invited talk at Oculus Research on “Holographic Photopolymers”
- Rafael Piestun gave an invited talk at the Latin America Optics & Photonics Conference (Lima)
- Rafael Piestun gave an invited talk at the European Optical Society Biennial Meeting (Delft)
- Kelvin Wagner: Editorial Board for 3-D research
- Kelvin Wagner: Conference Program Committee for Information Photonics 2019
- Carol Cogswell was voted as the first "Conference Chair Emeritus" by the SPIE society
- Carol Cogswell is an ongoing member of the International Advisory Committee of Focus on Microscopy (one of the leading international conferences on optical microscopy).
- Stephen Becker was invited to give a short-course at Cambridge this June on optimization
- Mark Borden was funded by GIAN to give a 1-week short course on “Microbubbles for Biomedical Applications” at the India Institute of Technology in Gandhinagar
- Mark Borden was appointed to Scientific Committee for the European Contrast Ultrasound Symposium
- Mark Borden was Elected to the Technical Program Committee for the International Ultrasound Symposium
- Mark Borden was invited to give a master class on ultrasound contrast agents at the International Ultrasound Symposium in Kobe, Japan (October 21-25, 2018)
- Mark Borden: Agreement for Scientific and Cultural Exchange put in place between CU Boulder and the University of Florence
- Mark Borden: Session Chair, Ultrasound Mediated Agent Delivery, 2018 IEEE IUS, Kobe, Japan
- Mark Borden: Session Chair, Emulsions Bubbles & Foams, 2018 American Chemical Society, Colloids and Surface Science Symposium, Penn State
- Mark Boden: Invited Talk, 2018 American Institute of Ultrasound in Medicine, New York, NY
- Mark Borden: Two Invited Talks, 2018 Acoustical Society of America, Victoria, Canada.
- Mark Borden: Graduate student Alec Thomas completed his PhD on acoustic droplet vaporization for ultrasound imaging, and accepted a postdoctoral position at Oxford University to continue research in Imaging Science.
- Invited talk: J. T. Gopinath and M. Siemens, Generation and detection of tunable orbital angular momentum in polarization maintaining optical fiber, *Invited talk at OSA Incubator meeting on Orbital Angular Momentum*, Washington DC (2018).
- Andrew Goodwin co-chaired a symposium at the most recent ACS National Meeting in Boston on Biomaterials and Biointerfaces.
- Fatemeh Pourahmadian chaired a session (Digital Twin and Signal Processing) in QNDE2018.
- Fatemeh Pourahmadian presented an invited lecture at Duke in May 2018.

- Fatemeh Pourahmadian gave an invited lecture to the bureau of Reclamation in April on emerging imaging technologies for sensitive infrastructures. This work will be published in their State of the Art report to come out this December.

Proposals and Projects

Multi-department proposals/projects (> $1M)

- Mahmoud Hussein was awarded as PI (Multi-department) a grant from ARPA-E to develop a new type of thermoelectric device (nanophononic thermoelectric device). Project is for 3 years and is in collaboration with NIST and Colorado School of Mines 2.5M **(funded)**
- Svenja Knapp- DARPA N3: "Multifocal Integrated Non-Invasive Devise for Sensing and Stimulation (MINDSS)" subcontract to Teledyne Scientific; with Prof. Daniel Barth (Dept. Neuroscience and Psychology) CU portion: Phase 1: $1.1M **(funded)**, Phase 2: $780K, Phase 3: $670K
- Mark Borden, PI: Air Force, Supporting Study to Transform En Route Care Phase 3, 10/2018-9/2024, $3.7M. **(funded)**
- Bob McLeod (PI) was funded by Oculus, "High Performance Holographic Photopolymers for Augmented Reality," $1.5M **(funded)**
- Corey Ne (PI) NIH 2 R01 AR063712-07 / Probing Osteoarthritis Pathogenesis by Noninvasive Imaging of Cartilage Strain, 4/2019–3/2024 (This renewal application received a percentile score of 1.0) Goal: To utilize novel noninvasive imaging methods of measuring articular cartilage biomechanics to predict osteoarthritis pathogenesis in vivo following anterior cruciate ligament transection. Total funds requested: $3.1M **(pending, *very likely to be funded*)**
- IRT Members Todd Murray (PI), Mark Borden, Daria Kotys-Schwartz, Stephen Becker, Rafael Piestun, Fatemeh Pourahmadian, Andrew Goodwin, and Mahmoud Hussein; NSF NRT: Focusing Waves on Information, Safety, and Health, $3.0M **(not funded- will be revised and resubmitted)**
- Cogswell and Becker (with Restrepo and Gibson at Anschutz campus): NIH R01 proposal entitled: Validation of a novel approach to super-resolution optical fluorescence microscopy that can facilitate unprecedented analysis of brain microconnectivity. Total direct and indirect costs requested over three years: $2.5M. **(not funded)**
- Mark Borden submitted a NIH R01 proposal on Image-Guided Drug Delivery, $1.9M, scored 25%, **(not funded, was revised/resubmitted)**
- Kelvin Wagner established a new collaboration with Prof. Milos Popovic at BU to investigate a new approach to LIDAR imaging using a multi-aperture array of wavelength beam-steering Silicon photonic tiles containing 2-dimensional serpentine optical gratings. If successful, this phase 1 500K program may be graduated to a multi-million-dollar phase 2 effort. 9 **(planed future submission)**
- Kelvin Wagner established a new collaboration with Dr. Erich Grossman at NIST to investigate the mm-Wave imaging capabilities of an Optically Addressed mm-Wave Modulating Semi-conductor (OAMS) wafer addressed by traveling-wave acousto optically modulated fringes in order to probe the Fourier components of the reflectivity profile of a remote object. If successful, this phase 1 500K program may be graduated to a multi-million-dollar phase 2 effort. **(planned future submission)**

Center-scale proposals/projects (> $10M)

- Nothing to Report

APPENDIX

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